The Role of Temperament

5.1 Historical Perspective

While early versions of the concept of temperament might had existed in ancient Egypt and Mesopotamia, essentially this approach was developed by the school of Cos and specifically by Polybus who was a pupil and son-in-law to Hippocrates (fourth century BC) and author of the book 'Peri physeos anthropou' ('On the Nature of Man'). This theory is in fact a microcosmic form of the macrocosmic theory of the four elements (earth, water, air, fire) and the four qualities (dry, wet, cold, hot) as first proposed by Empedocles (fifth century BC). According to this ancient approach, temperament (in Greek crasis or idiosyncrasia), health and disease are the products of the balance four body humours (in Greek choli). According to the predominance of a given humour, four temperamental types were described: the choleric (yellow bile from the liver; cyclothymic), the sanguine (blood from the heart; hyperthymic), the melancholic (black bile from the kidneys; depressive) and the phlegmatic (phlegm from the lungs; self-content). The theory was further elaborated by Erasistratos, Asclepiades (first century BC) and eventually by Galen (second century AD) with his treatise 'Peri crasaion' ('De temperamentis'). This approach was the standard until the sixteenth century and in the India and the Muslim world constituted the basis of Yunani or Unani medicine (after Yunan that is Iones-Greeks in Eastern languages). In 'The Canon of Medicine', Avicenna (980-1037 AD) extended the theory of temperaments to include 'emotion, mental ability, moral attitudes, self-awareness, movement and dreams'. In English texts, temperament is mentioned in Wycliff's sermons (1380), in the writings of Shakespeare and in Robert Burton's Anatomy of Melancholy (Table 5.1).

The word 'temperament' itself comes from the Latin word 'temperare', which means 'to mix', while the Greek original word is 'crasis' or 'idiosyncrasia', standing for 'mixture' and 'unique admixture', respectively.

Temperament theory influenced philosophical thinking and played a predominant role in the shaping of the anthropological and humanitarian sciences. Prominent scholars like Ernst Platner (1744–1818), Immanuel Kant (1724–1804),

 Table 5.1 Chronological chart of theoretical elaboration on temperament

Theorist	Time period	Contribution	
Polybus (school of Cos)	Fourth century BC	'Peri physeos anthropou' ('On the Nature of Man'). Theory of the four humours	
Eristratos, Asclepiades	First century BC	Further elaboration on Polybus' theory	
Galen	Second century AD	'Peri crasaion' ('De temperamentis')	
Avicenna	980–1037 AD	Canon of medicine (includes emotion, mental ability, moral attitudes, self-awareness, movement and dreams)	
Nicholas Culpeper	1616–1654	The first to disregard the idea of fluids as defining human behaviour	
Georg Ernst Stahl	1660–1734	Animism/vitalism	
Friedrich Hoffmann	1660–1742	Iatromechanism (hydraulic based theory)	
Immanuel Kant	1724–1804	Anthropologie	
Ernst Platner	1744–1818	Philosophische Aphorismen	
Friedrich Schiller	1759–1805	Human types: idealist and realist	
Franz Joseph Gall	1758–1828	Phrenologistic teachings; considered the study of temperaments as the first step in phrenology	
Johann Spurzheim	1776–1832		
Friedrich Schelling	1775–1854	'Naturphilosophie'	
Jacob Henle	1809–1885	The first to base a theory of temperaments on the tone of the nervous system	
William James	1842–1910	Tough-minded and tender-minded temperaments	
Friedrich Wilhelm Nietzsche	1844–1900	The Apollonian, or rational, and the Dionysian, or passionate, element of human nature (the birth of tragedy)	
Carl Spitteler	1845–1924	Prometheus (forethinker, introvert) and Epimetheus (after-thinker, extrovert)	
Rudolf Steiner	1861–1925	Suggested that temperament is under the persons' partial control, changes and matures; persons are a mixture of different temperaments which are characterized by different levels of maturity	
Erich Adickes	1866–1928	'Four world views' in 1907: 'dogmatic', 'agnostic', 'traditional' and 'innovative'	
Carl Gustav Jung	1875–1961	Interplay between an outer public self and a secret inner self as determining the direction of the libido (extroversion vs. introversion)	
Alfred Adler	1879–1937	Four mistaken goals: 'recognition', 'power', 'service' and 'revenge'	
Eduard Spränger	1882–1963	Four human values: 'religious', 'theoretic', 'economic' and 'artistic'	

Table 5.1 (continued)

Theorist	Time period	Contribution
Ernst Kretschmer	1888–1964	Three body types (asthenic/leptosomic, athletic and pyknic/extrovert) and two temperaments ('schizothymic' with the hyperaesthetic–sensitive and anaesthetic–cold characters and the 'cyclothymic' with depressive–melancholic and the hypomanic characters)
William Sheldon	1898–1977	Three body types (endomorphic, mesomorphic and ectomorphic) and three related groups of temperament traits: 'viscerotonia' (relaxation, comfort, sociability, gluttony for food, for people and for affection), 'somatotonia' (muscular activity and of bodily assertiveness) and 'cerebrotonia' (restraint, inhibition, concealment)
Erich Fromm	1900–1980	Eight basic needs (relatedness, transcendence, creativity, rootedness, sense of identity, frame of orientation, excitation and stimulation, unity, effectiveness) and two factors (acquiring and assimilating things (assimilation) and reacting to people (socialization)) forming five types of malignant character (receptive, exploitative, hoarding, necrophilous and marketing) and one positive character (productive)
Hans Eysenck	1916–1997	The first psychologist to analyse personality differences using an empirical/statistical method
		He suggested that temperament is biologically based. Three dimensions of personality: neuroticism (tendency to experience negative emotions), extraversion (tendency to enjoy positive events) and psychoticism (cognitive style)
		His theory and the theories that derived from it, all concern approach/reward, inhibition/punishment and aggression/flight
Solomon Diamond	1957	In order to distinguish between 'the essential foundations of individuality and its cultural elaboration', one has to look at the animal world
		Four temperament traits in primates: fearfulness, aggressiveness, affiliativeness and impulsiveness
David Keirsey	1921–	Four temperament patterns (sensing perceiver, sensing judger, intuitive thinker and intuitive feeler) and 16 characters
Jeffrey Gray	1934–2004	Neural theory of the Behavioural Inhibition System (BIS) and Behavioural Approach System (BAS)

(continued)

Table 5.1 (continued)

Theorist	Time period	Contribution
Alexander Thomas, Stella Chess, Herbert G. Birch	1956	The 'New York Longitudinal Study' began in 1956 Nine dimensions of temperament (activity level, rhythmicity of biological functions, approach/ withdrawal, adaptability, threshold of responsiveness, intensity of responses, quality of mood, distractibility and persistence) and three distinct temperaments: the 'easy children' (40 % of sample, characterized by regularity, ease of approach, adaptability, mild to moderate mood intensity and a generally positive mood), the 'difficult children' (10 % of the sample with opposite qualities to the 'easy' type) and the 'slow-to-adapt children' (50 %) They put the emphasis on 'goodness of fit'
Buss and Plomin	1973	Temperament traits show early appearance in ontogenesis (infancy), are heritable and are predictive of later development Four temperament traits (emotionality, activity,
Robert Cloninger	1944–	sociability and impulsivity) He developed a theory of hierarchical temperament and character traits and dimensions; he attempted to intimately connect temperamental characteristics and neurotransmitter systems His theory suggests a link between novelty seeking
H. Hill Goldsmith and Joseph Campos	1990	and dopamine, harm avoidance and serotonin and reward dependence and noradrenaline Temperaments are individual differences in the primary emotions. Emphasis on the basic/primary emotions (anger, fear and pleasure) and also the way of regulating them. Central to this notion are three characteristics of response: threshold, latency and intensity
Hagop Akiskal	1945–	He focused on the affective components of temperament and their relationship to mood disorders and creativity
Mary Rothbart	1940–	She emphasized reactivity (meaning biological arousability), self-regulation (increase, decrease, maintain and restructure the patterning of reactivity) and cognitive processes (focus of attention) She identified three broad dimensions of temperament: surgency–extraversion (positive anticipation, activity level and sensation seeking), negative affectivity (fear, anger/frustration and social discomfort) and effortful control (inhibitory control, attentional focusing and perceptual sensitivity)
Jerome Kagan	1929–	Described two types of children: the 'inhibited' (cling to their mothers, cry and hesitate with unfamiliar persons or events, are timid and shy and represent about 20 %) and the 'uninhibited' (or exuberant) Inhibition can be better understood as intolerance of uncertainty and not as a proneness to fear

Friedrich Schiller (1759–1805) and Friedrich Wilhelm Nietzsche (1844–1900) included concepts similar to temperament in their writings. Gradually physiology and medicine returned to the field and eventually, on the borderline and interface between philosophy, sociology, psychology, anthropology and medicine, Rudolf Steiner (1861-1925), Ernst Kretschmer (1888-1964) and Erich Fromm (1900-1980) described human types and temperaments. Ernst Kretschmer (1888–1964) described the asthenic/leptosomic, athletic and pyknic body types with the pyknic body type being extrovert and related to manic depression. He also divided personality into two temperaments: The 'schizothymic' (with the hyperaesthetic-sensitive and anaesthetic-cold characters) and the 'cyclothymic' (with depressive-melancholic and the hypomanic characters). Hans Eysenck (1916–1997) was the first to analyse personality differences using an empirical/statistical method. He proposed that the basic factors were neuroticism (tendency to experience negative emotions), extraversion (tendency to enjoy positive events) and psychoticism (cognitive style). Eysenck's theory and all the theories that derived from it concern approach/reward, inhibition/punishment and aggression/flight (Eysenck and Eysenck 1962, 1964, 1967, 1968, 1969, 1972, 1977; Eysenck et al. 1974, 1976, 1977).

McCrae and Costa proposed the five-factor model (Big Five) (McCrae and Costa 1987) which includes neuroticism, extroversion agreeableness, openness and conscientiousness and constitutes a further development of Eysenck's theory. The older concept of 'psychoticism' was substituted by agreeableness and conscientiousness, while openness has some degree of overlap with extroversion (Markon et al. 2005).

The work of Robert Cloninger is characterized by an attempt to intimately connect temperamental characteristics with individual differences in genetics, neurotransmitter systems and behavioural conditioning. He described novelty seeking (anger), harm avoidance (fear), reward dependence (attachment) and persistence (ambition) (Cloninger 1987; Cloninger et al. 1993). His research suggests that temperament components can be assessed as early as preschool age (Constantino et al. 2002) and remain moderately stable throughout a person's lifespan except for changes from behavioural conditioning (Josefsson et al. 2012).

Hagop Akiskal has conceived temperament as the affective predisposition or reactivity, based on the original descriptions by Kraepelin (1921) of fundamental states (manic or hyperthymic, irritable, cyclothymic, anxious and depressive). Empirical research has confirmed the hypothesized four-dimensional factor structure and is in agreement with those previously proposed on clinical populations. In an additional exploratory analysis, a depressive type constituted the antipode of hyperthymia and was distinguished from cyclothymia; the irritable temperament appeared somewhat independent. These are close to the classic descriptions of Kraepelin, Kretschmer and Schneider (Akiskal et al. 1998b) (Table 5.2).

While personality refers to goals, coping styles, defensive styles, motives, self-views, life stories and identities (McAdams and Pals 2006), basic personality traits (e.g. extraversion or neuroticism) are essentially parts of temperament (Rothbart et al. 2000). The major theories taken together suggest that four-temperament model of Akiskal (Akiskal and Akiskal 2005), the cube model of Cloninger (Cloninger et al. 1999), the five-factor model represented by the NEO-PI (Costa and McCrae 1990), the seven-factor model of Tellegen (Tellegen et al. 1991) and Cattell's 16-factor

Researcher	Time period	Results	
Alexander Thomas, Stella Chess, Herbert G. Birch	1956	Nine dimensions of temperament (activity level, rhythmicity of biological functions, approach/ withdrawal, adaptability, threshold of responsiveness, intensity of responses, quality of mood, distractibility and persistence) and three distinct temperaments: the easy, the difficult and the slow-to-adapt children. Emphasis on 'goodness of fit'	
Solomon Diamond	1957	Fearfulness, aggressiveness, affiliativeness and impulsiveness	
Hans Eysenck	1964	Neuroticism (tendency to experience negative emotions), extraversion (tendency to enjoy positive events) and psychoticism (cognitive style)	
Buss and Plomin	1973	Emotionality, activity, sociability and impulsivity	
Robert Cloninger	1987	Four temperaments (novelty seeking, harm avoidance, reward dependence and persistence), 3 characters (self-directedness, cooperativeness, self-transcendence) and 25 facets	
Mary Rothbart	1988	Reactivity, self-regulation and cognitive processes	
		Three dimensions of temperament: surgency–extraversion, negative affectivity and effortful control	
Jerome Kagan	1989	The inhibited and the uninhibited children	
H. Hill Goldsmith and Joseph Campos	1990	Anger, fear and pleasure and the way of regulating them (threshold, latency and intensity)	
Jeffrey Gray	1991	Behavioural Inhibition System (BIS) and Behavioural Approach System (BAS)	
Hagop Akiskal	1998	Hyperthymic, cyclothymic, depressive, irritable and anxious	
Diogo Lara and Hagop Akiskal	2006	The fear and anger model	

Table 5.2 Summary of the results of empirical studies on temperament

model (Cattel et al. 1970) may in fact represent different levels of an hierarchical structure of normal and pathological personality with a two-superfactor solution at the top largely reflecting ego control and ego resiliency (Akiskal et al. 2005a; Cohen 1999), a limited number of temperaments in the middle (named under many labels, but significantly overlapping) (Maremmani et al. 2005) and many characters (15 or more) at the bottom. 'Temperament' corresponds to the 'higher' levels, while 'personality' and 'character' to the 'lower' (Cloninger et al. 2011).

The relationship of temperament to health suggests a strong link to general health and mortality (Friedman et al. 1993) to future mental health (Conley 1985) and to anxiety (Rosenbaum et al. 1988, 1991; Biederman et al. 1990, 2001; Kagan and Zentner 1996; Kagan et al. 1999, 2001; Smoller et al. 2005). It is established that premorbid temperamental predispositions are often present in mood patients and their relatives. These temperamental traits have a disorder-specific pattern of distribution (Evans et al. 2005; Kesebir et al. 2005; Akiskal et al. 2005a, b, c).

The anxious temperament seems to constitute a generic vulnerability factor and was shown to be a robust predictor of most mental disorders. On the contrary, the hyperthymic temperament has shown a uniquely protective effect on most mental disorders (with few exceptions including bipolar disorder) (Karam et al. 2010; Pompili et al. 2008). The dysthymic, cyclothymic and anxious temperaments are related to hopelessness and the irritable temperament to suicidality (Pompili et al. 2008).

Temperament assessment might help in differentiating between unipolar and bipolar depression. This is very important since in many patients the manifestation of a manic or mixed episode comes after several years of suffering and failed or false treatment efforts. The problem is that this 'temperament assessment' might reflect subclinical residual features of bipolar disorder (state) rather than true 'temperament' (i.e. basic long-standing characteristics of the patients or traits). To further complicate the picture, the assessment of temperament changes the definition of bipolarity itself and contributes to the concept of the 'bipolar spectrum'. In this frame it is one of the crucial factors in the increasing prevalence of bipolar cases (especially bipolar II) at the expense of unipolar ones. Although these above-mentioned thoughts constitute significant limitations, the presence of an affective temperament contributes additional affirmation of the early occurrence of mood symptoms in early-onset forms of both unipolar and bipolar depressions (Oedegaard et al. 2009).

The literature suggests that the clinical constellation of 'euphoric-grandiose', 'paranoid-anxious' and 'accelerated-sleepless' symptoms is related to the hyperthymic temperament, while the 'depressive' constellation is related to the depressive temperament and the cluster of 'irritable-agitated' symptoms is related to both temperaments (Perugi et al. 2001). Thus, 'hyperthymic' temperament characterizes manic patients with or without psychotic features (Perugi et al. 1997, 1998b; Dell'Osso et al. 1993) and its assessment reveals that one-third of depressed patients belong to the bipolar spectrum (Cassano et al. 1989).

The subgroup of 'unipolar' patients with hyperthymic temperament (12.4 % of unipolar cases) is similar to BD-II patients in terms of gender and bipolar family history (Cassano et al. 1992b). BD-II patients (40 % of depressed patients after systematic evaluation) manifest high scores on hypomania scales and cyclothymic and irritable temperaments. On the other hand, 88 % of cases, for which a cyclothymic temperament is recognized by clinicians, are diagnosed as BP-II. Cyclothymic temperament is significantly elevated in the bipolar vs. the unipolar depressive group (Mendlowicz et al. 2005a), but it seems that it is a robust clinical marker specifically for BP-II disorder (Hantouche et al. 1998) and is also higher in patients with a family history of bipolarity (Akiskal et al. 2005b).

BD-II patients with cyclothymia differ from those without as having younger age at onset and age at seeking help, higher depressive scores, more atypical features, longer delay between onset of illness and recognition of bipolarity, higher rate of psychiatric comorbidity and different personality disorders profiles (i.e. more histrionic, passive–aggressive and less obsessive–compulsive). Also, cyclothymic BP-II scored significantly much higher on irritable–risk-taking than 'classic' driven–euphoric items of hypomania (Akiskal et al. 2003). In comparison to hyperthymic patients, they might be more frequently females with more depressive

and hypomanic episodes and suicide attempts and more comorbidities (most often panic disorder/agoraphobia and social anxiety disorder); they meet more borderline personality disorder criteria and have higher rates of first-degree family history for both mood and anxiety disorders. On the other hand, hyperthymic patients might have more frequent manic episodes and hospitalizations and more antisocial personality disorder features (Perugi et al. 2010).

Marked irritable–explosive traits (occurring in 2–3 % of young persons and tending to attenuate by middle age) often coexist with the mood-labile cyclothymic type, representing the dark 'borderline' side of this cyclothymic temperament (Akiskal et al. 2003; Merikangas et al. 2007, 2011). The type BP-II ½ manifests early onset, complex temperament structure and high mood instability, rapid switching, irritable ('dark') hypomania and suicidality and seems to be the most prevalent and severe expression of the bipolar spectrum, accounting for 33 % of all depressions (Akiskal et al. 2006a). BP-III which is associated with antidepressant treatment is reported to arise from depressive temperament and bipolar family history (Akiskal et al. 2006b).

More than half of depressed patients with atypical features are reported to have antecedent cyclothymic or hyperthymic temperaments and often family history for bipolar disorder (Perugi et al. 1998a). Most of them (78 %) could meet the criteria for bipolar spectrum (mainly BD-II). Atypical patients with cyclothymic temperament manifest higher reactivity of mood, interpersonal sensitivity, functional impairment, avoidance of relationships, other rejection avoidance and, on the interpersonal sensitivity, phobic anxiety, paranoid ideation and psychoticism (Perugi et al. 2003). Reversely, as mentioned before, cyclothymic BD-II patients are reported to manifest more atypical features (Akiskal et al. 2003).

The psychotic mixed patients seem to be closer to the BD-I and are characterized by a hyperthymic temperament with a familial background of psychotic mood disorders, while the nonpsychotic mixed patients are closer to the BD-II and more often have a cyclothymic temperament and a family background of nonpsychotic disorders and substance abuse (Dell'Osso et al. 1993). The EPIMAN study in France suggests that the higher prevalence of hyperthymic temperament in males is responsible for the higher frequency of pure mania in men and the higher prevalence of depressive temperament in females is responsible for the more frequent mixed episodes in women (Akiskal et al. 1998a). Mixed episodes in BD-I women are related to both hyperthymic and depressive temperaments and familial depressive (rather than bipolar) disorders (Dell'Osso et al. 1991; Perugi et al. 1997).

Suicide is related to hopelessness and in turn the dysthymic, cyclothymic and anxious temperaments are related to hopelessness with the irritable temperament relating specifically to suicidality (Pompili et al. 2008). Lifetime suicide is related (among others) to depressive or mixed polarity of first episode and cyclothymic temperament (Azorin et al. 2009).

Patients with non-violent suicide attempts in the past have higher depressive, cyclothymic, irritable and anxious temperaments, but they do not differ from the general population in terms of hyperthymic temperament (Rihmer et al. 2009; Azorin et al. 2010).

Patients with high depressive and low hyperthymic temperament seem to be more likely to have higher hopelessness scores, more white matter hyperintensities, higher suicidal risk and more recent suicide attempts than the rest (Serafini et al. 2010). Late-onset mood disorder is characterized by hyperthymic, cyclothymic and irritable temperaments (Ng et al. 2008).

In summary, the hyperthymic temperament is related to euphoria, grandiose and paranoid thinking, antisocial behaviour, psychomotor acceleration and reduced sleep, as well as to higher frequency of manic episodes and hospitalizations. The cyclothymic temperament is related to the BD-II bipolar type, the presence of panic disorder, agoraphobia and social anxiety disorder, nonpsychotic mixed episodes and suicidality. The depressive temperament is related to depressive symptoms and the irritable to suicidality.

A summary of the relationship of various temperaments and the clinical manifestations of bipolar illness is shown in Table 5.3.

The differences between genders concerning the manifestation of mood disorders can be explained at least partially through differences in temperament. Women are much higher in need for approval (reward dependence) and cooperativeness than men (Cloninger et al. 1994). Females manifest less hypomanic, and more depressive, episodes and more anxiety and somatization. Gender differences in temperament (higher prevalence of the depressive temperament in women vs. higher hyperthymic temperament in men) might account for the differences in rates between genders (Perugi et al. 1990). It has also been proposed that sexes are distinguished by the 'ruminative' and the 'active' cognitive response styles. It seems also possible that women are more vulnerable to childhood adversities and to adult stressors especially related to bonding with men and child rearing (Nolen-Hoeksema and Girgus 1994; Nolen-Hoeksema et al. 1999; Nolen-Hoeksema 2011), which is consistent with gender differences in personality being closely related to traits important for attachment.

Mixed episodes in BD-I women are related to lower hyperthymic temperament and familial depressive, rather than bipolar, disorders (Dell'Osso et al. 1991). These temperamental dysregulations seem to constitute the intermediate step between predisposing familial-genetic factors in affective illness and gender-related clinical expressions of mood disorders (Cassano et al. 1992a). Differences in clinical manifestations might also include more anxiety—depressive features in females (which is in line with female overrepresentation in mixed mania) vs. more social disinhibition in males (Hantouche et al. 2001).

Unipolar and bipolar depressive patients with hyperthymic temperament are reported to have high rates of bipolar family history (Kendler 1997; Kendler and Karkowski-Shuman 1997). In comparison, patients with depressive temperament are reported to have a higher familial loading for mood disorders in general (Cassano et al. 1992a). Cyclothymic patients have also bipolar family history (Akiskal et al. 2005b; Hantouche and Akiskal 2006). Many monozygotic twins discordant for full-blown mood disorders manifest temperamental features strongly suggesting the presence of a genetic component (Bertelsen 1978; Bertelsen et al. 1977).

Table 5.3 Summary of the relationship of bipolar clinical features with various temperaments

Bipolar clinical feature	Temperament	
Classic bipolar disorder		
Euphoric-grandiose	Hyperthymic	
Paranoid-anxious	Hyperthymic	
Accelerated-sleepless	Hyperthymic	
Manic patients with or without psychotic features	Hyperthymic	
More frequent manic episodes and hospitalizations and more antisocial personality disorder features	Hyperthymic	
Depressive' constellation	Depressive	
Mixed episodes		
'Irritable-agitated' symptoms	Hyperthymic, depressive	
Psychotic mixed patients	Hyperthymic	
Nonpsychotic mixed patients	Cyclothymic	
Mixed episodes in females	Hyperthymic, depressive	
Comorbidity		
Panic disorder, agoraphobia and social anxiety disorder	Cyclothymic, anxious	
Suicidality		
Hopelessness	Dysthymic, cyclothymic and anxious	
Suicidality	Irritable	
Lifetime suicidality	Cyclothymic	
Non-violent lifetime suicidality	Depressive, cyclothymic, irritable, anxious	
Bipolar spectrum types		
BD-II	Cyclothymic	
BD-II ½	Cyclothymic, irritable	
BD-III	Depressive	
Atypical depression	Cyclothymic, hyperthymic	
Late-onset mood disorder (BD-VI)	Hyperthymic, cyclothymic and irritable	

In terms of relatives of patients, the cyclothymic temperament is more frequently present in first-degree relatives of patients with BD-I, followed by persons with family history of mood disorders. This loading was more pronounced in females. In the frame of a spectrum concept of bipolar disorder, cyclothymic temperament is distributed in ascending order in the well-relatives of patients from unipolar depression to bipolar disorders, thus possibly constituting a link between molecular and behavioural genetics (Chiaroni et al. 2005). Although peculiar, it is reported that controls have higher hyperthymic temperament in comparison to relatives of bipolar patients (Evans et al. 2005; Mendlowicz et al. 2005b). This is in accord with the above, but in contrast to the results of another study which suggests that BD-I patients and their relatives had significantly higher frequency of hyperthymic temperament than the controls (Kesebir et al. 2005). Relatives of bipolar probands

showed lower cyclothymic temperament scores than bipolar patients but higher scores than controls. Patients and their relatives showed higher anxious temperament scores than controls (Mendlowicz et al. 2005b). It seems that the composition of the sample in terms of diagnosis might determine the outcome, by giving weight to depressive, anxious, irritable or cyclothymic temperament, but not hyperthymic which might be higher in controls. The presence of these temperaments might impact on the quality of life of relatives of mood patients (Vazquez et al. 2008). Finally it has been shown that personality traits of high harm avoidance and low self-directedness are heritable risk factors for major depression in the never depressed sibs of depressives (Farmer et al. 2003).

It is often very difficult to distinguish between 'personality' from one hand and 'bipolar disorder' on the other, especially if bipolar disorder has a very early onset with complex residual symptoms between episodes.

Many of subthreshold mood conditions that constitute subeffective disorders were previously subsumed under such rubrics as 'neurotic', 'characterological' and 'existential' depressions and more recently personality disorders. It is relevant that measures of Beck's dysfunctional attitudes are strongly correlated with low self-directedness but not with temperament. Any temperament profile as measured by Cloninger may occur in people who are well adjusted and clinically normal – it is individual differences in character that determine whether a person can self-regulate their emotional drives (temperament) and thereby function in a healthy adaptive manner regardless of stress (Cloninger and Zohar 2011; Cloninger et al. 2010).

Cluster B personality disorders are closer to mood disorders in terms of clinical manifestations. Depending on the population studied, anywhere from half to two-thirds of DSM-III borderline disorders seem to represent subaffective expressions, principally on the border of bipolar disorder, characterized by dysthymic, irritable and cyclothymic temperaments or anxious-sensitive temperament in continuum with hysteroid dysphoric and atypical depressive disorders (Akiskal 1994). This is particularly true for cyclothymic BD-II patients, who are often misclassified as borderline personality disorder because of their extreme mood instability (Perugi and Akiskal 2002).

Cyclothymic BP-II patients were more histrionic, passive–aggressive and less obsessive–compulsive in terms of personality disorders (Akiskal et al. 2003).

The concept of temperament has been developed since antiquity to serve the comprehensive understanding of how the human body works and more important what determines human behaviour. The many theories on temperament included biological interpretations, philosophical and ethical approaches as well as psychological and sociocultural elements. Therefore, a large amount of information concerning the patient is gathered under the umbrella of temperament, and thus it is reasonable to assume that by utilizing temperament and related concepts, one can understand mental illness in a more comprehensive way. This has been studied especially for mood disorders with fruitful results, although many areas remain to be further clarified.

Within the area of mood disorders, specific affective temperaments might constitute vulnerability factors, clinical picture and illness course modifiers, residual syndromes or genetically determined variations of mood disorders, or even the

source of creativity. Considering the temperament issue in a wider sense, temperaments could constitute all the above in different proportions, but even in the same patient (Akiskal et al. 1989, 1997; Akiskal 1998, 2000, 2001; von Zerssen and Akiskal 1998; Kendler et al. 1992; Maier et al. 1992; Remick et al. 1996; Akiskal and Akiskal 2007). Affective temperaments seem to relate also to mood disorder family history, thus constituting an endophenotype bridge between genes and mood disorders (Cassano et al. 1992a; Akiskal et al. 2005b; Hantouche and Akiskal 2006; Chiaroni et al. 2005; Mendlowicz et al. 2005b). Viewing mood disorders under this prism gives birth to the concept of the bipolar spectrum with major implications for all aspects of mental health research and providing of care (Akiskal 2007).

Research so far indicates that the hyperthymic and the depressive temperaments are related to the more 'classic' bipolar picture (i.e. euphoria, grandiose and paranoid thinking, antisocial behaviour, psychomotor acceleration and reduced sleep and depressive episodes, respectively). On the contrary, cyclothymic, anxious and irritable temperaments are related to more complex pictures and might predict poor response to treatment, violent or suicidal behaviour and high comorbidity. Coexistence of temperaments or intrusion of a mood episode on a temperament of the opposite polarity also produces complex clinical manifestations and might lead to poor outcome. Often this poor outcome does not reflect inherent properties of the illness, but instead reflects the inability of the therapist to understand the illness and adequately plan treatment (Pompili et al. 2008; Oedegaard et al. 2009; Perugi et al. 1997, 1998b, 2001; Dell'Osso et al. 1993; Cassano et al. 1989, 1992b; Akiskal et al. 2005b, 2006a, b; Azorin et al. 2009, 2010; Rihmer et al. 2009; Ng et al. 2008). Temperament assessment could be especially helpful in understanding gender differences and plan treatment accordingly (Perugi et al. 1990; Dell'Osso et al. 1991; Cassano et al. 1992a; Hantouche et al. 2001).

Finally, the widening of our view concerning the information that could be useful for the diagnosis and treatment of bipolar disorder not only radically changes our understanding of the disease but also leads to better treatment and outcome of patients and probably can also lead to saving and better allocation of resources. Incorporating the concept of temperament and the bipolar spectrum in the standard training of psychiatric residents emerges as a pressing issue, but the way this can be achieved remains a challenge.

References

Akiskal HS (1994) The temperamental borders of affective disorders. Acta Psychiatr Scand Suppl 379:32–37

Akiskal HS (1998) The childhood roots of bipolar disorder. J Affect Disord 51(2):75–76. doi:S0165032798001736 [pii]

Akiskal HS (2000) Temperament and mood disorders. Harv Ment Health Lett 16(8):5–6. doi:M0100b [pii]

Akiskal HS (2001) Dysthymia and cyclothymia in psychiatric practice a century after Kraepelin. J Affect Disord 62(1–2):17–31. doi:S0165-0327(00)00347-5 [pii]

Akiskal HS (2007) The emergence of the bipolar spectrum: validation along clinical-epidemiologic and familial-genetic lines. Psychopharmacol Bull 40(4):99–115

Akiskal H, Akiskal K (2005) Epilogue. The renaissance of the ancient concept of temperament (with a focus on affective temperaments). In: Mai M, Akiskal H, Mezzich J, Okasha A (eds) Personality disorders. Wiley, San Diego, pp 479–500

- Akiskal HS, Akiskal KK (2007) In search of Aristotle: temperament, human nature, melancholia, creativity and eminence. J Affect Disord 100(1–3):1–6. doi:10.1016/j.jad.2007.04.013, S0165-0327(07)00139-5 [pii]
- Akiskal HS, Cassano GB, Musetti L, Perugi G, Tundo A, Mignani V (1989) Psychopathology, temperament, and past course in primary major depressions. 1. Review of evidence for a bipolar spectrum. Psychopathology 22(5):268–277
- Akiskal HS, Judd LL, Gillin JC, Lemmi H (1997) Subthreshold depressions: clinical and polysomnographic validation of dysthymic, residual and masked forms. J Affect Disord 45(1–2):53–63. doi:S0165-0327(97)00059-1 [pii]
- Akiskal HS, Hantouche EG, Bourgeois ML, Azorin JM, Sechter D, Allilaire JF, Lancrenon S, Fraud JP, Chatenet-Duchene L (1998a) Gender, temperament, and the clinical picture in dysphoric mixed mania: findings from a French national study (EPIMAN). J Affect Disord 50(2–3):175–186
- Akiskal HS, Placidi GF, Maremmani I, Signoretta S, Liguori A, Gervasi R, Mallya G, Puzantian VR (1998b) TEMPS-I: delineating the most discriminant traits of the cyclothymic, depressive, hyperthymic and irritable temperaments in a nonpatient population. J Affect Disord 51(1): 7–19. doi:S0165-0327(98)00152-9 [pii]
- Akiskal HS, Hantouche EG, Allilaire JF (2003) Bipolar II with and without cyclothymic temperament: "dark" and "sunny" expressions of soft bipolarity. J Affect Disord 73(1–2):49–57. doi:S0165032702003208 [pii]
- Akiskal H, Akiskal K, Haykal R, Manning J, Connor PD (2005a) TEMPS-A: progress towards validation of a self-rated clinical version of the temperament evaluation of the Memphis, Pisa, Paris, and San Diego autoquestionnaire. J Affect Disord 85(1–2):3–16
- Akiskal HS, Akiskal K, Allilaire JF, Azorin JM, Bourgeois ML, Sechter D, Fraud JP, Chatenet-Duchene L, Lancrenon S, Perugi G, Hantouche EG (2005b) Validating affective temperaments in their subaffective and socially positive attributes: psychometric, clinical and familial data from a French national study. J Affect Disord 85(1–2):29–36. doi:10.1016/j.jad.2003.12.009, S0165032704000242 [pii]
- Akiskal HS, Mendlowicz MV, Jean-Louis G, Rapaport MH, Kelsoe JR, Gillin JC, Smith TL (2005c) TEMPS-A: validation of a short version of a self-rated instrument designed to measure variations in temperament. J Affect Disord 85(1–2):45–52. doi:10.1016/j.jad.2003.10.012, S0165032703003215 [pii]
- Akiskal HS, Akiskal KK, Lancrenon S, Hantouche E (2006a) Validating the soft bipolar spectrum in the French National EPIDEP Study: the prominence of BP-II 1/2. J Affect Disord 96(3): 207–213. doi:10.1016/j.jad.2006.03.011, S0165-0327(06)00131-5 [pii]
- Akiskal HS, Akiskal KK, Lancrenon S, Hantouche EG, Fraud JP, Gury C, Allilaire JF (2006b) Validating the bipolar spectrum in the French National EPIDEP Study: overview of the phenomenology and relative prevalence of its clinical prototypes. J Affect Disord 96(3):197–205. doi:10.1016/j.jad.2006.05.015, S0165-0327(06)00248-5 [pii]
- Azorin JM, Kaladjian A, Adida M, Hantouche E, Hameg A, Lancrenon S, Akiskal HS (2009) Risk factors associated with lifetime suicide attempts in bipolar I patients: findings from a French National Cohort. Compr Psychiatry 50(2):115–120. doi:10.1016/j.comppsych.2008.07.004, S0010-440X(08)00105-3 [pii]
- Azorin JM, Kaladjian A, Besnier N, Adida M, Hantouche E, Lancrenon S, Akiskal H (2010) Suicidal behaviour in a French Cohort of major depressive patients: characteristics of attempters and nonattempters. J Affect Disord 123(1–3):87–94. doi:10.1016/j.jad.2009.09.004, S0165-0327(09)00422-4 [pii]
- Bertelsen A (1978) A Danish twin study of manic-depressive disorders. Prog Clin Biol Res 24A:119–124
- Bertelsen A, Harvald B, Hauge M (1977) A Danish twin study of manic-depressive disorders. Br J Psychiatry 130:330–351

- Biederman J, Rosenbaum JF, Hirshfeld DR, Faraone SV, Bolduc EA, Gersten M, Meminger SR, Kagan J, Snidman N, Reznick JS (1990) Psychiatric correlates of behavioral inhibition in young children of parents with and without psychiatric disorders. Arch Gen Psychiatry 47(1):21–26
- Biederman J, Hirshfeld-Becker DR, Rosenbaum JF, Herot C, Friedman D, Snidman N, Kagan J, Faraone SV (2001) Further evidence of association between behavioral inhibition and social anxiety in children. Am J Psychiatry 158(10):1673–1679
- Cassano GB, Akiskal HS, Musetti L, Perugi G, Soriani A, Mignani V (1989) Psychopathology, temperament, and past course in primary major depressions. 2. Toward a redefinition of bipolarity with a new semistructured interview for depression. Psychopathology 22(5):278–288
- Cassano GB, Akiskal HS, Perugi G, Musetti L, Savino M (1992a) The importance of measures of affective temperaments in genetic studies of mood disorders. J Psychiatr Res 26(4):257–268
- Cassano GB, Akiskal HS, Savino M, Musetti L, Perugi G (1992b) Proposed subtypes of bipolar II and related disorders: with hypomanic episodes (or cyclothymia) and with hyperthymic temperament. J Affect Disord 26(2):127–140
- Cattel R, Eber H, Tatsuoka M (1970) The handbook for the sixteen personality factor questionnaire. Institute for Personality and Ability Testing, Champain
- Chiaroni P, Hantouche EG, Gouvernet J, Azorin JM, Akiskal HS (2005) The cyclothymic temperament in healthy controls and familially at risk individuals for mood disorder: endophenotype for genetic studies? J Affect Disord 85(1–2):135–145. doi:10.1016/j.jad.2003.12.010, S0165032704000254 [pii]
- Cloninger CR (1987) A systematic method for clinical description and classification of personality variants. A proposal. Arch Gen Psychiatry 44(6):573–588
- Cloninger CR, Zohar AH (2011) Personality and the perception of health and happiness. J Affect Disord 128(1–2):24–32. doi:10.1016/j.jad.2010.06.012, S0165-0327(10)00425-8 [pii]
- Cloninger CR, Svrakic DM, Przybeck TR (1993) A psychobiological model of temperament and character. Arch Gen Psychiatry 50(12):975–990
- Cloninger CR, Przybeck TR, Svrakic DM, Wetzel RD (1994) The Temperament and Character Inventory (TCI): a guide to its development and use. Washington University Center for Psychobiology of Personality, St. Louis
- Cloninger C, Svrakic D, Bayon C, Przybeck T (1999) Measurement of psychopathology as variants of personality. In: Cloninger C (ed) Personality and psychopathology. American Psychiatric Press Inc., Washington, DC, pp 33–65
- Cloninger CR, Zohar AH, Cloninger KM (2010) Promotion of well-being in person-centered mental health care. Focus 8(2):165–179
- Cloninger CR, Abou-Saleh MT, Mrazek DA, Moller H-J (2011) Biological perspective on psychiatry for the person. Int J Person Cent Med 1 (1) (in press)
- Cohen P (1999) Personality development in childhood: old and new findings. In: Cloninger C (ed) Personality and psychopathology. American Psychiatric Press Inc, Washington, DC, pp 101–127
- Conley JJ (1985) Longitudinal stability of personality traits: a multitrait-multimethod-multioccasion analysis. J Pers Soc Psychol 49(5):1266–1282
- Constantino JN, Cloninger CR, Clarke AR, Hashemi B, Przybeck T (2002) Application of the seven-factor model of personality to early childhood. Psychiatry Res 109(3):229–243. doi:S0165178102000082 [pii]
- Costa P, McCrae R (1990) Personality disorders and the five-factor model of personality. J Personal Disord 4:362–371
- Dell'Osso L, Placidi GF, Nassi R, Freer P, Cassano GB, Akiskal HS (1991) The manic-depressive mixed state: familial, temperamental and psychopathologic characteristics in 108 female inpatients. Eur Arch Psychiatry Clin Neurosci 240(4–5):234–239
- Dell'Osso L, Akiskal HS, Freer P, Barberi M, Placidi GF, Cassano GB (1993) Psychotic and non-psychotic bipolar mixed states: comparisons with manic and schizoaffective disorders. Eur Arch Psychiatry Clin Neurosci 243(2):75–81
- Evans L, Akiskal HS, Keck PE Jr, McElroy SL, Sadovnick AD, Remick RA, Kelsoe JR (2005) Familiality of temperament in bipolar disorder: support for a genetic spectrum. J Affect Disord 85(1–2):153–168. doi:10.1016/j.jad.2003.10.015, S0165032703003252 [pii]

References 177

Eysenck HJ, Eysenck SB (1962) A factorial study of an interview-questionnaire. J Clin Psychol 18:286–290

- Eysenck SB, Eysenck HJ (1964) An improved short questionnaire for the measurement of extraversion and neuroticism. Life Sci 3:1103–1109
- Eysenck SB, Eysenck HJ (1967) Physiological reactivity to sensory stimulation as a measure of personality. Psychol Rep 20(1):45–46
- Eysenck SB, Eysenck HJ (1968) The measurement of psychoticism: a study of factor stability and reliability. Br J Soc Clin Psychol 7(4):286–294
- Eysenck SB, Eysenck HJ (1969) Scores on three personality variables as a function of age, sex and social class. Br J Soc Clin Psychol 8(1):69–76
- Eysenck SB, Eysenck HJ (1972) The questionnaire measurement of psychoticism. Psychol Med 2(1):50–55
- Eysenck SB, Eysenck HJ (1977) The place of impulsiveness in a dimensional system of personality description. Br J Soc Clin Psychol 16(1):57–68
- Eysenck SB, Eysenck HJ, Shaw L (1974) The modification of personality and lie scale scores by special 'honesty' instructions. Br J Soc Clin Psychol 13(1):41–50
- Eysenck SB, White O, Eysenck HJ (1976) Personality and mental illness. Psychol Rep 39(3):1011–1022
- Eysenck SB, Adelaja O, Eysenck HJ (1977) A comparative study of personality in Nigerian and English subjects. J Soc Psychol 102(Second Half):171–178
- Farmer A, Mahmood A, Redman K, Harris T, Sadler S, McGuffin P (2003) A sib-pair study of the temperament and character inventory scales in major depression. Arch Gen Psychiatry 60(5):490–496. doi:10.1001/archpsyc.60.5.490, 60/5/490 [pii]
- Friedman HS, Tucker JS, Tomlinson-Keasey C, Schwartz JE, Wingard DL, Criqui MH (1993) Does childhood personality predict longevity? J Pers Soc Psychol 65(1):176–185
- Hantouche EG, Akiskal HS (2006) Toward a definition of a cyclothymic behavioral endophenotype: which traits tap the familial diathesis for bipolar II disorder? J Affect Disord 96(3):233–237. doi:10.1016/j.jad.2004.08.013, S0165-0327(04)00279-4 [pii]
- Hantouche EG, Akiskal HS, Lancrenon S, Allilaire JF, Sechter D, Azorin JM, Bourgeois M, Fraud JP, Chatenet-Duchene L (1998) Systematic clinical methodology for validating bipolar-II disorder: data in mid-stream from a French national multi-site study (EPIDEP). J Affect Disord 50(2–3):163–173
- Hantouche EG, Allilaire JP, Bourgeois ML, Azorin JM, Sechter D, Chatenet-Duchene L, Lancrenon S, Akiskal HS (2001) The feasibility of self-assessment of dysphoric mania in the French national EPIMAN study. J Affect Disord 67(1–3):97–103. doi:S0165032701004426 [pii]
- Josefsson K, Jokela M, Cloninger CR, Hintsanen M, Salo J, Hintsa T, Pulkki-Raback L, Keltikangas-Jarvinen L (2012) Maturity and change in personality: developmental trends of temperament and character in adulthood. Development and Psychopathology (in press)
- Kagan J, Zentner M (1996) Early childhood predictors of adult psychopathology. Harv Rev Psychiatry 3(6):341–350
- Kagan J, Snidman N, Zentner M, Peterson E (1999) Infant temperament and anxious symptoms in school age children. Dev Psychopathol 11(2):209–224
- Kagan J, Snidman N, McManis M, Woodward S (2001) Temperamental contributions to the affect family of anxiety. Psychiatr Clin North Am 24(4):677–688
- Karam EG, Salamoun MM, Yeretzian JS, Mneimneh ZN, Karam AN, Fayyad J, Hantouche E, Akiskal K, Akiskal HS (2010) The role of anxious and hyperthymic temperaments in mental disorders: a national epidemiologic study. World Psychiatry 9(2):103–110
- Kendler KS (1997) Social support: a genetic-epidemiologic analysis. Am J Psychiatry 154(10):1398–1404
- Kendler KS, Karkowski-Shuman L (1997) Stressful life events and genetic liability to major depression: genetic control of exposure to the environment? Psychol Med 27(3):539–547
- Kendler KS, Neale MC, Kessler RC, Heath AC, Eaves LJ (1992) A population-based twin study of major depression in women. The impact of varying definitions of illness. Arch Gen Psychiatry 49(4):257–266

- Kesebir S, Vahip S, Akdeniz F, Yuncu Z, Alkan M, Akiskal H (2005) Affective temperaments as measured by TEMPS-A in patients with bipolar I disorder and their first-degree relatives: a controlled study. J Affect Disord 85(1-2):127-133. doi:10.1016/j.jad.2003.10.013, S0165032703003227 [pii]
- Kraepelin E (1921) Manic-Depressive Insanity and Paranoia. Edinburgh: Livingstone
- Maier W, Lichtermann D, Minges J, Heun R, Hallmayer J (1992) The risk of minor depression in families of probands with major depression: sex differences and familiality. Eur Arch Psychiatry Clin Neurosci 242(2–3):89–92
- Maremmani I, Akiskal H, Signoretta S, Liguori A, Perugi G, Cloninger C (2005) The relationship of Kraepelian affective temperaments (as measured by TEMPS-I) to the tridimensional personality questionnaire (TPQ). J Affect Disord 85:17–27
- Markon KE, Krueger RF, Watson D (2005) Delineating the structure of normal and abnormal personality: an integrative hierarchical approach. J Pers Soc Psychol 88(1):139–157. doi:10.1037/0022-3514.88.1.139, 2004-22407-010 [pii]
- McAdams DP, Pals JL (2006) A new Big Five: fundamental principles for an integrative science of personality. Am Psychol 61(3):204–217. doi:10.1037/0003-066X.61.3.204, 2006-03947-002 [pii]
- McCrae RR, Costa PT Jr (1987) Validation of the five-factor model of personality across instruments and observers. J Pers Soc Psychol 52(1):81–90
- Mendlowicz MV, Akiskal HS, Kelsoe JR, Rapaport MH, Jean-Louis G, Gillin JC (2005a) Temperament in the clinical differentiation of depressed bipolar and unipolar major depressive patients. J Affect Disord 84(2–3):219–223. doi:10.1016/j.jad.2004.01.013, S0165032704000849 [pii]
- Mendlowicz MV, Jean-Louis G, Kelsoe JR, Akiskal HS (2005b) A comparison of recovered bipolar patients, healthy relatives of bipolar probands, and normal controls using the short TEMPS-A. J Affect Disord 85(1–2):147–151. doi:10.1016/j.jad.2004.01.012, S0165032704000825 [pii]
- Merikangas KR, Akiskal HS, Angst J, Greenberg PE, Hirschfeld RM, Petukhova M, Kessler RC (2007) Lifetime and 12-month prevalence of bipolar spectrum disorder in the National Comorbidity Survey replication. Arch Gen Psychiatry 64(5):543–552. doi:10.1001/arch-psyc.64.5.543, 64/5/543 [pii]
- Merikangas KR, Jin R, He JP, Kessler RC, Lee S, Sampson NA, Viana MC, Andrade LH, Hu C, Karam EG, Ladea M, Medina-Mora ME, Ono Y, Posada-Villa J, Sagar R, Wells JE, Zarkov Z (2011) Prevalence and correlates of bipolar spectrum disorder in the world mental health survey initiative. Arch Gen Psychiatry 68(3):241–251. doi:10.1001/archgenpsychiatry.2011.12, 68/3/241 [pii]
- Ng B, Camacho A, Lara DR, Brunstein MG, Pinto OC, Akiskal HS (2008) A case series on the hypothesized connection between dementia and bipolar spectrum disorders: bipolar type VI? J Affect Disord 107(1–3):307–315
- Nolen-Hoeksema S (2011) Emotion regulation and psychopathology: the role of gender. Annu Rev Clin Psychol 8:161–187. doi:10.1146/annurev-clinpsy-032511-143109
- Nolen-Hoeksema S, Girgus JS (1994) The emergence of gender differences in depression during adolescence. Psychol Bull 115(3):424–443
- Nolen-Hoeksema S, Larson J, Grayson C (1999) Explaining the gender difference in depressive symptoms. J Pers Soc Psychol 77(5):1061–1072
- Oedegaard KJ, Syrstad VE, Morken G, Akiskal HS, Fasmer OB (2009) A study of age at onset and affective temperaments in a Norwegian sample of patients with mood disorders. J Affect Disord 118(1–3):229–233. doi:10.1016/j.jad.2009.01.030, S0165-0327(09)00047-0 [pii]
- Perugi G, Akiskal HS (2002) The soft bipolar spectrum redefined: focus on the cyclothymic, anxious-sensitive, impulse-dyscontrol, and binge-eating connection in bipolar II and related conditions. Psychiatr Clin North Am 25(4):713–737
- Perugi G, Musetti L, Simonini E, Piagentini F, Cassano GB, Akiskal HS (1990) Gender-mediated clinical features of depressive illness. The importance of temperamental differences. Br J Psychiatry 157:835–841
- Perugi G, Akiskal HS, Micheli C, Musetti L, Paiano A, Quilici C, Rossi L, Cassano GB (1997) Clinical subtypes of bipolar mixed states: validating a broader European definition in 143 cases. J Affect Disord 43(3):169–180. doi:S0165-0327(97)01446-8 [pii]

Perugi G, Akiskal HS, Lattanzi L, Cecconi D, Mastrocinque C, Patronelli A, Vignoli S, Bemi E (1998a) The high prevalence of "soft" bipolar (II) features in atypical depression. Compr Psychiatry 39(2):63–71. doi:S0010-440X(98)90080-3 [pii]

- Perugi G, Akiskal HS, Rossi L, Paiano A, Quilici C, Madaro D, Musetti L, Cassano GB (1998b) Chronic mania. Family history, prior course, clinical picture and social consequences. Br J Psychiatry 173:514–518
- Perugi G, Maremmani I, Toni C, Madaro D, Mata B, Akiskal HS (2001) The contrasting influence of depressive and hyperthymic temperaments on psychometrically derived manic subtypes. Psychiatry Res 101(3):249–258. doi:S0165-1781(01)00232-3 [pii]
- Perugi G, Toni C, Travierso MC, Akiskal HS (2003) The role of cyclothymia in atypical depression: toward a data-based reconceptualization of the borderline-bipolar II connection. J Affect Disord 73(1–2):87–98. doi:S0165032702003294 [pii]
- Perugi G, Toni C, Maremmani I, Tusini G, Ramacciotti S, Madia A, Fornaro M, Akiskal HS (2010)
 The influence of affective temperaments and psychopathological traits on the definition of bipolar disorder subtypes: a study on bipolar I Italian National sample. J Affect Disord. doi:10.1016/j.jad.2009.12.027, S0165-0327(10)00006-6 [pii]
- Pompili M, Rihmer Z, Akiskal HS, Innamorati M, Iliceto P, Akiskal KK, Lester D, Narciso V, Ferracuti S, Tatarelli R, De Pisa E, Girardi P (2008) Temperament and personality dimensions in suicidal and nonsuicidal psychiatric inpatients. Psychopathology 41(5):313–321. doi:10.1159/000146069, 000146069 [pii]
- Remick RA, Sadovnick AD, Lam RW, Zis AP, Yee IM (1996) Major depression, minor depression, and double depression: are they distinct clinical entities? Am J Med Genet 67(4):347–353. doi:10.1002/(SICI)1096-8628(19960726)67:4<347::AID-AJMG6>3.0.CO;2-J [pii]
- Rihmer A, Rozsa S, Rihmer Z, Gonda X, Akiskal KK, Akiskal HS (2009) Affective temperaments, as measured by TEMPS-A, among nonviolent suicide attempters. J Affect Disord 116 (1–2):18–22. doi:10.1016/j.jad.2008.10.024, S0165-0327(08)00438-2 [pii]
- Rosenbaum JF, Biederman J, Gersten M, Hirshfeld DR, Meminger SR, Herman JB, Kagan J, Reznick JS, Snidman N (1988) Behavioral inhibition in children of parents with panic disorder and agoraphobia. A controlled study. Arch Gen Psychiatry 45(5):463–470
- Rosenbaum JF, Biederman J, Hirshfeld DR, Bolduc EA, Faraone SV, Kagan J, Snidman N, Reznick JS (1991) Further evidence of an association between behavioral inhibition and anxiety disorders: results from a family study of children from a non-clinical sample. J Psychiatr Res 25(1–2):49–65
- Rothbart MK, Ahadi SA, Evans DE (2000) Temperament and personality: origins and outcomes. J Pers Soc Psychol 78(1):122-135
- Serafini G, Pompili M, Innamorati M, Fusar-Poli P, Akiskal HS, Rihmer Z, Lester D, Romano A, de Oliveira IR, Strusi L, Ferracuti S, Girardi P, Tatarelli R (2010) Affective temperamental profiles are associated with white matter hyperintensity and suicidal risk in patients with mood disorders. J Affect Disord. doi:10.1016/j.jad.2010.07.020, S0165-0327(10)00501-X [pii]
- Smoller JW, Yamaki LH, Fagerness JA, Biederman J, Racette S, Laird NM, Kagan J, Snidman N, Faraone SV, Hirshfeld-Becker D, Tsuang MT, Slaugenhaupt SA, Rosenbaum JF, Sklar PB (2005) The corticotropin-releasing hormone gene and behavioral inhibition in children at risk for panic disorder. Biol Psychiatry 57(12):1485–1492. doi:10.1016/j.biopsych.2005.02.018, S0006-3223(05)00183-6 [pii]
- Tellegen A, Grove W, Waller N (1991) Inventory of personality characteristics #7 (IPC7). University of Minnesota Department of Psychology, Minneapolis
- Vazquez GH, Kahn C, Schiavo CE, Goldchluk A, Herbst L, Piccione M, Saidman N, Ruggeri H, Silva A, Leal J, Bonetto GG, Zaratiegui R, Padilla E, Vilaprino JJ, Calvo M, Guerrero G, Strejilevich SA, Cetkovich-Bakmas MG, Akiskal KK, Akiskal HS (2008) Bipolar disorders and affective temperaments: a national family study testing the "endophenotype" and "subaffective" theses using the TEMPS-A Buenos Aires. J Affect Disord 108(1–2):25–32. doi:10.1016/j.jad.2007.09.011, S0165-0327(07)00340-0 [pii]
- von Zerssen D, Akiskal HS (1998) Personality factors in affective disorders: historical developments and current issues with special reference to the concepts of temperament and character. J Affect Disord 51(1):1–5. doi:S0165032798001517 [pii]