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Review article

Temperament correlates in adult ADHD: A systematic review★★

Vito Pinzone[a,1], Pietro De Rossi[a,b,c,1], Guido Trabucchi[a], David Lester[d], Paolo Girardi[a], Maurizio Pompili[a,*]

[a] Department of Neurosciences, Mental Health and Sensory Organs, Suicide Prevention Center, Sant'Andrea Hospital, Sapienza University of Rome, Rome, Italy
[b] Department of Neurology and Psychiatry, Sapienza University of Rome, Rome, Italy
[c] ASL RM5, Monterotondo, Rome, Italy
[d] Stockton University, Galloway Township, NJ, United States

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ABSTRACT

Background: Attention deficit and hyperactivity disorder (ADHD) is the most common neurodevelopmental disorder in children, but adult-ADHD is still an under-diagnosed and untreated condition. Treating adult-ADHD is complex and requires effective strategies for ADHD symptoms and comorbidities. Because of its high comorbidity rate with mood disorders and the growing interest in symptoms of emotional dysregulation in these patients, our aim was to collect studies that investigated temperament correlates in adult people with ADHD, to better understand the association between them and the eventual role of temperament as a prognostic-therapeutic marker.

Methods: We performed a systematic review of the literature. We included only studies that measured temperament traits in ADHD adults using the Temperament Evaluation of Memphis, Paris and San Diego-Autoquestionnaire (TEMPS-A) or the Temperament and Character Inventory (TCI).

Results: We retrieved 15 papers that used the TCI and 6 papers that used the TEMPS-A. In the TCI studies, ADHD was associated with high scores on Novelty Seeking and Harm Avoidance and low scores on Persistence. For the TEMPS-A studies, ADHD and Bipolar Disorders share some similarities in temperament scores, except for the hyperthymic temperament score.

Limitations: A comparison between the TCI and TEMPS-A results was not possible. The number of papers included was small. Among them, the type of sample, the number of recruited subjects and the ADHD assessment were very different.

Conclusions: The majority of ADHD individuals share temperament traits such as lability, irritability and excessiveness of emotional responses. Further research is needed to better understand whether temperament influences the pharmacological response of ADHD patients and whether temperament scores affect the long-term therapeutic outcome.

1. Introduction

1.1. ADHD

Attention-deficit hyperactivity disorder (ADHD) is a chronic, multifactorial and heterogeneous disorder characterized by symptoms of inattention, hyperactivity and impulsivity (APA 2013; Faraone et al., 2015). ADHD is the most common neurodevelopmental disorder in childhood, affecting approximately 5–8% of children (Faraone et al., 2003; Polanczyk et al., 2014). Persistence of symptoms into adulthood occurs in two-thirds of early-diagnosed patients (Turgay et al., 2012), with an estimated worldwide prevalence of 3–5% for affected adults

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* Corresponding author at: Sant'Andrea Hospital, Sapienza University of Rome, 1035-1039, Via di Grottarossa, 00189, Rome, Italy.
E-mail address: maurizio.pompili@uniroma1.it (M. Pompili).
[1] Vito Pinzone and Pietro De Rossi contributed equally to this paper.

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(Fayyad et al., 2007; Retz et al., 2011; Newcorn et al., 2007; Simon et al., 2009). During childhood, there is a higher ADHD prevalence in males than in females, but the gender distribution of ADHD in adults is still unclear (Rucklidge et al. 2010; Biederman et al., 2004). ADHD is an underdiagnosed and undertreated condition in adulthood (Katzman et al., 2016). Less than 20% of adults with ADHD are diagnosed and treated properly (Fayyad et al., 2007; Retz et al., 2011). Pharmacological and non-pharmacological treatment of adult ADHD is usually complex, and this warrants the search for clinical markers bearing prognostic-therapeutic potential relevant to treatment strategies which are effective for ADHD symptoms and comorbidities. In this scenario, temperament could be an easily obtainable index that would serve this purpose.

1.2. Comorbidities

Psychiatric comorbidities are frequent in adult ADHD patients and include anxiety, mood disorders, bipolar disorders (Meinzer et al., 2014; Torres et al. 2015), oppositional-defiant disorder, conduct disorders, substance use disorders, learning disabilities, sleep disorders, eating disorders and personality disorders (Connor et al., 2010; Hazell et al. 2010). Between 17%–22% of adults attending psychiatric outpatient clinics for conditions other than ADHD suffer from this disorder (Almeida Montes et al. 2007). Personality disorders are frequently associated with ADHD. Comorbidity with Cluster B disorders is well-known (primarily Borderline Personality Disorder) but Cluster C disorders, when measured, are frequently identified (May and Bos 2000; Burket et al., 2005; Miller et al. 2007; Williams et al., 2010.) Furthermore, up to 80% of patients affected by autism spectrum disorders have a coexistent ADHD (Van der Meer et al. 2012; Murray 2010). In addition, some medical comorbidities are associated with ADHD, including obesity, asthma and migraine (Cortese et al., 2013; Fasmer et al., 2011a, 2011b).

1.3. Clinical presentation

ADHD is characterized by a persistent and pervasive pattern of inattention and/or hyperactivity-impulsivity beginning during childhood, often prior to 12 years of age (APA 2013). Diagnosis is possible when 6 or more inattentive or hyperactivity-impulsivity symptoms are present for a minimal duration of 6 months, and in at least 2 settings (e.g., home, school or other activities), causing significant impairment or negatively impacting on social and occupational activities.

According to DSM-5 there are 3 main categories of ADHD:

- Combined presentation: if both inattention criteria and hyperactivity-impulsivity are present;
- Predominantly inattentive presentation: inattention criteria were met but hyperactivity-impulsivity criteria were not met over the past 6 months;
- Predominantly hyperactive/impulsive presentation: hyperactivity-impulsivity criteria are met but inattention criteria were not met over the past 6 months. (APA 2013)

It is noteworthy that, in DSM 5, the concept of “type” was replaced by the concept of “presentation”. This is consistent with the fact that this disorder can present with different features over the course of time rather that displaying “fixed” clinical features.

1.4. The impact of ADHD during life

Starting in early childhood, ADHD can lead to scholastic and occupational dysfunctional patterns (Kieling et al., 2010; Kessler et al., 2005). This impairment tends to persist into adulthood. An association between ADHD and scholastic underachievement has been reported (De Zeeuw et al. 2017). Individuals affected by ADHD have impaired and conflictive relationships in their family, at work and in other social settings. As a result of inattention and hyperactivity-impulsivity symptoms, these individuals have difficulties in holding a job and maintaining a stable relationship with their partner, and these problems can lead to a higher intensity of depressive symptoms (Halmoy et al., 2009; Biederman and Faraone 2006). Early diagnosis and treatment can positively influence such outcomes (Halmoy et al., 2009). When there is comorbidity with a substance abuse disorder, ADHD patients are more likely to have developed an early substance dependence, and their remission rates are lower (Arias et al., 2008; Schubiner 2005). The association between ADHD and antisocial personality disorder is a demonstrated risk factor for criminal behavior and subsequent confinement in jails (Ginsberg et al., 2010; Von Polier et al. 2012). Early treatment is a protective factor for criminal behavior (Lichtenstein et al., 2012).

1.5. Emotional dysregulation

Impairment and clinical outcome of ADHD patients are related also with emotional dysregulation, a common feature in all of the neurodevelopmental disorders. In a recent review, Shaw et al. (2014) defined emotional dysregulation (ED) as *“emotional expressions and experiences that are excessive in relation to social norms and context-inappropriate; rapid, poorly controlled shifts in emotion (‘lability’); and the anomalous allocation of attention and to emotional stimuli,”* and they estimated that the prevalence in adult ADHD patients is between 34 and 70% (Able et al., 2007; Surman et al., 2013).

Authors reviewed the possible mechanisms underlying emotional dysregulation in ADHD, including deficits in orienting towards, recognizing and/or allocating attention to emotional stimuli.

They also suggested three models to explain the association with ADHD: (1) ED can be considered as a dimensional entity that co-occurs with ADHD, (2) ED is a core-symptom of ADHD, (3) ADHD with ED may constitute a different nosological entity. According to these findings, emotional dysregulation seems to play a fundamental role in the pathophysiology and treatment of ADHD, but an understanding of the underlying mechanisms still requires further research. Given the lability, irritability and excessiveness of emotional responses, analogies between emotional dysregulation and temperamental traits are likely, as discussed below.

1.6. Treatments

Treatments for ADHD include medications and behavioral therapies. The first-line pharmacotherapy are stimulant medications such as methylphenidate and other amphetamine formulations.

Atomoxetine, a selective noradrenergic reuptake inhibitor, is a non-stimulant medication and represents second-line treatment when stimulants are contraindicated. Compared with immediate-release stimulants, recent studies showed that atomoxetine has the same efficacy on ADHD symptoms in both adults and children (Bushe and Sayill 2014; Bushe et al., 2016). Evidence indicates good efficacy for this medication in ADHD patients with comorbid anxiety disorder and opposition-defiant disorder (Clemow et al., 2017).

Behavioral therapies mostly consist of cognitive-behavioral therapy (CBT) (Seixas et al., 2012) Although the efficacy of CBT as a sole treatment for adult ADHD is not supported by evidence, a multimodal approach consisting of pharmacotherapy and adjunctive CBT lead to better outcomes (Hirvikoski et al., 2011; Philipsen et al., 2015).

Diagnosing and treating ADHD in adulthood, especially when it was not diagnosed at an earlier age, is challenging because of the complexity of the clinical picture and difficulty in managing comorbidities. In this context, the development and use of simple clinical tools that are potentially useful as reliable indices of diagnostic and prognostic/therapeutic relevance is critical.

1.7. Temperaments

The concept of temperament was first described in the ancient era. Hippocrates and Galen supposed that alteration of "humors" in the body could lead to the development of diseases (Rothbart and Derryberry 1981). Kraepelin, inspired by Galen's theory, described four temperaments (manic, depressive, cyclothymic and irritable) and considered them to be subclinical manifestations of manic-depressive disorder (Kraepelin 1921). A modern definition of temperament was provided by Cloninger who described temperament as *"individual differences in associative learning in response to novelty, danger or punishment, and reward"*. He noted that temperaments are stable over time, and he suggested the possibility of a genetic predisposition (Cloninger et al., 1993).

There is no universal consensus about differentiating between temperament and character, but temperament appears to be a basic behavioral predisposition with a partial genetic determination, based on the interactions that exist between genes, individuality and environmental stimuli (Goldsmith et al., 1987; Sanson et al., 2004; Saudino 2005). Kagan noted the differences between personality and temperament, writing: *"The environment acts on that temperament to produce personality"* (Kagan 1997).

Research into the role of temperament in neurodevelopmental disorders such as ADHD has grown in recent years. The most commonly used instruments to evaluate temperament are two self-report questionnaires, based on two different theoretical models: the Temperament Evaluation of Memphis, Paris and San Diego-Auto-questionnaire (TEMPS-A) and the Temperament and Character Inventory (TCI).

The TEMPS-A was created by Akiskal and his colleagues and is based on an interview protocol for the depressive, cyclothymic, irritable, hyperthymic and anxious temperaments. It is a self-report, questionnaire designed to quantify temperament in both psychiatric patients and healthy individuals. The long version of TEMPS-A consists of 110 items (Akiskal et al., 2005).

Screening for affective temperaments is important for the majority of psychiatric disorders (Akiskal et al., 1998). For affective disorders, temperaments can be predictors of health and functional impairment (Pompili et al., 2013) as well as comorbidities and disorder severity (Qiu et al., 2017). Because of the high comorbidity rates of ADHD with Bipolar Disorder (Milberger et al., 1995; Kessler et al., 2006), researchers investigated the clinical and biological overlaps between the disorders (Kent and Craddock, 2003) and proposed that the evaluation of temperament in ADHD patients could lead to better treatment results (Torrente et al., 2017). For these reasons, the assessment of affective temperaments seem to have an important role also in ADHD. The TCI is another important instrument for measuring temperaments based on Cloninger's psychobiological theory of temperaments (Cloninger et al., 1994). The TCI consists of 240-items answered yes or no, with 5 validation items for the assessment of response accuracy and carelessness. The TCI explores seven dimensions: four of them are named "temperaments" and the other three "characters". Cloninger described four temperaments - novelty seeking (NS), harm avoidance (HA), reward dependence (RD) and persistence (PS) – and three characters - self-directedness (SD), cooperativeness (CO) and self-transcendence (ST).

According to Cloninger, people with high scores of Novelty Seeking tend to be curious, disordered, impulsive and easily bored. These features often occurs in ADHD and, for example, these individuals can find it difficult to maintain a job or a relationship. As we mentioned, impulsivity can be a prominent symptom of ADHD and it is not surprising that high scores for Novelty Seeking seem to be predictive of a lifetime diagnoses of ADHD (Lynn et al., 2005). High scores for Harm Avoidance can represent the tendency of people being easily worried, fearful, shy and tired. Another important domain of Cloninger's classification is Self-Directedness that reflects responsibility, goal-orientation, self-confidence and resourcefulness.

The main features of temperaments for both the described classifications are shown in Table 1a and b. The aim of the present review was to collect studies that investigated temperamental correlates in adult people with ADHD, to better understand the relationship between them. In particular, we focused on temperament as tools commonly used in clinical practice to assess this construct that are simpler and less time-consuming than a more detailed personality evaluation. As previously stated, the most frequent comorbidities of adult ADHD are mood disorders, and ADHD pharmacological treatments could be either poorly effective or detrimental if mood is not adequately treated (Scheffer et al. 2005). For these reasons, the purpose of our review is to provide state-of-the-art evidence on temperament and ADHD in adults, supporting temperament evaluation as a potential therapeutic-prognostic index in order to personalize treatment at the very beginning of the diagnostic process.

Table 1
(a) Akiskal's Classification of Temperaments. (b) Cloninger's Classification of Temperaments.

A TEMPERAMENTS (Akiskal's Classification)	Main features
Hyperthymic	Exuberance Tirelessness Risks seeking High energy Sensation seeking
Depressive (Dysthymic)	Introversion Pessimism Excessive worrying Easy fatigability and low energy Discouragement and guilt
Cyclothymic	Alternation of the features of Hyperthymic and Dysthymic Temperaments showing unstable productivity and functioning
Irritable	A combination of Hyperthymic and Dysthymic Temperaments with impulsiveness, restlessness and dissatisfaction
Anxious	Harm avoidance Dependence Shyness Anxiety Hyper-arousal

B TEMPERAMENTS (Cloninger's Classification)	Main features
Novelty Seeking	Impulsive decision making Exploratory activities and sensation seeking Extravagance Avoidance of frustration Disorderliness
Harm Avoidant	Shyness Pessimism Excessive worrying Easy fatigability
Reward Dependent	Social Approval Seeking Sentimentality Dependence
Persistent	Persistence despite fatigue or frustration Ambitious Work-hard

2. Method

A systematic review of articles published in English was performed. The databases Pubmed and PsychInfo were searched using the following key words: ("attention deficit hyperactivity disorder" OR "adhd") AND ("temperament" OR "temperament evaluation"). The studies were reviewed by two independent reviewers using the PRISMA statement (Moher et al., 2009), as shown in Fig. 1. The bibliographies of the retrieved papers were searched by hand for additional publications.

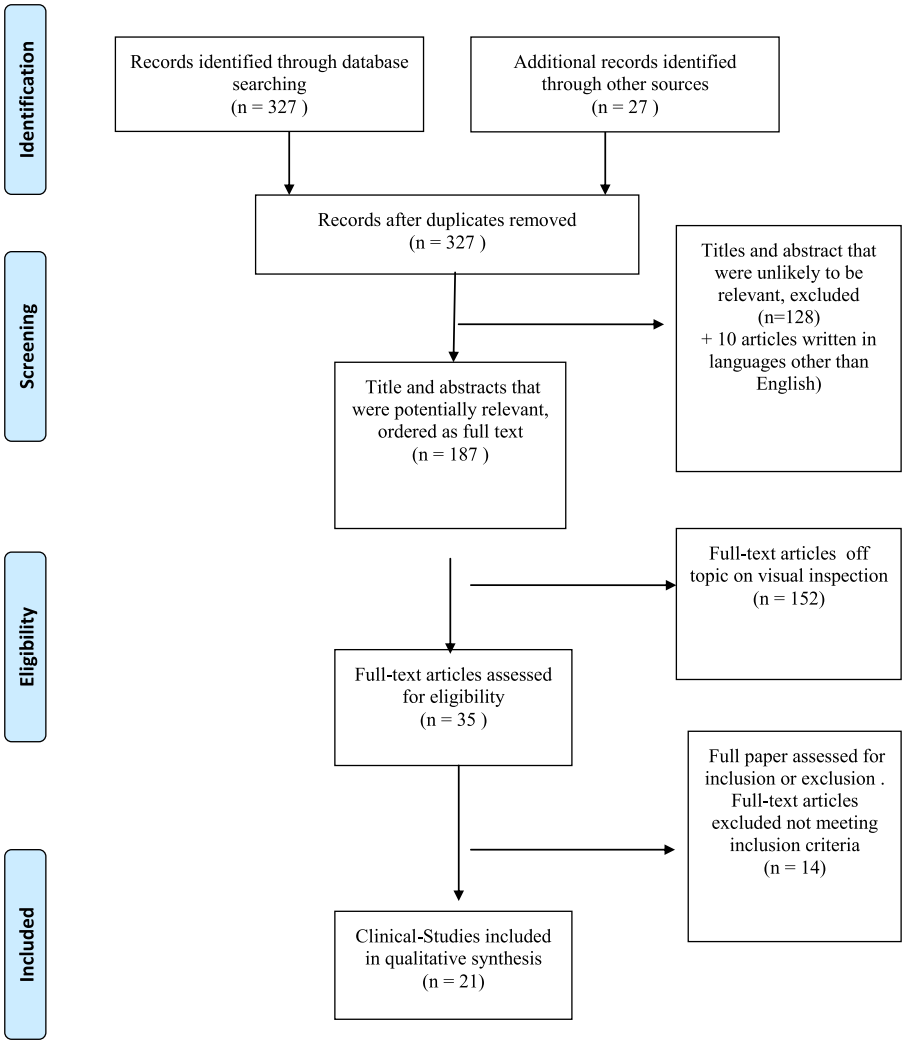

Fig. 1. Stages of the screening process: Temperamental Correlates in Adult ADHD: A systematic review.

Studies were included only if they measured the temperament in adult ADHD patients using the most common and validated inventories - the Temperament and Character Inventory (TCI) and the Temperament Evaluation of Memphis, Paris and San Diego-Auto-questionnaire (TEMPS-A). We retrieved a total of 327 studies and applied the following exclusion criteria: (1) papers written in languages other than English, (2) studies based on temperament evaluation in children and adolescents, and (3) off-topic papers. A total of 21 papers were included in this review.

3. Results

The results are shown in Tables 2 and 3. The retrieved papers examined adult patients with a diagnosis of ADHD or people testing positive for ADHD symptoms. The assessment of ADHD symptoms in undiagnosed adults was based on different scales such as the DSM-IV-TR ADHD interview (DIVA, Kooij 2012) and the Adult-ADHD Self-Report Scale (ASRS). We found no studies that used both the TEMPS-A and TCI for the evaluation of temperament. Thus, the results of studies based on the TCI and studies based on the TEMPS-A are presented and discussed separately.

3.1. TCI scores in ADHD adults

We found 15 studies that used the TCI for the assessment of temperament in ADHD patients.

In a sample of 429 Korean college students, Kim et al. (2017) evaluated the presence of ADHD symptoms using the Korean Scale for ADHD Symptoms, and they administered the TCI, the Beck Depression Inventory (BDI) and the Beck Anxiety Inventory (BAI). They confirmed higher NS and HA scores and lower PS scores in students with ADHD symptoms compared with the students without ADHD symptoms. Depressive and anxious symptoms evaluated using the BDI and the BAI were also higher in the group with ADHD symptoms. These results are consistent with results from a study by Park et al. (2016) on 2917 college students tested with the ASRS and the TCI. Higher NS scores were associated with ADHD symptoms, as were lower SD and CO scores.

Perroud et al. (2016) found a significant correlation between ADHD and high NS, HA and ST scores in a group of ADHD outpatients compared with controls, and also after controlling for psychiatric comorbidities. They recruited 119 adult ADHD patients and divided them into three groups to highlight the correlation between the ADHD subtype and the corresponding temperament. Diagnoses were made using the DIVA, and the subtypes were (i) Predominantly Inattentive ADHD, (ii) Predominantly Hyperactive-Impulsive ADHD and (iii) Combined ADHD. Inattention symptoms positively correlated with HA scores and negatively with SD scores, whereas hyperactive symptoms positively correlated with NS and ST scores. The severity of symptoms was assessed with the ASRS and showed a positive association with high NS scores and low SD scores.

The association between the severity of ADHD symptoms and

Table 2
TCI IN ADHD ADULTS: Note that the following TCI results refers to research on ADHD patients or people positive for ADHD symptoms. ↑ and ↓ indicate higher or lower TCI scores in people with ADHD symptoms or syndromes compared with non-ADHD people/healthy controls.

Authors/Year	Participants	TCI RESULTS
Kim et al., 2017	429 college students tested for ADHD, depressive and anxious symptoms	*Temperament Dimension:* ↑ Novelty seeking ↑ Harm avoidance *Character dimension:* ↑ Self-transcendence ↓ Self-directedness ↓ Cooperativeness.
Park et al., 2016	2917 college students tested for ADHD symptoms	*Temperament Dimension:* ↑ Novelty Seeking (hyperactive and inattentive groups) ↑ Harm Avoidance ↓ Persistence *Character dimension:* ↑ Self-Transcendence (hyperactive group) ↓ Self-Directedness (inattentive group) ↓ Cooperativeness (hyperactive group)
Perroud et al., 2016	522 subjects • 119 ADHD • 403 HC	*Temperament Dimension:* ↑ Novelty Seeking (hyperactive and inattentive groups) ↑ Harm Avoidance ↓ Persistence *Character dimension:* ↑ Self-Transcendence (hyperactive group) ↓ Self-Directedness (inattentive group) ↓ Cooperativeness (hyperactive group)
He et al., 2015	329 subjects • 206 ADHD • HC controls	*Predictors of Functional Impairment* *Temperament Dimension:* ↑ Novelty Seeking ↑ Harm Avoidance ↓ Persistence *Character dimension:* ↑ Self-Transcendence ↓ Self-Directedness ↓ Cooperativeness
Sizoo et al., 2015	128 subjects • 75 ASD • 53 ADHD	Similar Harm Avoidance and Self-directedness scores in ADHD and ASD.
Instanes et al., 2016	131 subjects • 63 ADHD • 68 controls	↑ Novelty Seeking: some relation with a lifetime diagnosis of ASPD ↑ Harm Avoidance (except when comorbid with depression or anxiety
Merwood et al., 2013	886 adult twin pairs	• Novelty Seeking genetically associated with both inattentive and hyperactive symptoms • HA genetically associated with inattentive ADHD only • Unique profiles of temperament are genetically related to the two ADHD symptoms dimension in adults.
Van Dijk et al. *2012*	103 females	↑ Novelty Seeking associated with full symptomatic ADHD + BPD traits
Sousa et al., 2011	422 ADHD	↑ Novelty Seeking ↓ Harm Avoidance in patients with smoking habits
Muller et al., 2010	110 ADHD	ADHD Severity significantly related to ↑ harm avoidance and ↑ Self directedness
Sizoo et al., 2009	128 ADHD/ASD	ADHD: ↑ novelty seeking ASD: ↓ reward dependence, ↑ harm avoidance
Salgado et al., 2009	296 ADHD	ADHD combined presentation ↑ Novelty Seeking ↓ cooperativeness Inattentive Symptoms associated with ↓ Self-Directedness ↑ Harm Avoidance Hyperactivity-Impulsivity symptoms associated with ↑ Novelty Seeking ↑ persistence
Faraone et al., 2009	370 - 247 ADHD: • 41 Subthreshold ADHD • 79 Late-onset ADHD (onset between 7–45 yrs., *n* = 79) • 127 Full-ADHD (onset in the prior 7yrs) - 123 HC	Full ADHD and late-onset ADHD show similar personality profiles with significant deviations on all TCI scales except reward dependence and self-transcendence. Subthreshold cases show deviations on Novelty seeking and Self-directiveness.

(*continued on next page*)

Table 2 (*continued*)

Authors/Year	Participants	TCI RESULTS
Anckarsater et al., 2006	273 patients • 147 ADHD69 Combined Type • 44 Inattentive Type • 16 Hyperactive Type • 18 In Remission 126 patients with other diagnoses	↑ NS and HA in the ADHD group, compared to patients with other diagnoses.
Lynn et al., 2005	171 parents of children with ADHD (tot. 56 families) • History of ADHD: 56 • No History of ADHD: 115	Parents with History of ADHD have ↑ NS and ST scores compared to parents without history of ADHD.

ADHD: ATTENTION DEFICIT AND HYPERACTIVITY DISORDER; **HC:** HEALTHY CONTROLS; **ASD:** AUTISM SPECTRUM DISORDERS; **ASPD:** ANTISOCIAL PERSONALITY DISORDER; **BPD:** BORDERLINE PERSONALITY DISORDER.

temperament was also investigated by Muller et al. (2010) in a sample of 110 ADHD patients. ADHD diagnoses were assessed using the Wender Utah Rating Scale (WURS) and Conners' Adult ADHD Rating Scale (CAARS). The assessment of the severity of symptoms was made using the Brown Attention Deficit Disorder Scale (BADDS). The authors also studied genetic variations of the sample by extracting genomic DNA from white blood cells. A total of 9 polymorphisms (SLC6A3, DBH, DRD4, DRD5, HTR2A, CHRNA7, BDNF, PRKG1 and TAAR9) were investigated, but the authors did not find a relation between genetic variations and the severity of symptoms. The severity of symptoms was associated significantly with the temperament trait of HA and the character trait of SD. In particular, ADHD symptom severity was positively associated with the HA scores and negatively associated with SD scores.

He et al. (2015) reported that functional impairment in ADHD patients was associated with low SD scores, even after controlling for ADHD symptoms. Low SD scores also predicted executive function deficits and psychiatric comorbidities.

Sizoo et al. (2009, 2015) compared patients with ADHD and Autism Spectrum Disorders (ASD) to see if temperament characteristics were shared. Using the abbreviated version of the TCI, they found differences between the two groups of patients. ADHD patients had high NS scores, while ASD patients had low RD scores. The authors suggested that temperament could be related to eventual substance use.

In a case-control study, Instanes et al. (2016) evaluated a total of 131 individuals (63 with a previous diagnosis of ADHD and 68 population controls) using the Mini International Neuropsychiatric Interview Plus to check for comorbidities. On the TCI, the ADHD patients had higher NS scores, but similar HA scores when adjusted for the presence of comorbid anxiety or depression disorder.

Merwood et al. (2013) studied 886 adult twin pairs selected from the Swedish Twin study of Child and Adolescent Development (TCHAD), a longitudinal study of all twin pairs born in Sweden between May 1985 and December 1986. The sample included 140 monozygotic males, 214 monozygotic females, 83 dizygotic males, 145 dizygotic females and 286 dizygotic opposite-sex pairs. The mean age of the twins was 19.66. ADHD symptom dimensions (inattention and hyperactivity-impulsivity) were assessed using a Likert-type scale of 18 DSM-IV based items for ADHD. The results showed a modest phenotypic correlation of NS scores with Inattentive Symptoms and Hyperactivity-Impulsivity

Table 3
TEMPS in ADHD ADULTS
↑ and ↓ indicate higher or lower TEMPS-A scores in people with ADHD symptoms or syndromes compared with standard cut-offs.

Authors/Year	Participants	TEMPS Results in ADHD
Ozdemiroglu et al., 2018	• 81 ADHD	• ↑ cyclothymic, irritable and anxious in adult ADHD than childhood ADHD • Scores of cyclothymic and irritable temperaments significantly associated with symptoms' severity in adult ADHD
Torrente et al., 2017	• 60 ADHD • 50 BD • 30 HC	• ↑ depressive, cyclothymic, irritable and anxious in ADHD patients and BD patients compared with controls • No temperament differences between ADHD and BD group. • ADHD and BD showed similarity in the levels of depressive symptoms compared to controls. • more neurovegetative symptoms in BD than ADHD • ADHD with TEMPS + showed ↑ depression and ↑ impulsivity than ADHD with TEMPS-. • ADHD TEMPS + and Bipolar Disorder Groups have similar results.
Harmanci et al., 2016	300 subjects • 100 BD patients • 100 MDD patients • 100 HC Tested for ADHD symptoms	• ↑ depressive, cyclothymic, irritable, and anxious all the three groups positive for ADHD symptoms. • No significant association with hyperthymic temperament.
Skala et al., 2016	3280 men	Cyclothymic, Irritable and Anxious temperaments are related with occurrence and severity of ADHD Symptoms.
Ekinci et al., 2013	120 subjects • 40 ADHD • 40 BD • 40 HC	• No dominant temperament in HC • ADHD: ↑ scores on all domains (depressive, cyclothymic, irritable and anxious) except hyperthymic. • ↑ Irritable temperament in ADHD than BD • Similar results for ADHD and BD on all domains (except Irritable)
Landaas et al., 2012	• 586 ADHD • 721 HC	*TEMPS-A Scores:* • 13.0 in ADHD, 4.6 in controls • 71% of ADHD patients have cyclothymic temperament • 13% of controls have cyclothymic temperament *ADHD Patients + Cyclothymic Temperament Associations:* • ↑ childhood and adult ADHD symptoms • Underachievement • ↑ psychiatric comorbidity (Bipolar Disorder 10%) 49% screened positive on the Mood Disorder Questionnaire.

ADHD: ATTENTION DEFICIT AND HYPERACTIVITY DISORDER; **BD:** BIPOLAR DISORDER; **MDD:** MAJOR DEPRESSIVE DISORDER; **HC:** HEALTHY CONTROLS.

symptoms. In contrast, HA scores were significantly correlated only with Inattentive symptoms. These associations were greater in monozygotic than in dizygotic twin pairs for most variables, suggesting a probable genetic influence.

Van Dijk et al. (2012) investigated the association between ADHD, temperament and borderline personality disorder (BPD) in a group of 103 female patients recruited from ADHD and BPD outpatient clinics. NS scores were associated with ADHD and BPD symptoms. The highest NS temperament scores were found in that class of patients with both symptoms of BPD and symptoms of all of the areas of ADHD. BPD symptoms were specifically associated with high HA scores, low CO scores and low SD scores.

Sousa et al. (2011) reported that smoking behavior was associated with high NS scores and low HA scores in a sample of 422 adult ADHD patients. They suggested that smoking habit in adults with ADHD is related to the inability to inhibit pleasurable albeit dangerous or maladaptive impulses. Their TCI result of high NS scores in smokers is consistent with a previous study conducted in a population of adolescents (Audrain-McGovern et al., 2006).

In a sample of 296 adult ADHD patients, Salgado et al. (2009) evaluated ADHD dimensions and their correlation with temperament/personality dimensions. For the evaluation of ADHD symptoms, they used SNAP-IV scores. They found that patients with the ADHD-combined type (inattention and hyperactivity-impulsivity) had higher NS scores and lower CO scores than patients with the inattentive-type ADHD. Higher Inattention scores were significantly associated with lower SD scores and higher HA scores. Hyperactivity-impulsivity symptoms were associated with higher NS scores and higher PS scores.

Faraone et al. (2009) recruited 123 non-ADHD controls and 247 ADHD patients. The latter were recruited from referrals to the psychiatric clinics at the Massachusetts General Hospital and the Boston area population. The SCID-IV was given to all of the subjects. They divided the ADHD patients into three different subgroups: (i) Subthreshold ADHD (n = 41), (ii) Late-onset ADHD (onset between 7–45 yrs., n = 79), and (iii) Full-ADHD (onset in the prior 7 yrs. n = 127). Subthreshold-ADHD was defined as never having met DSM-IV criteria for ADHD but reporting a chronic history of three or more inattentive symptoms or three or more hyperactive-impulsive symptoms. Definition of symptom cut-off scores was based on the researchers' previous work (Biederman et al., 2004). Full ADHD and late-onset ADHD did not significantly differ from each other in any TCI domains. Full ADHD and late-onset ADHD subjects had significantly higher scores for NS and HA and significantly lower PS, SD and CO scores compared to non-ADHD subjects. No significant differences between these groups were found for RD and ST scores. Subthreshold ADHD subjects showed higher scores for NS compared to the non-ADHD subjects, but significantly lower scores when compared to the late-onset and full ADHD patients. SD scores were significantly lower in the full and late-onset ADHD patients compared to Subthreshold ADHD subjects.

Anckarsater et al. (2006) focused the differences of temperamental traits in a sample of 273 individuals referred to their neuropsychiatric outpatient clinics. The diagnoses were made using SCID, DSM IV criteria checklist for ADHD and other disorders not included in the SCID, Yale-Brown Obsessive Compulsive Scale and Asperger Syndrome and High-Functioning Autism Screening Questionnaire. They found that 147 of these patients met the criteria for ADHD (Combined Type: 69; Inattentive Type: 44; Hyperactive Type: 16; In remission: 18). Temperament traits were investigated using TCI and the researchers reported high scores of Novelty Seeking and Harm Avoidance in the ADHD group, compared to the others. On the other hand, people with an autism spectrum disorder had lower Novelty Seeking and Reward Dependance scores, suggesting some specific temperamental differences between ADHD and ASD.

Lynn et al. (2005) conducted a molecular genetic study in a sample of 171 parents from 96 families of children with ADHD. For the assessment of ADHD authors used the behavioral disorders section of the Schedule for Affective Disorders and Schizophrenia for School-Age Children—Present and Lifetime Version. Also, they included a spousal report to confirm the diagnosis. Authors reported higher scores on NS and SD in parents with history of ADHD (N = 56) compared to the ones without history of the disorder. No correlations between Dopamine D4 Receptor gene variant and temperament were found.

3.2. TEMPS-A scores in ADHD adults

We found 6 studies using the TEMPS-A in individuals with diagnosed ADHD or with present and past symptoms of the disorder. The results were consistent, with significant associations between ADHD symptoms and depressive, cyclothymic, anxious and irritable temperament scores.

Ozdemiroglu et al. (2018) studied a sample of 81 subjects (48 women and 33 men) with a lifetime diagnosis of ADHD, recruited in their outpatient clinic. Diagnoses were assessed using SCID-I, while the severity of childhood ADHD symptoms was retrospectively assessed by using the Turkish version of the Wender Utah Rating Scale (WURS-25). A Turkish version of Turgay's Adult ADD/ADHD Diagnosis and Evaluation Scale was used for the assessment of symptom severity in childhood and adulthood ADHD. The aim was to investigate affective temperaments and their role in persistent adult ADHD without comorbid Bipolar Disorder. The sample was divided into two groups: those with childhood ADHD (n = 46) and those with adult ADHD (n = 35). They found that the Adult ADHD group had significantly higher scores on cyclothymic, irritable, and anxious subscales of the TEMPS-A. The scores for cyclothymic and irritable temperaments were significantly associated with the severity of adulthood symptoms of ADHD.

A comparison between patients with Bipolar Disorder (BD) and ADHD patients was made by Torrente et al. (2017). Their sample included 60 ADHD patients, 40 BD patients (36 BD-type II, 6 BD-type I, 8 BD-nos) and 30 healthy controls. The results regarding temperament were consistent with previous research. ADHD patients had significantly higher scores for cyclothymic, irritable, depressive and anxious temperaments on the TEMPS-A compared with healthy controls, but there were no significant differences in temperament no scores between the ADHD and BD groups. Twenty-three of the 60 ADHD patients recruited had a dominant temperament. The most common was cyclothymic, followed by irritable, depressive and anxious temperaments. The patients were also administered the Beck Depression Inventory II (BDI-II) and the ADHD rating scale for Adults. The ADHD and BD patients had similar BDI-II scores for depressive symptoms, but neurovegetative symptom scores were higher in BD patients than in ADHD patients. Both groups were found to have higher depressive symptoms in all BDI-II domains compared with healthy controls. Finally, those ADHD patients who scored above the cut-off scores on the TEMPS-A (and also the BD patients) showed significantly higher scores for depressive symptoms compared to ADHD patients with scores below the cut-off and healthy controls.

Skala et al. (2016) studied 3280 18-year-old men during their military evaluation. Those with past or present symptoms of ADHD had higher scores for the cyclothymic, irritable and anxious temperaments.

Harmanci et al. (2016) investigated ADHD as a comorbid diagnosis in 100 patients with Bipolar Disorder, 100 patients with Major Depressive Disorder (MDD) and 100 Healthy Controls (HC). The evaluation of symptoms was made by using the ASRS and the Wender Utah ADHD Rating Scale (WURS). The results indicated that 48% of the BD patients had ADHD symptoms, while the percentage was lower in the MDD patients (25%) and the healthy controls (12%). A higher incidence of a suicidal history was found in patients with both BD and ADHD compared with the other groups. Regarding the temperament evaluation, higher scores for cyclothymic, anxious irritable and depressive temperaments were found in the ADHD patients of all three groups compared to the patients without co-occurring ADHD. The

scores for the hyperthymic trait did not show a significant difference between the ADHD and the non-ADHD subjects in any of the groups.

Ekinci et al. (2013) evaluated 40 ADHD patients, 40 BD patients and 40 healthy controls. The ADHD patients had significantly higher scores for depressive, cyclothymic, irritable and anxious temperaments, but not for the hyperthymic temperament when compared to the healthy controls. ADHD patients did have significantly higher scores for the irritable temperament compared with BD patients.

Landaas et al. (2012) studied 586 ADHD patients and 721 healthy controls. Roughly 71% of ADHD patients were positive for the cyclothymic temperament compared to 13% of the healthy controls. Overall, the patients with both ADHD and a cyclothymic temperament had a higher incidence of childhood and adult ADHD symptoms and more frequent psychiatric comorbidity than the healthy controls, as well as lower educational and occupational achievements.

4. Discussion

All of the TCI studies produced results consistent with one another and with previous studies. There was a positive association between ADHD and higher scores for Novelty Seeking and Harm Avoidance and lower scores for Persistence. In four of these studies (Kim et al., 2017; Park et al., 2016; Merwood et al., 2013; Lynn et al., 2005), participants did not receive a prior diagnosis of ADHD but were tested for ADHD symptoms. The positive association between ADHD symptom dimensions and the above temperaments is consistent with studies that included a sample of ADHD patients diagnosed in outpatient clinics, suggesting that a novelty seeking and a harm avoidance temperament has an association with ADHD symptoms, as well as their severity and functional impairment.

For the TEMPS-A, only one study was performed outside an ADHD outpatient setting (Skala et al., 2016) and another study did not include patients with a prior ADHD diagnosis but merely tested the subjects for ADHD symptoms (Harmanci et al., 2016). When comparing ADHD patients with Bipolar Disorder patients, some similarity in the temperament scores existed, and both disorders seem to share higher TEMPS-A scores in all domains except the hyperthymic temperament (Torrente et al., 2017; Ekinci et al., 2013). Bipolar patients with ADHD symptoms may score higher on a TEMPS-A evaluation when compared with individuals without ADHD symptoms (Harmanci et al., 2016). In the largest study, the most frequent temperament in ADHD patients was cyclothymic, and it was related to higher psychiatric comorbidity in these patients (Landaas et al., 2012). Some temperament traits such as cyclothymia and irritability seem to predict the persistence of ADHD symptoms from childhood into adulthood in patients without a comorbid mood-disorder (Ozdemiroglu et al., 2018).

When trying to compare temperament assessment tools, limitations come from three important facts. (1) At the moment, a TCI versus TEMPS-A comparison is impossible as there is no study directly comparing the two tools, and these two tools were conceived on the basis of two different theoretical approaches. (2) Adult ADHD, even in the DSM-5 era, is still a challenge in terms of diagnosis, and its presence can be under-diagnosed. (3) The studies reviewed in the present paper differ in the type of sample, the number of recruited subjects and the ADHD assessment.

Despite the aforementioned limitations, the picture that emerges is that adult ADHD patients show temperament traits associated with emotional dysregulation even in absence of a co-occurring mood disorder. This is the only fact on which both temperament assessing methods converge. We suggest that emotional dysregulation in adults with ADHD could be an independent feature of a subgroup of these individuals and could play a role in predicting the persistence of ADHD symptoms into adulthood and their severity. It is known that emotional dysregulation is a clinical dimension peculiar to ADHD itself, although it is not part of the diagnostic criteria, and it usually responds to standard ADHD treatments. However, in a considerable number of cases, emotional dysregulation does not respond entirely, and additional treatment strategies are needed (Shaw et al., 2014). In this regard, temperament traits could be useful for identifying patients who are less likely to benefit from standard ADHD treatments alone in order to control emotional dysregulation. At the present time, temperament traits do not seem to show sufficient specificity to serve as a tool for differentially diagnosing ADHD, bipolar disorder, and ADHD-BD comorbidity.

In order to understand whether and how temperament influences the clinical course of ADHD and ADHD-oriented treatment strategies, longitudinal studies are needed on adult ADHD patients tested for temperament at baseline and also for depressive, anxious and hypomanic symptoms and their changes after appropriate ADHD-specific treatments. Finally, further studies on childhood ADHD could lead to a better understanding of the role of temperament in differentiating the two disorders and their developmental trajectories.

5. Conclusions

In recent years, there has been an increase in the number of studies on the association between ADHD and specific temperaments. The papers we examined in this review show consistent results in indicating that ADHD is associated with specific temperament traits whose severity might be a potential marker warranting additional treatments for emotional dysregulation in some patients. On the TCI, ADHD patients have high Novelty Seeking and Harm Avoidance temperament scores. On the TEMPS-A, ADHD patients have higher scores on the cyclothymic, depressive, anxious and irritable temperament scales. However, a direct comparison of the two temperament assessment methods has not been performed, and current evidence does not support a role for temperament traits in differential diagnosis or personalized early treatment decisions that can improve treatment effectiveness. This warrants future research aimed at delineating the weaknesses and strengths of the two methods of assessing temperament from a diagnostic, prognostic and therapeutic point of view.

The research using the TCI and TEMPS-A indicates that emotional dysregulation is a key feature of bipolar spectrum disorders and ADHD. However, it is unclear how emotional dysregulation could impact the clinical management of adult ADHD patients. Future research is needed in order to study how temperament influences the pharmacological response of ADHD patients and the course of their illness, and whether temperament scores affect the long-term therapeutic outcome.

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Conflict of interest

None to declare.

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