Chapter 8 Executive Dysfunction During Normal and Abnormal Aging



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8.1 Introduction

The neuroscience literature has established that the cognitive processes mediated by the frontal lobes undergo progressive changes as we age (Rosselli & Jurado, 2013). The vulnerability of the frontal lobe to aging and the parallel decline of executive and metacognitive functions are the bases for the frontal lobe hypothesis of aging (West, 1996). This hypothesis proposes that the prefrontal cortex (PFC) begins deteriorating before other regions (Rodríguez-Aranda & Sundet, 2006). The cerebral volume of the PFC (specifically, the orbitofrontal cortex) suffers a greater reduction compared to limbic areas and other brain regions (Lindberg, 2012). Kennedy and Raz (2015) also reported these changes in the PFC, as well as in the cerebellum and neostriatum. Shrinkage of the PFC, as well as the entorhinal cortex, has been linked to declines in cognitive performance or reduced ability to benefit from repeated testing (for a review, see Raz & Daugherty, 2018). The effects of aging have been demonstrated with interruptions of frontal tracks that connect the frontal lobe with other cortical and subcortical structures, such as the cortico-cortico and cortico-subcortical tracks (Sullivan, Rohlfing, & Pfefferbaum, 2010), with larger age effects in association tracks connecting frontal and parietal multimodal cortices than in projection fibers (Salat, 2014). This pattern of aging effects is in accordance to the first-in-last-out hypothesis (Raz & Daugherty, 2018): regions of the brain that develop later are more vulnerable to age-associated degeneration than those that evidence early growth.

The frontal lobe hypothesis of aging has been complemented with results from functional neuroimaging studies, showing that compared to young adults, older adults have reduced activity in some brain regions but increased activity in others (Cabeza,

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McIntosh, Tulving, Nyberg, & Grady, 1997). The age-related increases and decreases in neural activity are noticeable within the PFC (Cabeza, 2002). When comparing older and younger adults, older adults show a more bilateral pattern of activation of the PFC during tasks of verbal recall, implying a decreased activation of the left PFC and increased activation of the right PFC. These findings support the notion that cognitive processing in the aging brain differs from that of younger brains (Cabeza & Dennis, 2013).

The frontal lobes are the bases for executive functions (EFs). Age-related anatomical and functional changes of the frontal lobe are accompanied by EF changes. EF is an umbrella term covering cognitive and behavioral processes mediated by the frontal lobes (Rodríguez-Aranda & Sundet, 2006). EFs are regarded as a construct that includes numerous abilities required for the initiation and organization of activities and functions that contribute to the executive process of reaching a goal; these capabilities support various phases of the executive process, with the assumption that systematic monitoring of each phase provides insight into the overall process (Hanna-Pladdy, 2007). Intentionality seems to be an important component of EFs (Lezak, Howieson, & Loring, 2004), suggesting that the cognitive and behavioral processes of EFs are reflected in actions.

EFs can be separated into two processes: one relating to affective operations and the other to cognitive operations. EFs that have an affective/emotional component are considered "hot," while those that are relatively abstract and non-affective while relating to cognition (e.g., working memory and multitasking) are known as "cool" or "cold" (these include self-management skills without the involvement of emotion, such as updating, inhibition, and set-shifting; Ho, Hsu, Lu, Gossop, & Chen, 2018). "Hot" EFs include affective decision-making for events with emotionally significant consequences (i.e., meaningful rewards and/or losses; Kerr & Zelazo, 2004). Ardila (2013) suggested that cool EFs constitute a metacognitive group of EFs abilities, whereas hot EFs comprise the emotional/motivational EFs. The latter EFs include abilities required to fulfill basic impulses following socially accepted strategies in which inhibitory control plays a major role.

Failure to respond in a particular way during neuropsychological tasks or to environmental circumstances may reflect a dysexecutive syndrome (DES), a group of problems in inhibitory control, poor cognitive flexibility, and the inability to follow a plan. In the cognitive DES, deficits are found in metacognitive abilities (cool EFs), whereas in the behavioral DES, deficits are mainly observed in the form of behavioral disinhibition, global hypoactivity with apathy, perseverative behavior, and impulse control disorders (Godefroy et al., 2018). During complex interactions, the individual who wants to reach a goal may need to generate a plan while monitoring internal and external information. This individual must simultaneously maintain some information online and suppress inappropriate behaviors, as well as avoid distractions by irrelevant stimuli while initiating appropriate responses to changing environmental stimuli (Jurado & Rosselli, 2007). Therefore, adapting to a complex and changing environment requires a diverse range of EFs including problem-solving, set-shifting, self-monitoring, initiation, inhibition, planning, and sequencing. EF deficits in normal aging may affect behavior as well as cognition. In elderly individuals, cognitive deficits

in planning, decision-making, organization, and self-control are expected to negatively affect their daily lives (Amieva, Phillips, & Della Sala, 2003).

Age-related deficits in EF can be observed by using standardized neuropsychological tests presumed to assess frontal function or in experimental paradigms focused on various executive processes (Cabeza & Dennis, 2013). The most studied EF processes are inhibitory control, cognitive flexibility, and set-shifting, planning, and initiation or self-generation (Hanna-Pladdy, 2007; Jurado & Rosselli, 2007). Age-related changes in these processes vary among individuals; some present with changes in only one process while others are affected in several domains (Byczewska-Konieczny, 2019). The effect of age on EFs may be a continuum, with the most extreme being the DES. Although there is no consensus regarding the diagnostic criteria for this syndrome, it may include objective changes in several behavioral and cognitive EF domains with preserved non-EF skills (Godefroy et al., 2018).

Baddeley and Wilson (1988) coined the term DES as a functional characterization of patients with deficits in the central executive component of working memory. This syndrome was later characterized in reference to a patient who had amnesia with confabulation after bilateral traumatic frontal damage (Baddeley & Wilson, 1988). This patient's DES included the following: (1) reduced performance and numerous perseverations on a test of cognitive flexibility (e.g., Wisconsin Card Sorting Test [WCST; Heaton, Chelune, Talley, Kay, & Curtis, 1993]); (2) poor thinking as reflected on their performance on the Cognitive Estimation Test (Shallice & Evans, 1978), and in other reasoning tests; (3) the inability to generate words in letter and semantic fluency tests; and (4) a change in behavior (from apathetic to charming and amusing).

The initial description of the DES was associated with focal frontal lobe pathology, but more recently, the field has recognized that it may arise from other neurological disorders, which explains why the term evolved to executive disorders (Godefroy et al., 2018; Hanna-Pladdy, 2007). Godefroy et al. (2018) stressed that the term "dy-sexecutive disorder" should be used to refer to all disorders related to decreased control of EFs, independent of their neurological etiology. Subsequently, "cognitive dysexecutive disorders" refer to the impairment of control processes that are assessed by cognitive tests and "behavioral dysexecutive disorders" refer to behavioral changes that are assessed by the direct examination of the subject's behavior or the use of behavioral inventories (Karzmark, Llanes, Tan, Deutsch, & Zeifert, 2012).

This chapter aims to review the findings that relate age to EF declines and to present evidence of the DES in abnormal aging. Dysfunctions in EF in cases of Mild Cognitive Impairment, different types of dementia, and other diseases are described. We highlight the idea that alterations of EFs in abnormal aging involve a neurological condition, whereas EF changes in healthy adults result from the normal processes of aging.

8.2 Dysexecutive Syndrome in Normal Aging

Consistent with the frontal lobe hypothesis, cognitive deficits in healthy older adults are greater for tasks that are highly dependent on executive control processes. These include inhibiting irrelevant information, switching in response to environmental changes, implementing planning strategies to achieve a goal, and initiating an action or response (Rosselli & Jurado, 2013).

8.2.1 Attentional Control/Response Inhibition

Attentional control is defined as the selective and inhibitory component of attention (Anderson, 2002) allowing us to focus our cognitive resources on specific aspects of the environment. The simultaneous inhibition of irrelevant information is essential in situations with high attentional demands. This control will vary depending on the length of the sustained attention and the depth of engagement with the source of information (Tas, Luck, & Hollingworth, 2016). Attentional control plays an important role in accomplishing goals by directing resources to systems related to the relevant task while inhibiting orientation to the irrelevant one.

Deficits in this ability can be explained by the inhibitory deficit hypothesis (Hasher & Zacks, 1988) which suggests that dysfunctions in the inhibitory mechanisms of attention are responsible for age-related cognitive deficits. The lack of inhibitory control would reduce working memory capacity due to the intrusion of irrelevant information, which will limit the processing capacity of relevant information. Because of this deficit, elderly individuals may get distracted easily, generate task errors, and increase the response processing time.

The Stroop test (Stroop, 1935) is the most common paradigm used to measure response inhibition. The Stroop requires participants to read color words (i.e., blue, green, red) printed in conflicting colored ink, which requires the suppression of reading while having to provide the color of the ink (e.g., the word "blue" printed in red ink). Previous research showed that elderly participants present inhibitory difficulties, as measured by response time. Older individuals appear to require more time to inhibit the automatic tendency to read the word compared to younger ones, thereby showing a larger Stroop effect (Van der Elst, Van Boxtel, Van Breukelen, & Jolles, 2006). Interestingly, West and Baylis (1998) found that the age-related increases in the Stroop effect were observed only when the proportion of incongruent trials was high, requiring a high demand of inhibitory processes, suggesting that older adults have a limited amount of inhibitory resources.

Although these outcomes support the idea of age-related declines in inhibitory processes, other research has suggested that general slowing can also explain the increases in the Stroop effect (Fisk & Warr, 1996). West and Alain (2000) tested this idea using Event Related Potentials (ERPs) and hypothesized that differences in the amplitude of ERP modulations between younger and older adults would reflect

inhibitory attentional processes. Results showed an age-related decline in inhibitory processing resulting in a reduction in the amplitude of modulations differentiating incongruent trials from neutral and congruent trials over the midline frontocentral region and left parietal and bilateral frontal regions. Although older adults had a higher response time, age-related declines in inhibitory control contributed to the increased Stroop effect observed in the older adults of this study. Analyses of the response latency data revealed an age-related increase in the magnitude of the Stroop effect in older adults. The effect of age on incongruent trials remained significant after controlling for age-related differences in response latency on neutral trials. The authors concluded that there is a unique effect of age, beyond that of general slowing, that contributes to the larger Stroop effect observed in older adults.

Besides inhibitory control, vigilance, a type of sustained attention required for monitoring rare but critical events (Thomson & Hasher, 2017) also shows age-related changes. The alternating programs and go-no go paradigms that measure response inhibition are also sensitive to aging impairments (Gaál & Czigler, 2015).

8.2.2 Planning

Planning is essential for reaching a goal and includes the organization of behaviors in subgoals (Luria, 1976). A decreased capacity to make plans is seen in elderly individuals as early as age 60 and can be observed with the tower tests. After this age, adults being making errors in the Tower of London (Zook, Welsh, & Ewing, 2006) or the Tower of Hanoi (Sorel & Pennequin, 2008). These tests include the following detailed rules that need to be followed to successfully complete the final configuration: (1) only one disk can be moved at a time, and therefore, participants cannot hold more than one disk at a time; (2) smaller disks must always be placed above larger disks; and (3) the final configuration should be achieved in the least number of moves possible. Elderly adults make more moves and have higher completion times than younger adults (Andrés & Van der Linden, 2000; Sorel & Pennequin, 2008). Also, more rule-breaking is seen in the elderly (Passingham, 1993).

The effects of aging on planning tasks could also be influenced by the characteristics of the task and the participant's non-verbal abilities. Brennan, Welsh, and Fisher (1997) used two levels of complexity on the Hanoi tower test to compare three age groups: the young group, with a mean age of 19, the young old group, with a mean age of 65, and an old group, with a mean age of 75. Results showed no group differences when the task only used two disks, however, the performance of the young group was significantly better compared to the other groups when the number of disks was increased to four. These results underlined the interaction of aging effects with task difficulty. Similarly, Zook et al. (2006) found that low scores on the Tower of London test in elders over the age of 60 correlated with their non verbal skills; these are abilities traditionally included in the fluid intelligence category, which is very sensitive to aging (Jurado & Rosselli, 2007). Rönnlund, Lövdén, and Nilsson (2001) observed that the negative effects of aging on the Tower of Hanoi test were evident after the age of 65 and correlated with a greater number of moves and increased completion time. The same group of authors (Rönnlund et al., 2007) reported limited planning problems on the Tower of Hanoi test between the ages of 30 and 60 but a significant increase in the number of errors and in slowing after age 65.

Similarly, Allain et al. (2005) found that elderly participants (mean age of 80) made a greater number of errors when compared to younger participants (mean age of 29) in planning a visit to the zoo. Using ecologically valid tasks may be more appropriate for older adults, but age differences are not consistently reported in these types of studies (Phillips, Kliegel, & Martin, 2006).

In conclusion, research seems to suggest that healthy older adults have planning impairments when compared to younger healthy participants, with deficits appearing to subside with the use of ecologically valid tasks. Some research suggests that planning difficulties in normal aging result from issues in predetermining a complex course of action aimed at achieving a goal, more so than in guiding the execution of a sequence (Rosselli & Jurado, 2013).

8.2.3 Cognitive Flexibility/Set Shifting

Cognitive flexibility refers to the capacity to change a behavior or a mindset as a consequence of behavioral feedback (Jurado & Rosselli, 2007). This flexibility of the human mind allows us to appropriately adjust our behavior in response to environmental contingencies (Hanna-Pladdy, 2007). The most common neuropsychological tests used to study cognitive flexibility are the WCST and the Trail-Making Test-B (TMT-B; Reitan & Wolfson, 1993), with the go-no go paradigm occasion-ally included in this category (Hanna-Pladdy, 2007). This paradigm, despite being commonly used to measure response inhibitory control, requires cognitive flexibility.

The WCST, originally developed by Grant and Berg (Berg, 1948; Grant & Berg, 1948), is used to measure the ability to think in an abstract manner. The WCST assesses the capability of changing cognitive sets under shifting task demands that are unknown to the participants by employing cards that change in color, form, or number. Participants have to correctly sort the cards according to these three dimensions/categories using feedback (right or wrong) provided by the examiner. Dimensions are changed by the examiner without notice and participants must determine the rules of the test, understand when the rules have arbitrarily changed, and adjust their behavior accordingly (Bryan & Luszcz, 2000). Axelrod and Henry (1992) found a significant reduction in the number of correct categories and in an increase in the number of errors and perseverative responses (the continued incorrect response to one category despite receiving feedback) after the age of 60. Additionally, Daigneault, Braun, and Whitaker (1992) reported an increase in perseverative errors and a decrease in correct WCST categories at an earlier age (between 50 and 59 years). Bryan and Luszcz (2000) found a significant negative association (r = -0.56) between age and

the number of categories on the WCST in a group of 60 older (aged between 65 and 88 years) and 60 younger (aged between 17 and 48 years) participants.

Several theories have attempted to explain these age effects on the WCST. Ridderinkhof, Span, and Van der Molen (2002) suggested that elders have an impaired ability to develop hypotheses when rules change constantly. Offenbach (1974) proposed that age affects the ability to use feedback information and consequently, working memory is impaired in tasks such as the WCST. Finally, Salthouse (1996) concluded that the decline in cognitive flexibility results from the slowing of the speed of processing, which reduces the amount of information that can be activated simultaneously.

Another neuropsychological test used to measure cognitive flexibility is the TMT-B, a visuomotor test in which the score corresponds to the time it takes to draw lines between alternating numbers and letters in consecutive order (Reitan & Wolfson, 1993). To be successful in this visuomotor test, conceptual flexibility is needed to alternate between numbers and letters (Kortte, Horner, & Windham, 2002). Typically, elderly participants make a greater number of errors and have longer completion times compared to younger participants (Ashendorf et al., 2008).

The influence of age on tests of cognitive flexibility is not always reported. For example, Mejía, Pineda, Alvarez, and Ardila (1998) did not observe differences on the WCST between two age groups of individuals between the ages of 55 and 70 and between 71 and 85. Surprisingly, Haaland, Vranes, Goodwin, and Garry (1987) reported a decrease in the number of perseverative errors along with an increase in the number of categories obtained by the older groups compared to younger groups. This group of authors only reported deficits in cognitive flexibility after 80 years of age.

In summary, most research on cognitive flexibility shows that increasing age is related to a higher number of perseverative errors and longer completion times (Bryan & Luszcz, 2000). However, other research does not support these results. These differences may be partially attributed to the variability of sample sizes and varying educational levels of the participants (Jurado & Rosselli, 2007). In addition, it is important to note that the cognitive flexibility tests mentioned above also require attentional control and working memory, and may have a motor component (e.g., the TMT-B).

The differences in cognitive flexibility that distinguish young adults from older adults have been correlated with variations in the activation level of prefrontal regions (Laguë-Beauvais, Brunet, Gagnon, Lesage, & Bherer, 2013). In general, studies of executive control using functional Magnetic Resonance Imaging (fMRI) show that older adults have increased activation in frontal regions, and this increase is positively correlated with task performance, suggesting that it plays a role as a compensatory mechanism. Madden et al. (2010) found that the pattern of event-related activation for task switching is similar for young and older adults, but older adults activate multiple prefrontal regions during task performance, not limiting the activation to regions specific to task switching. fMRI studies have shown that task switching involves activation of the frontoparietal network, although the regional patterns vary in response to individual task demand (Slagter et al., 2006). Additionally, differences

in the integrity of the functional connectivity of the frontal lobe with other cortical areas have been observed, particularly with the parietal lobe (Gold, Powell, Xuan, Jicha, & Smith, 2010). Finally, Madden et al. (2010) compared the functional connectivity of a group of senile participants and a group of younger adults and reported that the senile group had less functional connectivity with other brain regions in tasks of cognitive flexibility, particularly when cue processing was involved. In this study, cueing indicated that a categorization decision needed to be made in relation to a target. Performance on this type of task is typically slower and less accurate when the categorization of the current trial switches from the previous trial, relative to when it repeats.

8.2.4 Initiation and Self-generation

The productivity of an individual is determined in part by his/her own behavioral initiative. Reduced initiation or latency in responding can modify the response efficiency. Tests that require the timed generation of items (verbal with phonological or semantic fluency or nonverbal with design fluency) with specific task constraints have been used to estimate the generational capacity of an individual (Lezak et al., 2004). To be successful on these tests, participants need to implement a recall strategy (words or designs), followed by an additional strategy to keep responses within the mandated category with the corresponding inhibition of irrelevant words, while also monitoring recall to avoid repetitions. Also, these tasks require the flexibility to move within the subcategories to have a more efficient word recall. For example, within the animal category, there are subcategories of mammals, birds, reptiles, etc. (Rosselli, Tappen, Williams, Salvatierra, & Zoller, 2009).

Research on the effects of age on fluency tests has produced contradictory results. Some authors have concluded that there are no age effects, while others suggest that young adults outperform older adults (Jurado & Rosselli, 2007). Fisk and Sharp (2004) found no evidence to support the theory of a negative effect of age on word fluency, however, these effects were found during paradigms that required the simultaneous manipulation of information. Similarly, Rodríguez-Aranda and Sundet (2006) found age differences in different types of EF tests, except for verbal fluency. Some researchers suggest that verbal fluency remains unchanged by age because it depends on a source of verbal knowledge that remains intact over the years (Crawford, Bryan, Luszcz, Obonsawin, & Stewart, 2000). In fact, several authors have found that the level of vocabulary is not sensitive to the passage of time and changes are evident only in the eighth decade of life (Emery, 1985). Bryan, Luszcz, and Crawford (1997) evaluated older adults whose ages ranged from 72 to 95 and found small age-related declines on phonological fluency, demonstrating that this ability is somewhat preserved in old age.

On the other hand, Brickman et al. (2005) reported a linear decline in verbal fluency function as age progressed. These authors replicated previous findings that suggest that semantic fluency is impaired before phonological fluency. Likewise,

Bolla, Lindgren, Bonaccorsy, and Bleecker (1990) found a significant age effect on phonological and semantic fluency when studying a group of elderly people with a high level of education.

Two meta-analyses demonstrated a slow deterioration of phonological fluency functions after the age of 40, which became faster after 60 (Rodríguez-Aranda & Martinussen, 2006; Loonstra, Tarlow, & Sellers, 2001). A recent longitudinal study shows the deterioration of both semantic and phonological fluidity in 96 patients with normal aging and with an average age of 74 years. The decrease in semantic fluency (number of recalled animals and supermarket items) over time was significantly faster than the decrease in phonological fluency (words beginning with F, A, and S) (Clark et al., 2009). It is unclear why there are divergent results, but it is possible that these are related to different education levels (Rosselli & Jurado, 2013). The effect of education on verbal fluency tests has been clearly established (Ardila, Ostrosky-Solis, Rosselli, & Gómez, 2000; Rosselli et al., 2009); these levels must be strictly controlled along with other socioeconomic variables (Jurado & Rosselli, 2007).

The performance of young and old adults on tasks of verbal fluency correlates with the activation of the frontal (inferior and medial portion) and temporal lobes (superior and medial turns) of the left hemisphere (Baldo, Schwartz, Wilkins, & Dronkers, 2006). It has been observed, however, that in old age, activation of these areas is more extensive and is accompanied by additional activation of the right frontal lobe (Cabeza & Dennis, 2013). This supplementary activation has been positively correlated with performance on memory tasks (Cabeza, Anderson, Locantore, & McIntosh, 2002) but negatively correlated with performance on verbal fluency tasks (particularly, semantic verbal fluency; Meinzer et al., 2009). That is, greater bilateral activation was associated with superior performance on memory tests (Cabeza et al., 2002), but worse performance on verbal fluency. Meinzer et al. (2012) reported that in phonological fluency tasks, but not semantic fluency, young adults can, like older adults, present activation in the right frontal lobe, but this activation is limited to one frontal region, in contrast to the broad activation observed in older adults. Additionally, this study found that the presence of negative bilateral activation (areas that are active during rest and are inhibited during the task) of anterior and posterior areas of the midline and temporal and parietal regions (especially the frontal lobe and precuneus during semantic fluency) during fluency tasks differed between young and older adults. During phonological fluency tasks, a pattern of negative activation was observed, very similar to that found in semantic fluency tasks. Compared with the young adults, the brains of the older adult sample in Meinzer et al.'s (2012) study were characterized by a much lower negative activation.

Nonverbal equivalents of the verbal fluency tasks include design fluency tasks such as the 5-Point Test (Regard, Strauss, & Knapp, 1982). This task requires participants to generate as many designs as possible in three minutes using 5-dot matrices. Participants have to connect two or more dots within the time frame without repetitions. This test appears to place greater demands on executive control mechanisms than semantic fluency tests (Foldi, Helm-Estabrooks, Redfield, & Nickel, 2003). Research on the influence of age on design fluency is mixed; some studies found no influence of age (Daigneault et al., 1992) and others report detrimental age effects

(Mittenberg, Seidenberg, O'Leary, & DiGiulio, 1989). It is possible that this test is sensitive to age only when comparing extreme age groups (Bryan & Luszcz, 2000).

8.2.5 Behavioral/Emotional Dysexecutive Syndrome

Problems with response inhibition can be evident in a patient's failure to inhibit inappropriate verbal or behavioral responses, and ideally, the assessment should be done by observing behavior during a clinical examination and using family reports. Response inhibition often presents as behavioral impulsivity, which can affect a wide range of everyday behaviors with significant consequences on effective functioning in the real world (Hanna-Pladdy, 2007). Most of the studies on dysexecutive functions associated with aging have analyzed cognitive abilities, while the behavioral component of the syndrome has rarely been investigated. The nature of behavioral dysexecutive symptoms in aging has been explored using the Dysexecutive Questionnaire (DEX; Burgess, Alderman, Evans, Emslie, & Wilson, 1998). This 20-item questionnaire assesses EF problems in four areas: personality, motivation, behavioral, and cognitive. Amieva et al. (2003) conducted a pilot study using the DEX with 20 elderly Scottish participants and identified five factors that accounted for 75.6% of the variance of DEX scores. The factors were related to intentionality/initiative (factor 1), coping with interfering events (factor 2), euphoria, perseveration, and confabulation (factor 3), planning and thinking ahead (factor 4), and social regulation (factor 5). All factors except for factor 4 correlated with EF measures; the strongest and most significant correlation (r = 0.574, p = 0.008) was found between factor 5 (social regulation) and completion time on the Zazzo Cancelation task. Byczewska-Konieczny (2019) replicated Amieva et al.'s (2003) study by administering the DEX to a larger sample of elderly Polish participants (N = 40). Additionally, DEX scores were correlated with performance on three neuropsychological measures of EF (Zazzo Cancelation task, Simon Task, and OSPAN task). Items from the DEX loaded onto three factors (F1, ability to plan and monitor of one's behavior; F2, emotional regulation; and F3, ability to cope with interfering events) that accounted for 43.38% of the total variance. The author did not find significant associations between these behavioral factors and scores on cognitive EF tasks in the sample of normally aging individuals. These findings are in contradiction to those by Chan (2001), who found significant correlations between cognitive EF tests and five factors from the DEX (F1, inhibition; F2, goal-directed behavior; F3, knowing-doing dissociation; F4, "in resistance" of both thinking processes and behavior; and F5, social regulation) in a sample of younger healthy Chinese adults. These age-discrepant results question the validity of the DEX with older individuals, as results have been obtained in younger samples. The limited theoretical validity across age groups makes the characterization of DES difficult in older groups; therefore, future research is needed to determine the relationship between cognitive and behavioral aspects of dysexecutive symptoms among elderly people from a nonclinical perspective.

Finally, since studies testing the validity of the DEX use samples from different cultures (Scottish, Polish, and Chinese), the potential contribution of cultural and socioeconomic factors on the reported results seems relevant.

The areas of the brain involved in emotional processing overlap with those associated with EF declines in aging. Therefore, van Reekum et al. (2018) suggested that the capacity to adaptively respond to emotional information declines with age. Recent evidence using neuroimaging suggests that when older adults process emotional facial expressions, they engage different cortical networks compared to younger adults. These networks involve dorsal areas in the medial PFC (mPFC; e.g., Williams et al., 2006) or ventrolateral PFC (VLPFC) when processing complex negative images (Dolcos, Wang, & Mather, 2014). van Reekum et al. (2018) demonstrated less activation in the left ventrolateral PFC (VLPFC) and greater ventromedial PFC (VMPFC) activity with increasing age during negative-picture viewing, while age was not correlated with amygdala activation (a structure for the acquisition and expression of emotions). The authors suggested that aging impacts activity in PFC systems that compute negative affect without necessarily altering the emotional response. This suggests that there is a compensatory mechanism with advancing age, reflected in greater engagement of medial rather than lateral PFC areas during the processing of emotion-laden information, preserving emotional reactivity.

8.3 Dysexecutive Syndrome in Abnormal Aging

As stated above, DES may be identified when there is frontal lobe damage as a result of disease (associated with aging) or injury (Poletti, Cavallo, & Adenzato, 2017) and includes cognitive impairment (dysregulation of EF) as well as emotional and behavioral concerns (Godefroy et al., 2010). It is important to note, however, that there is currently little consensus regarding the diagnosis and definition of DES, and terms are often used interchangeably to describe EF impairment (e.g., frontal lobe disorders or dysexecutive disorders; Godefroy et al., 2018).

It is essential to determine whether there are behavioral issues in DES, and it is important to assess cognitive changes with neuropsychological tests and behavioral changes with behavioral scales and by observing the patient (Hanna-Pladdy, 2007).

Within the EF disorders, Godefroy et al. (2018) described that the most common behavioral impairment is global hypoactivity with apathy, in which there is reduced motivation and activity, as well as disinhibition. The most commonly observed cognitive impairments were related to difficulties in self-initiating action.

8.3.1 Mild Cognitive Impairment and Dementia

While executive dysfunction (ED) is often seen as a sign of several dementia subtypes, it has also been described in amnestic Mild Cognitive Impairment (aMCI; Blanco Martín et al., 2016) in which cognitive deficits are not severe enough to constitute functional impairment (Petersen et al., 1999). aMCI is considered a prodromal stage of dementia and is associated with a greater likelihood of progressing to dementia (Petersen et al., 2001). Blanco Martín et al. (2016) evaluated cognitively normal and aMCI individuals with neuropsychological and clinical tests. Their results suggest that executive changes are present in aMCI and that among the three tests included measuring EF, semantic fluency (specifically animals) was associated with progression from aMCI to dementia. Similarly, Peter et al. (2016) found that patients with aMCI perform significantly worse and use fewer strategies during semantic and design fluency compared to healthy controls (HC). Both groups, however, benefited equally from repeated assessment, highlighting the groups' abilities to increase performance with practice (fluency tasks were administered three times within two days). In aMCI, performance during semantic fluency was significantly predicted by design fluency performance, while in HC, it was significantly predicted by naming performance. These findings suggest that in aMCI, participants use an executive strategy rather than a semantic strategy. In HC, the volume of the superior frontal gyrus (SFG) significantly predicted semantic and design fluency performance and strategy use during design fluency. In aMCI, the SFG and the inferior frontal gyrus (IFG) predicted performance during semantic and design fluency. The IFG significantly predicted strategy use during semantic fluency in both groups. The authors concluded that the reduced semantic fluency performance in aMCI seems to be primarily due to dysfunctional executive control mechanisms rather than impaired semantic knowledge.

Similarly, in cases of non-amnestic dysexecutive vascular MCI (VaMCI), a review by Sudo et al. (2012) described the disconnection of the fronto-parietal-subcortical network. Sachdev et al. (2009) evaluated post-stroke patients with vaMCI between the ages of 45 and 87 who did not have a dementia diagnosis or other neurological disorders before vascular incidents. The authors used a neuropsychological battery that tested a wide range of domains and concluded that in vaMCI patients, EFs, assessed with the Controlled Oral Word Association Test (Benton & Hamsher, 1976; Morris et al., 1989) and language (tested with the shortened Boston Naming Test; Mack, Freed, Williams, & Henderson, 1992) declined more than other domains over three years.

ED is common in Alzheimer's disease (AD), but the main impairment in this case relates to memory deficits resulting from damage to medial temporal lobes. However, Godefroy et al. (2018) reported that in AD, over 75% of individuals have the behavioral and/or cognitive DES, while around 90% have some type of initial EF disorder (Godefroy et al., 2016). These individuals have impairments in planning, inhibition, and flexibility, as well as global hypoactivity apathy (Godefroy, Barbay, Andriuta, Tir, & Roussel, 2017).

Within AD, there are rare cases in which there may be a "frontal variant" of the disease (fvAD). This variant is also known as the behavioral/dysexecutive variant of AD (Ossenkoppele et al., 2015) which primarily presents with cognitive impairments (working memory, cognitive flexibility, planning, and problem-solving) and little behavioral concerns. In these patients, the atrophy mainly compromises the

medial temporal lobes instead of the frontal lobes, which are significantly damaged in the behavioral variant of frontotemporal dementia (bvFTD). The damage in the behavioral/dysexecutive AD is in line with what is traditionally found in classical AD. However, due to the clinical similarities between fvAD and bvFAD, the differential diagnosis is challenging (Wong et al., 2019).

bvFTD is accompanied by changes in social cognition and EF, however, this impairment (particularly in the early stages of the disease) may only be observed using ecologically valid EF tests that include real-life EF and complex decision-making tasks (Torralva, Roca, Gleichgerrcht, Bekinschtein, & Manes, 2009). Specifically, bvFTD patients show impairments in planning, flexibility, complex decision-making, and organization. Similarly, Gansler, Huey, Pan, Wasserman, and Grafman (2017) evaluated patients with bvFTD, primary progressive aphasia (PPA), and corticobasal syndrome (CBS). The authors found that bvFTD patients had lower scores on EF tasks and a greater degree of dysexecutive behavior (DB) compared to the other two groups. Importantly, these authors emphasized the importance of combining EF as well as DB measures to assist in the diagnosis of the three disorders.

8.3.2 Subcortical Disorders

ED is also present in individuals with Parkinson's disease (PD), in which the hallmark symptoms are motor disturbances. This ED is reflected by worsened performance in several aspects of EF (e.g., set shifting, inhibitory control, reasoning, planning, and problem solving) which impacts the patients' daily lives (Kamei et al., 2008). This dysfunction includes behavioral as well as cognitive disturbances, whose impact should be carefully assessed (Ceravolo, Pagni, Tognoni, & Bonuccelli, 2012; Gruszka, Hampshire, Barker, & Owen, 2017).

Moreover, DES has been described at the early stages of PD (Foltynie, Brayne, Robbins, & Barker, 2004) and could include deficits of working memory, planning, attentional control, and set-shifting performance. However, one of the most common deficits is set-shifting difficulties which are evident in cognitive and motor tasks. These deficits are associated with hypoactivation in the inferior frontal sulcus (IFS), the striatum, and the anterior cingulate gyrus (ACC) (Gruszka et al., 2017).

Within PD, researchers also examined the incidence of dementia and explored whether certain variables could predict cognitive decline (Williams-Gray, Foltynie, Brayne, Robbins, & Barker, 2007). Their results suggested that 10% of their patients progressed to dementia after 3.5 years, while two-thirds developed cognitive deficits in this period. They additionally described that this rate may be influenced by age, the motor phenotype, and deficits in semantic fluency and a pentagon-copying task, all of which increased the risk of progressing to dementia.

DES has also been examined in nondemented PD patients (Roussel et al., 2017). The authors reported that DES was present in 81% of PD patients, with either cognitive or behavioral impairments observed in most patients. Behaviorally, these patients

often presented global hypoactivity, while cognitive impairments included deficits in inhibition and flexibility.

8.3.3 Vascular Disorders

Besides neurological diseases in aging, ED has been identified as a factor for the risk of stroke in cognitively unimpaired individuals (Oveisgharan & Hachinski, 2015). Additionally, following a stroke, individuals may develop DES (Godefroy et al., 2018). More specifically, strokes in the thalamus (i.e., ischemic thalamic stroke) have also been shown to impair EF (Liebermann, Ploner, Kraft, Kopp, & Ostendorf, 2013). The authors found that their subjects, who mostly presented with ventral thalamic lesions, performed worse on the WCST while performance on other tests of EF (e.g., semantic and phonological fluency and the Stroop test) was normal. This suggests that different EF abilities may rely on diverse thalamic regions.

DES has also been characterized in individuals with ischemic vascular disease (IVD), in which patients exhibit difficulties in engaging in a certain task, inhibiting irrelevant answers, and continuing adequate behavior for the task (Lamar, Price, Giovannetti, Swenson, & Libon, 2010). These impairments were attributed to damage of the basal ganglia and thalamus and their connections to the frontal lobe.

8.4 Conclusion

In general, there is evidence suggesting that age-related changes in the frontal lobe (in volume and in the degree of functional connectivity with other regions) are associated with EF declines. These can be observed in healthy and abnormal aging and may influence several EF domains. DES appears to be the most severe manifestation of these deficits and is present in neurological disorders. Normally aging individuals suffer from deficits in attentional control and inhibiting unwanted responses, with impairments leading to greater distractibility and slower processing time during neuropsychological testing. Other theories propose that adulthood is characterized by general slowing, which may result in these deficits, however, there appears to be a unique effect beyond slowing accounting for inhibitory difficulties. Older adults also exhibit issues with planning for future actions to achieve a goal, particularly after the age of 65, as well as impairments in cognitive flexibility, possibly due to the inability to update hypotheses with constant rule changing, or, like inhibition, general slowing. Impairments in initiating behaviors are also seen in healthy adults, traditionally observed with fluency tests. Neuroimaging findings suggest that older adults use a compensatory mechanism during these tasks, resulting in greater activation than in younger adults.

Behavioral DES, unlike cognitive DES, is better captured using questionnaires and behavioral observations, however, the validity of these measures has yet to be established for aging populations. In older adults, there are emotional processing changes, with activation of different brain areas compared to younger adults. Conflicting results across cognitive and behavioral domains in aging may be related to different levels of education in the groups or the variety of the EF paradigms used, which tend to heavily rely on several lower-level functions.

Besides normal aging, DES (cognitive and behavioral) is present in several neurological diseases that are prevalent in older adults. In aMCI and VaMCI, EF is impaired, and this is reflected by deficits in fluency tests, highlighting the sensitivity of these measures in the early stages of AD and vascular dementia. In AD and in rare cases of a frontal variant, ED is present as well, resulting in difficulties with planning, cognitive flexibility, and other domains. In bvFTD, ED is reflected by impairments in planning, flexibility, complex decision-making, and organization. Lastly, the executive dysfunctions in PD have been described in the early stages of the disease (in working memory, planning, shifting, and attentional control) and in demented and nondemented PD patients. It appears that DES is prevalent in this condition and is associated with hypoactivation of the ACC, IFS, and striatum (brain regions associated with learning). Finally, the presence of DES in post-stroke patients has been identified in individuals with thalamic damage, emphasizing this structure and its numerous frontal connections as an important neural underpinning of EFs.

Overall, ED is prevalent in healthy older adults as well as in those with a wide range of neurological diseases. Cognitive impairments appear to be more accurately characterized with the use of ecologically valid tasks, which present participants with novel requirements, while behavioral impairments may only be observed with interviews and observations.

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