Affective Temperament Traits Measured by TEMPS-A and Their Associations with Cognitive Functions among Offspring of Parents with Bipolar Disorder with and without Subthreshold Symptoms

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Abstract

Background: To our knowledge, there have been no studies that have examined affective temperament traits in offspring of parents with bipolar disorder (BD). The aim of this study was to identify affective temperamental characteristics and their relationships with cognitive functions in BD offspring.

Methods: A group of BD offspring were enrolled in this study. Subthreshold symptoms were used to categorize participants as either symptomatic offspring (SO) (n=60) or asymptomatic offspring (AO) (n=52). Healthy controls (HCs; n=48) were also enrolled for comparison. We used the Chinese Short Version of Temperament Evaluation of Memphis, Pisa, Paris, and San Diego, Auto-questionnaire (TEMPS-A) to measure temperament traits, and MATRICS Consensus Cognitive Battery (MCCB) to measure cognitive functions.

Results: We observed higher cyclothymic, irritable, depressive and anxious temperament scores in SO than AO when compared to HCs. In BD offspring (SO and AO), cyclothymic individuals performed better in processing speed and verbal learning than depressive individuals and better in attention/vigilance than irritable and anxious individuals; hyperthymic individuals performed better in processing speed

than depressive individuals. We also observed that a higher cyclothymic score was associated with better verbal learning and verbal fluency, a higher hyperthymic score was associated with better processing speed and verbal learning; while a higher depressive score was associated with worse processing speed, verbal learning and verbal fluency and a higher irritable score was associated with worse attention/vigilance.

Conclusions: The relationships between cognitive functions and measures of temperament suggest that these features may share neurobiological substrates and appear to be heritable.

Keywords: affective temperament, cognitive function, bipolar disorder, offspring

1. Introduction

Affective temperament is a genetically-determined biological personality substrate and reflects an "endophenotype" trait of individuals (Nuttin, 1985), which can be evaluated by the Temperament Evaluation of Memphis, Pisa, Paris, and San Diego, Auto-questionnaire (TEMPS-A) compiled by Akiskal and his colleagues (2005). The TEMPS-A measures five types of affective temperaments: cyclothymic, hyperthymic, irritable, depressive and anxious temperaments (Akiskal et al., 2005). Recently, it has been reported that the affective temperament measured by TEMPS-A in first-degree relatives (FDRs) (i.e. parents, siblings, offspring) of persons affected by bipolar

disorder (BD) may be used to search for trait-markers. Several studies suggested that FDRs of persons affected by BD had greater cyclothymic, irritable, anxious or depressive temperaments (Chiaroni et al., 2005; Mahon et al., 2013; Mendlowicz et al., 2005; Vázquez et al., 2008), while a few studies suggested that the FDRs demonstrated greater hyperthymic temperament (Kesebir et al., 2005; Gandotra et al., 2011).

Failing to accurately identify symptomatic and asymptomatic FDRs of BD patients may partly explain the inconsistency in findings to date. A large proportion of FDRs of persons affected by BD suffer from subthreshold symptoms (e.g. minor depression, hypomania, anxiety, attention deficits, hyperactivity); however, they do not meet diagnostic criteria for BD (Axelson et al., 2015; Duffy et al., 2014). Prior studies have found offspring of BD patients with subthreshold symptoms and those without subthreshold symptoms showed largely non-overlapping patters of brain function connectivity and displayed differential cerebellar grey matter volume (Lin et al., 2018b; Lin et al., 2018c). In addition, associations between subthreshold manic or hypomanic and depressive episodes and conversion rate to BD in FDRs of BD patients are significant (Axelson et al., 2015). Risk of developing BD is higher in FDRs of BD patients that demonstrate subthreshold symptoms (Birmaher et al., 2018). The biological mechanism underlying the development of BD in FDRs may differ between individuals with subthreshold symptoms and individuals that are asymptomatic. Thus, to examine affective temperamental characteristics in FDRs of individuals with BD, it is critical to conduct separate investigation between subgroups

based on the presence or absence of symptoms.

Meta-analyses have suggested that FDRs of BD patients suffered from significant cognitive deficits (Arts et al., 2008; Bora et al., 2009; Bora, 2017). There is a wide overlap between the brain regions underlying affective temperaments and those underlying cognitive functions, such as prefrontal, hippocampal and amygdala neural systems (Nigg, 2000; Schilling et al., 2013; Turken et al., 2008; Zakzanis et al., 2005). To our knowledge, there have been no studies to examine the associations between affective temperament and cognitive functions in the FDRs of BD patients. Our previous study showed BD patients with hyperthymic temperament demonstrated worse working memory and set shifting than those without temperaments (Xu et al., 2014). Nevertheless, an association between greater hyperthymic temperament and better processing speed was also showed in BD patients (Russo et al., 2014). Meanwhile, contradictory associations between greater cyclothymic temperament and better or worse cognitive functions were also suggested in BD patients (Romero et al., 2016; Russo et al., 2014). These findings are inconsistent.

Compared with BD patients, studies in BD offspring excluded the impacts of psychiatric medication. Mood stabilizers, antipsychotics and antidepressants have been reported to have long lasting effects on cognition (Karson et al., 2016; Papakostas, 2015; Rybakowski, 2016). In addition, studies in BD offspring could observe whether these affective temperaments have effects on cognitive functions before the onset of BD.

Herein, we compared the affective temperaments among medication-naïve symptomatic offspring (SO) and asymptomatic offspring (AO) of parents with BD to healthy controls (HCs). Our study aimed to identify the affective temperament characteristics of BD offspring. Furthermore, we compared the cognitive functions among the groups on the basis of dimensional temperament measures and computed the associations between affective temperaments and cognitive functions in BD offspring. We explored whether there are differences across cognitive functions that are associated with the presence of temperamental characteristics. We hypothesized some affective temperaments could be considered trait-markers before BD onset and relate to some cognitive functions.

2. Methods

This study is a part of the Recognition and Early intervention on Prodromal Bipolar Disorder (REI-PBD) project (ClinicalTrial.gov Identifier: NCT01863628), which is an ongoing longitudinal study (Lin et al., 2015). The research ethics committee (the Ethics Committee of the Affiliated Brain Hospital of Guangzhou Medical University) approved this study. All participants (for participants older than/equal to 18 years old) or their guardians (for participants under 18 years old) signed informed consents after a full explanation of this study.

2.1. Participants

A group of BD offspring (n=112) were enrolled in this study. Based on subthreshold symptoms, the offspring were categorized as being either symptomatic offspring (SO) (n=60) or asymptomatic offspring (AO) (n=52). All subjects were recruited from the Affiliated Brain Hospital of Guangzhou Medical University between March 2013 and March 2019, and 8 to 28 years old and had at least one biological parent with BD. DSM-IV criteria based on the Structured Clinical Interview for DSM-IV-TR Axis I Disorders (SCID-I) was administered for the diagnosis of BD. Demographics and clinical variables were collected by the psychiatrists who belonged to the trained research team. Hamilton Depression Rating Scale (HAMD) and Young Mania Rating Scale (YMRS) were used to assess their clinical variables. The intraclass correlation coefficients (ICCs) assessing inter-rater reliability for SCID-I was 0.95 and for the clinical scales (HAMD and YMRS) were between 0.89 and 0.93.

Offspring of parents with BD were considered in the SO group if they manifest at least one of the following symptoms: 1) two or more hypomania symptoms lasting for at least 4 days but failing to meet DSM-IV criteria for hypomanic episode; 2) two or more major depressive symptoms lasting for at least 1 week but failing to meet DSM-IV criteria for a major depressive episode; 3) one or more of the following attenuated psychotic symptoms lasting at least 10 minutes for each manifestation and 2-7 manifestations per week for at least 3 months: ideas of reference, odd ideas, odd beliefs, unusual perceptual experiences, bizarre thought or speech, grandiosity, suspicious ideas, paranoid ideas, odd mannerisms, hallucination(s),

disorganized/catatonic behavior; and 4) two or more of the hyperactive and/or impulsive symptoms defined by the DSM-IV for attention deficit hyperactivity disorder (ADHD), observable by teachers, peers, and/or parents. BD offspring were considered in the AO group if they did not have any of these symptoms.

The exclusion criteria for both SO and AO groups included the followings: 1) any DSM-IV-TR Axis I disorders; 2) alcohol, drug or other psychoactive substance abuse or dependence; 3) pregnant or postpartum women; 4) hyperthyreosis; 5) a history of organic brain disease or brain trauma; 6) without ability to complete temperamental or cognitive tests.

Forty-eight healthy controls (HCs) aged 8 to 28 years were recruited from Guangzhou China. The exclusion criteria included the followings: 1) any DSM-IV-TR Axis I disorders; 2) alcohol, drug or other psychoactive substance abuse or dependence; 3) pregnant or postpartum women; 4) hyperthyreosis; 5) a history of organic brain disease or brain trauma; 6) inability to complete temperamental or cognitive tests; or 7) a family history of psychiatric disorder.

2.2. Affective temperament

A short version of TEMPS-A, consisting of 45 items validated by us previously, was used to assess affective temperaments among the adults of ages older than or equal to 16 years (Lin et al., 2018a). At present, the Chinese Short Versions of the TEMPS-A are mainly used for adult assessment (Lin et al., 2013; Lin et al., 2018c;

Yuan et al., 2014). Some items are related to adult experiences, love affairs and sex, which are generally not applicable to children and adolescents. Hence, a short version of the TEMPS-A consisting of 60 items validated by us previously was used to assess affective temperaments among the children and adolescents aged 8 to 15 (Lin et al., 2016). The two versions of TEMPS-A assess five affective temperaments: depressive, cyclothymic, hyperthymic, irritable and anxious temperaments. All participants completed this assessment in a quiet environment.

We computed the Z-score of each temperamental subscale for each subject (Xu et al., 2014), according to the criteria that the highest determined the predominant affective temperament (Akiskal et al., 1998; Conio et al., 2019; Placidi et al., 1998). BD offspring were subdivided into 38 cyclothymic-temperament individuals, 40 hyperthymic-temperament individuals, 28 irritable-temperament individuals, 29 depressive-temperament individuals and 22 anxious-temperament individuals. There were differences in age (Cyclothymic individuals, Irritable individuals < Hyperthymic individuals) and education level (Cyclothymic individuals, Irritable individuals, Depressive individuals < Hyperthymic individuals) and no difference in gender ratio among these five groups with different temperaments.

2.3. Cognitive function

All participants were tested with the Chinese version of the MATRICS Consensus Cognitive Battery (MCCB). These tests were taken in the same order in a quiet

environment, and were completed by the participants in about 30 minutes. Participants missing data from three or more cognitive tests were excluded from analyses. Three BD offspring were exclude due to missing cognitive data.

Several domains of cognition were assessed by the following tests: 1) processing speed was measured by the Trail Making Test Part A (TMT-A) and the Brief Assessment of Cognition in Schizophrenia (BACS)-symbol coding; 2) verbal learning was measured by the Hopkins Verbal Learning Test-Revised (HVLT-R); 3) working memory was measured by the Wechsler Memory Scale-III Spatial Span (WMS-III SS); 4) reasoning and problem solving was measured by the Neuropsychological Assessment Battery (NAB) mazes; 5) visual learning was measured by the Brief Visuospatial Memory Test-Revised (BVMT-R); 6) verbal fluency was measured by animal naming; 7) attention/vigilance was measured by the Continuous Performance Test-Identical Pairs (CPT-IP). The detailed neurocognitive scores of a large subset of the present participants were reported in Lin et al. (2017).

2.4. Statistical analysis

SPSS 26 software (SPSS Inc, Chicago, IL, USA) was used to conduct statistical analyses. Variables were evaluated for homogeneity of variance with Levene's test. Demographics, clinical variables and temperament scores were analyzed using χ^2 test, one-way analysis of variance (ANOVA) or Kruskal–Wallis tests. A one-way ANOVA test was conducted if the variance of continuous variable was homogeneous. A

Kruskal-Wallis test was conducted if the variance of continuous variable was not homogeneous. Cognitive functions among the BD offspring with different affective temperaments were examined by using multivariate analysis of variance (MANOVA) controlling for confounders, including gender, age, years of education and clinical scale scores (HAMD and YMRS). Interactions were assessed by adding the product term (i.e. affective temperaments × BD offspring subgroups) to the tested models. Associations between temperaments and cognitive functions were evaluated by using multivariable linear regression model controlling for confounders, including gender, age, years of education and clinical scale scores (HAMD and YMRS). The level of significance was set at $p< 0.05$, two-sided.

3. Results

3.1. Sample characteristics

Table 1 describes the demographic and clinical characteristics for the subjects. 60 SO, 52 AO and 48 HCs were included in this study. The three groups were matched according to age ($F = 0.95$, $p = 0.390$), gender ($\chi 2 = 0.69$, $p = 0.707$) and education level ($F = 1.22$, $p = 0.298$). As for clinical variables, there were significant differences in HAMD and YMRS scores between groups ($\chi 2 = 53.92$, $p < 0.001$; $\chi 2 = 41.03$, $p < 0.001$, respectively), SO scored higher than AO and HCs in these two scale scores ($p < 0.05$), and no differences between AO and HCs were evident.

3.2. Comparisons of TEMPS-A subscale Z scores

As shown in Table 2, there were significant differences in cyclothymic, irritable, depressive and anxious scores among the three groups (SO, AO and HCs) ($\chi 2$ = 11.22, p = 0.004; $\chi 2$ = 14.06, p = 0.001; $\chi 2$ = 8.29, p = 0.016; $\chi 2$ = 6.04, p = 0.049, respectively). Cyclothymic score was higher in SO than AO ($p < 0.05$), and irritable and depressive scores were higher in SO than AO and HCs ($p < 0.05$) and no differences in irritable and depressive scores between AO and HCs were showed, and anxious score trended to be higher in SO than AO and HCs (p = 0.052).

3.3. Comparisons of cognitive functions with different affective temperaments

As shown in table 3, there were significant differences in processing speed measured by TMT-A (F = 3.75, p = 0.007) and BACS-symbol coding (F = 2.54, p = 0.045), verbal learning measured by HVLT-R (F = 3.27, p = 0.015) and attention/vigilance measured by CPT-IP (F = 3.32, p = 0.014) among BD offspring (SO and AO) with different affective temperaments. Cyclothymic and hyperthymic groups performed better in processing speed measured by TMT-A than depressive group ($p < 0.05$) and no difference between cyclothymic and hyperthymic groups was found. Cyclothymic group also performed better in processing speed measured by BACS-symbol coding ($p < 0.05$) and verbal learning ($p < 0.05$) than depressive group ($p < 0.05$), and better in attention/vigilance than irritable and anxious groups ($p < 0.05$) and no difference in attention/vigilance between irritable and anxious groups was

found.

There were no significant interaction effects of affective temperaments and BD offspring subgroups (SO and AO) on cognitive functions.

3.4. Associations between affective temperaments and cognitive functions

As shown in table 4, in BD offspring including SO and AO, higher cyclothymic score was associated with better verbal learning (β = 0.312, p = 0.005) and verbal fluency (β = 0.215, p = 0.048). Higher hyperthymic score was associated with better processing speed measured by TMT-A (β = -0.244, p = 0.042) and verbal learning (β = 0.288, p = 0.008). Higher depressive score was associated with worse processing speed measured by TMT-A (β = 0.253, p = 0.023) and verbal fluency (β = -0.243, p = 0.033). There were trends for associations between higher depressive score and worse processing speed measured by BACS-Symbol Coding (β = -0.192, p = 0.054) and verbal learning (β = -0.219, p = 0.056). Higher irritable score was associated with worse attention/vigilance (β = -0.215, p = 0.046).

In SO, we did not find any associations between subscale scores of affective temperaments and cognitive functions.

In AO, only an association between higher cyclothymic score and better vernal memory was showed (β = 0.297, p = 0.036).

4. Discussion

We observed SO had more predominant cyclothymic, irritable, depressive and anxious temperaments than AO and HCs, AO and HCs showed similar affective temperament traits. In BD offspring (SO and AO), cyclothymic group performed better in processing speed and verbal learning than depressive group, and better in attention/vigilance than irritable and anxious groups; hyperthymic group performed better in processing speed than depressive group. We also observed that higher cyclothymic score was associated with better verbal learning and verbal fluency, higher hyperthymic score was associated with better processing speed and verbal learning while higher depression score was associated with worse processing speed, verbal learning and verbal fluency, higher irritable temperament score was associated with worse attention/vigilance.

Our findings are in accordance with Vázquez et al., (2008), which reported that FDRs of BD patients had higher cyclothymic, irritable, depressive and anxious scores than HCs.[4] Similarly, some other studies also reported that FDRs of BD patients were characteristic with more predominant cyclothymic, irritable and/or anxious temperaments than HCs (Chiaroni et al., 2005; Mahon et al., 2013; Mendlowicz et al., 2005). A meta-analysis of four studies also reported more predominant cyclothymic, irritable and anxious temperaments in FDRs than HCs (Solmi et al., 2016).

We observed that there were associations between clinical scale scores (HAMD and YMRS) and subscale scores of affective temperaments in this study (Supporting

Information Table S1), which suggests subthreshold symptoms may have associations with affective temperaments. These associations may be a cause of BD offspring with subthreshold symptoms having more obvious affective temperament traits. Our study found that SO had four more predominant temperaments (cyclothymic, irritable, depressive and anxious temperaments) than HCs, while other studies reported FDRs of BD patients only had two or three predominant affective temperaments (Chiaroni et al., 2005; Mahon et al., 2013; Mendlowicz et al., 2005). This may be due to the fact that these scholars mixed SO and AO, while we separated SO from BD offspring and compared them with HCs.

We observed that hyperthymic temperament was not different between groups. It is in accordance with the majority of studies (Chiaroni et al., 2005; Mahon et al., 2013; Mendlowicz et al., 2005; Solmi et al., 2016; Vázquez et al., 2008). However, the findings of two studies were different from ours, and they showed BD patients and FDRs of BD patients had the greater hyperthymic temperament (Kesebir et al., 2005; Gandotra et al., 2011). The inconsistency in findings across studies may be partially attributed to the variation across methodologies with identifying affective temperament across studies. The two inconsistent studies were comparing ratios of individuals with predominant affective temperaments between groups, to show the difference of temperament traits, while our study was comparing the TEMPS-A scores. In the study by Gandotra and colleagues (2011), they divided the subjects into those either with the high hyperthymic temperament (score ≥ 7) or the low hyperthymic temperament (score < 7) according to the subscale score. Kesebir et al. (2005) found

the FDRs of BD patients had greater hyperthymic temperament than HCs only when the predominant temperament was determined using a z-score cut-off and ratio of this temperament was compared, while the hyperthymic trait of FDRs of BD patients was similar to HCs when scale score was compared as a continuous variable.

In our study, we also found BD offspring with cyclothymic temperament performed better in processing speed and verbal learning than those with depressive temperament and better in attention/vigilance than those with irritable and anxious temperaments. BD offspring with hyperthymic temperament performed better in processing speed than those with depressive temperament. Meanwhile, we observed the greater cyclothymic temperament was associated with better verbal learning and verbal fluency, greater hyperthymic temperament was associated with better processing speed and verbal learning; while greater depressive temperament was associated with worse processing speed, verbal learning and verbal fluency, and greater irritable temperament was associated with worse attention/vigilance. Our results suggest the cyclothymic and hyperthymic temperaments may be associated with better cognitive functions. In contrast, depressive, irritable and anxious temperaments may be associated with reduced cognitive functions in offspring of individuals with BD.

Previous findings of associations between cyclothymic and hyperthymic temperaments and cognitive functions are inconsistent (Poyraz et al., 2017; Romero et al., 2016; Russo et al., 2014). Russo and colleagues (2014) reported that higher cyclothymic score was associated with better processing speed, working memory and

global cognition, while higher hyperthymic score was associated with better processing speed in stable BD patients.[22] In healthy individuals, predominant cyclothymic temperament was characterized by increased physiological arousal and faster information processing (Poyraz et al., 2017). However, associations between greater cyclothymic temperament and worse visual memory and attention, and greater hyperthymic temperament and worse working memory in patients with BD were also showed (Romero et al., 2016). In our previous study, we showed cognitive impairments in working memory and set shifting in depressive BD patients with the hyperthymic temperament were greater than non-temperamental individuals (Xu et al., 2014), which was also inconsistent with our present findings. We inferred that the cyclothymic and hyperthymic temperaments in individuals with normal mood (including healthy individuals, BD offspring who did not develop BD, and remitted patients with BD) are associated with better cognitive functions, while they may damage cognitive functions in BD patients during depressive or hypomanic/manic episode.

Viewpoints of most previous studies on associations between the depressive temperament and cognitive functions are similar to ours (Poyraz et al., 2017; Romero et al., 2016; Russo et al., 2014). Our study also observed BD offspring with greater irritable and anxious temperaments performed worse in attention/vigilance, and greater irritable temperament was associated with worse attention/vigilance. Our findings suggest irritable and anxious temperaments may reduce attention/vigilance in BD offspring. Additionally, Romero et al. (2016) also reported the greater irritable

temperament was associated with worse attention and set shifting, and greater anxious temperament was associated with worse attention. Conversely, Russo et al., (2014) observed an association between greater irritable temperament and worse attention and social cognition in healthy individuals, while an association between greater irritable temperament and better processing speed and working memory in BD patients. Impact of irritable temperament on different aspects of cognitive functions may be different, it may have a harmful impact on attention and other cognitive functions relating to attention, while may be beneficial to processing speed and working memory. Additional studies investigating the effect of affective temperament on cognitive function in BD offspring are required to further elucidate the association between affective temperament and genetic predisposition of BD in FDRs.

Some potential limitations of our study should be considered. First, the sample sizes of subgroups (SO, AO and HCs) were relatively small. We did not find any associations between subscale scores of affective temperaments and cognitive functions in SO, only an association between a higher cyclothymic score and better vernal memory in AO was showed. After subgroups analyses, our study still had some statistical findings in each subgroup, but the number of statistical findings was significantly reduced. Relatively small sample size of each subgroup may impair the statistical power and result in false negative results in our study. Second, we did not control for intelligence quotients (IQs) in all statistical analyses. The IQs has impacts on cognitive functions (Martínez-Arán et al., 2004; Skakkebæk et al., 2017).

In conclusion, these findings suggest that BD offspring with subthreshold

symptoms are more likely to demonstrate more predominant cyclothymic, irritable, depressive and/or anxious temperaments than BD offspring without subthreshold symptoms and healthy individuals. Moreover, greater cyclothymic and hyperthymic temperaments may be associated with better cognitive functions. In contrast, greater depressive, irritable and anxious temperaments may be associated with worse cognitive functions in offspring of individuals with BD. The relationship between cognitive function and measures of temperament suggest that these features may share neurobiological substrates and appear to be heritable.

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Table 1

Demographic and clinical characteristics for the three groups.

Characteristics	Symptomatic offspring (n=60)	Asymptomatic offspring (n=52)	Healthy controls (n=48)	*F* or χ^2	*p*	Post hoc[a]
Age (years)	15.57 (5.77)	16.83 (5.48)	15.63 (4.50)	0.95	0.390	
Male/female	31/29	23/29	22/26	0.69	0.707	
Education (years)	8.62 (4.18)	9.62 (3.91)	9.67 (3.92)	1.22	0.298	
HAMD score	3.0 (0.0-10.0)	0.0 (0.0-0.0)	0.0 (0.0-0.0)	53.92	<0.001	SO > AO, HCs
YMRS score	1.0 (0.0-3.0)	0.0 (0.0-0.0)	0.0 (0.0-0.0)	41.03	<0.001	SO > AO, HCs

Abbreviations: SO, symptomatic offspring; AO, asymptomatic offspring; HCs, healthy controls; HAMD, Hamilton Depression Rating Scale; YMRS, Young Mania Rating Scale.

Notes: [a] significance values have been adjusted by the Bonferroni correction for multiple tests.

Table 2

Comparisons of TEMPS-A Z scores among the three groups [Median (IQRs)].

TEMPS-A T scores	Symptomatic offspring (n=60)	Asymptomatic offspring (n=52)	Healthy controls (n=48)	χ^2	*p*	Post hoc[a]
Cyclothymic score	51.95 (42.52-62.15)	44.58 (40.05-51.94)	48.26 (42.03-54.99)	11.22	0.004	SO > AO
Hyperthymic score	46.24 (39.34-59.19)	49.70 (40.20-58.19)	49.17 (46.24-59.59)	1.12	0.570	
Irritable score	54.66 (42.77-64.22)	43.94 (42.77-52.41)	42.77 (42.77-49.88)	14.06	0.001	SO > AO, HCs
Depressive score	50.22 (45.85-59.00)	45.90 (45.85-45.90)	45.90 (45.90-50.22)	8.29	0.016	SO > AO, HCs
Anxious score	51.70 (44.03-62.16)	44.03 (44.03-50.98)	44.03 (44.03-52.41)	6.04	0.049	

Abbreviations: TEMPS-A, Temperament Evaluation of Memphis, Pisa, San Diego-auto questionnaire; SO, symptomatic offspring; AO, asymptomatic offspring; HCs, healthy controls.

Notes: [a] significance values have been adjusted by the Bonferroni correction for multiple tests.

Table 3

Comparisons of cognitive function in BD offspring with different affective temperaments [Estimated marginal mean (S.E.)]

	Temperament groups							
	Cyclothymic	Hyperthymic	Depressive	Irritable	Anxious			
Cognitive domains and Tasks	(n=25)	(n=26)	(n=22)	(n=19)	(n=15)	*F*	*p*[a]	Post hoc[b]
Processing speed								
TMT-A	30.13 (2.80)	32.54 (2.50)	43.58 (2.54)	35.92 (2.95)	36.77 (3.22)	3.75	0.007	C, H < D
BACS-Symbol Coding	60.94 (2.17)	58.33 (1.94)	52.53 (1.97)	54.48 (2.29)	57.57 (2.49)	2.54	0.045	C > D
Verbal learning								
HVLT-R	30.28 (0.99)	28.74 (0.89)	25.87 (0.90)	27.37 (1.05)	26.31 (1.14)	3.27	0.015	C > D
Working memory								
WMS-III SS	17.93 (0.90)	17.04 (0.80)	16.84 (0.81)	17.78 (0.95)	16.40 (1.03)	0.44	0.778	
Reasoning and problem solving								
NAB-Mazes	16.39 (1.34)	16.63 (1.20)	14.83 (1.21)	15.07 (1.41)	15.39 (1.54)	1.36	0.252	
Visual learning								
BVMT-R	25.64 (1.34)	25.81 (1.20)	22.72 (1.21)	23.50 (1.41)	22.57 (1.54)	0.40	0.812	
Verbal fluency								

Animal naming	20.66 (1.25)	19.27 (1.12)	18.19 (1.13)	18.68 (1.32)	19.64 (1.43)	0.61	0.66	
Attention/vigilance								
CPT-IP	2.79 (0.16)	2.43 (0.14)	2.36 (0.15)	2.05 (0.17)	2.05 (0.18)	3.32	0.014	C > I, A

Abbreviations: BD, bipolar disorder; C, cyclothymic; H, hyperthymic; D, depressive; I, irritable; A, anxious; TMT-A, Trail Making Test Part A; BACS-Symbol Coding, Brief Assessment of Cognition in Schizophrenia-Symbol Coding; HVLT-R, Hopkins Verbal Learning Test-Revised; WMS-III SS, Wechsler Memory Scale-III Spatial Span; NAB-Mazes, Neuropsy- chological Assessment Battery mazes; BVMT-R, Brief Visuospatial Memory Test-Revised; CPT-IP, Continuous Performance Test-Identical Pairs.

Notes: [a]Adjusted for gender, age, educational level and clinical scale scores; [b]The threshold for significance was $p< 0.05$, with the Bonferroni correction.

Table 4

Associations between subscale scores of affective temperaments and cognitive functions among BD offspring

	Cyclothymic socre		Hyperthymic score		Depressive score		Irritable score		Anxious score	
Cognitive domains and Tasks	*β*	*p*	*β*	*p*	*β*	*p*	*β*	*p*	*β*	*p*
Processing speed										
TMT-A	-0.056	0.597	**-0.244**	**0.042**	**0.253**	**0.023**	-0.077	0.488	-0.043	0.725
BACS-Symbol Coding	-0.005	0.954	0.057	0.542	**-0.192**	**0.054**	0.032	0.749	0.040	0.714
Verbal learning										
HVLT-R	**0.312**	**0.005**	**0.288**	**0.008**	**-0.219**	**0.056**	0.113	0.322	-0.225	0.074

Working memory										
WMS-III SS	-0.088	0.451	-0.116	0.314	-0.081	0.507	0.161	0.192	-0.150	0.264
Reasoning and problem solving										
NAB-Mazes	-0.072	0.544	-0.049	0.678	-0.016	0.900	0.181	0.146	0.003	0.980
Visual learning										
BVMT-R	0.069	0.533	0.106	0.345	-0.014	0.906	-0.005	0.965	-0.064	0.621
Verbal fluency										
Animal naming	**0.215**	**0.048**	0.171	0.109	**-0.243**	**0.033**	-0.021	0.857	-0.040	0.747
Attention/vigilance										
CPT-IP	0.018	0.851	0.080	0.403	0.057	0.572	**-0.215**	**0.046**	-0.139	0.206

Abbreviations: BD, bipolar disorder; TMT-A, Trail Making Test Part A; BACS-Symbol Coding, Brief Assessment of Cognition in Schizophrenia-Symbol Coding; HVLT-R, Hopkins Verbal Learning Test-Revised; WMS-III SS, Wechsler Memory Scale-III Spatial Span; NAB-Mazes, Neuropsy- chological Assessment Battery mazes; BVMT-R, Brief Visuospatial Memory Test-Revised; CPT-IP, Continuous Performance Test-Identical Pairs.