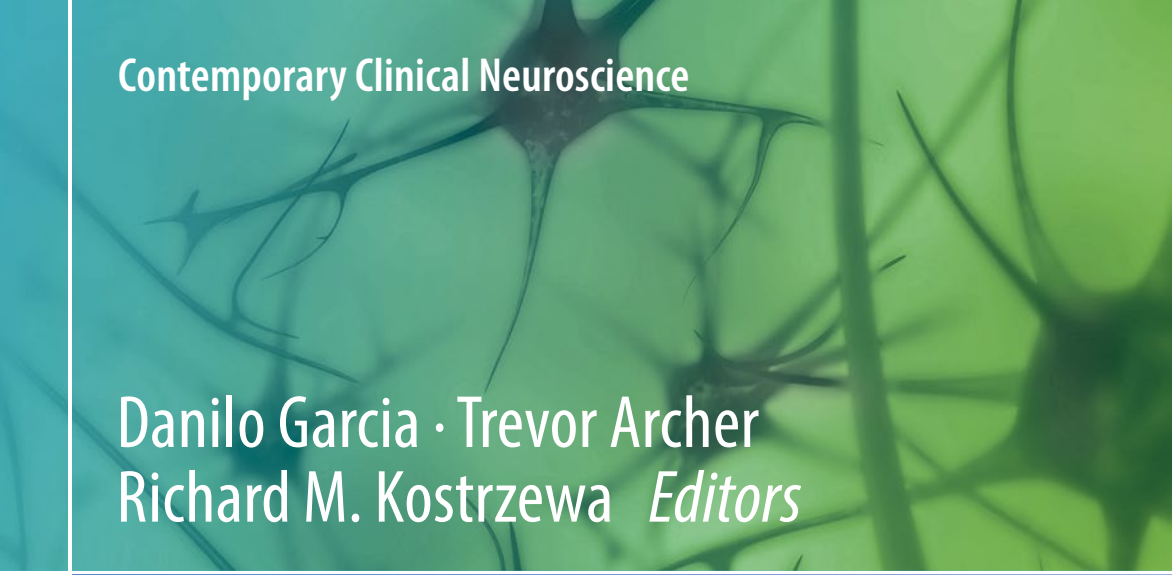

Contemporary Clinical Neuroscience

Danilo Garcia · Trevor Archer
Richard M. Kostrzewa *Editors*

Personality and Brain Disorders

Associations and Interventions

Springer

Contemporary Clinical Neuroscience

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To Sophia and Linnéa for being the ones testing my temperament in order to help me build my character… I'm One with the Force, the Force is with me

DG

Preface

The human brain, the body's control center, is composed of billions of glia, 100 billion neurons, and 1 quadrillion neural connections. The brain is part of the nervous system, which also includes the spinal cord and a large network of peripheral neurons and nerve terminals. The nervous system controls everything from the five senses, the muscles throughout the body, to thought pattern and the apprehension of life as a whole. Therefore, damage to the brain can affect many different things, including memory, sensation, and even personality. Brain disorders include any conditions or disabilities, such as illness, genetics, or traumatic injury, which affect the brain. In other words, brain disorders consist of a myriad of conditions including neurodevelopmental, neurodegenerative, and affective disorders, which might be investigated, possibly abated, and prevented using person-centered methods. However, since personality is a phenomenon that is debated as either changeable or stable, current research has not been able to definitively denote ways to engage person-centered methods in the care of people with brain disorders. Here, human personality has been defined as the dynamic organization, within an individual, of psychobiological systems that modulate adaptation to a changing environment (Cloninger, Svrakic, & Przybeck, 1993). Throughout the book, however, personality is conceptualized using different models. The first part of this book aims to outline the associations between brain disorders and personality. The second part outlines different approaches used in the health care and education of people suffering from different brain disorders. The third part focuses on challenges and new venues.

More specifically, in chapter "Personality and the Brain: Person-Centered Approaches", the authors briefly introduce how personality reflects our brain's history of development through three major systems of learning and memory in a long series of steps through evolution: the procedural, the propositional, and the episodic memory systems. In addition, the authors of chapter "Personality and the Brain: Person-Centered Approaches" also explain new innovative methods that were developed based on these facts. In chapter "Personality Stability and Change in Alzheimer's Disease and Major Depressive Disorder", the author explores personality change and stability by focusing on two disorders: Alzheimer's disease, which

has a chronic and progressive course, and major depressive disorder, which is episodic in nature. In chapter "Stress, Affective Status and Neurodegenerative Onslaughts", the authors outline how distressful, negative affect and depressive mood are associated with destructive neurodegenerative progressions involving pro-inflammatory dispositions, stroke and cardiovascular complications, and even diabetes and metabolic syndrome. The reader will also get the opportunity to more deeply explore how personality change is part in different stages of the cognitive continuum toward dementia in chapter "Aspects of Personality Traits and Changes in Different Stages of Dementia Disorders". In this line, in chapter "The Study of Personality Traits in the Blekinge Part of the Swedish National Study on Aging and Care (SNAC-B)", the authors present results from the Swedish National Study on Aging and Care with respect to stability and change of personality during the ages of 60 to 90 and also its relation to health. The last chapter in Part I of this book concerns how temperament and character is associated to childhood-onset autism spectrum disorders and ADHD. Importantly, in this chapter, the authors lay the ground for the second part of the book by stating that it is reasonable to include the full person, his or her personality and surroundings, in all assessments and treatments.

In Part II, the authors of chapter "A Case Study in Sweden: The Need for Person-Centred Methods in the Care of Dementia Patients with Severe Aggressive Behaviour" focus on the authentic case of a patient suffering of dementia with severe behavioral and psychological symptoms. Here, the authors discuss the pharmacological treatment that is often still used, even though side effects are common and may make the symptoms even more problematic. Finally, the authors discuss person-centered methods in relation to patients with dementia with very severe to extreme behavioral and psychological symptoms. In chapter "Transcranial Magnetic Stimulation in the Treatment of Major Depressive Disorder: A Personalized Approach", the reader gets the opportunity to get a review of the possible role of repetitive transcranial magnetic stimulation in the treatment of depression. In addition, based on the literature, the authors evaluate current potential difficulties in diagnosing major depression and review a personalized approach as a model that may help with diagnosing major depression more accurately as well as improving existing transcranial magnetic stimulation treatment. In chapter "Person-Centered Schools", the authors argue that personality development is a core dimension of holistic development and that the most promising pathway for societies to promote a holistic development in youths is to shift toward person-centered schools. Thus, the authors put conventional and mainstream schools in perspective; they revisit the classical concept of person-centered schools and review evidence supporting the need for person-centered approaches in the school context. In this line, in chapter "Integrating Healthy Personality Development and Educational Practices: The Case of Student Engagement with School", the authors describe how the promotion of healthy personality development is possible within the context of current educational practices, including school improvement efforts to reach educational excellence and equity.

Finally, in Part III, the book gets a more global perspective of the implication of how the human brain works, how it has developed, and how personality mirrors this

evolution. In chapter "Current Directions in Psychiatric Classification: From the *DSM* to RDoC", the author describes the conceptualization of personality disorders from Diagnostic and Statistical Manual of Mental Disorders III (DSM-III; APA, 1980) and forward, including the differences between categorical and dimensional models of psychopathology. The author also presents some of the fundamental differences between the DSM-5 and Research Domain Criteria (RDoC) perspectives and describes challenges for the RDoC framework along with a possible alternative to it, namely, the network approach to psychological disorders. In a creative way, the author of chapter "The Future of Personalized Care: Scientific, Measurement, and Practical Advancements in Personality and Brain Disorders" attempts to present glimpses into the future of personalized care. In short, the author presents three broad developments: (1) scientific advancements in understanding how personality and genetics are central in predicting mental health and disorders, with the potential to increase predictive diagnosis and treatment validity; (2) measurement advancements with help of trait dimensions and latent structures, with the potential to increase reliability in assessing personalized care needs and functioning; and (3) practical advancements in implementing a personalized approach in care services, with the potential to increase effectiveness and satisfaction with patients. The last chapter of the book is a brief note in which the authors recap the latest research that have succeeded in identifying nearly all the genes for human personality. Since human personality is highly complex and the strongest predictor of our physical, mental, and social health overall as well as the actual cause of most mortality and chronic disease, the authors suggest that these revolutionary findings might make it possible to understand the basic mechanisms that influence our emotions as well as the way we can self-regulate our feelings, goals, and values in order to live healthy and satisfying lives. This recent finding might serve as a stepping stone for a systematic understanding of the complex molecular and brain processes that regulate human health and well-being.

We wish the reader an informative, interesting, and happy reading even though this book is not a total book.

> *"I cannot think it unlikely that there is such a total book*
> *on some shelf in the universe. I pray to the unknown gods*
> *that some man--even a single man, tens of centuries ago--*
> *has perused and read this book. If the honor and wisdom*
> *and joy of such a reading are not to be my own,*
> *then let them be for others. Let heaven exist,*
> *though my own place may be in hell.*
> *Let me be tortured and battered and annihilated,*
> *but let there be one instant, one creature,*
> *wherein thy enormous Library may find its justification."*
> *In "The Library of Babel" by Jorge Luis Borges*

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Contents

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Part I
Personality and Its Association to Different Brain Disorders

Personality and the Brain: Person-Centered Approaches

Danilo Garcia, Nigel Lester, Franco Lucchese, Kevin M. Cloninger, and C. Robert Cloninger

Abstract Human personality has been defined as the dynamic organization, within an individual, of psychobiological systems that modulate adaptation to a changing environment (Cloninger, Svrakic, & Przybeck, 1993). In this chapter, we briefly outline the ancestral lineage of human beings as five major transitions and then describe how human personality has evolved through three major systems of learning and memory in a long series of steps through evolution. The first one is the procedural system, which regulates different emotional responses such as anger, fear, disgust, and ambition, that is, the temperament dimensions of personality. The second system, the propositional system, is present in primates and helps the individual to be self-directed and cooperative in a social environment. The third system, the episodic system, exists only among humans and stands for humans' capacity for self-awareness, which allows introspection and recollection of autobiographical memories. The second and third systems are responsible for the presence of the character dimensions of personality, which can be defined as individual differences in values, goals, and self-conscious emotions (e.g., hope, love, and faith). Importantly, character regulates the expression of temperament predispositions, so character is the regulator of well-being regardless of underlying

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temperament. But the person needs to learn to know and understand her whole being (i.e., temperament and character) to integrate them in order to promote resilience and well-being. Thus, we also present the Temperament and Character Inventory (TCI) and also discuss how interactions between traits within the individual serve as a good description, measurement, and base for dialogue in person-centered approaches.

Keywords Brain development · Character · Human evolution · Personality · Person-centered care · Temperament · Temperament · and Character inventory

> Why is thought being a secretion of the brain, more wonderful than gravity a property of matter? It is our arrogance...our admiration of ourselves
> Charles Darwin

Evolution is a complex adaptive process in which multiple genetic and environmental events are constantly interacting, shifting the balance of reproductive fitness from situation to situation and time to time (Wright, 1982). Hence, genetic influences on personality and other human characteristics show extensive gene–gene and gene–environmental interactions (Cloninger, 2004; Keltikangas-Jarvinen et al., 2009; Keltikangas-Jarvinen, Raikkonen, Ekelund, & Peltonen, 2004). As such, human evolutionary history provides a solid scientific basis for describing the functional structure of consciousness (Cloninger, 2004; Cloninger, 2009). We know, for example, that individual differences in human temperament traits were well developed in the common ancestor shared by reptiles and humans (Cloninger, 2009). Furthermore, neocortical development in mammals proceeded in five major transitions: from early reptiles to early mammals, early primates, simians, early *Homo*, and modern *Homo sapiens* (Cloninger, 2009). Consequently, it is important to follow the thread of evolution leading to humans as it unfolded in response to the unrepeatable ecological complexities of the past. Next, adapted from earlier literature reviews (see Cloninger, 2004, 2009; Cloninger & Cloninger, 2011), we briefly outline these important major transitions. We briefly describe how human personality has evolved through three major systems of learning and memory (i.e., the procedural system, the propositional system, and the episodic system) in a long series of steps through evolution. Last but not the least, we present the Temperament and Character Inventory (TCI) as a tool for the measurement of a biopsychosocial model of personality and how interactions between traits within the individual serve as a good description, measurement, and base for dialogue in person-centered approaches.

The Major Transitions in Human Evolution

The major transitions in brain system structure and function in human evolution can be traced by studying the emergence of clades,[1] usually with some living descendants of the common ancestor shared with human beings (Cloninger, 2009). The

[1] A clade (from Ancient Greek, κλάδος, klados, "branch"), also known as monophyletic group, is a group of organisms that consists of a common ancestor and all its lineal descendants and represents a single "branch" on the "tree of life." From https://en.wikipedia.org/wiki/Clade

ancestral lineage leading to humans includes the first eukaryotes, craniates, and amniotes, thereby leading to the common ancestor shared by reptiles and mammals. Among mammals, the line continues from the earliest nonplacental mammals to tree shrews and then the proto-primates called plesiadapiforms. The tree shrews, for instance, has been suggested to be the closest living example of the common ancestor of primates (Janecka, Miller, Pringle, et al., 2007). Among primates, the line continues through ancestors in common with prosimians, simians, and then great apes. Prosimians are typically nocturnal and solitary foragers, whereas simians (monkeys and apes) are typically diurnal and active in social groups most of the time (Sussman, 2003; Sussman, Andrianasolondraibe, Soma, & Ichino, 2003; Sussman & Chapman, 2004). The great apes show warm emotional expressions and affectivity, including ventral hugging, in addition to more complex imitation learning, more flexible dominance hierarchies, and communication with concrete symbols such as sign language (Preston & Waal, 2002; Sussman & Chapman, 2004). Furthermore, among the hominoids, the line continues through ancestors of australopiths to early *Homo*. The details of the lineage are intensively debated, but the functional and structural changes are fairly clear even when the precise transitional form remains uncertain. Australopithecines had well-developed erect bipedal walking, as was shown in the fossilized footprints preserved at Laetoli in Africa (Wood & Collard, 1999). *Homo habilis* is classified as the earliest human species on the basis of an average brain volume of >600 cm^3 and development of brain regions that support language functions in modern humans. Some argue, however, that it should be grouped with australopiths, not *Homo*, because its body was similar to that of an australopith (Wood & Collard, 1999). It is clear that between australopiths and *Homo erectus* there was a revolutionary increase in the size of the brain and body of human beings (Hawks, Hunley, Lee, & Wolpoff, 2000). This increase required a new way of obtaining nutrients to support the greater energy consumption of a larger body and brain.

Indeed, every transition in the ancestral lineage leading to modern humans involved adapting to a novel ecological challenge. In other words, every transition was associated with different challenges that the existing species had to adapt to or face extinction. Mass extinctions occurred often, shifting the balance of dominance from one life form to another (Stanford, 2001). Moreover, animals co-evolved with plants, just as both plants and animals had to adapt to the changing climate and tectonic shifts. The adaptive challenge helps to recognize the functional shifts that occurred at each transition leading to modern human beings. The extinction of the dinosaurs, for example, allowed mammals to diversify and they rapidly became the dominant land animals. The emergence of fruit-bearing trees provided the circumstance in which sexually prolific mammals were selected for greater agility, taste discrimination, and maternal care (Sargis, 2002; Sussman, 1991). When vegetation changed in response to a warmer climate, during the late Eocene, competition for resources increased, and diurnal animals emerged, including the first simians. Simians are typically diurnal and social and have higher rate of oxygen consumption than prosimians, which allows them being active during the day and foraging in social groups. All this, in turn, gave an energy advantage that supported larger bodies and brains (Armstrong, 2005). When grasslands become widespread, replacing

forest, most large herbivores became extinct. In contrast, australopiths adapted well to the grasslands. They walked upright and also consumed grass or the meat of grass-grazers, giving them an advantage over apes that did not adapt for grass consumption (Sponheimer & Lee-Thorp, 1999). Early humans developed larger bodies and brains, which required a means of richer nutrition. Hunting, fishing, tool-making, and the use of fire, all these contributed to the supplementation of high-fiber diets by early humans with meat for adequate nutrition during the Paleolithic Ice Age (Richards, 2002). They had the intelligence to migrate out of Africa and colonize areas throughout most of the world during the Pleistocene epoch. The end of the Ice Age made the development of agriculture feasible, providing a more reliable source of nutrition for modern *Homo sapiens. (*cf. Harari, 2015).

The Brain Structures that Emerged

The transitions mirror the emergence of specific aspects of consciousness. The five major transitions are briefly described in Table 1 and are the root of each functional development. In reptiles, for example, sensory information is first processed in the basal forebrain before being relayed to the thalamus and dorsal cortex, but these brain areas do not reciprocate with output that could modulate the hypothalamus (Nieuwenhuys, 1994). In other words, in reptiles, central regulation of brain functions is organized in the hypothalamus. A multi-layered neocortex first emerges in early mammals, and there is a progression of five transitions whereby the neocortex takes control of central regulatory functions from the hypothalamus. In early mammals and tree shrews, the major neocortical function is voluntary control of copulation, which is reflexive in reptiles (Wersinger & Baum, 1997). Early mammals noted for their prolific sexuality (i.e., copulation), such as rodents and rabbits, are a sister clade of tree shrews (Murphy et al., 2001). Primary somatosensory cortex is clearly developed in early mammals and tree shrews (clades 6/7), but there is little or no differentiation of sensory neocortex from motor neocortex (Kaas, 2006, 2008). In proto-primates and prosimians, there is functional development of motor agility, better discrimination of the taste of a varied diet, more maternal care of young, and more time spent in grooming and related forms of appeasement. These functions involve regulation of material things such as food and activities of daily living (i.e., materiality). Unlike rodents, in primates there is no direct path from the brainstem taste areas such as the nucleus of the solitary tract to the hypothalamus and amygdala. Information about taste in primates, in contrast, reaches the amygdala and orbitofrontal cortex from the primary taste cortex, which is in the frontal operculum and insula (Verhagen, Kadohisa, & Rolls, 2004). Prosimians have well-differentiated sensory and motor neocortical areas, in contrast to tree shrews. Detailed studies of galagos indicated several changes in brain structure that support enhanced motor agility with advanced grasping and leaping adaptations, such as greater topographical ordering of sensory input for the hands and feet, premotor and supplementary motor areas, at least two motor areas in the cingulate cortex, and feedback circuits

Table 1 Cladistic staging of evolution of the functional components of self-aware consciousness in human beings: five basic stages

Clades	Emergent brain network	Major voluntary function	Component functions
4/5 Early mammals	Somatosensory neocortex-regulating sexuality	Copulation	Sex drive Longing (Pleasure) (Eroticism) (Tenderness)
6/7 Early primates	Differentiation of sensory and motor neocortex; neocortex regulating taste	Materiality	Rhythmicity Agility Sensation (Movement) (Transformation)
8/9 Simians	Prefrontal cortex regulating limbic system; von Economo neurons in anterior insular cortex/ anterior cingulate cortex; mirror neuron system	Affectivity	Fulfillment Friendship Emotional awareness Romanticism (Devotion)
10/11 Early *Homo*	Auditory association cortex regulates cross-modal symbolism; brain default network regulates attention and daydreaming; frontoparietal perceptual–motor praxis system permits refined tool-making	Symbolism	Taboo Allegory Empathy Discernment Aesthetics
12 Modern *Homo sapiens*	Autonoetic system unifying frontoparietotemporal association areas, which are linked by visual projection system	Unity	Harmony Sublimation Adoration Contemplation Universal awareness

Note: Functions in parenthesis are found in human beings but not in original ancestor in which major function came under neocortical regulation. Adapted from Cloninger (2009)

between prefrontal cortex, premotor cortex, and primary motor cortex (Kaas, 2006, 2008). In addition, prosimians have an enlarged posterior parietal cortex for processing visual, auditory, and somatosensory information to form and relay instructions about hand and eye movements to premotor areas. In simians there is emergence of affectivity with patterns of emotional expression, attachment, and friendship that are similar to human affectivity as noted by Darwin (Darwin, Ekman, & Prodger, 1998) and Bowlby (1983). Related brain changes include the development of the prefrontal cortex for regulation of emotional functions (Semendeferi, Armstrong, Schleicher, Zilles, & Van Hoesen, 2001), a distinctive system for interoceptive processing of sensual aspects of touch (Craig, 2004, 2005, 2009a, 2009b), and the emergence of the mirror neuron system on frontal and parietal cortical areas (i.e., affectivity; Rizzolatti & Craighero, 2004). In early *Homo* there is emergence of symbolism, including capacities for taboo, allegory, language, empathy, and discernment (Craig, 2005). Symbolism builds on the abilities needed for cooperative

group foraging in simians (Craig, 2005). *Homo erectus* showed aesthetic appreciation in the making of refined tools in their Acheulian culture (Stout, Toth, Schick, & Chaminade, 2008; Stout, Toth, Schick, Stout, & Hutchins, 2000). These symbolic functions depend on processing in the inferior parietal cortex, which is a convergence area for touch, hearing, and vision, allowing cross-modal transformations important for language and other forms of symbolism (Deacon, 1997). The angular gyrus in particular has an important role in the comprehension of metaphor and allegory (Ramachandran, 2005). Symbolic activity enhances the capacity of the brain default network, which allows first-person perspective talking and daydreaming, as when a person is letting his or her mind freely wander about inner thoughts and feelings (Buckner, Andrews-Hanna, & Schacter, 2008; Raichle et al., 2001).

Finally, in modern human beings, there is self-aware perception of a sense of unity, manifested by emergent capacities for harmony, sublimation, spiritual adoration, and contemplation (Cloninger, 2004). These abilities give modern human beings their potential in art, science, and spirituality, sometimes leading to transcendent joy, oceanic feelings, or even cosmic consciousness (Cloninger, 2004; Mithen, 1996). Such integrated awareness is supported by autonoetic system of learning and memory (Tulving, 1987). Such self-aware consciousness allows a person to travel in space and time in their recollection of episodic events. Such autobiographical thinking involves a distributed frontoparietotemporal network (Levine, 2004). Essentially, the visual projection system connects all tertiary association cortices so that the brain can function as a coherent whole (Cloninger, 2009).

What and How Is Human Personality?

Human personality has been defined as the dynamic organization, within an individual, of psychobiological systems that modulate adaptation to a changing environment (Cloninger et al., 1993). This includes metacognitive patterns and systems that regulate cognition, emotion and mood, personal impulse control, and social relations. In this context, personality traits are enduring patterns of perceiving, relating to, and thinking about oneself, other people, and the world as a whole (Cloninger, 2004, 2009). These three aspects of being are associated to physical, mental, social, and spiritual health (Cloninger, 2003, 2004). Many theories of personality, however, focus on different parts of human life and experience, such as sexuality, physicality, emotionality, sociality, cognition, or spirituality (Hall & Lindzey, 1978). Moreover, some scientists, such as Freud (1938), Piaget (1954), and Maslow (1948), have given birth to broad theories that were intended to serve as a coherent theory of theories (i.e., metatheory). Nevertheless, despite being useful, even these metatheories still focused on a particular aspect of being, such as sexuality, cognition, or spirituality, which impairs our understanding of both the effects and relationships of human personality on important outcomes, such as health. As a matter of fact, health is indeed an integrated state of physical, emotional, social, cognitive, and spiritual well-being (Vaillant & Vaillant, 1990; WHO, 2001). Hence, no models of

neurobiology or personality provide an adequate explanation of human beings' subjectivity (i.e. self-aware consciousness) (Cloninger, 2009). There are of course several promising neurobiological insights for explaining different components of consciousness that might be integrated in a unified general model of self-aware consciousness (e.g., Buckner et al., 2008; Craig, 2009a, 2009b; Gusnard, Akbudak, Shulman, & Raichle, 2001; Levine, 2004; Pribram, 1993; Raichle et al., 2001). Furthermore, as detailed in the first part of this chapter, human evolutionary history provides a solid scientific basis for describing the functional structure of consciousness (Cloninger, 2004, 2009).

According to Cloninger, human personality has evolved through three major systems of learning and memory in a long series of steps through evolution (Cloninger, 2004, 2008, 2009; see Table 2). The first one is the procedural system, which regulates different emotional responses such as anger, fear, disgust, and ambition, that is, the temperament dimensions of personality. Temperament has been variously defined as those components of personality that are heritable, fully manifest in infancy, and stable throughout life (Goldsmith et al., 1987). Fortunately, each approach defines essentially the same traits, which are all present from infancy onwards and are moderately heritable and stable throughout life. The four temperament traits are as follows: (1) *novelty seeking*, associated with the neurotransmitter dopamine, is the tendency of frequent activation or initiation of behaviors in response to novel stimuli and potential rewards and punishments expressed as frequent exploration of new unfamiliar places or situations, quick loss of temper, impulsive decision-making, and active avoidance of monotony; (2) *harm avoidance*, associated with the neurotransmitter serotonin, is the tendency to avoid or cease behaviors due to intense response to aversive stimuli expressed as fear of uncertainty, shyness of strangers, quick fatigability, and pessimistic worry of future problems; (3) *reward dependence*, associated with the neurotransmitter noradrenaline, is the tendency to respond intensively to reward expressed as sentimentality, social attachment, and dependence of approval of others; and finally (4) *persistence*

Table 2 Distinctive properties of three systems of learning and memory in human beings

System	Form of learning	Qualitative properties
Procedural	Habits and skills	Prelogical
		Emotion-laden
		Quantitative
		Variable strength, not self-aware
Prepositional	Facts and propositions	Logical
		Algorithmic
		Hierarchical
		Not self-aware
Episodic	Intuitions and narratives	Self-aware
		Holistic biographical
		Creative and freely willed

Note: Adapted with permission from C. Robert Cloninger

is also associated with the brain's noradrenergic system and is the tendency to persevere despite fatigue or frustration, overachieving, and perfectionism. Importantly, the temperament dimensions are useful to predict disorders and destructive behaviors (e.g., substance abuse is associated to high levels of novelty seeking) but not sufficient to predict who will develop a disorder or maladaptive behaviors (Cloninger, 2004). For example, not all individuals who are high in novelty seeking develop substance abuse problems.

The second system of learning and memory, the propositional system, is present in primates and helps the individual to be self-directed and cooperative in a social environment. The third system, the episodic system, exists only among humans and stands for humans' capacity for self-awareness, which allows introspection and recollection of autobiographical memories (Cloninger, 2008). The second and third systems are responsible for the presence of three dimensions of character, which can be defined as individual differences in values, goals, and self-conscious emotions (e.g., hope, love, and faith) or what the individual makes of her/himself intentionally (Cloninger et al., 1993). That is, as temperament refers to the way we are born (i.e., our emotional predispositions), character traits describe individual differences in our self–object relationships, which begin with parental attachments in infancy, then self–object differentiation in toddlers, and continue to mature in a stepwise manner throughout life (Cloninger, 2004). The three character traits are: (1) *self-directedness*, which refers to self-determination; being able to control, regulate, and adapt behavior in accordance to own goals and values; and being self-sufficient, self-acceptant, responsible, reliable, and effective; (2) *cooperativeness*, which accounts for individual differences in acceptance of and identification with other people, tolerance, helpfulness, and empathy; and (3) *self-transcendence*, which refers to individual differences in selflessness or self-forgetfulness, patience, spirituality, and identification with something bigger than the self that gives meaning to one's existence (Cloninger et al., 1993; Köse, 2003).

Furthermore, temperament and character configurations are related to one another in complex but systematic ways. Temperament influences choices of behavior in different situations that are automatized and subsequently constrain character development but does not fully determine it because of the systematic effects of sociocultural learning and the stochastic effects of experience (Cloninger, 2004; Garcia et al., 2014). For example, individuals who are high in the temperament dimensions of novelty seeking and harm avoidance in conjunction with low reward dependence are predisposed for the underdevelopment of self-directedness and cooperativeness (Cloninger, 2009). Again, temperament's influence is not an inevitable or necessary determinant of character structure, which also depends substantially on social learning and random environmental events that can be measured but not predicted in advance. In other words, normal personality development is a complex adaptive system of patterns of relationships between temperament structure, character structure, and histories of behavioral conditioning and insight (social) learning, which can be measured as a biopsychosocial model of personality (see Fig. 1).

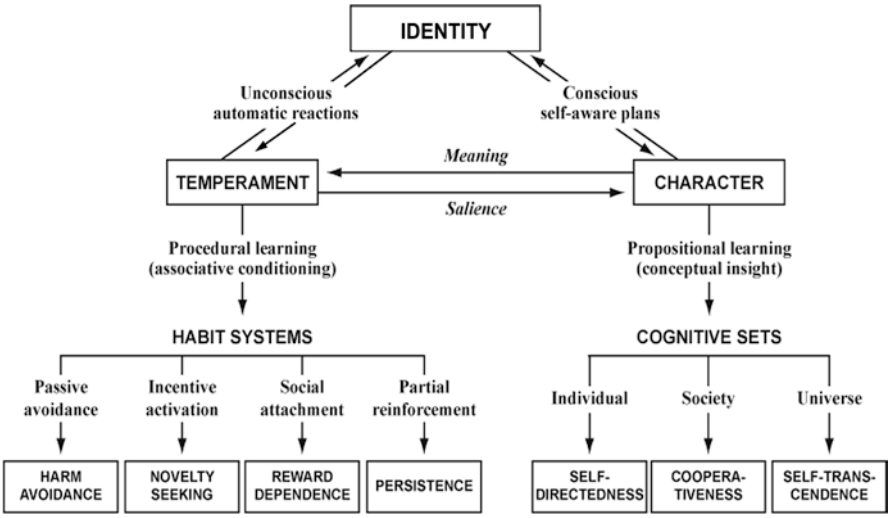

Fig. 1 The biopsychosocial model of temperament and character. (Note: Reproduced with permission of Washington University Center for Well-Being)

Personality as a Complex Adaptive System: The Temperament and Character Inventory

The Temperament and Character Inventory (TCI) is a tool for personality assessment (http://anthropedia.org) that was developed to provide a comprehensive biopsychosocial model of personality as it develops within individuals (Cloninger et al., 1993). It deconstructs personality into the seven dimensions theorized by Cloninger, which vary widely in the general population, rather than focusing only on pathology or abnormal traits. Nevertheless, it was designed to be equally applicable to clinical populations without being stigmatizing or pathologizing (see also Garcia, Lester, Cloninger, & Cloninger, 2017). The TCI is based on the complex interactions among genetic, psychological, social, cultural, and spiritual variables, rather than assuming that personality can be decomposed into independent dimensions (Cloninger, 2004; see Table 3 for a definition of high/low levels in each temperament and character traits). For instance, Cloninger and his colleagues showed, in three different cultural diverse samples, that the heritability of temperament and character can be nearly fully explained by a large number of genetic variants that are unique for multi-trait profiles, not single traits (Zwir et al., 2018a, 2018b; see also Cloninger & Zwir, 2018). Without claiming that it is the only way to understand personality rigorously, we argue that the TCI is a well-validated system for assessment; its basis recognizes the nonlinear nature of personality development that is crucial for treatment planning and has been shown to be useful and practical in clinical practice for treatment across the full range of personality and psychopathology (Cloninger, 2004; cf. Gould, 1981; Gunderson, Triebwasser, Phillips, & Sullivan, 1999).

Table 3 Description of the temperament and character dimensions

	Temperament and character descriptors		
		High scorers	*Low scorers*
Temperament	Harm avoidance	Worrying and pessimistic	Relaxed and optimistic
		Fearful and doubtful	Bold and confident
		Shy	Outgoing
		Fatigable	Vigorous
	Novelty seeking	Exploratory and curious	Indifferent
		Impulsive	Reflective
		Extravagant and enthusiastic	Frugal and detached
		Disorderly	Orderly and regimented
	Reward dependence	Sentimental and warm	Practical and cold
		Dedicated and attached	Withdrawn and detached
		Dependent	Independent
	Persistence	Industrious and diligent	Inactive and indolent
		Hardworking	Gives up easily
		Ambitious and overachiever	Modest and underachiever
		Perseverant and perfectionist	Quitting and pragmatist
Character	Self-directedness	Mature and strong	Immature and fragile
		Responsible and reliable	Blaming and unreliable
		Purposeful	Purposeless
		Resourceful and effective	Inert and ineffective
		Self-accepted	Self-striving
		Habits congruent with long-term goals	Habits incongruent with long-term goals
	Cooperativeness	Socially tolerant	Socially intolerant
		Empathic	Critical
		Helpful	Unhelpful
		Compassionate and constructive	Revengeful and destructive
		Ethical and principled	Opportunistic
	Self-transcendence	Wise and patient	Impatient
		Creative and self-forgetful;	Unimaginative and self-conscious
		United with the universe	Pride and lack of humility

Note: Reproduced with permission from C. R. Cloninger

The TCI provides a quick, reliable, and clinically meaningful description of the person without judging or blaming. The most important, for the understanding of a person, are the interactions between traits (see Fig. 2a, b). For example, excessive imagination associated with high self-transcendence often leads to perceptual aberrations and vulnerability to over-valued ideas or psychosis if there is not the solid reality testing associated with high self-directedness (Smith et al., 2008). In other words, unless the person is both highly self-directed and self-transcendent, she/he is likely to have an attitude of separateness, which leads to superstitious or magical thinking without the realistic and selfless qualities of truly self-transcendent atti-

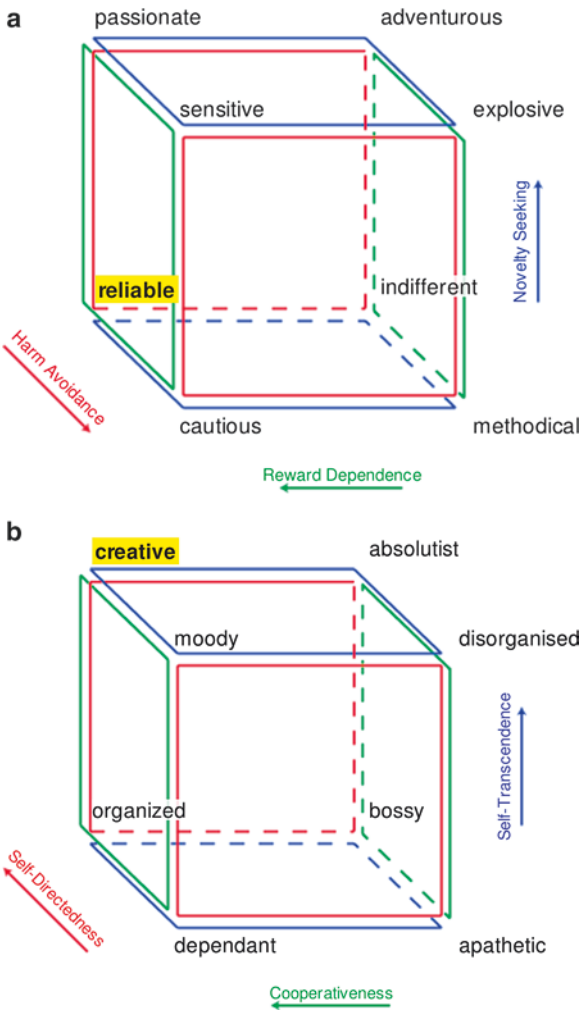

Fig. 2 The temperament cube (**a**) representing the eight possible combinations of high and low scores in the temperament traits. The character cube (**b**) representing the eight possible combinations of high and low scores in the character traits. (Note: Reprinted with permission from Anthropedia Foundation)

tudes like altruism and benevolence to others. The creative and organized character (see Fig. 2b) configurations consistently have the highest levels of well-being, whereas the apathetic (melancholic) and disorganized (schizotypal) configurations consistently have the lowest levels of well- being (Cloninger, 2004). People with an apathetic profile are low in all three traits of character, so they often say "life is hard, people are mean, and then you just die!" Not surprisingly, they are unhappy, alienated, and physically unhealthy and fearful of death with high rates of mental and physical disorders (Cloninger, 2004). In contrast, creative people are high in all three traits of character, so they often regard life as filled with opportunities to learn from their mistakes and to serve others, enjoy helping others with tolerance and compassion, and seek to grow in awareness of the inexhaustible mysteries of life and what is beyond human existence.

In other words, seeing personality as a dynamic complex adaptive system entails a person-centered approach in which an individual is not only adapting to the environment but also to the traits within the being—that is, the notion of the individual as a whole system unit which is best studied by analyzing patterns of information or profiles (Bergman & Wångby, 2014). Although at a theoretical level there is a myriad of probable patterns of combinations of individuals' levels of character traits, if viewed at a global level, there should be a small number of more frequently observed patterns or "common types" (Bergman & Magnusson, 1997; Bergman & Wångby, 2014). Indeed, the development of character is best explained by nonlinear dynamics in complex adaptive systems that have led to a triune model of character (see Fig. 2b; Cloninger, Svrakic, & Svrakic, 1997). In Table 4, for example, we present data from 524 patients who answered the TCI (see Falhgren, Nima, Archer, & Garcia, 2015; Garcia, Lester, Fahlgren, Rozsa, & Cloninger, 2016). The patients' temperament profiles were constructed by first dividing their percentile scores in high/low (N/n = high/low novelty seeking, H/h = high/low harm avoidance, R/r = high/low reward dependence) and then creating all possible eight combinations: NHR "sensitive," NHr "explosive," NhR "passionate," Nhr "adventurous," nHR "cautious," nHr "methodical," nhR "reliable," and nhr "independent." The patients' character profiles were constructed in the same way (S/s = high/low self-directedness, C/c = high/low cooperativeness, T/t = high/low self-transcendence): SCT "creative," SCt "organized," ScT "absolutist," Sct "bossy," sCT "moody," sCt "dependent," scT "disorganized," and sct "apathetic." We compared the patients' temperament profiles to their own character profiles to see whether there was an agreement between the different combinations of personality dimensions using an exact cell-wise analysis conducted using the ROPstat software (http://www.ropstat.com). In short, if a specific cell contains more cases than expected under this base model, this cell indicates a relationship that exists only in this particular sector of the cross-classification, that is, it constitutes a *type*. If a cell, in contrast contains fewer cases than expected under the base model, this cell also indicates a local relationship, that is, it constitutes an *antitype*. The results showed, for example, that a "disorganized" character profile (scT) was typical for both an "explosive" (NHr; $Chi^2 = 13.06$, $p < 0.001$) and a "methodical" (nHr; $Chi^2 = 6.89$, $p < 0.01$) temperament profile. Moreover, both of these temperament profiles were also typical for the "apathetic" character profile (sct; $Chi^2 = 3.23$, $p < 0.05$ and $Chi^2 = 15.03$, $p < 0.001$, respectively). Indeed, as earlier stated, individuals who are high in the temperament dimensions of novelty seeking and harm avoidance in conjunction with low reward dependence are predisposed for the underdevelopment of character (Cloninger, 2009). These results, however, suggest that some patients with these temperament profiles might also need to, besides working on their relations to the self and others, address aspects related to spirituality to improve their health. This complexity is expected; more than 30 years of research have confirmed the nonlinear dynamics of personality development, such as equifinality and multifinality,[2] and that the step-

[2] Equifinality: high scores in each one of the character traits might have different antecedents, for example, individuals who are high in self-directedness might have different temperament basis. Multifinality: antecedent variables have different outcomes, for example, not all individuals who are high in novelty seeking end up scoring high in self-directedness (Cloninger & Zohar, 2011; Garcia & Rosenberg, 2016a, 2016b).

Table 4 Exact cell-wise analysis of two-way frequencies of osteopathic patients' temperament and character profiles

	SCT "creative"	SCt "organized"	ScT "absolutist"	Sct "bossy"	sCT "moody"	sCt "dependent"	scT "disorganized"	sct "apathetic"
NHR "sensitive"	–	ANTITYPE	–	–	TYPE	–	–	–
Observed frequency	7	3	2	5	12	3	13	10
Expected frequency	9.1	8.6	3.4	5.7	6	2.5	10	9.6
Chi-square	0.5	3.63*	0.58	0.09	5.85*	0.09	0.89	0.02
NHr "explosive"	–	ANTITYPE	–	–	–	–	TYPE	TYPE
Observed frequency	4	1	3	3	3	2	20	14
Expected frequency	8.3	7.8	3.1	5.2	5.5	2.3	9.1	8.7
Chi-square	2.23	5.93**	0	0.93	1.14	0.04	13.06***	3.23*
NhR "passionate"	TYPE	–	–	–	–	–	ANTITYPE	ANTITYPE
Observed frequency	34	16	5	9	10	2	6	1
Expected frequency	13.8	12.9	5.1	8.6	9.1	3.8	15.1	14.4
Chi-square	29.68***	0.72	0	0.02	0.08	0.87	5.49**	12.51***
Nhr "adventurous"	–	–	–	–	–	–	–	–
Observed frequency	8	11	7	8	4	3	5	9
Expected frequency	9.1	8.6	3.4	5.7	6	2.5	10	9.6
Chi-square	0.14	0.68	3.78	0.91	0.69	0.09	2.51	0.03
nHR "cautious"	–	–	–	–	–	–	–	–
Observed frequency	7	11	2	7	6	4	14	14
Expected frequency	10.8	10.1	4	6.8	7.2	3	11.8	11.3
Chi-square	1.33	0.07	1.02	0.01	0.18	0.34	0.4	0.64
nHr "methodical"	ANTITYPE	ANTITYPE	–	ANTITYPE	–	–	TYPE	TYPE
Observed frequency	3	6	5	3	10	5	27	31
Expected frequency	14.9	14	5.6	9.4	9.9	4.1	16.4	15.7
Chi-square	9.54***	4.60**	0.06	4.32*	0	0.18	6.89**	15.03***

(continued)

Table 4 (continued)

	SCT “creative”	SCt “organized”	ScT “absolutist”	Sct “bossy”	sCT “moody”	sCt “dependent”	scT “disorganized”	sct “apathetic”
nhR “reliable”	–	TYPE	–	–	–	–	ANTITYPE	ANTITYPE
Observed frequency	12	16	3	3	7	2	2	3
Expected frequency	8	7.5	3	5	5.3	2.2	8.7	8.4
Chi-square	2.04	9.68**	0	0.79	0.56	0.02	5.19**	3.43*
nhr “independent”	–	TYPE	–	TYPE	–	–	ANTITYPE	–
Observed frequency	8	14	4	14	3	2	4	5
Expected frequency	9	8.4	3.3	5.6	5.9	2.5	9.8	9.4
Chi-square	0.1	3.69*	0.13	12.52***	1.46	0.09	3.46*	2.06

* $p < .05$, ** $p < .01$, *** $p < .001$.

Note: Type (gray fields): the observed cell frequency is significantly greater than the expected ($p < 0.05$). Antitype (black fields): the observed cell frequency is significantly smaller than the expected ($p < 0.05$). –: the observed cell frequency is as expected

wise development of character determines large differences between individuals in their risk of psychopathology, as well as varying degrees of maturity and health that are best conceptualized as eight character profiles (Cloninger, 2004, 2006; Cloninger et al., 1997).

Unfortunately, most contemporary medical treatment is focused on relief of acute symptoms of illness rather than the promotion of health and well-being (Cloninger, Zohar, & Cloninger, 2010; Wong & Cloninger, 2010). As a result, contemporary medical practice is ineffective in the prevention and management of chronic diseases, which are common and complex in their etiology and treatment. Drop-out, relapse, and recurrence rates are also high even for acute illness when treatments are not directed toward promotion of well-being (Cloninger, 2006). Furthermore, impersonal approaches to therapeutics have failed to increase physical, emotional, or social well-being in the general population, despite substantial advances in technical capacities and health care expenditure (Mezzich et al., 2010; Cloninger, 2004, 2013a, 2013b).

Treatments directed at acute symptoms of illness, rather than its causes, result in temporary relief, frequent relapse and recurrence, and no lasting improvement in public health (Cloninger, 2006). The inadequacies of impersonal approaches have led to a widespread and growing interest in alternative therapies that are more person-centered. Evidence-based treatments for medical conditions are highly diverse, including physical exercise, diet, sleep hygiene, deep breathing exercises, muscular relaxation, mood self-regulation, guided imagery, meditation, and acts of kindness and gratitude (Bertisch et al., 2009; Chiesa & Serretti, 2009; Servan-Schreiber, 2005). Such self-regulatory and alternative treatments produce results that are often indistinguishable from more conventional allopathic interventions, suggesting that a common mechanism is being influenced by complementary pathways (Targ & Levine, 2002). Success in self-regulation from repeated practice in one type of situation, such as exercises for monitoring and improving posture, monitoring and regulating mood, or monitoring and recording eating, consistently leads to greater self-control (i.e., willpower or free will) in other unpracticed situations, again suggesting a common underlying mechanism, or a synergistic set of mechanisms of well-being (Baumeister et al., 2006; Baumeister, Bauer, & Lloyd, 2010; Muraven, Baumeister, & Tice, 1999).

Where Does Health, Happiness, and Wisdom Come From?

The conditions that promote well-being and recovery from illness involve a set of common features of health that include hope, empathy, and respect for one's self and others (Amering & Schmolke, 2009). These common characteristics of well-being emerge from a self-transcendent outlook on life with a sense of participation in the boundless unity of all things or inseparable connectedness with nature and other people (Cloninger, 2004). Self-transcendent outlooks and values are typical of healthy and creative people in all human cultures (Schwartz, 1992). An outlook of

separation predisposes a person to feelings of fear, alienation, and individual pride or shame, thereby predisposing to dissatisfaction with life and ill health. Hence, person-centered approaches aim to promote health by providing the experience of an outlook of unity in the client/patient alliance, which can later be generalized beyond the alliance. An outlook of unity fosters well-being by activation of a synergistic spiral of increasing self-directedness, cooperativeness, and self-transcendence (Cloninger, 2004, 2006; Cloninger et al., 2010). As a matter of fact, only about 15% of the variance in treatment outcome is attributable to specific techniques of different psychotherapeutic schools, whereas about 85% of the variance in psychotherapy outcomes is explained by common factors shared by different approaches (Joyce et al., 2006; Lambert, 2003, 2005). What is attributed to the strong placebo effects observed in most drug or psychotherapy trials is substantially determined by common psychosocial factors, which can be as large or larger than putatively specific treatments (Lambert, 2005). The common factors in all treatments include:

1. The patient's characteristics and the therapist's qualities of respect (i.e., prizing, unconditional positive regard, acceptance, trust)
2. Empathic understanding and genuineness (i.e., realness, authenticity)
3. The quality of the therapeutic alliance between them (shared goals, emotional engagement, and exchange)

In other words, a clinician's effectiveness in treatment depends substantially on his or her attitude toward—and understanding of—the patient. When physicians rely only on symptom-based diagnosis and treat patients without respectful exchange in dialogue, there are usually high rates of dropout and non-compliance with treatment prescriptions, as well as high rates of burnout in the physician and stigma in the patient (Cloninger, 2006). Most physicians today will often describe a person' s illness only in terms of a checklist of symptoms and perhaps the course of their past medical history without integration of additional information about personal, social, cultural, and spiritual history. Even with a thorough symptom-based diagnosis, most physicians do not really appreciate who the person is, or, if they do know intuitively, they have still not integrated their appreciation of the patient with an understanding of the causes of the illnesses or the unique set of strengths that will allow the person to recover their health. Accordingly, effective clinical practice depends on tools that facilitate non-stigmatizing personality assessment, rapid facilitation of a therapeutic alliance, and guided development of self-awareness for people to learn how to live well and develop a creative character profile. We argue that the TCI is an adequate tool in these endeavors, as it is used in the *Know Yourself* program about well-being promoted by the Anthropedia Foundation (visit http://anthropedia.org; see also chapter "The Future of Personality Research and Applications – Some Latest Findings" in this volume). Personality assessment helps a clinician to know who the person is, stimulates the patient to reflect on their strengths and weaknesses in regulating their emotions in accord with their goals and values. Instead of merely generating a pejorative categorical label of personality traits and disorders, both the clinician and patient need to understand how a patient's personality profile is organized and may contribute to his or her health and illness.

To give a short answer to the question labeling this subsection, the health, happiness, and wisdom of creative people come from them actually living the three practices of well-being: working in the service of others (i.e., acts of unconditional kindness; cf. cooperativeness), letting go (i.e., no fighting or worrying; self-directedness), and growing in awareness (i.e., seeking to understand the mysteries and wonders of life and what is beyond human existence; self-transcendence) (Cloninger, 2004). As a result of their outlook and practices, people with a creative character configuration have integrity, resilience, and are well satisfied with their life despite all its challenges, difficulties, and disappointments. As a result, a creative character is strongly predictive of all aspects of well-being, including health, happiness, and virtue in prospective studies of both mental and physical health. Individual differences in a person's outlook on life strongly determine their capacity to work, love, and serve others with satisfaction and health. Nevertheless, a creative outlook on life is often associated with challenges and disappointments, as exemplified in the lives of positive philosophers like Lamartine or Gandhi (Cloninger, 2004). As in the history of human evolution, failure and suffering in life are often the stimulus for development of greater well-being by means of reflection and contemplation on the causes of our ill-being. Creative characters are self-transcendent enough to accept the human condition with its unavoidable disappointments, suffering, and death. Such humble acceptance of one's limitations promotes well-being by helping people to let go of complaining and selfish striving so that a person can be more grateful and enjoy the wonders and mysteries of life.

Conclusion and Final Remarks

Using past literature reviews (Cloninger, 2004, 2009; Cloninger & Cloninger, 2011), we have briefly outlined the ancestral lineage of human beings. We have identified five major transitions in functionality through evolution: copulation, materiality, affectivity, symbolism, and unity. We have also described the structure of personality based on the development of different memory systems that each have served as a base for the development of human personality and also as a solid foundation for a model of personality that is biopsychosocial in nature. Here, the TCI has also been briefly explained and also how interactions between traits within the individual serve as a good description, measurement and base for dialogue in person-centered approaches. The methods for promoting healthy character development are described more fully elsewhere (e.g., Cloninger, 2004; Cloninger et al., 2010).

In short, we argued that the neocortical development in mammals, from early reptiles to early mammals, early primates, simians, early *Homo*, and modern *Homo sapiens*, provide the foundation for human self-awareness (Cloninger, 2009). This foundation suggests that the promotion of well-being must begin by a person recognizing what brings them health and lasting satisfaction. A humanistic dialogue is, for instance, the foundation for developing shared goals in a therapeutic alliance that will lead to well-being (Ryan & Deci, 2001; Tournier, 1997; Wong & Cloninger,

2010). Here, we suggest that this dialogue should include the way the components of personality interact to produce illness or health, in order to make the therapeutic encounter truly person-centered and also to initiate a process of rapid spontaneous change (Wong & Cloninger, 2010). In some, but not all people, an increase in self-awareness automatically potentiates synergy among a person's way of functioning, plasticity, and virtue, as described elsewhere (Cloninger & Cloninger, 2011). More work is needed to recognize what blocks this synergy in other people. Certainly, everyone has a spontaneous need to be self-actualizing, that is, to become a fully functioning human being. However, different people may be receptive and responsive to different treatments depending on their personality and circumstances. Nevertheless, there are also often obstacles to change so a person must learn many things in order to live well. What a person needs and wants to learn must be skillfully tailored to their individual needs using person-centered approaches, such as a biopsychosocial model of human personality.

> I follow Nature, the best of guides, as I would a god, and am loyal to her commands.
> Cicero.

Conflict of Interest The authors declare that there are no competing interests. The views and ideas expressed here are those of the authors and do not necessarily reflect the official policy or position of any agency of the Swedish government.

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Personality Stability and Change in Alzheimer's Disease and Major Depressive Disorder

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Abstract *Background*: Is personality a source of resilience and/or diathesis for behavioral disorders? Alternately, are some personality profiles part of the pathology of these disorders? Answers to these questions inform our understanding of personality and the brain and the etiology of behavioral disorders. Our understanding of these issues is constrained in three ways: (1). much of the research is cross-sectional and thus does not allow for inference about precedence or causality. (2). Many behavioral disorders are not curable, and hence we cannot contrast the post-recovery and premorbid personality with that measured while the disorder was present. (3). Different disorders exhibit different relationships with personality. *Aims*: This chapter explores personality change and stability by focusing on two disorders: Alzheimer's disease (AD) which has a chronic and progressive course and major depressive disorder (MDD) which is episodic in nature. Both are contrasted with age-appropriate normal development (ND) in controlled studies. These disorders were chosen because they are serious and debilitating but have contrasting courses. *Results*: Personality profiles do indeed provide protection or increase risk for both disorders. Resilience to both AD and MDD is conferred by high self-directedness and low harm avoidance or, in other terms, low neuroticism and high conscientiousness; and the inverse profile increases risk for both. There is an association between the change in personality and brain pathology and biomarkers of disease progression, suggesting distinct mechanisms of pathophysiology for AD and MDD. The degree of change seen in the course of AD is greater than that seen in MDD and much greater than that seen in ND over development. For MDD personality change is linked to depressive episodes, and although personality changes more in MDD patients than in the ND controls, the change is reversible for patients who respond to therapy. *Conclusions*: There does seem to be a causal relationship between personality profiles and AD and MDD and between the progression of the disorders and personality change. The extent and pathophysiology need further research and elaboration.

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There is a very impressive body of literature on personality, AD, and MDD. A search of major databases including Medline, Embase, and PsycINFO, as well as the combined resources covered by EBSCO in December 2017 from 2007 to 2017, for "Alzheimer's disease and personality" turned up 18,000 references; the search for "depression and personality" turned up 895,000 references. Some of these are reviews and or meta-analyses. Therefore, this chapter does not attempt a complete and systematic review, but is a narrative review in which central contributions are included. Only studies that included a comparison group of normally developing (ND) individuals were included.

Stability and Change in Personality in Alzheimer's Disease

Cross-Sectional Studies

There is considerable cross-sectional research on AD and personality. Overall, the cross-sectional studies support an association between AD and high Harm Avoidance, and low Self-Directedness – or in 5 factor terms high neuroticism, low conscientiousness, agreeableness, and openness.

Duchek, Balota, Storandt, and Larsen (2007) thoroughly examined 287 individuals who presented at the Washington University Alzheimer's Disease Research Center and grouped them by age and health status: middle-aged healthy adults with no dementia ($N = 36$; age 52 ± 4.9), old healthy adults with no dementia ($N = 131$, age 75 ± 10), old adults with *very mild* dementia ($N = 74$, age = 75 ± 14), and old adults with *mild* dementia ($N = 46$; age 78 ± 9). All participants were medically screened to exclude competing explanations including depression and hypertension and then individually and comprehensively assessed for neuropsychological and cognitive function. Participants self-reported on a short form of the Neuroticism Extraversion Openness Personality Inventory (NEO PI; 1992) to assess the five personality factors and a carefully selected informant reported on each participant as well. The results of this study showed differences between the healthy and the cognitively impaired (very mild and mild dementia) groups on all 5 personality scales although the informant reports showed greater differences than did the self-reports. By informant report healthy individuals were more open, more conscientious, more extravert, more agreeable, and less neurotic; by self-report the direction was the same, but the differences that were significant were for neuroticism and for openness. The use of informant report over self-report is typical in this area of study, as cognitive and functional decline make it increasingly harder for AD patients to self-report as the disease progresses. Moreover, Ruby, Collette, D'Argembeau, Péters,

Degueldre, Balteau, and Salmon (2009) showed under functional magnetic resonance imaging (fMRI) that in AD patients, self-reflection is extremely effortful and relies more on reasoning than on memory, suggesting that self-report on personality may be less reliable than informant report even when AD patients are capable of self-reporting.

Pocnet, Rossier, Antonietti, and Gunten (2013) compared 54 AD patients attending a memory clinic (age 76.9 ± 8.5) with 69 healthy community volunteers (age 69.3 ± 8.7). For each study participant, an informant was selected who reported on behavioral symptoms as well as on the NEO PI-R (this is the full 240-item form; Costa & McCrae, 1992) once for the current situation and once retrospectively for the participant's personality from young adulthood until 5 years previously. For premorbid personality, patients were rated as more neurotic, less open, less extravert, and less conscientious than the comparison group. For current ratings (post AD diagnosis for the patient group), the differences between the personality scores for the patient and comparison group increased so that patients were rated as much more neurotic and much less open, extravert, and conscientious than healthy controls. Pocnet et al. (2013) conclude that AD is related to a personality profile that constitutes a diathesis for the disease, which is then magnified by its progress.

Henriques-Calado, Duarte-Silva, and Ferreira (2016) following a similar methodology, compared 44 women diagnosed with AD (age 81.3 ± 4.3) and 80 healthy female community volunteers (age 76 ± 4.1). Informants reported on current personality as well as on personality in the past using the 60-item form of the NEO PI (Costa & McCrae, 1992). Post diagnosis the AD group was elevated on neuroticism and lower than the healthy controls on openness, agreeableness, and extraversion. However, contrary to expectation, there was no difference between the groups on conscientiousness. This may be due to the fact that on premorbid personality the AD group was rated particularly high on conscientiousness, significantly higher than the healthy controls. Thus, in this study, conscientiousness cannot be said to present a diathesis to AD although, as in other studies, the post-diagnosis personality of the AD patients is rated lower on conscientiousness than was their premorbid personality.

Roy et al. (2016) compared 119 patients diagnosed with AD (age 75 ± 9.2) to 63 healthy community volunteers (age 68 ± 6). Personality was assessed by informant report on the 60-item version of the NEO PI (Costa & McCrae, 1992). AD patients were found to be less open, extravert, and conscientious than controls, and more neurotic. These results are consistent with the results of previous cross-sectional studies (Duchek et al., 2007; Pocnet et al., 2013; and in the main Henriques-Calado et al., 2016).

There is also cross-sectional research showing that with the progression of the disease, premorbid personality traits predict further decline in personality, as well as the number and severity of neurobehavioral symptoms that accompany AD. Prior et al. (2016) recruited 217 patients with a probable diagnosis of late onset AD from nursing homes in the greater London area, ranging in age from 67 to 98. Informants were close relatives or cohabiters who had known the patients in their 40s. They reported on the personality of the patients in midlife using the Standardized

Assessment of Personality (SAP; Mann, Jenkin, Cutting, & Cowen, 1981). The SAP is a semi-structured interview that begins with an open enquiry about the patient's personality. The assessment then probes for key features of specific personality disorders. If traits are identified, the rater proceeds with a series of questions probing for more specific features. It rates individuals on the key traits of the three personality disorder clusters. The personality traits identified by the SAP were then tested against current neuropsychiatric symptoms as reported by daily caregivers. Cluster A personality traits, especially being solitary or paranoid in midlife, predicted current hallucinations, depression, and anxiety. Having antisocial (Cluster B) traits in midlife, predicted current aggression and irritability. Cluster C traits in midlife had no predictive validity. As there was no comparison group, it is difficult to determine whether these interesting associations are typical and unique for late onset AD. However, using a very different methodology from the previous studies reviewed, Prior et al. (2016) found that premorbid personality affected the quality of late onset AD.

Tabata et al. (2017) used personality informants on participants at midlife to predict neuropsychiatric symptoms in 98 old AD patients (80.6 ± 5.66 years of age). Premorbid high neuroticism predicted depression in AD; low agreeableness predicted agitation, apathy, and irritability.

To summarize the results of the cross-sectional research reviewed, high neuroticism and low openness, agreeableness, extraversion, and conscientiousness constitute risk for developing AD, become more extreme over the course of AD, and predict the neuropsychiatric behaviors that accompany AD. In personality disorder terms, having type A cluster personality disorder traits at midlife is a predictor of AD onset and of the accompanying neuropsychiatric behavioral problems that accompany AD.

Longitudinal Studies

Duberstein et al. (2011) followed up 767 healthy adults over the age of 72 for 6 years; personality was measured at outset using the 60-item informant version of the NEO PI-R (Costa & McCrae, 1992), and the outcome variable was the clinical diagnosis of AD within the study window. Education, gender, race, depression, and anxiety were controlled for. AD status within the 6-year window was predicted by higher initial neuroticism, and lower initial openness and conscientiousness.

Sutin, Stephan, Luchetti, and Terracciano (2018) examined 1988 deceased patients from the health and retirement plan, who had cognitive decline at the end of life for neurobehavioral symptoms accompanying cognitive loss at the end of life. Predictors were self-reported personality traits measured 8 years prior to cognitive decline. Neuroticism increased the risk for all of the following subsequent symptoms: getting lost in familiar places, wandering off, hallucinations, depression, periodic confusion, uncontrollable temper, and not being able to be left alone.

Conscientiousness was protective against two of the symptoms (getting lost in familiar places and not being able to be left alone) as well as for the symptom sum.

Terracciano et al.(2014) followed up 1671 healthy adults in the community for up to 22 years. Participants over the age of 60 and under the age of 80 were examined bi-annually for cognitive decline and AD; participants over the age of 80 were examined annually. Personality was assessed on enrollment using the 240-item NEO PI self-report (Costa & McCrae, 1992). In addition, Terraciano et al. (2014) found suitable published prospective studies and entered their own data and previously published data into a meta-analysis resulting in a combined sample of over 5000 participants. Participants were grouped by premorbid personality trait quartiles. The participants in the highest quartile of neuroticism and those in the lowest quartile of conscientiousness were at threefold risk to develop AD over the follow-up period, contributing 13% and 11% explained variance, respectively. Terraciano et al. (2014) conclude that personality constitutes a potent risk factor for AD: "these effect sizes are comparable to those reported for recognized clinical and lifestyle risk factors for AD …" (page 5). However, epidemiological studies typically do not include personality as a risk factor among the psychosocial risk factors. For example, Qiu, Kivipelto, and von Strauss (2009) list as psychosocial risk and protective factors: high educational attainment, mentally stimulating activities, social activity and enriched social network, and physical activity as having moderate or sufficient epidemiological evidence. The epidemiological studies do not include personality, although the effect sizes for personality (as in the Terracciano et al., 2014 paper) are as strong and stronger.

Using Biomarkers to Measure AD Progress Versus Personality Change

The ultimate biomarker for AD is brain pathology as seen post-mortem. Terracciano et al. (2013) prospectively followed up 111 individuals. When healthy they were tested for personality, and 13–17 years later, they were tested for cognitive function and dementia. Post-mortem their brains were examined for the neurotic plaques and neurofibrillary tangles that are the brain pathology diagnostic of AD. This research design allowed for comparing three groups: those who showed no AD cognitive decline and were later shown to have no AD brain pathology, the normal group ($N = 27$, 24.3% of the participants, at death 78 ± 9); those who showed no AD cognitive decline and were later shown to have extensive AD brain pathology, the ASYMAD group ($N = 29$, $N = 26.1\%$; at death 72 ± 10;); and those who were behaviorally diagnosed with AD and later were shown to have extensive brain pathology the AD group ($N = 55$, 49.5%; at death 89 ± 7). Other than age at death, the three groups were comparable in their demographic composition and known risk factors. The ASYMAD groups' personality profile was highest of the three groups in conscientiousness and lowest in neuroticism suggesting that even in the

presence of brain pathology low neuroticism and high conscientiousness confer resilience against the cognitive decline and dementia that is the behavioral hallmark of AD. Combining the ASYMAD group and AD group, there was a positive and significant correlation between the extent of the neurofibrillary tangles and premorbid neuroticism and a negative and significant correlation between the extent of the neurofibrillary tangles and premorbid agreeableness.

The original biomarkers for AD are the known genotypes that have been shown to increase AD risk. Ringman et al. (2015) studied middle-aged adults in families of probands with dominant autosomal Alzheimer's disease. Participants were genotyped for APP, PSEN1, PSEN2, and APOE. Of the participants, N = 106 (age 38 ± 10) were noncarriers, N = 97 were asymptomatic carriers (age 35 ± 9), N = 25 were mildly symptomatic carriers (age 43 ± 11), and N = 33 were demented (age = 49 ± 8). The asymptomatic carriers were no different from the noncarriers in their neuropsychiatric behaviors; however, the mildly symptomatic and the overtly demented had considerable neuropsychiatric symptoms, with the overtly demented exhibiting about double the number of symptoms (6.23 vs. 3.95, $p < 0.0001$).

There are a few studies that use imaging techniques to characterize the brain pathology as it accrues and to quantify it. Snitz et al. (2015) studied healthy adults over the age of 65 who were screened clear of any medical condition or cognitive decline but had subjective complaints of memory loss. They assessed personality using the 60-item NEO PI (Costa & McCrae, 1992) and brain amyloid-β deposition via PiB-PET imaging. Snitz et al. (2015) found that the personality trait of neuroticism was a moderator between brain amyloid-β deposition and memory loss as shown in the Memory Functioning Questionnaire (Zelinski, Gilewski, & Anthony-Bergstone, 1990). Only for those high in neuroticism did brain deposition of amyloid-β predict memory loss. Snitz et al. conclude that certain personality traits might act as catalysts of cognitive impairment and dementia.

Tautvydaitė, Antonietti, Henry, von Gunten, and Popp (2017) compared 66 AD patients with mild cognitive impairment (age 74 ± 6.5) with 44 healthy controls (age 66 ± 6.6). Informants reported on the participants' personality using the 240-item version of the NEO PI (Costa & McCrae, 1992) both currently (post diagnosis for patients) and retrospectively for 5 years before the study took place. In addition, biomarkers for the progression of AD pathology were extracted from lumbar puncture CSF for all participants. Healthy controls had higher CSF concentrations of Aβ1–42 and lower concentrations of tau and ptau-181; they also had smaller ratios of tau/Aβ1–42 and of ptau-181/Aβ1–42. The AD group's rise in neuroticism and decline in extraversion, agreeableness, and conscientiousness were significantly larger than the changes in personality reported for the healthy controls. Within the AD patients, the biomarkers were significant predictors of the change in personality traits; in particular, a lower concentration of Aβ1–42 was predictive of rising neuroticism and declining conscientiousness even when controlling for cognitive decline. Tautvydaitė et al. (2017) conclude that initial differences in personality may indicate diathesis to AD and then also drive further changes in personality as well as actively partaking in the advance of brain pathology as measured in CSF biomarkers.

Zufferey et al. (2017) studied 97 healthy older adults, collecting informant report on their personality using the full 240-item NEO PI (Costa & McCrae, 1992) and MRI biomarkers, gray matter volume (GMV), and gray matter mean diffusivity (GMMD) in the medial temporal lobe. Based on the mini-mental state examination, the participants were classified as normal controls (NCI; $N = 68$, age 66 ± 6) or as mildly cognitively impaired (MCI; $N = 29$, age 68 ± 8). There were no demographic differences between the two groups, nor were there differences in the level of depressive and anxiety symptoms. However, there were significant differences in personality: neuroticism was significantly higher in the MCI group while extraversion, openness, agreeableness, and conscientiousness were significantly lower. Imaging showed that the MCI group was significantly higher in GMMD in several locations of the right and left hippocampus; multi-linear modeling revealed that while neuroticism was correlated with the extent of brain pathology, the other four personality traits conferred some protection in particular extraversion and agreeableness. The neuroticism subscales of hostility, depression anxiety, and vulnerability to stress were those implicated in more extensive GMMD brain pathology.

There is convergence between the cross-sectional, longitudinal and biomarker research on AD and personality. Personality is a risk factor for AD; the vulnerable personality profile exacerbates over the course of AD and is intimately related to the development of the brain pathology cognitive decline; these in turn exacerbate the personality profile and make it more extreme. A simple integrative model of the relationships between premorbid personality diathesis, brain pathology, cognitive decline, and neuropsychiatric behavioral symptoms is presented in Fig. 1.

Stability and Change in Personality in Depression

Premorbid Personality as a Risk Factor for Depression

"Good morning, Pooh Bear," said Eeyore gloomily. "If it is a good morning," he said. "Which I doubt," said he (Milne, 1966, p. 70). In other words, personality configuration might predispose to depression, shaping experience as negative and stressors as insurmountable.

Cloninger, Svrakic, and Przybeck (2006) followed up a representative sample of adults from the community over 12 months for personality and for depressive symptoms. Over this time window, two temperament traits and one character trait proved predictive of depressive symptoms: harm avoidance and persistence contributed to future depressive symptoms, and self-directedness was protective against depressive symptoms; however after controlling for baseline depressive symptoms, the contribution of personality, although significant, was small.

Why should personality traits predispose an individual to develop the symptoms of depression? The most likely explanation is that individuals with a vulnerable personality profile find it more difficult to deal with major and minor life stresses.

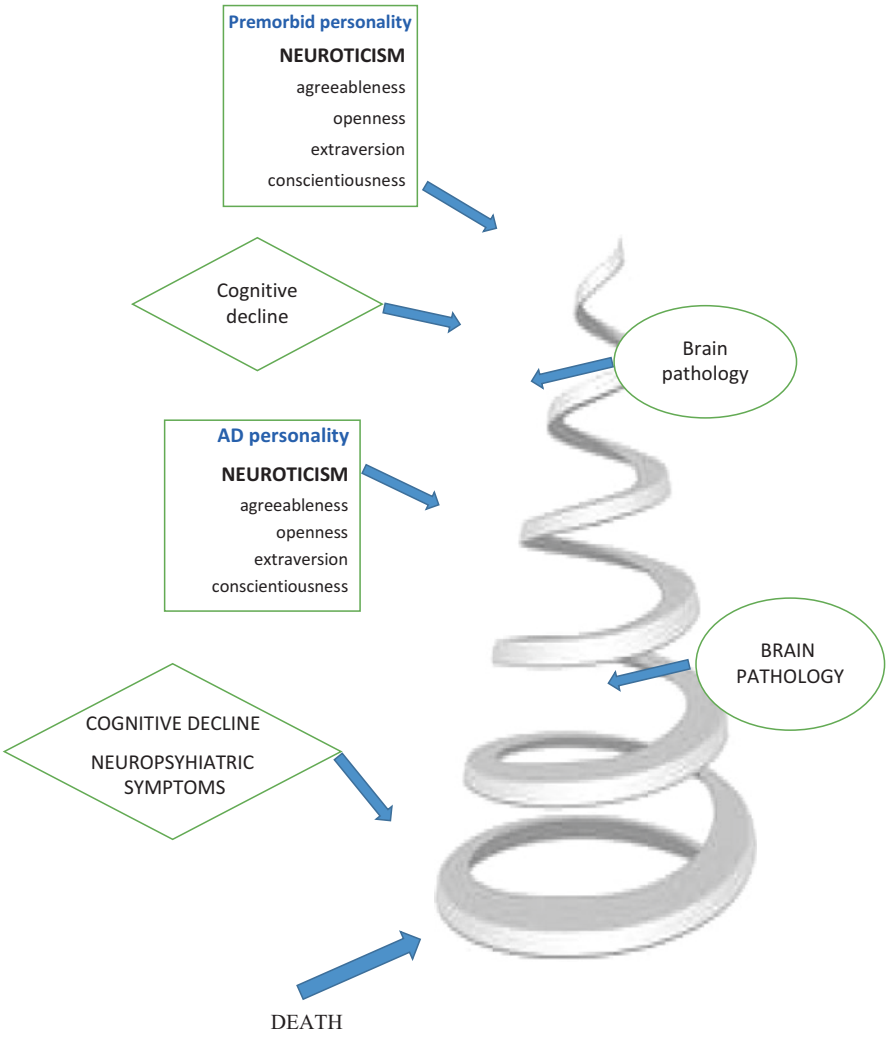

Fig. 1 Interplay of personality, brain pathology, cognitive decline, and AD pathology

Because they start out with a lot of negative affect to begin with, and because their lessened ability to down-regulate negative affect exposure to stress leaves them depleted and subject to depression. Kopala-Sibley et al. (2016) assessed positive emotionality (PE) and negative emotionality (NE), as well as a history of depression in over 300 women over the 5 years before they were exposed to Hurricane Sandy. They found that in women high in NE or low in PE there was a strong correlation between the level of exposure to the hurricane and depressive symptoms even when controlling for previous depressive symptoms and episodes, but not in the others. The strength of the hurricane and the destruction that it brought was objectively

measurable and thus was an excellent opportunity to study stress resilience. Kopala-Sibleyet al. (2016) conclude that the extreme stress of a hurricane interacted with the women's pre-hurricane personality to predict depression, because those who were high in NE or low in PE did not have the emotional resources to weather the stress.

Hakulinen et al. (2015) reviewed and meta-analyzed 10 prospective cohort studies that amounted to over 115, 000 participants, with an age range of 15–104 of whom 54.7% were women. Each of the studies was a large-scale national cohort study, and they were from Britain, Australia, Germany, and the United States. When controlling for depressive symptoms at outset and for many potentially confounding demographic variables, low extraversion, high neuroticism, and low conscientiousness were predictive of future depressive symptoms. The strongest and most consistent predictor was high neuroticism. The meta-analytic effect size of neuroticism was moderate, accounting for about 20% of explained variance.

Noteboom, Beekman, Vogelzangs, and Penninx (2016) followed up more than 1000 Dutch adults, of whom 40% had experienced a depressive episode at outset, for 2 years. Among those who had already had a MDE higher extraversion, agreeableness and higher conscientiousness reduced the odds ratio of contracting another MDE significantly although the effect size was small. For those who at outset were screened clear of MDD, the risk of a first-episode depression was significantly predicted by higher neuroticism. Thus personality is a risk factor for first episode, and complimentary traits might be protective against recurrence.

Hengartner, Ajdacic-Gross, Wyss, Angst, and Rössler (2016) followed up over 500 individuals in Switzerland over a 30-year span. When excluding those who at study onset (1988) had a history of depression or anxiety, high neuroticism at outset predicted first-episode depression within 10 years with an OR of 1.53.

This predictive validity of personality for depression persists throughout the lifespan. While most of the studies reviewed so far have spanned adult life, there is also information on adolescence and old age. Prenoveau et al. (2011) followed up adolescents for 3 years for personality, anxiety, and depression. They found that personality traits were very stable and were related to depressive symptoms which were on the whole more changeable and less trait-like. For old adults, Chow and Roberts (2014) studied a national cohort of over 5000 individuals who were assessed for personality at outset (67 ± 9.8) and for depression at conclusion (71 ± 9). They found that neuroticism positively predicted and that conscientiousness negatively predicted later depression. Both results were highly significant, but neuroticism had a bigger contribution, of about 0.4SD. Even after recovery from previous depressive episodes, in later life, Steunenberg, Braam, Beekman, Deeg, and Kerkhof (2009) found in a longitudinal Dutch study that high neuroticism predicted an old-age end-of-life depressive episode, and Duberstein, Pálsson, Waern, and Skoog (2008) showed that these same personality traits predicted the incidence of a first depressive episode in adults over the age of 70 followed up for 15 years.

Personality as Predictor of Treatment Response for Depression

Joyce et al. (2007) conducted a randomized trial of treatment for depression and used the temperament and character inventory (Cloninger, Przybeck, Svrakic, & Wetzel, 1994) to predict the outcome. High initial harm avoidance and low reward dependence were predictive of less therapeutic response, while high initial self-directedness predicted better treatment response. Thus the personality profile that indicates diathesis when inversed is indicative of better treatment response.

However, not all studies find that personality is predictive of treatment response. In a randomized controlled study of medication and IPT, of nearly 200 patients, Blom et al. (2007) found that only features of the depressive episode itself were predictive of treatment response, personality as measured by the NEO PI (Costa & McCrae, 1992) at outset had no predictive power.

Personality Change After Recovery from a Depressive Episode

Corruble, Duret, Pelissolo, Falissard, and Guelfi (2002) followed up 57 patients who were hospitalized for severe MDD a month after release as well as at follow-up 12 months after. The patients ranged in age from 18 to 65 years and completed assessment on temperament and character (Cloninger et al., 1994) at three time points: before treatment commenced and then twice again at the follow-up points. For the patients whose depression improved, but not for those who did not respond to treatment, there were significant changes in personality. At 1-month follow-up, the responders showed a dramatic decline in harm avoidance and a growth of the character traits of self-directedness and cooperation; at 12 months further growth of self-directedness and cooperation was observed as well as a growth in self-transcendence. Corruble et al. (2002) conclude that for patients recovering from depression character growth must bestow protection from relapse in the future.

Tang et al. (2009) compared three groups of patients with moderate to severe MDD who entered a randomized control trial: those who received paroxetine ($N = 120$), those who were given placebo ($N = 60$), and those who were treated with cognitive therapy (CT; N = 60). All three groups of patients showed improvement when assessing their depressive symptoms and changes in personality when comparing pre- and posttreatment self-reports. However, at 12-month follow-up, patients who had taken paroxetine reported greater personality change than placebo patients, even after controlling for depression improvement; they reported a seven-fold reduction in neuroticism vs. placebo patients and a 3.5-fold growth in extraversion. Furthermore, neuroticism reduction during treatment predicted lower relapse rates among paroxetine responders but not among CT responders. Tang et al. (2009) conclude that paroxetine influences personality traits even when controlling for the lifting of depression and that this personality change is lasting and protective against future episodes.

De Fruyt, Van Leeuwen, Bagby, Rolland, and Rouillon (2006) assessed 600 outpatients in a multisite study; they followed up the patients monthly for 6 months for personality and depression. The patients were randomized to treatment groups for one of two medications and one of three psychotherapy approaches. Substantial improvements were found for depression, with no differences among therapy conditions. The changes in personality over 6 months were significant for all the personality traits measured, but small for all but neuroticism/emotional stability for which there was a substantial change with an effect size of d = 0.55.

Roberts, Luo, Briley, Chow, Su, and Hill (2017), in a systematic review of more than 200 studies, showed that clinical interventions do indeed bring about personality change. For depression, clinical interventions of all kinds showed changes in neuroticism /emotional stability; the effect size was between 0.52 and 0.76 standard deviations. Moreover, most of the personality change happened quite rapidly within the first month of the clinical intervention, rather than slowly and incrementally.

Biomarkers for Depression and Personality

There is genetic diathesis to depression, and as in many other disorders, earlier onset and greater depression severity are associated with more familial transmission. However, the identification of relevant genotypes has been mired by non-replication in case-control studies and by non-replication in large-scale genome-wide association studies.

A possible explanation for the missing depression genotypes is that of reactive-responsive genotypes, predispositions that moderate the response to environmental events. If there is a genotype-environment interaction, so that the very same genotype will increase the risk of depression when the environment is unfavorable but confer protection when the environment is favorable, then we should be searching not for depression genotypes but for these reactive-responsive genotypes.

There is substantial research from the last two decades suggesting that over development and particularly in early childhood a given genotype might dispose an individual to good outcomes if the environment does not pose particular challenges and to grave outcomes if there are adverse childhood events (ACE). Saleh et al. (2017) compared non-medicated depressed and healthy adults who had been exposed to ACE and showed that greater ACE exposure was associated with slower processing speed and smaller orbital frontal cortex volumes in depressed subjects, but not in the healthy adults; thus, brain dysfunction was moderated by ACE and by depression. There is extensive replicated research identifying reactive-responsive genotypes and the neuro-modulation that leads from a particular genotype to the social-emotional processing of the individual as encapsulated in personality traits and in the vulnerability to depression (Moore & Depue, 2016).

Some of the inconsistencies between studies might also be due to sex differences. One of the most studied neuro-modulators of major depression is brain-

derived neurotrophic factor (BDNF), which is a product of a polymorphic autosomal gene active in the central and peripheral nervous systems. The Val66Met allele of the BDNF gene was found to be associated with lower levels of BDNF activity and increased risk of depression and other brain disorders. A rigorous large-scale study of adult community volunteers (Terracciano et al., 2010) failed to find an association between the Val66Met genotype and the BDNF levels and personality traits for all participants. However, for men, an interesting though reverse relationship was discovered: neuroticism subscales of depression and vulnerability to stress were positively associated with BDNF plasma concentration, and extraversion and conscientiousness were negatively associated with BDNF levels.

Although reduced BDNF levels have been repeatedly found for depressed vs healthy controls, the association between levels of BDNF and depression severity is still not completely clear. In a systematic review of the literature up to 2014 of treatment for depression and BDNF levels, Polyakova et al. (2015) estimated that BDNF in serum (the part of the blood which excludes clotting factors) showed significantly increased levels in MDD treatment responders vs. MDD non-responders, d = 1.27, and concluded that recovery of premorbid BDNF levels could be incorporated into assessment of treatment effects and MDD severity. However, a recent study of 163 moderately to severely depressed patients failed to find a significant and robust association between BDNF levels and symptom severity (Caldieraro et al., 2017). In a subsequent study, on a smaller series of depressed patients, Caldieraro et al. (2017) showed that BDNF reduction in depression was associated with inflammatory response in carriers of the Val66Met allele. Thus the relationship between the BDNF chromosome 11 genotype, levels of BDNF in the CNS, personality traits, and immune response sketches possible complex pathways in which personality traits and depressive episodes might change mediated by complex gene environment and sex-specific processes.

There is evidence that depressive episodes are associated with reduced hippocampal volume; and while the number, severity, and duration of depressive episodes are related to the volume reduction, there is also evidence that this brain damage is reversible (Czéh & Lucassen, 2007). Krzak, Cao, Agius, and Hoschl (2017) suggest that the reversibility of the damage might be explained by changes in rates of neurogenesis rather than changes in rates of cell death; if depression slows neurogenesis and treatment revitalizes the process, the hippocampal damage might be reversed through the depression treatment and the recovery process.

There is some evidence that the personality traits that confer risk or protection for depression are associated with brain function, and in particular with default normal (DN) brain function. The DN includes spontaneous and self-generated cognition, such as mind-wandering, episodic memory retrieval, future thinking, mental simulation, theory of mind reasoning, and creative cognition. Beaty et al. (2016) found that openness to experience was positively associated with DN and explained 18% of the variance in DN even when taking into account other personality traits, and controlling for gender and IQ. Thus people low in openness who are more vul-

nerable to future depression have less DN brain function and less efficient information processing.

Brain function in depression can be distinguished from that in other disorders and from brain function of normal age-matched individuals. In a controlled fMRI study of patients with dissociative disorder, depression, anxiety, and other disorders, the regions of the brain particularly activated in response to happy or sad faces in patients with depression were the right pulvinar (happy) and left amygdala (sad) regions; for all other patient groups, the right or left temporal gyrus was activated for either sad or happy faces or for both (Lemche et al., 2016). Thus, the processing of emotion in facial expressions is different in the brains of individuals while depressed.

The pathophysiology of brain and depression may also depend on age and development. In a longitudinal prospective study, Harrington et al. (2017) used positron emission tomography (PET) to classify healthy and cognitively intact older adults over the age of 65 into those with high-amyloid-β (Aβ) levels ($N = 81$) and low-amyloid-β (Aβ) levels ($N = 278$). At baseline and again at 18 and 36 months, there was no relationship between initial Aβ levels and depression. However, at the last follow-up, 54 months after the initial PET scan, there was a 4.5-fold incidence of depression in the high-Aβ group vs. the low-Aβ group. The accretion of Aβ in the brain is also part of the pathophysiology of AD and might be evidence of shared causality of the two disorders in old age. However, it is clear from the study that this is a slow process and thus would mainly explain the brain pathology of depression in old age.

In summary, the extensive research on personality and brain in MDD is consistent with viewing personality traits and profiles as predisposing to the onset of depression as well as being potentially protective. There is evidence that episodes of depression are associated with change in personality and in brain structures and function; however, unlike these processes in AD, the changes are reversible in treatment responders, with both personality and brain recovering to their premorbid levels. The complexity of the results may indicate heterogeneity in causes, processes, and personality-brain-disorder pathways, which in a disorder as common as MDD would not be surprising.

Overall, in comparing the literature on AD and MDD, personality plays a role in both disorders, as a predisposing factor, as a protective shield and in association with the brain pathology that accompanies the disorders. This relationship holds for MDD throughout the lifespan, and is shown for AD in old age. The profiles that confer risk or protection and that are associated with the two disorders are very similar, although the brain pathology appears to be mainly distinct, both in structure and in function.

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Stress, Affective Status and Neurodegenerative Onslaughts

Trevor Archer and Max Rapp-Ricciardi

Abstract Stress, i.e. distressful, negative affect and depressive mood are associated with destructive neurodegenerative progressions involving pro-inflammatory dispositions, stroke and cardiovascular complications, and diabetes and metabolic syndrome all of which present harbingers for poor health and ill-being. Negative affect, as an indicator of anxiety and neuroticism, has repeatedly been linked to exposure to adverse and traumatic environments concomitant with psychological distress that underlie maladaptive and self-destructive behaviours expressed in psychopathology. Eustress, from the Greek 'Good stress', implies beneficial stress whether psychological, physical, neurochemical or radiological and is not defined by form or type but rather perception and 'appraisal' of the stressors. It is linked to hormesis-based adaptive neuronal response mechanisms, such as fasting, sustained physical exercise and intellectually challenging lifestyles, that provide a protection against protect against neuronal damage from neurodegenerative and corrosive onslaughts of chronic and traumatic stress. The reciprocal determinant relationship between 'hormesic stressors' and individuals and organisms furnishes a springboard of beneficial development and health manifestation.

Keywords Stress · Affect · Neurodegeneration · Inflammation · Trauma · Eustress · Hormesis · Exercise · Health

Inability and/or incapacity to balance the reciprocal determining interactions between environmental demands (social, physical, interoceptive, etc.) and individual resources (neurobiological and neurogenetical accomplishment, cognitive-emotional coping attributes, cognitive flexibility, etc.) precedes the maladaptive development of a myriad of stressors and their neurobehaviour, neuroendocrine and neuro-immune expressions, all of which are damaging to greater or lesser

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degrees, generally instigating further stress intensification and deterioration of well-being, e.g. violent displays of discipline through physical punishment in certain types of schools continue to be widespread across the globe despite their known damaging effects. In a study applying structural equation modelling methods, the links between (i) violent exercising of discipline, (ii) symptoms of burnout and job perceptions of pressure within the school context and problems with pupils in the class as self-reported by 222 teachers derived from 11 secondary schools in Tanzania indicated that a strong relationship between perceived stress and emotional violent discipline and violent physical punishment discipline (Hecker, Goessmann, Nkuba, & Hermenau, 2017), i.e. the involved teachers' personal perceptions of their assignment and directive and their burden of stress (i.e. expressions of burnout), exerted a critical influence upon their disciplining behaviour to mutual detriment. These types of cognitive-emotional and social behaviour disruptions are associated with several conditions and expressions of neurodegeneration, e.g. alterations in connectivity and regional volumetric reductions (Apostolova & Cummings, 2008; Balthazar et al., 2014; Bora, Fornito, Pantelis, & Yucel, 2012; Lopes et al., 2013). Psychopathological symptoms arising from severe and long-lasting stress in combination with chronic negative affect (NA) and absence of positive affect (PA), a so-called 'self-destructive syndrome', underlie the outcome of neurodegenerative destruction that provides powerful model systems (Levenson, Sturm, & Haase, 2014; Sturm et al., 2013), such as AD and PD. Taking into account the stressfulness of the caregiver role with accompanying levels of NA, it has been found that caregiver mental health deterioration and ill-being predicted increased mortality among neurodegenerative patients (Lwi, Ford, Casey, Miller, & Levenson, 2017). Vulnerability factors for adverse psychological health outcomes include daily stress and the tendency to react to stress with heightened levels of NA. Mindfulness-based stress reduction decreases the extent of NA while alleviating the extent to which individuals perceive their days as stressful (Snippe, Dziak, Lanza, Nyklíček, & Wichers, 2017).

Although the presence of provocative, stressful environments and situations are associated with both acute and chronic somatic health issues, such as diarrhoea and other expressions of illness, it has been demonstrated that the relative impact of these types stressors may be regulated by the animals', e.g. rhesus macaques, personality (Gottlieb et al., 2018). Taking into account a large number of linked factors for posttraumatic stress disorder (PTSD); personality factors, e.g. neuroticism, extroversion, openness to experience, agreeableness and conscientiousness; as well as serving in the army, service-rank, trauma severity, presence of perceived threat, peri-traumatic dissociation, recent life stress and social support, personality factors and baseline PTSD avoidance symptoms, higher baseline psychological inflexibility predicted unique variance in 1-year PTSD symptom severity (Meyer et al., 2018).

Stress and Pro-inflammatory Neurodegeneration

Recent and past evidence implies that individuals' lifestyles consisting of intermittent bio-energetic challenges, such as physical exercise, dietary energy restriction and selective diets, may insure the likelihood that the brain-body interaction will function optimally with limitations upon the occurrences of disease states throughout the life cycle. Adverse neurodevelopmental environments, e.g. early social isolation, increase anxiety-like behaviour, reduce social behaviour and elevate cellular apoptosis, synaptic protein loss, myelination defect and microglial activation in the hippocampus and medial prefrontal cortex; all these developments abolish brain and brain plasticity, thereby rendering individuals susceptible to the destructive demands of the environment. For example, the exposure of mice to stressors, i.e. chronic mild unpredictable stress, prior to administration of a neurotoxin, such as the DA denervating effects of the neurotoxin, MPTP, induced low levels of motor behaviour associated with greater anxiety states accompanied by the most extenuating enhancement of neuro-inflammatory processes and other markers of stress, thereby accelerating the Parkinsonian neurodegenerative advance in laboratory mice. Chronic stress reduces the density of protective microglia, rendered increasingly dysfunctional and overexpressing pro-inflammatory cytokines, in several brain regions (Branchi, Alboni, & Maggi, 2014). Thus, it has been observed that stress causes alterations in the composition of the gut microbiota, which in turn influences microglial activity inducing an avenue that results in affective disorder and depression (Erny et al., 2015; Erny, Hrabě de Angelis, & Prinz, 2017; Erny & Prinz, 2017) with neurodegeneration propensities (Andrés et al., 2017; Singhal & Baune, 2017). It is becoming increasingly evident that microglia-regulated mechanisms may determine the differential susceptibility to stressful events and subsequently the vulnerability to brain affective disorders triggered by the experience of stressful events with neurodegenerative propensity (Milior et al., 2016). Using ultrastructural analysis, the loss of synapses due to microglial involvement in the cognitive decline across chronic stress, ageing and neurodegenerative disorders may be examined. A novel type of microglial phenotype, imperceptibly present under steady-state conditions, in the hippocampus, cerebral cortex, amygdala and hypothalamus, attains an abundance during chronic stress, ageing and fractalkine-signalling deficiency (in CX3 CR1 knockout mice) and in Alzheimer's disease pathology (in APP-PS1 mice), thereby expressing various markers of oxidative stress, such as a condensed, electron-dense cytoplasm and nucleoplasm rendering these in the form of 'dark' microglia as mitochondria with extensive re-modelling of nuclear chromatin (Bisht et al., 2016). These 'dark microglia' greatly more active than normal microglia reach the synaptic clefts with extensive encircling of axon terminals and dendritic spines with their highly bifurcated and thin processes. It ought to

be noted that the status of regional brain integrity, e.g. hippocampus, under conditions of selective serotonin reuptake inhibitor antidepressant compounds, e.g. fluoxetine, under conditions of environmental stress or enrichment is accompanied by a complex arrangement of pro-inflammatory or anti-inflammatory microglial outcomes (Alboni et al., 2016, 2017).

Despite these hazards, both neurobehavioral and neuropharmacological interventions continue to proliferate upon the treatment horizon although it remains unclear whether or not current practitioners/general physicians are fully aware of these advantages. Thus, the successful regulation of behavioural, neurogenic, metabolic and oxidative stress offers much scope for the maintenance of brain health through prevention of neurodegenerative onslaughts, thereby ensuring a healthy and productive ageing and/or disorder prognosis. Cushing's syndrome presents an assortment of signs and symptoms, including high blood pressure, abdominal obesity accompanied by thin arms and legs, a round face and fat lump between the shoulders, weak muscles, weak bones, acne and poorly healing skin as well as mood fluctuations and fatigue and chronic pain in various limbs and body parts all due to prolonged and excessive exposure to cortisol (Newell-Price, 2016; Newell-Price, Bertagna, Grossman, & Nieman, 2006; Valassi et al., 2017); they express a neuropsychological status defined by depressiveness, anxiety, mania, absence of well-being, increased negative affect and lack of positive affect and poor health-related quality of life (Dorn & Cerrone, 2000; Szcześniak et al., 2017; Tiemensma et al., 2010). Problematically, not all the symptoms of disorder are alleviated following treatment for hypercortisolism (Santos et al., 2012; Sonino, Guidi, & Fava, 2015; Wagenmakers et al., 2012). Indeed, there appears to be a long-lasting overproduction of pro-inflammatory cytokines with accompanying epigenetic alterations (Woda, Picard, & Dutheil, 2016). It has been shown also that Cushing's syndrome patients in remission, but not active patients, presented more severe white matter lesions than the control group which correlated positively with diastolic pressure and the duration of hypertension (Santos et al., 2015), with depressive mood scores correlating negatively with fractional anisotropy and positively with radial diffusivity values (Pires et al., 2017, see also Pires et al., 2015). Furthermore, among so-called 'cured' Cushing's syndrome patients, depressiveness, anxiety and impaired stress perception, i.e. poor affective integrity estimated with positive affect and negative affect scales (PANAS), were associated with low levels of serum brain-derived neurotrophic factor (BDNF) and high levels of cortisol (Valassi et al., 2017).

Stress Markers for Neurodegeneration

In diffusion kurtosis imaging, an advanced neuroimaging modality which is an extension of diffusion tensor imaging by estimating the kurtosis, skewedness, Cushing's syndrome patients demonstrated altered diffuse parameters in the grey matter and white matter of the left medial temporal lobe and elevated radial diffusivity in grey matter of the left hippocampus/parahippocampal gyrus that was correlated positively

with the clinical severity of hypercortisolism (Jiang et al., 2017), as well as altered kurtosis parameters in the cerebellum and frontal lobe. Further to the neurodegenerative progression, abnormal brain metabolite concentrations, glutamate and N-Acetylaspartate + N-acetylaspartylglutamate, in the ventromedial prefrontal cortex correlated negatively with hypercortisolism and anxiety levels (Crespo et al., 2016), in addition to early markers for glucocorticoid neurotoxicity which preceded decrements in hippocampal functioning and volume (Resmini et al., 2013). The neurodegenerative aspect of these biomarkers is confirmed by the narrowing of cortical tissue and impaired decision-making by Cushing's syndrome patients and underlines the neurotoxic propensities of exogenous/endogenous glucocorticoids on the brain tissues, as depicted by functional magnetic resonance imaging (Andela et al., 2015). Finally, dyslipidaemia and chronic markers for inflammation, interleukin-6 and C-reactive protein, were associated with telomere length shortening and consequently to premature ageing and increased morbidity (Aulinas et al., 2015), as well as the finding that hypercortisolism may impact negatively upon telomere maintenance and integrity (Aulinas et al., 2014).

Chronic and/or repetitive exposure to stress leads eventually to long-lasting or permanent deficits in neurobiological functioning and cognitive-affective behavioural expression (Yuen et al., 2012). In a comparison of male and female laboratory rats, it has been observed that, regardless of the specific chronic stress regimen and conditions, male rats showed greater vulnerability to the somatic effects of chronic stressors, whereas female rats expressed greater susceptibility to the neuroendocrine and behavioural alterations involved (Vieira et al., 2017). Exposure to early-life stress, such as maternal separation, provokes long-term alterations and impediments in the brain and behaviour and may aggravate the outcome of neurological insults (Markostamou et al., 2016); thus, prolonged maternal/caregiver separation stress promotes neurobehavioral hyperarousal, alterations in hypothalamic-pituitary-adrenal (HPA) axis expressions and alterations to hippocampal and prefrontal cortical neurobiology over multiple neurotransmitter systems (Faure, Uys, Marais, Stein, & Daniels, 2007; Hernaus, Quaedflieg, Offermann, Santa, & van Amelsvoort, 2017; Laine et al., 2017; Uys et al., 2006). Marked deficits in novel object recognition and re-recognition together with exploratory behaviour in the open-field test, an estimation of affective status among rodents (Emack, Kostaki, Walker, & Matthews, 2008), were accompanied by elevated plasma concentrations of corticosterone and reduced hippocampal concentrations of BDNF in those animals exposed to the repetitive stress (Makhathini, Abboussi, Stein, Mabandla, & Daniels, 2017). Concurrently, both glucocorticoid and mineralocorticoid receptor RNA were reduced markedly in the stressed animals who expressed decreased global DNA hypomethylation of the hippocampal genome, all of which contributed to the hippocampus-associated abnormalities. Furthermore, several avenues of observation have indicated that stress, particularly through the corticosterone stress hormones, produces complex changes in glutamatergic signalling in prefrontal cortex, which leads to the alteration of cognitive processes defined and modulated by this cortical region, as expressed by presynaptic glutamate release, postsynaptic glutamate receptor

membrane trafficking and degradation, spine structure and cytoskeleton network and epigenetic control of gene expression (Yuen, Wei, & Yan, 2017). Finally, chronic, unpredictable restraint stress and the arrest of adult neurogenesis induced the atrophy of hippocampal pyramidal cell apical dendrites in the dorsal CA3 region and the promotion of neuronal reorganization in the ventral CA3 region while affecting the integrity of granule cell dendrites markedly (Schoenfeld, McCausland, Morris, Padmanaban, & Cameron, 2017).

Stress responses and reactivity affecting brain circuitries, such as reward and cognition, vary according to age and gender-hormonal properties selective to female rats. In this regard, female rats exposed to the same repetitive stress regimes demonstrated a normal type of synaptic functioning and prefrontal cortex-mediated cognitive performance; remarkably, aromatase, the enzyme necessary in the biosynthesis of oestrogen, remains markedly higher in the PFC of females than male which points to a protective effect of the hormone (Yuen et al., 2016), and dopamine D4 activation induced a potent reduction of excitatory transmission in the acutely stressed rats concomitant with a marked increase of excitatory transmission in repeatedly stressed rats (Yuen, Zhong, Li, Wei, & Yan, 2013). In a chronic, unpredictable, repeated stress paradigm that induced depressiveness and mood problems, differences between ovariectomized and intact female mice were obtained through which the former showed greater levels of anxiety and reactivity in the open-field test, despair in the stress paradigm in the latter, that was alleviated by oestrogen administration, with significant impact upon hippocampus-related spatial behaviour and affective behaviour, prefrontal cortical BDNF levels and hypothalamic transcriptome profiles (Karisetty et al., 2017; Karisetty, Joshi, Kumar, & Chakravarty, 2017; Karisetty, Khandelwal, Kumar, & Chakravarty, 2017). In this context, endocannabinoid CB1 receptor antagonism (using AM251) and stress exposures (1 hour of confinement stress) during adolescence (daily, postnatal days 30–44) combined to alter neuroendocrine stress responses and anxiety with both male and female rats sensitive to this treatment (Simone, Baumbach, & McCormick, 2017). Nevertheless, the authors found that female rats were markedly more sensitive to the disruption, i.e. AM251-induced antagonism, of the CB1 receptor under stress conditions, with increased social behaviour, decreased CB1 receptor expression in the dorsal hippocampus and elevated GAD67 expression in the prefrontal cortex during adolescence than the male rats.

Stress, Affective Status and Stroke

Stress, whether occurring during neurodevelopment, infancy and childhood, adolescence and young adulthood or during any other phase of the lifespan, promotes the progression, provokes and/or aggravates the severity of neuropsychiatric and neurologic conditions (Schoenfeld et al., 2017; Shields et al., 2017; Shields & Slavich, 2017; Slavich, 2016). An abundance of evidence implicates chronic stress/trauma/co-morbid stress in the epidemiology of stroke incidence and mortality, a

pro-inflammatory status and impaired endothelial function and accelerated ageing (Edmondson et al., 2017; Gilsanz et al., 2017; Roberts et al., 2017; Stuller, Jarrett, & DeVries, 2012; Sumner et al., 2017). Patients presenting cardiovascular and cerebrovascular disorders in co-morbidity with mood and affective disorders, particularly bipolar disorder and major depressive disorder, are afflicted with reduced quality of life and significant disability, bidirectionally, according to their years of life and mortality with a concurrent necessity for neurobehavioural lifestyle interventions that target nutrition and exercise, coping strategies and attitudes towards health (Fornaro et al., 2017). Indeed, the prior exposure to stressful events during the pre-stress phase of stroke emergence exacerbates the extent and severity of neuronal-glial damage and inflammation (Espinosa-Garcia et al., 2017; Khoshnam, Winlow, Farzaneh, Farbood, & Moghaddam, 2017; Sorrells et al., 2013). Activation of resident immune cells, e.g. microglia with either detrimental or beneficial influence depending on polarization or microglial phenotype (M1 or M2), the infiltration of peripheral inflammatory cells and pro-inflammatory cytokine release characterize the inflammatory processes in stroke that are potentiated by stress-promotion conditions, such as ageing/sleep parameters (Jin et al., 2017; Kluge et al., 2017; Pan et al., 2017; Plaza-Zabala, Sierra-Torre, & Sierra, 2017; Yin et al., 2017; Zhao, Ma, et al., 2017; Zhao, Zhang, et al.,2017). Taken together, these divergent observations imply that selective regulation of the M1 or M2 microglia phenotypes, thereby affecting microglial polarization, may offer avenues for inhibiting or abolishing the pro-inflammatory neurodegenerative progression with subsequent neuroprotective outcomes (Espinosa-Garcia et al., 2017). In a 1-month post-bilateral carotid artery stenosis-induced injury model of stroke in rodents, which induces microglial activation, production of associated pro-inflammatory cytokines and priming of microglial polarization towards the M1 phenotype, it was observed that fingolimod, which reduces microglia-mediated neuroinflammation after WM ischemia and promoted oligodendrocytogenesis by shifting microglia towards M2 polarization, decreased the cognitive decline and ameliorate the disruption of WM integrity (Qin et al., 2017).

The co-occurrence of different ischaemia-induced neurobiological dysfunctions in combination with psychosocial distress with resulting damage to frontal-basal ganglia brainstem pathway monoaminergic neurotransmitter systems, e.g. serotoninergic pathways, contributes to pathophysiology of post-stroke depression (Bergersen et al., 2010). A powerful relationship exists between neuro-inflammatory outcomes to acute ischaemic stroke, stress/trauma activation of the HPA axis and the impairment of adaptive response, i.e. neuroreparation/neurogenesis, against a background of altered energy metabolism, such as mitochondrial dysfunction (Barra de la Tremblaye & Plamondon, 2016; Chen et al., 2017; Niu et al., 2016). In a prospective study of 25,335 older women (mean age 72.2 ± 6.04 years) not presenting at baseline responding and at 3-year follow-up registering their experiences with stress, particularly cumulative, that included perceived stress, work stress, work-family spill-over stress, financial stress, traumatic and major life events, discriminatory events and neighbourhood environment/stressors, as well as other domains that involved sleep quality, anger and its management, cynical hostility, depression, anxiety, social support, intimate partner relations and volunteer and social activities

(Albert et al., 2017), the influences of adversity was associated with marked decline in cardiovascular integrity. They obtained higher levels of cumulative stress that were related to younger age and black race/ethnicity, divorced or separation marital status, elevated prevalence of obesity and overweight, smoking habits, diabetes, depressiveness and anxiety. Selective serotonin reuptake inhibitors (SSRIs), atypical antidepressant compounds, despite certain drawbacks, have been shown to induce limited clinical activity for treatment and prevention of post-stroke depression (Villa, Ferrari, & Moretti, 2017). Further, in the context of depression and metabolic conditions, diabetes, leading to stroke and neurodegenerative disorders, rosiglitazone, the anti-diabetic compound, administered to laboratory mice reversed depressive indications in the forced-swim and open-field test of an established mouse model of depression (Zhao et al., 2017). Additionally, it inhibited the pro-inflammatory effect of unpredictable, chronic mild stress, decrease corticosterone levels, and promoted astrocyte proliferation and neuronal axon plasticity in the pre-frontal cortex of the depressed mice. Early-life adversity stress immune phenotype is described by and leads to inflammatory processes, impaired cellular immunity and immunosenescence co-occurring with an elevated state of immune activation (Elwenspoek, Hengesch, et al., 2017; Elwenspoek. Sias, et al., 2017; Elwenspoek, Kuehn, Muller, & Turner, 2017).

Stress, Hormesis and 'Eustress'

Several major disease states, including neuropsychiatric and neurologic disorders, cardiovascular diseases and metabolic syndrome, and neuro-inflammatory conditions and cancer arise from the biological processes underlying ageing which may be described as the structural and functional decline of individuals at molecular, cellular, circuitry, regional and physiological levels, such as immunosenescence and sarcopenia (Kroemer, 2015, 2017; López-Otín, Blasco, Partridge, Serrano, & Kroemer, 2013, López-Otín, Galluzzi, Freije, Madeo, & Kroemer, 2016; Stoll et al., 2015). Contrastingly, hormesis, processes providing biphasic responses to exposure of increasing amounts of damaging entities (e.g. toxins) and which offer an organo-protective/cytoprotective impact, is directly associated with organisms' (or cells') capability to survive under pathological conditions most often ageing and age-related diseases (Zimmermann, Bauer, Kroemer, Madeo, & Carmona-Gutierrez, 2014); it consists of moderate environmental or self-imposed challenges through which the system improves its functionality and/or tolerance to more severe challenges (Calabrese & Mattson, 2017). Those environmental factors that induce positive or protective adaptive responses may be expressed as 'eustress'; certainly, in the context, the influence of 'stress resistance' or 'stress resilience' (Melinder et al., 2017; Waltz et al., 2017) as devices for the 'slowing' of ageing and anti-ageing devices may be argued (Hamilton and Miller, 2016; Lomeli, Bota, & Davies, 2017; Stringer and Rossiter, 2017). For example, male mice and male Syrian hamsters were phenotyped for stress resilience in rodent models of social defeat, and it was

observed that animals resistant to social defeat stress also show increased concentration of molecules to protect against oxidative stress in the nucleus accumbens and dorsomedial prefrontal cortex (Dulka et al., 2017). The acquisition of positive personal attributes, such as competence and social support which imply a degree of hermetic adaptive behaviour, seems to offer possibilities for stress resilience: Among a cross-sectional sample of 1183 human adolescents, there was a significant positive association between stress and symptoms of depression and anxiety, with personal competence negatively associated with depression and anxiety and social support negatively associated with anxiety, all of which implied the compensatory role of stress resilience upon the relationship between stress and emotional symptoms (Moksnes & Lazarewicz, 2017).

Hormesis-based adaptive neuronal response mechanisms arising from stimulation of mitochondrial biogenesis and cellular stress resistance, e.g. fasting, sustained exercise and intellectually challenging lifestyle, that initiate brain-intrinsic and peripheral organ-derived signals, including glutamic acid and BDNF, protect against neuronal damage from neurodegenerative and traumatic onslaughts (Raefsky & Mattson, 2017). On the other hand, epigenetic regulation of gene expression in environmental interactions presents a critical molecular mechanism relating environmental factors with the genome with subsequent outcomes for individual health status throughout the lifespan. Stress resilience attributes developed through hermetic adaptive responses have been estimated both as behavioural entities and neural biomarkers (Gerber et al., 2017). Exercise-induced reactive oxygen species provides a particular form of hormesis, a bell-shaped response curve, to prevent/intervene against a wide range of disorders with exercise intensity a critical factor for the efficacy of supplementary antioxidant treatment, whereas physical inactivity and a sedentary lifestyle, ageing or pathological disorders increase the sensitivity to oxidative stress by altering the bell-shaped dose-response curve (Radak et al., 2017). 2,4-Dinitrophenol (DNP), as an obesity treatment, exerts an hermetic effect by stimulating several adaptive cellular stress-response signalling pathways in neurons involving BDNF, the transcription factor cyclic AMP response element-binding protein and autophagy (Febbraro, Svenningsen, Tran, & Wiborg, 2017; Geisler, Marosi, Halpern, & Mattson, 2017). Physical exercise apportions several stressors upon skeletal muscle and the cardiovascular system, including mechanical, metabolic, oxidative stressors, for induction of hormesis and exercise preconditioning. This latter combination of stress response and antioxidant enzyme induction provides protective influences against striated muscle damage, oxidative stress and injury (Lawler, Rodriguez, & Hord, 2016).

Physical exercise renders individuals an improved cognition and flexibility, i.e. smarter, greater satisfaction and self-esteem, i.e. happier and a higher level of neurogenesis and neuroreparation, i.e. more neurons, as a function of dose (intensity), frequency and duration of the training schedules maintained. In this regard, exercise offers a hormesic agent to promote resilience, both cellular and neurobehavioral, thereby providing greater resistance to distressful stress in response to a range of sensory provocations (Archer & Lindahl, 2018). Exercise, as a potent epigenetic regulator, implies the potential to counteract pathophysiological pro-

cesses and alterations in most cardiovascular/respiratory cells and tissues not withstanding a paucity of understanding the underlying molecular mechanisms and dose-response relationships (Archer, 2015). The relationship between physical exercise and brain information processing offers greater relevance than merely correlational associations; the causal relations are evidenced by performance, biomarkers and angiogenesis. Adult hippocampal neurogenesis, a putative physical substrate for hormetic responses to exercise, subtends a hormesis-like, biphasic dose-response to physical training (Gradari, Pallé, McGreevy, Fontán-Lozano, & Trejo, 2016). It induces oxidative stress with downstream consequences involving the generation of reactive oxygen species in the mitochondria of contracting skeletal myocytes, with modest increases caused by moderate intensity exercise involving redox-sensitive signalling effects rather than oxidative damage. The responses of muscle and non-muscle cells to exercise-associated redox-sensitive signalling consist of transcription factors such as peroxisome proliferator-activated receptor gamma and liver X receptor alpha that comprise redox-activatable signalling systems that have been located in, and we and others have reported exercise-associated modulation of peroxisome proliferator-activated receptor gamma- and/or liver X receptor alpha-regulated genes in skeletal myocyte and in non-muscle cell-types, such as monocyte- macrophages to protect against chronic inflammation (Webb, Hughes, Thomas, & Morris, 2017). Although epigenetic dysregulation is associated with a variety of neurodegenerative inclinations, the reversible nature of epigenetic factors, rendering them mediatory between the genome and the physical/social environment, promoting epigenetic regulation in neurogenesis offers a parallel process in conjunction with ongoing hormetic actions (Delgado-Morales, Agís-Balboa, Esteller, & Berdasco, 2017). In this regard, the 'heat acclimation' form of hormesis provides for 'thermo-tolerance' involving the enhancement of innate cytoprotective pathways mediated through cross-tolerance mechanisms. It has been indicated that epigenetic markers such as post-translational histone modification and altered levels of chromatin modifiers during acclimation and its decline suggest that dynamic epigenetic mechanisms controlling gene expression induce heat acclimation-mediated cross-tolerance and acclimation memory of epigenetic regulation as, for example, post-translational histone modification and altered levels of chromatin modifiers during acclimation and its decline implicate the dynamic epigenetic mechanisms controlling gene expression to promote heat acclimation-mediated cross-tolerance and acclimation memory (Horowitz, 2017). There is an accumulation of evidence that adaptive epigenetic rearrangements can transpire both during early stages of developmental and concurrently through the individual's adulthood, via the induction of hormesis, induced by the adaptive responses to low doses of otherwise harmful conditions enhancing the functional ability of cells and organisms (Vaiserman, 2011, 2014). Examples of hermetic agents abound: physical exercise, mithridatic drug self-administration, intermittent fasting and calorie restriction. 'Mitohormesis', the form of hormesis induced by those stressors that are activated by mitochondrial retrograde signalling, such as the increased production of mild reactive oxygen species, and 'xenohormesis', a phytochemical-

induced hormesis, present the aspect of a reciprocal determinant relationship between plants and animals that evolutionary adaptational pressures have exposed humans and other beings to stressors, thereby assuring hormetic health benefits (Kim, Lee, Choi, Jacobs Jr, & Lee, 2017).

Conclusions

The bereaved survivors of natural catastrophe or terrorism, having lost loved one or friend, present the psychological, physical, everyday behavioural and physiological components forming extensive reporting of posttraumatic stress disorder, depression, anxiety, negative affect, deteriorated mental health, adverse physical health symptoms, alcohol consumption, family conflicts and fear, despite their own personal survival. In the present account, the concatenation of stress (acute, chronic, traumatic and non-traumatic), affective status and neurodegenerative assailment, including inflammatory neuronal-glial events, as well as metabolic and cardiovascular perturbation, is examined from several convergent and divergent perspectives, not least trauma and negative affect. The 'over-compensation' of a variety of adaptive responses through cellular stresses, hormesis, thereby the achievement of 'eustress', attains a non-linearity in the effects of exposure to harmful environmental agents and stressors through the agency of mild to moderate intermittent stressors from any source but most regularly through exercise, calorie restriction, intermittent fasting, cognitive stimulation and phytochemicals.

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Aspects of Personality Traits and Changes in Different Stages of Dementia Disorders

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Abstract Personality change is part of the dementia syndrome. In this chapter, we aim to outline aspects of personality in different stages of the cognitive continuum towards dementia. Research studies suggest that personality traits may be risk/protective factors for dementia. Personality changes have been reported to appear early in the disease progress, even before the first cognitive signs. It may be part of a psychological reaction to dysfunction, but also directly related to neurodegeneration in the brain. Some cognitive disorders are associated with different patterns of personality change. Premorbid personality may be associated with the expression of behavioural and psychological symptoms (BPSD) in later stages of dementia. The decreased symptom insight in dementia leads to methodological difficulties when assessing personality changes. Knowledge of personality alterations in dementia may help relatives to understand these difficult changes and may be important information for clinicians and researchers to identify the early signs and distinguish between dementia disorders.

Keywords Personality · Dementia · Mild cognitive impairment · BPSD · Alzheimer's disease dementia · Vascular dementia · Lewy body dementia · Frontotemporal dementia · Cognition

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The Multifaceted Role of 'Personality' in Relation to Dementia

Cognitive decline – progressing impairment regarding memory, language, visuospatial, attention and executive functions – is a hallmark symptom of dementia. Other dementia-related changes, such as changes in personality and behaviour, are often described as 'non-cognitive' symptoms.

Personality may be described as 'the combination of characteristics or qualities that form an individual's distinctive character' (Oxford dictionary). Regarding dementia and personality, the first thing that comes to mind may be the rather extensive personality changes associated with specific manifest dementia syndromes such as frontotemporal dementia. That is, personality changes as part of the *manifest* dementia stage. However, personality traits and changes also play a role *prior* to disease onset, as there is some evidence to suggest that certain traits may actually function as *risk*- or *protective* factors in relation to dementia development – before the onset of any brain changes. Personality change may also be a possible *early indicator* of an underlying dementia disorder – after the onset of brain changes but prior to a clinically manifest dementia syndrome – and consequently have a potential value in the diagnostic procedure. Furthermore, there has been reports of an association between *premorbid* personality traits and how behaviour is expressed in the later, manifest states of dementia, e.g. 'behavioural and psychological symptoms in dementia' (BPSD). Personality may also affect *other aspects* of the disease, such as early vs late help seeking and how a person copes with receiving a diagnosis. Thus, aspects of personality may have implications for the risk of dementia, as well as for signs in the prodromal phase and coping and expression of the manifest phase of dementia. In this chapter, we aim to outline aspects of personality in different stages of the cognitive continuum towards dementia and to highlight that personality factors may play a role throughout the development of dementia. Knowledge in this area is potentially important to better understand the often complex symptomatology of different dementia disorders, not the least for caregivers who struggle with the changes of their loved one.

Dementia: Short Characteristics

The World Health Organization (WHO) has estimated the worldwide prevalence of dementia to 47 million, with 10 million new cases each year. As the average life expectancy increases globally, so does the occurrence of dementia. Prognoses indicate that the prevalence of dementia will nearly triple in the next 33 years – to 132 million cases in 2050 (World Health Organization, 2012).

Dementia is not a disease in itself, but a syndrome characterized by progressing loss of cognitive functions, which is caused by an underlying disease. Several different diseases lead to a dementia state, and Alzheimer's disease is believed to be

the most common aetiology. The clinical signs of prodromal Alzheimer's disease dementia usually start with a decreased ability to remember recent events – the episodic memory function. Gradually, other cognitive domains such as language, attention, visuospatial and executive functions are also affected. Besides Alzheimer's disease, many other conditions may lead to a dementia state. The International Classification of Diseases (ICD-10) lists no less than 25 different underlying physiological conditions that may lead to a dementia state, although many are very rare. Some of the most common dementia types following Alzheimer's disease dementia are vascular dementia, frontotemporal dementia, Lewy body dementia and Parkinson's disease dementia (refer to chapter "Personality Stability and Change in Alzheimer's Disease and Major Depressive Disorder" of this book for more about Parkinson's disease). There are also mixed forms, such as simultaneous presence of both Alzheimer type and vascular type dementia. Each different underlying disease implicates a different pattern of progression, neurobiologically as well as cognitively and behaviourally. The onset of neural degradation starts in different anatomical areas depending on specific disease, which lead to different expressions of the diseases.

Most dementia forms progress during years, perhaps even decades. There are still knowledge gaps about the actual neuronal causes of the common dementia forms. Dementia research largely focuses on identifying the starting point of the dementia disorders, especially concerning Alzheimer's disease. There is also still no efficient medical cure for dementia, and treatment options are to date still limited to symptom relief. Eventually, all dementia states lead to a complete loss of abilities.

Changes of the personality are undoubtedly a part of the dementia syndrome and seem to progress in a linear fashion alongside the disease progression (Helmes, Norton, & Østbye, 2013). However, the type and temporal onset of personality changes differ for different dementia disorders. In some dementia disorders, personality change may be an important early sign, while in others such changes appear later in the disease progress. Thus, it is not possible to establish only one type of personality change that is specific for dementia. Disease-specific personality changes have been associated with specific degenerative lesions to brain structures in neurodegenerative diseases (Sollberger et al., 2009). For example, interpersonal traits high in 'agency' (a person's assertiveness towards others) have been associated with left dorsolateral prefrontal and left lateral frontopolar regions, whereas interpersonal traits high in 'affiliation' (social/emotional engagement) were in the same study related to right ventromedial prefrontal and right anteromedial temporal regions (Sollberger et al., 2009).

Dementia: A Timeline

According to a model operationalized as the Global Deterioration Scale (GDS) (Reisberg, Ferris, de Leon, & Crook, 1982), the phases leading to dementia can be divided into seven stages. The seven stages are summarized in Fig. 1.

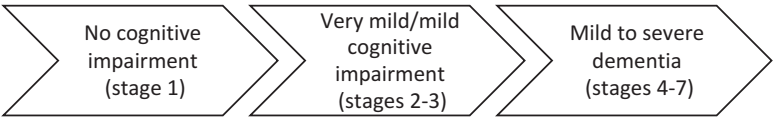


Fig. 1 The progression from healthy to dementia as stages

Stage 1 – *no cognitive decline*. There are no clinical changes, neither subjective nor objective, although neural changes have started for individuals who will develop dementia.

Stage 2 – *very mild cognitive decline*. Neural changes have started, and first cognitive difficulties may be noticeable by the affected individual (subjective cognitive decline) although cognitive tests are still in the normal range.

Stage 3 – *mild cognitive decline.* Decline become gradually more noticeable by neuropsychological tests and family members may begin to notice signs of change. Instrumental activities of daily living such as managing personal finances or meal preparations may be mildly affected.

Stage 4 – *moderate cognitive decline*. Clinical signs are now noticeable by others and can be detected during interview and exam. Instrumental activities of daily living, such as managing finances and personal transportation, are affected. Basic activities of daily living such as maintaining personal hygiene and dressing oneself start to become affected. Social withdrawal is common.

Stage 5 – *moderately severe cognitive decline*. The cognitive and functional problems are now widely spread and affect most parts of everyday activities, such as dressing and bathing. People may have difficulty orientating themselves in time and place and, for example, may forget their own address.

Stage 6 – *severe cognitive decline*. In this stage, people are often incontinent and may also forget the name of loved ones. It is common with delusions, anxiety and agitation. The affected person needs constant care.

Stage 7 – *very severe cognitive decline*. The ability to speak and communicate is lost. Eventually, the affected person can no longer walk.

Aspects of personality are potentially relevant for all seven stages of cognitive decline, in various ways. In the following text, this timeline will be followed to outline different aspects of personality and personality changes related to dementia progression.

Personality Theories

Various different theories and models of personality have been developed during the last century, some driven by psychological or psychobiological theories and other by statistical analyses. An example of the former is Cloninger's psychobiological model of personality which was developed to predict vulnerability to mental disorders proposing that personality is structured in the connection between

neurobiology and temperament (Cloninger, 1986). The 'five-factor model' or 'big-five theory' has perhaps been the most influential model, suggesting that personality may be described as traits that may be more or less occurring in an individual (i.e. dimensions) – as opposed to 'type' – theories that describe personality more in terms of categories.

This chapter is not written from the standpoint of a specific theory or model of personality. The aspects of personality mentioned here rather reflect which models and instruments have been used in related research studies – most often variants of the 'five-factor model'. Thus, we use the term 'trait' throughout the chapter.

Is Personality Stable Across the Lifespan?

The risk of developing dementia increases with age. The global prevalence of dementia in 65-year-olds is approximately 1–2% and 29–64% for 90-year-olds, with large variations for different regions of the world (Prince et al., 2013). Normal age changes are therefore important to take into account when examining possible signs and symptoms of dementia. The personality continuity vs change that may be expected in normal ageing is a large separate research area. In short, earlier accounts often described personality traits as generally stable across the lifespan, at least after the age of 30 (Conley, 1985; Costa Jr. & McCrae, 1988), but more recent research has shown that personality actually may change somewhat throughout the lifespan (Allemand, Gomez, & Jackson, 2010; Allemand, Zimprich, & Martin, 2008; Helson, Jones, & Kwan, 2002; Jeronimus, Riese, Sanderman, & Ormel, 2014; Lucas & Donnellan, 2011; Mroczek & Spiro, 2003; Roberts, Walton, & Viechtbauer, 2006). However, considering the many life-changing events that a person goes through during life, personality can still be considered as remarkably stable (Caspi, Roberts, & Shiner, 2005). The theories about which mechanisms cause the degree of continuity span from genetic influence (e.g. McCrae et al., 2000; McGue, Bacon, & Lykken, 1993) to environmental and psychological factors. For example, people develop a psychological maturity over time, which may enhance certain traits such as agreeableness and openness, while, e.g. neuroticism may be reduced. People tend to create, seek out or 'end up' in specific environments that are correlated with their traits ('niche building'), and people commit to certain identities that provide reference points to life decisions, which may also serve the continuity of personality traits. A key point is that life experiences, such as career choices, does not happen randomly – they are to some extent created by people in a fashion that corresponds to their traits, which are thereby further deepened (Caspi et al., 2005). Specific examples from research on personality in old age suggest that neuroticism decreases during adulthood but later increases in the oldest old (Mroczek & Spiro, 2003) and extraversion was seen to decline in another 79-year-old cohort (Mottus, Johnson, & Deary, 2012). Another study on 80 + -year-olds found that extraversion decreased, whereas neuroticism remained stable (Berg & Johansson, 2014). To complicate the

matter of normal age-related changes even further, there also seem to be cohort effects – for example, individuals born around 1900 scored lower on extraversion compared to cohorts born later (Mroczek & Spiro, 2003).

Personality Traits as Risk vs Protective Factors

Most dementia disorders develop gradually and it is not fully understood when, or how, they begin. Therefore, it is an essential topic of dementia research to investigate potential risk factors, which may play a role for the development of the disease, in – or prior to – early disease stages (Fig. 2). Can certain personality traits increase the risk of developing a dementia disorder? Some studies support such an association (Johansson et al., 2014; Low, Harrison, & Lackersteen, 2013; Terracciano, Stephan, Luchetti, Albanese, & Sutin, 2017; Wang et al., 2009; Wilson et al., 2005). A large US population-based study (Terracciano et al., 2017) investigated associations between personality traits and subsequent dementia in a large sample of over 10,000 50 + -year-old participants. The follow-up time was up to 8 years. The results indicated that low conscientiousness, high neuroticism and low agreeableness were significantly and independently associated with higher risk of incident dementia, also after accounting for age and sex, socio-economic status, health behaviours and clinical risk factors. They also investigated the association between personality traits and conversion from healthy to a milder form of cognitive impairment not yet reaching the dementia state ('cognitive impairment no dementia' – CIND). Persons who declined from healthy to CIND scored higher at baseline on neuroticism and lower on conscientiousness compared to those who did not decline cognitively. Similar results were reported from a 2013 meta-analysis of fifteen relevant studies (Low et al., 2013). It was concluded that higher neuroticism was associated with greater risk of subsequent dementia. Considering specific facets, anxiety and vulnerability to stress, rather than depression, were associated with dementia. Extraversion and agreeableness were not associated with dementia risk.

A memory clinic study from 2015 (Ramakers et al., 2015) reported opposite results. Neuroticism-related traits and rigidity were associated with a *decreased* risk of dementia in this study, while no personality traits predicted conversion to dementia. How can we understand these conflicting results regarding the role of the neuroticism trait in relation to dementia risk? It is likely that a major factor has to do

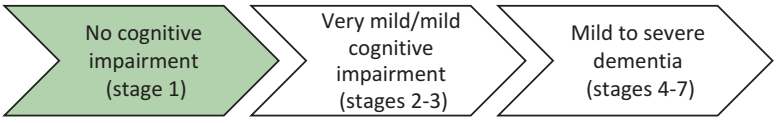


Fig. 2 The current text section highlights aspects of personality/personality changes that may be relevant before or at the stage of 'no cognitive impairment' – that is, prior to clinical symptoms, which corresponds to GDS stage 1

with the type of population in focus. The two most common types of study of dementia risk include on the one hand population-based studies, in which community-dwelling individuals are randomly selected and invited to participate, and on the other hand clinically based studies, which investigate patients who are in the medical health care system because of related health issues – in this case, most frequently memory problems. Dementia disorders are often slowly and gradually developing. The point of help seeking for cognitive problems that could possibly be caused by a dementia disorder largely differs between individuals. Some people do not seek medical help until they are in a manifest dementia state, when they can no longer manage basic activities of daily life. However, memory clinics also frequently see individuals seeking help for very subtle self-perceived cognitive changes, which could potentially be (but often are not) the first cognitive symptoms of a dementia disorder. Subtle memory complaints may be associated to multiple factors – personality is one of them. Once again, a higher level of neuroticism has been associated with an increased prevalence of memory complaints (Comijs, Deeg, Dik, Twisk, & Jonker, 2002). Persons with only subjective cognitive decline still have a somewhat larger risk to develop dementia compared to the general population (Mitchell, Beaumont, Ferguson, Yadegarfar, & Stubbs, 2014). However, studies indicate that the prevalence of depressive symptoms, anxiety and stress is high in this help-seeking group (Eckerstrom et al., 2016; Elfgren et al., 2003), which may be a more plausible cause than an underlying dementia, of their self-experienced cognitive problems. The difference between help-seeking individuals and the general population may explain why population-based studies and memory clinic studies have reported contradicting results. Obviously, high neuroticism is related to a higher tendency to worry and likely also a higher tendency to seek medical care even for very subtle cognitive changes that are less likely to be related to dementia. Therefore, in memory clinic patients, it may be speculated on that high scores on neuroticism may actually be more common in patients who will not decline cognitively.

There are several suggested mechanisms used to describe in what way personality traits induce an increased risk of dementia. Some personality traits may be indirect risk factors, because they increase the probability of the presence of *direct* risk factors for dementia. For example, studies have reported an association between personality traits and the likelihood of cigarette smoking, a sedentary lifestyle and other cardiovascular or metabolic risk factors for dementia (Jokela et al., 2014; Sutin, Ferrucci, Zonderman, & Terracciano, 2011; Terracciano & Costa Jr., 2004). These are known as *mediating factors*. However, the large study from Terracciano and colleagues found that these factors did not fully account for the relation between personality traits and dementia development (Terracciano et al., 2017). An alternative, or perhaps additional hypothesis, is that personality traits modulate dementia through its associations with specific brain changes – whole brain integrity, brain-tissue loss and white matter hyperintensities (Booth et al., 2014). For example, neuroimaging findings have indicated that higher neuroticism is associated with smaller

regional brain volumes and greater decreases in volume with increasing age, while higher conscientiousness is associated with larger regional brain volumes and less decline in higher age (Jackson, Balota, & Head, 2011).

It is also important to acknowledge the methodological challenges associated with studying dementia risk. Dementia is in most cases developed over a long time, with subtle symptoms emerging gradually. This makes it difficult to draw the line between risk factors and symptoms that are more likely to be early manifestations of the diseases. To clarify which factors are actual long-term risk factors, studies need to follow large populations over several decades.

Personality Traits as a Protective Factor Against Dementia

If some personality traits may infer an increased risk to develop dementia, could other sets of personality traits be associated with a decreased risk to develop dementia and thus act as possible protective factors? Higher conscientiousness – referring to being more careful, dutiful, organized and thorough – may be protective against dementia according to some studies (Duberstein et al., 2011; Wilson, Schneider, Arnold, Bienias, & Bennett, 2007). Two studies have pursued to analyse which facets of the conscientiousness trait are specifically related to a decreased dementia risk. Terracciano et al. (2014) found that being *organized*, *responsible*, *disciplined* and *capable* was associated with a lower risk of dementia. Another study reported similar results – high scores on *responsibility* showed the greatest risk reduction, followed by *self-control* and *industriousness* (Sutin, Stephan, & Terracciano, 2017). High scores on these facets were also related to a reduced risk of developing CIND, which is a state characterized by milder cognitive impairment. Higher scores on *openness* have also been associated with a decreased risk of dementia (Low et al., 2013).

What could then be the mechanisms behind this association? As stated previously, one possibility is that certain personality traits during life reduce the risk of engaging in behaviours that are direct risk factors to develop dementia, such as smoking and physical inactivity. However, in the study by Sutin et al. (2017), the association between specific facets of conscientiousness and dementia remained even after accounting for smoking, physical inactivity and low educational attainment. Thus, the complex interrelationship between personality and underlying brain structure may again be part of the explanation for decreased risk. Although several studies have reported an increased or decreased risk for the development of manifest dementia associated with certain personality traits, it is however not clear to what extent personality changes can be directly linked to the underlying neuropathology that is believed to act as the neural basis for dementia disorders. One study based on brain imaging reported that specific regions of the brain were associated with personality-related traits in patients with neurodegenerative disease (Sollberger et al., 2009). Further, the fact that different dementia disorders lead to different patterns of personality change – for example, differences between

temporal and frontal variants of frontotemporal dementia (Rankin, Kramer, Mychack, & Miller, 2003) – implies that there is a relationship between personality and brain structure (Sollberger et al., 2009). However, there are also studies that could not find associations between personality traits and typical dementia pathology (e.g. Wilson, Begeny, Boyle, Schneider, & Bennett, 2011). A possible explanation could be that psychosocial behaviour may modify the association of pathology with cognition (Wilson & Bennett, 2017). In other words, a person with personality traits that, for example, make it more likely to engage in social activities and thus maintain a larger social network may have an increased cognitive resistance to the neuropathological changes.

Personality Changes as Early Signs of a Dementia Disorder

Dementia research is largely focused on identifying early signs of prodromal dementia, that is, objective but mild signs before the dementia has become manifest (Fig. 3). The medical treatment options for dementia are still very limited, but early identification will likely be increasingly important when efficient treatment is developed. Early identification may also give families more time to plan for the following functional decline. One aspect of personality dementia research concerns the hypothesis that there may be changes in personality preceding a dementia diagnosis – thus, not as a risk factor but rather as an early sign of an already ongoing underlying disease that will progress. Such changes could then be potentially helpful non-cognitive clues when trying to establish the correct diagnosis. The results from studies (Ausen, Edman, Almkvist, & Bogdanovic, 2009; Balsis, Carpenter, & Storandt, 2005; Lykou et al., 2013; Smith-Gamble et al., 2002; Wilson et al., 2007; Yoneda, Rush, Berg, Johansson, & Piccinin, 2017) that have examined personality-related changes as possible early signs of dementia are summarized in Fig. 4. Increased neuroticism has been associated with both a higher risk of converting to dementia and with fulfilling the criteria for mild cognitive impairment – the possible transitional stage between healthy and dementia. Other changes that have been reported before the transition to dementia – e.g. increased stubbornness, apathy, rigidity and irritability – borders what could also be assessed as psychiatric symptoms, for instance, related to depression or anxiety, and also the challenging 'behavioural and psychological symptoms' (BPSD), which we discuss later in this chapter.

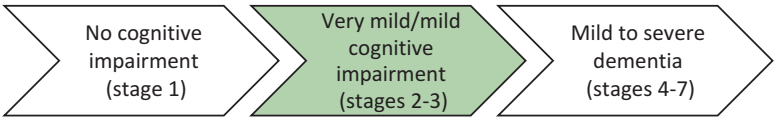


Fig. 3 The current text section highlights aspects of personality/personality changes that may be relevant for the stage of very mild/mild cognitive impairment, which corresponds to GDS stages 2–3

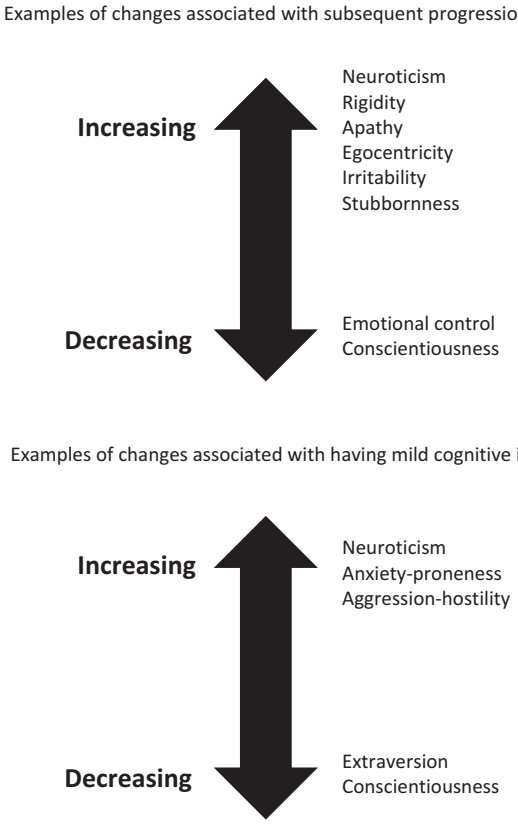


Fig. 4 Personality-related changes as possible early signs of a dementia disorder

Obviously, there is no sharp borderline between changes in personality and long-lasting psychiatric symptoms.

One study also performed post-mortem pathology examinations of the brains of study participants (Balsis et al., 2005). Interestingly, the same pattern of personality changes that was identified in individuals who later progressed to dementia was also frequently occurring in persons who did *not* develop clinical dementia during their lives but who had Alzheimer pathology in their brains (Balsis et al., 2005). These results suggest that personality changes, for some individuals, could emerge even before the cognitive changes, on the progressive continuum towards dementia. However, this is a complicated issue, since it is not possible to know if persons with Alzheimer pathology would remain cognitively intact if they would have lived longer or if they would eventually develop symptoms (Iacono et al., 2009).

Considering extraversion, one study reported that this trait seemed stable in persons who later were diagnosed with dementia (Yoneda et al., 2017), while another study observed that extraversion seemed to decrease, and anxiety proneness seemed

to increase, in persons with mild cognitive impairment (Ausen et al., 2009). In the group with mild cognitive impairment, some but far from all persons will progress to dementia. This clinical group also includes help seekers who have a mild cognitive decline due to other factors than an underlying dementia – such as psychiatric disorders, somatic disease or stress. It is therefore not surprising that individuals with mild cognitive impairment tend to become more socially withdrawn and anxious. Individuals who are close to converting to dementia may already have a slightly decreased insight into their symptoms, which possibly makes it emotionally easier for some individuals to engage in social activities compared to in earlier stages of the disease when symptom insight was at its peak.

Dementia Camouflaged as a Personality Disorder

The process of diagnosing dementia may be hampered when a patient also fulfils a psychiatric disorder that may alter the manifestations of symptoms. For example, presence of a personality disorder may complicate the clinical picture. Researchers often want to include as homogeneous patient samples as possible, to decrease the effects of confounding factors. However, real life is not as simple, and different syndromes often occur simultaneously.

Hellwig, Dykierek, Hellwig, Zwernemann, and Meyer (2012) describe the case of a 61-year-old female patient who presented with a progressive memory impairment. The patient had a medical history of repeated help seeking for symptoms that had generally been assessed as somatoform (psychogenic), as no organic causes could be identified: gastric pain, migraine, psychogenic muscle twitching, limb pain and fluctuating inability of leg movement. Together with other aspects of her behaviour, such as 'theatrical behaviour', inadequate boasting about personal merits, lack of empathy and excessive preoccupation with her physical appearance, she was assessed as fulfilling criteria for a histrionic personality disorder. Consequently, her impaired cognitive performance – which was measured by neuropsychological examination – was initially considered yet another aspect of the somatoform symptomatology. However, subsequent investigations using magnetic resonance imaging, 18F-fluorodeoxyglucose positron emission tomography (^{18}F-FDG-PET), Pittsburgh Compound-B (PiB-PET) and analysis of Alzheimer typical markers in cerebrospinal fluid, showed typical signs of Alzheimer's disease, and deteriorating cognitive deficits helped confirm the diagnosis (Hellwig et al., 2012).

The process of diagnosing dementia is a time-consuming puzzle and often includes several different measures – clinical as well as neuropsychological, brain imaging and neurochemical markers. Furthermore, patients often need to be followed over time to investigate whether the symptoms progress. This case exemplifies the additional difficulties that emerge in cases of personality disorders.

Personality Changes and Expressions of Manifest Dementia

Specific Dementia Disorders and Related Personality Changes

Alzheimer's Disease Dementia

The *manifest* dementia stages (Fig. 5) ranges from 'mild dementia' or 'moderate cognitive decline', which is the first stage of a manifest clinical dementia syndrome, while 'severe dementia' is a term to describe the very last stages of the syndrome, when the abilities to speak, communicate and eventually also to walk, are lost. Dementia of the Alzheimer type is often described as the most common dementia form. The neural changes in Alzheimer's disease include presence of amyloid plaques and neurofibrillary tangles, which lead to neuron malfunction. The typical neural damage associated with Alzheimer type dementia includes atrophy in the temporal and parietal regions of the brain, due to loss of neurons and synapses. Except for a few known genetic mutations, the cause of Alzheimer's disease is still unknown. The brain changes occur for years and perhaps decades before the clinical signs appear. The first symptoms may be merely self-experienced, but will develop into a measurable cognitive decline that often is characterized by a poor ability to recall recent information and events.

Personality changes occur in almost all individuals with Alzheimer's disease dementia and tend to progress alongside the disease (Aitken, Simpson, & Burns, 1999). The changes are often noted even before the clinical diagnosis (Balsis et al., 2005).

The pattern of personality change in Alzheimer's disease dementia has been summarized in a meta-analysis covering nine relevant studies (Robins Wahlin & Byrne, 2011). They outlined four possible different patterns of personality change: (i) an exaggeration of premorbid personality; (ii) the development of a specific Alzheimer disease personality type; (iii) changes that may develop in a stereotypic pattern but still reflect individual variability; and (iv) changes develop without any clear pattern, without reflecting the premorbid personality. However, most researchers seem to argue against the hypothesis of a unified shift in personality that would lead to a converged 'Alzheimer type personality'. Rather, the changes in personality seem to reflect the premorbid personality (Balsis et al., 2005). The most marked change in patients developing Alzheimer type dementia seem to be a decrease in *conscientiousness*. *Neuroticism* is often clearly increased and *extraversion* decreased, while *openness* and *agreeableness* have been observed as modestly

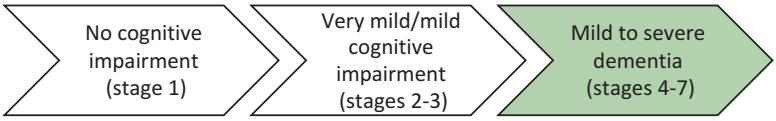


Fig. 5 The current text section highlights aspects of personality/personality changes that may be relevant for the stage of mild to severe dementia, which corresponds to GDS stages 4–7

reduced (Robins Wahlin & Byrne, 2011). Thus, this meta-analysis supported the view of a clear and consistent systematic stereotypic personality change in Alzheimer type dementia, consisting of changes towards a specific direction, but still with maintained individual variability reflecting the premorbid personality. In other words, those who were high on one trait remained high also after disease onset (Robins Wahlin & Byrne, 2011).

Recent studies have focused on the associations between neurochemical Alzheimer disease biomarkers and premorbid personality. Findings have suggested that there is an interaction between personality traits and Alzheimer pathology, which predicts cognitive functioning (Tautvydaite et al., 2017). Possibly, personality traits may affect cognitive reserve (resistance to brain damage), but more studies are needed.

Vascular Dementia

Vascular dementia is the second most common form of dementia (Roman, 2003). It is related to reduced blood flow to the brain which may be caused by a large incident such as a stroke or narrowing and/or blockage of the small blood vessels. Common symptomatology includes, e.g. slowness of thought, difficulties with planning and organizing (executive functioning), depression, gait disturbance, restlessness, confusion and emotional lability. The literature on the vascular dementia phenotype is limited compared to the Alzheimer type, possibly due to debated and unclear boundaries between these two syndromes. Five-factor personality traits in relation to vascular dementia have seldom been investigated. Some findings have suggested that white matter lesions, which are a common finding in vascular dementia, are related to reduced conscientiousness and increased neuroticism (Duron et al., 2014). Early accounts describe personality as ‘relatively preserved’ in vascular dementia, compared to Alzheimer’s disease dementia. For example, relatively preserved personality was listed as a criterion in the Hachinski Ischemic Score (Hachinski et al., 1975), which was previously frequently used to identify vascular dementia. However, contradicting findings suggest that personality traits do in fact change to a similar extent in vascular dementia and dementia of the Alzheimer type (Verhey, Ponds, Rozendaal, & Jolles, 1995). Furthermore, ‘personality and mood changes’ are listed as clinical criteria in the frequently used diagnostic criteria for vascular dementia: the National Institute of Neurological Disorder and Stroke-Association Internationale pour Recherche et l’Enseignment en Neuroscience (NINDS-AIREN) (Roman et al., 1993; Roman, Erkinjuntti, Wallin, Pantoni, & Chui, 2002). These contradicting accounts of personality within the literature on – and criteria for – vascular dementia forms likely have to do with terminology. An increase in emotional lability is a well-established symptom of the vascular dementia phenotype (O'Brien, 2003). That is, changes that could be described as ‘increased neuroticism’ are rather described as ‘increased emotional lability’, and the conceptual boundaries between personality traits and emotional expression are unclear. Taken together, vascular dementia undoubtedly is associated with changes that are likely to be perceived as a change of personality by loved ones, often related to the person's emotional expression.

Lewy Body Dementia

Lewy body dementia (LBD) is often described as the third most common dementia disorder, after Alzheimer type dementia and vascular dementia. The related pathology known as Lewy bodies (after neurologist Frederic Lewy) – consisting of abnormal levels of the protein alpha-synuclein – was observed already in the early 1900s. The disease was not described until much later and the diagnosis was not fully established until the mid-1990s. This is a plausible reason for the, to date, relatively limited amount of studies focusing on this specific disorder. The cognitive symptomatology and brain pathology in LBD is somewhat overlapping with e.g. Alzheimer's disease dementia in many patients, which complicates the diagnostic procedure (Galvin, 2003). However, the clinical picture of LBD frequently displays other specific characteristics. Memory impairment is generally the primary symptom of Alzheimer's disease dementia, but LBD is rather characterized by fluctuations in cognitive functioning. One typical symptom related to early signs of LBD is vivid dreaming, which often is physically acted out by movements during sleep. Another hallmark symptom is visual hallucinations, often in the form of living creatures such as people or animals. Hallucinations in LBD are non-psychotic, as the affected individuals generally are not delusional but are aware that the visions are not real. LBD also includes severe medical sensitivity, which may potentially be life-threatening if patients are misdiagnosed and, for instance, medicated with antipsychotic drugs. These can induce neuroleptic malignant syndrome in patients with LBD, which may lead to kidney failure. Furthermore, LBD is closely associated with Parkinson's disease dementia, both regarding brain pathology and the typical motor symptoms including e.g. gait disturbance and stiffness. The only established clear difference between LBD and Parkinson's disease dementia involves the order of symptoms – cognitive symptoms should present earlier than motor symptoms in LBD, but vice versa in Parkinson's disease. The aspects of personality in relation to LBD are not thoroughly described in research studies. Clinical experience suggests that the personality in patients with LBD is often largely intact for a relatively long time into the disease progress. However, one study (Galvin, Malcom, Johnson, & Morris, 2007) observed some aspects of personality that separated between LBD and Alzheimer's disease dementia patients. Personality-related factors that distinguished LBD were diminished emotional responsiveness, relinquishing hobbies, growing apathy and purposeless hyperactivity. They also found that these changes were associated with presence of visual hallucinations, but not associated with Parkinsonism.

Frontotemporal Dementia (FTD)

The term frontotemporal dementia (FTD) is inconsistently used and debated in the literature, but has previously often been divided into three specific phenotypical syndromes: a behavioural variant (bvFTD) and two temporal variants – semantic dementia and primary-progressive non-fluent aphasia (Neary et al., 1998). Since

2011, new criteria have been published in which the language variants are more distinctly separated from FTD (Gorno-Tempini et al., 2011; Rascovsky et al., 2011) and described as primary-progressive aphasia with three main variants. The age of onset is relatively low – typically at 45–65 years. Neuropathologically, dementia disorders within the FTD spectrum comprise atrophy in the frontal and/or anterior temporal cortex (Neary, Snowden, & Mann, 2005), with atrophy in the right lobe being associated with far more pervading personality changes compared to left lobe atrophy (see Mychack, Rosen, and Miller (2001) for case studies).

The frontal area of the brain, especially the prefrontal area, is central for executive functions such as planning, control, complex attention and impulse inhibition. The prefrontal cortex is usually regarded as the most important neuroanatomical structure for the development of personality. Consequently, neurodegeneration in this area leads to extensive personality alterations, which is also known as a hallmark symptom of bvFTD. One study reported that 50% of patients with bvFTD showed behaviours that could be classified as 'misdemeanours' – especially shoplifting and physical threats (Diehl et al., 2006). The other dementia syndromes related to frontotemporal lobar degeneration – primary-progressive aphasia and subtypes – include atrophy in the temporal region which primarily leads to the specific symptomatology of impaired ability to find and understand words (semantic dementia) or to pronounce words and use correct grammar (primary-progressive aphasia).

Frontotemporal Dementia: Behavioural Variant

Personality change is a core criterion of bvFTD (Neary et al., 2005), and changes related to all five-factor model traits have been reported, e.g. Mahoney, Rohrer, Omar, Rossor, and Warren (2011). Abnormal social behaviour is common. Personality changes appear early in the disease and are often much more pronounced than the cognitive deficits. A person with FTD generally has very reduced insight into these changes (Salmon et al., 2008) which differentiates them from persons with Alzheimer type dementia who generally show more self-awareness regarding personality dimensions (Rankin, Baldwin, Pace-Savitsky, Kramer, & Miller, 2005). Not surprisingly, many persons who are later diagnosed with FTD start out as patients in psychiatric care, because their symptoms are poorly understood (Wittenberg et al., 2008).

A case study published in Military Medicine (Faber, Hill, & Kim, 2003) describes the progression of bvFTD in S.C., a 51-year-old former US air force officer. Previously, S.C. had maintained 'impeccable standards of personal presentation and behaviour necessary for an officer of that rank'. During a 9-year period, his behaviour and personality went through dramatic changes. The first signs, according to retrospective accounts by family members, were subtle but inadequate behaviours – such as hanging up the telephone in the middle of a conversation without warning. During the subsequent years, his behaviour became increasingly impulsive and socially unacceptable: he developed an excessive interest in pornography;

he attended a family wedding unwashed and physically abused one of the guests and suddenly left abroad for a 3-year contract without giving notice to his family. These incidents were typically accompanied by a total lack of remorse or empathy from S.C.'s part. His eating habits became unhealthy consisting of soft drinks and candy, leading to a weight gain of 88 kg. Eventually, the changes led up to a divorce from his wife and discharge from the army. He was not able to hold down even simpler jobs, such as working at a fast food restaurant. Prior to inevitable hospital admission, his behaviours developed to the extreme, including defecating in inappropriate places (even though he was not incontinent). Despite these extensive behavioural changes, S.C.'s memory functions, as well as comprehension, reading, spelling and calculating, were intact. He scored 30 of 30 on the Mini-Mental State Examination (MMSE). He declined having any suicidal or homicidal thoughts or any auditory or visual hallucinations. His insight into his problems was poor, and his behaviour during medical and psychological evaluation was characterized by restlessness, inattention, distractibility and occasional inappropriate personal questions.

Frontotemporal Dementia: Temporal Variants

Dementia characterized by atrophy in the predominantly left temporal brain regions often leads to a deterioration of language functions, with three different but overlapping main variants as described within the diagnostic concept of primary-progressive aphasia: non-fluent/agrammatic variant, semantic variant and logopenic variant (Gorno-Tempini et al., 2011). In short, these three variants are characterized by impairments in grammar and motor speech (non-fluent/agrammatic variant), single-word comprehension and object/people knowledge (semantic variant), repetition (logopenic variant), confrontation naming and reading/spelling (semantic and logopenic variants) and sentence comprehension (logopenic and agrammatic variants) (Gorno-Tempini et al., 2011). Changes in personality traits may appear in the different primary-progressive aphasia variants (Multani et al., 2017), but to a much lesser extent compared to right-sided bvFTD (Mesulam, 2013). The semantic variant has been associated with a decline in warmth, extraversion, agreeableness, openness and dominance and an increase in neurotic traits (Mahoney et al., 2011; Sollberger, Stanley, et al., 2009; Sollberger, Neuhaus, et al., 2011).

Differences Between Different Dementia Disorders

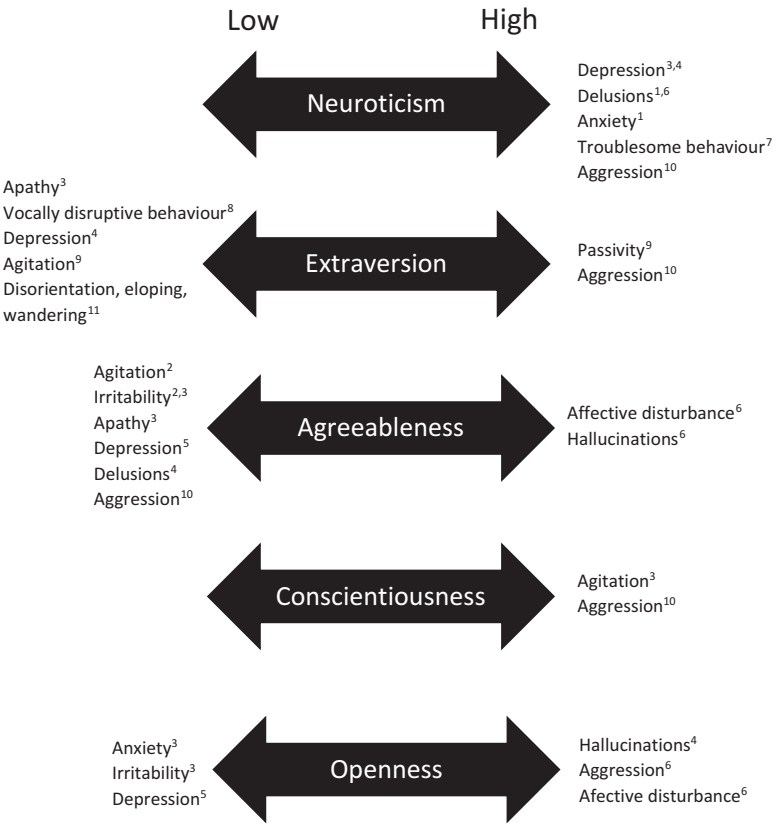
Is it possible to distinguish different dementia disorders by different patterns of personality changes? There are still only a limited number of studies, although some have addressed this specific issue, e.g. between frontotemporal dementia, Alzheimer type dementia and mild cognitive impairment (Lykou et al., 2013); Lewy body dementia and Alzheimer type dementia (Galvin et al., 2007); Alzheimer type

dementia, head injuries and stroke (Golden & Golden, 2003); and bvFTD, primary-progressive aphasia and Alzheimer type dementia (Sollberger et al., 2011; Torrente et al., 2014). The most specific patterns of personality change are generally observed in cases of frontotemporal dementia and can give a clear early indication of that specific dementia diagnosis. For instance, a lack of warmth has been reported as the clearest difference between frontotemporal dementia forms and Alzheimer type dementia (Sollberger et al., 2011). However, for other dementia disorders, the boundaries are generally not as clear, and most dementia disorders are associated with some degree of, e.g. increased apathy, social withdrawal and emotional lability – even if these symptoms may present earlier in vascular dementia forms. Increased neuroticism is a recurrent theme across dementia disorders. However, as personality traits have been associated with specific underlying neural networks (Sollberger et al., 2009), it is reasonable to assume that there are more specific personality differences in dementia disorders that still remain to be identified by research studies. Many studies have so far only reported the broader personality traits/domains such as 'neuroticism' and 'extraversion'. Personality assessment would perhaps provide more information that is useful considering the differential diagnostic procedures if studies would further pursue in-depth study of specific facets.

BPSD: Behavioural and Psychological Symptoms in Dementia

'Behavioural and psychological symptoms in dementia' (BPSD) is a term describing a heterogeneous group of non-cognitive symptoms and behaviours occurring in dementia (Cerejeira, Lagarto, & Mukaetova-Ladinska, 2012). These include symptoms such as irritability, insomnia, agitation, hallucinations, wandering, screaming, paranoid delusions and depressive symptoms/anxiety, with great individual variability considering the severity of symptoms. The prevalence of BPSD in old age cognitive impairment (occurrence of at least one symptom) was recently reported as 66% in persons with mild cognitive impairment, 86% in mild dementia and 91% in moderate dementia (Boccardi et al., 2017). For most types of dementia, BPSD is most common in later phases. The distinction between what should be considered a 'change of personality' and what is better described as BPSD symptoms is not clear (von Gunten, Pocnet, & Rossier, 2009). Both are matters of behaviour, and it is likely not possible to establish any clear-cut boundaries. The complex relationship between personality and BPSD can be described as 'pathoplastic' (von Gunten et al., 2009), meaning that personality has an effect on how the symptoms develop and thus may partly explain why individuals who are diagnosed with the same disease may display variations in symptoms.

Needless to point out, BPSD symptoms induce very difficult challenges for caregivers as well as immense suffering for both the affected individuals and family members. Knowledge of how personality, as well as cognition, emotion and behaviour, may change during dementia, is likely important to help family members cope with these challenges.



1. (Strauss, Lee, & DiFilippo, 1997); 2. (Archer et al., 2007); 3. (Tabata et al., 2017); 4. (Chatterjee, Strauss, Smyth, & Whitehouse, 1992); 5. (Wilson, Arnold, Beck, Bienias, & Bennett, 2008); 6. (Low, Brodaty, & Draper, 2002); 7. (Meins, Frey, & Thiesemann, 1998); 8. (Holst, Hallberg, & Gustafson, 1997); 9. (A. Kolanowski & Litaker, 2006); 10. (A. M. Kolanowski, Strand, & Whall, 1997); 11. (Song & Algase, 2008).

Fig. 6 Premorbid personality traits in relation to BPSD symptoms

Figure 6 shows summarized results from 11 studies on the subject of personality traits (using only five-factor traits) in relation to BPSD symptoms. Clearly, even across this limited number of studies, a complex pattern of relationships between personality traits and challenging non-cognitive behaviours emerges.

The most marked associations appear to be evident between BPSD symptoms and high premorbid levels of neuroticism, low premorbid levels of extraversion and agreeableness. Additionally, *low* premorbid levels of neuroticism and conscientiousness were not associated with any BPSD symptoms.

A review (Osborne, Simpson, & Stokes, 2010) included 18 studies published between 1992 and 2008 that investigated the relationship between premorbid

personality and challenging behaviour in dementia. Most studies (n = 14) used informant report as a measure of behaviour, and the four remaining used observational methods. All studies used informant report to assess personality traits, mostly in accordance with the NEO five-factor model. Five studies reported that there were no significant relationships between premorbid personality traits and challenging behaviours, which could perhaps partly be explained by low sample sizes. The remaining 13 studies reported significant relationships between challenging behaviours and premorbid personality. The most frequently reported relationships included aggressive behaviour (aggression, irritability, agitation) and mood-related behaviour (depression, passivity, apathy), which were positively associated with higher neuroticism. Two studies reported that agreeableness was negatively related to aggression-related behaviours. Two studies focused on wandering behaviour, which was significantly associated with 'extraversion', although in two opposite directions.

One such case was described by Poletti and Bonuccelli (2011), focusing on the relation between personality disorders – the pathological expression of personality – and dementia. They present the case of U.C., a 73-year-old retired chemical engineer.

Throughout adulthood, he had displayed several characteristics typical for a narcissistic personality disorder. During decades, he prepared thousands of lawsuits and studied law textbooks to denounce individuals and institutions who he thought were guilty of misconduct. Further, he wrote an erotic version of a best-selling novel. He described himself as having a superior intelligence. The authors describe that his behavioural pattern was also compatible with a paranoid personality disorder, given his extensive distrust and suspiciousness of others. At the age of 72, his wife reported that his behaviours changed to include new patterns, such as hypersexuality, disinhibition and verbal aggression. Brain imaging using MRI revealed leukoencephalopathy, and ^{18}F FDG-PET showed a bilateral prefrontal hypometabolism, which was marked on the right side, and a less marked mesial temporal hypometabolism especially on the right side. His clinical symptoms as well as the imaging findings were compatible with a diagnosis of FTD.

Methodological Challenges When Studying Personality in Dementia

It is well known that the level of awareness of cognitive functioning and insight into disease gradually declines during dementia development. This process may begin even before the dementia is manifest, even though the pattern of how and when awareness is affected may differ for different dementia disorders. In later stages, anosognosia – decreased awareness of one's own disability – is inevitable in all dementia disorders. The reduced insight also affects the persons' ability to assess their own behaviour accurately and consequently also when asked to rate their own

personality traits (Robins Wahlin & Byrne, 2011). Persons with dementia may tend to report on their former personality traits rather than their current traits, which makes it difficult to investigate possible personality changes (Rankin et al., 2005). Consequently, in studies including persons with manifest dementia, self-assessment is not possible, or of very limited value (von Gunten et al., 2009). A few studies have been based on materials in which personality was assessed prospectively, before disease onset (e.g. Ausen et al., 2009; Berg & Johansson, 2014; Yoneda et al., 2017). However, in most studies, researchers have had to use retrospective informant-reported personality measures as a second-best alternative, which undoubtedly gives rise to questions of validity. Although there is evidence of a high correlation between informant-reported and self-rated personality (Bagby et al., 1998), it is not certain whether retrospective informant-reported assessment is valid (Low et al., 2013). When a family member rates the patient's personality, what is actually assessed? Personality consists of both a person's view of herself and of behaviour. In informant-based personality rating, the self-viewing perspective will inevitably be lost. The methodological problem of assessing personality retrospectively has been highlighted by several researchers (Balsis et al., 2005; Osborne et al., 2010; Robins Wahlin & Byrne, 2011). Investigating self-reported personality traits in relation to dementia would require large and longitudinal prospectively collected data sets, which is rare.

Another methodological difficulty concerns what comprises the concept of personality and its complex associations with emotion, behaviour and cognition. What is a change of personality? When is the change best described as a personality change, and when is it a change of behaviour and emotion that is an inevitable consequence of decreased functioning? To what extent are the personality-related changes direct effects of damage to neural circuits, or indirect effects of cognitive impairment and dysfunction in everyday life? Plausibly, early changes may be more related to coping and reactions to the emerging dysfunction, and later changes are likely to be related to the progressing neurodegeneration of the brain.

Implications of Personality Research in Dementia

Dementia disorders gradually deprive affected individuals of their functions and lead to extensive changes in cognition, emotion and behaviour – essential aspects of what a person is. It is a painful journey for friends and family members to see a loved one be gradually broken down until there is not much left of what characterized them previously in life. Not seldom, spouses of patients with mild dementia find it very difficult to deal with the changes of personality and behaviour, which may lead to irritability and conflicts within affected families. The knowledge of that these personality changes partly are caused by underlying brain changes may help relatives to accept these changes as a part of the disease itself and not as a matter of choice. Knowledge of personality changes and related emotional/behavioural changes are also potentially useful in the planning of interventions and health care.

For clinicians and researchers, evidence suggesting that personality changes may help differentiate between different dementia disorders and that personality changes often appear in an early stage – perhaps even earlier than the first cognitive signs – are important as part of the complex process of identifying early signs of dementia. Not least for clinical drug trials, the identification of early signs is a key issue.

Personality is a complex phenomenon and the clinical usefulness and possibilities are limited. Studies on personality traits and changes tend to be primarily descriptive. More in-depth studies into associations and mechanisms between personality and dementia-related brain changes are needed. Nevertheless, the procedure of diagnosing dementia is a puzzle, and aspects of personality change may be one useful piece of that puzzle.

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The Study of Personality Traits in the Blekinge Part of the Swedish National Study on Aging and Care (SNAC-B)

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Abstract *Background*: Personality has been shown to be related to numerous health-related factors. In the SNAC-B study, relationships between health variables and the personality traits of neuroticism (N), conscientiousness (C), agreeableness (A), openness (O), and extraversion (E) have been investigated. *Aim*: In this chapter, stability and change of personality during the ages of 60 to 90 years are explored. In addition, relationships between personality traits and health-related variables are presented. *Methods*: The results are based on data from the SNAC-B studies of 1402 men and women aged 60 to 90. The participants have been followed up during 12 years, while data on health, well-being, and autonomy have been continuously collected. In addition, variables assumed to influence health have been collected, such as lifestyles, demographic factors, social environment, and personality. *Results*: The results show personality to be stable over time according to rank order, but all personality traits except neuroticism were shown to have small but significant mean level changes. In addition, connections between a number of health-related variables and personality traits, such as mortality, self-care, work ability, and perception of pain, were indicated. *Conclusions*: The results indicate that the role of personality should be taken into account in research on health and aging. Personality traits have a lifelong influence on health behaviors and have been shown to affect both subjective and objective aspects of health and the way we cope with health-related experiences.

Keywords SNAC · Personality and stability

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Introduction

The study of personality concerns several human aspects including behavior, cognitive function, attitudes, and emotions. These aspects are strongly related to adaptation to the environment and are supposed to have a considerable impact on health and well-being as well as on how the individual aging process takes place more generally. As individuals in old age have been exposed to their own personality traits for many years, the personality of each individual should be taken into account in the study of aging, health, and well-being. The stability and change of personality and the relationships between personality and health have been poorly investigated. Therefore, personality traits have been included in the Swedish National study on Aging and Care (SNAC), which is a national, longitudinal study aimed to follow the aging Swedish population with the focus on good health and illness as well as the need for care and social services.

This chapter summarizes findings regarding the stability and change of personality during a 12-year period among participants of the SNAC study aged 60 to 96. In addition, relationships between personality traits and well-being, health, and longevity, found in the SNAC study, are described and discussed.

The SNAC Study

Care and social service of good quality presuppose knowledge about both existing needs and available resources. In the area of health care and social service for the aging population in Sweden, this knowledge is particularly important as the older part of the population is increasing while the resources remain limited. The SNAC study aims to generate such knowledge. The study was initiated in 1998 by the Swedish government, which continually supports it together with county councils, municipalities, and universities in the four Swedish regions, where the study is located. The basic idea behind the study is to build a database on individual level that describes the aging process in terms of health, illnesses, and the development of care and social service needs. The SNAC database comprises medical as well as social, demographical and psychological aspects, and the data is collected longitudinally. More specifically, the aim is to follow the participants and the health care and social service efforts and to study how the resources match the needs. In short, the study aims to give information about how the resources are used in terms of who gets what or how the limited resources are used in relation to the existing needs in a given situation. In addition, changes in these relationships between needs and resources are studied longitudinally. As the SNAC study is conducted in four Swedish areas including both big and middle-sized cities and in rural areas, the database is supposed be representative for the older Swedish population. The big cities are represented

by Kungsholmen (a part of Stockholm) and Malmö; the middle-sized cities include Karlskrona, Ystad, and Hässleholm; and the rural areas consist of the municipalities of Osby and Nordanstig. The SNAC study comprises one care system part, in which the registers of care and service efforts are collected and analyzed, and one population part, in which data about the health, illnesses, and needs are collected on a population level together with information about social, demographical, and psychological factors supposedly connected with health and the development of illnesses and the need for care and social service efforts from society.

The longitudinal data collection in the population part includes health, illness, functional capability, social situation, care need, cognitive functions, and personality traits. Initially, a baseline data collection was made on individuals aged 60, 66, 72, 78, 81, 84, 87, 90, 93, and 96. These individuals are then followed up regularly – every 6 years those aged 60 to 78 and every 3 years those aged 81 to 96. Every sixth year, a new cohort of 60- and 81-year-olds is added to the study. This enables both following separate age groups and comparing cohorts. As a consequence of this design, it is possible to study changes over time in any variable, for example, the stability and change of personality traits. In addition, relationships between personality traits and either good health variables or other possibly health-related variables such as self-care, experience of pain, work disability, and even longevity.

The baseline data collection was completed at all sites in 2004. After that, all participants have been reexamined twice and those 81 years of age and older four times. The design of the SNAC study has been previously described by Lagergren et al. (2004).

The Population Part of SNAC-B

In SNAC-B, comprising the Karlskrona part of the study, the population-based data on personality traits is complete in all phases. Therefore, the focus in the following section will be on the population part of SNAC-B. In SNAC-B, 1402 individuals participated in the baseline data collection. In the various age cohorts, the participation rate varied between 50 and 75% with a mean rate of 62%. The second phase involving the reexamination of those 81 years of age or older was completed in 2004 with 513 participants. The rate of mortality was 27% in that group at the time. For those still living, the participation rate was more than 80% in all phases. A reexamination of the total sample was made 2007–2009. The third reexamination of those aged 81 years or older was carried out 2010–2012. During 2013–2015 the fourth data collection phase was performed, reexamining the whole study population (Fig. 1).

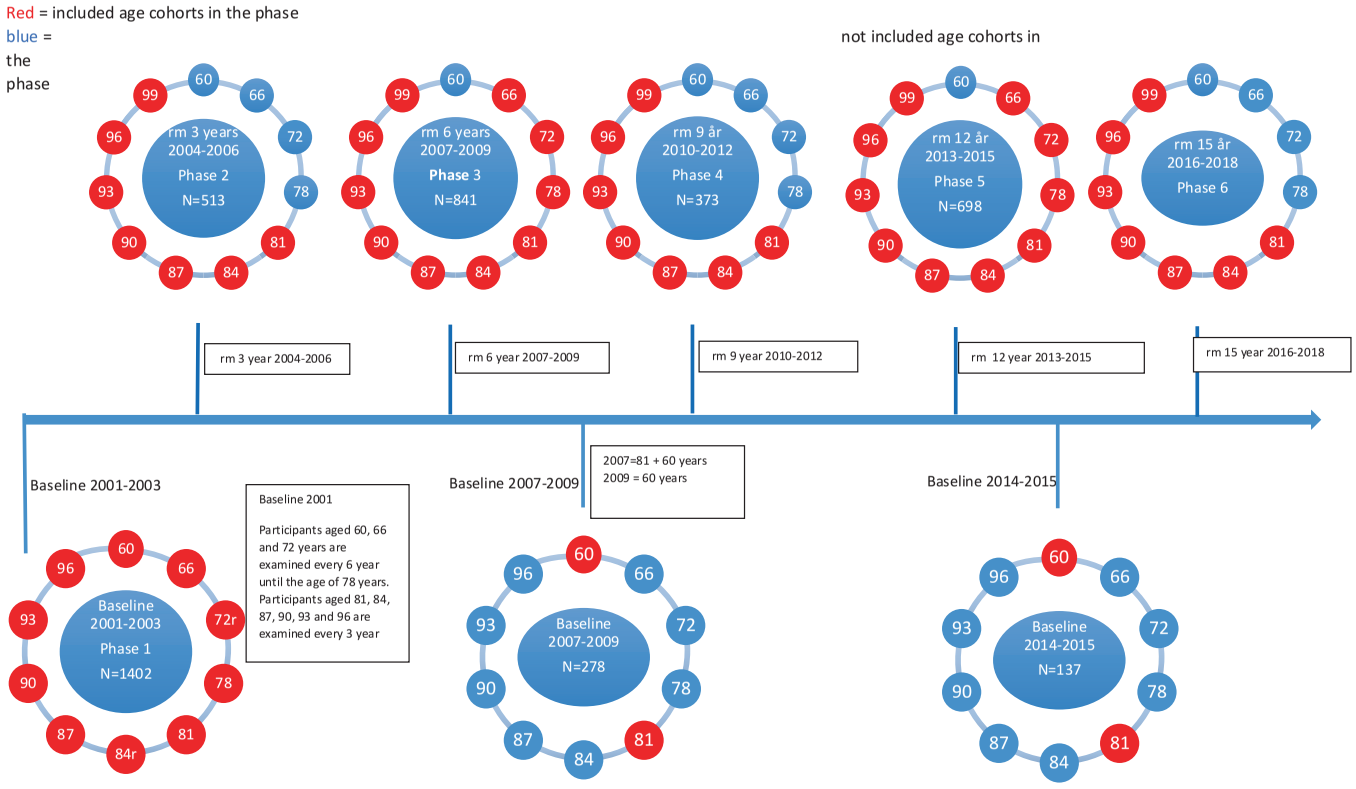

Fig. 1 Baseline and the process of repeated measures in SNAC-B

Perspectives on Personality

One of the earliest definitions of personality was made by Allport (1937). He defined personality as "the dynamic organization within the individual of those psychophysical systems that determine his characteristic behavior and thought." There is, however, no single definition of personality. Various theoretical perspectives, e.g., the psychodynamic, the social-cognitive, or the trait-theoretical perspectives, lead to different definitions. In the psychodynamic perspective, the personality can be described within the structural model of superego, ego, and id and is a result of the dynamic processes between these structures. The personality can be described as the way the individual balances these structures and adapt to external and internal demands by adaptation strategies or defense mechanisms (Cervoe & Pervin, 2016). In a social-cognitive perspective, personality can be described by a cognitive model of competence, beliefs, expectations, personal goals, and behavioral norms. This model mainly focuses on individual cognitive skills and how they are used for problem solving (Mishel & Shoda, 2008). In this perspective, personality is a result of these cognitive models in interaction with the social environment.

Most current research on personality is, however, based on a trait-theoretical perspective. In this perspective, personality is described in less theoretical terms which enable the categorization of individuals, based on traits. The advantage of the trait perspective in research is that it makes it possible to study personality by interviews and questionnaires. The description of an individual's personality is founded on the establishment of a general taxonomy or a terminology system that enables describing an individual in as simple terms as possible. For this purpose, a lexical method was developed in which terms for personal behaviors were selected from dictionaries. By using factor analyses, 12 to 16 factors were developed (Catell, Eber, & Tatsuoka, 1970; John, 1990). By extended factor analyses, the number could be reduced to five factors, which were able to give a broad description of the personality of an individual (Costa & McCrae, 1985). These factors, often called the big five comprise extraversion (E), agreeableness (A), conscientiousness (C), openness (O), and neuroticism (N). According to the trait theory, traits are supposed to constitute stable internal dispositions to behave in a specific way in a given situation (McCrae & Costa, 1988).

Stability and Change in Personality Traits

Trait-related definitions of personality imply that traits are relatively stable over time and situation (Roberts, Walton, & Viechtbauer, 2006). A basic assumption has been that personality traits develop and, consequently, change during childhood and adolescence until the age of about 30 and then stabilize throughout adulthood (Costa & McCrae, 1988). This assumption has, however, been questioned (Srivastava, John, Gosling, & Potter, 2003). Although evidence has shown that personality may

change over time even during adulthood, traits are still assumed to be mostly stable (Roberts et al., 2006), while the degree and nature of stability and change are still debated (Specht, Egloff, & Schmukle, 2011). In addition, there is no consensus with regard to trends in stability and change of personality during the aging process (Hutteman, Hennecke, Orth, Reitz, & Specht, 2014; Kandler, Kornadt, Hagemeyer, & Neyer, 2015). In this chapter, the question of stability and change will be looked into on the basis of analyses of longitudinal data from the SNAC-B study. Before that, definitions of stability and change need, however, to be clarified.

In the study of stability and change of personality, stability has been defined as rank-order stability (Roberts et al., 2006). This shows to what degree individuals keep their relative position in comparison with the other individuals in the group under study. Change, on the other hand, is defined as an individual's mean value changes on personality traits between repeated measures. Stability and change may thus occur simultaneously and are mutually independent.

Research on rank-order stability indicates a moderate to high stability with a correlation coefficient of 0.4 to 0.6 (Ardelt, 2000; Roberts & DelVecchio, 2000) and increases with the increased time span between measurements (Caspi, Roberts, & Shiner, 2005). In addition, rank-order stability has been shown to increase from adolescence to the age of 50 (Pullmann, Raudsepp, & Allik, 2006; Roberts & DelVecchio, 2000). However, it has not yet been clarified whether the increase in stability continues in older age groups. Although according to "the cumulative continuity principle" (Caspi et al., 2005), personality is assumed to be strengthened and cemented during the aging process, empirical findings show contradictory results. In a meta-study, Roberts and DelVecchio (2000) showed that the rank-order stability was straightened out after the age of 50, and in another study, Ardelt (2000) found that it evefdn decreased during the same age period. More recently, Ardelt's findings have been supported in several studies (Kandler et al., 2015; Lucas & Donnellan, 2011; Specht et al., 2011; Wortman, Lucas, & Donnellan, 2012).

Mean value change is assumed to follow "the maturity principle" (Caspi et al., 2005; Wortman et al., 2012). According to this assumption, healthy maturity is indicated by an increased A and C together with a decreased N during the aging process. The two other personality dimensions (O and E) have not been assumed to be connected to the maturity principle.

Empirical results generally supports the maturity principle (Bleidorn, Kandler, Riemann, Angleitner, & Spinath, 2009; Roberts et al., 2006; Soto, John, Gosling, & Potter, 2011). As some studies, however, show ambiguous results (Lucas & Donnellan, 2011; Specht et al., 2011) and recently, Kandler et al. (2015) recently questioned the relevance of the maturity principle when it comes to older ages. In their study, a decrease in A and C was shown. Other studies (Lucas & Donnellan, 2011; Specht et al., 2011) support their findings in samples of individuals aged 80 years or older and have also found an increase of N in older ages. Hutteman et al., (2014) suggests that these findings mirror age-related changes in abilities and relationships in older ages but may not necessarily indicate lower maturity or mental health levels. On the contrary, they argue that decreased agreeableness and

conscientiousness may reflect functional maturity in relation to age-related changes such as fewer social roles to fulfill and fewer relationships to adapt to. In addition, higher neuroticism may reflect a mature strategy toward a more frail body.

Personality and Health

Both well-being and health and even longevity are multi-determined and can never be explained by any single factor alone. Previous research indicates, however, personality traits to be related to aspects of health. N and E have, for example, been shown to be related to both morbidity and mortality, although the findings are both complex and contradictory. In addition, these personality traits have been shown to be related to life satisfaction, neuroticism, with a negative direction and extraversion positively (Kämpfe & Mitte, 2010). Most research on the relationships between personality and health has been performed on young and middle-aged individuals. Still, in a PhD thesis, Stalbrand (2011) explored the role of N, E, and O in relation to life satisfaction in a sample of 2109 individuals aged between 60 and 93. The results confirmed previous findings, showing E to be positively and N to be negatively related to life satisfaction. On the other hand, the relation of O to life satisfaction was more complex, as it was positive in some subgroups and negative in others. According to the relationships between self-reported health and personality traits, Jerram and Coleman (1999) found that N was negatively related to medical status and positively related to attendance to the health-care visits. E was positively related to health behaviors generally and O and A to good reported health. Women scoring high on A reported fewer medical problems and lower attendance to their health, while men scoring high on C reported good health and low number of health-care visits. As regards longevity, C has repeatedly been shown to be positively related (Terracciano, Löckenhoff, Zondermann, Ferrucci, & Costa, 2008; Weiss & Costa, 2005).

Relationships between personality and perceived pain have also been reported. It has been suggested that psychosocial functioning in patient with pain is influenced by their personality with N being shown to make them more vulnerable (Goubert, Crombez, & Damme, 2004). In addition, N, O, and A have been able to significantly predict pain anxiety (Martinez, Sanches, Miro, Medina, & Mami, 2011).

Methods

Participants

Data from the SNAC-B were used in the empirical studies that are presented below. Design, number of participants, participation rates, and descriptions of the participants are described previously, under the heading “The population Part of SNAC-B.”

Instruments

Personality was measured by a Swedish version of the NEO-FFI five-factor inventory (Bratt, Stenstrom, & Rennemark, 2015; Costa & McCrae, 1988; Rennemark & Berggren, 2006). The questionnaire consists of 60 items describing personality traits and are answered on a Likert scale with alternatives from 1 (do not agree) to 5 (agree completely). Higher scores on each personality factor indicate stronger inclination to behave in line with the description of the factor. In each study presented below, other instruments and sources of data are presented separately. All data are taken from the SNAC-B database.

Procedures

A written invitation to participate in the study was given to 2312 randomly selected individuals by mail of which 1404 (62%) did choose to participate. All participants were invited to visit the research center. After having filled in a written informed consent, they were examined medically and given both survey questions and various psychological tests. Examinations and tests were conducted by trained research staff and took about 3 h. Participants who were unable to visit the research center were offered to be examined in their homes.

Results from SNAC-B

Stability and Change of Personality in Old Age

In a master thesis, Axbrink and Lindén (2017) investigated both rank-order stability and mean level change in the SNAC-B sample of 72–90-year-old participants, using the SNAC-B baseline database and a follow-up measure 12 years later. On the basis of previous findings, they investigated the rank-order stability of the Big Five personality dimensions in the total group as well as mean age changes in both the younger age cohorts (72–79 years) and the older age cohorts (84–90 years).

The results showed moderate to high rank-order stability in the Big Five personality domains in terms of test–retest stability, as measured by Spearman's rank-order correlation for N (N = 315), A (N = 317), and C (N = 315) and Pearson product-moment correlation for E (N = 314) and O (N = 302) (Table 1).

Mean value change was measured by paired samples t-test, showing small but significant changes for E (mean value difference 1.57***), O (mean value

Table 1 Rank-order stability as measured by test–retest correlations during a 12-year period

Personality dimension	Correlation coefficient
Neuroticism	654***
Extraversion	719***
Openness	628***
Agreeableness	424***
Conscientiousness	596***

***$p < 0.001$

Table 2 Mean value changes as measured by paired sample t-test for the younger group (aged 60 to 66 years)

Personality dimension	M (SD)	M (SD)	Difference	Cohen's d
Neuroticism	25.74 (6.31)	25.99 (6.73)	−0.25	0.05
Extraversion	41.16 (5.76)	39.92 (5.59)	1.25***	0.28
Openness	38.12 (5.10)	37.30 (4.42)	0.82**	0.20
Agreeableness	42.22 (4.02)	41.44 (4.16)	0.78*	0.17
Conscientiousness	43.92 (4.92)	42.79 (5.19)	1.13***	0.25

*$P < 0.05$, **$P < 0.01$, ***$P < 0.001$

Table 3 Mean value changes as measured by paired sample t-test for the older group (aged 84–90 years)

Personalit dimension	M (SD)	M (SD)	Difference	Cohen's d
Neuroticism	27.69 (5.37)	28.41 (5.78)	−0.72	0.14
Extraversion	39.28 (5,69)	36.90 (5.68)	2.38***	0.62
Openness	35.93 (5.03)	35.31 (4.73)	0.62	0.14
Agreeableness	41.20 (4.36)	40.96 (3.96)	0.24	0.06
Conscientiousness	42.75 (4.86)	41.35 (5.15)	1.40**	0.33

**$P < 0.01$, ***$P < 0.001$

difference 0.71**), A (mean value difference 0.69**) and C (mean value difference 1.21***). Thus, only N showed no significant change (mean value difference – 0.39). The same pattern emerged when the analyses were carried out using only the younger group (aged 60–66 years) (Table 2). As can be seen in Table 2, the direction of changes involves that all mean values become somewhat lower in the follow-up measure, except for N. In the older age group, however, changes emerged only in E and C, with the mean values also decreasing in the follow-up measure (Table 3). In Tables 2 and 3, effect sizes are shown as Cohen's d values (1992).

Relationships Between Personality and Health

Work Status and Personality

In a study, aimed to investigate the predictive values of extraversion (E), the number of leisure activities and of symptoms of the tendency to retire from work before the age of 60, Rennemark and Berggren (2006) used 184 participants from the SNAC-B baseline database. The participants were divided into three subgroups based on their work status; the first group consisting of those still working ($N = 122$), the second of those who had left work due to health problems ($N = 29$) and the third those who had left work for other reasons ($N = 31$).

The number of symptoms was measured by 30 questions about symptoms of illness during the last 3 years, while survey items were used for measuring the number of leisure activities, asking whether the respondents had participated in various activities during the last year. E, finally, was measured by a Swedish version of the Costa and McCrae (1988) NEO-FFI questionnaire. In multiple logistic regression analyses, household economy, work satisfaction and education level were used as covariates.

The results showed E to predict work status. Lower scores on E increased the odds to be retired marginally although significant. In comparison with those who had left work due to health problems, the odds ratio was 8% higher (OR1.08, 95%, CI 0.98–1.19).

The Use of Nature-Cure Medicine and Personality

Differences between users and nonusers of nature-cure medicine were investigated according to personality, age, and gender in a sample of 60- and 66-year-old participants from the SNAC-B baseline database (Olofsson & Rennemark, 2007). The aim of the study was to identify the typical user of such medicine.

The personality traits studied comprised E, A, C, N, and O (Costa & McCrae, 1988). Information on the use of nature-cure medicine was gathered from the medical protocol of the database, which includes a questionnaire about medicines that participants use. Participants' whose answers were positive have also filled in the name of the medicine.

The results showed that O was positively related to the use of nature-cure medicine. The difference between users and nonusers as measured by t-test was 3.7, $p < 0.001$.

Personality and Mortality Risk

The role played by N and C for mortality risk in old age was investigated in a study comprising older adults who had lost a child or/and spouse (Bratt et al., 2015). In this study, 976 individuals from the SNAC-B study were included in Cox proportional hazard regression analyses in order to predict the value of child, spouse, and

child–spouse bereavement on mortality. According to the personality variables, N but not C turned out to significantly affect the hazard function. For each increase in the N score, the mortality risk increased by 1.8% (HR = 1.08*, 95% CI = 1.00–1.037). In further analyses, child-bereaved men had a 2.7% higher mortality risk than child-bereaved women for each N score increase. In addition, child-bereaved men were found to have an increased mortality risk by 1.7% for each increase in the C.

Personality and Pain

The influence of personality traits on the perception of pain was investigated in the SNAC-B baseline database (Wranker et al. 2015). Pain was measured by self-reporting, to which was added the possibility to answer yes or no to the question "have you suffered from ache/pain during the last 4 weeks." Personality was measured by the five personality domains included in the NEO-FFI questionnaire (Costa & McCrae, 1988). In the analyses, different patterns of relationships between pain and personality traits emerged for men and women. For women, only N predicted perceived pain with an increased odds ratio for reporting pain by 5% (OR 1.05***, CI 1.03–1.08), and for men, both N and O increased the odds ratio for an increased pain report by 4% and 2%, respectively (OR 1.03*, CI 1.00–1.07 and OR1.04*, CI 1.01–1.08). These results were stable and did not change when the covariates age, insomnia, economic status, and education levels were included in the logistic regression analyses.

Discussion

Stability and Change

The results of the SNAC analyses indicate personality to possess moderate to high rank-order stability. On the other hand, all personality traits except N were shown to have small but significant mean value changes in the total group as well as in the younger group (60–66 years of age) during the observed 12 years, while in the older group (84–90 years of age), only E and C changed. All significant changes were in the direction of decreasing in the follow-up measure. According to rank-order stability, the results confirm previous findings (Ardelt, 2000; Roberts & DelVecchio, 2000; Specht et al., 2011). The mean value changes show a more complex pattern and do not support the maturity principle assumed by Caspi et al. (2005) and previously supported by results from other studies (Bleidorn et al., 2009; Roberts et al., 2006; Soto et al., 2011). On the other hand, the results partly support other previous findings, indicating a decrease of A and C during older ages. The decrease in A has been interpreted as mirroring age-related changes such as the diminishing number of social roles relationships. The decrease in C may also mirror fewer demands in older age due to retirement and a lower level of societal responsibility.

In addition, the SNAC studies have shown connections between a number of health-related variables and personality traits, such as mortality, self-care, work ability, and perception of pain.

Relationships Between Personality and Health

In the SNAC studies, all personality traits included in the five-factor model except A were shown to be related to one or more health-related variables. C has been shown to be negatively related to an increased mortality risk among child-bereaved men; O shows the increased inclination to use nature-cure medicine for both men and women but also to experiencing pain among men. A low level of E was related to early retirement, and a high N applies to perception of pain in both sexes and for child- and/or spouse-bereaved women, also to an increased mortality risk.

As C has, in previous studies been repeatedly shown to be positively related to longevity (Terracciano et al., 2008; Weiss & Costa, 2005), the relationship between mortality risk and C in the child-bereaved male group is not surprising. There was, however, no connection between mortality and C in the bereaved female group. In both male and female groups, N increased the mortality risk for child- and/or spouse-bereaved parents. To the best of our knowledge, no comparable data are available on the relationships between N and mortality risk in this specific groups, but a connection between N and mortality has been generally reported (Mroczek, Spiro III, & Turiano, 2009), whereas some other studies indicate that N may be a protective mortality factor (Weiss & Costa, 2005). N also showed to be connected to the perception of pain among both men and women. This finding confirms previous findings indicating relationships between N and pain (Goubert et al., 2004). Among men alone, O was also related to the perception of pain albeit in a positive direction, a finding that is confirmed by Martinez et al., (2011) in a previous study. E was found to be related to work ability and overall retirement age. Connections between E and life satisfaction (Kämpfe & Mitte, 2010) as well as to positive health behaviors (Jerram & Coleman, 1999) have been reported previously and may supposedly explain these connections.

Strengths and Limitations

The SNAC-B database possesses several strengths. It is a randomly selected sample which reflects the population of a suburban Swedish region and closely resembles the population of older adults in Sweden. In addition, it contains a broad range of data including psychological, biological, social, and demographical information, and this information has been collected repeatedly, so far over 12 years. Some limitation should however be mentioned. The personality traits are based on self-reports, and, generally, effect sizes and OR values in the above-presented results on the

relationships between personality and health are low. Therefore, interpretations of the findings should be made with some care.

Future Analyses of the SNAC Database

On the basis of the present findings, future analyses of the SNAC database will be focused on possible relationships between personality changes and life changes such as major life events, the onset of illness, and other age-related changes. As we now know that personality does change during the aging process and that there exists relationships between personality and health, it is also of interest to investigate factors possibly generating personality changes and influencing the relationships between personality and health variables.

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Temperament and Character in Childhood-Onset Neurodevelopmental Disorders (Autism Spectrum Disorders and ADHD)

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Abstract Neurodevelopmental disorders, such as autism spectrum disorders (ASD) and attention-deficit/hyperactivity disorder (ADHD), express aberrant neurocognitive functions in social communication, flexibility and executive control from an early age, not seldom casting extensive consequences long into adulthood. They exist along a continuum from severe disorders to broader phenotypes or "shadow syndromes". In recent years, several studies have assessed the relation between these conditions and associated personality traits in terms of Cloninger's temperament and character model in both children and adults. The aim is to clarify to what extent neurodevelopmental challenges are associated with adult personality and elucidate the link between symptom severity and specific personality traits. Findings give support for specific temperaments (previously known as constitutions) with high Novelty Seeking in ADHD and low Reward Dependence with high Harm Avoidance in ASD, while low scores on the character dimensions of Self-Directedness and Cooperativeness are a shared feature of both disorders (and more

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so the more severe the disorder is). This replicates previous findings of the same character deficits across adult mental disorders, forming a common ground for mental health problems. This pattern is proposed to be a window of opportunity for treatment interventions aiming at enhancing agency, communion, resilience and well-being.

Keywords ADHD · Autism · Character · Cloninger · Personality · Temperament

Background

Personality has been a concept and focus of study since antiquity and the humoral pathology. A choleric person had an excess of green bile, while a phlegmatic was considered to be under the influence of mucous, a sanguine under that of blood and a melancholic under black bile. The Latin word "persona" initially referred to the masks worn by actors in ancient Rome, playing stereotypic roles marked through masks and costumes. In the sixth century, Boëthius came to define personality as "persona est naturae rationalis individua substantia", that is, an individual with reasonable thinking (Piltz, 1978). Until the advent of modern psychiatry and psychology, personality was a characteristic of the individual. Soon after the introduction of medical–scientific psychiatry during the French Revolution, not only symptomatic mental illnesses but also maladaptive personalities became the focus of study. Around the beginning of the twentieth century, emphasis was put on traits, seeking systematic differences and their patterns of convergence or discordance in groups or populations rather than individuals. Personality in a psychological sense has since then been conceptualized in terms of degrees of traits, either empirically generated or derived from theoretical constructions of typologies. Several models of personality structure have consequently come to be fairly established with a solid empirical basis, for example, the basic axes of intro-/extraversion (Eysenck, 1971), the Big Five model (Costa & McCrae, 1992) and Cloninger's seven-factor Temperament and Character model (Cloninger, Svrakic, & Przybeck, 1993).

The clinically based research on personality *disorders* has followed another path, mainly using categorical diagnoses to capture personalities so unusual or fragile that they give rise to significant dysfunction and/or suffering (even if the evidence for these being true taxons is scarce or non-existent). This literature is now dominated by studies using the DSM-IV classification that classified personality disorders into three clusters, where Cluster A comprises the odd and eccentric, B the dramatic and emotional and C the anxious and fearful, with ten specific, named personality disorders (subtypes). A true integration of models was long the aim of the DSM-5, but when it was finally presented in 2013, it was obvious that this had been thwarted. At least two models, one with its roots in biological processes and one in dimensional measures of psychopathology, currently attract interest in the scientific community, that is, the Research Domain Criteria (Insel et al., 2010) and the Hierarchical Taxonomy of Psychopathology (Kotov et al., 2017). Also, in the last decade, the concept of person and personality has come back to the centre of

development not only in psychiatry but also in all of medicine, with the focus on "person-centred" healthcare.

"Person" in the latter definition, just as in the original, refers to the individual human, while "personality" mostly refers to systematic differences between humans, and "personality disorders" refer to reified clinical conditions. No clear-cut definitions of these terms have been established. As the Boëthian definition emphasizes the individuality of the person, this concept lends itself to an integrative perspective on the body with the mind and/or the soul. In contrast, the body (or brain) has little relevance for the established models of personality variance, with the notable exception of Cloninger's model, in which three of the four temperament factors were initially hypothesized to express the variance in activity of three different monoaminergic transmitter systems of the brain and/or patterns of neurophysiological responses to stimuli. The aetiologies of the personality disorders have been sought along the same lines as other mental disorders, on the one hand, in genetics, neurobiology and cognitive tests and, on the other hand, in intraindividual experiences and narratives. Relatively little attention has been given to group and cultural effects in the Western-dominated traditions of psychiatry and psychology. Generally accepted influences over personality include (a) genetic predispositions, (b) attachment experiences, (c) traumatic events, (d) family constellation and dysfunction and (e) sociocultural and political forces (Magnavita, 2004).

Three models or principles to study and treat personality are generally accepted: (a) the biopsychosocial model (aetiological heterogeneity), (b) the stress–diathesis model (the overall compensatory power of the personality structure depends on its robustness and the amount of stress it suffers) and (c) the chaos model (even small changes can lead to major effects, in both positive and negative directions, without this being obvious from before). There is no clear contradiction between these three models, which all may be used in the same research paradigm. Personality has traditionally been studied from either a lumping or splitting approach, using overarching dimensions or typologies to establish basic differences or a fine-grained description aiming at comprehensiveness.

Overall, rather few attempts have so far been made to find the personality profiles or dimensions studied in brain anatomy or physiology. Early hypotheses, such as those based in humoral pathology, craniometry or body constitution (pyknic, athletic and asthenic), were soon discarded as simplistic and non-useful for lack of empirical support. Similarly, the later decades have seen a number of proposed models based in transmitter metabolism, electric activity and sympathetic tone, brain imaging and molecular genetics. Likewise, in spite of huge efforts, rather little has come out of these studies, either to explain the differences in personality, to diagnose clinical disorders or to treat the malfunctioning, besides very strong evidence that at least half the variance, in principle, of every interpersonal variance in a given population may be referred to genetic effects (Plomin, 2018). Thus, clinicians of different schools concur in regarding symptomatic, "productive" or egodystonic disorders (formerly diagnosed on Axis I in the DSM-III and DSM-IV systems to separate them from personality disorders that were lumped in with

learning disabilities on Axis II) as more theoretically understandable and clinically treatable than personality disorders.

In this chapter, we have reviewed studies of how personality traits are related to childhood-onset neurodevelopmental disorders in order to bridge the literature on personality with that of cognitive neuroscience. Examinations of the link between personality and disorders that have been defined not only in terms of neurocognitive (dys)function but also by intensive scientific mapping of what is known (or even knowable) by today's methods in neuroscience, during the recent "decade of the brain" and "decade of the genome", hold promise to deepen our understanding of how the brain interacts with the mind and soul in mental (un)health and even to identify new inroads for treatment of both types of clinical conditions. We have chosen Cloninger's model of personality because of its theoretical distinction between temperament and character and the two most well-studied childhood-onset neurodevelopmental disorders, autism spectrum disorders (ASD) and attention-deficit/hyperactivity disorder (ADHD).

Cloninger's Model

Cloninger has developed a comprehensive biopsychosocial model of personality intended both to cover wide variations in the general population and to explain pathology. This model comprises seven dimensions, of which four are referred to as temperaments and three as characters. The four temperament dimensions are Harm Avoidance, Novelty Seeking, Reward Dependence and Persistence, while character consists of Self-directedness, Cooperativeness and Self-transcendence. Temperament, which reflects patterns of reactions to stimuli, is presumed to be genetically determined to 40–60% and has been shown to remain comparatively stable over time (Heath, Cloninger, & Martin, 1994; Zwir et al., 2018a, 2018b). Cloninger has also proposed associations between the temperament dimensions and the monoaminergic systems (Novelty Seeking and dopamine, Harm Avoidance and serotonin, Reward Dependence and norepinephrine) (Cloninger, 1986). The temperament Harm Avoidance is associated with passive avoidance; individuals high in this dimension are fearful, pessimistic, shy and easily fatigued. Novelty Seeking is associated with incentive activation of behaviours, suggesting that those high in this dimension are exploratory, impulsive and monotony avoidant. Social attachment is a core feature of Reward Dependence, expressed in behaviours such as sentimentality, social attachment and dependence on others' approval. Persistence, finally, is the tendency to persevere despite frustration and fatigue.

Character is thought to reflect degree of maturity in the personality (based on conceptual learning) in relation to self (Self-directedness), to others (Cooperativeness) and to a universal wholeness (Self-transcendence), reflecting individual differences in values, goals and self-conscious representations of emotions (Cloninger et al., 1993). Self-directedness refers to the ability to control oneself, to regulate behaviour in accordance with goals and values, and to be self-sufficient and self-acceptant

(on a metacognitive level). Cooperativeness captures individual differences in being accepting, tolerant, helpful and empathic towards other people and understanding relations and ethical principles on the metacognitive level. Self-transcendence refers to individual differences in self-forgetfulness, spirituality and transpersonal identification and abilities that involve metacognitive insights into the self's relation to a higher or larger whole that gives meaning to one's existence. The sum of the scores for Self-directedness and Cooperativeness forms a measure of character maturity that predicts the risk of having a personality disorder, while the type of disorder is determined by the temperaments configuration, just as certain temperament configurations are linked to specific DSM Axis II personality disorders (Svrakic, Whitehead, Przybeck, & Cloninger, 1993).

These seven personality dimensions are assessed in the self-rating questionnaire Temperament and Character Inventory (TCI), of which the current version has 259 questions rated on a five-point Likert scale (Garcia, Lester, Cloninger, & Cloninger, 2017). The TCI has been validated on normal populations in a large number of countries, including Sweden (Brandstrom et al., 1998). Since it is designed to cover all kinds of personality constellations, it has been widely studied in relation to almost all types of adulthood psychopathology (e.g. psychoses (Fresan et al., 2015), mood disorders (Hansenne et al., 1999) and substance-related disorders (Gutierrez, Sangorrin, Martin-Santos, Torres, & Torrens, 2002)).

Childhood-Onset Neurodevelopmental Disorders: Autism Spectrum Disorders (ASD) and ADHD

Aberrant development of cognition, motor coordination and social communication will result in at least 6% of all children meeting the criteria for one or more neurodevelopmental disorders before age 6 years (Fernell & Gillberg, 2010), and at least 10% of children under 18 years of age will be diagnosed with one or more such disorders (12% of boys, 8% of girls) (Gillberg, 2010). Autism spectrum disorder (ASD, in DSM-5) is one of these diagnoses, previously referred to as pervasive developmental disorders (PDD) in DSM-IV (including autistic syndrome and Asperger syndrome), while various forms of attention-deficit disorders with hyperactivity and impulsivity such as ADHD are another. These conditions are defined through behavioural reactions to stimuli, similar to adult temperament dimensions, but are thought to be related to neurodevelopment based on associations with (a) lower or uneven results on neurocognitive tests, thought to express extremes in neurocognitive abilities (Matsuura et al., 2014), (b) strong heritabilities (Homberg et al., 2016) and (c) abnormal motor functions (Spittle, FitzGerald, Mentiplay, Williams, & Licari, 2018); reflexes (Kuiper et al., 2018); sensory processing aberrations (Little, Dean, Tomchek, & Dunn, 2018); outright symptoms of brain disorder, such as epilepsy (Gillberg, Lundstrom, Fernell, Nilsson, & Neville, 2017); and minor physical anomalies (Manouilenko, Eriksson, Humble, & Bejerot, 2014).

There is a link between these conditions and learning disabilities, but by definition, they exist on all levels of IQ, from clear mental retardation to very high IQ. This paper does not address the question of personality in severe forms of learning disabilities (corresponding to intellectual disability), as this is a highly specific field of research that calls for systematic studies to a completely different degree than what has been done up until today. Very few studies have really aimed at mapping personality traits in representative, large groups of developmentally charged persons. Personality disorders are generally not diagnosed in combination with intellectual disability. Furthermore, in groups of persons with a shared aetiology, commonalities, rather than variation and individuality, in behaviour and functioning ("behavioural phenotypes") have been described, which has given rise to typologies that tend towards the stereotypic (e.g. persons with Down syndrome who are often assumed to all be happy and outgoing, which is far from the truth).

Neurodevelopmental disorders overlap frequently with each other, as with other child psychiatric disorders, especially with affective and anxiety disorders (Davidsson et al., 2017; Shephard et al., 2018), eating disorders (Rastam et al., 2013; Westwood & Tchanturia, 2017) and physical disorders (Alabaf et al., 2019; Taljemark, Rastam, Lichtenstein, Anckarsater, & Kerekes, 2017).

The DSM definitions for ASD are organized around three behavioural domains, corresponding to the three areas in Wing's triad, describing problems with social interaction, communication and imagination (stereotyped and inflexible interests and activities) (Wing, 1981). In the DSM-5, the three symptom domains are condensed into two domains (social–communication and repetitive behaviours and problems with sensory processing) (American Psychiatric Association, 2013). The essential core of these social skills problems could be described as impairments in reciprocal communication and interaction in combination with restricted and repetitive patterns of behaviour. There is a wide variation in severity between affected individuals, ranging from rather mild problems more or less restricted to one of these domains to those with severe problems in all domains of social skills.

ADHD is characterized by persistent problems with attention and regulation of activity and impulses. Attentional difficulties are mainly manifested as being inattentive, easily distracted and disorganized, while problems in the area of regulating one's activity are manifested as hyperactivity and impulsivity with an inability to adapt and control impulses in accordance with the situational demands. Symptoms of ADHD vary widely from individual to individual, but three subtypes are described, that is, the primarily inattentive type, the primarily hyperactive/impulsive type and the combined type, those with problems within both domains.

During the last 50 years or so, empirical findings have led to an emerging consensus that neurodevelopmental disorders are not discrete, but rather describe the lowermost extremes of normally distributed abilities, blending into "normality" over an intermediary zone referred to as "broader phenotypes" or "shadow syndromes" (Rydell, Lundstrom, Gillberg, Lichtenstein, & Larsson, 2018; Whitehouse et al., 2017).

Associations Between Neurodevelopmental Disorders and Personality Traits According to Cloninger's Temperament and Character Model

Temperament and Character Profiles in Children and Adolescents with ADHD

Several studies have investigated Cloninger's temperament and character dimensions in relation to ADHD in children and adolescents, covering both clinical and community samples. A recurring, quite stable pattern of high scores in the temperament dimension Novelty Seeking and low scores in the character dimensions Self-directedness and Cooperativeness compared to normal controls has emerged in a majority of these studies. (See Table 1 for a summary of studies on TCI in children with ADHD.) These dimensions have also repeatedly been found to correlate in the range from modest to strong with measures of ADHD, that is, positively for Novelty Seeking and negatively for Self-directedness and Cooperativeness. This pattern seems to be valid in younger children as well as in adolescents, regardless of whether they are clinically recruited or from the community and whether ADHD is diagnosed in accordance with the DSM system or measured by different self-rated or parent-rated scales. It has even been seen in children with subthreshold ADHD, indicating that this pattern is closely related to the neurodevelopmental deficiencies or diathesis that give rise to the clinical picture of ADHD (Cho et al., 2009). Furthermore, the validity of this pattern is also supported by the fact that it is found cross-culturally, reported in data from, at least, Asia, North America and Europe.

A somewhat inconsistent pattern has emerged with regard to the three temperament dimensions of Harm Avoidance, Reward Dependence and Persistence. They have, at times, been low compared to normal controls or have been found to correlate negatively with measures of ADHD. Low Persistence is the dimension that has most often been associated with ADHD or ADHD symptoms, even if not in all identified studies (see Table 1). It is also the only temperament dimension beside Novelty Seeking where there is some evidence for a genetic association with the two problem areas of ADHD (i.e. inattention and hyperactivity/impulsivity) (Merwood, Asherson, & Larsson, 2013). Results concerning Harm Avoidance and Reward Dependence appear less stable across studies. Only among younger children (thus, by parent-rated scales) have low Harm Avoidance and/or Reward Dependence been associated with ADHD. To summarize, the results of the identified studies support a temperament profile of high Novelty Seeking and low Harm Avoidance in combination with low scores in the character dimensions of Self-directedness and Cooperativeness as a childhood personality profile connected to ADHD.

Table 1 Main features and results of studies analysing ADHD and personality dimensions according to Cloninger's model of temperament and character in children and adolescents

Neurodevelopmental disorder	Author/s and year	Methodology	Sample	Assessment instrument/s	Results
ADHD in children/ adolescents, original research	Tillman et al. (2003)	Group comparison	$N_1 = 101$ children with a prepubertal and early adolescent bipolar disorder phenotype (PEA-BP) $N_2 = 68$ children with ADHD $N_3 = 94$ normal controls	All diagnoses were assigned in accordance with DSM-IV The Washington University in St. Louis Kiddie Schedule for Affective Disorders and Schizophrenia (WASH-U-KSADS) The Children's Global Assessment Scale (CGAS) The Pubertal Status Questionnaire The self-rated and parent-rated versions of the Junior Temperament and Character Inventory (JTCI)	Parent-reported JTCI data for children with ADHD revealed that they had higher scores on Novelty Seeking, and lower on Reward Dependence, Persistence, Self-directedness and Cooperativeness than normal control cases. When they were compared to parent ratings for children with PEA-BP, the only difference found was a significantly lower score on Cooperativeness in the latter group. Child-reported JTCI data showed no difference between either the ADHD group versus normal controls or the ADHD group versus the PEA-BP group.

	Yoo et al. (2006)	Cross-sectional	N_{Tot} = 516 elementary school children n_1 = 52 children with ADHD n_2 = 52 age- and sex-matched non-ADHD control children	The ADHD Rating Scale-IV – Parent and Teacher Version (ARS-IV, 0.77 ≤ α by age ≤ 0.89) The Korean version of the Child Behavior Checklist (CBCL, 0.61 ≤ α by age ≤ 0.86) The Korean Junior Temperament and Character Inventory (JTCI, α for temperament dimensions ranges from 0.48 to 0.80 and for character dimensions from 0.63 to 0.69)	Novelty Seeking correlated positively with inattention and hyperactivity/impulsivity symptoms in both parent and child ratings. Persistence, Self-directedness and Cooperativeness correlated negatively with these symptoms. Children with ADHD had significantly higher scores of Novelty Seeking and lower scores of Self-directedness and Cooperativeness compared with those in the control group.
	Cho et al. (2008)	Group comparison	N_1 = 51 children with ADHD N_2 = 51 age- and sex-matched healthy children	Diagnostics according to DSM-IV criteria Korean version of Junior Temperament and Character Inventory (JTCI), both self-rated and parent-rated versions DuPaul's ADHD Rating Scale (ARS-IV)	Both self-rated and parent-rated scores of the temperament dimension Novelty Seeking were significantly higher in children with ADHD, while they were significantly lower for the character dimension Self-directedness. Low Self-directedness scores were the only TCI dimension that significantly predicted total scores in ARS-IV, indicating more severe symptoms.

(continued)

Table 1 (continued)

Neurodevelopmental disorder	Author/s and year	Methodology	Sample	Assessment instrument/s	Results
	Cho et al. (2009)	Cross-sectional	N_{Tot} = 2493 elementary school children n_1 = 97 children with full syndrome ADHD n_2 = 148 children with subthreshold ADHD n_3 = 185 children randomly selected from those who did not meet criteria for full syndrome or subthreshold disorder	DSM-IV psychiatric disorders were assessed by the Diagnostic interview schedule for children version-IV (DISC-IV) The Korean version of the Child Behavior Checklist (CBCL) The Korean version of the Junior Temperament and Character Inventory (JTCI)	The group of subthreshold ADHD did not differ from the group of full syndrome ADHD in any of the JTCI personality dimensions, while the former showed higher Novelty Seeking and lower Persistence and Self-directedness than were found in the control group.

	Purper-Ouakil et al. (2010)	Group comparison with follow-up	$N_1 = 95$ boys with ADHD $N_2 = 87$ controls	Parents were interviewed by the use of K-SADS lifetime version The French version of the ADHD Rating Scale-IV, clinician rated (ADHD-RS, $\alpha = 0.70$) The French parent-rated Junior Temperament and Character Inventory (JTCI, $0.59 \leq \alpha \leq 0.79$) The French version of the Child Behavior Checklist (CBCL) The Clinical Global Impression-Severity scale (CGI-S)	Boys with ADHD showed higher scores for Novelty Seeking and lower scores for Reward Dependence and Persistence compared to controls, while they showed significantly lower scores for Self-directedness and Cooperativeness. Externalizing symptoms were positively correlated with Novelty Seeking and negatively with Persistence, Self-directedness and Cooperativeness in controls. Likewise, the attention problem subscore was negatively correlated with Persistence, Self-directedness and Cooperativeness, and positively with Novelty Seeking. Total ADHD-RS at baseline was significantly positively correlated with Novelty Seeking and negatively with Self-directedness, Cooperativeness and Self-transcendence. Finally, the only treatment variable that was related to any temperament and character dimension was in remission, which was significantly predicted by high Persistence and low Self-directedness.

(continued)

Table 1 (continued)

Neurodevelopmental disorder	Author/s and year	Methodology	Sample	Assessment instrument/s	Results
	Merwood, Asherson, and Larsson (2013)	Twin methodology	N_{Tot} = 868 Swedish twin pairs n_1 = 140 monozygotic males n_2 = 214 monozygotic females n_3 = 83 dizygotic males n_4 = 145 dizygotic females n_5 = 286 dizygotic opposite-sex pairs	Self-rated ADHD symptoms according to 18 DSM-IV-based items Subscale of inattention (IA: 9 items, α = 0.79) Subscale of hyperactivity/impulsivity (HI: 9 items, α = 0.76) The Temperament and Character Inventory, short version (TCI), subscales of Novelty Seeking, Harm Avoidance, Reward Dependence and Persistence	Novelty Seeking correlated positively with both IA and HI. Harm Avoidance correlated positively with IA. Persistence correlated negatively with IA and positively with HI. Novelty Seeking was genetically associated with both IA and HI, while Harm Avoidance was genetically associated with only IA. Finally, the study also found some evidence for that Persistence was genetically associated with both IA and HI.
	Donfrancesco et al. (2015)	Group comparison	N_1 = 146 children with ADHD N_2 = 223 age- and gender-matched control children	A clinically established diagnosis of ADHD The Italian parent version of Junior Temperament and Character Inventory The Italian version of The Strengths and Difficulties Questionnaire	A MANOVA showed that ADHD children with regard to temperament dimensions displayed higher scores for Novelty Seeking and lower scores for Persistence, and with regard to character dimensions lower scores for Self-directedness and Cooperativeness. In addition, Novelty Seeking and Persistence emerged as significant predictors of presence of ADHD due to a logistic regression analysis.

	Melegari et al. (2015)	Cross-sectional	N_{Tot} = 120 parent-rated children n_1 = 30 children with ADHD n_2 = 30 children with oppositional deviant disorder (ODD) n_3 = 30 children with generalized anxiety disorder or social phobia n_4 = 30 control children	The Child Behavior Checklist (CBCL) The Preschool Age Psychiatric Assessment PAPA) The Preschool Temperament and Character Inventory (PsTCI)	ADHD children showed lower scores in Reward Dependence compared to controls. They also showed significantly lower scores in Harm Avoidance compared to ODD, while they showed higher scores in Novelty Seeking compared to controls and the group with anxiety disorders. A discriminant analysis correctly classified 80% of ADHD children, where only temperament dimensions contributed significantly. ADHD children were according to this analysis characterized by high Novelty Seeking and low Persistence.

(continued)

Table 1 (continued)

Neurodevelopmental disorder	Author/s and year	Methodology	Sample	Assessment instrument/s	Results
	Peyre, Speranza, Cortese, Wohl, and Purper-Ouakil (2015)	Cross-sectional with follow-up of sub-sample	N_{Tot} = 173 outpatient children with ADHD n_1 = 136 reassessed children after optimal adjustment of methylphenidate (≥15 days and ≤ 3 months)	Parents were interviewed by the use of K-SADS lifetime version The French version of the Child Behavior Checklist (CBCL) The Clinical Global Impression-Severity scale (CGI-S) The French version of the ADHD Rating Scale-IV (clinician rated) (ADHD-RS) The French parent-rated Emotionality Activity Sociability scale (EAS) The French parent-rated Junior Temperament and Character Inventory (JTCI) Neuropsychological testing by the Trail Making Test, the Stroop Color and Word Test, and the Conner's Continuous Performance Test (CPT)	Low Self-directedness together with clinical severity due to ADHD-RS, presence of internalized disorders and high EAS were independently associated with CBCL Dysregulation Profile. Harm Avoidance and Persistence were significantly associated with treatment response.

	Yoo, Ha, Yu, Park, and Ryu (2016)	Cross-sectional	N_{Tot} = 694 pre-school children n_1 = 74 pre-school children with ADHD n_2 = 74 randomly selected age- and sex-matched controls	The Korean version of the DuPaul's ADHD rating scale, parent version (ARS-IV, α = 0.88), where the upper 10th percentile was chosen as criteria for occurrence of ADHD The Korean version of the pre-school Temperament and Character Inventory (psTCI, α for temperament scales range from 0.62 to 0.78 and for the character scales from 0.62 to 0.77)	Novelty Seeking correlated positively with ARS-IV total score, and symptoms of inattention and hyperactivity. Persistence and Self-directedness correlated negatively with total score, and inattention and hyperactivity symptoms. Harm Avoidance correlated positively with total score and inattention symptoms. Children with ADHD showed significantly higher scores of Novelty Seeking, and lower of Persistence and Cooperativeness compared to the control group.

Temperament and Character Profiles in Adults with ADHD

Temperament and character profiles related to ADHD have not only been studied in children and adolescents but also in several adult clinical and community samples, with and without formal ADHD diagnostics. Broadly, the same profile as that seen in children has recurred in adults, regardless of whether clinically diagnosed or general population samples. (See Table 2 for a summary of research on TCI in relation to ADHD in adult samples.) Thus, the temperament dimension of Novelty Seeking has repeatedly appeared as significantly higher compared to controls, while the character dimensions of Self-directedness and Cooperativeness have been lower. Judging from findings seen in studies on adult samples, this profile seems even more stable with a larger effect size than in the child studies, and documented both in individuals with childhood-onset, persistent adulthood ADHD or childhood-only ADHD, and in general population samples. Harm Avoidance, in contrast, tends to be increased in adult ADHD, while it was lower in childhood studies. Low Reward Dependence and Persistence have also been found in a few studies (e.g.He, Antshel, Biederman, & Faraone, 2015; Instanes, Haavik, & Halmoy, 2016; Park, Suh, Lee, & Lee, 2016).

A further unresolved question is any possible sex differences in associations of temperament and character profiles with ADHD. Studies touching upon this are almost non-existent, but there is one where females with ADHD were found to have higher raw scores on Harm Avoidance, Reward Dependence, Cooperativeness and Self-transcendence than males (Salgado et al., 2009). The difference seen here between genders might be one of the reasons why there have been contradictory findings with regard to Harm Avoidance and Reward Dependence, as the gender ratios have varied between different studies with no control for this variation or no compensation for uneven rates of males versus females.

The variations between study settings lend weight to the validity of the profile of high Novelty Seeking and Harm Avoidance and low character scores of Self-directedness and Cooperativeness as related to ADHD. Study samples exhibiting this profile have been recruited not only clinically among those formally diagnosed with ADHD but also among young adults (e.g. students) and from the general population covering different parts of the world such as Asia, the Middle East, Europe and Australia. Furthermore, different measures reflecting not only a diagnosis of ADHD but also symptoms of inattention as well as hyperactivity and impulsivity have been used in these studies, and the number of included individuals exceeds 200 in about half of all studies. The recurrence of this profile in varying cross-cultural samples and in relation to different measures is an argument supporting a genuine relationship between these personality traits and the corresponding neurodevelopmental problem constellations. This profile is in terms of temperament characterized by an energetic, easily aroused and impulsive disposition (with rather less anxiety and fear of punishment in childhood, which in adulthood has changed to a more anxious and asthenic temperament) in combination with a self-conceptualization far more immature and inconsistent than what normally is the case.

Table 2 Main features and results of studies analysing associations between ADHD and personality dimensions according to Cloninger's model of temperament and character in adults

Neurodevelopmental disorder	Author/s and year	Methodology	Sample	Assessment instrument/s	Results
ADHD in adults, original research	Lynn et al. (2005)	A latent variable modelling study	N_{Tot} = 171 parents with an affected sibling pair with ADHD n_1 = 56 with a lifetime history of ADHD n_2 = 28 of those in n_1 with persistent ADHD	The Schedule for Affective Disorders and Schizophrenia – Lifetime Version Modified for the Study of Anxiety Disorders The behavioural disorders section of the Schedule for Affective Disorders and Schizophrenia for School-Age Children – Present and Lifetime Version The Temperament and Character Inventory (TCI) Genotyping for polymorphic region in the DRD4 gene consisting of a variable number of 48-bp repeats was scored by polymerase chain reaction, where genotypes were coded 0 or 1 reflecting occurrence or not of the 7-repeat variant.	By the use of confirmatory factor models, the contribution of factors underlying temperament and character to lifetime ADHD diagnosis or symptom variability was tested. At best, the temperament and character inventory factors explained 49% of the variance in ADHD diagnosis. Novelty Seeking was the single TCI factor that contributed the most, accounting for 26% of variance in a lifetime ADHD diagnosis. The DRD4 gene variant independently predicted ADHD, but the amount of explained variance was small (5%). However, this gene variant did not predict Novelty Seeking.

(continued)

Table 2 (continued)

Neurodevelopmental disorder	Author/s and year	Methodology	Sample	Assessment instrument/s	Results
	Salgado et al. (2009)	Cross-sectional with group comparison	N_{Tot} = 296 adults with ADHD n_1 = 128 inattentive subtype of ADHD n2 = 168 combined subtype of ADHD	The Portuguese version of the Schedule for Affective Disorders and Schizophrenia for School-Aged Children, Epidemiologic Version (K-SADS-E) The Mini International Neuropsychiatric Interview, sections of conduct and antisocial personality disorder (MINI) The Structured Clinical Interview for DSM-IV-R, other lifetime psychiatric disorders The Brazilian Portuguese version of the self-administered SNAP-IV rating scale The Portuguese version of the Temperament and Character Inventory (TCI)	Individuals belonging to the combined ADHD subtype showed higher Novelty Seeking and lower Cooperativeness when compared to inattentive subtype individuals. Females showed higher Harm Avoidance, Reward Dependence, Cooperativeness, and Self-transcendence compared to males. Regression analyses revealed that SNAP-IV scores of inattention were negatively associated with Self-directedness and positively with Harm Avoidance. Scores on the hyperactivity/impulsivity scale were positively associated with Novelty Seeking, and negatively with Persistence.

	Müller et al. (2010)	Cross-sectional	$N = 110$ adults with ADHD	A diagnosis of ADHD according to DSM-IV The Wender Utah Rating Scale The Brown Attention Deficit Disorder Scale The Conners' Adult ADHD Rating Scale Adverse life events were assessed by a structured interview consisting of 61 items A genetic analysis covering common polymorphisms in nine important candidate genes (SLC6A3, DBH, DRD4, DRD5, HTR2A, CHRNA7, BDNF, PRKG1 and TAAR9)	Harm Avoidance and Novelty Seeking scores significantly contributed to the differentiation of ADHD subtype. The highest scores for the former were found in the inattentive subtype, while this group also showed significantly lower scores for the latter compared to the hyperactive subtype as well as the combined group. Overall, ADHD symptom severity was significantly positively correlated with Harm Avoidance and negatively with Self-directedness.

(continued)

Table 2 (continued)

Neurodevelopmental disorder	Author/s and year	Methodology	Sample	Assessment instrument/s	Results
	Gomez, Woodworth, Waugh, and Corr (2012)	Cross-sectional	$N = 231$ adults from the general population	The Temperament and Character Inventory 125-items version (TCI-125) Current Symptom Scale (CSS, corresponding to DSM-IV symptoms of ADHD and ODD)	ADHD correlated significantly and positively with Novelty Seeking and Harm Avoidance, and negatively with Reward Dependence, Self-directedness, and Cooperativeness. Inattention correlated positively with Harm Avoidance, and negatively with Reward Dependence, Self-directedness, and Cooperativeness. Hyperactivity/impulsivity showed a positive significant correlation with Novelty Seeking and Harm Avoidance, and a negative correlation with Reward Dependence, Self-directedness, and Cooperativeness. According to regression analyses, ADHD was predicted significantly and negatively by Self-directedness, inattention positively by Harm Avoidance and negatively by Self-directedness, while hyperactivity/impulsivity was predicted significantly and positively by Persistence.
ADHD in adults, original research	Akbas, Kilic, Zahmacioglu, Atalay, and Goktuna (2015)	Cross-sectional with group comparison	$N = 122$ university students	Turgay's Adult ADHD scale The Turkish version of the Temperament and Character Inventory (TCI)	Students with moderate ADHD symptoms showed statistically significantly lower scores in Self-directedness and Cooperativeness compared to those with mild or no symptoms of ADHD. A positive significant correlation was found for Novelty Seeking with hyperactivity/impulsivity and total ADHD scores, and a negative significant correlation was found for both Self-directedness and Cooperativeness with attention deficit, hyperactivity/impulsivity and total ADHD scores. Finally, a regression analysis showed that total ADHD scores significantly predicted Self-directedness and Cooperativeness scores.

	He, Antshel, Biederman, and Faraone (2015)	Group comparison	N_1 = 206 adults with ADHD, consisting of 185 clinically recruited and 21 community-recruited individuals N_2 = 123 non-ADHD adults from the greater Boston area	Diagnostics according to the Structured Clinical Interview for DSM-IV (SCID-I) Functional outcomes were addressed in a structured interview covering domains such as academics, motor vehicle operation and legal/criminal activity Quality of Life Enjoyment and Satisfaction Questionnaire, short form (Q-LES-Q-SF) Social Adjustment Scale–Self Report (SAS-SR) Family Environment Scale (FES) The Temperament and Character Inventory (TCI) A binary measure of executive functioning based on Arithmetic and Digit Span from the WAIS-III, the Wisconsin Card Sorting Test, the Stroop Color and Word Test, the California Verbal Learning Test, and the Seidman auditory working memory continuous performance test	The ADHD group showed significantly higher scores on Novelty Seeking and Harm Avoidance, and significantly lower scores on Reward Dependence, Persistence, Self-directedness, and Cooperativeness. Novelty Seeking predicted the total number of ADHD symptoms in the ADHD group, that is, the higher the scores, the more symptoms. Cooperativeness and Novelty Seeking predicted lifetime incidence of ever being arrested after controlling for ADHD symptoms, executive functioning deficits and psychiatric comorbidities, such that lower levels of Cooperativeness and higher of Novelty Seeking were associated with ever being arrested in participants with ADHD. Low Self-directedness predicted more impaired work and primary relationship functioning in the ADHD sample, while low scores of Harm Avoidance predicted more impaired primary relationship functioning. A more impaired family functioning in the ADHD sample was predicted by lower scores on Cooperativeness. Self-directedness emerged as the strongest predictor related to quality of life outcome variables in the ADHD sample, that is, higher Self-directedness scores were associated with higher values on the quality of life variables. Overall, among the TCI dimensions associated with functional outcome in the ADHD sample, Self-directedness emerged as the one with the strongest significant association when controlling for ADHD symptoms, executive function deficits and current psychiatric comorbidities.

(continued)

Table 2 (continued)

Neurodevelopmental disorder	Author/s and year	Methodology	Sample	Assessment instrument/s	Results
	Instanes, Haavik, and Halmoy (2016)	Group comparison	$N_1 = 66$ adult ADHD patients $N_2 = 69$ adult controls	The Norwegian version of the Adult ADHD Self-Report Scale (ASRS) The Norwegian version of the Temperament and Character Inventory (TCI) The Mini International Neuropsychiatric Plus Version 5.0.0 (MINI Plus)	The ADHD group showed significantly higher scores on Harm Avoidance, Novelty Seeking and Self-transcendence, and significantly lower scores on Reward Dependence, Self-directedness, and Cooperativeness in comparison to the control group. However, when controlling for lifetime anxiety the significant association between Harm Avoidance and ADHD ceased. Similarly, the association between high Novelty Seeking, high Self-transcendence, low Self-directedness, and low Cooperativeness and ADHD disappeared when controlling for comorbidity, while the association with low Reward Dependence remained.
	Park, Suh, Lee, and Lee (2016)	Group comparison	$N_{Tot} = 2917$ Korean college students $n_1 = 140$ individuals in Inattention symptom subgroupz (IA) $n_2 = 61$ individuals in hyperactivity/impulsivity and combined symptom subgroup (HI) $n_3 = 2716$ controls	The Korean version of the Temperament and Character Inventory – Revised Short Version (TCI-RS) The Attention Deficit/Hyperactivity Disorder Self-Rated Scale (ASRS)	Novelty Seeking and Harm Avoidance were significantly higher in the two groups of IA and HI compared to controls. Persistence was significantly lower in the two symptom subgroups compared to controls. Scores of Self-directedness and Cooperativeness were significantly lower for the IA and HI groups compared to controls. Self-transcendence was significantly higher in the HI group than what was found for the IA group and controls. According to multinomial logistic regression, the IA group was associated with high Novelty Seeking and low Self-directedness in relation to controls, while the HI group was associated with high Novelty Seeking and Self-transcendence and low Cooperativeness in relation to controls.

	Perroud et al. (2016)	Group comparison	N_1 = 119 outpatients with adult ADHD N_2 = 403 adult controls from the general population	In N_1, a semi-structured interview assessing childhood as well as adult ADHD based on DSM-IV criteria was conducted together with the Diagnostic Interview for Genetic Studies (DIGS). They also completed the Wender Utah Rating Scale (WURS) In N_2, 191 subjects were screened for DSM-IV Axis I disorders by the use of the Mini International Neuropsychiatric Interview (MINI) All subjects in both groups completed the Temperament and Character Inventory (TCI, with α values ranging from 0.89 to 0.93)	The ADHD group showed significantly higher scores of Novelty Seeking, Harm Avoidance, and Self-transcendence, and lower scores of Self-directedness and Cooperativeness, in comparison to the control group. The predominantly inattentive ADHD type was associated with lower Novelty Seeking and higher Harm Avoidance scores in comparison to the ADHD combined and hyperactive/impulsive subtype. Symptoms of inattention correlated positively with Harm Avoidance and negatively with Self-directedness, while hyperactive symptoms correlated positively with Novelty Seeking and Self-transcendence. Severity of ADHD in childhood correlated negatively with Self-directedness and Cooperativeness. Severity of current ADHD symptoms correlated positively with Novelty Seeking, Reward Dependence, and Self Transcendence, and negatively with Self-directedness.

(continued)

Table 2 (continued)

Neurodevelopmental disorder	Author/s and year	Methodology	Sample	Assessment instrument/s	Results
	Kim et al. (2017)	Group comparisons	N_{Tot} = 429 university students n_1 = 53 persistent adult ADHD n_2 = 56 with only childhood ADHD n_3 = 320 healthy controls	The Korean version of the Adult Attention/Hyperactivity Disorder Scale (AADHD, α = 0.82) The Korean version of the Wender-Utah Attention Deficit/Hyperactivity Disorder Rating Scale (WU-ADHD, α = 0.92) The Korean version of the Barratt Impulsiveness Scale (BIS, α = 0.91) The Korean Young Internet Addiction Scale (YIAS, α = 0.93) The Korean version of the Beck Depression Inventory-II (BDI-II, α = 0.90) The Korean version of the Beck Anxiety Inventory (BAI, α = 0.91) The Korean version of the Rosenberg Self-Esteem Scale (RES, α = 0.93) The Korean version of the Lubben Social Network Scale (LSNS) The Korean version of the Temperament and Character Inventory (TCI)	Novelty Seeking scores were significantly higher in those with persistent ADHD compared to healthy controls. Scores on Harm Avoidance were also higher for this group compared to both those with only childhood ADHD and healthy controls. Self-directedness scores were significantly lower in the adult persistent ADHD group compared to both healthy controls and childhood ADHD only. Cooperativeness scores were significantly lower in the group of persistent adult ADHD compared to healthy controls. Scores on Self-transcendence, finally, were significantly lower in healthy controls compared to the two ADHD groups, for which no significant differences were seen. A binary logistic regression analysis for ADHD symptoms showed that low Self-directedness was a predictor for the continuation of these symptoms into adulthood.

Cloninger's temperament and character dimensions have also been studied in relation to different measures of outcome in adults with ADHD. According to these findings, the character dimension Self-directedness emerged as a strong predictor of functional outcome (e.g. impaired work, primary relationship and quality of life) in individuals with ADHD (e.g. He et al., 2015). Low Self-directedness has also been found to predict ADHD symptom severity and continuation of symptoms from childhood into adulthood. Among the temperament dimensions, Novelty Seeking arose as a factor strongly related to a diagnosis of ADHD. It explained in a study as much as 26% of the variance in lifetime occurrence of an ADHD diagnosis. Harm Avoidance is another temperament for which data supports an association with outcome, especially in the form of ADHD symptom severity.

Temperament and Character Profiles in Individuals with Autism Spectrum Disorder (ASD)

The number of studies investigating the relations between Cloninger's temperament and character dimensions and ASD are much fewer than in the case of ADHD. Somewhat surprisingly, we could not identify any study that focused on ASD in children or adolescents, despite it being a disorder with childhood onset. However, a handful of studies have examined these dimensions in adult samples, with results supporting a temperament profile of high Harm Avoidance and low Novelty Seeking and Reward Dependence, in combination with an immature character with low Self-directedness and Cooperativeness. (See Table 3 for a summary of research on TCI in relation to ASD in adult samples.) This profile has without exception been found in every sample, regardless of whether participants were clinically recruited or drawn from or reflected the general population. It has, thus, been seen in those with a diagnosis on the ASD spectrum and in parents to children with ASD as well as in a large sample of students, either in comparison to normal controls or in relation to symptoms of ASD or autistic-like traits. One study also compared genders without finding any differences, supporting the notion that gender has no substantial effect on the associations between personality dimensions and ASD (Kunihira, Senju, Dairoku, Wakabayashi, & Hasegawa, 2006).

There are, even if all identified studies exposed signs of the same personality profile in individuals with ASD, some reasons why its validity should be taken with some caution. The variety of samples covering not only clinical and non-clinical populations but also such different sociocultural regions as Asia, the Middle East and Europe speaks in favour of the validity of this profile, together with some reports of shared genetic effects behind the phenotypic correlations between ASD symptoms and temperament and character dimensions (Picardi et al., 2015). However, the fact that almost every study used the same instrument to measure symptoms of ASD, that is, the Autism Spectrum Quotient (AQ), is a limitation. A larger number of different instruments measuring ASD might have led to a more varied profile

Table 3 Main features and results of studies analysing associations between autism spectrum disorder (ASD) and personality dimensions according to Cloninger's model of temperament and character in children and adults

Neurodevelopmental disorder	Author/s and year	Methodology	Sample	Assessment instrument/s	Results
Autism spectrum disorder in adults, original research	Soderstrom, Rastam, and Gillberg (2002)	Cross-sectional	*N* = 31 adult outpatients with Asperger syndrome	The Swedish version of the Temperament and Character Inventory	The Asperger syndrome group differed significantly with regard to temperament dimensions from normative data in the following way: high Harm Avoidance (HA) and low Novelty Seeking (NS) and Reward Dependence (RD). However, when classified according to Cloninger's temperament type, quite a wide variation emerged beside the "obsessional" type defined by low NS, high HA and low RD. This group differed also with regard to character in the following way: significantly lower Self-directedness (SD) and Cooperativeness (C), and higher Self-transcendence. The combined result on SD and C is presumed to reflect character maturity, here indicating that an immature character characterized 27 of those with Asperger syndrome.
	Kunihira et al. (2006)	Cross-sectional	*N* = 1364 Japanese university students	The Japanese version of the Autism Spectrum Quotient (AQ) A short 60-item version covering only the temperament dimensions of the Temperament and Character Inventory The Japanese version of the Self-Rating Depression Scale (SDS) The Japanese version of the State-Trait Anxiety Inventory (STAI) Questionnaire About Bullying Experiences	AQ score was negatively and significantly correlated with Novelty Seeking and Reward Dependence, and positively correlated with Harm Avoidance. When divided by gender, similar results occurred, indicating that gender has no substantial effect on the relation between AQ scores and temperament as measured by items from the Temperament and Character Inventory. Further on, structural equation modelling was used to depict the relations between AQ and personality traits. The model with the best goodness-of-fit measures indicated that AQ had some effect in the following direction: low Novelty Seeking and Reward Dependence, high Harm Avoidance, high depression and anxiety and high tendency to experience being bullied.

	Anckarsater et al. (2012)	Longitudinal group comparison follow-up study	$N_1 = 51$ subjects with adolescent-onset anorexia nervosa, fourth wave of data $N_2 = 51$ age-, gender- and education-matched healthy controls, fourth wave of data	Among a multitude of instruments, the following are of importance here: the Structured Clinical Interview for DSM-IV Axis I (SCID-I), the Cluster C module of the SCID-II, the Asperger Syndrome Diagnostic Interview (ASDI), the Swedish version of the Autism Spectrum Quotient (AQ), the Swedish version of the Temperament and Character Inventory (TCI)	Group comparisons showed that those with anorexia nervosa plus autism spectrum disorder had significantly lower Novelty Seeking, Reward Dependence and Self-directedness, and significantly higher Harm Avoidance in comparison to healthy controls.
	Kadak, Demirel, Gokalp, Erdogdu, and Demirel, (2015)	Cross-sectional	$N = 70$ parents to children with autism spectrum disorder	The Turkish version of the Autism Spectrum Quotient (AQ) The Turkish version of the Temperament and Character Inventory (TCI)	Harm Avoidance correlated positively with score on AQ, and Self-directedness and Cooperativeness negatively. A stepwise regression analysis showed that Self-directedness together with education predicted autistic traits according to AQ, explaining 35% of the variance.

(continued)

Table 3 (continued)

Neurodevelopmental disorder	Author/s and year	Methodology	Sample	Assessment instrument/s	Results
	Picardi et al. (2015)	Twin methodology	N_{Tot} = 266 adult twin pairs from the Italian Twin Register N_1 = 160 monozygotic twin pairs (MZ; 45 male–male, 115 female–female) N_2 = 106 dizygotic twin pairs (DZ; 11 male–male, 49 female–female, 46 unlike gender pairs)	The Italian version of the Autism Spectrum Quotient (AQ, α for total score = 0.70) The 12-item version of the General Health Questionnaire (GHQ-12, α = 0.86) The 125-item version of the Temperament and Character Inventory (TCI-125)	The AQ score was correlated negatively with Novelty Seeking, Reward Dependence, Self-directedness and Cooperativeness, and positively with Harm Avoidance. Cross-twin/within-trait correlations for the TCI dimensions were generally much higher in MZ than in DZ twin pairs, indicating that additive genetic factors contributed to the individual differences in these scores. Genetic correlations between AQ and all TCI dimensions except Persistence and Self-transcendence were significant, suggesting that the sets of genes underlying the expression of autistic traits and these personality traits may overlap. The amount of shared genetic effects that were explained with regard to the phenotypic correlation between AQ and TCI scores ranged from 43% for AQ and Harm Avoidance to 73% for AQ and Cooperativeness. However, overlapping individual-specific environmental factors were also responsible for important portions of the phenotypic correlations between AQ and TCI scores, ranging from 27% for AQ and Cooperativeness to 57% for AQ and Harm Avoidance.

reflecting the huge variation in symptoms and suffering within this "spectrum" of conditions. Another aspect that does not seem to have been studied with regard to personality and ASD is whether these profiles are related to various aspects of outcome in individuals with ASD. We saw that this was the case for ADHD, supporting the intertwined character of personality traits and neurodevelopmental problems seen among individuals with ADHD. Nevertheless, it is noteworthy that low character maturity, especially in the form of low Self-directedness and Cooperativeness, has been shown to characterize a very large range of different mental disorders and was found in adult ASD, just as in all other studied conditions (Svrakic et al., 1993).

Temperament and Character Profiles in Studies Comparing ADHD and ASD

A couple of studies have also focused on investigations of temperament and character traits in individuals with ADHD and/or ASD. All of them focused on adult clinical samples, with one exception, a Swedish twin study investigating the association between temperament and character dimensions and scores of ADHD and ASD in children aged 9 and 12 years old (Kerekes et al., 2013). (See Table 4 for a summary of research on TCI in relation to mixed samples of ADHD and/or ASD.) This study found strong negative correlations between scores for ASD and ADHD and the character dimensions of Self-directedness and Cooperativeness. Among the temperament dimensions, Novelty Seeking correlated positively with ADHD scores and Harm Avoidance with ASD scores. Low character immaturity, that is, a value more than one standard deviation below the mean in Self-directedness and/or Cooperativeness, was clearly related to number of symptoms on ADHD or ASD. Finally, cross-twin, cross-trait correlations identified genetic effects behind the phenotypic associations between identified personality traits and the neurodevelopmental problems of ADHD and ASD.

The adult studies on clinical samples with ADHD and/or ASD found, when comparing only those with one of these diagnoses to normal controls, personality profiles largely identical to those in the diagnosis-specific studies presented above. This adds further support for the validity of specific temperament and character profiles in ADHD and ASD. Comparisons between these two diagnostic groups revealed higher scores of Novelty Seeking in ADHD, while higher scores in Harm Avoidance characterized ASD. Data for individuals with comorbid ADHD and ASD indicated a personality profile reflective of both ADHD and ASD, that is, high Novelty Seeking and Harm Avoidance in combination with low Self-directedness and Cooperativeness. However, it seems that those with comorbid states have an even more immature character compared to those with a single diagnosis, owing to especially low scores in Self-directedness. This is in line with the strong negative correlation between symptom severity and scores on character dimensions (i.e. Self-directedness and Cooperativeness) reported in several studies. Immature character seems, thus, to be a continuous concomitant to neurodevelopmental problems from childhood into adulthood, even if there are subgroups of diagnosed patients still scoring in the normal zone.

Table 4 Main features and results of studies analysing associations between ADHD and/or autism spectrum disorder (ASD) and personality dimensions according to Cloninger's model of temperament and character in children or adults

Neurodevelopmental disorder	Author/s and year	Methodology	Sample	Assessment instrument/s	Results
ADHD and autism spectrum disorder in children, original research	Kerekes et al. (2013)	Twin methodology	N_{Tot} = 1886 children, 9- and 12-year-olds, from the Swedish twin register n_1 = 471 children from monozygotic pairs n_2 = 752 children from same-sex dizygotic pairs n_3 = 612 children from opposite-sex dizygotic pairs n_4 = 51 children with unknown zygosity	The autism – tics, ADHD and other comorbidities inventory (A-TAC) The Swedish version of the parent-rated junior Temperament and Character Inventory (JTCI)	Strong negative correlations were found between A-TAC ADHD and autism spectrum disorder (ASD) scores and the two character dimensions Self-directedness and Cooperativeness. Score on the ADHD module correlated also positively with Novelty Seeking, while ASD score correlated positively with Harm Avoidance. Low character maturity, defined as more than one SD below the mean in Self-directedness and/or Cooperativeness, was seen in 25% of the study population. The risk of character immaturity was clearly related to number of ADHD or ASD scores on A-TAC, especially with regard to Self-directedness in children with high ASD scores. Analyses of cross-twin, cross-trait correlations showed a pattern for both ADHD and ASD where twice as strong correlations with Novelty Seeking, Persistence, Self-directedness and Cooperativeness were seen in monozygotic pairs as in dizygotic pairs, indicating a strong genetic effect behind the phenotypic covariation between these neurodevelopmental problems and personality traits.

ADHD and autism spectrum disorder in adults, original research	Anckarsater et al. (2006)	Cross-sectional with group comparison	N_{Tot} = 273 consecutive adults referred for neuropsychiatric investigation n_1 = 240 who completed the Temperament and Character Inventory n_2 = 100 with a diagnosis of ADHD n_3 = 66 with an autism spectrum disorder (ASD) n_4 = 47 with both ADHD and ASD	Diagnoses were assigned in accordance with DSM-IV, allowing for all diagnoses whose criteria were fulfilled, fully covering the pattern of comorbidity The Swedish version of the Temperament and Character Inventory (TCI)	Patients with autism spectrum disorders showed significantly higher scores on Harm Avoidance and lower scores on Reward Dependence, Self-directedness and Cooperativeness in comparison to the norm group. Those with a diagnosis of ADHD showed significantly higher scores on Novelty Seeking and Harm Avoidance, and lower scores on Self-directedness and Cooperativeness compared to the normal group. Patients with both ADHD and autism spectrum disorders showed a pattern similar to that found in the ADHD group. Finally, those with ADHD significantly differed from those with autism spectrum disorders in the following way: higher scores in Novelty Seeking, Reward Dependence and Self-directedness.

(continued)

Table 4 (continued)

Neurodevelopmental disorder	Author/s and year	Methodology	Sample	Assessment instrument/s	Results
	Sizoo, van den Brink, Gorissen van Eenige, and van derGaag (2009)	Cross-sectional with group comparison	N_{Tot} = 128 adult Dutch patients n_1 = 75 with an autism spectrum disorder (ASD) n_2 = 53 with a diagnosis of ADHD	All diagnostics according to DSM-IV Current substance dependence or abuse status was established The abbreviated Dutch 105-item version of the Temperament and Character inventory (VTCI)	Significantly higher scores for Harm Avoidance and Self-transcendence were seen in comparison to the normal group, and significantly lower scores for Reward Dependence, Self-directedness and Cooperativeness. For the ADHD group scores were significantly higher for Novelty Seeking, Self-transcendence and Harm Avoidance when compared to the normal group, while lower scores were seen for Self-directedness and Cooperativeness. An ANOVA test for effect of substance use disorder (SUD) status on personality dimensions in ASD and ADHD found a strong and significant effect of diagnosis on Novelty Seeking (higher in ADHD), a modest effect on Harm Avoidance (higher in ASD) and a small effect on Self-transcendence (higher in ASD). It also found a modest effect of SUD status for Persistence and Self-directedness, where all SUD groups differed with regard to the former (highest in previous SUD now abstinent for 6 months), but only between no SUD and current SUD for the latter. Finally, an interaction effect between diagnosis and SUD was found for Reward Dependence, such as that it was significantly lower in the ASD no SUD subgroup compared to the ADHD no SUD subgroup.

	Sizoo, van derGaag, and van den Brink (2015)	Cross-sectional with group comparison	N_1 = 75 adult outpatients with autism spectrum disorder (ASD) N_2 = 53 adult outpatients with ADHD	The Dutch version of the Autism Spectrum Quotient (AQ) The abbreviated Dutch 105-item version of the Temperament and Character inventory (VTCI, α ranging from 0.67 to 0.87)	The ADHD group scored significantly higher on Novelty Seeking compared to the ASD group. The former also showed a significantly higher score than was seen in the normal group. The ASD group, on the other hand, scored significantly higher than the ADHD group on Harm Avoidance, where both diagnostic groups also significantly differed from the normal group, showing enhanced scores. The two diagnostic groups showed similar scores on Self-directedness, which in both cases were significantly lower than in the normal group. Finally, the ASD group, but not the ADHD group, showed significantly higher scores on Self-transcendence than were seen in the normal group. Total AQ score within the ASD group correlated positively with Harm Avoidance, and negatively with Reward Dependence, Self-directedness and Cooperativeness. In the ADHD group total AQ correlated positively with Harm Avoidance, and negatively with Self-directedness. Thus, among the personality dimensions, only Harm Avoidance and Self-directedness were associated with AQ scores in both diagnostic groups.

Discussion

Background

Cloninger's first two character scales, Self-directedness and Cooperativeness, are valid predictors of whether an individual has the kind of adaptive personality that yields resilience and stress-coping abilities (Josefsson et al., 2011; Svrakic et al., 1993). As demonstrated here, they function as a general measure of mental (un) health, not only for mental disorders and personality disorders in adulthood but also for childhood-onset neurodevelopmental disorders. The latter are heterogeneous problem constellations first manifested during childhood and commonly thought to reflect abnormal cognitive functioning due to deviant brain development and/or brain pathology. General IQ and learning disorders owing to low IQ have been regarded as expressing a deficient "general" intellectual development or learning disorder, while other "specific" learning disorders have been defined by problems in various areas of scholastic development (reading/writing, arithmetic, athletic coordination). ASD and ADHD are thought to express dysfunctions in cognitive systems that are necessary not only for functioning in school and for learning but also for personal functioning in the family and among peers. These diagnoses are, therefore, obvious candidates for research comparing neurodevelopmental disorders with personality, reconnecting to Sjöbring's original model of personality as constitution. In his model, intelligence was one dimension of personality (in terms of "capacity") (Sjobring, 1973), and the other constitutions are various forms of mental capacities that a person could have in excess, normally, or to such a low extent that it gave rise to clinical problems (validity/energy, stability/balance, solidity/steadfastness).

Tics and Tourette disorder forms another important diagnostic category in childhood-onset neuropsychiatry. These conditions, related to obsessive-compulsive disorder (OCD), have been proposed to include explosive and compulsive personality traits (Shapiro, 2015), but formal studies on this association are almost non-existent. One hypothesis is that the tics-OCD spectrum is alien to other mental disorders by virtue of expressing a clear-cut basal ganglia dysfunction that can arise from, for example, infections. Anorexia nervosa has teenage onset and is generally not counted among the childhood-onset neuropsychiatric disorders, even if autistic-like traits or socio-communicative problems have been reported in a subgroup of those afflicted (Anckarsater et al., 2012).

Temperament

The present review shows that a growing literature has identified two temperament profiles specifically related to ASD and ADHD. This means that neurodevelopmental disorders diagnosed on clinical (including both anamnestic and observational) symptoms and test assessments by multi-professional assessors are also expressed

in the everyday emotions, behaviours and relations asked about in items that constitute personality scales. Of course, it can be argued that these are just reflections of the innate cognitive limitations carried by the disorders, but as we will see, such an epiphenomenalistic view may be unwarrantedly narrow and poor.

It even seems that the personality covariates have yielded more consistent and specific characteristics for ASD and ADHD than the vast literature trying to pin these disorders to cognitive tests. This is the case, regardless of whether they are thought to probe socio-communicative abilities (e.g. the Sally–Anne test (Baron-Cohen, Leslie, & Frith, 1985), the Reading the Mind in the Eyes Test (Baron-Cohen, Jolliffe, Mortimore, & Robertson, 1997), social stories (Happe, 1994)), executive functions (Wisconsin card sorting test (Romine et al., 2004), CANTAB (Fried, Hirshfeld-Becker, Petty, Batchelder, & Biederman, 2015)) or the ratios between various Wechsler scales (Nyden et al., 2010).

The literature on ASD and ADHD also relies on studies using proxies for clinical diagnoses in rating scales validated to assess their symptoms in the general population. Such studies have largely confirmed the temperament profiles linked to disorders in population-based samples. From these studies, the most clear-cut findings regarding the nature of these problems have merged. That disorders and traits alike are under strong genetic effects cannot reasonably be doubted nor that this is mainly due to excessive loads of genetic variants (polymorphisms, i.e. distributed in the normal population, often with unclear effects on proteins and biology but implicated in complex pathways necessary for processes that occur in all humans, included in so-called polygenetic risk scores (Taylor et al., 2018)). The symptom load has a smooth distribution from the most challenged percentile into the normal population, and the same statistic effects have been shown to give rise to disorders and subthreshold traits alike (Larsson, Anckarsater, Rastam, Chang, & Lichtenstein, 2012; Lundstrom et al., 2012). The axes of interindividual differences in problems seem to convert rather than being orthogonal, so that one problem increases the risk for all others. Furthermore, the overlap between clinical conditions is high, and there seems to be a general genetic effect driving some individuals towards the extreme in several dimensions (the "p-factor" (Caspi et al., 2014; Pettersson, Larsson, & Lichtenstein, 2016) or, rather, driving the majority of individuals towards the average normal, resourceful handling of quite challenging situations during the lifespan). In contrast, comparing disorders (and traits) to other "biomarkers" and neurocognitive test scores, findings have been notoriously difficult to replicate and have yielded no models that could be used to screen for or identify diagnoses or traits. The literature on ASD and ADHD was also long ambivalent about whether they constituted personality variants, constitutions or neurodevelopmental (or neuropsychiatric) disorders. They have also been used as typologies for personality profiles per se, reflecting the degree of severity of subthreshold symptoms, such as the Asperger quotient, schizoid personality and hyperactive–impulsive personalities in the context of antisocial PD/psychopathy (Baron-Cohen, Wheelwright, Skinner, Martin, & Clubley, 2001; Still, 1902; Wolff, 1991).

Taken together, there seems to be little evidence that ASD and ADHD, in the absence of mental retardation or identified syndromes (with brain pathology, such

as tuberous sclerosis, neurofibromatosis or malformations or clear-cut genetic aberrations, such as fragile X or CATCH-22), should constitute taxons of delimitated disorders qualitatively different from extremes in normal personality variation, or specifically "neuro"-derived mental health problems. Instead, they seem to be extremes of interindividual differences in constitutions and abilities, which have implications on all levels of personhood, from perception and motor coordination to metacognitive abilities like relations and identity. Systematic personality differences seem to come closest to being the "endophenotypes" of the diagnoses.

Character

Even more importantly, the review shows that neurodevelopmental disorders create obstacles in the maturation of character, just as extreme temperament profiles do (Svrakic et al., 1993), so that deficient development of Self-directedness and Cooperativeness forms a shared feature of most persons with clinical mental disorders, also correlating with the symptom load in the subthreshold ("broader phenotype") persons. Character was conceptualized to reflect the metacognitive understanding of, and strategies to regulate, one's perceptions, reactions, impulses and behaviours. The two first scales are thought to give a crude measure of a person's maturity, that is, adaptation, control and freedom from disorder. These two scales have been shown to consistently identify psychopathology across the spectra of child and adult psychiatry alike. This is not only important with regard to diagnostics, but especially for identifying a window of treatment opportunities that are not aimed at specific symptoms of a mental disorder, but rather at a person's broad ability to function without suffering in everyday life and to deal with the inevitable larger challenges of life.

Cloninger and his collaborators in the Anthropedia Foundation are now developing treatment interventions with this aim, in the form of a DBT-like structured coaching programme of psychoeducation, aimed at developing agency, resilience and well-being through cognitive–behavioural and body-centred training in awareness techniques (Cloninger & Cloninger, 2011). In addition, a number of quite simple, common-sense interventions may contribute to character maturity as well, which has long been a mainstay in clinical and therapeutic work and therefore less systematically studied as compared to manual-based or structured interventions. Regular habits regarding sleep, social interaction, occupation, money and physical activity (including aerobic training, healthy food and responsible medical checks), refraining from alcohol in excess and focusing on stable relations in the family and a close circle of friends, are all sound advice to achieve character maturity. Such sociocultural changes may also prevent susceptible individuals from developing the degree of dysfunction or suffering that is required for clinical diagnoses, influencing the elusive "prevalences" of the disorders (which depend not only on the wording of the criteria but also on how conducive the sociocultural circumstances are to the development of resilience to susceptibility factors).

Implications

Explanatory models that regard only one or another aspect of individuals (such as the brain in epiphenomenalism) may harm both agency and communion by letting people understand that problems arise solely in the brain and remain constant, with nothing to be done about them apart from brain-acting therapies and/or making other people more accommodating. Knowledge about individual differences in an integrative approach bridging the brain, genetics, temperament and character maturity would open therapeutic windows to help people manage their lives and provide science with a more fruitful model than looking only at the brain to explain the individual and his or her peculiarities and problems. Child psychiatry has been successful in emphasizing the "neuro" in developmental disorders rather than focusing on difficult constitutions or deficient character. Many patients, and especially parents, have felt that the new definitions were less blaming and more exculpating, as more medical and neutral, than the older terminology based on personality. Regardless of utility, however, empirical data not only fail to confirm "zones of rarity" around categorical diagnoses but also indicate that brain function is influenced by behaviours, thoughts and stimuli just as genetics plays an important part in shaping personality (i.e. mental and brain events are intrinsically linked rather than unidirectionally caused). In addition, diagnostic tests based on neuroscience have failed to emerge. Striving to master oneself in the rather challenging situations of any normal life is a superb giver of meaning, and using everyday habits and neuroscience together in psychiatric/psychological workups and treatment planning may get people involved in a way that simplistic medical models do not. Therefore, it seems reasonable to include the full person, his or her personality and surroundings, in all assessments and treatments of (normal-intelligence) ASD and ADHD, just as neurocognition and child development are essential for understanding the problems referred to as personality (disorders) in adulthood.

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Part II
Person-Centered Approaches

A Case Study in Sweden: The Need for Person-Centred Methods in the Care of Dementia Patients with Severe Aggressive Behaviour

Ulrika Harris, Inger Jönsson, and Cecilia Fagerström

Abstract This chapter focuses on giving an overview of the current care of dementia patients with very severe to extreme behavioural and psychological symptoms (BPSD), particularly aggressive behaviour. We start with an authentic case which will be the heart of this chapter. We also discuss the pharmacological treatment that is often still used, even though side effects are common and may make the symptoms of BPSD even more problematic. The chapter continues discussing person-centred methods in relation to dementia patients with very severe to extreme BPSD. We expected to find answers in the literature on how to manage severe or extreme BPSD and aggression in a person-centred way, but this proved to be difficult. As a conclusion, we offer a discussion on how future care might improve for this group of patients.

Keywords Aggression · Behavioural and psychological symptoms · BPSD · Dementia · Person-centred care · Sweden

How Do We Care for Tom?

Tom,[1] 85, was suffering from dementia, but he was still living by himself in the house he and his wife bought 50 years ago. This particular day he had his mind set on buying a new car and went to a car sales company. The staff at the company thought Tom was acting strange and Tom got more and more upset, because no one gave him the help he wanted. Tom got physically and verbally aggressive, and the police was sent for. In the commotion with the police, Tom fell over and hit his head.

[1] Tom is not his real name.

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The police found Tom's behaviour so erratic and aggressive that they brought him to the psychiatric emergency unit who stated that "we don't accept patients with dementia." After some discussion between the psychiatric staff and the police, Tom ended up at a medical ward, due to the head injury from the fall at the car company. Tom was at this stage even more agitated since he was in a situation that he did not have any control over. Tom's aggression increased while he was admitted to the ward, and his behaviour made it impossible to perform any medical procedures. He was placed under compulsory care, and security guards were called in. It took 3–4 staff, all male, to give him his medication. Tom thought that the food was poisoned and refused to eat. He also thought that the staff was trying to shoot him. Due to these delusions, Tom was throwing things and physically attacking staff. He did not want to stay in the bed, so most of the time he was on a mattress on the floor, sometimes crawling around naked. For security reasons, staff had to leave the door open which meant that everyone passing his room could see him. Tom was later discharged to a dementia care home, and he died there ten days after discharge from the hospital.

In Blekinge County in Sweden, a recent evaluation focused on the consequences of closing the psychogeriatric wards (Harris, Ström, & Wennstig, 2017). Tom's case was one of many cases described to the authors of this evaluation by hospital personnel.

In this chapter, we will describe the current care for Tom and other patients with similar problems and thoughts on what a more person-centred care would look like.

Dementia

Dementia is a cognitive impairment caused by specific brain diseases. Since no cure of any dementia disease is yet available, the goal in caring for dementia patients is to reach the highest possible level of well-being during the development of the disease. The criteria for dementia diagnosis are pronounced cognitive impairment and decreased cognitive function affecting the patient's daily life. Early in the process other conditions that can be confused with dementia symptoms have to be excluded. This is important in order to give adequate treatment, prognosis and follow-ups of the progress.

The risk of dementia increases with age; almost half of all people aged 90 and older have dementia (National Board of Health and Welfare, 2016). There are various types of dementia where Alzheimer's is the most common one followed by vascular dementia. Lewy body and frontotemporal dementia are other types. The symptoms and development of the disease will vary depending on the type of dementia. In this chapter, the behaviour is central, not the type of dementia.

When it comes to physical aggression, a recent Swedish study shows that there are differences between the various types of dementia (Liljegren, Landqvist Waldo, & Englund, 2017). Patients with frontotemporal dementia are physically aggressive

at an earlier stage of the disease compared to patients with Alzheimer's, and the violence is also more "brutal and unprovoked" compared to Alzheimer's.

Dementia involves gradually losing your abilities. A few symptoms at the start will increase in number and severity and affect the person's life more and more. Difficulty communicating symptoms and needs will increase the risk of not getting the right treatment for minor physical illnesses such as urinary infection, etc. There is also a risk of overmedication, which we will come back to later.

Persons suffering from dementia are especially vulnerable and fragile in a hospital care setting. According to George, Long, and Vincent (2013), persons with dementia are a discriminated group of patients. They are often not getting adequate medical assessment and treatment. They also risk getting inappropriate treatment with medication that can potentially worsen their dementia symptoms. The longer they stay in the hospital, the higher the risk of falls, confusion and decreased functional capacity (George et al., 2013).

The world is facing a major challenge in terms of providing healthcare for individuals affected by dementia. There is a growing population of people over 65, due to the so-called baby boom generation born shortly after WWII. They tend to live longer, and subsequently they also live longer with diseases such as dementia. It is estimated that we now have almost 50 million people in the world living with dementia and that the number will rise to 131.5 million in 2050 (Alzheimer's Disease International, 2016). In Sweden, the current number of people living with dementia is 170,000, with a total population of almost ten million. Sweden is expected to follow the international prediction, and the estimated number for 2030 is 230,000 (Alzheimer Sverige, 2017). A recent report from Swedish National study on Aging and Care (SNAC) calculates the number of dementia patients over the age of 60 in Sweden to 126,000–130,000 in 2015, a lower number compared to previous predictions (Fratiglioni et al., 2017).

BPSD: Behavioural and Psychological Symptoms of Dementia

It is estimated that about 90% of people with dementia will suffer from BPSD in some form at some stage of the disease. BPSD involve a variety of symptoms such as hallucinations, delusions, aggression, shouting, acting out, uninhibited behaviour (socially, sexually), anxiety, apathy and more (Brooker & Latham, 2016; Preuss, Wong, & Koller, 2016). BPSD are not connected to any particular dementia diagnosis and are unpredictable in the way they can appear during the progression of the illness. Results from a systematic review indicate that BPSD are major risk factors for an earlier move to a dementia care home and a potentially more severe course of dementia over time (Kales, Gitlin, & Lyketsos, 2015).

In this chapter, we are focusing on the small group of patients suffering from very severe or extreme BPSD, particularly those exhibiting aggressive behaviour. The aggression can be verbal or physical, as in Tom's case, sometimes resulting in violence towards caregivers or other residents. This group of patients is estimated to

be less than 1% of all suffering from dementia, but it is a group that requires extensive specialized care. In Fig. 1, the square at the top of the triangle marks the group we are referring to (Brodaty, Draper, & Low, 2003). The triangle shows the percentage of people with dementia who falls into different levels of BPSD and the level of care required.

A recent study showed that 35% of all patients with frontotemporal dementia and Alzheimer's disease displayed physical aggression (Liljegren et al., 2017). Both verbal and physical aggression put a lot of strain on caregivers, professional as well as family. It is stressful and exhausting caring for a person who is violent, and personal safety issues are real (injuries, stress). In a Swedish study, 134 (68.4%) of a total of 196 caregivers in 3 nursing homes reported that they had experienced violence in their workplace during the previous year (Isaksson, Graneheim, Richter, Eisemann, & Åström, 2008).

Family members struggle to recognize their loved one, and, when the behaviour is violent and causes much pain, there is a risk of forgetting the person behind the behaviour. Family caregivers are risking decreased health and reduced quality of life, when experiencing for example lack of sleep and constant stress which can lead to depression (Kales et al., 2015).

The evaluation report mentioned earlier (Harris et al., 2017) showed that patients with very severe or extreme BPSD are often being treated like Tom. There is

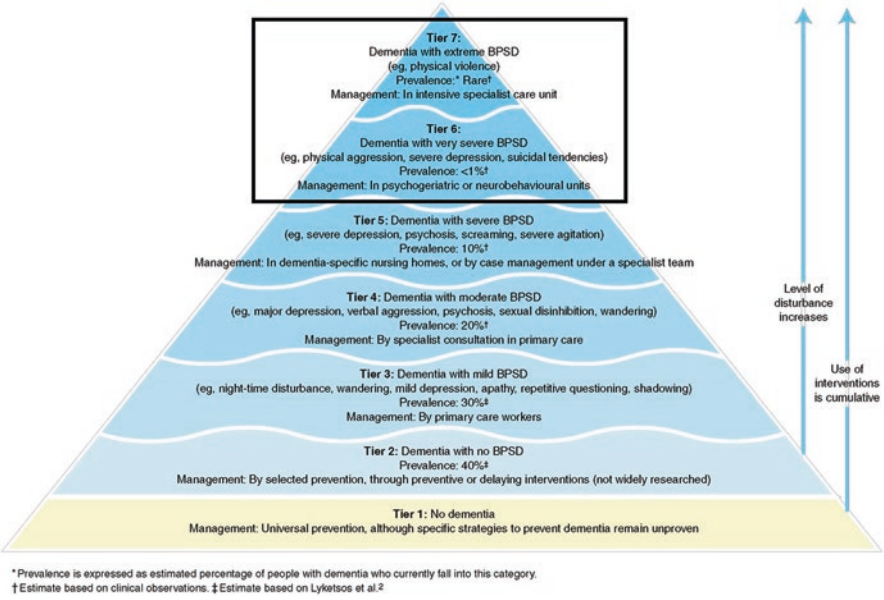

Fig. 1 The Brodaty triangle. * Prevalence is expressed as estimated percentage of people with dementia who currently fall into this category. † Estimate based on clinical observations. ‡ Estimate based on Lyketsos et al. (Brodaty et al., 2003). (© Copyright 2003 The Medical Journal of Australia – figure adapted and reproduced with permission)

currently no place of care for these individuals in a county such as Blekinge, and the solutions are either to quickly create a temporary place for them or to send them to a specialized unit in another county. All of the interviewed professionals agreed that there is a need for a consistent and permanent solution that will provide the best care and safety for patients, their families and staff. The situation for these patients is similar throughout Sweden.

BPSD have many causes: physical, psychological, general care and treatment or the care environment (Kales et al., 2015). Cohen-Mansfield (2013) stresses unmet needs as the most important reason for behavioural disorders. The dementia patient's inability to clearly communicate pain or discomfort is a major factor that can lead to spiralling anxiety or aggression. Pre-existing personality and characteristics may play a part in the development of BPSD, for example, an aggressive behaviour existing before the dementia debut might be accentuated (Pulsford & Duxbury, 2006). In some cases, there is an underlying personality disorder that has never been diagnosed (Enmarker, Olsen, & Hellzen, 2011). This disorder might present itself as violent behaviour of some sort, and it is logical to assume that the person still reacts with violence after the dementia debut. According to Enmarker et al. (2011), a dementia patient experiencing pain often becomes aggressive. If the carer understands that pain is the underlying cause, that person can help alleviate the pain, and the aggression stops. This requires the carer to see the patient as a person that is trying to convey something with his behaviour. Otherwise the carer will neglect the message sent through the aggressive behaviour, thinking that the patient is only being "difficult." It might end with even more pain and thus more aggression.

Another major trigger of BPSD is a change of environment, especially admission to the hospital. A hospital ward is often not designed for people with dementia. In an acute hospital setting, the BPSD symptoms affect 75% of patients with dementia at some point during their stay, aggression being the most common disturbance (Sampson et al., 2014). In hospitals, they are seen as an unwanted group of patients, as in Tom's case (George et al., 2013). Hospital staff often lack knowledge of dementia and are therefore not fully prepared for dealing with dementia patients. A contributing factor to this might be that the curriculum for medical and nursing studies does not include enough about dementia and BPSD (Clissett, Porock, Harwood, & Gladman, 2013).

Patients suffering from BPSD have difficulties interpreting and understanding communication and different impressions and situations. Behaviour and expressions in a person with BPSD can be challenging to understand, but they are relevant for the person experiencing them. There is logic behind the behaviour, and it is important to try to understand in order to ease the worry or fear that is being expressed. It is mentioned in one study (Pulsford & Duxbury, 2006) that difficulties in understanding might even lead to the use of physical restraints, like in the case with Tom when 3–4 persons had to hold him down in order to give him his medications.

Pharmacological Treatment of Dementia

One major aspect of dementia care today involves pharmacological treatment. In this section, we describe the current treatment and some of its possible complications.

According to Ballard, Corbett, Chitramohan, and Aarsland (2009) and Yeh and Ouyang (2012), a careful identification of target symptoms and their consequences, initial trials of non-pharmacological approaches, continuous treatment monitoring and use of the least harmful medication for the shortest period of time should be principals of treatment of BPSD in the dementia care. This is in accordance with Swedish national guidelines (National Board of Health and Welfare, 2010b). However, these guidelines are not always followed. Instead, pharmacological treatment of BPSD is a central but complex element in the management of dementia.

In order to slow down the decline of cognition and function, drugs like cholinesterase inhibitor and memantine are often used in persons with Alzheimer's disease. These two types of drugs do not impact the progress of the disease but have behaviour-stabilizing effects (Rodda, Morgan, & Walker, 2009), and cholinesterase inhibitors are seen as useful for symptoms such as apathy and psychosis. They are also used to reduce agitation in dementia (Lockhart, Orme, & Mitchell, 2011) as well as to delay transfer to a nursing home (Feldman et al., 2009). Memantine have a potential effect on agitation and aggression (Ballard & Corbett, 2010). However, the evidence in dementia is still limited (Declercq et al., 2013; Rodda et al., 2009; Sink, Holden, & Yaffe, 2005) and is even seen as not useful at all (Howard et al., 2007) in part due to methodological considerations.

The most common treatment for BPSD is psychotropic drugs (affecting mental activity, behaviour or perception, as a mood-altering drug), particularly antipsychotic drugs (Sultzer, 2004). There is limited evidence of antipsychotic treatment effects in older people with dementia. The medical treatment of BPSD has repeatedly been noticed, debated and criticized, especially concerning patient safety (Bishara, Taylor, Howard, & Abdel-Tawab, 2009) and the potential risks of the antipsychotic drugs. In persons with dementia, side effects of the treatment like stroke and falls are increased, and that is why the use of antipsychotic drugs should be minimized and even be avoided (Mittal, Kurup, Williamson, Muralee, & Tampi, 2011; Oderda, Young, Asche, & Pepper, 2012). Simultaneous treatment with other psychotropics also increases the risks of potential side effects (National Board of Health and Welfare, 2013). Furthermore, benzodiazepine is often used to handle BPSD symptoms (Bishara et al., 2009) and used as a replacement or in combinations with antipsychotic drugs in the treatment of BPSD. Benzodiazepines are calming but also highly addictive and should be prescribed carefully.

The prevalence of antipsychotic drug use differs (12–48%) across countries in Europe depending on cohorts included (Karlsson, Rahm Hallberg, Midlöv, & Fagerström, 2017). The same pattern is shown within Sweden, and the prevalence differs (6–38%) depending on regional location and time of data collection. A review performed by Karlsson et al. (2017) showed that the highest rates of usage

were found in persons with cognitive impairment especially in those who were younger elderly people, with moderate cognitive impairment and living in nursing homes specialized in dementia care. The good news is that a general positive trend in usage of antipsychotics was indicated, i.e. there was a decreased prescribing of antipsychotics over time (Karlsson et al., 2017).

Although national recommendations from Swedish authorities have been more restrictive in the last years, resulting in fewer prescriptions of antipsychotics, there are still older patients with dementia who are given antipsychotics over a long period of time (Karlsson et al., 2017). Current recommendations from Swedish national authorities state that individuals with dementia should have the same doctor (National Board of Health and Welfare, 2010a; *Patientlag*, SFS 2014:821, ch. 6) with whom they discuss (together with primary caregiver) the continuous antipsychotic treatment with the aim of decreasing the usage and dosage (Medical Products Agency, 2008). Antipsychotic drugs should only be used when people with dementia suffer from delusions and hallucinations (National Board of Health and Welfare, 2010b).

When directives regarding antipsychotics become more restrictive, other psychotropics may be introduced in order to minimize the risk of under-treatment of BPSD symptoms. This problem has been identified by Vasudev et al. (2015). The increased awareness about negative side effects of antipsychotics may result in other care alternatives such as non-pharmacological interventions. Strategies including both pharmacological and non-pharmacological treatments for an optimal dementia care are recommended (Preuss et al., 2016), and new perspectives on additional management could be helpful in the discussion of the complexity of treatment and management of BPSD.

Person-Centred Care

In this section, we first tell the story of person-centred care by describing the theory behind it. This is followed by a discussion on the connection between person-centred theory and method.

The Story of Person-Centred Care

Person-centred care has its roots in psychology with psychologist Carl Rogers focusing on the client's perspective and experience in the client-centred psychotherapy (Rogers, 1946). From this method, psychologist Tom Kitwood formed the theory of personhood and connected that to the context of dementia care (Kitwood & Bredin, 1992).

Kitwood stated that a patient is not just a diagnosis, but also a person. He saw that this aspect was often neglected when the person became sick and needed care.

The person then was reduced to a diagnosis that should be cared for. This diminishes the patient and makes him vulnerable and dependent in an unhealthy way.

Instead, Kitwood created the theory of personhood as a way of thinking about the patient that would take into account the whole human being and not just the illness. He argued that people caring for dementia patients should remember to learn about the patients' opinions, preferences, history and everything else that turn humans into individuals. Kitwood's point was that everyone is part of a biological, social and psychological context. The key to a dementia patient's well-being is for the caregivers to understand this context and apply it to the care given.

As already mentioned, persons suffering from dementia become especially vulnerable in a care situation, because in a way the disease has already taken away some or most parts of their personhood. Person-centred care focuses mainly on the person and not on the diagnosis, and this might be even more important when it comes to people suffering from dementia. Knowing the person you take care of is of utmost importance if you want to give the best possible care.

In person-centred care, it is also important to focus on the professional caregiver, since the basic idea is to make sure that everyone is seen, heard, respected and appreciated, including the ones who are meant to give the person-centred care (Charmel & Frampton, 2008; Nilsson, 2013). Studies show that staff appreciate getting to know the people they are caring for, when they are given the appropriate time and structure for it. They start to see the person with dementia in a different light, and previous attitudes, sometimes coloured by prejudice or assumptions, fade away (Egan et al., 2007; Kolanowski, van Haitsma, Penrod, Hill, & Yevchak, 2015). It also gives the professional the self-esteem and joy back, since working with people with severe dementia and BPSD can be upsetting when they aim their aggression towards you (Charmel & Frampton, 2008).

What Is in the Black Box We Call Person-Centred Care?

It proved to be a challenge to find research that has studied the effect of person-centred care on patients suffering from BPSD. We expected to find answers in the literature on how to manage severe or extreme BPSD and aggression in a person-centred way. Instead, we found a plethora of articles relating more or less to the topic. One major question arose: What exactly is person-centred care?

We found a lot of studies related to person-centred care in general, whether the authors are calling it person-centred care or not. It can be anything that considers the individual before the symptoms of disease and takes into account personal habits, values, needs, history and personality. Some examples of various interventions are music therapy (Svansdottir & Snaedal, 2006; Thomas et al., 2017), hospital clowns (Kontos et al., 2016), sensory stimulation (Lykkeslet, Gjengedal, Skrondal, & Storjord, 2014), aquatic exercise (Neville, Henwood, Beattie, & Fielding, 2014) and staff education (Spector, Orrell, & Goyder, 2013). As Cohen-Mansfield (2013) points out, there are a number of different non-pharmacological methods that can be

used for behavioural disorders, but it is not so much the method itself but the person-centred approach that matters. The caregiver has to be genuinely interested in the patient in order to provide the best care, according to Kitwood.

Even studies that focus on person-centred care do not always base it on a specific person-centred theory, which makes it difficult to compare with other studies in the same field. The few studies that made the connection between theory and method referred to Kitwood. Also, every intervention has its own way of measuring the outcome of the intervention. If healthcare services are supposed to work according to person-centred methods, it needs to be clear exactly what those are; otherwise, it is difficult to say what we are measuring. In some sense, the studies we found made a claim to assess some sort of person-centred intervention without clarifying what characterizes person-centred care. It is difficult to evaluate something that does not have a clear definition.

During the work with this chapter, we have tried to find the best possible person-centred method to care for these patients, but to the best of our knowledge, no method can be recommended as better than any other. Many methods claim to be person-centred, but not many studies connect this person-centredness to a clearly stated theory, which creates some uncertainty about the validity and usability of those methods in the context of aggressive persons.

Improving the Situation for Tom Through Person-Centred Care

According to Brooker and Latham (2016), all behaviour, such as aggression, has a logic reason and makes sense to the person expressing it. If person-centred care is applied, caregivers ought to look for the reason behind the behaviour. This requires an attitude based on genuine curiosity in the caregiver. There are a lot of questions that could be asked in reference to Tom and his situation, questions that the staff might have asked Tom or his family. That does not mean that Tom would have got whatever he wanted, but at least someone would have listened to him and explained why he could not go home or buy a new car. Instead, it seems that the situation escalated, and the more aggressive Tom got, the less of a person he became. He turned into a problem that needed a solution, not a person in distress or a patient with medical needs.

Unmet needs can trigger aggression (Cohen-Mansfield, 2013). We do not know why Tom got aggressive or crawled on the floor; maybe he was in pain, felt too hot, and felt fear and had traumatic memories and hallucinations. Tom was degraded when everyone could see him crawling on the floor. The whole situation must have been strange for both visitors and staff. Even if Tom himself did not understand (or maybe he did?) the indignity of everyone seeing him in this state, other people did. It is not hard to imagine how upsetting it would be for Tom's family to see him crawling around naked on the floor or being held down by a whole team of nurses.

Other patients and their families would most likely have reacted to the situation as well, maybe wondering who would be the next patient up for the same treatment.

Tom was given medication; we do not know which ones. Antipsychotics are still prescribed to dementia patients, in spite of research listing the disadvantages and national guidelines recommending non-pharmacological methods first hand. This is a fact that everyone working with dementia patients must be aware of and "rather than to reflexively *prescribe* medications, they need to automatically *look for* underlying modifiable causes" (Kales, 2015, p. 1210). This, plus raised awareness and status of non-pharmacological methods, would be of utmost importance for caring for dementia patients, especially in inpatient hospital care.

People with dementia and severe/extreme BPSD and aggression are a group of patients that are seen as unwanted. An individual with these problems is seen as hard to deal with and hard to place. In interviews with staff (Harris et al., 2017), they expressed the following concerning Tom:

> He doesn't belong here. We're an acute hospital ward; it's not suited for patients like that. We were under a lot of stress dealing with many patients; we couldn't put 2–3 of our own staff watching him all the time. This patient was a risk to himself and to others. He shouldn't be here.

The evaluation report (Harris et al., 2017) showed that patients with extreme BPSD are often treated like Tom, maybe due to a lack of time or to a lack of staff with specialized competence. Time pressured caregivers without this special competence feel stressed and frustrated, and present a risk of being verbally or physically abused by the patient, and vice versa. It is not an easy situation for healthcare professionals, family or caregivers. While staff is expressing an extremely stressful situation, it is still notable how the patient's point of view is nearly erased. Tom is seen as just a problem that they have to deal with or try to find someone else to deal with it. Unfortunately, this view is not uncommon in healthcare, where patients with dementia and/or confusion are seen as undesired (George et al., 2013). Caregivers are usually the ones at the greatest risk of being targets of physical aggression. It can affect the quality of care through adverse attitudes but also in aggressive acts towards the person with dementia (Liljegren et al., 2017).

A dementia register is one way of providing structure in the professional dementia care. In Sweden, the BPSD register started in 2010 and aims to decrease BPSD symptoms and to improve quality of care for dementia patients. The symptoms are measured with Neuropsychiatric Inventory (NPI). The measurements are used as a basis for discussion among staff regarding the problems and possible solutions. A checklist is used to assess possible causes like pain, constipation, urinary infection, etc. This is followed by discussing possible changes in the care plan which is documented for consistency (Sjöström, 2017). The BPSD register is widely used in the residential care but not so much in the hospital care (BPSD, 2017). Since the implementation of the BPSD register in the local councils in Sweden, the quality of the dementia care has improved, and knowledge and awareness of person-centred care have increased (Sjöström, 2017). As a complement to using the BPSD register, staff education about dementia (Clissett et al., 2013), BPSD and person-centred care

would be beneficial (Enmarker et al., 2011; Kolanowski et al., 2015). Curriculum for medical and nursing studies should include greater focus on dementia and BPSD (Clissett et al., 2013).

Since the dementia patients themselves might have great difficulties recalling their history, preferences, etc., it is particularly important for the carers to do that for them. When working with older patients, especially persons with dementia, the patient's life story is especially important. A life story includes important events, experiences and feelings that have formed a person's life, from childhood through adulthood and old age (Santamäki Fischer, 2010).

Personnel working with dementia patients have to know the person behind the dementia to be able to care for the patient in the best way possible. Knowing a patient well might also be a help if the patient becomes aggressive or gets other symptoms of BPSD. The reason for the behaviour might be found in the patient's life story. Knowing the life story might help solving the problem (Egan et al., 2007). Even though professionals in dementia care are positive regarding the use of life stories, the actual usage is still relatively low. The main reason is lack of routines and structure concerning life stories (Wennstig & Fagerström, 2017).

So what can you do in a situation like Tom's? First, talk and listen to the man and those nearest to him to get a picture of who this man has been and is today, his personality, habits, what he prefers, his values and needs. It is about trying to understand and interpret the patient's behaviour from his or her perspective, in other words try to "walk in their shoes" (Nilsson, 2013). Studies show that this is a way of reducing an aggressive or agitated behaviour in persons with dementia (Enmarker et al., 2011).

Conclusion

A small group of people with very severe to extreme BPSD will require intensive specialist care in a high-security unit with specially trained staff. Brodaty's triangle, mentioned earlier, refers to them as tiers 6 and 7. These patients will end up here after all other attempts have been exhausted. We believe that person-centred care needs to be applied before the patient reaches the top of the Brodaty triangle and the sooner the better, in order to avoid severe or extreme BPSD. From targeting symptoms, pharmacological and non-pharmacological approaches, to continuous treatment and care, the person-centred glasses should be worn.

In the light of what we have found, the Swedish BPSD register seems to be a great tool for implementing person-centred care. It is mainly used in nursing homes, but we believe it might be used in hospital settings as well. It provides staff with the possibility to actually talk about what is happening with the patients and about how to consider dementia patients primarily as persons and not diagnoses. We believe that staff working in acute hospital settings would benefit from learning more about BPSD and aggressive behaviour in particular. This is not their primary patient group, but the number of patients with these symptoms will increase over the years

to come. By using this register, or a similar systematic way of working, the hospital departments would be able to identify causes of BPSD and evaluate the different solutions presented in a structured way.

In summary, treatment and management based on evidence on person-centred methods is essential to improve care for this group of patients but is still insufficiently described in the literature. We expected to find answers in the literature on how to manage severe or extreme BPSD and aggression in a person-centred way, but this proved to be difficult. In order to endorse optimal care using the least harmful medication for the shortest period of time, more focus needs to be put on person-centred methods in the care of dementia patients with severe aggressive behaviour.

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Transcranial Magnetic Stimulation in the Treatment of Major Depressive Disorder: A Personalized Approach

Marko Mihailovic and Mehmet E. Dokucu

Abstract A growing body of evidence suggests that magnetic and electrostimulation of certain parts of the brain can alleviate depressive symptoms. Repetitive transcranial magnetic stimulation (TMS) as a treatment for depression has shown statistically significant effects, but the clinical significance of these effects has been questioned. Major depression is often difficult to diagnose accurately. Even when the diagnosis is properly made, standard treatment approaches (e.g., psychotherapy, medications, or their combination) are often inadequate to control symptoms or maintain initial benefit. There is a need for more effective and better-tolerated treatments.

TMS is a noninvasive and easily tolerated method of altering cortical physiology. It is effective in treating depression with minimal reported side effects. The existing literature supports a possible role for TMS in the treatment of depression and suggests concurrent biomarkers, which may help in determining which group of patients would have a positive response to TMS treatment for major depressive disorder (MDD). Temperament and Character Inventory (TCI) appeared to be a cost-effective, promising predictor to TMS treatment response. The authors evaluated current potential difficulties in diagnosing MDD accurately and reviewed a personalized approach as a model that may help with diagnosing MDD more accurately as well as improving the existing TMS treatment.

Keywords Major depressive disorder · MDD · TMS · rTMS · Personalized medicine · Treatments for MDD · Biomarkers · TCI

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Introduction

Depression is highly prevalent across the globe and is one of the major contributors to disability worldwide (Kessler & Bromet, 2013; Kessler, Ruscio, Shear, & Wittchen, 2010). This condition is not only an individual burden but also causes significant costs to society (Murray et al., 2012). Furthermore, even experienced clinicians have difficulties in treating individuals who suffer from depression. Moreover, it is challenging to recognize and diagnose patients who suffer from this disorder (Janicak & Dokucu, 2015). There are important controversies related to diagnosing and treating individuals with depression (Reynolds, 2004). Therefore, there is a clear need to understand this condition better, to address barriers to care, and to improve treatment outcomes.

In this chapter, we will review historical perspectives on models of mental disorders, differences and similarities between those models, current treatments for depression, pros and cons of the current treatments, new approaches to the treatment of depression, and potential personalization of those approaches.

Categorical Versus Dimensional Classification of Mental Disorders

Diagnosis is at the core of the medical model of psychopathology and is the first task from which all other steps flow. A diagnostic system classifies disorders and provides a description of the types of disorders likely to be found in a particular domain. Advanced diagnostic systems are not only descriptive but also predictive and prescriptive because they carry implications for underlying pathology, etiology, course, and prognosis (Kihlstrom, 2002).

Kraepelin developed the first systematic classification of mental illnesses that went beyond citations of symptoms (Shorter, 2011). He begrudgingly acknowledged that a more desirable classification based on pathological anatomy was impossible due to the state of medical knowledge and also openly admitted that most of the etiologies given in his text were speculative and tentative. Following on Kraepelin's work, diagnostic classification based on syndromes is justified despite the fact this was the practice he was trying to avoid (Kihlstrom, 2002).

The first and the second editions of *Diagnostic and Statistical Manual for Mental Disorders* (DSM-I and DSM-II) (American Psychiatric, 1952, 1968) were diagnostic classifications based on lists of symptoms and signs that were largely presumed to arise as a reaction to intrapsychic conflicts or external events. These early classifications suffered from poor inter-rater reliability such that empirical investigations showed that the probability of two psychiatrists agreeing on the diagnosis of a mental disorder in the same patients hardly exceeded chance (Kendler, Munoz, & Murphy, 2010). The "St. Louis Group," based at Washington University School of Medicine in Saint Louis (Feighner et al., 1972; Woodruff, Goodwin, & Guze, 1974),

advocated a medical model for psychiatry in which diagnosis had a central role and psychiatric disorders had to be treated as were other medical disorders. This group created the Feighner criteria that led to a paradigm shift that had profound effects on the course of American and, ultimately, world psychiatry. The third and fourth editions of the *Diagnostic and Statistical Manual for Mental Disorders* (DSM-III, DSM-III-R, and DSM-IV) (American Psychiatric, 1984, 1987, 1994) were very highly influenced by this group's approach (a.k.a Neo-Kraepelinian).

Feighner criteria were instrumental in the renaissance of psychiatric research in the subsequent decades (Kendler et al., 2010). However, neither the developers of the criteria nor we would claim that assigning operationalized diagnostic criteria is all that is required for what should be considered a good psychiatric evaluation. Our diagnostic criteria, however detailed, never contain all the important features of psychiatric illness that we should care about in clinical practice, but the task of developing more reliable and valid psychiatric diagnoses will probably remain central to the research mission of psychology and psychiatry for the foreseeable future.

In contrast to the medical psychiatric tradition, psychology has long pursued dimensional features of personality using empirical data. The best-known and most commonly used personality tests are the Temperament and Character Inventory (TCI) and Big Five Questionnaire (BFQ) (Baeken et al., 2014). These self-report-based questionnaires capture the variability and nuance of personality but do not make sharp normal-versus-abnormal distinctions. Each person exhibits one trait to a certain degree, the next trait to another degree, and so forth and the combinations are nearly infinite.

The present trend in medicine is, essentially, to identify biomarkers for psychiatric diseases (Fidalgo et al., 2014). Psychiatrists and psychologists attempt to test for differential psychological deficits by testing blood for the presence of antigens and antibodies or by scanning the brain to detect lesions or changes in the structure or function in order to create a new nosology based on psychopathological findings (Fidalgo et al., 2014). It is hoped that a new nomenclature would be more closely tied to underlying psychopathology.

The Holistic and Humanistic (Person-Centered) Approach to Mental Illness

The holistic approach to medicine has ancient roots and can be found in major Eastern civilizations such as Chinese and Ayurvedic (Patwardhan, Warude, Pushpangadan, & Bhatt, 2005). The term "holistic" originates from the Greek word "holos," which literally means whole. It is an approach that appreciates each individual as a whole interacting with the social and physical environment. The holistic approach is based on Plato's philosophical premises that the whole is more than the sum of its parts (Cloninger, Cloninger, & Mezzich, 2016). Holistic and integrative medical approaches are fundamentally person-centered. Health is considered to be

a state of physical, mental, social, and spiritual well-being (Cloninger et al., 2016). This approach implies a profound complexity of the human being and also suggests that biological, psychological, and social factors should be taken into consideration in our attempts to address mental illness.

Balancing "What Disease Does the Patient Have?" with "What Patient Has the Disease?"

The traditional medical model endorses the concept of "patient" that implies a person who must wait patiently for detailed directions from the expert. Clinical experience and literature suggest that the focus of contemporary medicine should be shifted from disease and patient to person (Mezzich, Botbol, Christodoulou, Cloninger, & Salloum, 2016; Mezzich, Snaedal, van Weel, & Heath, 2010). Holistic medicine emphasizes that the patient is a person, not a disease or separate organ. The person-centered approach is at the core of holistic medicine because it emphasizes the importance of unconditional positive regard in addition to respect for each person being responsible for their own health and recognizes the role of physician's subjectivity as a diagnostic and treatment tool (Mezzich et al., 2016).

Major Depressive Disorder

Major depressive disorder (MDD) is a common condition in the population and constitutes a grave public health concern (Kessler & Bromet, 2013). MDD was ranked as the fourth leading cause of disability worldwide by the World Health Organization (WHO), which projects that by 2020, it will be the second leading cause of handicap and premature death in the world after coronary diseases (Kessler & Bromet, 2013; Mathers, 2008). Community-based surveys conducted in several countries using the International Classification of Diseases (ICD) 10th revision criteria have shown a lifetime prevalence of MDD ranging from 6% to 12%, with an annual prevalence of 3–11% (Anderson, Joyce, Carter, McIntosh, & Bulik, 2002; Waraich, Goldner, Somers, & Hsu, 2004). MDD is a chronic, recurrent disorder, with nearly 80% of patients relapsing after the treatment of an episode (Brunoni et al., 2010). Finally, about one third of patients have treatment-resistant depression, which is defined as the failure to achieve adequate alleviation of symptoms after 2 or more standard antidepressant (AD) treatment trials (Pridmore, 1999; Zobel, Yassouridis, Frieboes, & Holsboer, 1999). In fact, the high prevalence of treatment-resistant depression associated with failure to respond to AD is an important concern when managing major depression (Fidalgo et al., 2014).

MDD is conceptualized as a medical disorder that is rooted in the brain and is mediated by the brain systems responsible for mood regulation, emotional

expression, reward processing, motivation, and responses to stress (Drevets, Price, & Furey, 2008). The medial prefrontal cortex (subgenual cingulate), amygdala, hippocampus, and ventromedial parts of the basal ganglia have been identified as possible regions in the brain responsible for depressive symptoms. Dysfunction in these regions may play a role in disturbances in neurotransmission, autonomic regulation, neuroendocrine responses, emotional behavior, and cognitive performance that characterize depression (Drevets et al., 2008).

Clinicians have difficulties identifying and appropriately diagnosing MDD and this leads to under-treatment of individuals with MDD. Only half of those individuals who are diagnosed with MDD and receive treatment actually benefit from the treatment (Miller et al., 1998). It is confirmed that many of these individuals either do not receive an adequate trial of therapy, or initially benefit but then lose this effect over time, or do not tolerate the standard approaches (Janicak & Dokucu, 2015). The Sequenced Treatment Alternatives to Relieve Depression (STAR*D) study emphasized this issue. This large semi-naturalistic clinical trial found that approximately one third of the patients had not achieved remission in the 12-month naturalistic follow-up phase to four aggressive AD treatment strategies (Rush et al., 2006).

Available Treatments for Depression

AD medication is the best established pharmacotherapy treatment for depression and has been shown to be efficacious, particularly in more severe cases of MDD (Fournier et al., 2010).

Review of the current body of effective and well-tolerated treatments for MDD suggests that there is a need for better understanding of alternative treatments and the discovery of more effective novel treatments for MDD with milder safety profiles (Bulteau et al., 2017). Therapeutic neuromodulation is one of the alternative treatment approaches. As the brain is an electrochemical organ, it can be modulated by electrical as well as pharmacological means, and there are several devices which can be used to alter electrical activity in the central nervous system. The main therapeutic focus of neuromodulation is MDD, but this strategy might benefit other neuropsychiatric disorders (e.g., bipolar disorder, schizophrenia, pain disorders, Gilles de la Tourette syndrome) (Lefaucheur et al., 2014).

Existing neuromodulation devices appear to impact areas of the brain (e.g., mesocortical limbic mood circuit) involved in the pathophysiology of MDD. Electroconvulsive therapy (ECT) has been available for about 75 years (Bulteau et al., 2017; Janicak & Dokucu, 2015). A number of patients are not ideal candidates for ECT or refuse to receive the treatment due to its adverse cognitive effects, substantial relapse rates after a successful acute treatment course, and negative public image (Barker & Freeston, 2007; Janicak & Dokucu, 2015). Therefore, a number of new neuromodulation approaches are being developed. For instance, vagus nerve stimulation (VNS) and transcranial magnetic stimulation (TMS) are

already cleared by the US Food and Drug Administration (FDA) as effective and safe treatments for MDD. VNS has been available since 2005 but has not been widely utilized because of a surgical procedure that is needed to implant the device and the need for prolonged exposure over months to achieve optimal results (Rado & Janicak, 2007). On the other hand, TMS was FDA cleared in 2008 and is a non-invasive procedure with very few adverse effects. There is evidence that TMS is better tolerated than medications or other therapeutic neuromodulation approaches (Janicak et al., 2008). Safety and efficacy of TMS in the treatment of MDD have been confirmed with over 35 randomized, sham-controlled trials (Janicak & Carpenter, 2014).

Transcranial Magnetic Stimulation

TMS is a noninvasive brain stimulation technique that uses a highly targeted pulsed magnetic field to stimulate cortical neurons. The magnetic field produced by TMS is similar in type and strength to those produced by a magnetic resonance imaging (MRI) machine except that it focuses on a limited area of the cortex. The magnetic field produced by TMS passes through the scalp and skull unimpeded and it varies from 1.5 to 3 Tesla in strength (Janicak & Dokucu, 2015). TMS induces currents in focal brain areas by electromagnetic stimulation (Fitzgerald & Daskalakis, 2011). The mechanisms of action of TMS are explained in the literature as: improvement in prefrontal hypometabolism (Bestmann, Baudewig, Siebner, Rothwell, & Frahm, 2005), neuromodulation of remote cerebral areas (especially the subgenual region) (Baeken et al., 2015), regulation of the hypothalamohypophyseal axis (Baeken et al., 2015), modulation of cortical excitability and synaptic plasticity (Baeken & De Raedt, 2011; Hoogendam, Ramakers, & Di Lazzaro, 2010; Pell, Roth, & Zangen, 2011) and dopaminergic secretion (Shaul, Ben-Shachar, Karry, & Klein, 2003; Strafella, Paus, Fraraccio, & Dagher, 2003).

In clinical use, TMS is administered as several 1000 pulses that are usually applied over a period of minutes to hours. This is called repetitive transcranial magnetic stimulation or "rTMS" (as an abbreviation, TMS is used more often). When these pulses are delivered in a high frequency (HF; 10–20 Hz), they enhance cortical activity. On the contrary, when pulses are delivered in a low frequency (LF; 1 Hz), they inhibit cortical activity (Janicak & Dokucu, 2015). Both TMS methods appear to be equally effective therapies for MDD (Isenberg et al., 2005; Pallanti, Bernardi, Di Rollo, Antonini, & Quercioli, 2010; Rossini et al., 2010).

The use of TMS devices was validated for this indication by the US Food and Drug Administration (FDA) in 2008 and by the European Union (EU) in 2012 (Bulteau et al., 2017). Of note, one of the most recent analyses highlighted a three-fold greater response and remission rate for left prefrontal cortex stimulation at high-frequency versus sham treatment (Berlim, van den Eynde, Tovar-Perdomo, & Daskalakis, 2014). TMS has an adherence rate of 97% versus 60% traditionally recorded compliance for medication. Several meta-analyses based on randomized,

controlled, double-blind studies refer to the therapeutic efficacy of TMS in the management of resistant depression (Bulteau et al., 2017). Furthermore, once AD drugs have failed, TMS would be less expensive and would allow a better quality of life and greater function compared to conventional treatment strategies (Simpson, Welch, Kozel, Demitrack, & Nahas, 2009).

The superiority of rTMS over sham stimulation is confirmed in randomized controlled trials conducted over 20 years. Effect sizes in the range of 0.4–0.6 were identified in meta-analytic studies. Reported response and remission rates in different studies varied in the range of 50–58% and 24–37% (Taylor et al., 2017). There is strong evidence that the effect size for TMS antidepressant efficacy is comparable to that of antidepressant medications (Janicak & Dokucu, 2015).

There is an increased body of evidence for supporting TMS augmentation with other treatment modalities. TMS in combination with ECT (versus ECT alone) for acute treatment of depression reduced the number of ECT sessions required, thus minimizing the adverse effects (Pridmore, 2000). Preliminary data and increasing clinical experience also suggest a potential maintenance role with TMS after a successful acute trial of ECT (Cristancho, Helmer, Connolly, Cristancho, & O'Reardon, 2013). Previous research based on meta-analysis showed that augmentative TMS therapy was significantly superior to sham condition in treatment-resistant depression (TRD). For TRD patients, augmentative TMS after the failure of medications significantly increases the effect of ADs, and TMS was a safe strategy with relatively low adverse events and low dropout rate, suggesting that augmentative TMS is an effective intervention for TRD (Janicak & Dokucu, 2015). More studies are required to replicate these findings and to identify predictive factors for patient selection and treatment response.

Biomarkers as Predictors of TMS Treatment Response

There is substantial evidence for the efficacy of TMS treatment and thus there has been increased interest in finding potential predictors of clinical response. Clinical factors are not helpful in predicting treatment outcome in MDD (Bagby, Ryder, & Cristi, 2002; Simon & Perlis, 2010) and a shift toward biomarkers is noticeable (Arns, Drinkenburg, Fitzgerald, & Kenemans, 2012). Biological markers (BMs) are defined as biochemical, physiological, or anatomical traits that are specific to particular conditions. BMs can be used as diagnostic tools and should have predictive power and allow the identification of individuals at risk. Past studies have revealed encouraging results for the therapeutic use of these techniques (Hahn et al., 2011; Schneider, Hampel, & Buerger, 2009) which can be grouped into three main categories: neuroimaging, electrophysiological, and neuroimmunoendocrine. A review of these three BM categories follows.

Neuroimaging was the most commonly used BM. Functional magnetic resonance imaging (fMRI), SPECT, positron emission tomography (PET), and magnetic resonance spectroscopy (MRS) are among the most frequently used

neuroimaging modalities. For instance, fMRI studies showed a bilateral reduction in task-related prefrontal cortex (PFC) activation as related to the AD effects of TMS (Fidalgo et al., 2014). fMRI, PET, and SPECT studies confirmed that TMS effect was associated with an increase in cerebral blood flow (CBF) at the site of stimulation and in connected limbic regions (Malhi & Lagopoulos, 2008; Rahmim & Zaidi, 2008). SPECT images after TMS stimulation in treatment-resistant patients showed a significant increase in CBF in the left DLPFC (Kito, Fujita, & Koga, 2008). Using MRS, specific brain metabolites such as F-aminobutyric acid (GABA) and glutamate (Thaker, 2008; Ziemann, 2011) can be investigated by examining the area under each peak produced. MRS showed that the baseline glutamate concentrations in the DLPFC were lower in responders than those for non-responders. After the treatment, these concentrations were elevated in responders and decreased in non-responders (Luborzewski et al., 2007).

Previous studies suggest that EEG could be used as a predictor for AD response to rTMS because they identified that increased low-theta power in the subgenual anterior cingulate cortex was associated with AD response (Narushima, McCormick, Yamada, Thatcher, & Robinson, 2010). TMS-indexed cortical excitability is a technique that utilizes a TMS approach to measure cortical excitability by assessing the integrity of central motor pathways (Kobayashi & Pascual-Leone, 2003). Single-pulse TMS can measure motor threshold and motor-evoked potentials (Bajwa et al., 2008; Kobayashi & Pascual-Leone, 2003), while the paired-pulse technique gauges intracortical inhibition or facilitation, indexing gabaergic and glutamatergic activity (Chistyakov et al., 2005). TMS may be an especially important marker to measure interhemispheric differences. In fact, there are studies which showed that patients with major depression presented interhemispheric differences in motor threshold with lower excitability in the left side, which may be related to an imbalance of neurotransmitters on left hemisphere of the brain (Crevits, Van den Abbeele, Audenaert, Goethals, & Dierick, 2005; Fidalgo et al., 2014).

Neuroimmunoendocrine factors proved to be promising BMs for the treatment response in MDD patients. Previous research studies showed serum cortisol may be a potential BM for TMS response and may also be useful to identify risk of relapse (Fleck et al., 2009; Gratacos et al., 2007). Brain-derived neurotrophic factor (BDNF) may provide a general index of neuroplasticity and it has been studied as a main marker to identify responders to TMS treatment (Fidalgo et al., 2014). There is a negative correlation between BDNF serum levels and the severity of the disease (Stipcevic, Pivac, Kozaric-Kovacic, & Muck-Seler, 2008). Research also showed that TMS was able to increase the serum BDNF levels in MDD patients. This data suggested a normalizing effect of the TMS treatment (Zanardini et al., 2006). Increased levels of hippocampal BDNF produced AD-like effects (Steingard et al., 2000), whereas an impairment of BDNF signaling produces depression-related symptoms and impairs ADs effects (Shirayama, Chen, Nakagawa, Russell, & Duman, 2002). Dopamine is responsible for the experience of pleasurable feelings and reward mechanisms and thus plays an important role in terms of MDD treatment response (Meltzer et al., 1998). The 5-HT systems of serotonin extend throughout the brain and disturbances in their pathways have been linked to impulsivity,

depression, and, in some cases, suicide and other violent behavior (Souery, Papakostas, & Trivedi, 2006). There is no clear relationship between clinical response and biochemical outcomes of dopamine and serotonin, but there are indications that observed improvement is partially attributed to the effects of TMS on the dopaminergic system (Kuroda et al., 2006). A study (Esel et al., 2002) showed a reduction in depression as well an association between TMS response and LH, FSH, and estradiol levels in women.

The significance of genetic variability and its influence in treatment responses is becoming an area to explore in the fields of genetic/epigenetic research. For instance, BDNF polymorphisms have a direct impact on the promotion of synaptic plasticity (Fidalgo et al., 2014). Therefore, biomolecular assessments intended to identify such genetic variations may become the foundation for personalized pharmacological and nonpharmacological treatments including neuromodulation (Fidalgo et al., 2014). It is also important to consider the role of cognitive performance as a functional marker in the treatment of MDD because cognitive dysfunction may also be a functional and therapeutic marker for disorders such as MDD (Zheng et al., 2010).

TCI and Its Use in Predicting MDD Treatment Response

Temperament and Character Inventory (TCI) is a psychometric instrument that assesses a seven-factor psychobiological model of quantifiable personality traits. These personality traits have been validated on the basis of genetic and neurobiological data. The TCI determines four temperament dimensions: Harm Avoidance (HA: measures fear and behavioral inhibition), Novelty Seeking (NS: exploratory and impulsive vs. reserved and stoical), Reward Dependence (RD: approval seeking vs. aloof), and Persistence (P: industrious and determined vs. lazy and underachieving). These dimensions are rooted primarily in various neurobiological data (Cloninger & Svrakic, 1997). Also described are three character dimensions—Self-Directedness (SD: modulates emotional conflicts such as being responsible and having determination), Cooperativeness (CO: helpful and empathic vs. hostile and aggressive), and Self-Transcendence (ST: creative and spiritual vs. alienated and skeptical). These dimensions develop mostly based on social learning (Cloninger & Svrakic, 1997).

All aspects of personality interact and influence an individual's susceptibility to depression (Cloninger, 1994). A large number of studies have been conducted to determine the clinical use of this personality theory in patients with MDD. In pharmacotherapy research, the TCI has been evaluated to examine its ability to predict clinical outcome in MDD (Kaneda, Yasui-Furukori, Nakagami, Sato, & Kaneko, 2011; Mulder, 2002; Newton-Howes, Tyrer, & Johnson, 2006). The temperament dimension HA and the character dimension SD have been related to depression, and these two dimensions are usually negatively correlated (Hansenne et al., 1999; Hirano et al., 2002; Nery et al., 2009; Spittlehouse et al., 2010). In general, MDD patients compared to healthy controls score higher on HA and lower on SD, and it

was also reported that successful treatment interventions may "normalize" the two TCI scales (Hirano et al., 2002). Furthermore, these two TCI dimensions have been reported to be indicative of treatment response in patients with MDD (Celikel et al., 2009; Cloninger, Svrakic, & Przybeck, 2006; Margetic & Jakovljevic, 2013). High pre-treatment levels of HA have been found to be correlated with response to selective serotonin reuptake inhibitors (SSRI); reduction in HA mediates the reduction in depressive symptoms in treatment responders (Joyce, Mulder, McKenzie, Luty, & Cloninger, 2004; Kampman et al., 2012; Quilty, Godfrey, Kennedy, & Bagby, 2010). Moreover, response to cognitive behavioral therapy has been found to be correlated with increased initial levels of SD (Johansson, Lyssarides, Andersson, & Rousseau, 2013), which further increase in responders.

Harm avoidance has been correlated with serotonin transporter polymorphisms (Mandelli et al., 2009) and has repeatedly been shown to predict response to serotonergic pharmacotherapy (Joyce et al., 2004; Kampman et al., 2012; Quilty et al., 2010). Furthermore, self-directedness has been correlated with response to cognitive-behavioral therapy in MDD (Johansson et al., 2013) and various other illnesses, such as obsessive-compulsive disorder and eating disorders (Corchs et al., 2008; Johansson et al., 2013). The use of the TCI should be explored further because it appears to be a good predictor for the treatment response and its use is easy and cost-effective compared to the cost of obtaining other BMs.

Previous research indicated that NS, RD, P, and ST are relatively stable over time (16 weeks) in patients with MDD, while HA, SD, and CO were significantly correlated to the level of depression. These dimensions (HA, SD, and CO) were greatly changed during an effective AD treatment, which suggests that these dimensions are dependent on state of depression (Hirano et al., 2002). Hirano and his collaborators' results suggested that both SD and CO were significantly affected by depression (Hirano et al., 2002). The timing of the administration of TCI during a depressive episode is very important because it may indicate a significantly elevated HA score and significantly decreased SD and CO scores (Hirano et al., 2002). Previous research (Akiskal, Hirschfeld, & Yerevanian, 1983; Hirschfeld et al., 1983) indicated that a depressive episode may cause long-lasting personality alteration and thus significant differences in HA between responders (after treatment) and controls (Hirano et al., 2002) may not even be a trait characteristic because it may only reflect the long-lasting personality alteration.

The findings related to predictive properties of certain TCI dimensions for clinical response in MDD have been inconsistent. For instance, HA scores were not indicative for clinical outcome in all AD trials (Marijnissen, Tuinier, Sijben, & Verhoeven, 2002; Newman et al., 2000). Research suggests that the lower scores on SD indicate that low SD may be associated with depression (Takahashi et al., 2013) and higher scores on SD predicted better clinical outcome (Joyce, Mulder, & Cloninger, 1994; Sato et al., 2001; Tome, Isaac, Harte, & Holland, 1997). Previous studies also suggest that SD and CO may be related to comorbid personality disorders (PD) in patients with mood disorders (Hirano et al., 2002; Svrakic, Whitehead, Przybeck, & Cloninger, 1993). MDD patients with comorbid PD may not be as responsive to treatment as patients without PD regardless of the chosen intervention

(Rosenbluth et al., 2012). These results raise interesting questions as to whether the TCI dimensions have the capability to distinguish responders and non-responders to an AD treatment and whether the initial scores on the TCI can accurately predict response to the AD.

Good Predictors of Positive Treatment Response to TMS

Although TMS on the DLPFC is an established antidepressant treatment, little is known about predictors of response. It is difficult to predict which patients will respond to TMS resulting in significant financial and time investment in TMS treatment (Siddiqi, Chockalingam, Cloninger, Lenze, & Cristancho, 2016). To address this concern, there have been efforts to identify predictors to TMS response. Current literature suggests certain clinical features are associated with higher response rates such as concurrent AD pharmacotherapy (Dumas, Padovani, Richieri, & Lancon, 2012), fewer earlier treatment failures, a shorter duration of the current mood episode, and absence of a concurrent anxiety disorder (Lisanby et al., 2009). Inadequate response to TMS treatment is associated with the use of benzodiazepine or anticonvulsant pharmacotherapy (Dumas et al., 2012). In addition to these above-mentioned predictors, some TCI dimensions have also predicted response to TMS (as well as pharmacotherapy and cognitive-behavioral therapy).

Current evidence suggests that persistence (P) is the only personality dimension which can predict TMS response. In one particular study, it was showed that P is independent of illness severity because it was not correlated with severity of depressive symptoms at baseline, while SD was directly correlated with depression severity at baseline (Siddiqi et al., 2016). Previous studies also demonstrated that MDD is associated with lower SD (Hansenne et al., 1999; Zaninotto et al., 2015). Using optical neuroimaging, it was found that P was inversely proportional to baseline left hemispheric motor cortical reactivity and this finding may help to understand the association of P with response to TMS (Ito, Fukuda, Suto, Uehara, & Mikuni, 2005). Since there is evidence that TMS enhances cortical excitability (Pell et al., 2011), patients with lower baseline excitability may be more likely to respond to TMS (Cheeran et al., 2008). According to the findings discussed in this paragraph, it is suggested that a high level of P may be a useful predictor to AD response to TMS.

Psychotherapy in Conjunction with TMS Treatment for MDD

TMS in conjunction with psychotherapy presents an effective adjunctive treatment for MDD. Previous research suggested that HF and LF TMS combined with psychotherapy resulted in an overall response rate of 77.8% (Arns et al., 2012). One study (Keller et al., 2000) demonstrated that psychotherapy combined with medication also resulted in a large response rate of 73%, whereas TMS treatment as a

monotherapy had a response rate of 48%. This data is impressive because most TMS studies involve participants with moderate to high treatment resistance, which is known to result in lower response rates (Fregni et al., 2006; George et al., 2010). Therefore, these results tend to be in line with results from combined psychotherapy and AD medication trials and further demonstrate the feasibility of combining psychotherapy and TMS treatment in clinical practice (Arns et al., 2012). Since TMS is a passive treatment, some investigators have administered psychotherapy in conjunction with TMS while the patient is undergoing TMS therapy (Vedeniapin, Cheng, & George, 2010). It could therefore be hypothesized that a more personalized approach to the treatment of MDD patients with TMS should mostly also include its combination with psychotherapy.

Personalized TMS Treatment

Psychotherapy in conjunction with standard treatments for MDD, AD medications, and TMS was shown to improve treatment response and remission rate compared to AD monotherapies (Keller et al., 2000). The rates of response of AD monotherapies were similar (approximately 50%), but the standard AD treatments in conjunction with psychotherapy has a response rate over 70% (Keller et al., 2000). According to the existing data, the combination therapy is superior over AD monotherapy and provides a clinically meaningful advantage. Cognitive behavioral therapy (CBT) is supported by research, and it is considered to be an evidence-based approach for the treatment of MDD (Anderson et al., 2002). Previous research suggested CBT may change brain function and even brain structure. There are indications that TMS stimulation of the prefrontal cortex might synergistically reinforce effects of CBT by increasing resilience (Vedeniapin et al., 2010). Psychotherapy, particularly CBT, might help individuals with depressive symptoms by meeting personal needs and addressing specific personal problems. Thus, the standard AD treatments in conjunction constitute a personalized and promising form of the treatment for MDD.

Besides psychotherapy, we should think about other available approaches that might even further improve TMS treatment by making it tailored to personal needs. As we mentioned earlier in this chapter, there is evidence that biological, psychological, and social factors interact and play a significant role in contributing to MDD. Therefore, we hypothesize that a person-centered well-being coaching might be another effective treatment option in conjunction with TMS for MDD. One such system is the Know Yourself coaching and DVD series. This integrative approach is a holistic method that integrates biological, psychological, and social approaches to increase self-awareness and provides individuals with tools to strengthen their resilience in all domains of their lives (Cloninger, 2006). This type of coaching has been shown to reduce mental illness as well as increase well-being and resilience (Cloninger, 2013; Cloninger & Cloninger, 2011). It involves a structured and manualized approach to well-being that utilizes a series of prerecorded DVDs that describe a multi-pronged positive psychological approach to personal growth,

depression, and distress. As a pilot observational and feasibility study, the authors have played KY DVDs concurrently to patients while they are receiving TMS treatment. The authors' clinical observations and the patient testimonials and requests have been very encouraging to conduct controlled studies to test this hypothesis.

Future Research

The "personalized medicine" approach to depression is becoming broadly accepted (Williams et al., 2011). As a key component of this approach, both genetic and neuroimaging biomarkers have been explored and both are showing promising results in aiding treatment prediction using pre-treatment measures (Williams et al., 2011).

Personality assessment may be a useful component of precision medicine initiatives in TMS use for depression. Future studies examining the clinical effects of TMS treatment paradigms in refractory MDD may do well to screen for possible PD. Therefore, more studies involving TCI as an effective clinical tool to screen for PD are needed. Furthermore, follow-up studies are needed to evaluate whether the relatively lower scores in SD even in HF TMS responders are predictors of relapse for another MDD episode. Studies suggest that identifying a high level of P may be a useful tool for determining which patients are likely to respond to TMS. These findings should be further confirmed by future studies with larger participant numbers. Future research should include baseline neuroimaging to prospectively investigate the relationship between TMS response, persistence, and cortical excitability.

Conclusion

In summary, TMS is a promising, novel antidepressant treatment relatively early in its development. Its efficacy and safety have improved significantly with continued research and clinical experience. The effect size for TMS antidepressant response is at least comparable to those of AD medications. This evidence base has satisfied the critical thresholds for FDA clearance and approval of coverage by most third-party payers in health care. Further, there is a signal that TMS may benefit certain subgroups of patients who previously would be referred for ECT. Finally, the durability of AD benefit of TMS and its safety and tolerability profile make it an attractive treatment option for selected patients. Although TMS is labor intensive compared with medications, its efficacy, safety, and tolerability for depression and possibly other disorders are driving additional research to refine and improve its therapeutic potential. Thus, TMS has promise that it can be refined and enhanced to become more person-centered. Along with the TCI, biomarkers such as fMRI, EEG and plasma BDNF can be further refined to be good predictors for TMS patient selection and treatment response. The TCI can be utilized in clinical practice as a way to

identify who would benefit from TMS treatment and to help with screening for PD to identify a subgroup of patients who are not likely to respond to standard MDD treatments. TMS in conjunction with psychotherapy is proven to be more effective than either medication or TMS treatment alone. Therefore, more personalized TMS treatment involving BM and a biopsychosocial therapy approach might be an answer for treating MDD effectively with a personalized medicine approach.

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Person-Centered Schools

Paulo A. S. Moreira and Danilo Garcia

Abstract *Background*: Technological and material resources are available for humans at an unprecedented level, and yet a significant percentage of the population report some degree of subjective suffering, functioning impairment, or medical ill-being associated with patterns of maladaptive psychosocial functioning/lifestyles. This suggests that there is a vital need for new approaches to promoting human development. School is one of the most powerful contexts for implementing such approaches. However, a new paradigm in education is required to help schools be more efficient at preparing their students to deal adaptively with the challenges facing humanity. Schools need to be able to promote the processes underlying human holistic development, rather than emphasizing the development of mainly logical-propositional dimensions, as is the case of materialistic-oriented conventional schools.

Aims: In this chapter, we argue for two points: (1) personality development is a core dimension of holistic development and (2) the most promising pathway for societies to promote a holistic development in youths is to shift towards person-centered schools. Although the need for person-centered schools was advocated decades ago, we argue that its relevance is more evident at present because of the availability of new research findings. We put conventional and mainstream schools in perspective; we revisit the classical concept of person-centered schools and review evidence supporting the need for person-centered approaches for contemporary and short-term future schools.

Conclusions: School is an ideal context for implementing a holistic approach to the promotion of human functioning. However, the effectiveness of any means

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aiming to promote positive adaptation in (person-centered) schools depends on intentionality, coordination, systematization, continuity, evaluation, and monitoring. We need to develop and test coherent frameworks that describe the common factors, and dynamics amongst them, involved in changing conventional schools to person-centered schools. This process is in its embryonic phase and is one of the current main challenges for research and practices of behavioural sciences. If done effectively, it will have substantial implications, not only for individuals' well-being, but also for societal organization and development.

Keywords Person-centered · Education · Schools · Personality · Holistic · Development

Being Human in Technological Contexts: The Quest for Positive Adaptation

Societies are changing at an exponential rate, and today we exist within societies that are profoundly different to what they were in the not-too-distant past. The reality that our parents experienced as children is likely to be somewhat different from the reality that we ourselves experienced, and this effect is likely to be amplified for our own children. Indeed, the current pace of change leads to substantial differences in societies, not across generations as it might once have been but within single lifetimes. Those of us who are adults should have no difficulties identifying considerable differences, at various levels, between the characteristics of contexts, technology, routines, values, or societal dynamics of our childhoods and those of our present. Such rapid changes can be attributed to the ever-increasing capacity of humans to develop technology, to alter environments, and, ultimately, to construct or shape reality. This exponential complexification of society has consequences at multiple levels, but at the level of preparing young people for the future, we can synthesize these into two major adaptation challenges:

(a) Many of the jobs that exist today did not exist a decade ago, and many of the children who are currently in school will have jobs that do not exist now (European Commission, 2017). The instrumental capacities and knowledge required by individuals to make appropriate use of the products of human action, and thus to move adaptively in societies, must satisfy the most basic needs of performing functions to guarantee sustenance.
(b) Young people are exposed to an exponential (and often toxic) increase in information, opportunities, and possible selves in an extremely volatile and globalized world. There is thus a need for them to develop psychobiological organizations and lifestyles that foster a coherent and harmonious perspective of their multiple possible selves in an identity that favours positive adaptation.

In short, the challenges faced by young people are to keep up with the pace of rapid societal change, to deal with exposure to a huge amount of information, and to allocate internal resources to meet the challenges for instrumental adaptation.

Simultaneously, young people need to allocate resources and actively engage with individual well-being and happiness, and the common good, which implies a respect for others and the environment.

Society and School Change: Are They on the Same Page?

Historically, there have been essentially two types of knowledge and accumulated knowledge transmission. The first, and oldest, is the most instrumental. This principally concerned learning about the most effective ways to solve survival problems at a level of concrete experience and a level of procedural learning. The second has crystallized over time, with increasing levels of abstraction made possible by the development of systems of symbolization (writing) and the means of easy reproduction of information.

Education and school as a mass phenomenon as we know it today has resulted from an appreciation of the need to integrate these two types of knowledge to prepare children for adult life.

Indeed, the history of education and schooling can be thought of as the story of how societies have understood and achieved the integration of these two components. The massification of education was originally justified as a means to satisfy the need for individuals to occupy a profession. This was considered vitally important since, once achieved, employment was expected to lead to the satisfaction of other needs. Indeed, it was via this logic that education was affirmed as a universal societal priority and the replacement for a scholastic tradition of transmitting accumulated knowledge to a certain historical point, which, for most of human history, had been limited to a restricted elite of individuals.

Contemporary schools are now at a crossroads. There is a need to reconcile the transmission of knowledge acquired by previous generations with the need to keep up to date with, and simultaneously transmit, the knowledge being obtained in the present. This is vital for two reasons. Firstly, doing so has the potential to contribute to the change of reality in a short space of time (indeed, within such as short timeframe that those who think about education consider it in terms of what they themselves have learned, but at a time when this is already outdated). Secondly, such a reconciliation should extend the scope of education beyond the transmission of knowledge of facts and to a recognition that the development of the individual as a whole (including holistic health) is at least as worthy of being an object of education as the traditional dimensions. Factors that were once seen as the responsibility of other areas (health, spirituality, etc.) now need to be integrated into education. Schools must assume themselves as platforms of excellence for integrating these various dimensions and promoting an integrated development.

In an attempt to respond to the challenges of today's societies, schools have confused the expression of the specialization of areas or domains of functioning (thematic areas, problems, contents) with the processes underlying this expression. Schools need to make an effort to understand that preparing individuals for

successful adaptation requires less focus on specific outcomes (which are circumstantial and can take different forms) and more on the underlying processes that mediate the individual's expression in context (with plasticity for adaptation to various contexts).

With an exponentially complexifying society, the challenges that individuals face become more complex and more numerous. These challenges, in turn, challenge schools from their essence (conception) to their practices. Of course, the needs of students might be met by alternative methods (homeschooling, sole responsibility of the family, or other modalities). It is possible, in the future, that societies organize themselves differently, and it is highly likely that in the near future there will be a greater expression of hybrid models (between school and homeschooling). But regardless of how evolution happens, this does not dispense with the need to question schools as they currently are, or will be, in the near future. On the contrary, it makes the need to rethink current schooling more evident. How we run schools today in order to satisfy current needs is of great relevance for the social construction of reality and societies (as described by constructivism and social constructionism) in terms of the development of trends for the future.

Despite the great transformations that we have witnessed, at least two certainties remain. One of the main challenges for human beings remains adaptation, and this process of adaptation is not a given, rather a process that benefits from learning. The school has become increasingly important in the process of preparing individuals for successful adaptation, but as societies become more complex and challenging to the process of successful adaptation, schools need to adapt.

There is a growing consensus about the need for a paradigm shift in education, and several authors have recently emphasized that this is urgent. As just two examples, Jacobs (2015) suggests that this change needs to be made at several levels: rediscovering pedagogy, restoring life to education, trans-disciplinarity, reuniting life and knowledge, values-based education, conception of knowledge, and person-centered education. Similarly, for Harish (2015), education needs to redefine its purpose, make students the subject, and highlight the value of values. In short, there is a growing agreement across different scientific disciplines that a new humanism is needed to aid individuals in their quest to adapt to current societies (e.g. Cloninger, 2004; d'Orville, 2015).

Humanism Person-Centered Approaches

> We are, in my view, faced with an entirely new situation in education where the goal of education, if we are to survive, is the facilitation of change and learning. The only man who is educated is the man who has learned how to learn; the man who has learned how to adapt and change; the man who has realized that no knowledge is secure, that only the process of seeking knowledge gives a basis for security. Changingness, a reliance on process rather than upon static knowledge, is the only thing that makes any sense as a goal for education in the modern world. (Rogers, 1969, p. 104)

In an ever-changing world, the need for individuals to adapt to their realities calls for education at school, from the individual to macro/societal level of conceptualization,[1] to be dynamic and flexible. Fortunately, this is made possible for a number of reasons. Firstly, humans are malleable, both as objects and agents of change, meaning that education is amenable to intervention in terms of policy and decision-making. Secondly, education is a powerful tool for influencing human development, and a structural vehicle for societal evolution and human differentiation. Thirdly, education is a socially constructed phenomenon meaning (a) its characteristics are defined by policies and (b) that educational agents define and implement school strategies and practices. These three reasons allow for a certain degree of optimism concerning our current and future generations of students: at least to some degree, their ability to adapt to the ever-changing world depends on us. But if this (the fact that educational agents can exert a significant role in shaping the development of societies) seems like good news, it comes with a big responsibility. We argue there is an ethical, moral, and possibly even legal responsibility to rely on scientific evidence for defining educational policies and strategies. As we will describe later in this chapter, such evidence comes from a number of different behavioural disciplines, but all converge on the conclusion that schools need to be person-centered schools. Prior to that, however, we shall consider person-centered schools in more detail.

As a first point, person-centered approaches to education are not new. Carl Rogers (1902–1987) and Abraham Maslow (1908–1970) were both important proponents of a paradigmatic shift in the conception of the human being at the level of the psychological self. At a time when the different therapeutic approaches tended to value aspects of psychological functioning (unconscious aspects and early experiences for psychoanalysis, behaviours for behaviourism, cognitions, and representations of reality for cognitivism), the proposal that the understanding of human functioning required a consideration of the individual as a whole, humanism, was both bold and visionary. Humanism combines elements of two major philosophical perspectives with psychology theory. The first perspective, existentialism, emphasizes the responsibility of the individual – a result of an awareness of reality – and that more than any kind of determinants the individual constructs himself (Kierkegaard, 1959; Sartre & Mairet, 1960). The second, phenomenology (e.g. Husserl, 1970), emphasizes subjective experience and the objective study of subjective phenomena, of which phenomena and psychological processes are an example.

In summary, the individual and his/her development require the holistic understanding of all different dimensions. The Gestalt theory (and its assumption that the whole is different from the sum of its parts, Köhler, 1947, 1959) has influenced the emphasis on the consideration of the individual as a whole. Human beings have a set of basic and instinctive needs, hierarchically organized, and their satisfaction leads to personal fulfilment (Maslow, 1975, 2013). Actualization refers to the natural and innate tendency, common to all organisms, to develop one's capacities in

[1] Please refer to Table 6 for a consideration of the different levels of conceptualization.

order to maintain and improve one's current state of being. In humans, this concretizes as self-actualization: the motivation to try to reach ones full potential and achieve a better life (Rogers, 1969, 2012a, b). This process of self-actualization tends to be spontaneous, but requires three conditions, which, if necessary, are also sufficient: empathy, positive regard, and congruence. For Rogers, being in an environment offering these common factors should guarantee self-actualization (although Maslow considered that this result was only reserved for some individuals). Indeed, Rogers applied this approach to education in his book *Freedom to Learn: A View of What Education Might Become* (Rogers, 1969) in which he emphasized the role that education could play in promoting the self-actualization of students.

In Table 1, Rogerian foundational assumptions, objectives, and means of person-centered approaches applied to education imply specific pedagogic approaches to teacher classroom management (Table 2) and learner-centered principles (Table 3).

From Person-Centered Approaches to Person-Centered Schools

So, what is new about current person-centered approaches applied to education? Unlike when Rogers and Maslow made their proposals, we now live in an era where a robust body of evidence from different scientific disciplines is available. Moreover, this research evidence mainly supports the assumptions and principles of person-centered approaches. In Table 4 we present a synthesis of such by levels of evidence, and then briefly elaborate on each type.

1. *The person-centered approach (and its assumptions and principles) has received a substantial amount of evidence when applied to a wide range of contexts and phenomena.*

The person-centered approach emerged from the client-centered approach and developed as an alternative to the existing, more expressive, approaches to psychotherapy (especially behaviourism and psychoanalysis, and later cognitivism). However, it rapidly evolved into a theory of personality development, and remains one of the most relevant theories of human and personality development. Its application has been expanded to a wide range of contexts, and its assumptions and principles have been gradually applied to learning, education, schools, organizations, all kinds of helping relationships, and more recently the field of medicine. Person-centered approaches have been highly prevalent in science and professional practice, a status highlighted by Kirschenbaum and Jourdan's (2005) meta-analysis of the large quantity of books, book chapters, and scientific journal articles published on the topic since the works of Carl Rogers, and the existence of hundreds of person-centered organizations around the world. That said, person-centered approaches are undergoing a new revival in light of recent developments, particularly

Table 1 Rogerian assumptions, objectives, and means of person-centered schools

Assumptions
Human beings are complex and their functioning involves dynamic and interconnected systems that need to be seen from a holistic perspective. Humans are individuals with needs at different levels, including psychological needs. Individuals have, within themselves, innate resources for self-actualization and for reaching their full potentials (which refers to a continuous process of self-understanding, updating and changing self-concepts, basic attitudes and personal agency mechanisms or self-directed behaviour). As relational beings, self-actualization occurs within the context of interpersonal contexts. Facilitative interpersonal contexts are characterized by relationships where the conditions for the satisfaction of psychological needs are provided. These facilitating conditions are a necessary condition for humans to develop adaptively, but when present, are also sufficient for self-actualization. These conditions are empathy, unconditional positive regard, and genuineness/congruence. These imply nondirective relationships, valuing processes and subjective experiences (at several levels, including emotional, cognitive, behavioural, and spiritual), and valuing positive aspects of the individual. Applied to learning and education, individuals learn and teach better when within interpersonal contexts characterized by reciprocal empathy, warmth, and congruence amongst their members
Objectives
To build interpersonal contexts with others that offer the conditions for development and self-actualization. In other words, to create interpersonal contexts that allow individuals to express themselves in all their levels of functioning (from a holistic perspective) and to experience reality in a secure environment, in order to learn and grow by integrating all the aspects of existence into a unique self and identity
Means
The most powerful means are the positive, respectful, and caring relationships between teachers and students. These are characterized by three types of attitudes: *Educator is empathic*: Educator understands the student's subjective experiences (emotions, cognitions, behaviours, and meaning making, including identity uniqueness) and communicates in an explicit, simple, and delicate way to the student that his or her subjective experiences are understood *Educator is warm and accepting*: Educator accepts students' subjective experiences in an unconditional way. The educator has a non-judgemental attitude towards students' characteristics and experiences; has a sincere interest, care, and appreciation of students' levels of experience (including subjective states); and unconditionally accepts and respects all the students' experiences and attitudes. The educator believes that – as self-actualizing human beings – students are trustworthy in their capacities and therefore gives the physical and relational "space" for students' experiences and the self-growth resulting from learning at all levels of experience *Educator is genuine/congruent*: Educator is in touch with his/her own subjective experience and internal states. The educator is aware of, and accepts, his/her own reality (without distortion or defensiveness) as a whole person, which allows him/her to relate with others in a way that is congruent with his/her own holistic experience (including emotions, cognitions, behaviours, and identity). The educator is honest with the students, which in turn becomes a stimulus (both as a feedback or an element of reality) for students to integrate into their own experiences

From (Rogers, 1959, 1969, 2012a, 2012b; Rogers, Lyon, & Tausch, 2013)

Table 2 Classroom management and learning facilitator principles

Learning facilitator principles
The teacher promotes the construction of a positive relational environment and facilitates the expression of students' experiences
The teacher creates an environment conducive to learning by identifying and accepting the goals of each member of the class (even if they may seem antagonistic or conflicting)
The teacher considers and stimulates the interests of each student as a motivator for learning
Organizes educational resources (at the level of different domains of operation) to be explored by the students
The teacher is a resource at service to the group
The teacher values and considers the different types of student reaction, both intellectual and affective
The teacher must be particularly attentive to forming deep and affective reactions to promote a climate of unconditional acceptance and express acceptance, trust, and respect
The teacher can express personal opinions in the relational climate of unconditional acceptance
The teacher accepts when sharing their feelings and thoughts (in an egalitarian design of roles) that students can accept or reject them
The teacher is conscious of their own characteristics, including limits, and accepts them

Note. Adapted from Freiberg and Lamb (2009)

those concerned with the application of person-centered approaches to medicine and health care.

The theory is that interpersonal relationships characterized by unconditional positive regard, empathic understanding, and congruence offer individuals the necessary, but sufficient, conditions for positive personality change. After decades of research, this hypothesis has been supported in full by an impressive amount of evidence, particularly concerning the principles of empathy and unconditional positive regard (Kirschenbaum & Jourdan, 2005). Indeed, a meta-analysis of studies–especially those related to the efficacy of psychotherapy – has confirmed that relationships are a core component of therapeutic change, regardless of the theoretical model used, and there is a growing body of evidence indicating that relationships are a common factor across different modalities of psychotherapeutic approaches (Norcross, 2002; Lambert, 2005; Wampold & Imel, 2015). Such findings are contributing to theoretical integration and technical eclecticism, not only across psychological models but across scientific disciplines.

2. *Growing consensus about the need for multiple-system transdisciplinary approaches (holistic perspective) in behavioural sciences.*

Contemporary schools are products of the first, second, and third industrial revolutions. They are, therefore, strongly influenced by the notion of individuals as predominantly rational beings, and subsequently assume this rationality is responsible for a large part of human adaptation, even in contemporary societies. Because of this assumption, educational policies and school practices are still frequently oriented towards prioritizing the promotion of rational components. This can account for the common emphasis on logical-propositional knowledge, which is considered

a central component of providing students with the resources required to survive (i.e. via working and earning an income). It has also led to a conception of human beings as rational actors, or what Gintis conceptualized as beliefs, preferences, and constraints (the BPC model). However, as Gintis himself highlighted, the BPC model's conception of human beings is inadequate because it relies on several misconceptions. Indeed, contrary to the BPC, individuals do not have unlimited rationality, decision-makers are not consistent (substance abuse disorders are prime

Table 3 Learner-centered psychological principles

Factors	Principles
Cognitive and metacognitive factors	*Principle 1: Nature of the learning process* The learning of complex subject content is most effective when it is an intentional process of constructing meaning from information and experience *Principle 2: Goals of the learning process* The successful learner, over time and with support and instructional guidance, can create meaningful, coherent representations of knowledge *Principle 3: Construction of knowledge* The successful learner can link new information with existing knowledge in meaningful ways *Principle 4: Strategic thinking* The successful learner can create and use a repertoire of thinking and reasoning strategies to achieve complex learning goals *Principle 5: Thinking about thinking* Higher-order strategies for selecting and monitoring mental operations facilitate creative and critical thinking *Principle 6: Context of learning* Learning is influenced by environmental factors, including culture, technology, and instructional practices
Motivational and affective factors	*Principle 7: Motivational and emotional influences on learning* What, and how much, is learned is influenced by the learner's motivation. Motivation to learn, in turn, is influenced by the individual's emotional states, beliefs, interests and goals, and habits of thinking *Principle 8: Intrinsic motivation to learn* The learner's creativity, higher-order thinking, and natural curiosity all contribute to motivation to learn. Intrinsic motivation is stimulated by tasks of optimal novelty and difficulty, relevant to personal interests, and providing for personal choice and control *Principle 9: Effects of motivation on effort* Acquisition of complex knowledge and skills requires extended learner effort and guided practice. Without learners' motivation to learn, the willingness to exert this effort is unlikely without coercion
Developmental and social factors	*Principle 10: Developmental influences on learning* As individuals develop they encounter different opportunities for, and experience different constraints on, learning. Learning is most effective when differential development within and across physical, intellectual, emotional, and social domains is taken into account *Principle 11: Social influences on learning* Learning is influenced by social interactions, interpersonal relations, and communication with others

(continued)

Table 3 (continued)

Factors	Principles
Individual-difference factors	*Principle 12: Individual differences in learning* Learners have different strategies, approaches, and capabilities for learning that are a function of prior experience and heredity *Principle 13: Learning and diversity* Learning is most effective when differences in learners' linguistic, cultural, and social backgrounds are taken into account *Principle 14: Standards and assessment* Setting appropriately high and challenging standards and assessing the learner and learning progress (including diagnostic, process, and outcome assessment) are integral parts of the learning process

Note. Summarized from APA Work Group of the Board of Educational Affairs (1997)

examples of the inconsistencies between choice and well-being), and individuals are faulty logicians, amongst others (Gintis, 2007, 2014). In other words, by promoting logical-propositional knowledge only, and thus neglecting other functioning dimensions, schools adopt a philosophy consistent with Cartesian "mind/body" dualism, which is evident in other dualisms such as emotion/cognition, facts/values, and the academic and so-called soft skills.

Concerning education and the impact that school actions have on individual functioning, research evidence demonstrates that there are reciprocal influences between education processes and outcomes at several levels: better health, better social organization and functioning, and less crime (Blundell, Dearden, Meghir, & Sianesi, 1999; Checchi, 2006; Cutler & Lleras-Muney, 2006; Lochner, 2011; Psacharopoulos, 2014; Von demKnesebeck, Verde, & Dragano, 2006) amongst others. Empirical evidence concerning the dynamics and mutual influences of different systems on individual functioning is also available for educational- and school-related processes and outcomes. Examples include the influence of gene-environmental interactions on education (Keltikangas-Järvinen et al., 2008); interactions between emotion, cognition, and performance (Pekrun, 2006); and the ability of psychobiological organizations (e.g. persistence and self-directedness) to predict academic processes and outcomes (Duckworth & Seligman, 2005; Moreira et al., 2012) and improve the likelihood that students from under-resourced high schools will graduate (Eskreis-Winkler, Duckworth, Shulman, & Beal, 2014).

As a result of this evidence, there is a growing consensus about the need for a multiple-systems transdisciplinary approach that incorporates perspectives from fields such as genetics, neuroscience, developmental epidemiology, contextual behavioural science, environmental sciences, and professional practices (Fishbein & Ridenour, 2013). However, contributions from different disciplines need to be integrated in coherent frameworks that allow for a more holistic understanding of phenomena. Recently, there has been a movement towards disciplinary integration, and this need becomes increasingly evident (Gintis, 2007, 2014). An integration of knowledge from different disciplinary areas is the basis for what has been called intentional change (Wilson, Hayes, Biglan, & Embry, 2014). The most striking support for this is that advances in different areas are converging on a consensus that a

Table 4 Person-centered schools. Levels of evidence that support the need of person-centered schools

Disciplinary integration	1. The person-centered approach (and its assumptions and principles) has received a substantial amount of evidence when applied to a wide range of contexts and phenomena
	2. Growing consensus about the need for multiple-system transdisciplinary approaches (holistic perspective) in behavioural sciences
Conceptual, theoretical, and methodological tools	3. Substantial advances in concepts, constructs, and theory have been made, and we now have a larger number of more accurate conceptual tools suited to capturing phenomena underlying holistic functioning
	4. Substantial advances have been made in methodological and analytic tools, which allows for a more reliable description of the phenomena underlying holistic functioning
Subjective experience	5. Academic indicators are better understood when conceptualized as processes rather than outcomes
	6. Student academic performance is better understood when considering individuals' subjective experiences, rather than focusing on objective indicators
Holistic functioning	7. Learning (including knowledge about facts and logical-propositional processes) is influenced by the interactions amongst different dimensions, including physical, emotional, and social dimensions (and not by rational ones only)
	8. Non-cognitive (logical-propositional) dimensions are strong predictors of multiple functioning domains, health, and death
Positive aspects of holism	9. Adaptive development benefits from an emphasis and promotion of positive dimensions and strengths, rather than focusing on deficits
	10. There are substantial individual differences in positive functioning and strengths
	11. Positive functioning is amenable to intervention
	12. Positive development is multidimensional and needs to be conceptualized in terms of dynamic organizations resulting from the non-linear interactions amongst different domains of functioning
School characteristics	13. School characteristics matter: different school dimensions have different effects on different functioning domains
	14. School-based interventions for the promotion of positive functioning and strengths are effective
	15. The most efficient school-based interventions for the promotion of positive functioning/strengths are multidimensional
	16. School-based interventions promoting non-academic skills have a positive and significant impact on learning, including classic indicators of academic performance
Importance of the relation	17. Relationships matter: Relationships are the school characteristic with the most powerful effect on students' processes and outcomes
	18. We better understand that teachers' functioning also matters and that it impacts on the youth development
	19. Different teacher characteristics have different effects on students' functioning domains

(continued)

Table 4 (continued)

School professional development	20. Scientific and professional organizations acknowledge the need for person-centered approaches and principles: integrating person-centered principles as common factors for different scientific disciplines and professional activities
	21. Professional roles of the short-term future require psychological plasticity from individuals more than the acquisition of conventional academic contents
Educators need expertise on behaviour sciences	22. Education and school efficacy require scientific knowledge and expertise and highly specialized professionals
Global sustainability	23. Global development and sustainability (including world order, social organization, and planet sustainability) depend on individuals' holistic development

complete understanding of human behaviour requires a holistic conception of human functioning.

In short, because of the importance that education and schools have for human development, we need to ensure that existing schools keep up to date with available knowledge. Such knowledge includes current conceptions of human beings (where multiple systems interact dynamically) and schools (with a need to incorporate and integrate contributions from different disciplines).

3. *Substantial advances in concepts, constructs, and theory have been made, and we now have a larger number of more accurate conceptual tools suited to capturing phenomena underlying holistic functioning.*

There has been a proliferation of approaches to non-cognitive individual characteristics from different research traditions. Examples include emotional intelligence, character, social-emotional skills, social learning, competences, strengths, positive development, personal qualities, non-cognitive attributes, and virtues. This increase serves as an indicator of the growing interest by different disciplinary traditions in human functioning and allows for a more fine-grained holistic analysis of the positive aspects of human functioning. Unfortunately, it also presents a challenge for the integration of research into a coherent, multidimensional, and multidisciplinary understanding of human development.

Research has also allowed for the development and testing of more holistic and more specific theoretical models. These are of two kinds. The first are frameworks derived from person-centered principles and assumptions, including the learning-centered model (e.g. Cornelius-White, Hoey, Cornelius-white, Motschnig-Pitrik, & Figl, 2013) or self-determination theory. According to self-determination theory, individuals have basic psychological needs (relatedness, competence, and autonomy) that need to be fulfilled for individuals to have a healthy psychological development and to be psychosocially adapted (Deci & Ryan, 2012). Adaptive student functioning requires that schools can provide the necessary conditions (including activities, positive relationships) for students to fulfil their needs for relatedness (support from others, acceptance, and warm interactions), autonomy (sense of

agency, opportunities, and control over decisions), and competence (self-perceived competence, self-efficacy, and self-regulation). Students tend to be engaged in activities and contexts that provide the conditions for the fulfilment of these psychological needs (Jang, Reeve & Deci , 2010).

The second are theories consistent with a holistic perspective of human functioning. The bio-ecological theory of human development (Bronfenbrenner, 2005) highlights the importance of school as an important developmental context that exerts a significant impact on student development. This impact occurs via the interactions between the most proximal processes within school, the teacher-student and student-peer interactions. Models addressing sociocultural inequalities on health and education posit that individual functioning refers to, and results from, dynamic and malleable selves that are modified by the interactions between individual and sociocultural dimensions, including interpersonal dimensions (Stephens, Fryberg, Markus, Johnson, & Covarrubias, 2012). Interactionist frameworks highlighting the dynamics between individual and contextual characteristics have been also proposed. These include regulatory fit theory (Higgins, 2006) and expectancy-value theory (Eccles & Wigfield, 2002), which suggest that adaptive/maladaptive development and functioning depends on the fit between individuals psychological needs and school conditions to meet them (Ames, 1992; Lau & Nie, 2008; Peng, Cherng, & Chen, 2013). Finally, Cloninger's psychobiological model of personality, which is a model specific to personality, is consistent with the assumptions and principles of person-centered approaches such as holism (it integrates contributions from behavioural genetics, neurosciences, psychology, and psychiatry) and the role of therapeutic relationships or alliance in the description of human personality (Cloninger, 1999; Cloninger, 2004).

4. *Substantial advances have been made in methodological and analytic tools, which allows for a more reliable description of the phenomena underlying holistic functioning.*

The interaction between individual and contextual characteristics (especially interpersonal contexts) is at the core of the person-centered approaches. Over recent decades sufficient methodological and analytical advances have been made for researchers to have a variety of good tools for capturing interactionist phenomena.

Individual-centered research approaches are relevant methodologically and analytically because they have made substantial contributions to the more prevalent and traditional variable-centered approaches (Hayenga & Corpus, 2010; Laursen & Hoff, 2006; Moreira, Dias, Vaz, & Vaz, 2013; Muthén & Muthén, 2000). The use of individual-centered approaches is expanding, evident by the growing amount of publications describing research using person-centered approaches, particularly in the educational sciences (Moreira et al., 2013; Murdock & Miller, 2003; Wormington & Linnenbrink-Garcia, 2017).

Multilevel analytic approaches, which are relatively new, allow for researchers to estimate the effects of individual and contextual characteristics (and the interactions amongst them) as a means to understanding human development processes and outcomes (e.g. Raudenbush & Bryk, 2002). The use of these methodological and ana-

lytical techniques allows for a more reliable description of the multilevel effects and interactions involved in human and personality development. Studies using such techniques have, for example, offered an empirical validation of the importance of teacher-student relationships to positive student development in school contexts (Lee, Dedrick, & Smith, 1991; Lee & Burkam, 2003; Lee & Smith, 1999; Moreira, Dias, Matias, Castro, Gaspar, & Oliveira, 2018; Wang & Fredricks, 2014, Wang & Eccles, 2012, Wang & Eccles, 2013).

5. *Academic indicators are better understood when conceptualized as processes rather than outcomes.*

There has been a marked shift from an emphasis on academic outcomes to an emphasis on academic processes. In other words, there is a general consensus that education and school processes and outcomes are better conceptualized as developmental phenomena. Rather than being static and discrete products of individual processes, educational outcomes are better conceptualized as developmental trajectories. In the same manner as developmental cascades, academic trajectories are *cumulative consequences for development of the many interactions and transactions occurring in developing systems that result in spreading effects across levels, among domains at the same level, and across different systems* (Masten & Cicchetti, 2010, pg. 491). Academic trajectories are also malleable and sensitive to several influences, including the influences of other processes, the influence of time (e.g. maturation of psychobiological processes), and the cumulative and cascade effects over time and contexts (Haller, Handley, Chassin, & Bountress, 2010; Masten et al., 2005; Moilanen, Shaw, & Maxwell, 2010; Swanson, Valiente, & Lemery-Chalfant, 2012; van Lier, & Koot, 2010).

6. *Student academic performance is better understood when considering individuals' subjective experiences, rather than focusing on objective indicators.*

In recent years, there has been a marked shift from an almost exclusive emphasis on objective outputs (academic performance and related outcomes, such as school dropout) to an acknowledgement of the importance of students' subjective experiences towards school (Appleton, Christenson, & Furlong, 2008; Fredricks, Blumenfeld, & Paris, 2004). A paradigmatic example of this is the construct of student engagement with school, which has received growing attention from researchers across different educational sciences (Christenson, Reschly, & Wylie, 2012) from around the world (e.g. Virtanen et al., 2017). Research also shows that this subjective experience has dynamic and reciprocal interactions with other psychological processes such as behavioural problems (Wang & Fredricks, 2014) and well-being (Lewis, Huebner, Malone, & Valois, 2011; Upadyaya & Salmela-Aro, 2013). These interactions are sensitive to contextual characteristics (Salmela-Aro, & Upadyaya, 2014). Moreover, students' subjective experiences towards school are the strongest predictors of academic performance and school dropout (Archambault & Dupéré, 2017; Lee, 2014; Lee, & Burkam, 2003), and are amenable to intervention. Indeed, they are one of the promising factors for the early prevention of maladaptive academic trajectories and for the promotion of improvement of processes

and outcomes in low achievers or students with prior poor academic performance (Moreira et al., 2018).

7. *Learning (including knowledge about facts and logical-propositional processes) is influenced by the interactions amongst different dimensions, including physical, emotional, and social dimensions (and not by rational ones only).*

Learning (broadly understood) and educational/school processes and outcomes are multidimensional – a result of the dynamics amongst different systems and dimensions (Credé & Kuncel, 2008, Moreira et al. 2013; Mullis, Rathge & Mullis, 2003). Learning and academic processes and outcomes also depend on the interactions between individual and context dimensions and amongst the different individual systems. Significant contextual influences include family and school characteristics (including family involvement with school and support for learning) (e.g. Moreira et al., 2013). These influences occur at different levels, from gene-environmental interactions (Keltikangas-Järvinen et al., 2008) to the effect of school characteristics on student academic trajectories, and include school dropout (Lee & Burkam, 2003), the likelihood of graduation in students from disadvantaged backgrounds (Eskreis-Winkler, Duckworth, Shulman, & Beal, 2014), and in buffering the negative impact of prior academic performance in student engagement with school (e.g. Moreira et al., 2018). There has been an increasing consensus that, contrary to conventional perspectives of academics and school performance, the consideration of rational aspects alone is not sufficient for a full understanding of learning (including classic academic processes and outcomes). Cloninger's psychobiological model of personality posits a convincing integration of the systems of learning and memory as an explanation of human personality. It incorporates the influences that genetics, neuroanatomic circuitries, and psychological processes have on the organization of psychobiological systems, including emotional and cognitive systems. Academic processes and outcomes, including academic performance (Duckworth, & Seligman, 2005; Moreira et al., 2012), can be considered, in this light, as a result of the interactions between emotion and cognition (e.g. persistence and self-directedness). Indeed, non-cognitive skills (referred to differently by different authors, including terms such as character dimensions, strengths, etc.) account for about half of what matters for positive academic, post-secondary, labour market, and general life outcomes for young people (Heckman et al. 2006).

Paradigmatic examples of the contemporary acknowledgement of the importance of considering non-cognitive factors include the recent development and testing of models describing the role of emotions in school achievement situations (e.g. Pekrun, 2006). But perhaps the best example comes from the acknowledgment and conceptualization of non-cognitive dimensions as the so-called soft skills. This is an indicator that society is aware of the importance of these dimensions, but also that the current approach to them is superficial, inaccurate, diffuse, and unscientific. This is an example of one of the main challenges for the integration of behavioural sciences. Improving the current approach will allow for an integrative scientific-based understanding and conceptualization of the multiple systems, and the interac-

tions amongst them, which education policies and practices need to adopt if person-centered schools are to be a reality.

8. *Non-cognitive (logical-propositional) dimensions are strong predictors of multiple functioning domains, health, and death.*

Humans comprise much more than rational dimensions. Indeed, research converges on the conclusion that the rational and logical-propositional aspects of humanity are insufficient for a full understanding of individual and societal processes and outcomes. Research associated with personological epidemiology has repeatedly confirmed that emotional and personal agency mechanisms are amongst the strongest predictors of education, social relationships, societal behaviours (including crime), performance at different levels of functioning, health behaviours, morbidity and illness (including all states on the continuum of physical/mental health and illness), and even mortality. Accordingly, a meta-analytic review has supported the need to integrate the rational and non-rational components of human functioning by combining cognitive epidemiology and personological epidemiology in an integrative differential epidemiology (Deary, Weiss, & Batty, 2010).

The body of evidence supporting a need to consider the non-rational components of human beings in an integrative way is robust. This is particularly evident for two major assumptions of person-centered approaches. First, evidence shows that non-rational dimensions are amongst the strongest predictors of processes and outcomes, including education, health, morbidity, longevity, and even causes of death (Chapman, Roberts, & Duberstein, 2011; Chapman, Fiscella, Kawachi, & Duberstein, 2009; Deary, Weiss, & Batty, 2010; Dodge et al., 2014; Jokela et al., 2013; Jokela, Pulkki-Råback, Elovainio, & Kivimäki, 2014). Second, evidence also indicates that emotional and socio-cognitive processes are the strongest predictors of what is considered the ultimate objective of all humans: to be happy. Personality is one of the strongest predictors of each state in the continuum between subjective ill-being and well-being (Cloninger, 1999; Cloninger, 2004; Cloninger, 2006; Cloninger, & Zohar, 2011; Cummins, Gullone, & Lau, 2002; Josefsson et al., 2011; Krueger, & Tackett, 2006; Moreira et al., 2015; Steel, Schmidt, & Shultz, 2008). In sum, research supports the need to consider all dimensions in the promotion of individual functioning and to integrate the subjective aspects of experience into schools' policies and practices.

9. *Adaptive development benefits from an emphasis and promotion of positive dimensions and strengths, rather than focusing on deficits.*

In an attempt to resolve specific difficulties, behavioural sciences have traditionally focused on peoples' problems, dysfunctions, pathology, or morbidity. This has been the status quo for several decades and characterizes the first systematic scientific approach to applying evidence to the improvement of peoples' lives. This focus was understandable at the time. From a societal point of view, problems at the group and societal level were more salient than problems at an individual level because they are more likely to disturb societal organization and functioning. The problems faced by individuals with a need for special attention were a secondary

priority for societies and scientific disciplines and remain so for modern governments and public policies. This approach to human functioning gave answers to societal and individual problems from a remedial perspective and was perceived by both science and society (including those who receive the interventions) as not only the most adequate but also, in the long term, the only possible thing to do. Obviously, this is closely related with the historical moment (including the societal organizations) and the science available, but as a consequence, the conceptions and practices within behavioural sciences were clearly oriented towards problems and deficits. This was also the case within education systems and schools, for which the effect was potentiated in modern societies by the conception of the state and public policies. The state has been perceived as the ultimate advocate for those who are most vulnerable and who also tend to register more needs, and accordingly accumulated taxes were considered to be of better use helping people with salient problems rather than promoting things that were good already. Positive functioning and strengths were considered a "luxury" or something for privileged populations, frequently those with more financial and economic resources. This was even more evident in education, where the majority of schools available in democratic societies were publicly funded. Advancements in research allowed for a better understanding of the aetiology and maintenance processes involved in deficit conditions and of the efficacy of the practices and interventions of professional practices. Such advancements converged on two main conclusions that are transversal to different behavioural sciences. Firstly, the conventional professional approach focused on symptoms and deficits and was inefficient in promoting positive functioning in individuals, including in the most vulnerable ones. Secondly, these conventional approaches failed to guarantee equity in terms of offering the needed conditions for an optimal development to all individuals. For example, there is a growing consensus that traditional approaches to mental health (from psychotropic drugs to psychotherapy) have failed to improve the average levels of happiness and well-being in the general population because of the excessive focus on deficit and symptoms and the neglect to actively consider positive dimensions (e.g. Cloninger, 2006).

There is also a growing consensus on the benefits of promoting positive aspects of experience, such as well-being and happiness, even in terms of the efficacy of interventions such as therapeutic medicine, preventive medicine, and psychoeducational interventions. This is especially true for educational and school practices. As highlighted by Zins and colleagues, an emphasis on positive aspects of functioning is needed in schools if they want to promote a positive development in all their students (Zins, Payton, Weissberg, & O'Brien, 2007; Zins, & Elias, 2007). Person-centered schools require a shift from the emphasis on the deficit to the strengths, both in terms of assessment (Duckworth, & Yeager, 2015) and intervention (e.g. Peterson, & Seligman, 2004; Shoshani, & Slone, 2013).

10. *There are substantial individual differences in positive functioning and strengths.*

Having a person-centered approach implies an acknowledgment of the idiosyncrasies, specific background conditions, and exposure to different developmental

conditions that result in individual differences. Indeed, one of the main assumptions of person-centered approaches is an acknowledgment of each individual's uniqueness. This needs to become an accepted truism for educational and school practices as a means to promoting holistic functioning, but remains a challenge for conventional schools, even in terms of conventional rational knowledge. As a result, asking schools to take responsibility for accepting student uniqueness in their conceptions and practices is an even tougher task.

There is, however, no alternative given the large amount of evidence suggesting there are a) substantial individual differences in the positive aspects of student functioning and b) that these differences are present from early stages of development, including at preschool (Grist & McCord, 2010). This is unsurprising given that aspects of positive functioning express the interactions between complex psychobiological organizations and characteristics of contexts and experiences. As an example, there is a growing consensus that differences in biopsychosocial functioning in adolescents are associated with a small number of higher-order emotional (Pitzer, Esser, Schmidt, & Laucht, 2007) and even socio-cognitive (Moreira et al., 2012; Moreira et al., 2015) dimensions. Therefore, the consideration of individual differences in students (including in terms of non-rational components of learning and development) is an educational imperative.

11. *Positive functioning is amenable to intervention.*

A shift from a paradigm focused on deficits to the consideration of positive dimensions and strengths, and from an emphasis on rational aspects of learning to a holistic vision of learning, requires that educational agents are aware that the educational conceptions and practices characterized by a deterministic approach to student development are equally inadequate for both logical-propositional learning and holistic development promotion. The fact that individuals differ in their background characteristics does not mean that nothing can be done to promote different development trajectories, nor that it is acceptable that schools adopt a passive attitude towards those background differences.

On the contrary, there is a rapidly growing body of evidence that non-rational dimensions of functioning and learning (including positive aspects and strengths) are malleable. Fortunately, many of the strongest predictors of positive functioning/psychological strengths (Moreira, et al., 2015) are also amongst the psychobiological processes susceptible to change (Josefsson et al., 2013). More importantly, beyond the simple fact that these dimensions are malleable, this malleability implies that and they can be improved by intentional interventions (Ciocanel, Power, Eriksen, & Gillings, 2017; Durlak, Weissberg, Dymnicki, Taylor & Schellinger, 2011; Greenberg et al., 2003; Jones, Brown, & Lawrence Aber, 2011; Taylor, Oberle, Durlak, & Weissberg, 2017).

12. *Positive development is multidimensional and needs to be conceptualized in terms of dynamic organizations resulting from the non-linear interactions amongst different domains of functioning.*

As previously stated, positive development dimensions/psychological strengths are expressions of the interactions between complex psychobiological organizations and characteristics of contexts and experiences. The different systems involved in psychobiological organizations suggest multidimensionality of positive development/psychological strengths, and this has been supported by several studies (Taylor, Oberle, Durlak, & Weissberg, 2017). Evidence of this multidimensionality comes from a variety of studies and research traditions, including studies promoting specific and narrow social and emotional skills (e.g. Moreira, Crusellas, Sá, Gomes & Matias, 2010; Moreira et al., 2014), studies supporting transactional models of personality change (Heaven, Leeson, & Ciarrochi, 2009; Willie et al., 2012), empirically tested models of personality-mental health in children and adolescents (Tackett, 2006), and evidence that personality development mediates the impact of negative life events on different processes and outcomes, such as traumatic symptoms, anxiety and depression symptoms, and subjective well-being (McCullough, Huebner, & Laughlin, 2000; Moreira, Stevanovic, et al., 2018; Olayinka, Stevanovic, Moreira, et al., 2018).

13. *School characteristics matter: different school dimensions have different effects on different functioning domains.*

Studies, mostly from the area of sociology, have devoted a great deal of effort into understanding whether school characteristics matter for students' academic trajectories and how they influence different dimensions. This line of research started as a means to better understanding why some schools systematically had better academic results than others (Lee, & Holland, 1993). Following studies have investigated the effects of school characteristics on different dimensions. By using the appropriate multilevel analytic approaches (Raudenbush, & Bryk, 1986; Raudenbush, & Bryk, 2002), the first of such studies estimated school effects on academic-related outcomes, such as academic performance (Lee, Dedrick, & Smith, 1991; Raudenbush, & Bryk, 1986; Lee, & Smith, 1999; Lee & Burkam, 2003). A subsequent second wave of studies have shown that school characteristics have significant effects on other psychological phenomena from self-concepts to mental health (e.g. Anderman, 2002), and that school characteristics moderate the effects of school-based universal interventions for the promotion of social and emotional learning (Bierman, Coie, Dodge, Greenberg, Lochman, McMahon, & Pinderhughes, 2010). This line of research continues to be very active and has evolved to the estimation of school effects on students' subjective experiences and to the description of how school characteristics model different processes along the time (Wang, & Eccles, 2013; Wang & Fredricks, 2014). Additionally, interactions between individual and contextual characteristics may assume different patterns of match/fit and mismatch/misfit (Lau & Nie, 2008). Studies have shown that school characteristics really matter and that different characteristics are associated with different outcomes, with some characteristics favouring a match, and others a mismatch, between context and individuals' characteristics (Lau & Nie, 2008; Murayama & Elliot, 2009). Further studies have shown that school characteristics have a significant effect on teacher functioning (Lee, Dedrick, & Smith, 1991; Van Maele, & Van

Houtte, 2009). The importance of these studies for person-centered school is evident: school characteristics can ameliorate students' existing vulnerabilities and can potentiate positive development.

Person-centered classroom management facilitates higher achievement by promoting more positive learning environments and stronger teacher-student relationships. The most promising and efficient components of person-centered classroom management are social-emotional emphasis, school connectedness, positive school and classroom climate, and student self-discipline (Freiberg & Lamb, 2009).

14. *School-based interventions for the promotion of positive functioning and strengths are effective.*

School is a context that should not be exclusive to interventions promoting scholastic dimensions. Instead, it is a suitable context for promoting a holistic positive development (Masten, Herbers, Cutuli, & Lafavor, 2008). A paradigmatic example is "school-based prevention programmes", which refer to a type of systematic interventions for the promotion of functioning domains other than academic outcomes in school settings (Humphrey, Lendrum, &Wigelsworth, 2013). The ever-increasing number of studies evaluating the efficacy of school-based programmes, including meta-analyses, is converging on the conclusion that these programmes are effective (Camilli, Vargas, Ryan, & Barnett, 2010; Domitrovich, Durlak, Staley, & Weissberg, 2017; Durlak, Weissberg, Dymnicki, Taylor & Schellinger, 2011; Greenberg, Domitrovich, Weissberg, & Durlak, 2017; O'Conner, De Feyter, Carr, Luo, & Romm, 2017; Taylor, Oberle, Durlak, & Weissberg, 2017; Yeager, 2017). Moreover, the programmes appear to be cost-benefit effective (Klappa et al., 2017). Additionally, although the advantages of attending early childhood education programmes for academic outcomes begin to disappear in early elementary school, the advantages for other levels of functioning, such as social and emotional skills, persist. Indeed, individuals who attended early childhood education programmes tend to report better long-term life outcomes such as employment, earnings, and less involvement criminal justice system (Schweinhart et al. 2005).

15. *The most efficient school-based interventions for the promotion of positive functioning/strengths are multidimensional.*

An important question for the promotion of positive development/psychological strengths is "What components do intervention programmes need to include in order to be effective?". Clearly the answer to this question depends on the characteristics of the target population, including their background and dispositional characteristics, their developmental history, their current interpersonal contexts, the challenges they are facing, etc. However, available research is consistent in suggesting that the most successful programmes are multi-component based (covering several domains) and of medium- to long-term duration since they are more likely to foster enduring benefits (Greenberg et al., 2003). These interventions need to conceive human development from an holistic perspective, including interpersonal contexts that favour procedural learning, self-knowledge (including automatic responses, adaptive coping skills, flexibility in dealing with internal states),

awareness about the others (social skills, and psychological strengths such as understanding perspectives of the others) and awareness about the wider an transcendent reality (including imagination, etc.) (Moreira et al., 2010). Consistent with the holistic nature of human functioning, promoting different dimensions independently has limited effects: dimensions of positive functioning/psychological strengths need to be promoted in an integrated and coordinated way in order to complement each one another.

16. *School-based interventions promoting non-academic skills have a positive and significant impact on learning, including on classic indicators of academic performance.*

Meta-analytical research has shown that programmes for the promotion of social and emotional skills encourage positive outcomes at several other functioning domains and reduce risk behaviour (Ciocanel, Power, Eriksen, & Gillings, 2017). Interestingly, interventions aiming to promote positive functioning and psychological strengths (such as social and emotional skills) also have a significant positive effect on academic-related processes and outcomes (Ciocanel, Power, Eriksen, & Gillings, 2017; Durlak, Weissberg, Dymnicki, Taylor & Schellinger, 2011; Greenberg, Weissberg, O'Brien, Zins, Fredericks, Resnik, & Elias, 2003; Jones, Brown, & Lawrence Aber, 2011; Taylor, Oberle, Durlak, & Weissberg, 2017). Of equal importance is that the effect of school-based interventions on promoting social-emotional learning is moderated by school characteristics (Bierman, Coie, Dodge, Greenberg, Lochman, McMahon, & Pinderhughes, 2010), which reinforces the importance of this question for person-centered schools.

17. *Relationships matter: Relationships are the school characteristic with the most powerful effect on students' processes and outcomes.*

For educators, the importance of teacher support for students' development is clear, even if this impression comes solely from their own experiences. Fortunately, an increasing number of research studies have concluded that the teacher-student relationship is the most relevant educational tool for promoting a holistic development in youths. Specifically, meta-analytic review confirms that learner-centered principles (Table 3) and relationships are effective (Cornelius-White, 2007; Cornelius-White, Motschnig-Pitrik, & Lux, 2013).

Multilevel research has confirmed that, of all the school characteristics, relationships with teachers have the strongest effects on students' processes and outcomes. Effects are evident across a wide range of functioning domains, from outcomes (such as academic performance) to processes (such as engagement with school), along the time (Klem, & Connell, 2004; Vollet, Kindermann, & Skinner, 2017; Wang, & Eccles, 2012; Wang, & Eccles, 2013). Of equal importance, positive relationships between teachers and students serve to buffer the impact that prior low academic performance has on student engagement with school, meaning that it is a crucial component for promoting educational equity (Moreira et al., 2018). Indeed, effective helping relationships, and especially teacher-student relationships, have a significant effect, not only in reducing deficits, but also in promoting positive

functioning (Jackson, 2016; Levitt, 2009). Meta-analytical research (Thoits, 2011) offers an empirically based understanding of the importance of the school interpersonal context and social support for the promotion of students' positive development. The importance of school for student development relies on the fact that it allows the interaction amongst types of support, types of supporters, and mechanisms of action involved in the influences of the social context on individuals functioning (Thoits, 2011).

18. *Teachers' functioning also matters, and it impacts on the youth development.*

Regardless of the school, teachers are important. Teachers are, of course, people too, and they matter for schools not just from the perspective of secondary agents at the service of students but also as individuals. Although conventional schools have consistently neglected teachers' functioning dimensions and well-being, person-centered schools need to be aware that the promotion of both student and teacher positive functioning is equally important. There is little doubt that teachers are sensitive to school conditions, that their functioning (including their relationships with students) can be seriously impaired, and that any such impairments will impact negatively on students. Evidence in support of this comes mostly from research on the topic of burnout (Aloe, Amo, & Shanahan, 2014; Aloe, Shisler, Norris, Nickerson, & Rinker, 2014). More recent approaches are also addressing teachers' functioning from the perspective of positive functioning. There is also a growing consensus that schools need to intentionally create the required conditions for teachers' positive functioning and development (Van Maele, & Van Houtte, 2009). This is because teachers' well-being and positive functioning reflects on teachers' relations with students and thus will have significant influences on students' functioning, including on positive functioning (Klassen, & Tze, 2014; Roffey, 2012; Schonert-Reichl, 2017).

19. *Different teacher characteristics have different effects on students' functioning domains.*

Conventional schools have typically selected teachers based on criteria including initial disciplinary training, mobility, and experience. In schools more oriented towards school success, the criteria may also include the degree to which teachers are demanding of established higher academic expectations and patterns for their students. However, for person-centered schools, it is insufficient for a teacher to be an expert in his/her academic domain. He/she also needs to demonstrate an ability to create secure relationships and to make a good use of these relationships for the service of student positive development. In this respect, the most striking studies are those that have investigated how different teacher characteristics are associated to different domains of efficacy. For example, a recent study has shown that teachers are crucial agents in the promotion of non-rational dimensions and positive functioning. Most importantly, this study also showed that the teacher characteristics involved in promoting social and emotional functioning were different from those involved in promoting academic achievement, such as test scores (Jackson, 2016). Interestingly, students acknowledge the importance of teachers with both

characteristics, including for the long-term (Jackson, 2016). Such findings have the important implication for educational policies and school organizations that more attention should be paid to teacher characteristics. Certainly, person-centered schools need to consider teachers' interpersonal relationships (including positive functioning, psychological strengths) during the recruitment process (e.g. Casey & Childs, 2017) and when creating conditions at schools for teacher development. This depends on school leadership, which is yet another critical dimension of person-centered schools (Combs, Midser, & Whitaker, 1999).

20. *Scientific and professional organizations acknowledge the need for person-centered approaches and principles: integrating person-centered principles as common factors for different scientific disciplines and professional activities*.

Person-centered approaches have been widely accepted. They have inspired institutions across the globe, and there are now over 200 person-centered organizations worldwide (Kirschenbaum & Jourdan, 2005). Person-centered principles and assumptions are also being adopted across different scientific domains, particularly by disciplines where the helping-relationship plays an important role. For example, in 1993 the American Psychological Association (APA) established a task force, which was later renamed in 1997 as the APA Work Group, with the role to systematize a framework of learner-centered psychological principles (see Table 3). More recently, there has been a renewed interest in the application of the person-centered principles, including in fields such as medicine and its sub-disciplines. Paradigmatic examples of this include the formation of several scientific journals devoted to person-centered approaches in different contexts, including the *International Journal of Person-Centered Medicine* and *European Journal of Person Centered Healthcare*. Interestingly, beyond medicine, person-centered approaches have also started to be considered in the context of non-human environments, including artificial intelligence or digital contexts (McCombs & Vakili, 2005).

21. *Professional roles of the short-term future require psychological plasticity from individuals more than the acquisition of conventional academic contents.*

In the conventional school paradigm, the founding rational is that schools need to promote the specific skills and competences considered to be crucial for students to undertake a specific professional role. Historically, it was common for people to have the same profession, and even the same job, for the entirety of their career. Recently, however, there have been substantial and rapid changes to this trend. Furthermore, there have been rapid developments in terms of technology and its importance in a revolution in the organization of society regarding the satisfaction of the different needs. On the one hand, many traditional jobs are being automated and workers replaced by machines. On the other hand, other realities emerge, and other new jobs are created. Many of the jobs that exist today did not exist a decade ago, and many of the children who are currently in school will have jobs that does not exist now (European Commission, 2017). As such, this implies a marked uncertainly that people will need to manage. Additionally, with globalization and changes to societal organization, humanity is creating more volatile environments and

increasing the demand for resources. This is a great challenge for human adaptation and requires, at least, that individuals have greater flexibility and resilience in order to have a positive adaptation. A paradigmatic example is the case of the coherence of the self and of identity. As the volatility of individual roles in society increases, individuals will need to become more flexible concerning role-identity. At the same time, individuals will need to develop the necessary psychosocial resources for him/her to maintain a sense of coherence for the self and identity. This is one of the main indicators of the individual as a holistic self and includes the higher-order level of psychological functions that result from the dynamics between different systems, including emotional, cognitive, and behavioural, as well as experiences. Consequently, person-centered schools will need to be able to promote, in all their students, a development of the psychological strengths and resources that will allow them to succeed in a positive adaptation, including health and well-being.

22. *Education and school efficacy require scientific knowledge and expertise and highly specialized professionals.*

As we described earlier, there is evidence to indicate what schools can do to effectively promote a holistic development of students. But, in order for this to happen, several challenges must be overcome. One of the biggest is the educators' profiles. In the paradigm of conventional schooling, the subjective nature of human functioning has often been misunderstood and confounded as easy, unintentional, or irrelevant. However, just because education refers to, and implies everybody, just because we all were students once, just because we have opinions about how to best educate our own children, it does not mean that we have sufficient expertise to take on a role that will have a major influence on individuals' lives and societal functioning. We all have a heart, but does that make us able to make decisions regarding a child's healthy heart development? Would it be acceptable for people coming from other scientific disciplines, without expertise in medicine and in cardiology, to be in charge or to take decisions regarding institutional policies and practices concerning the heart's functioning? Promoting human positive development and psychological strengths in a combined, integrated, intentional, and systematized way is a complex issue that requires a high level of expertise. An effective educator – and particularly an effective education policy-maker or decision-maker – needs to be a highly competent scientist and able to integrate the available knowledge from different behavioural sciences into a coherent framework that is efficient in addressing the main processes underlying human functioning. Unfortunately, it remains prevalent in modern societies for educational policy- and decision-makers, educational leaders, and educational stakeholders to be professionals without expertise in behavioural science. The result of this is that many institutions are wasting resources, time, and opportunities to effectively promote student holistic development. Furthermore, without this necessary expertise, bad decisions are made (reflecting the erroneous conception of the educational subject and object and their dynamics), educational and schools conceptions and practices become diffuse, and within schools decisions can be contradictory. This strongly relates to the initial training, continuous learning, and development of educational agents and needs to involve all educational

stakeholders (including researchers, universities, schools, NGO, parents, etc.). It is now up to the behavioural sciences (with a special emphasis on educational agents) to create the possibility described by research evidences into a reality for all.

23. *Global development and sustainability (including world order, social organization, and planet sustainability) depend on individuals' holistic development.*

Evidence suggests that dysregulated development (without the harmonious integration of all dimensions) has a negative impact on the environment and that a pervasive emphasis on individualism and competitiveness is menacing the sustainability of the planet itself. Ecological conditions are responsible for suffering and death of millions of people (Hughes, Chu, & Mason, 2018; Otto, Reckien, Reyer, Marcus, Le Masson, Jones, et al., 2017; Stern, 2008; World Health Organization, 2016). Furthermore, these conditions are deteriorating on a huge scale due to the action of humans (Burroughs, 2007; Houghton, Ding, Griggs, Noguer, van der Linden, Dai et al., 2001; Intergovernmental Panel on Climate Change, 2014; Vitousek, Mooney, Lubchenco, & Melillo, 1997).

Global development and sustainability are also dependent on the success of shifting the educational paradigm towards person-centered schools. Without promoting holistic development in present and future generations, individuals' (and thus societies) awareness about themselves, others, and the planet is less likely to improve. This is mainly because an unbalanced development tends to result in an individualist and self-centered personality profile (Cloninger, 2004). This pattern of functioning is largely responsible for the prevalent behavioural patterns in societies causing dramatic changes to the conditions for life on earth. We are consuming resources at a pace that is not sustainable. The way we are treating our environment (destroying the conditions that support life) suggests a lack of awareness of us as part of the environment too. This means that humanity (in general) is failing in regulating their behavioural pattern and to move from a dysregulated and self-centered patterns of relations with the earth's resources and the environment. The only way of changing the current relationship that humans have with the planet is to develop individuals' intrapersonal (about ourselves), interpersonal (about the others), and transpersonal (about the holistic reality) knowledge in an integrated way (Cloninger, 2013a), with a special effort on the development of transpersonal awareness or self-transcendence (Cloninger, 2013a, 2013b). The most promising avenue towards reaching this important goal for humanity is, without doubt, person-centered schools.

On Becoming Person-Centered Schools: The Quest for All Schools

Each student is unique. They are unique regarding who they are at a specific moment and in whom they will become. Each individual thus has the right of seeing his/her uniqueness acknowledged, and to have the necessary conditions to express his or her full potential, because it is the expression of potential that forms the basis of

individual differentiation. We are not a mere result of random biological and contextual coincidences, but in fact, continually developing beings. We are, therefore, a phase of a process, a link in the process of being. Being human implies the question "How are we being?"

As we described earlier, research evidence suggests that there is a need to shift the current paradigm from schools simply applying some person-centered principles (and applying them under other approaches) to schools fully adopting the ideology of person-centered education. Person-centered schools must be more than conventional schools where some teachers, sometimes, apply person-centered principles. Person-centered schools are holistic in all their dimensions: from how they conceptualize student as persons to the mission of the school and the educational practices. That said, schools are complex, meaning that while they need to be ambitious in their aim to shift towards the person-centered approach, they need to be realistic about the process of doing so.

- As dynamic and complex organizations, schools should not consider their person-centered status as being either all or nothing. Such schools should consider this status from a dimensional perspective (meaning that schools vary in the degree to which they are person-centered).
- Person-centered schools are multidimensional. Schools need to consider interacting dimensions, including conceptions about the object of education (the person) and the educational agents who implement the means (also the person).
- There are already schools implementing person-centered assumptions and principles efficiently and systematically. These can be considered person-centered schools. Other schools are far from achieving this.
- Schools are dynamic organizations, and this applies to the way they change practices. This means that some schools will be able to move towards a conception of person-centered schools more quickly than others will.

In order to conceptually and graphically represent these ideas, we propose that the move towards person-centered will include dynamic and non-linear interactions between two major axes. These correspond to the two major dimensions of what we will call the *Epistemology of Person-Centered Schools*: the conception of "what" we want to educate (and education is aimed at educating people, so the object of education is the Person) and of "who" educates (and teachers and educators are educational agents, so the educational subject is also the Person).

The vertical axis of Fig. 1 reflects the conception of students as the *object of education*. The extremes of this axis are a reductionist conception of students (with an emphasis on parcelled human functioning and a value for the rational dimensions of learning in which the other functioning domains do not exert a relevant role) to a holistic perspective of the person (with an emphasis on the dynamics amongst the different systems underlying the individual's positive development). On this continuum person-centered schools are characterized, at several levels of analysis, by the features described in Table 6. An increasing number of researchers from different disciplines are advocating the need to shift from a reductionist/parcelled perspective to a holistic perspective of students. As an example, Cloninger's

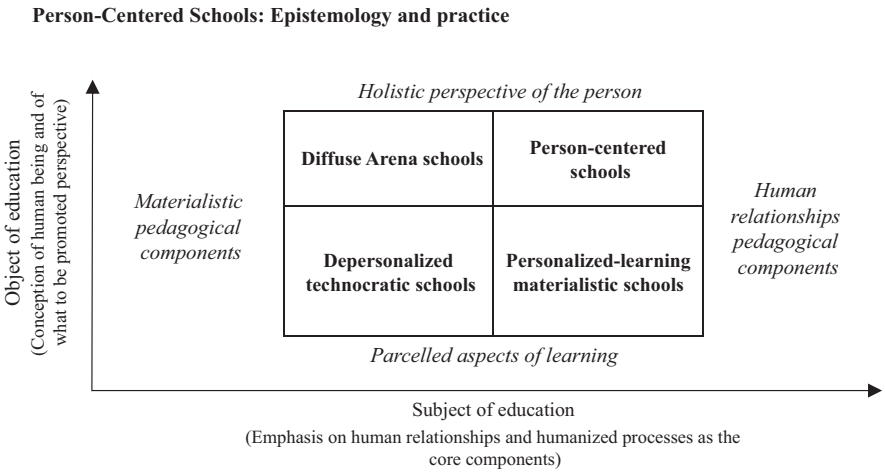

Fig. 1 Person-centered schools: epistemology and practice

psychobiological model of personality demonstrates the growing multidisciplinary and integrated understanding of students. Students are not rational recipients, but, instead, existential beings whose subjective experiences are their most relevant reality. Physical, psychological, relational, and contextual systems interact dynamically and influence (and are influenced by) health, interpersonal relations, and external conditioners. The dynamics amongst these factors are relevant components of individuals' processes of integration and meaning making of experiences including self-actualization, self-growth (Rogers), or positive personality development and plasticity (Cloninger) that allow for the person to experience beneficial states of being (see Table 5).

The horizontal axis of Fig. 1 refers to the manner that schools consider the needed pedagogic tools to promote students' learning, and specifically the role that positive interpersonal relations play in this. Some schools have a materialistic/technological orientation concerning the nature of the pedagogic instruments (those at the left of the horizontal axis). Others consider that positive teacher-student relationships are the most central pedagogic tool (at the right side of the horizontal axis).

Each school is located in a unique context: they have different resources; their social compositions differ substantially in terms of socio-economic backgrounds; their educators (including school leadership and school staff) have different conceptions about students; and the process of individual and student development, the role of schools in promoting student development, and finally teachers have different teaching and relational characteristics. The combination of all these factors results in very different types of schools. When considering the combinations of the dimensions of the conception of the student (object of education) and the conception of the education agents (subject of education), we propose there are four broad types of schools: depersonalized technocratic schools, diffuse or arena schools, personalized-learning materialist schools, and person-centered schools.

Table 5 Human being as existential being: the person and the self

System	Higher order processes	Beneficial states of being
Body Soma *Psychological* Emotional Cognition Previous learning and identity	Health	Composite Well-being Physical well-being Mental well-being Social well-being Spiritual well-being
Relational	Interpersonal contexts	
Contextual Time Space	External conditioning	
Self-actualization/self-growth, plasticity/flexibility		

Depersonalized technocratic schools These schools are the most proximal to conventional schools, which themselves follow the traditional perspective of how a school should be (including their functions and dynamics). Students are considered as mini-adults preparing themselves to play a professional role in society, and schools are conceived as contexts where students develop the skills and instrumental, rational, and procedural knowledge that will allow them to obtain a profession. Educational practices and pedagogy are a means to developing student expertise in the identified scientific and societal domains. Therefore, the objective (rational knowledge and procedural skills) justifies and requires consistent educational and pedagogic tools. These include teacher expertise in transmitting knowledge and skills; high-quantity, high-intensity exposure of students to the contents to be learned and skills to be acquired; and use of technology (often the most advanced technology available) to facilitate the acquisition of rational knowledge and procedural skills as they exist in the market labour. These schools establish their intentional focus on logical-propositional knowledge and procedural skills clearly. At the same time, they tend to encourage students to be disciplined in their approach to investing in these priorities and avoiding distraction by functioning domains and activities. These schools tend to promote self-directedness and competitiveness and neglect cooperativeness and self-transcendence. The indicators of success are predominantly grades, admissions to top universities (for non-vocational schools), and integration in the labour market (for vocational schools).

Diffuse arena schools These are schools with a diffuse conception of students as persons and no clear understanding of what really matters in students' development. Because schools are open spaces, these schools acknowledge the different outcomes of developmental trajectories. In other words, they acknowledge that education is involved in different phenomena (such as academic performance, professional success, societal roles, risk behaviours, health, etc.). Consequently, they deliver packages of interventions, each one addressing a different outcome, as if they were not different expressions of the same underlying psychobiological mechanisms. They might, for example, offer additional courses for maths alongside programmes

Table 6 Levels of analysis and specific features of conventional and person-centered schools

Levels of Analysis	Conventional Schools	Person-Centered Schools
Conceptual	- Unidimensional underpinnings of learning (rational system) - Emphasis on individual/innate/competencies - Determinism - Linearity - Positivism and post-positivism - Outcomes - Structural dualisms (e.g. emotion vs. cognition) - Functional sectarianism -Knowledge acquisition at the centre of the school mission -Materialism	- Multidimensional underpinnings (dynamics between cognition, emotion, behavioural and social) - Emphasis on relational conditions - Non-determinism - Non-linearity - Constructivism and social constructionism - Processes - Structural holism - Functional holism -Personal development at the centre of the school mission -Holism
Politics	- Students' as mini-citizens, who need to learn how to play a productive role for society - Instrumental and productive-centered - Transmission of knowledge as main pedagogical process is legitimized by the teacher's authority - Playing a productive role in society leads to societal integration and success, and this leads to happiness/wellbeing and positive functioning - "Blaming the victim": poor outcomes are a result of student and/or family background characteristics - Dehumanized - Materialistic orientation	- Students' as developing human beings who need to develop holistically. Their role in society derives from this - Person-centered - Provision of basic conditions for relationships as main pedagogic component to developing students as a whole person - Developing as a whole person, developing the conditions for self-growth, and plasticity leads to happiness/wellbeing, positive functioning and these lead to a productive role and integration in society - Contextual (also school) responsibility for the students outcomes (including negative) - Humanized - Humanistic orientation
Structure	- Schools are conceived as tailoring contexts, oriented toward preparing students for specific technocratic societal roles - Rigid functioning (from conceptions to boundaries) - Schools neglect the need of teachers having characteristics for effective logical-propositional learning AND for effective relationships -Teachers as a scholastic authority -Teachers as a transmitter of knowledge -Teacher quality based on content expertise or bureaucratic competence	- Schools are conceived as relational contexts, oriented toward preparing students for holistic development and plasticity - Flexible functioning (from conceptions to boundaries) - Schools acknowledge that the teacher characteristics involved in the effective learning of logical-propositional knowledge are different from the teacher characteristics of teachers adept at promoting effective relationships - Teachers as participants in interpersonal relations - Teachers as facilitators of learning - Teacher quality based on competence for creating the conditions for students' development (positive relationships)
Processes	- At their core, schools offer "packages of knowledge", and these are the most relevant and differentiating aspects - Parallel existence of multiple non-integrated (competing and frequently contradictory) domains and content dimensions coming from different behavioural sciences as educative offer - Content reproduction - External/Hetero – regulation - Rigidity of organizational procedures - Reification of human processes -Materialist learning (emphasis on knowledge and skills)	- At their core, schools offer the development of positive human relationships and holistic development, and this is their most relevant and differentiating aspect - Conditions for holistic development, self-growth and plasticity (with identification with the common factors coming from the different behavioral sciences) as educative offer - Promoting conditions for self-actualization - Self-regulation - Flexibility of organizational procedures - Dereification of processes as dynamics - Holistic learning (including knowledge about the self, the other and the transcendence)
Outcomes	- Knowledge /skills/ expertise - Conformity - Comparability and competitiveness - Logical-propositional knowledge - Learning of facts and materialistic skills - Reproduction of social and educational inequalities - Objective static indicators - Scholastic achievement and performance and indicators of materialistic success (labour market, earnings, etc.)	- Holistic development and self-growth - Creativity - Happiness and well-being - Holistic development (including experiential and existential knowledge) - Learning about intrapersonal, interpersonal and transpersonal aspects of being - Equity schools - Subjective dynamic processes - Self-actualization, self-growth and well succeed adaptation (wellbeing, health, flexibility or plasticity)

for prevention of substance abuse, intimate partner violence, sustainable food systems, reduction of car accidents, politics understanding, civic rights, and financial literacy. In short, these schools tend to offer as many intervention packages as staff and students can take and which are mostly dependent of what is – at a given moment – salient or popular in the community. These schools vary from being

highly demanding in terms of outcomes (which encourage students to be the best in everything, where there is no room for failure), or undemanding. In all cases, what they tend to do is materialize in grades and reproduce the existing differences in students' background characteristics. These schools may or may not select their students based on good predictors of academic performance (e.g. socio-economic status or prior academic performance), without providing the necessary interpersonal conditions for holistic development. These schools are arena-like contexts (like the arenas of the Roman gladiators), where student performance depends almost exclusively on their background resources (each man for himself), and this is "observed" by an "audience" of teachers, parents, community, etc. These schools promote competition, rather than cooperation, and tend to have a high-level of inequity amongst students.

Personalized-learning materialistic schools These schools place a large emphasis on student performance and academic outcomes. They value, and aim towards, rationality and the acquisition of logical-propositional knowledge. These schools acknowledge students' differences and their implications for academic performance. Moreover, they acknowledge the benefit of tailoring conditions according to student characteristics, because this will improve student learning and outcomes. Particularly, they acknowledge the importance of adapting the means to the student and of giving more teacher support to students. These schools vary in their student social compositions, some with low SES student populations and others with high SES student populations. Consequently, the use that these schools make of personalized-learning varies from excellence-oriented goals (the cases of schools with students mostly with high socio-economic backgrounds) to remedial- or compensatory-oriented goals (the case of schools with students mostly with low socio-economic backgrounds). Similar to depersonalized technocratic schools, indicators of success are predominantly grades, admission to top universities (for non-vocational schools), and integration into the labour market (for vocational schools).

Person-centered schools Person-centered schools are contexts intentionally organized around the main aim of offering suitable conditions for students to develop his/her full potential. By doing so this enables successful adaptation, both from the perspective of performance at the various roles in this process and the level of subjective experience of reality. Such schools understand individuals as holistic beings whose optimal functioning results from the interaction between various dimensions, and not from an exclusive or majority stimulation of instrumental skills or knowledge of facts and logical-propositional. This means that schools consider individuals as beings who experience reality in a multicomponential way, whose existence includes experiential dimensions, and who feel reality in a positive and optimal way, including happiness. These schools consider education as a means to promote the expression and experience of humanity to its fullest in students, not just the materialistic part of the human condition. In other words, person-centered schools are about offering the conditions for humans to be "human". According to Jacobs, *The real subject and object of education are the same. The subject of education is a human being. The*

object of education is to develop the mind and personality of that human being. Everything else is secondary, often irrelevant and many times detrimental to mental, emotional, social and physical health and wellbeing (2015, pag.13).

A person-centered school is necessarily a context that simultaneously promotes self-actualization and equity. Although Maslow considered that self-actualization is only accessible to some individuals, others, including Rogers and Cloninger, have proposed that self-actualization is accessible to all individuals. A person-centered school provides the conditions for *all* their students to reach their potential, thus promoting self-actualization (Rogers) and plasticity (Cloninger). The history of education has always been characterized by marked inequalities in the degree to which schools dealt with students from different backgrounds (including demographic, socio-economics, or psychobiological characteristics). Regardless of the perceived inequalities in how schools provide knowledge and skills, the inequality between schools in the degree to which they are person-centered is clearly substantial. The challenge of shifting to person-centered school paradigm is thus coupled with the no less demanding challenge of equity.

Person-Centered Schools as a Research, Political, and Intervention Agenda

Academic results are more an expression of the idiosyncratic conditionalisms of each individual than the mechanisms underlying positive holistic adaptation. The two, therefore, cannot be confounded and schools need to keep in mind that education should be about the second rather than the first.

> A main objective of equitable educational systems is how to offer to all students the same educational opportunities' and how to succeed in diminishing the existing differences in student outcomes resulting from students' background characteristics (including families SES). When schools fail in this quest, it means that those schools are doing little more than to reproduce the inequalities already existing at other societal levels (for example, at the level of wealth distribution) and apply them to education. This is unfortunate in any time and society. However, it is even more disturbing in contemporary societies that have the necessary knowledge and resources to make a real difference to students developmental trajectories, and ultimately to students' lives. (Moreira et al., 2018)

As we described earlier in this chapter, *a growing body of evidence suggests that person-centered schools are a privileged avenue for promoting holistic development for all children and that teachers are the most powerful agents in that process.* However, we need to develop and create testable interventions promoting an effective shift from conventional to person-centered schools. Once accomplished, policymakers and educators need to implement these effective interventions.

We need an agenda of research, policy, and intervention for transforming our schools into person-centered schools. We suggest that the pathway to person-centered schools includes making good use of the science of intentional change. Understanding the relevance of person-centered schools may lead to a clear research

agenda focused on creating testable interventions and identifying effective processes of building person-centered schools. This process needs to be a systematic and integrative one and needs to address four main challenges: identifying common factors, defining concepts and consistent objectives, creating the structurally needed conditions, and implementing the effective components and dynamics.

Identifying Common Factors

We need to move away from the prevailing school emphasis on transmitting knowledge of concepts and facts and logical-propositional components of learning. Schools do not yet fully acknowledge that what really matters for positive student development is the healthy organization of interacting psychobiological factors common to different outcomes. Under specific circumstances, the underlying dynamics of psychobiological processes can lead to different outcomes (e.g. school absenteeism, uncivil behaviours, disruptive behaviours, drug abuse, interpersonal violence, affective disorders, and traffic accidents), all of which are important to consider by societies and individuals. However, rather than being independent and discrete phenomenon, these are all expression of maladaptive patterns of functioning, the frequency and severity of which depends on developmental trajectories and circumstantial stressors. Schools need to have a full understanding of these common organizations of interacting psychobiological factors, and how they impact on different outcomes, rather than focusing on the specific outcomes themselves without consideration of their causing mechanisms.

Schools frequently over-emphasize the importance of interventions targeted at these specific outcomes and are thus compartmentalizing students in terms of outcomes or functioning domains rather than considering them holistically. This approach has many negative aspects. Firstly, education agendas and interventions are influenced by trends and the salient issues for educators and policy-makers and thus neglect student needs. Secondly, an emphasis on providing many specific interventions covering different functioning domains, as well as being a logistical burden, can lead to schools burning resources. These resources include teachers' energy and capacity to focus on the elements important to student development. Thirdly, specific interventions are often unsustainable in the long term and eventually discontinued.

Defining Concepts and Objectives

There has been a proliferation of approaches to non-cognitive student characteristics from different research traditions, which accounts for the abundance of psychological constructs described in scientific literature (including emotional intelligence, character, social-emotional skills, competencies, strengths, positive development,

personal qualities, and non-cognitive attributes). There is a need to integrate and clarify these constructs. Doing so should have considerable implications for research that will inform educational policies and school strategies and therefore influence school practices.

An implication of these advances in knowledge on psychological strengths is that it will allow practitioners to identify students at risk for the development of maladaptive developmental processes. This will only be possible when reliable and sound assessment instruments are available. Having reliable assessments is also crucial for a phase prior to intervention: it is equally important to an integrative understanding of the phenomenon itself and for the construct integration. The development of reliable assessments will allow for an integrative understanding of evidence coming from different research traditions and using different constructs. In fact, this has been considered by several authors as one of the major challenges in this field (Bollich et al., 2016; Duckworth & Yeager, 2015). This will have clear implications for both theory and practice as it is a necessary condition for the development and testing of coherent frameworks that describe the common factors, and the dynamics amongst them, involved in the changing of conventional schools to person-centered schools. There is a growing consensus that we need to make this a priority for research and practice (e.g. Sokatch, 2017).

Creating the Needed Structural Conditions

Spontaneous learning experiences and dynamics do not exist in a physical or temporal vacuum. Similarly, intentional and systematized educational dynamics exist in a context (space, time and relational) aimed at guaranteeing the necessary conditions for educational and learning experiences to be effective.

Extensive research has shown that school characteristics have the potential to buffer the risk factors associated with individual and family characteristics (Gut, Reimann, & Grob, 2013; Blatchford et al., 2011; Eccles & Roeser, 2011; Zimmer-Gembeck et al., 2006; Van Maele & Van Houtte, 2011; Wang & Eccles, 2012; Wang & Eccles, 2013; Waters, Cross, & Shaw, 2010a, 2010b). This means that schools can diminish the impact that student background characteristics (such as family vulnerabilities) have on student functioning, and by doing so, diminish the degree to which background vulnerabilities impair the fulfilment of student potential.

Fortunately, we have the necessary scientific knowledge to allow us to form an integrated understanding of the psychobiological dimensions and dynamics underlying positive adaption. The most efficient path is to promote the development of human beings from a holistic perspective, which itself is the best means to promote positive human development. The result is positive adaptation and resilience. Person-centered schools are the ideal context for the pursuit of this societal challenge. Therefore, we need to allocate the necessary resources (both material and human) to the development of the necessary structural conditions for person-centered schools to flourish. As existing typologies of school characteristics are

described, school and educational structural characteristics are multidimensional (from school structure to social and professional organization). The structural conditions required for the existence of person-centered schools begin with school autonomy (an ability to define policies and make decisions), and require the necessary material resources. However, although important, these are just a part of the whole picture. School autonomy and material resources are of little importance without the appropriate structural interpersonal conditions. These include school leadership (which needs to combine research-based school vision and humanistic sensitivity) and teachers who are competent at integrating knowledge from different behavioural disciplines and forming positive interpersonal relationships. The structural conditions for person-centered schools also require other school staff (competent in establishing positive and care relationships) and the student population (who feels that their needs at several levels are fulfilled). At a community level, person-centered schools are also dependent on families (who are sensitive to, and advocates of, a holistic perspective of the student) and on wider community stakeholders (supportive of person-centered driven community involvement).

Implementing Efficient Components

Preparing individuals for contemporary societal demands requires educational leaders to adopt an attitude of promoting intentional change via considering students as a whole. Indeed, the human phenotypic plasticity that enables individuals to respond adaptively to their environments requires – in order to promote effective intentional change in conceptions and practices – an integration of knowledge coming from different research traditions. These include the basic behavioural sciences (e.g. behaviourism, social constructivism, social psychology, cognitive psychology, and evolutionary psychology), neurosciences, educational sciences, social sciences, and political sciences.

As Wilson and colleagues highlight, there are several examples that humans can promote science- and evidence-based change, from small groups to large populations (which are examples that it is possible for humans to manage evolved mechanisms of phenotypic plasticity) (Wilson, Hayes, Biglan, & Embry, 2014).

We argue that the task of transforming our current conventional schools into person-centered schools is urgent. We argue that to be successful, we need to integrate the basic and applied behavioural sciences to make best use of the science of intentional change. Doing so will have huge implications on how societies deal with these challenges, from policy to practice, because individuals tend to demand leadership and governance consistent with their vision of reality. In turn, these policies are likely to have a large impact on how societies manage to make good use of the products of human activity in the construction of reality including societal organization, the use of technology, the sustainability of the planet, and individual experience.

In order to be effective at shifting from conventional to person-centered schools, we need systematic research on the effective processes of becoming a person-centered school. Robust methodological and analytical approaches need to be applied to compile evidence about how effectively this change can be made. Because of the nature of school organizations, a purist kernel approach (Jäkel, Schölkopf, & Wichmann, 2009) may be insufficient. However, we need a kernel-like approach for this process to help identify the fundamental units of behavioural influence that underlie effective change (Embry, & Biglan, 2008) and shift to person-centered schools. In fact, by identifying the fundamental common factors underlying the school promotion of holistic positive development, and by implementing them successfully, we may be able to produce longer-lasting organizational shifts.

In sum, we need to develop and test coherent frameworks that describe the common factors, and dynamics amongst them, involved in the changing of conventional schools to person-centered schools. We are all – researchers, policy-makers, educators, and the wider community – an important component of these frameworks.

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Integrating Healthy Personality Development and Educational Practices: The Case of Student Engagement with School

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Abstract *Background*: Positive, or healthy, personality development is a strong predictor of major lifelong adaptive processes and outcomes across different functioning domains. Consequently, the systematic promotion of healthy personality in children and adolescents via education contexts and practices is an imperative for contemporary societies. There is a growing consensus about the need for societies to shift from a paradigm of conventional schooling to person-centered schools. Structural features of person-centered schools include (a) a conception of individuals as whole persons, (b) an emphasis on subjective experience and on processes, (c) centrality of positive relationships, and (d) an emphasis on positive features of psychobiological functioning. This shift may be perceived as intangible, or as implying abrupt and disruptive changes. However, the promotion of healthy personality development in schools is not a question of all or nothing, but rather a continuum. Further, there are a substantial number of schools already promoting healthy or positive development, even if unintentionally or via means of processes and constructs more typical of school and educational traditions. *Aims*: We argue that student engagement with school is a paradigmatic example of a narrower expression of personality in the education and school context. We aim to describe how the promotion of healthy personality development is possible within the context of current educational practices, including school improvement efforts to reach educational excellence and equity. *Conclusions*: As an expression of personality, student engagement with school is a process that is malleable to intervention and particularly sensitive to interpersonal influences (including teacher-students relationships). Student engagement with school is, therefore, an example of how personality and educational constructs can be integrated into effective educational and school practices, including in school improvement and re-restructuring efforts.

Keywords Student engagement · Person-centered schools · Character · Health

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Students' Experiences at School Matter for Personality Development

Personality is a dynamic psychobiological organization resulting from the interactions between dispositional characteristics, contextual characteristics, and experiences (including learning). It influences how individuals experience and construct reality at any given time and is amenable to reorganization based on experience. Childhood and adolescence are developmental periods in which the differentiation of psychobiological organizations is more substantial and, within these periods, school is a context where characteristics and dynamics have an important influence on the development of psychobiological organizations. Person-centered schools are particularly adept at promoting the development of healthy personalities. This implies there is a need to change the traditional conception of the school at both the student and school levels. At the student level, it is fundamental to value and consider, among other things, the school organization and educational practices concerning student subjective experience (not only the valuation of objective results) and the various domains of experience (including emotions, cognitions, and behaviors). At the level of the conditions that schools offer to students, interpersonal relationships with the various educational actors, including teachers, auxiliaries, and peers (but also family support for learning), are the most powerful instruments for promoting healthy personality organizations.

Despite the apparent challenge this might pose to societies, shifting the paradigm to person-centered schools does not imply abrupt and disruptive measures. Moreover, doing so is not an unknown, or even new, concept for educational agents. Indeed, there are clear signs that this shift is already happening, slowly but surely, in research and educational practices. In this chapter, we describe this shift in terms of student engagement with school because of this constructs rapid and widespread validation and acceptance by educational communities. Specifically, student engagement with school concerns the subjective experiences (including emotions, cognitions, and behaviors) that lead to an experience of identification and involvement with school. It is a malleable process and influenced by different significant relational contexts (support of teachers, peers, and family for learning).

The consideration of engagement with school as a fundamental element in the conceptualization of students' academic trajectories is an approach that, consistent with the characteristics of person-centered schools, favors a consideration and adaptation by schools to the subjective experiences of students. This approach emphasizes the processes involved in the construction of reality and encourages schools to consider, and adapt to satisfy, the psychological needs of the students, which in turn enhance the positive role of the school in promoting development of a healthy personality.

Engagement as Both a Process and an Outcome

A classic question concerning educational systems is "Why do some students learn more than others?". Some students learn more because they are more able (better cognitive ability). Others work harder (more persistent). Others still come from families with more desirable pro-school characteristics (e.g., high socioeconomic status, SES) (Moreira et al., 2012; Moreira, Dias, Vaz, & Vaz, 2013). Characteristics such as these are mostly unchangeable and typically mediate the impact of educational activities on students' outcomes and processes. Fortunately, there are other strong predictors of students learning that are malleable, including student engagement with school. Beyond a sole reliance on performance indicators, schools also need to consider indicators of academic developmental processes. Students' engagement with school needs to be considered as both a process and as an outcome.

Engagement as a Process

As a process, engagement is a core component for the understanding of students' cognitions, emotions, and behaviors toward school. Students' subjective experiences toward school (including cognitive representations) are a multidimensional and malleable process: students' feelings, cognitions, and behaviors are responsive to, and shaped by, the interpersonal contexts relevant to school (Fredricks, Blumenfeld, & Paris, 2004). As a process, student engagement involves the collation of experiences into psychological organizations and representations concerning the self, others, school, and the future. Each experience is processed in reference to current psychological organizations, but is also able to reinforce these organizations, or to actualize qualitatively different organizations, if the experience has both the valence and the strength to be meaningful.

Engagement as a Feature of Personality/Psychobiological Organizations

As a subjective experience, students' engagement with school refers to psychobiological organizations comprising affective, cognitive, and behavioral dimensions related to school. As a process, student engagement with school refers to the differentiation of psychological organizations as a function of the interactions between contextual and individual characteristics. The differentiation of psychological organizations related to school involves the same mechanisms involved in the psychological organizations specific to other functioning domains. Specifically, in order

for students to develop psychological organizations consistent with being engaged with school (including undesirable or maladaptive organizations consistent with disengagement), intentional strategies to promote students' engagement with school need to consider the fundamental psychological processes underlying behavioral learning and modification: emotion, cognition, and contextual stimuli. Change to engagement involves core systems of learning and memory that underlie the differentiation of psychological organizations. As in the case of many other psychological phenomena, a positive change in engagement involves growth in students' psychological organizations or subjective experiences integrating the several aspects of learning and memory.

Human psychobiological development happens via the dynamics and organizations of learning and memory. In terms of learning, change in engagement involves a procedural learning of habits and skills, semantic learning of facts and propositions, and a self-awareness of one's identity that develops over time and place (Cloninger, 2009, 2013). Procedural learning of habits and skills refers to the acquisition and modification of behavior via associative learning (including the operant conditioning of behaviors, habits, and affective responses which underlie dispositional and stable patterns of responses) (Cloninger, Svrakic, & Przybeck, 1993). This type of learning results from the formation of associations between the perceptual experiences of stimuli/events/contextual contingencies and emotional responses. Such procedural learning of habits and skills does not require an awareness of the stimuli and contextual contingencies, the responses to them, or the associations between them (Cloninger et al., 1993). Study habits, study skills, and school behaviors, as well as the patterns of automatic responses and behaviors involved in behavioral self-regulation, are all acquired via procedural learning. Procedural learning is also responsible for some dysregulated patterns of behavior and can lead to the disruptive behaviors that are frequently expressed at school (e.g., indiscipline, truancy, failure to complete schoolwork) and which elicit negative responses and feedback. The procedural learning of habits and skills influences the conditioning of school-related behaviors, emotions, and cognitions via the cumulative experience of family and parental practices that give structure and stimulation concerning school and the feedback students receive (including consequences on attendance, grades, schoolwork completion, study skills, etc.). Procedural learning is also influenced by early school experiences including feedback from the school context concerning the automatic pattern of students' behavioral systems. A lack of adequate contextual structuring and pro-school interpersonal structures (including from family and school) from an early stage places students at increased risk for interactions that do not favor the experience of positive emotional responses to school-related experience. These constitute the context for the development of organizations of disengagement with school. There is a need for students be exposed to, and interact with, stimuli and characteristics that favor the learning of new patterns of thinking, feeling, and acting. To achieve this, students need to be exposed to interactions that allow them to feel autonomy, relatedness, and competence as these favor the reorganization of the students' cognitive representations. In turn, such reorganizations modulate the connectivity between the objective characteristics of reality and their cognitive representation.

Semantic learning refers to the acquisition of concepts and values that are captured within psychological organizations via language and symbolic processes. Conceptual memory is influenced by the concepts individuals construct from the different forms of information available in their interpersonal contexts, such as school value. Semantic and conceptual learning involve neurobiological and sociocultural mechanisms of semantic and self-aware learning (i.e., self-concepts about goals and values or what people make of themselves intentionally) (Cloninger, 2009, 2013; Garcia et al., 2013), which lead to qualitative differences in the development of student engagement with school. These learned concepts underlie the development of beliefs, values, expectancies, and goals about the individual, the world, and the future. They are also conscious, symbolized by language in the processes of meaning making and differentiation of higher-order cognitive organizations, and involved in the higher-order cognitive self-regulatory processes that modulate the regulation of automatic tendencies and the expression of the responses acquired via associative learning (Cloninger et al., 1993). The propositional or semantic learning of goals and values influences the development of stable patterns of affect, cognition, and behavior at both broad and narrow levels.

Broad psychological organizations include personality, while narrower psychological organizations include engagement with school. The positive development of student engagement with school requires that students are exposed to, and consequently acquire, pro-school concepts, values, and goals (including relevance and importance of school, future academic goals, and control of schoolwork). These processes correspond to cognitive engagement. Moreover, this cognitive engagement follows from the acquisition of the pro-school beliefs, values, and goals learned from parents, teachers, and peers and their incorporation into psychological organizations. Early positive parent involvement with school, the transmission of pro-school values, and high expectations toward school all favor the development of pro-school beliefs and modulate the development of pro-school self-concepts consistent with school engagement.

Additionally, the development of both a greater self-awareness and the meaning-making process leads individuals to develop a greater sense of coherence concerning their experiences and, consequently, their identity. As with conceptual learning and propositional memory, episodic/narrative coherence and identity are crucial for the adoption and maintenance of a given behavior. Episodic/narrative memories allow for the development of a coherent differentiation of the self, which in turn allows for the differentiation of identity (Cloninger, 2004; Tulving, 1987). For example, the student integrates his/her experiences toward school (including family valuing of school, feedback from school behaviors, and feedback from grades) into his/her self-concepts as a student. The interactions between procedural and semantic learning thus underlie the progressive development and differentiation of the subjective experiences with school. In short, student engagement with school is a cumulative process, consisting of the progressive differentiation of psychological organizations underlying students' experiences with school.

Student engagement with school develops via perceptual processes and habit formation (study habits, rules, school stimuli, structures, grades, etc.), and concept-based processes (representations and beliefs about the importance of

school, etc.). These correspond to two different memory processes: perceptual memory (regulated by the cortico-striatal memory system), and conceptual memory (regulated by the cortico-limbo diencephalic memory system) (Cloninger et al., 1993). Development in awareness allows for these two learning mechanisms to be integrated as a coherent pro-school identity, which is differentiated by the forms of learning and memory.

Engagement with school involves perception-oriented and concept-based memories and their organization into coherent self-concepts (student identity). Consequently, the fostering of positive engagement requires a number of factors. Students should acquire pro-school habits and practices, and pro-school values and concepts. Students' conceptual insights should modify habits through disciplined practice. Moreover, the school context should offer the desirable stimulation and structuring for acquisition/modification of habits and practice. Teachers should be proficient at modifying pro-school concepts and values. Schools should offer opportunities for students (in a gradient of autonomy) to modify undesirable habits in order to be consistent with their pro-school concepts and values. Finally, there should be a context for students to have opportunities to develop coherent and stable preschool narratives and identity.

In order to promote the positive development of engagement in students, especially those at increased risk (such as students with a consistent history of poor academic performance), schools need to address the emotional, cognitive, behavioral, and contextual components of engagement in their daily practices. It is insufficient to tell students that school is important. Students, including those who are disengaged, are frequently told that school is important and are thus, in this manner, exposed to pro-school values and concepts. However, this seems inadequate as a means to altering the engagement organizations of disengaged students. This is probably because conceptual learning alone is not enough to maintain efficient and stable behavioral changes. Indeed, the conscious intention for change resulting from conceptual learning and propositional memory is "transient, effortful, and inefficient, whereas perceptual conditioning is more long-lasting, automatic, and efficient" (Cloninger et al., 1993). To be effective at promoting positive engagement for all their students, schools need to implement strategies that are informed by learning and memory systems (Cloninger et al., 1993). In other words, schools need to consider interventions aimed at:

- The adequate conditioning between students' habits and emotional responses. The school context is a stimulus for students' responses, and there is a need to elicit positive responses from students, including to the structures (rules) provided for students' behaviors.
- The transmission of pro-school concepts, values, and goals that can regulate the expression of automatic maladaptive behavior patterns. Examples include the school having high academic standards, and the climate characterized by pro-school beliefs and concepts.

- A higher-order meaning-making, sense of coherence, and pro-school identity. This implies that students develop more differentiated and conscious self-concepts and identity. Students require the appropriate conditions to develop a mature awareness of their experiences and to develop awareness and comprehension of his or her internal states (including emotions, impulses, cognitions, and behaviors) and the ability to regulate these internal states in order to respond adaptively to contextual demands and expectations.

Conceptualizing engagement as a cumulative process has the implication that because of the cascade effects associated with developmental processes and outcomes, the longer an individual is on a dysfunctional trajectory, the less likely that he/she can leave that dysfunctional trajectory. Interventions, therefore, need to be holistic and begin as early as possible. This is especially important for students at risk of poor academic trajectories because they are more dependent on what schools can do to buffer the effect of background risk factors.

Engagement Is Also an Outcome

As an outcome, student engagement with school reflects the quality of the cumulative experiences of school. The quality of such experiences is dependent on the interactions between the individual and contextual dimensions involved in students' experiences with school. As a result, engagement as an outcome reflects how well, or poorly, schools succeed in offering their students the necessary conditions for having school experiences that meet psychological needs and keep students involved with school.

Conceptualizing students' engagement as an outcome implies that schools consider engagement as an indicator of school quality. Indeed, according to OEDC data, student engagement with school (and particularly behavioral engagement, e.g., class attendance) is strongly associated with several indices of quality, including quality of schools' educational resources and school responsibility for curriculum and assessment. Student engagement is also able to account for differences between the quality of school's educational resources and socioeconomically advantaged and disadvantaged schools (OECD, 2013).

In other words, considered as an outcome, student engagement facilitates an understanding of how schools are able to do more for their students, indeed more so than sampling the vulnerabilities associated with students' background characteristics (e.g., SES, prior academic performance, etc.). If individual dimensions of student engagement are malleable, and therefore an influence on school characteristics, then these need to be considered by school policies and practices. It is crucial to understand how schools can have a significant influence on promoting positive students' engagement with school, and this is particularly important for at-risk students

because schools have the potential to buffer the negative impacts of individual and contextual factors.

Perceiving student engagement with school as an outcome highlights the necessity for schools to offer all students experiences that keep them engaged with school. Schools need to assume this responsibility by distributing educational resources and opportunities equally to students and making planned efforts to override the barriers imposed by socioeconomic constraints. Schools need to offer students opportunities that overcome the intergenerational pattern of SES disadvantage and which increase the odds for social class mobility and greater human development. Successful efforts will guarantee that schools make a difference to these students' lives, as schools are one of the few opportunities society gives to these disadvantaged populations to develop the internal resources necessary to move beyond educational and social inequalities.

It is vitally important that schools are able to create a more equitable distribution of learning opportunities and outcomes as a contrast to reproducing existing patterns of socioeconomic inequalities (OECD, 2013). However, this requires that schools are able to identify students vulnerable to poor academic trajectories (because of their background characteristics) and to implement systematic strategies to diminish the influence of their background-related deficits or school-related attitudes on their academic trajectories. This is especially important in societies and communities with high numbers of students at high risk for poor academic trajectories. In such communities, tackling the large number of students with early signs of disengagement is a major challenge to achieving greater educational equity (OECD, 2013). At the same time, it is also important that schools are able to offer opportunities for high achievers to reach their full potential and to promote educational excellence. As indicated by international organizations and research, it is desirable that educational systems are able to promote both excellence and equity. Indeed, being able to do this is a feature of excellent educational systems (OECD, 2013).

Indicators of Engagement and Mechanisms of Action

In order to illustrate how the shift from conventional schools to person-centered schools is already occuring, we will describe how the phenomenon of student engagement with school integrates with person-centered assumptions and principles. Specifically, the construct of student engagement refers to subjective experiences that are malleable to intervention and especially sensitive to school relationships, including teacher-student and peer-student relationships. In the following sections, we will elaborate on this by explaining how the indicators of cognitive engagement, and of teacher-student and peer-student relationships, are important to understanding student engagement with school. In order to do so, we will rely on examples of our own research on the interactions between student engagement and teacher- and peer-student support for learning.

Indicators of Cognitive Engagement

The Student Engagement Instrument (SEI; Appleton, Christenson, Kim, & Reschly, 2006) is an example of a useful assessment instrument for capturing cognitive engagement and teacher-student and peer-student relationships in different cultures (Moreira & Dias, 2018; Moreira, Vaz, Dias, & Petracchi, 2009; Virtaten et al., 2017). The items composing the cognitive scale of the SEI capture core components of students' cognitive representations about school, including future academic goals and control and relevance of schoolwork. The differentiation of these representations involves the processes of learning and memory underlying emotional, cognitive, and behavioral response acquisition and modification. These representations result from interactions between different systems of learning and memory. Items capturing associative learning and procedural memory components include the following items: Item 2 ("After finishing my schoolwork, I check it over to see if it is correct"); Item 15 ("When I do schoolwork I check to see whether I understand what I'm doing"); and Item 33 ("Learning is fun because I get better at something"). Items capturing conceptual learning and propositional memory components include the following: Item 8 ("My education will create many future opportunities for me"); Item 9 ("Most of what is important to know you learn in school"); Item 19 ("School is important for achieving my future goals"); Item 11 ("Going to school after high school is important"); and Item 34 ("What I'm learning in my classes will be important in my future"). Finally, items capturing higher-order self-narratives and identity components include the following: Item 25 ("When I do well in school it's because I work hard"); Item 17 ("I plan to continue my education following high school"); and Item 30 ("I am hopeful about my future").

Sources, Types, and Mechanisms of Social Support

To promote change to the school interpersonal context it is important to consider evidence on the mechanisms through which interpersonal context and social support impact on human development. Such evidence considers the types of support, types of supporters, and mechanisms of action involved in the influences of social context on individual functioning (Thoits, 2011). There are two types of social support: emotional sustenance and active coping assistance. There are also two broad categories of supporters, each offering a different form of support to distressed individuals. The first category includes significant others, who provide emotionally sustaining behaviors and instrumental aid. The second category includes experientially similar others, who offer empathy, active coping assistance, and role modelling. Finally, evidence presents seven principle mechanisms through which interpersonal context and social support act on human functioning: social influence/social

comparison, social control, role-based purpose and meaning (mattering), self-esteem, sense of control, belonging and companionship, and perceived support availability (Thoits, 2011).

Indicators of School Support for Learning (Teacher and Peer Support)

In order to illustrate how students' perceptions of support from teachers and peers are relevant to the monitoring and promotion of positive relations, we will again use examples of items from the SEI. We will also consider how these items relate to evidence on the relevance and functions of teacher-student and peer-student relationships for student functioning, particularly that highlighted by a relatively recent meta-analysis (Thoits, 2011).

Firstly, the SEI captures the influence of the two types of supporters previously highlighted: significant others and experientially similar others. Examples of items capturing support from significant others include Item 3 ("My teachers are there for me when I need them"), while items capturing support from experientially similar others include Item 7 ("Students at my school are there for me when I need them"). Secondly, the SEI also captures the two broad types of support (emotionally sustaining behaviors and instrumental aid). Item 13 ("Most teachers at my school are interested in me as a person, not just as a student") and Item 31 ("At my school, teachers care about students") are examples of support from teachers in the form of emotionally sustaining behaviors. Item 3 ("My teachers are there for me when I need them"), on the other hand, is an example of instrumental aid from teachers. In terms of peer support, Item 14 ("Students here respect what I have to say") is an example of empathy, while Item 7 ("Students at my school are there for me when I need them") is an example of coping assistance. Finally, the SEI captures most of the mechanisms through which social support impacts on individual's functioning:

- Social influence/social comparison. Includes items 16 ("Overall, my teachers are open and honest with me"), 21 ("Overall, adults at my school treat students fairly"), and 14 ("Students here respect what I have to say").
- Social control (e.g., Item 10 "The school rules are fair").
- Role-based purpose and meaning. Includes items 6 ("Other students at school care about me") and 31 ("At my school, teachers care about students").
- Self-esteem (e.g., Item 4 "Other students here like me the way I am").
- Sense of control (e.g., Item 27 "I feel safe at school").
- Belonging and companionship. Includes items 13 ("Most teachers at my school are interested in me as a person, not just as a student"), 23 ("I enjoy talking to the students here"), and 10 ("I have some friends at school").
- Perceived support availability. Includes items 3 ("My teachers are there for me when I need them") and 7 ("Students at my school are there for me when I need them") (Thoits, 2011).

Restructuring/Improvement Efforts: Toward Greater Educational Excellence and Equity

Studies have shown that some individual predictors of school dropout (such as SES and minority concentration) don't have a significant unique effect after controlling for school characteristics, meaning that specific school characteristics play a significant role in preventing undesirable outcomes (Lee & Burkam, 2003). We suggest that encouraging teachers and students to support the learning of others is crucial for the promotion of healthy personality development as it is amenable to direct policy intervention. In other words, those who direct and work in schools should work to change this particular characteristic of their school's social organization. We propose that promoting greater excellence and equity via the promotion of students' engagement in schools requires an integration of individual and contextual characteristics with an intentional, systematized and holistic approach to school improvement. To achieve this, schools need to first understand the specific dimensions involved in the development of students' subjective experiences toward school. This requires that schools are able to conceptualize student engagement as both a process and an outcome of students' developmental trajectories. Furthermore, schools need to be able to design and to implement strategies based on this conceptualization of student engagement to promote and maintain engagement in all of their students. In order to do this, school improvement efforts need to address what can be done to promote positive student engagement development.

Evidence accumulated over the past 30 years of school improvement efforts indicates that there is a need to develop holistic and multidimensional approaches to school improvement (Ainscow, Dyson, Goldrick, & West, 2013). However, recent efforts have mostly been developed in coherence with the paradigm of conventional schools: school improvement efforts have been oriented toward reaching higher levels of school efficacy in terms of indicators of academic performance. Because of the interactive influence between different dimensions of engagement and well-being (Van Ryzin, Gravely, & Roseth, 2009), schools' improvement efforts also need to allow them to be more effective at providing the relational conditions for the promotion of healthy personality development in *all* their students. As suggested by Ainscow and colleagues, we claim that these efforts need to be made at the within-school, between-school, and beyond-school levels (Ainscow et al., 2013).

Within-School *Efforts*

Within school strategies are those that affect a specific school population and are susceptible to change via school policies and practices. Most experiences of school occur at school. Fortunately, several within school dimensions are malleable and, thus, susceptible to being tailored to meet the psychological needs of a student

population. Within- school dimensions include those consistent with person-centered schools (Moreira, Cloninger, & Garcia, 2019):

- Conceptualization of school as a context for the promotion of holistic positive development.
- Holistic conceptualization of students.
- Students' academic outcomes and processes (from performance to engagement).
- Students' psychological strengths or qualities.
- Emphasis on positive dimensions of functioning (including healthy personality development and well-being).
- The organization of learning opportunities (e.g., contents and processes of learning opportunities).
- School social support for learning (teacher and peer support for learning).
- Positive relationships as the main pedagogical tool.
- School responses to student specificities (including demographic, socioeconomic background and individual psychobiological or personality dispositional characteristics).
- A school emphasis on the care of teachers as holistic persons, including in terms of well-being.
- Opportunities for the continuous professional development of teachers.
- Opportunities for the promotion of teacher self-growth and positive development.
- The relationships of schools with the community (including students' parents).

Each of these dimensions plays an independent contribution to students' experiences, although they also interact. In the following section, we describe how these dimensions might be internalized in school improvement efforts aiming to promote engagement in *all* students.

School Social Climate

A positive school climate is a necessary condition (or pre-condition) for enhanced student development, including in terms of academic performance. Achieving a positive school climate depends on the interaction between several factors including; school objectives, drive for excellence, autonomy, resources, quality of teachers, and continued improvement efforts. School social climate refers to the quality of the relational interactions within school. This includes the established values and the expectations defined by leadership and the interactions among all members of the school community as they actually happen. There is little doubt that establishing quality, including excellence and equity, is a priority for all schools. However, it is important that schools do not confound excellence with a sole emphasis on grades or academic performance, nor equity with low academic press. It is important to combine the promotion of holistic functioning with the acquisition and development of academic knowledge. In addition, it is also important to combine strong

support for learning and positive relationships with challenging learning opportunities and stimulation. As support of this, research has shown that students reporting high support from teachers *and* high academic press learned significantly more than students who reported high support from teachers, but who attended schools where they were not pushed academically (Lee & Burkam, 2003). Consequently, we suggest that a necessary condition for schools to achieve better educational excellence and equity is that they establish both as two main indicators of school quality. This is crucial because it will allow for a thoughtful planning of priorities and activities, and for a consistent allocation of school resources. Moreover, it should also allow for a systematic assessment of the impact of improvement efforts on academic indicators, especially on more vulnerable students.

Teachers and School Interpersonal Relations

What is it about teachers that make them so important for promoting gains in engagement, especially in at-risk students? Students' experiences with school and school engagement, rather than happening in a vacuum, occur within a unique developmental and relational context. As developmental science consistently shows, human development is modulated by interactions with significant others, especially parents and teachers. Indeed, teachers are the most proximal significant agents on structured developmental processes after parents.

A large body of evidence indicates that individual dimensions of engagement are modified by contextual characteristics, including teacher-student and peer-student interactions and support for learning (Archambault, Pagani, & Fitzpatrick, 2013; Baker, 2006; Baker, Grant, & Morlock, 2008; Chen, Chang, Liu, & He, 2008; Hughes, Luo, Kwok, & Loyd, 2008; Klem & Connell, 2004; Law, Cuskelly, & Carroll, 2013; Moreira et al., 2013; Moreira, Oliveira, Dias, Vaz, & Torres-Oliveira, 2014; Murray, 2009; Roorda, Koomen, Spilt, & Oort, 2011; Valiente, Lemery-Chalfant, Swanson, & Reiser, 2008; Wang & Eccles, 2013; Waters, Cross, & Shaw, 2010a, 2010b; Woolley, Kol & Bowen, 2009). In fact, student engagement with school is a malleable process affected by dynamic and interchangeable student-teacher interactions. Teacher-student interactions shape and modify the development of dimensions crucial to adaptive academic trajectories including students' self-concepts, standards, and goals/motivations about school (Hughes et al., 2008; Liew, Chen, & Hughes, 2010; Sanson, Hemphill, & Smart, 2004; Valiente et al., 2008; Wang, Brinkworth, & Eccles, 2013). In other words, student-teacher interactions constitute the relational context in which students' cognitive representations about school (cognitive engagement) are changed (e.g., Archambault et al., 2013; Rubie-Davies, Flint, & McDonald, 2012).

Student dimensions (including students' background characteristics such as SES, personality, disruptive behaviors, ability, motivations, positive involvement in classroom activities, and positive responsiveness to teaching) interact with teacher characteristics (including personality and interpersonal style, self-efficacy, sense of control, job satisfaction). In a transactional shaping of the quality of relationsips,

these student-teacher interactions modify teachers' interpersonal responses to student behaviors and their pedagogical practices (Rudasill, 2011; Rudasill, Reio, Stipanovic, & Taylor, 2010).

Schools characterized by high support for learning are more effective and more egalitarian than schools characterized by lower support for learning (Lee, 2000), including in regards to vulnerable students (Moreira et al., 2018). Schools with high support for learning are more effective because they are better at promoting higher levels of engagement in their students, and more egalitarian because they buffer the association between prior academic performance and students' engagement. In fact, school characteristics have bene shown to buffer the risk factors associated with multiple individual and family characteristics (Blatchford et al., 2011; Eccles & Roeser, 2011; Gut, Reimann, & Grob, 2013; Van Maele & Van Houtte, 2011; Wang & Eccles, 2012, 2013; Waters et al., 2010a; Zimmer-Gembeck, Chipuer, Hanisch, Creed, & McGregor, 2006). For example, our own research has demonstrated that teacher and peer support for learning is protective against the negative effects of poor prior academic performance and engagement: in school with higher teacher and peer support for learning, students with a history of poor academic performance were more engaged with school (Moreira et al., 2018).

What this indicates is that schools are able to diminish the impact that students' background characteristics (such as family vulnerabilities) have on student functioning, and by doing so reduce the degree to which students' background vulnerabilities impair the fulfilment of potential.

In addition to in-classroom teaching and instruction processes, teachers are agents who frequently deliver other types of interactions (e.g., extracurricular activities), and the influence of teachers' interactions on student functioning happens via the same processes involved in adaptive behavior organization, including emotional support and instrumental coping (Thoits, 2011). It is, therefore, unsurprising that teachers are able to exert a large influence over student development.

Having no doubts about the importance teachers have on student development, a natural question for schools is "What influence do we want our teachers to have on our students, especially those placed at special risk?". Educational policies intend for all students to access of the same necessary conditions for adaptive learning and development, but this outcome requires significant work from teachers. If schools want their teachers to be a positive influence on students, they must be aware that teachers have needs, and these needs must be satisfied for teachers to achieve their potentials. Teacher quality is multidimensional, involving individual and contextual influences. In the same way that schools have the responsibility for offering the necessary contextual conditions for students to reach their potentials, if good teachers are a necessary contextual and relational condition for adaptive student functioning, then schools need to ensure that they can offer the necessary contextual conditions for quality teachers.

It is the responsibility of schools to provide the required conditions for effective teachers by addressing the dimensions underlying teachers' expertise. Research evidence draws the conclusions that it is neither understandable nor acceptable for

educational systems to neglect their teachers' needs. Teacher efficacy and satisfaction are influenced by several dimensions, but there is substantial evidence that some dimensions are dissociable from teachers' expertise: e.g. teachers' initial training, teachers' continual development, working conditions, and school social organization (including quality leadership, communal school organization, and average levels of control granted to teachers) (Ainscow et al., 2013; Lee, Dedrick, & Smith, 1991; OECD, 2013). We propose that educational systems need to strengthen their efforts to provide quality teachers for all students. Such efforts require more emphasis on: teaching as a relational and psychosocial activity, with responsibility for students' processes; initial teacher training; incentives to attract and maintain quality teachers; continuous professional development; and teacher well-being.

Teachers need to be considered as agents of student-oriented interventions, but also targets for personal and professional development interventions. Integrative models of teacher development and teacher quality converge on the notion that teacher quality is multidimensional, involving dynamics between personal, professional, and environmental dimensions (e.g., Korthagen, 2004).

Disadvantaged schools tend to have difficulty attracting qualified teachers (OECD, 2013), and this can impair their conditions to reach equity and excellence. Promoting school engagement in high-risk students requires that teachers have suitable training and expertise on the relational components of teaching, including the mechanisms through which social support impacts on student development (Thoits, 2011). As such, schools need to succeed in attracting and maintaining good teachers in order to promote educational equity and excellence. This requires that educational systems adopt a systematic approach to allocating teachers to schools so that schools facing especially challenging circumstances can benefit from the contribution of teachers with high expertise. This is likely to require some specific methods such as developing strategies to; (a) attract high-quality teachers to in-need schools, (b) maintain them in the school for a substantial amount of time, and (c) to involve teachers from these schools in continual development and in-service training (OECD, 2013).

The main reasons teachers leave a school are low salaries, poor support from school administrators, a lack of student motivation, a lack of teacher influence over decision-making, and student discipline problems (Berry & Eckert, 2012). Schools need to consider and reward teachers' expertise. This is necessary so that expertise can be shared among colleagues (especially in disadvantaged schools) in order to improve teacher performance (at both curricular and social support dimensions) and ultimately help school improvement efforts. Several works have outlined their recommended incentives for attracting and maintaining good teachers, and we recommend readers to consult Berry and Eckert (2012). Educational systems from several countries have adopted such guidelines. In general, these guidelines recommend establishing excellence requirements (teachers need a teaching license), providing incentives for high-achieving students to become teachers, increasing salaries to make the profession more attractive, and retaining more high-quality teachers by offering incentives to engage in in-service teacher-training programs (OECD, 2013).

Other Evidence-Based Educational Opportunities

Individual schools can do plenty to tackle issues within their own organizations, and such actions are likely to have profound impacts on student experiences. But might issues of access (the allocation of students to schools) be more effectively addressed if schools work together on a common agenda (Ainscow et al., 2013)?

Schools can take several actions to promote the development of positive trajectories. Evidence from a large body of research supports a set of strategies for school promotion of student learning that are particularly effective in preventing disengagement with school, including school dropout. These work especially well with students at risk of poor academic trajectories. The National Dropout Prevention Centre/Network (NDPC/N), for example, has identified 15 effective strategies for preventing severe disengagement with school: active learning, after-school opportunities, alternative schooling, career and technology education, early childhood education, early literacy development, educational technology, family engagement, individualized instruction, mentoring/tutoring, professional development, safe learning environments, school-community collaboration, service-learning, and systemic renewal (Schargel & Smink, 2004). These strategies have the potential of reduce educational inequalities at several levels of functioning. For example, an early promotion of positive socio-emotional development overrides the inequalities in academic trajectories resulting from students' socioeconomic and other background characteristics (Becker & Luthar, 2002; Osher et al., 2008). All these strategies involve, or are delivered by, teachers. This reinforces the need of teachers' actions to be in accordance with what works in the pursuit of positive engagement in students. Research has also shown that students are more engaged in schools that implement school improvement efforts (Cavendish, 2013; Fullarton, 2002; Lee & Smith, 1995). To widen this effect, schools need to further evaluate the implementation and impact of these strategies on student functioning using assessment tools with acceptable evidence-based validity (e.g., Moreira et al., 2014). However, schools need to consider that when offering other educational opportunities these should be intentionally designed to promote student holistic development (including healthy personality development) and that educational opportunities, regardless of their nature, do not dismiss the importance of interpersonal relationships.

Between Schools

Much of what happens within school is influenced by what happens at the between-school level. Certainly, there is much schools can do beyond their school specific actions, and collaboration between schools and networking has been identified as an ideal pathway for schools to achieve higher excellence and equity (Ainscow et al., 2013; Ainscow & Sandill, 2010; OECD, 2013). *Between-school efforts* refer to the collaborative processes across different schools that aim to offer their school populations the best solutions to their needs.

Between school collaboration is of great importance for a number of reasons, especially in disadvantaged schools or schools facing substantive socioeconomic constraints. Disadvantaged schools have more difficulty in attracting and maintaining high-quality professionals with the potential to initiate or continue efficient school improvement plans and actions. Teachers in disadvantaged schools are frequently not up-to-date with current evidence and literature concerning concepts and practices due to a lack of time, motivation, continuous professional development, expertise and/or school leadership, and strategic vision. Disadvantaged schools do not benefit from the support of specialist school improvement organizations. Finally, disadvantaged schools are not involved in networks that might buffer the schools' vulnerabilities by allowing them contact with other experiences from which they may learn and benefit from shared resources (including material, modulation, and motivation). Because socioeconomic constraints are less changeable, school networking is an ideal pathway for schools to develop expertise on school improvement efforts.

Beyond School

This is a macrolevel context for school practices. This includes the national economic conditions and the human capital development, the socioeconomic characteristics of the school community, the political conceptualization of education (including priorities, policies, and resources for student development and teacher working conditions), and family characteristics (including structure, processes, and resources) (Ainscow et al., 2013). In order to achieve excellence and equity, educational systems need to:

- Establish excellence and equity as educational priorities.
- Allocate resources in a more equitable way between advantaged and disadvantaged schools and students.
- Make less use of stratification – no allocation of students to schools or classrooms based on ability or behavior.
- Make pre-primary education universal for all students, but especially disadvantaged students, for an early promotion of core competencies such as executive functions (early literacy and numeracy development promotion) and of socioemotional and personality development.
- Allow schools more autonomy for curriculum organization, teacher allocation, assessment of skills, and allocation of school resources to school priorities.
- Monitor school efficacy indicators (not only student grades but also student engagement) in the context of the wider educational system (OECD, 2013).

From these, school autonomy and school evaluation are especially amenable to policy interventions. Schools require more autonomy to recruit and maintain quality teachers. Schools facing particularly challenging circumstances should implement concrete and macro policies to empower them to address and meet the needs of all

their students. These could include increasing school autonomy to allocate resources, improving teacher participation and accountability, and increasing parent involvement with school, all of which should contribute to diminishing disparities in education (Pereira & Reis, 2012, 2014).

Evaluations of school quality are a second important beyond school feature. Such evaluations can assume different forms, but can be distinguished simply in terms of internal and external evaluations. Commonly, schools adopt a combination of both approaches as this allows for school autonomy over their own practices (internal control, called self-evaluation) and control by public authorities (external evaluation, frequently called inspection). External evaluations are associated with progress in school self-evaluation and school quality. Internal self-evaluations are positively associated with both student (Hofman, Dijkstra, & Hofman, 2009) and teacher processes and outcomes (Schildkamp, Visscher, & Luyten, 2009). As well as the involvement of educational agents, several methodologies include students in school self-evaluations, and this has been associated with greater educational equity (OECD, 2013). However, schools also benefit from further assistance in designing, making sense of assessment results and translating them into improvement efforts (Ainscow & Sandill, 2010; OECD, 2013). There is a growing tendency for school systems to involve specialist organizations that support schools in planning, implementing, and assessing the school quality dimensions of interest. These organizations, often called by School Improvement Officers (Ainscow & Sandill, 2010), play an important role in fostering school quality, including educational excellence and equity. That said, it is vital that school improvement organizations have a clear emphasis on the promotion of equity, specifically supporting schools to identify priorities, design interventions, and assess its impact on indicators of educational equity. School improvement organizations have the potential to help schools effectively integrate the numerous dimensions involved in the pursuit of excellence and equity. These include:

- Holistic conceptualization of students.
- Individual dispositional characteristics (personality organizations, cognitive abilities, and prior experiences).
- Students' families (structure, processes, resources, and health conditions).
- School characteristics (including deficits, constraints, and strengths of the different school dimensions).
- Socioeconomic characteristics of both distal and proximal contexts.
- Community resources.
- Educational policies.
- Theoretical, conceptual, and evidence-based foundations of the improvement efforts.
- Guidelines for systematic implementation of within- and between-school concrete actions.
- Support for the assessment of school improvement impact (from assessment selection, data collection procedures, data analyses, interpretation of results).

- Translation of the evidence coming from assessment into between-school, within-school, and community practices.
- Internal and external school evaluation.
- Opportunities for continuous professional development.
- Higher sense of control and support for the school improvement efforts.
- Professional motivation and well-being.

Conclusion

Non-familial social environments (particularly interactions with teachers and peers) have a significant impact, including in the long term, on several indicators of academic trajectories (Furrer & Skinner, 2003; Gut et al., 2013). School support for learning favors higher levels of engagement and also buffers the negative impact of prior academic performance on engagement. Because student engagement with school is one of the strongest predictors of academic trajectories, schools need to conceptualize student engagement as an outcome of school actions. This implies that schools assume a responsibility for keeping their students engaged with school and requires an adoption of specific strategies aimed at the promotion of students' engagement with school. Students' perceptions about school improvement efforts are associated with their engagement (Cavendish, 2013; Dias, Oliveira, & Moreira, 2014), attesting that the degree to which schools implement improvement efforts has a significant positive impact on students' engagement (Fullarton, 2002; Lee & Smith, 1995). If schools aim to promote engagement in all their students (especially those with individual and family risk factors), they need to be proactive in promoting the school dimensions that have been empirically supported to impact on students' engagement.

One of the main goals of equalitarian educational systems is finding a way to offer all students the same educational opportunities and to succeed in diminishing the existing differences in student functioning that arise from differences in students' background characteristics (including family SES). When schools fail to meet these objectives, it means they are doing little more than reproducing the inequalities found at other societal levels (e.g., at the level of the wealth distribution). This is always unacceptable, and particularly unacceptable in contemporary societies that have the means to make a real difference to students' developmental trajectories, and ultimately on students' lives. High educational excellence and equity are effective pathways for promoting the development of societies (from economic to human capital indicators), especially in the context of contemporary knowledge-based economies (OECD, 2013).

The positive development of personality and its narrower expressions, such as student engagement with school, is an effective pathway for promoting excellence and equity. Research (e.g., Wang & Eccles, 2012) and international organizations (OECD, 2013) acknowledge that disadvantaged students are typically less engaged with school (including energy, proactivity, pro-school motives and goals, confidence,

and sense of belonging). According to interactionist perspectives and self-determination theory, these are the core dimensions required for a healthy self-determination, positive functioning, and healthy personality development and engagement with school.

In sum, student engagement with school is an expression of personality organizations concerning experiences with school. It is a process malleable to intervention and particularly sensitive to interpersonal influences (including teacher-students relationships). In this light, student engagement with school can be considered an example of how personality and educational constructs might be integrated in effective educational and school practices, including in school improvement and re-restructuring efforts.

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Part III
Challenges and New Venues

Current Directions in Psychiatric Classification: From the *DSM* to RDoC

Björn N. Persson

Abstract In 2010, the National Institute of Mental Health initiated the Research Domain Criteria (RDoC), a new research framework for studying mental disorders. The RDoC is predicated on that psychiatric disorders are fundamentally disorders of the brain, which are best conceptualized as dimensional, and not discrete, phenomena. The RDoC approach stands in contrast to the more traditional *Diagnostic and Statistical Manual of Mental Disorders (DSM)*, which relies on discrete diagnostic categories such that patients either meet diagnostic criteria or not. The present chapter has three explicit aims: (a) to describe the conceptualization of personality disorders (PDs) from *DSM-III* (American Psychiatric Association, Diagnostic and statistical manual of mental disorders. Author, Washington, DC, 1980) and forward, including the differences between categorical and dimensional models of psychopathology; (b) to present some of the fundamental differences between the *DSM-5* and RDoC perspectives; and (c) to describe challenges for the RDoC framework along with a possible alternative to it, namely, the network approach to psychological disorders.

Keywords Psychiatric classification · Nosology · *DSM* · RDoC · Network psychometrics · Personality disorder · Psychopathology

In the past decade, a lot has happened in the realms of psychiatric classification, personality assessment, and neuroscience. One of the more important developments happened in 2010, when representatives of the National Institute of Mental Health (NIMH) initiated the Research Domain Criteria (RDoC), a new research framework for studying mental disorders (Cuthbert & Insel, 2013; Cuthbert & Kozak, 2013; Insel et al., 2010; Kozak & Cuthbert, 2016). A central tenet of RDoC is the

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conceptualization of mental disorders as brain disorders (Insel et al., 2010). The RDoC was developed as a response to increasing concerns (see Cuthbert & Insel, 2010; Insel et al., 2010) about the most recent version of the premiere psychiatric classification system – the fifth edition of the *Diagnostic and Statistical Manual of Mental Disorders* (*DSM-5;* 2013), produced and published by the American Psychiatric Association (APA). For a review of the development of the different *DSM* editions, see Blashfield, Keeley, Flanagan, and Miles (2014). To a certain extent, the *DSM* and RDoC present clashing diagnostic approaches (Lilienfeld & Treadway, 2016; Zachar & Kendler, 2017), insofar as they differ in fundamental assumptions about the nature of psychopathology. With that said, it should be noted that the RDoC is more research oriented, while the *DSM* serves the broader purpose of having clinical application (cf. Lilienfeld & Treadway, 2016). The goal of this chapter is to describe (a) the conceptualization of personality disorders (PDs) from *DSM-III* (APA, 1980) and forward, including the differences between categorical and dimensional models; (b) some of the fundamental differences between the *DSM-5* and RDoC perspectives; and (c) conceptual and psychometric challenges for the RDoC framework along with a possible alternative to it, namely the network approach (Borsboom & Cramer, 2013). It should be noted that many of the developments in personality psychology, both normal and abnormal, have paralleled—and to some extent caused (Krueger, 2013)—developments in psychopathology research, seen more generally. While the focus of this chapter is on personality, many of the issues raised pertain to both psychopathology more generally and personality, more specifically.

The *DSM-III* Paradigm

For a long time, mental disorders have been thought of as natural categories, or what is often referred to as taxa (Meehl, 1992). Taxa refers to discrete differences between conditions, such that one is either schizophrenic or not. A typical example, taken from medicine, is that one is either pregnant or not, one cannot be a little bit pregnant. Hence, pregnancy is a taxonic variable. A dimensional model, on the other hand, posits that an individual can present with a disorder (e.g., schizophrenia) to some degree. Evidence suggests that most *DSM* disorders are dimensional in nature (Haslam, Holland, & Kuppens, 2012; see also Borsboom et al., 2016), but it is only in recent years that this fact has received significant attention (Krueger et al., 2018).

The prevailing paradigm for psychiatric classification was established in the *DSM-III* (APA, 1980), in which the number of mental disorder categories increased from 163 to 224. *DSM-III* also introduced two major features not present in previous nosologies: diagnostic criteria for each mental disorder category and a multiaxial system (Blashfield et al., 2014). Editions prior to *DSM-III* did not use explicit diagnostic criteria but instead relied only on prose definitions for each mental

disorder, which led to poor inter-rater reliability (Blashfield et al., 2014). The multiaxial system was meant to be useful for providing a comprehensive diagnosis, as each patient was expected to be diagnosed on five separate axes (see Blashfield et al., 2014). The five axes described: (I) the presence of mental disorder categories (e.g., schizophrenia); (II) personality dysfunction and intellectual disability; (III) medical disorders relevant to the patient's psychiatric presentation; (IV) stressors in the social environment; and (V) an assessment of overall adaptive functioning. The *DSM-III* approach is often referred to as neo-Kraepelinian (Blashfield, 1984), as it shared the philosophy of Emil Kraepelin (1856–1926), in that it moved away from psychoanalysis and toward the methods of traditional medicine. The *DSM-III*, like Kraepelin, emphasized signs (observable manifestations), symptoms (subjective reports), and natural history (trajectory over time), instead of psychoanalytic concepts which were more influential in *DSM-I* and *DSM-II* (see Blashfield et al., 2014; Lilienfeld, Smith, & Watts, 2013; Lilienfeld & Treadway, 2016).

The *DSM-IV* (APA, 1994) grew in size, but not much changed in the approach or underlying philosophy. One of the things that did change was a gradual move toward polythetic criteria, which, as opposed to monothetic criteria, means that signs and symptoms are neither necessary nor sufficient for diagnosis (Lilienfeld et al., 2013). Monothetic criteria are useful as they maximize homogeneity within PD categories, as all individuals in a diagnostic category share traits. Conversely, the polythetic approach leads to diagnostic heterogeneity. For instance, borderline PD includes 256 different criteria combinations, all yielding the same disorder. Remarkably, for some diagnoses in the *DSM-IV*, it is possible for two patients to have no overlap in diagnostic criteria (Lilienfeld et al., 2013). This is not unique to PD categories. For instance, post-traumatic stress disorder combinations far outnumber those of PDs (Young, Lareau, & Pierre, 2014). For a clinician to be expected (perhaps required) to provide the same treatment for individuals who share no overlap in diagnostic criteria clearly points to an inherent problem in the *DSM-IV* model. Accordingly, polythetic criteria have been criticized for creating overly heterogeneous groups (Krueger, 2013), while monothetic criteria suffers from the opposite problem, creating overly narrow groups, thus not allowing for conditional indicators that may not be present in all cases (Widiger & Frances, 1985). The issues surrounding both monothetic and polythetic criteria are well established (see, e.g., Cooper, Balsis, & Zimmerman, 2010; Pfohl, Coryell, Zimmerman, & Stangl, 1986).

The *DSM-IV* model consists of 10 PDs: paranoid, schizoid, schizotypal, antisocial, borderline, histrionic, narcissistic, avoidant, dependent, and obsessive-compulsive. There is also an 11th category: PD not otherwise specified (PD–NOS) which was meant to be used when none of the other PDs fit a patient's symptoms. Because patients often do not fit neatly into PD categories, patients are either given multiple diagnoses (which is known as the problem of comorbidity, see Cramer, Waldorp, van der Maas, & Borsboom, 2010) or placed in the PD–NOS category (Verheul & Widiger, 2004). Both approaches cause substantial problems in clinical decision making: PD–NOS is unspecific and comorbidity dictates that an individual may fulfill criteria for multiple diagnoses, thus raising the question of which diagnosis to treat, and how.

DSM-5: Empirical Evidence, Opposition to Innovation, and Steps Forward

One major effort undertaken in the *DSM-5* was the attempt at replacing the previous (i.e., *DSM-IV-TR*, text rev.; APA, 2000) categorical model of PD with a dimensional model. This development was predicated on accumulating evidence that PDs are better conceptualized (and modeled statistically) as continuous and not as discrete phenomena (e.g., Markon, Chmielewski, & Miller, 2011; Trull & Durrett, 2005). These findings ran in parallel with the insight that taxonomies of normal personality could help shape models of pathological personality (see, e.g., Markon, Krueger, & Watson, 2005; Widiger & Mullins-Sweatt, 2009; Widiger & Trull, 2007).

In the traditional medical disease model of older *DSM* versions, diagnoses are discrete categories, meaning that a patient with major depression is qualitatively different from someone who is not suffering from major depression. In a dimensional model, there is a quantitative, continuous difference in level of depression, meaning that the boundary between normal and abnormal is inherently fuzzy. Ultimately, the effort to replace the categorical model fell short and the *DSM-IV-TR* personality disorder section was copied verbatim into the *DSM-5*.

The proposed dimensional model was placed in a separate section called "Emerging Measures and Models" (APA, 2013, p. 729). Plenty has been written about issues within the *DSM-5* task force (Frances, 2009; Spitzer, 2009), the inner workings of the Personality Disorder Work Group (Gunderson, 2013; Krueger, 2013; Skodol, Morey, Bender, & Oldham, 2013; Zachar, Krueger, & Kendler, 2016), including the resignation of two Work Group members (Livesley, 2012; Verheul, 2012), and finally reflections about the aftermath and efforts to improve future revisions of psychiatric classification systems (First, 2014; Gunderson, 2013; Lilienfeld, 2014a; Miller & Lynam, 2013; Mullins-Sweatt, Lengel, & DeShong, 2016; Pincus, 2013; Widiger & Crego, 2015). The intricacies of both the successes and failures of the *DSM-5* PD framework is highly important, but the utility of the dimensional model, including its consequences for the RDoC framework, is of greater relevance presently.

Dimensions of Normal and Abnormal Personality

During the *DSM-5* revision process, one concern was that much of the literature reviewed in support of a dimensional model contained studies of normal and not clinical populations. Much of this evidence, undoubtedly, relied on the Big Five (Goldberg, 1990) or Five Factor Model (FFM; Costa & McCrae, 2017; McCrae & John, 1992), which includes five broad bi-polar personality domains: extraversion, agreeableness, openness to experience, neuroticism, and conscientiousness. Together, these domains are both impressive descriptive taxonomies of personality

phenotypes and reliable predictors of a great variety of consequential outcomes (Grucza & Goldberg, 2007; Ozer & Benet-Martinez, 2006). The FFM facilitates individual profile scores, meaning that an individual is assessed on each of the five dimensions and is placed somewhere on a normal distribution. This procedure creates a more refined picture of an individual's personality than placement in a discrete category. In other words, knowing that one belongs to the 87th percentile in extraversion is more informative than being placed in a category of "extraverts," into which everyone with extraversion scores above the mean are placed. Translated into the language of psychopathology, knowing that a patient belongs to the 95th percentile on a specific diagnostic marker (e.g., trait antagonism) provides much more substantive information (cf. Markon et al., 2011) than the dichotomous information that a patient does or does not present with a diagnostic marker.

In commonly used personality inventories, the five domains are further divided into facets. These facets represent personality at a more detailed level of analysis. In recent years, describing personality at different levels of abstraction has become increasingly common, with analyses of "nuances," which refers to individual questionnaire items (Mõttus, Kandler, Bleidorn, Riemann, & McCrae, 2017), aspects (DeYoung, Quilty, & Peterson, 2007), and higher-order factors, or so-called metatraits, such as alpha-beta (Digman, 1997), stability-plasticity (DeYoung, 2006), and the general factor of personality (Musek, 2007; Rushton & Irwing, 2008). A lot of progress has been made in trying to understand how these different levels of abstraction relate to both normal and abnormal personality (Krueger & Markon, 2014; Markon et al., 2005; Wright & Simms, 2014).

During the process of updating the *DSM-5*, the Personality Disorder Work Group ultimately proposed a model inspired by the FFM, which included five broad maladaptive domains (with adaptive Big Five equivalents in parentheses): negative affectivity (neuroticism), detachment (introversion), antagonism ((dis) agreeableness), disinhibition (low conscientiousness), and psychoticism (openness to experience). In addition to these five broad domains, the model is further divided into 25 facets in total. During the process of validating this model, an instrument called the Personality Inventory for *DSM-5* was created (Krueger, Derringer, Markon, Watson, & Skodol, 2012; Suzuki, Samuel, Pahlen, & Krueger, 2015), which over the years has been proven to be psychometrically sound (Hopwood, Thomas, Markon, Wright, & Krueger, 2012; Morey, Krueger, & Skodol, 2013; Thomas et al., 2013), and more clinically useful than the *DSM-IV* model (Morey, Skodol, & Oldham, 2014). It should also be noted that substantial effort has been put into integrating normal and abnormal personality models, both historically (e.g., Cloninger, 1987; Cloninger, Svrakic, & Przybeck, 1993; Eysenck, 1947), and more recently (Conway, Latzman, & Krueger, 2019; Markon et al., 2005; Widiger & Simonsen, 2005), which has ultimately yielded FFM-based models that describe both normal and abnormal personality functioning across multiple levels of abstraction (Caspi et al., 2014; Hengartner, Ajdacic-Gross, Wyss, Angst, & Rössler, 2016; Kendler et al., 2017; Krueger & Markon, 2014; Mõttus et al., 2017).

Research Domain Criteria

When in 2010, the NIMH launched RDoC, they particularly emphasized that mental disorders should be viewed as brain disorders (Insel et al., 2010). Furthermore, it was assumed that these disordered circuits are identifiable using neuroscientific tools, such as electrophysiological measures, functional neuroimaging, etc. With what was arguably a failure of the *DSM-5*, the RDoC project garnered a lot of interest and in the years since has generated a number of studies across multiple scientific disciplines (see, e.g., Carcone & Ruocco, 2017).

The RDoC mission is relatively fluid, insofar as it is not looking to replace current psychiatric nosologies but rather allow researchers to study psychopathology within a given framework. Currently, this framework contains five broad domains: negative valence systems, positive valence systems, cognitive systems, systems for social processes, and arousal/regulatory systems. Each domain can be studied across seven units of analysis (or increasing levels of abstraction): genes, molecules, cells, circuits, physiology, behavior, and self-reports. Together, the domains and units of analyses create a two dimensional matrix (see, NIMH, 2017). The RDoC proposal thus allows researchers to study alternative models of psychopathology without being constrained by the traditional categorical system of the *DSM* (for pros and cons of diagnostic nosologies, see Markon, 2013; Zachar, 2013).

Issues Facing the RDoC Framework

In an excellent overview, Lilienfeld (2014b) presented some of the advantages the RDoC holds over the *DSM*, but also enumerated a number of methodological and conceptual challenges for the RDoC framework (see also Wakefield, 2014). Lilienfeld (2014b) posited four challenges: (a) an overemphasis on biological units and measures; (b) neglect of measurement error; (c) biological and psychometric limitations of endophenotypes; and (d) distinguishing biological predispositions from their behavioral manifestations. I briefly reiterate Lilienfeld's (2014b) challenges (c) and (d), and discuss (a) and (b) in more detail in the subsequent sections.

First, the term *endophenotype* refers to an internal process which can be objectively measured (Gottesman & Gould, 2003). Examples include biochemical markers, findings from brain imaging, or various neuropsychological tests (Lilienfeld, 2014b). Endophenotypes are perhaps more easily understood when distinguished from *exophenotypes*, which refers to the more traditional signs and symptoms (e.g., behaviors) found in *DSM* criteria. The rationale for using endophenotypes was to fill the gap between genes and the disease process, as endophenotypes are assumed to be closer to the gene than exophenotypes (e.g., behaviors) (Gottesman & Gould, 2003). There are many issues with endophenotypes (see, e.g., Lilienfeld et al., 2013; Lilienfeld, 2014b), but the main concern may be

that endophenotypes seem to be as complex as behavioral traits (Iacono, Malone, & Vrieze, 2017), which naturally limit their utility. However, these issues are just that, *issues*, and should not be seen as problems severe enough not to merit further research. In fact, for a more optimistic view regarding endophenotypes, see Miller, Rockstroh, Hamilton, and Yee (2016).

The next challenge, that of distinguishing biological predispositions from their behavioral manifestations, refers to a distinction between basic tendencies and characteristic adaptations. This distinction is meant to highlight a difference between, for instance, one's level of neuroticism (i.e., a basic tendency), and how one adapts to one's own neuroticism (i.e., the characteristic adaptation). Lilienfeld (2014b) writes that "an individual with high levels of negative emotionality may manifest this predisposition in an anxiety disorder; alternatively, she may manifest it in artistic productivity, which is associated with a disposition toward negative emotionality" (p. 135). This distinction has consequences for the RDoC, as similar predispositions may yield very different behavioral manifestations (cf. the concept of multifinality in the subsequent section). Progress in the RDoC framework may be impeded as physiological risk factors of psychopathology need to be separated from the psychopathology itself (Lilienfeld, 2014b; Wakefield, 2014).

Biological Overemphasis As mentioned previously, the RDoC conceptualizes mental disorders as "disorders of brain circuits." At this point in time, it has become axiomatic that all psychological phenomena are mediated by the brain, but as Lilienfeld (2014b) notes, biological mediation is not the same thing as biological etiology. A mental disorder may be caused by (have etiological roots in) environmental factors at time T_1 and manifest neurologically at time T2. Neither structural nor functional imaging at T_2 will shed light on the cause(s) at T_1. The psychometrician Frederick Lord is sometimes paraphrased as having said that "the numbers don't know where they came from" (Lord, 1953). This is true for all kinds of data, including data collected using neuroscientific methods. It is up to the researcher to provide an explanatory framework for how the collected data is best explained.

Furthermore, Lilienfeld (2014b) notes that data drawn from only the self-report domain fall outside the RDoC approach (Cuthbert & Kozak, 2013). This is potentially a problem as, in many cases, self-report questionnaires provide higher validity than biological measures. For instance, Iacono et al. (2017, p. 117) maintain that "there are no biomarkers that can be used clinically to confirm a diagnosis or identify a given individual as at risk, and it is not clear that the candidate biomarkers that exist do a better job identifying cases than existing interview methods." Accordingly, it seems reasonable to complement, but not supplant, self-report, and interview methods with other methods (e.g., physiological measures), but these methods too need to be thought of as fallible indicators.

It has long been known that developmental trajectories are not necessarily linear nor causally deterministic (Cicchetti & Blender, 2004). The concepts of equifinality and multifinality reflect this realization. Equifinality refers to the fact that multiple pathways can lead to the same outcome and multifinality reflects that

the same pathway may lead to multiple outcomes (Cicchetti & Toth, 2009). Similar concepts exist in the cognitive neuroscience literature, namely, that different brain structures may process information in ways that lead to similar outcomes and that similar processing may lead to different outcomes, depending on the brain structure (see, e.g., Sarter, Berntson, & Cacioppo, 1996). Crucially, the study of psychopathology needs to consider not only multiple levels of explanation but also how information across multiple levels interact over time. This idea traces back to the Cattell data box (Cattell, 1946), in which people and measures (e.g., personality items) were modeled across time, thus allowing both between subject and within subject comparisons. This idea never caught on in mainstream research, but has recently been revived (e.g., Molenaar & Campbell, 2009), and put to empirical use (Wright et al., 2017).

Measurement Error A final concern is the potential neglect of measurement error. Lilienfeld (2014b) captures some of the core issues inherent in an undue reliance on neuroscientific methods, for instance, the modest test-retest reliability of functional magnetic resonance imaging (fMRI) (Bennett & Miller, 2010; see also Friedman et al., 2008)—one of the most commonly used tools in neuroscientific research. While these issues are obviously very important, I will focus on a related idea which is consistent with RDoC approach, namely, that psychiatry should move into the laboratory in order to be more like medicine (see Widiger & Clark, 2000, for a review). This is an interesting idea, which I believe ties into Cronbach's (1957) classic distinction between two historic streams of psychology that are arguably present to this day: experimental and correlational psychology. Experimental psychology is mainly concerned with manipulating variables in order to understand some process. Correlational psychology is mainly concerned with phenomena that we cannot manipulate, for instance, individual differences in personality, and therefore focus on describing such differences.

This division was lamented by Cronbach, who believed that combining the two streams of psychology could eventually lead to a unification of psychology. Others take the view that this distinction emerges as a consequence of the fundamentally different levels of explanation on which experimental and correlational psychologists operate (Borsboom, Kievit, Cervone, & Hood, 2009; see also Hedge, Powell, & Sumner, 2018). The core issue is whether it is possible, and if so, how to integrate findings from multiple levels of explanation in the RDoC matrix (e.g., genes, physiology, behavior, and self-reports), being that experimental tasks and questionnaires intended to measure the same construct, may not produce reliable individual differences (Hedge et al., 2018). Laboratory measures have been known for a long time to be unreliable (Epstein, 1979), which is a consequence of large measurement error and high situational specificity. This fact does not seem to be unique to experimental psychology, as it is also present in contemporary neuroscience (Enkavi et al., 2019; Hajcak, Meyer, & Kotov, 2017; Luking, Nelson, Infantolino, Sauder, & Hajcak, 2017).

To exemplify this problem, consider that both behavioral and self-report measures of impulsivity independently predict impulsive behaviors, but the relation between

self-report and behavioral tasks is low (Sharma, Markon, & Clark, 2014), which suggests a lack of coherence between these two levels of explanation. Similarly, there seems to be a nonrelation between laboratory and self-reported empathy (Melchers, Montag, Markett, & Reuter, 2015) which may explain why there is an unexpected nonrelation between self-reported empathy and aggression (Vachon, Lynam, & Johnson, 2014). Both impulsivity and empathy are highly important for various personality disorders (e.g., narcissistic and antisocial) and have been subjected to a lot of research. Nevertheless, the current status of impulsivity and empathy is that self-report and behavioral tasks do not accurately measure the same phenomena. This is a critical problem for the RDoC, as findings from one level (e.g., laboratory/behavioral) may not correspond meaningfully with findings from another level (e.g., self-report).

There are many reasons for why these effects may occur. One may be the fundamentally different types of data (Borsboom et al., 2009; Hedge et al., 2018), or because a construct has been insufficiently defined or delineated (cf. Palminteri & Chevallier, 2018; Rossiter, 2005). Researchers must be aware that constructs may behave very differently across different levels of abstraction. Using multiple indicators is a step in the right direction, but a combination of a priori theorizing (Vaidyanathan, Vrieze, & Iacono, 2015), as well as the use of latent variable modeling (e.g., Patrick et al., 2013) is preferred, as it provides the opportunity to analyze different sources of variance in a theory-driven way. Even so, it was recently argued that clinical neuroscience may be lagging behind because of a failure to consider the basic measurement properties of the neural measures themselves (Hajcak et al., 2017). For instance, the internal consistency of fMRI measures is very rarely reported (Luking et al., 2017). Some consideration should also be given to the different time domains of laboratory and self-report measures. During collection of neuroscientific data, there are many sources of noise that needs filtering: the influence of physical movement, eye-blinks, heart rate, and deglutition can be major (Huettel, Song, & McCarthy, 2009; Luck, 2014). Such influences are not present in self-reports, where other types of noise are of greater concern, including method variance (Podsakoff, MacKenzie, & Podsakoff, 2012), and social desirability (Paulhus, 2002). Whether these measurement issues can be resolved by improving the conceptual domain (i.e., improving the conceptualization of constructs) or whether discrepant results are caused by fundamental differences in the nature of collected data remains to be seen. One may hope that finding such discrepancies paves a way toward more coherent constructs and improved research (see Cooper, Jackson, Barch, & Braver, 2019 for a measurement perspective on these issues). The importance of appropriate construct validation was recently described in a systematic and accessible fashion (Tay & Jebb, 2018).

The Network Approach

The RDoC introduces a more nuanced dimensional view of psychopathology than what the *DSM* approach offers, but there are other alternatives as well. The RDoC ultimately posits common biological causes for diagnostic categories, whereas the recently developed network approach conceptualizes mental illnesses in terms of causal dynamics between the symptoms themselves. In other words, in the network approach (Borsboom & Cramer, 2013; Schmittmann et al., 2013) the focus of analysis has shifted from the latent variables to the network itself. In conventional latent variable theory, the construct "depression" refers to a latent phenomenon which causes manifest signs and symptoms (indicators), such as sleep loss, disordered eating habits, suicidal thoughts, etc. In the network view, depression refers to the state of a system, and the system is not a latent variable but the indicators themselves (Borsboom & Cramer, 2013). In other words, depression emerges from the fact that an individual suffers from sleep loss, disordered eating habits, etc. One of the benefits of the network approach is that it removes some of the conceptual issues surrounding the ontological status of mental disorders (Borsboom, Mellenbergh, & Van Heerden, 2003; 2004). The question regarding the status of the manifest signs and symptoms are believed to be easier to explain: sleep loss is sleep loss. Network theory does not need to invoke an explanatory variable that in turn explains the presence of sleep loss (i.e., a latent variable). Nevertheless, it should be noted that the network approach does not abandon latent variables completely, insofar as it also allows for hybrid models. For example, mental disorder onset may have a common cause and the maintenance of the disorder could be governed by the interactions between symptoms (Fried & Cramer, 2017).

Network theory also deals with comorbidity in an interesting way (Cramer et al., 2010). In the latent variable view, the relation between a major depressive episode (MDE) and generalized anxiety disorder (GAD) is either that the two share a root cause, or that a patient has two simultaneous disorders. In the network view, comorbidity may arise because the two disorders share common symptoms. Borsboom, Cramer, Schmittmann, Epskamp, and Waldorp (2011, p. 1) provide the following example: "It is feasible that comorbidity between MDE and GAD arises from causal chains of directly related symptoms, e.g., Sleep deprivation (MDE) → fatigue (MDE) → concentration problems (GAD) → irritability (GAD)." Accordingly, network theory offers new creative solutions to old problems. The network approach is not necessarily incommensurable with the either the *DSM* or RDoC approaches. The network approach does, however, offer a different conceptualization of psychopathology than the other frameworks (see Borsboom & Cramer, 2013; Fried & Cramer, 2017).

Conclusion

There has been significant progress in psychopathology and personality research in recent years. In summary, the empirical evidence for the superiority of a dimensional classification system over the traditional categorical system used in the *DSM* is overwhelming. It seems probable that future nosologies (e.g., *DSM-6*) will utilize dimensional classification, in particular because of its greater reliability and validity. Whether this change will only entail personality disorders or include the entire range of psychopathology (see, e.g., Kotov et al., 2017) remains to be seen. Until then, the RDoC is a promising research framework, but also a difficult undertaking. A major concern is whether it is possible to mesh findings from different levels of explanation. Finally, the network approach offers an interesting alternative way of conceptualizing mental disorders. It has already generated a fair amount of discussion (cf. Cramer et al., 2010), but its ultimate standing in psychopathology research remains to be seen.

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The Future of Personalized Care: Scientific, Measurement, and Practical Advancements in Personality and Brain Disorders

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Abstract *Background*: Person-centered care sciences are experiencing rapid progress. Personalization in care services is becoming the norm, and implementation from scientific knowledge is increasingly acknowledged and mandated. Advances in personality and brain disorder research are crucial in assisting the future development of personalized care. *Aim*: We will attempt to present glimpses into the future of personalized care with support from frontline science, measurement, and practice, updating with input from personality genetics and measurement theory. *Outline*: We present three broad developments: (1) scientific advancements in understanding how personality and genetics are central in predicting mental health and disorders, with the potential to increase predictive diagnosis and treatment validity; (2) measurement advancements with help of trait dimensions and latent structures, with the potential to increase reliability in assessing personalized care needs and functioning; (3) practical advancements in implementing a personalized approach in care services, with the potential to increase effectiveness and satisfaction with patients. We review this glimpse into the future by referencing key findings in personality and assessment meta-analyses, genome-wide association studies (GWAS), and trait measurements in psychiatric disorders. *Conclusion*: Personalizing care services will benefit practitioners and patients. We suggest and recommend that personalized care diagnosis and treatment is the way forward and that the future will be potentially revolutionized by incorporating the presented advancements in personality research and brain sciences.

Keywords Person-centered care · Personality · Personality assessment · Genetics · Patient satisfaction

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Predicting the future of a field is naturally unwise, since predictions tend to go wrong. However, a sensible approach is to ponder upon the future based on present trends and long-term progress. It is much like forecasting long-term weather, which is not best done by speculating on incidental cloud formations but rather by browsing the calendar looking for a stable signal in the current climate trends.

The future of personalized care, which implies individualizing diagnosis and care treatment focusing on the unique functioning of a person, increasingly looks as one of the most important matters for modern welfare society. In the days ahead, personalized care has to be able to encompass both care effectiveness and citizen service satisfaction. In order to achieve this, health services will have to rely on the input from scientific research. The present chapter will attempt to outline the present scientific trends that likely can and will carry personalized care into the future. We show the exciting advancements from the last years in basic science, measurement, and practice. Diagnosis and treatment practice tend to depend on validity and reliability in measurement, which in turn tend to depend on the quality of scientific findings and theory. Together these intermingling trends help us navigate into the future of personalized care.

First, we present the consensual finding that personality traits are signals strong and stable enough to be able to predict mental health among individuals in entire populations across the life-span. One of the most replicable and sizable effects within the behavioral sciences is that genetics is the foundation of the lasting stability in personality across life-phases. This is a potential paradigm-shift in understanding mental disorders, benefitting both practitioners and patients. Second, we present evidence supporting that both personality and mental disorders are assessed better by dimensional and continuous measures, rather than the categorical and discrete measures. One of the consequences of this is that personality and mental disorders can be organized in a predictable hierarchy of structures, which has the potential to bring enduring order in earlier taxonomic and etiologic confusion. Third, we present that personalized care, knowing the individual person, works better than traditional, institutional care. A national Swedish study of care workers' personal approach towards a patient showed up to 50% explanation of the variance in care service satisfaction, while the care organizational level only explained up to 5% (Kazemi & Kajonius, 2016). Personalized care carries many names and is arguably already the most practiced method; however, fueled by the ongoing advancements in science and measurement, it has the potential to become even more effective and satisfying.

Scientific Advancements in Personality and Brain Sciences

Scientific Progress I: Personality Traits as Denominator for Life Outcomes

Some of the most useful and generalizable findings relevant for personalized care are found in personality research. Multiple meta-analyses as well as entire cohort-studies show that personality traits, including cognitive abilities, are among the

most predictive signals for functioning in a person's life (Deary, Pattie, & Starr, 2013). This signal is strong enough to be able to predict and differentiate longevity and mental health among individuals in entire populations; sometimes 50 years ahead into the future (Deary, Batty, Pattie, & Gale, 2008). In representative nation samples, some of the more notable personality traits, such as the basic temperaments of extraversion and neuroticism, predict socioeconomic success, educational attainment, and yearly income, better than family upbringing background (Cuijpers et al., 2010; Kajonius & Carlander, 2017). In other words, the future of personalized care can make use of individual traits being impactful. It should not be surprising that individual brain constitutions respond differently to life circumstances and treatments.

The finding that personality traits are stable has helped launch a burgeoning field of research called personality neuroscience, which is the combination of personality and brain research (Allen & DeYoung, 2017). One of the largest meta-analyses studying the biological base of personality is based on close to 15 million twin pairs and reports that personality traits are overall approximately 50% heritable (Polderman et al., 2015). This implies that genetics drive half of the variance in what makes one person different from the next. When furthermore controlling for measurement error, this further increases overall personality heritability to 60% (Kandler & Zapko-Willmes, 2017). In line with this, personality traits are found notably stable. Meta-analytic test-retest stability coefficients for personality traits are close to 0.90, when controlled for measurement error (Kandler & Zapko-Willmes, 2017). One meta-analysis based on over 300 samples showed that spurious environmental life effects, such as losing one's job or loved one, only accounted for 17% of the variance in personality over the life-span (Anusic & Schimmack, 2016). In other words, the future of personalized care can make use of personality traits being a stable foundation for diagnosing and treating individuals' recurring thoughts, emotions, and behaviors.

Scientific Progress II: Genes as Denominator for Life Outcomes

Parallel to the finding that personality is a common denominator in life outcomes, behavioral genetics, another burgeoning field, has progressed paradigmatically in the last decade. One of the most replicable and sizable effects within the behavioral sciences is that genetics is the foundation of all human behavior, which has been formulated as the first law of behavioral genetics (Plomin, DeFries, Knopik, & Neiderhiser, 2016). Recent meta-analyses, based on twin and adoption studies, conclude that *genetic* correlations are near identical after 30 years old and that the stability of personality traits are further cemented by individuals increasing control over their personal environment (Briley & Tucker-drob, 2014).

In the wake of almost 50 years of twin and extended family studies, the number of so called genome-wide association studies (GWAS) has in the last 10 years become commonplace. See a review by Visscher et al. (2017). GWAS

is characterized by studying individual differences on the genome level. For instance, 1 large study found 107 loci on 233 different genes associated with intelligence (Hill, Davies, McIntosh, Gale, & Deary, 2017). The challenges that are still ahead are that effects from gene variation on phenotypes are minutely small and that rare-gene variants, as well as gene-interactions, need very large population samples to be studied. To date, approximately only half of the variance found in common twin-studies is regularly found is GWAS research, which is called the "missing heritability"-problem (Chabris, Lee, Cesarini, Benjamin, & Laibson, 2015). Later studies utilize so-called linkage disequilibrium, which means that variations between families can be taken into account, and thus have been able to explain over 30% of the variance in cognitive ability on the genome level (Hill et al., 2018). In other words, the future of personalized care will likely make use of more precise predictions and diagnosis and based on genetic biology has the potential to revolutionize our view on what it means to be a human.

The mapping out of the human genome and linking genotypic variation in behavioral expressions also reveal and confirm which particular traits and life outcomes are primarily linked by genetics. For instance, it has long been known that cognitive ability and socioeconomic outcomes correlate highly, but it has been unclear how this relationship is mediated. Recent GWAS using large population samples show that cognitive ability and attained socioeconomic status are strongly genetically related ($r = 0.71$) (Bulik-Sullivan et al., 2015). Another GWAS shows that the personality trait Neuroticism genetically overlap strongly with subjective well-being ($r = -0.75$) (Okbay et al., 2016). Such findings may help illuminate why societal inequalities as well as individual mental disorders show stability despite social engineering and treatment interventions. A representative sample from the UK accounted for 20% of the variation in socioeconomic status using only common loci on the genome level (Hill et al., 2016). Future studies will bring more clarity into how to interpret the consequences of these findings. Another progress is the testing of the promising gene x environment hypothesis (Strachan, Duncan, Horn, & Turkheimer, 2016). This line of reasoning suggests that genetic influence can be accentuated as well as diminished by environmental factors, such as stress, poverty, or conflict (Sharma, Powers, Bradley, & Ressler, 2016). For instance, the genetic influence of cognitive ability may be enhanced in stable and resourceful environments, while the genetic potential of mental disorders may be triggered in more volatile and stressful environments. This is one of the many examples of unresolved issues with large relevance for the future of personalized care. The present implication for personalized care is that not only genetic potential should be increasingly diagnosed but also be complemented by the environmental context posing present risk factors.

Measurement Advancement in Personality and Brain Disorders

Measurement Progress I: Traits as the Basis for Disorders

The reviewed personality and behavioral genetic findings impact on psychiatry and the understanding of how to measure brain and mental disorders. Similarly, improvements in measurement validity and reliability have potential to increase effectiveness in diagnosis and treatment. Not everyone agrees with this, and many still rely on traditional symptom counting based on DSM taxonomies (American Psychiatric Association [APA], 2013). We are just in the aftermath of one heated scientific debate lasting over a decade and which is still not fully resolved concerning the nature and measurement of psychiatric disorders (Krueger, 2013). One thing, however, seems clear, which is that mental disorders are arguably assessed more precisely by using dimensional, continuous measures, rather than categorical, discrete measures – a large meta-analysis showed that by diagnosing with dimensional trait instruments, validity and reliability increase by up to 40% (Markon, Chmielewski, & Miller, 2011). This measurement approach, rather than relying only on expert opinion, also has the benefit of solving a host of issues with the former DSM-structure for mental disorders, such as the heterogeneity in diagnosis, treatment, and demarcation. In the latest DSM-5 (APA, 2013), a dimensional personality model (Personality Inventory for DSM-5; PID-5) is included in Section III. This model suggests that instead of estimating maladaptive symptoms, maladaptive trait levels should be measured, better revealing the potential and presence for mental disorders (former Axis II). Also, the World Health Organization's alternative to the DSM-5, International Classification of Diseases 11th Revision (ICD-11) is expected to follow suit and will build on a similar personality model (Bach et al., 2017). There are other pedagogically and theoretically strong alternatives as well, such as the Temperament and Character Inventory-approach (See Garcia et al., 2013; Wong & Cloninger, 2010). Using trait-based, dimensional assessment methods has the potential to clarify known issues in psychiatry such as etiology and comorbidity in mental disorders.

The release of DSM-5 and its complementary personality trait model has been foregone by decades of trait research, with substantial support for dimensional measurements. We today know much more of how maladaptive traits and disorders change and impact functioning throughout the life-span (Kajonius, 2017b). Key traits for diagnosis such as empathy can reveal the worldview of a person (Persson & Kajonius, 2016). As an example, antisocial disorders tend to fall almost by one standard deviation between 19 and 35 years of age, which implies that close to 90% of people above 35 years of age will have a lower score in antisocial tendencies than people in their late teens. Likewise, the trait agreeableness tends to increase and mature towards societal norms with age, which is one explanation behind the known decrease in criminality with age. Overall, for the benefit of personalized care, we

know that measurements of common personality traits can be utilized for predicting dispositions towards mental disorders (Kajonius & Dåderman, 2017). One of the more relevant meta-analyses for the future showed that maladaptive traits can be modeled and linked together with common personality traits (Markon, Krueger, & Watson, 2005). In other words, this suggests that there is potential for a coherent theoretical foundation for future personalized care diagnosis and treatment.

Measurement Progress II: The Structure and Organization of Disorders

Based on the improvements of understanding of how to measure traits and disorders, one of the achievements of modern personality research is also a much replicated hierarchical structure of mental disorders (Kotov et al., 2017). A structural model which is built on dimensionality in traits has the potential to bring order in the problematic historical approach of viewing disorders as set categories based on symptoms, ensuing etiologic and taxonomic confusion (Krueger, 2013). A complete structure of maladaptive traits would also be a guiding map of human (dys)functioning. One of the propositions from this body of accumulated research is that mental disorders are permeated by a general psychopathology-factor (p-factor) (Caspi et al., 2014), which is expressed in a large number of Externalizing and Internalizing maladaptive traits and dispositions. A latent p-factor would account for the comorbidity of mental health problems; that is the heightened likelihood of having multiple disorders. A critical view on this may suggest that a p-factor is theoretically problematic (i.e., what does it mean?) and practically meaningless (i.e., what does it predict?). Interestingly, studies on the structure of normal personality similarly suggest a general factor (General Factor of Personality; GFP), which is suggested to be a permeating conducive factor from an evolutionary perspective. The GFP is a highly replicated finding, expressed in Stability (Alpha; or normative) and Plasticity (Beta; or exploring) traits. One may argue that GFP may be mostly an expression of social desirability and method artifacts, but researchers generally agree that personality domains correlate and form a meta-trait structure (Kotov et al., 2017; Markon et al., 2005).

Personality structures are also more or less universal in similarity, even across countries and cultures (Kajonius & Mac Giolla, 2017). Whether we measure cognitions, emotions, or behaviors, they tend to align and organize in recognizable personality structures (Waszczuk, Kotov, Ruggero, Gamez, & Watson, 2017). Similarly, different instruments aspiring to tap into various maladaptive traits, even when based on different perspectives, align and organize well into the same structures when analyzed together (e.g., Wright & Simms, 2014). In other words, it seems that a personality constitution can be tapped into with various means and methods and that the underlying scientific and measurement foundation is rather coherent (cf. Markon et al., 2005).

In the present article, we attempt a novel sketch in how the general p-factor interlinks with the general GFP. See presentation in Fig. 1. Based on a Swedish community sample, there is a strong, but not perfect, negative correlation between the p-factor and GFP, $r = -0.65$ (Kajonius, 2017a). This can be taken as further proof for the appropriateness of a mutual personality platform. As an example, research advises that high maladaptive antagonism as well as low agreeableness traits is a prerequisite for narcissistic disorder or that psychopathy is constituted by disinhibition and antagonism maladaptive traits, which too is indicated by low conscientiousness and low agreeableness common traits (cf. Miller, Bagby, Pilkonis, Reynolds, & Lynam, 2005). The simplified model in Fig. 1 suggests a strong inter-

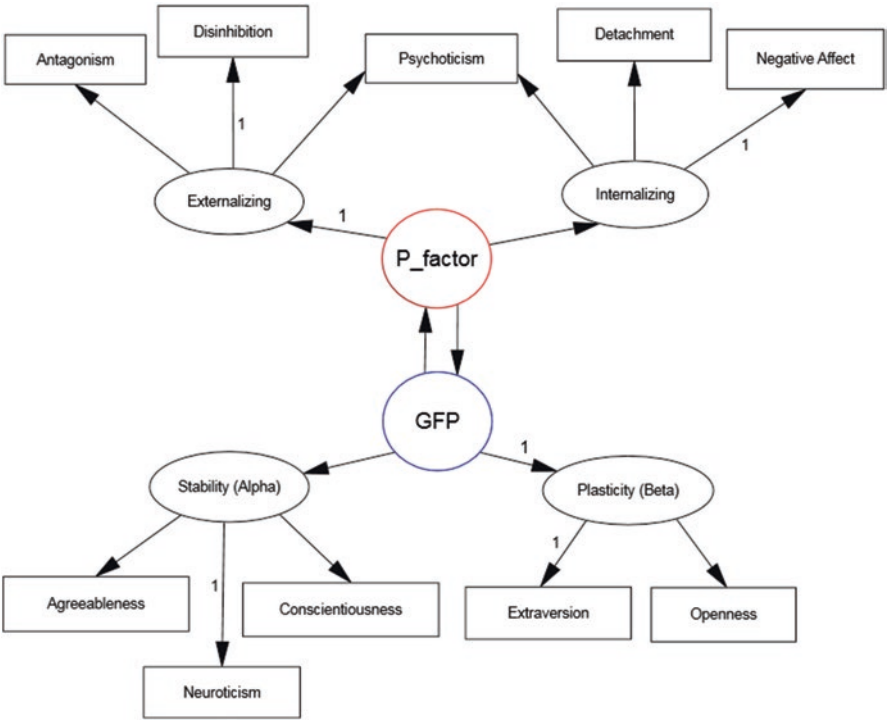

Fig. 1 The maladaptive traits and meta-traits (upper half of diagram) interlinking with common traits and meta-traits (lower half of diagram) proposed to underlie mental disorders. For example, antisocial disorder is known to be constituted by high externalizing traits of disinhibition and antagonism and is in reverse also indicated by low stability traits agreeableness and conscientiousness. Rectangles represent observed trait measurements, and round shapes represent latent and construed meta-traits. The figure shows how the structural relationships are linked by a proposed latent general psychopathology-factor (p-factor, separating into internalizing and externalizing traits) and a proposed latent general factor of personality (GFP, separating into stability and plasticity traits). Note that maladaptive psychoticism constitutes an anomaly by relating to two meta-traits and is also sometimes modeled as a third latent meta-trait called thought disorder (cf. Caspi et al., 2014). The illustrated model suggests a mutual foundation for personality traits and may be a useful map for future developments in personalizing care diagnosis and treatment

linking between maladaptive and common traits and may be a useful map for guiding personalized care into the future. The implication is that we will be able to approach the cores of mental disorders with help of mapped out meta-traits, as well as calibrate individual's disposition for general and specific mental disorders.

Practical Advancements: The Road into the Future

Personalized Care Is Recommended

Personalized care works and even more so when based on knowledge in personality and measurement structures. Present research indicates that accommodating individuals' traits is a foundation for effective and satisfying care services. For instance, it was shown in a large national sample that personalized elderly care, characterized by knowing the person and engaging in a care relationship on his or her terms, indeed alleviates the older person's disposition to feel lonely (Kajonius & Kazemi, 2015). Furthermore, when care workers utilize a personalized approach to care, user satisfaction is amplified (Kazemi & Kajonius, 2015). This method and perspective is recognized under different names with practitioners, such as individualized care, person-centered care, or user-oriented care. Researchers and decision-makers may argue about the differences between their meanings; however, the unifying feature is that the person in need is in focus, not the institution or the professional's needs.

A key research project covering all municipal care organizations in Sweden showed that a user-oriented approach by care workers not only is effective but is also related to satisfaction with the users. The study's conclusion was that a respectful and warm person-focused approach can explain up to 50% of the variance in older persons' care satisfaction, while the care organizational level (i.e., training, resources, and staffing) at most explain up to 5% (Kazemi & Kajonius, 2016). The remaining variance is explained of among other factors the personality traits of the older persons themselves (e.g., neurotic persons tend to score lower in satisfaction and extraverts higher, irrespectively of the quality of care). Based on this, one challenge for the future is to ensure that costs of care will be funneled to care workers to be able to supply the often time-consuming and resource-intensive personalized care (Kajonius & Kazemi, 2016). This will likely increase the quality of relationship with the older persons and result in higher user satisfaction with care services. Another challenge, shown in recent research, is for leadership and decision-makers to allow for an organizational climate of personalized care. One identified trend is that care organizations on the contrary tend to increase control and limit resources, often forced by well-meaning laws and regulations. This does often not allow for the necessary time and flexibility needed for personalizing the care to suit the older persons. Norms and leadership models are primary drivers in this development. Further in-depth case studies, based on interviews and participatory observations, have shown that management and organizational demands can suffocate motivation

for care workers, as well as inspire to more personalized efforts (Kajonius, Kazemi, & Tengblad, 2015). We recommend embracing the reviewed findings from the fields of personality and mental disorders into the practice of personalized care.

Personalized Care in the Future

In the future, it will likely be self-evident to complement mental as well as physiological diagnoses with personality trait instruments. Knowing the patient can optimize treatment processes. One such instrument is recommended in the latest manual for mental disorders, DSM-5 (APA, 2013), and a similar model is expected in the nearing release of another influential manual, ICD-11. Trait analyses can help pinpoint the core of respective conditions, as well as give individualized estimations of the severity of condition. For instance, facets of exploitation and self-grandeur are found to describe the core of narcissistic disorder, while individuals also can be scored on dimensional and specific trait continua. Anyone could be located on a scale ranging from normal, beneficial narcissism to clinical, malevolent narcissism (e.g., Kajonius, Persson, Rosenberg, & Garcia, 2016). See a fruitful person-centered example on how mental disorders can be structured and taxonomized in Wong and Cloninger (2010).

In the future, not only self and observer reports will benefit from increasing validity and reliability in measurement – fMRI studies will similarly be vastly improved by acknowledging personality traits in brain disorders (Dubois & Adolphs, 2016). The practice in experimental research today is most often to treat individual variance as error, instead of recognizing the inherent, valuable information beneficial for optimizing personalized treatment. Personality neuroscience is a nascent research field exploring how traits in both the common and clinical population tie into values and behaviors disposing for mental disorders. See one of the first studies and descriptions of this in Persson (2014).

In the future, not only trait measurements, but also genetic profiles, can predict everyday malevolent behaviors, thus enabling more proactive and timely interventions, for the benefit of both the individual and society. This progress is already underway, with the National Institute of Mental Health recommending all research and practices for the future to align with the RDoC approach (Lilienfeld & Treadway, 2016; Weinberger & Goldberg, 2014). This implies that all mental disorders will be delineated in levels and understanding of dimensional analysis, ranging from molecular to self-report (Krueger & DeYoung, 2016). Please read more of this endeavor with RDoC in an article designated to its methodological challenges (Persson & Kajonius, 2017) in the volume of Personality and Brain Disorders (Garcia, Archer, & Kostrzewa, 2017). It is our prediction that personalized care when based on personality and genetic dispositions will increase validity and reliability, theoretically ad infinitum, for all types of mental and brain disorders.

Future Note

Personalized services will be an increasing part of our future, both in private and public life. The rapid progress in personality and brain disorder research will be followed by moral challenges and may already be upon us. One challenge ahead, especially for practitioners, will be reconciling the general scientific advancements with the individual level application. How can we transform the growing knowledge into effective person treatment? Another challenge, especially for decision-makers, will be how to balance the opportunity for information with the protection of personal integrity, for instance, in regard to genetic data and handling of test results. Is there a limit for what can and should be known in regard to personalized care? In the midst of the reviewed advancements, it seems that personalized care in the future will both benefit and be provoked when incorporating the progress in personality and brain sciences.

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The Future of Personality Research and Applications: Some Latest Findings

Danilo Garcia, Kevin M. Cloninger, Nigel Lester, and C. Robert Cloninger

Abstract Human personality, although highly complex, is crucial to understand because it is the strongest predictor of our physical, mental, and social health as well as the actual cause of most mortality and chronic disease. However, despite the fact that earlier twin studies have found that the differences between people in personality are about 50% heritable, until recently only about 1% of this heritability has been explained by specific genes. Here we briefly outline current notions about the genetics of personality and also describe recent research that used novel and innovative person-centered methods to identify nearly all the genes for human personality. This international collaboration among 27 investigators at multiple sites comprised data from the Young Finns Study in Finland with independent replications in Germany and Korea (Zwir et al., Mol Psychiatry, 2018a, 2018b). In short, these results now make it possible to understand the basic mechanisms that influence our emotions as well as the way we can self-regulate our feelings, goals, and values in order to live healthy and satisfying lives. What is even more, these results provide a foundation for a thorough understanding of the complex molecular and brain processes that regulate human health and well-being. In this line, we also present preliminary

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results of a recent pilot study, in which interventions targeting character development among Swedish young adults suggest improvements in well-being after 6 months of well-being coaching. Importantly, it is argued that character regulates the expression of temperament predispositions, so character is the regulator of well-being regardless of underlying temperament. That is, since we are body, mind, and psyche at once (i.e., biopsychosocial in nature), the person needs to learn to both know and understand her temperament and her character to integrate them in order to adapt intelligently to who she is and the changing circumstances in the world around her.

Keywords Anthropedia well-being training · Character · Coaching · Genetics · Personality · Person-centered methods · Temperament

Human personality has been defined as the dynamic organization, within an individual, of psychobiological systems that modulate adaptation to a changing environment (Cloninger, Svrakic, & Przybeck, 1993). This includes metacognitive patterns and systems that regulate cognition, emotion and mood, personal impulse control, and social relations. In this context, personality traits are enduring patterns of perceiving, relating to, and thinking about oneself, other people, and the world as a whole (Cloninger, 2004, 2008). These three aspects of being are associated to physical, mental, social, and spiritual health (Cloninger, 2004; Cloninger, 2013a, 2013b; Roberts, Kuncel, Shiner, Caspi, & Goldberg, 2007). In the mid-1980s, observations about personality, rather than factor analysis of behavior or self-reports, provided a foundation for the development of a general model of temperament based on genetic, neurobiological, and neuropharmacological data (Cloninger, 1986, 1987). The adequacy of this structural model was tested by comparing this model of development within the individual (i.e., ontogeny) to the evolution of learning abilities in animal phylogeny (Cloninger, 1994; Cloninger & Gilligan, 1987). Cloninger described this model of temperament using four dimensions that were suggested as independently inherited: harm avoidance (anxious, pessimistic vs. outgoing, optimistic), novelty seeking (impulsive, quick-tempered vs. rigid, slow-tempered), reward dependence (warm, approval-seeking vs. cold, aloof), and persistence (persevering, ambitious vs. easily discouraged, underachieving) (Cloninger, 1987, 2004). These temperament dimensions proved to be a powerful way to distinguish subtypes of personality disorders and vulnerability to a wide range of mental disorders (Cloninger, 1999; Svrakic, Whitehead, Przybeck, & Cloninger, 1993).

However, Cloninger and his colleagues found that temperament alone did not capture the full range of personality (Cloninger et al., 1993; Cloninger, Przybeck, Svrakic, & Wetzel, 1994). They found that, by itself, temperament could not reveal whether a person was mature or had a personality disorder (Cloninger, 2004). On average, there were differences in the probability of personality disorder in people with different temperament configurations, but every configuration could be found in people who were mentally healthy as well as in people who had personality disorders (Cloninger, 2004; Cloninger, Svrakic, & Svrakic, 1997). Consequently, Cloninger identified a second domain of personality, using character traits to

measure a person's humanistic and transpersonal style: self-directedness (reliable, purposeful vs. blaming, aimless), cooperativeness (tolerant, helpful vs. prejudiced, revengeful), and self-transcendence (self-forgetful, spiritual vs. self-conscious, materialistic). These character dimensions measure the components of an individual's mental self-government and can strongly measure the presence and severity of personality disorder.

The character dimensions have been found to be as heritable as the temperament dimensions, each with about 50% heritability in twin studies (Gillespie, Cloninger, Heath, & Martin, 2003). All seven dimensions of temperament and character have been found to have unique genetic determinants (Garcia et al., 2013, 2014; Gillespie et al., 2003) and to be regulated by different brain systems as measured by functional brain imaging (Borg, Andree, Soderstrom, & Farde, 2003; Cloninger, 2004; Gusnard, Ollinger, Shulman, Cloninger, et al., 2003; Kaasinen, Maguire, Kurki, Brück, & Rinne, 2005; Tomer & Aharon-Peretz, 2004; Turner, Hudson, Butler, & Joyce, 2003). The temperament dimensions have strong relations with the older corticostriatal and limbic systems that regulate habits and skills (Turner et al., 2003; Kaasinen, Aalto, Nagren & Rinne, 2005; Tomer & Aharon-Peretz, 2004; Gusnard et al., 2003). In contrast, the character dimensions have strong relations with recently evolved regions of the brain—such as the frontal, temporal, and parietal neocortex—that regulate learning of facts and propositions (Borg et al., 2003; Cloninger, 2004; Kaasinen et al., 2005; Turner et al., 2003). Each dimension is influenced by complex interactions between many genetic and environmental variables, so personality develops as a complex adaptive system (Cloninger, 2004; see Fig. 1). Indeed, longitudinal studies show strong evidence of developmental complexity: individuals with

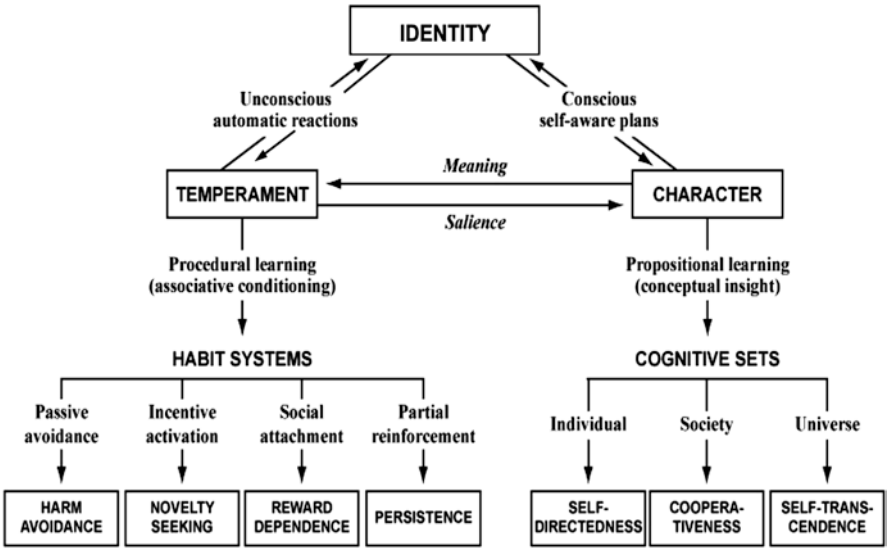
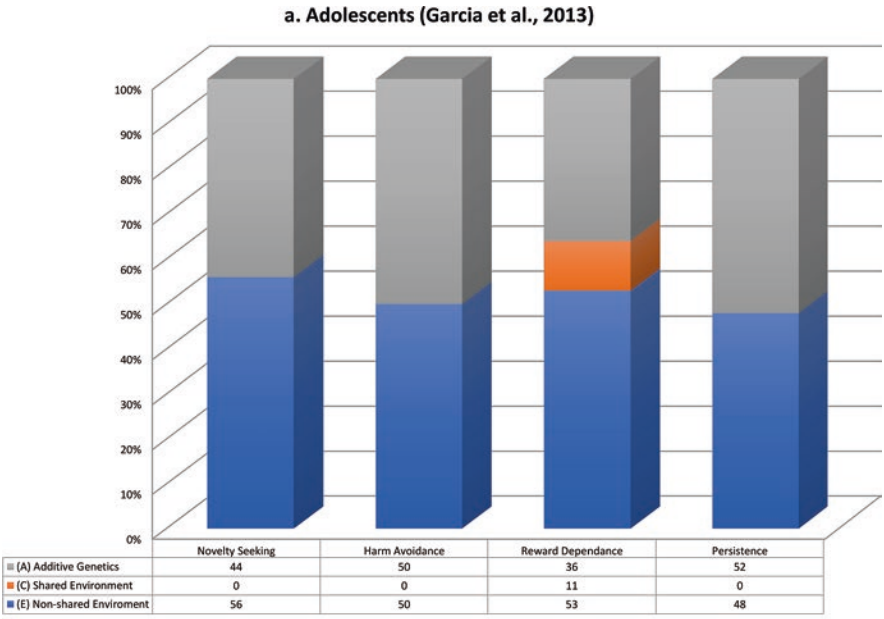


Fig. 1 Biopsychosocial model of temperament and character. (Reproduced with permission of Washington University Center for Well-Being)

the same antecedent traits may have different outcomes (i.e., multifinality), and those with different antecedent traits may have the same outcome (i.e., equifinality) (Cicchetti & Rogosch, 1996; Cloninger et al., 1997).

Although the character traits have indeed shown much the same levels of heritability as the temperament traits across several studies (e.g., Ando et al., 2004; Gillespie et al., 2003), there are some differences worth noting. For example, while character do not show common environmental influences in research among older adults (e.g., Gillespie et al., 2003), a small common environmental influence for self-directedness and cooperativeness has been found among young adults (20–30 years of age; e.g., Ando et al., 2004). In addition, recent research using one of the largest population-based twin studies among adolescents (see also Chap. "Temperament and Character in Childhood-Onset Neurodevelopmental Disorders (Autism Spectrum Disorders and ADHD)" in this volume) found suggestive evidence of common environmental influence for all of the character traits (Garcia et al., 2013). What is more, Gillespie et al. (2003) showed in adults and Garcia et al. (2013) in adolescents that the genetic structure of temperament shows no evidence of a shared or common environmental effect (C) across the four temperament traits. The exception being that in adolescents, in contrast to adults, there was a small shared environmental effect in the temperament dimension of reward dependence (i.e., the individuals' tendency to respond markedly to signals of social approval, social support, and sentimentality). The effect size was similar to that which is observed in adolescents' character dimensions. Overall the effect size of additive genetics (A) to nonshared environmental effect (E) is slightly larger across the temperament dimensions in adolescents compared to adults (see Fig. 2a, b). In contrast, the genetic structure of character in the adolescent sample shows a modest but noteworthy proportion of shared environmental influence that is not present in adult samples (e.g., Gillespie et al., 2003; see Fig. 3a, b). In other words, there is greater consistency, between the adolescent and the adult sample, in the proportion of additive genetic effect to nonshared environmental effect with respect to temperament but not with respect to character. These results suggest a "shift" in type of environmental influence (i.e., shared to nonshared) from adolescence to adulthood with regard to character. In this context, it is important to point out that character traits improve with cognitive-behavioral treatments and baseline levels of character are strong predictors of clinical outcomes (Anderson et al., 2002; Rowe et al., 2010; Mortberg & Andersson, 2013; Corchs et al., 2008; see also Chap. "Transcranial Magnetic Stimulation in the Treatment of Major Depressive Disorder: A Personalized Approach" in this volume). Lester and colleagues (Lester et al., 2016) argued that if the "shift" in environmental influence exists, then interventions targeting character development may be more successful if conducted during adolescence or young adulthood. Nevertheless, prior work that considered only the effects of individual genes on individual personality traits had been ineffective in unraveling the complex genetics of human personality. Moreover, up until recently, we still lacked studies investigating the effect of interventions that target character development per se.

Additionally, there is also fundamental doubt about whether the natural biological unit of measurement for personality corresponds to individual traits or multi-trait



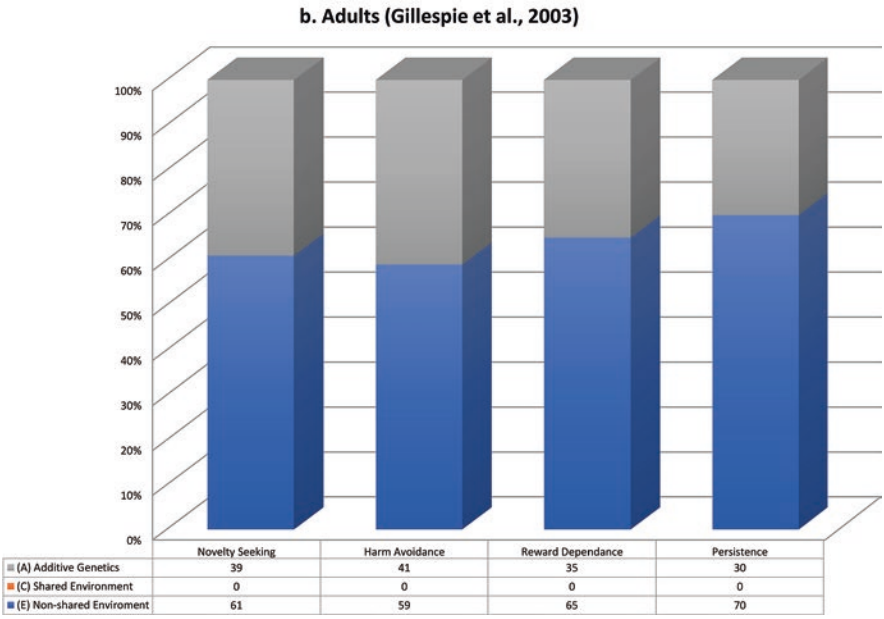
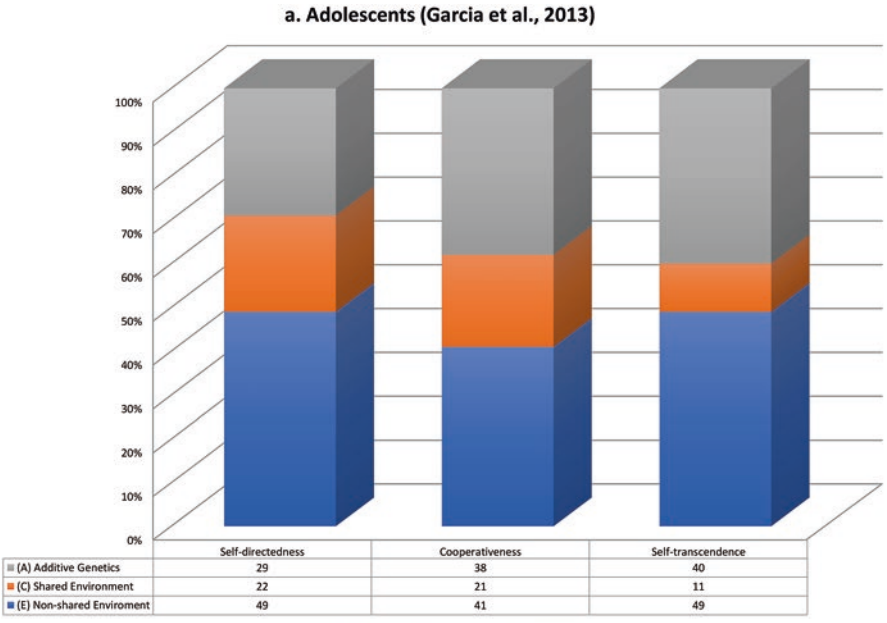


Fig. 2 (a, b) Showing the effect sizes of additive genetics (A) and nonshared environmental effect (E) across the temperament scales in (**a**) adolescents (Garcia et al., 2013) compared to (**b**) adults (Gillespie et al., 2003)



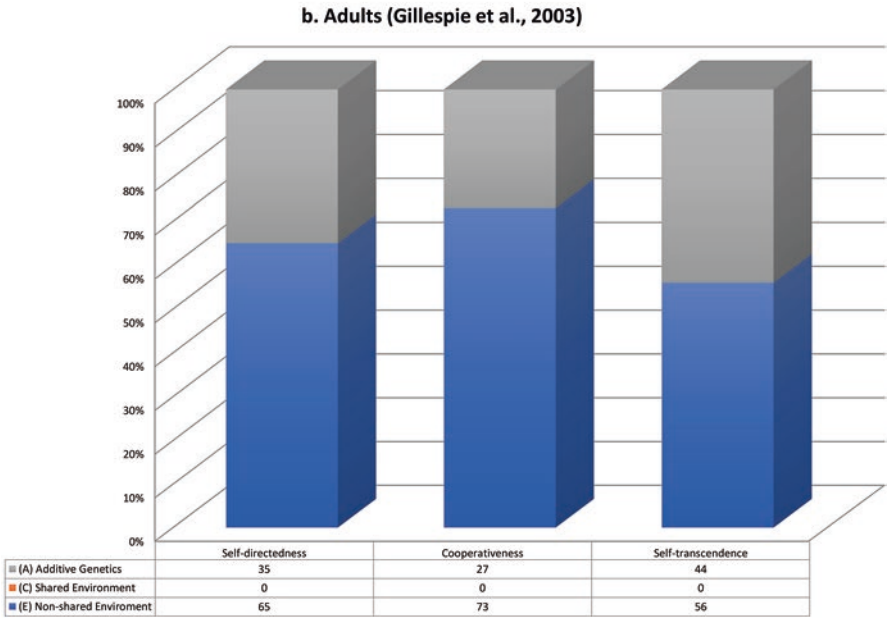


Fig. 3 (a, b) Showing the effect sizes of additive genetics (A), shared environment (C), and non-shared environmental effect (E) across the character higher-order scales in (**a**) adolescents (Garcia et al., 2013) compared to (**b**) adults (Gillespie et al., 2003)

configurations (cf. Cloninger & Zwir, 2018). Indeed, researchers of temperament and its biology usually focus on individual traits that differ between individuals (Shiner et al., 2012), while developmental and social-cognitive psychologists usually focus on multi-trait configurations within each individual because these are more stable developmentally and more informative about internal psychobiological processes (Cervone, 2004; Cloninger, 2003; Staudinger & Lindenberger, 2003). In this context, studies of twins along with other family members show that most of the heritability of temperament is likely to depend on complex interactions among multiple gene loci (i.e., epistasis) and environmental influences (i.e., gene–environment interaction) (Keller, Coventry, Heath, & Martin, 2005; Verweij et al., 2010, 2012). Hence, it is no surprise that genome-wide association studies (GWASs) that consider only the average effects of genes have explained little of the heritability of, for example, temperament (de Moor et al., 2012; Munafo & Flint, 2011; Service et al., 2012).

Advanced Methods of Deep Unsupervised Machine Learning

This failure to identify specific genes to account for the heritability of complex traits[1] has recently been approached using advanced methods of deep unsupervised machine learning. These methods have been developed for uncovering the hidden architecture of complex traits like personality in ways that are unencumbered by restrictive hypotheses like additive gene action (Arnedo et al., 2013; Arnedo, Mamah, et al., 2015; Arnedo, Svrakic, et al., 2015). These methods provide a data-driven way to describe the complex genotypic–phenotypic relationships needed to develop an adequate taxonomy and psychobiology of personality. These data-driven methods are useful to complement theory-driven approaches to these questions (Uher, 2013, 2015; Garcia, Cloninger, Sikström, Anckarsäter & Cloninger, 2019). Unsupervised machine learning provides a strictly data-driven method for uncovering complex latent architectures, such as patterns of connectivity in functional brain imaging and/or genotypic–phenotypic relationships in GWASs (Arnedo et al., 2013; Arnedo, Mamah, et al., 2015; Arnedo, Svrakic, et al., 2015; Hinton & Salakhutdinov, 2006). This person-centered approach focuses on identifying patterns of relationship within individuals, rather than on average differences between groups of people with heterogeneous features. Cluster analysis, without restrictive assumptions about the number or content of the clusters, based on nonnegative matrix factorization can be used to optimize pattern recognition and identification of naturally occurring associations of patterns across different types of data. This generalized clustering method, which is an extension of typical clustering methods, allows observations on subjects who may appear in multiple clusters in association with different features (Arnedo et al., 2013; Arnedo, Mamah, et al., 2015; Arnedo, Svrakic, et al., 2015).

[1] Often called the "missing" (Eichler et al., 2010) or "hidden" (Williams & Haines, 2011) heritability problem.

Two Multicultural Studies Identify Nearly All the Genes for Human Personality

Cloninger and colleagues have recently applied these person-centered methods to a GWAS of personality assessed by the Temperament and Character Inventory (Cloninger et al., 1993) in three large independent samples from Finland (Raitakari et al., 2008), Germany (Cook et al., 2015), and South Korea (Sung et al., 2006). Again, the temperament and character dimensions are about 40–55% heritable according to twin studies. However, temperament traits show strong evidence of nonadditive gene action. Thus, prior GWASs assuming that gene action was additive had failed to explain much of the expected heritability (Verweij et al., 2010, 2012). Indeed, only about 1% of personality's heritability has been explained by specific genes. The new method used by Cloninger and colleagues, however, allowed for the identification of clusters of genes that interact with each other and with the environment to influence profiles of traits that describe a person as a whole (Zwir et al., 2018a, 2018b). The investigators in the Young Finns Study (Raitakari et al., 2008) had measured the personality, health, and life experiences of more than 2000 people from 3 to 45 years of age. They measured both temperament and the aspects of personality that allow people to self-regulate their behavior intentionally (i.e., character). Cloninger and colleagues (Zwir et al., 2018a, 2018b) were able to find nearly 1000 genes that influence temperament and character. After identifying the genes in the Young Finns Study, Cloninger and his colleagues were able to confirm their findings in independent studies of about 1000 people in Germany (Cook et al., 2015) and 1000 people in Korea (Sung et al., 2006; see Zwir et al., 2018a, 2018b). In short, in both Eastern and Western cultures, the genes for temperament or basic emotional drives (such as being fearful or impulsive) and those for character or self-regulation of those emotions (such as being self-directed or cooperative) were nearly all expressed in the brain.

More specifically, 700 genes influenced human temperament. These genes occurred mainly in the molecular pathways for habit learning that are activated when nonhuman animals learn by reward and punishment in behavioral conditioning experiments. In this way, the new results about human temperament were confirmed both by replication in the German and Korean samples and by experimental studies of behavioral conditioning in other animals. Likewise, more than 700 genes were found to influence how well people are able to self-regulate their emotions and lifestyle behaviors that are critical for the physical, mental, and social aspects of their health. About 33% of the genes influenced both temperament and character, but 67% of the genes were unique for either temperament or character (Zwir et al., 2018a, 2018b). The genes for human character were often expressed in brain circuits known from functional brain imaging to regulate higher cognitive processes, such as intentional goal-seeking, reconciliation of social and emotional conflicts, symbolization, and self-awareness (Zwir et al., 2018a, 2018b).

From these findings, Cloninger argued that the natural building blocks of personality are multifaceted profiles of the whole person, not individual traits. Most prior

investigators, however, had focused on looking for the causes of individual traits like extraversion or neuroticism, but it turns out that individual traits are not the natural building blocks of personality. Moreover, this new research identified multiple molecular pathways that can produce the same individual traits. However, these pathways can be distinguished by profiles of multiple traits that have a more homogeneous genetic basis. Environmental influences, such as parental tolerance and emotional warmth, had small but significant interactions with the identified genes for temperament and for character (Zwir et al., 2018a, 2018b).

The Future of Personality Research and Applications

Human personality, although highly complex, is crucial to understand because it is the strongest predictor of our physical, mental, and social health as well as the actual cause of most mortality and chronic diseases. Cloninger's most recent work has succeeded in identifying nearly all the genes for human personality. In short, these results now make it possible to understand the basic mechanisms that influence our emotions as well as the way we can self-regulate our feelings, goals, and values in order to live healthy and satisfying lives, thus providing a foundation for a thorough understanding of the complex molecular and brain processes that regulate human health and well-being. According to Cloninger, the findings show that even at the most basic molecular genetic level, the health of human beings involves self-regulatory processes that influence the way we perceive the world and interact with one another. As a result, the treatment of disease and the promotion of health need to be person-centered and cannot be reduced to consideration of separate diseases or the identification of panels of genetic markers to predict disease. Instead, we need to recognize that it is the regulation of the expression of genes for personality that determines health and humanity, which depends on systems of learning to achieve valued goals that are meaningful and virtuous (e.g., moderate, altruistic). The findings provide crucial information about the basic mechanisms that regulate healthy lifestyle behaviors, which can inform a person-centered approach to health promotion and treatment that is solidly grounded in an understanding of the mechanisms that influence the development of a person physically, mentally, and socially. In other words, since as humans we are body, mind, and psyche at once (i.e., biopsychosocial in nature), the person needs to learn to know and understand her temperament and her character to integrate them in order to adapt intelligently to who she is and the changing circumstances in the world around her. For instance, the "shift" in type of environmental influence (i.e., shared to nonshared) from adolescence to adulthood with regard to character indicates that interventions targeting character development may be more successful if conducted during adolescence or young adulthood (Lester et al., 2016).

For instance, Anthropedia's well-being coaching was designed to increase physical and mental health, resilience, and overall well-being through character development (Cloninger, 2004, Cloninger, 2013a, 2013b; Cloninger & Cloninger, 2011;

Wong & Cloninger, 2010; see also Chap. "Personality and the Brain: Person-Centered Approache" in this volume). The coaching method uses a DVD series called *Know Yourself*, which was developed with the Anthropedia Foundation (https://anthropedia.org). The *Know Yourself* series is intended for use by a well-being coach or as an adjunct in psychotherapy. The exercises described by Cloninger and used by the coaches are intended to stimulate character development and self-awareness, thereby fostering a healthy way of living with three sets of goals and values:

(a) Working in the service of others, thereby increasing love and cooperativeness
(b) Letting go of fighting and worrying, thereby increasing hope and self-directedness
(c) Growing in awareness, thereby increasing faith and self-transcendence

This approach combines principles of cognitive-behavioral therapy, person-centered therapy (see also Person-Centered Care in this volume), and positive psychology with personality assessment and meditative practices that enhance mindfulness and self-awareness of the cognitive schemas that organize and direct our attention and motivation in different situations. This approach differs from other forms of psychotherapy by its emphasis on integration of a person's awareness of their body, thoughts, and psyche. As a matter of fact, the separation of biomedical, psychosocial, and spiritual approaches interferes with the development of well-being, whereas their integration has been shown to reduce drop-out, relapse, and recurrence rates in randomized controlled trials of well-being therapy (Cloninger, 2004). Well-being coaching has been implemented in different countries such as the USA, France, and Sweden. In Sweden, for instance, initiatives have led to community and research projects comprising well-being coaching of refugees (i.e., the Well-Being and Integration project financed by the European Social Fund), long-term unemployed young adults (i.e., the Sustainable Personal Development project financed by FINSAM and the Mind the Gap project financed by the European Social Fund), adolescents and health care personnel (i.e., the Resilience among Newly Graduated Nurses project financed by Human Resources at Region Blekinge).

Recently, in a series of pilot studies (Cloninger, Lester, et al., 2018; Cloninger, Muszynski, et al., 2018; Cloninger et al., 2019), we have been able to show that well-being coaching (see https://anthropedia.org/well-being-coach-certification/) significantly increases subjective well-being and significantly decreases depression and anxiety among Swedish unemployed young adults (see Fig. 4a, b). Specifically, at baseline, the participants showed lower levels of well-being compared to a

Fig. 4 (continued) The preliminary results indicate that young long-term unemployed adults who participated in the well-being coaching intervention showed significant increases in positive affect ($t = 2.31$, $df = 20$, $p < 0.05$, *Cohen's D* = 0.51), life satisfaction ($t = 2.94$, $df = 20$, $p < 0.01$, *Cohen's D* = 0.49), harmony in life ($t = 2.36$, $df = 20$, $p < 0.05$, *Cohen's D* = 0.59), and significant decreases in anxiety ($t = 3.08$, $df = 20$, $p < 0.01$, *Cohen's D* = 0.67) and depression ($t = 2.53$, $df = 20$, $p < 0.05$, *Cohen's D* = 0.54). The control group receiving commonly used interventions in this population in Blekinge, Sweden, showed the same baseline scores, low compliance answering the surveys, and small decreases in anxiety ($t = 2.9$, $df = 13$, $p < 0.05$, *Cohen's D* = 0.36)

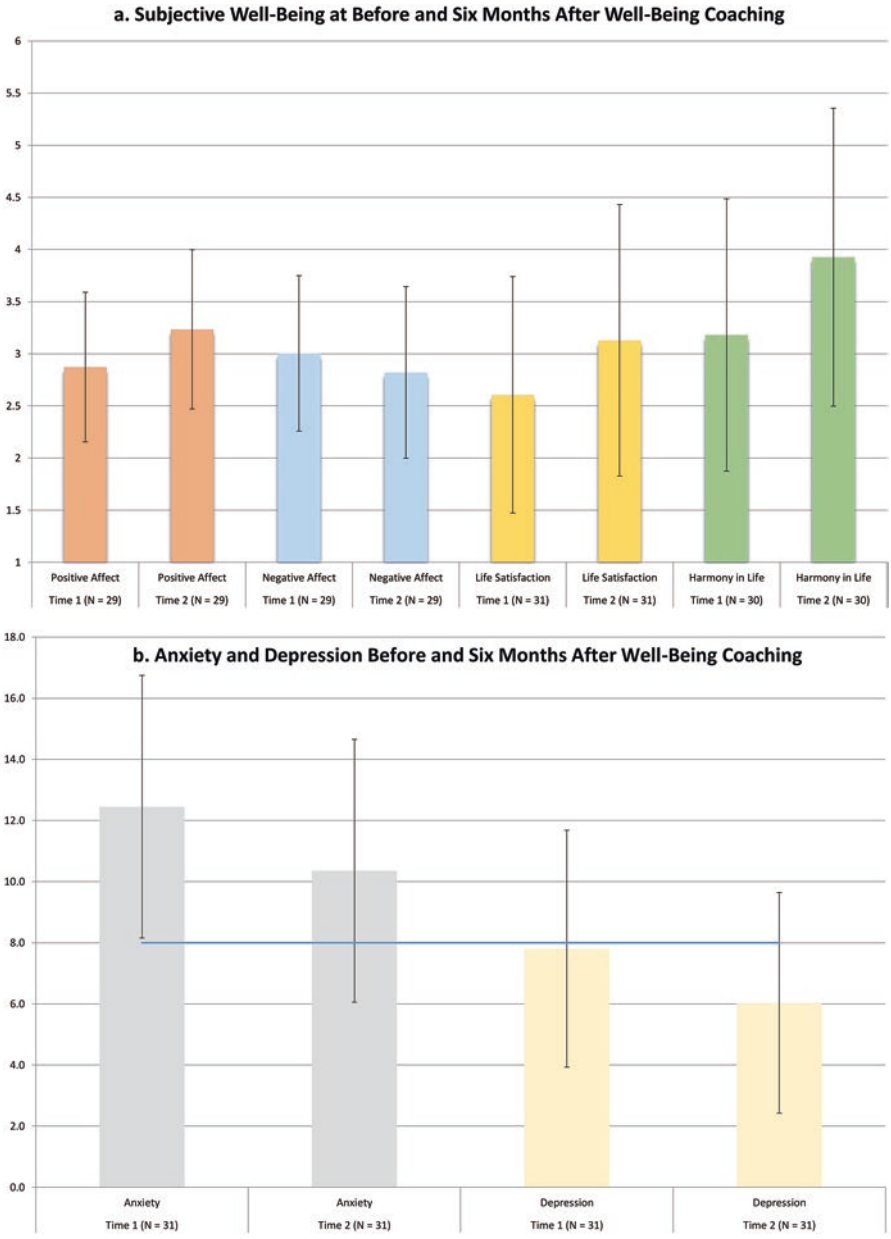


Fig. 4 (a, b) Showing the effect of well-being coaching on subjective well-being (**a**) and both anxiety and depression (**b**) in a 6-month pilot intervention study among young Swedish adults with long-term unemployment

Note: Subjective well-being was measured using the Positive Affect Negative Affect Schedule (Watson, Clark, & Tellegen, 1988), the Satisfaction with Life Scale (Diener, Emmons, Larsen, & Griffin, 1985), and the Harmony in Life Scale (Kjell, Daukantaitė, Hefferon, & Sikström, 2015). Anxiety and depression were measured using the Hospital Anxiety and Depression Scale (Zigmond & Snaith, 1983). The blue line indicates the cutoff for clinical levels of anxiety and depression.

Swedish normal population of young adults but the same levels of well-being as patients being treated for anorexia nervosa. The post-intervention scores, however, were at the same level as those of the Swedish normal population and indicate that young long-term unemployed adults who participated in the well-being coaching intervention showed significant increases in positive affect, life satisfaction, harmony in life, and significant decreases in depression and anxiety. The control group receiving commonly used interventions in this population in Blekinge, Sweden, showed the same baseline scores, low compliance answering the surveys, and small decreases in anxiety. Since well-being coaching is low-cost and easy to implement at an individual, institutional, or community level, Anthropedia's coaching shows great promise in addressing the rising rates of stress and depression of the twenty-first century. Importantly, the genes behind personality are expressed in each organ of the human body (Zwir et al., 2018a, b). Hence, changes in character should influence the person as a whole.

Conflict of Interest

The authors declare that there are no competing interests. The views and ideas expressed here are those of the authors and do not necessarily reflect the official policy or position of any agency of the Swedish government.

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The chapter 13 was inadvertently published with incorrect sentence and it is now updated in the revised version of the book.

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