The Functional Impairment of Different Subtypes and Occupational States in Euthymic Patients With Bipolar Disorder

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Research Article

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Abstract

Background

The aim was to explore the associations between clinical symptoms, demographic variables, social and neurocognitive functioning in euthymic patients with bipolar disorder (BD) stratified by subgroups of DSM-IV BD (BD-type I and BD-type II) and occupational status (employed/unemployed), and to highlight the significance of occupational status when assessing social and neurocognitive functioning in euthymic BD patients.

Methods

A total of 81 euthymic BD patients were participated in the study. The severity of the depressive and manic/hypomanic symptoms was measured using the 17-item Hamilton Depression Rating Scale (HDRS-17) and the Young Mania Rating Scale (YMRS), respectively. Social functioning and neurocognitive functioning were evaluated by the Functioning Assessment Short Test (FAST) and neurocognitive measures, respectively.

Results

Employed BD patients displayed greater social functioning (autonomy, occupational functioning, interpersonal relationship domain) and better verbal learning performance and speed of processing than unemployed BD patients. The correlation between neurocognitive functioning and social functioning was stronger in the employed group than in the unemployed group. There were no significant differences in neurocognitive and social functioning between the BD-I and BD-II groups, and the correlation between neurocognitive functioning and social functioning was similar between the BD-I and BD-II groups.

Conclusion

Employed BD patients may present greater occupational functioning and interpersonal relationships, as well as better verbal learning performance and speed of processing.

Background

As a recurrent and chronic illness, bipolar disorder (BD) is a complex mental disorder characterized by pathological mood instability (Grande et al., 2016), that affects 2.4% of the global population (Kathleen et al., 2011). The lifetime prevalence of bipolar disorder was 0.6% according to the China Mental Health Survey in 2012 (Huang et al., 2019). Bipolar disorder is reported to be one of the top 20 causes of the global disease burden (Vos et al., 2013), with documented moderate to severe social and neurocognitive functional impairment (Levy & Manove, 2012).

Despite optimal treatment with mood stabilizers and second-generation antipsychotics, social and neurocognitive dysfunction in BD remains a serious problem. It is reported that 60–70% of BD patients have varying degrees of impairment in social and occupational functions (Henry et al., 2015) and BD patients still suffer from impairment of attention, memory, information processing speed and executive function even in the stable period (Roux et
al., 2019). Social functioning is traditionally involved in autonomy, study, work, have leisure time, and engage in social relationships (Zarate et al., 2000). Previous studies have shown that gaps between clinical symptomatic remission and social and neurocognitive functioning are largely independent of clinical variables, such as the number of episodes, number of hospitalizations, and duration of illness (Martinez-Aran et al., 2007). Social dysfunction manifests itself in a subgroup of patients even at the onset of the disease (Tohen et al., 2000). Some findings have indicated that social and neurocognitive functional impairment persists among patients with bipolar disorder, not only at the acute stage of the illness but also in remission (Martinez-Aran et al., 2007; Suppes et al., 2001).

Despite the chronicity and high frequency of social and neurocognitive dysfunction in patients with BD, the possible associations between clinical symptoms and social and neurocognitive functioning in euthymic patients remain uncertain. Studies have identified depressive symptoms as a major cause of poor social functional outcomes in BD patients (Bonnin et al., 2010). Poor neurocognitive functioning, especially verbal memory deficits, are associated with poor social functioning (Bonnin et al., 2010). There is a complex interaction among neurocognitive function, social function outcome and residual depressive symptoms.

Although there are apparent social function deficits in BD patients (Hacimusalar et al., 2019), research on the differences in social function impairments between the bipolar disorder type I (BD-I) and type II (BD-II) is still inconsistent. Ruggero et al. did not find a difference in Global Assessment Functioning (GAF) scores between BD-I and BD-II patients (Ruggero et al., 2007). However, recent studies have found differences in social function between those with BD-I and BD-II in the early stage of BD (Vinberg et al., 2017), suggesting that BD-II patients presented more cognitive complaints and lower overall functioning. In contrast, Dell’Osso and his colleagues found that remitted BD and BD-I patients had significantly lower GAF scores than BD-II patients (Dell’Osso et al., 2007). The reasons for the discrepancy in functional outcomes may be due to different assessment tools, duration of illness, education level, and pre-disease cognitive reserve (Baune, et al., 2015; Vinberg et al., 2017). In terms of neurocognitive function, the prevailing view was that BD-II patients perform better than BD-I patients, but recent research has tended to support the opinion that there is no difference in neurocognitive function between the BD subtypes (Tsitsipa and Fountoulakis, 2015). A meta-analysis concluded that neurocognitive differences between BD-I and BD-II are not distinct (Bora, 2018), which is in line with Dittmann et al.’s findings (Dittmann et al., 2008).

Previous findings (Keck et al., 1998; Wingo et al., 2010) have revealed that social functional outcomes are associated with occupational status. Recent findings have indicated that social function may play a core role in employment development in BD patients (Bonnin et al., 2019). Patients with severe impairments of social function have a relatively higher rate of unemployment (Solé et al., 2018). However, few studies on the relationships between social dysfunction and occupational status have been conducted in BD patients. Moreover, the correlation between neurocognitive impairment and occupational status in BD patients has been mentioned in earlier studies. Altshuler et al.’s findings showed that sustained neurocognitive impairment may lead to decreased occupational opportunities (Altshuler et al., 2007). Further research suggested that working memory and speed of processing were significantly associated with occupational function (Bearden et al., 2011). Although the details of these findings differed, they all supported an association between neurocognitive function and occupational status.
Overall, studies of the differences in functional impairment between BD subtypes and between occupational status are still scarce. The differences in social and neurocognitive functioning between BD subtypes and between occupational status, as well as correlations between social and neurocognitive impairment and occupational status or subtypes in BD patients need further exploration. The purpose of this study was to examine the functional differences between occupational status and between subtypes in order to compare the correlation of neurocognition and psychosocial function in BD patients based on different occupational status and BD subtypes.

Methods

Participants

Euthymic patients with bipolar disorder aged 18–60 years were recruited consecutively from Tianjin Anding Hospital between June and December 2018. Euthymic BD patients were defined as those with YMRS total score \( \leq 6 \), HDRS total score \( \leq 8 \) and in clinical remission for at least one month (Zhang et al., 2018). Demographic information was obtained during clinical interviews. All patients met the diagnosis criteria for bipolar disorder according to the Diagnostic and Statistical Manual of Mental Disorders-fourth edition (DSM-IV) (APA, 1994). We had to exclude those patients who had manifested severe physical diseases or alcohol or substance abuse and other severe psychiatric disorders, such as schizophrenia and mental retardation. In addition, those who had received any psychological treatment, such as cognitive behavioral therapy and psychoeducation within the past six months were not included in this study. Patients who had received MECT treatment within the past six months were excluded. All recruited BD patients were permitted to use typical antipsychotic and mood stabilizer medications. We received approval from the Ethics Committee of Tianjin Anding Hospital. Written informed consent was obtained from all participants.

Occupational data was obtained as part of the clinical interview. All participants were divided into two groups based on current occupational status: employed and unemployed. Participants in the employed group consisted of individuals who were currently employed full-time (any occupational category) or enrolled as a full-time student. All participants in the unemployed group consisted of those who were currently unemployed. Participants who were retired (n = 1) or a "housewife" (n = 2) were excluded to clearly define both employed and unemployed groups (Ryan et al., 2013).

Assessments and Materials

We collected sociodemographic characteristics including age, sex, education level, employment, duration of BD, family history and medication treatments in the clinical interview. The severity of the depressive and manic/hypomanic symptoms was measured using the 17-item Hamilton Depression Rating Scale (HDRS-17) (Xie and Shen 1984) and the Young Mania Rating Scale (YMRS) (Young et al., 1978), respectively. Social functional impairment was measured using the Functioning Assessment Short Test (FAST) (Rosa et al., 2007); the Chinese version of the FAST has been shown to have satisfactory reliability and validity in BD patients (Zhang et al., 2018). The FAST comprises 24 items assessing six domains of functioning: autonomy, occupational functioning, cognitive functioning, financial issues, interpersonal relationships, and leisure time (Rosa et al., 2007). The total score is the sum of all items, with a higher score indicating more severe functional impairment. The
neurocognitive assessment tool was The MATRICS Consensus Cognitive Battery (MCCB), conducted by an experienced psychiatrist. The Chinese version of MCCB was translated and revised by Yu Xin’s team from the Sixth College of Peking University and established the Chinese population norm, which has excellent psychometric characteristics (Shi et al., 2015). The speed of processing was estimated with Trail Making Test-A (TMT-A) (Lezak et al., 2004) and the Symbol Digit Modalities Test (SDMT) (Smith, 1982); verbal learning and visual memory were rated by the Hopkins Verbal Learning Tests-Revised (HVLT-R) and Brief Visuospatial Memory Test-Revised (BVMT-R) (Nuechterlein et al., 2008). Executive function was evaluated by the Stroop Color-Word Test (SCWT) (Golden et al., 1978). Color blindness was assessed in all participants before applying Color Stroop Task.

**Statistical analysis**

Data analysis was performed using SPSS Version 25.0 (SPSS, Chicago, IL, USA). Demographic characteristics and clinical variables were compared between the groups using t-tests and chi-squared tests. Furthermore, an independent samples t-test was conducted to compare the differences in the HDRS, YMRS, FAST and neurocognitive measures between groups. The correlations between occupational status, demographic risk factors, clinical symptoms, social functional impairment and neurocognitive measures were assessed by Pearson’s partial correlation coefficients. All statistical tests were two-tailed, and alpha was set at 0.05.

**Results**

**Demographic characteristics for all participants**

Ninety euthymic BD patients were screened in this study, and data for nine patients were excluded due to incomplete assessments. A total of 81 patients (43 male and 38 female) completed all assessments in the interview, including 45 patients with BD-I, 36 patients with BD-II, 45 employed BD patients, and 33 unemployed BD patients. No significant differences were found in demographic characteristics, including age, educational level, marital status, family history, course of BD, and number of episodes, between genders or between BD subtypes. Moreover, we did not find differences in most demographic variables, except for educational levels, between the employed and unemployed groups (see table 1).

**Table 1** Demographic characteristics between employed and unemployed participants.
| Items                      | employed (n = 45) | unemployed (n = 36) | $\chi^2/t$ | $p$ value |
|---------------------------|-------------------|---------------------|-----------|-----------|
| Gender(female) (n(%))     | 21 (46.7%)        | 17 (47.2%)          | 0.002     | 0.96      |
| Age (year)                | 35.3 (7.2)        | 32.8 (10.2)         | 1.30      | 0.22      |
| Education levels (year)   | 14.0 (2.8)        | 11.8 (3.3)          | 3.23      | 0.002     |
| Marital status (n(%))     |                   |                     |           |           |
| -single                   | 9 (20%)           | 18 (50%)            |           |           |
| -married                  | 34 (75.6%)        | 10 (27.8%)          |           |           |
| -divorced                 | 2 (4.4%)          | 7 (19.4%)           |           |           |
| Duration of BD (year)     | 7.6 (5.5)         | 8.6 (6.1)           | -0.85     | 0.40      |
| Family history (yes/no)   | 8/37              | 8/28                | 0.25      | 0.62      |
| Number of episodes        | 3.4 (1.8)         | 3.6 (2.2)           | -0.54     | 0.59      |

**Comparison of the clinical variables between the groups**

We compared the clinical measures of HDRS, YMRS, and FAST (including its six domains), and the neurocognitive measures between genders, as well as between BD subtype groups. No significant differences in any of the above-mentioned variables were found between genders (all $p$ values > 0.05). There were highly significant group differences in the FAST total scores (including the occupational functioning, cognitive functioning and interpersonal relationship domains) between BD subtype groups. BD-I group had lower scores for these variables than BD-II group, but no differences in neurocognitive measures were found between BD subtype groups (see Table 2). We also compared the clinical measures and the functional measures between the employed group and unemployed group. We found no group differences in HDRS or YMRS scores ($p > 0.05$), but there were highly significant group differences in the FAST total scores, as well as in autonomy, occupational functioning, and interpersonal relationship domains, but minor differences in cognitive functioning domain. Employed patients reported lower scores in these domains than unemployed patients. In addition, the employed group reported higher scores on the Symbol Digit Modalities Test ($p < 0.001$) and Hopkins Verbal Learning Tests-Revised ($p < 0.001$) than the unemployed group. No other differences in neurocognitive measures were found between the employed group and unemployed group (see Table 2).

**Table 2** Comparisons of clinical variables by occupational states and by BD subtypes
| Items                        | employed (n = 45) | unemployed (n = 33) | t     | p value | BD-I (n = 45) | BD-II (n = 36) | t     | p value |
|-----------------------------|------------------|---------------------|-------|---------|--------------|---------------|-------|---------|
| HDRS                        | 3.7(0.9)         | 3.5(1.1)            | 0.96  | 0.338   | 3.6(1.0)     | 3.7(0.9)      | -0.68 | 0.501   |
| YMRS                        | 3.0(1.0)         | 3.5(1.3)            | -1.88 | 0.064   | 3.8(0.9)     | 3.6(1.4)      | 0.27  | 0.131   |
| FAST total                  | 17.5(2.4)        | 25.6(2.2)           | -15.76| < 0.001 | 19.5(4.0)    | 23.1(4.7)     | -3.81 | < 0.001 |
| -autonomy                   | 1.5(0.5)         | 1.9(0.7)            | -3.07 | 0.003   | 1.6(0.6)     | 1.8(0.6)      | 1.47  | 0.145   |
| -occupational functioning    | 5.2(1.3)         | 9.0(1.0)            | -15.13| < 0.001 | 6.1(1.8)     | 7.8(2.3)      | 3.64  | < 0.001 |
| -cognitive functioning       | 2.1(0.5)         | 2.4(0.5)            | -2.01 | 0.048   | 2.1(0.5)     | 2.3(0.5)      | 2.05  | 0.044   |
| -financial issues            | 1.6(0.5)         | 1.7(0.5)            | -0.87 | 0.385   | 1.7(0.5)     | 1.6(0.5)      | 0.51  | 0.610   |
| -interpersonal relationships | 5.3(1.2)         | 9.1(1.2)            | -13.61| < 0.001 | 6.3(2.0)     | 7.9(2.2)      | 3.39  | 0.001   |
| -leisure time               | 1.8(0.5)         | 1.6(0.5)            | 1.08  | 0.286   | 1.7(0.5)     | 1.7(0.5)      | 0.15  | 0.879   |
| TMT-A                       | 38.7(9.9)        | 38.6(9.1)           | 0.04  | 0.971   | 39.4(9.8)    | 37.8(9.2)     | 0.76  | 0.447   |
| SDMT                        | 49.1(5.7)        | 40.2(8.9)           | 5.21  | < 0.001 | 46.3(8.5)    | 43.8(8.5)     | 1.30  | 0.198   |
| HVLT-R                      | 25.6(3.6)        | 19.7(2.6)           | 8.17  | < 0.001 | 23.7(4.4)    | 22.1(4.1)     | 1.68  | 0.096   |
| BVMT-R                      | 22.7(4.8)        | 22.3(4.8)           | 0.34  | 0.735   | 22.0(4.7)    | 23.2(4.7)     | -1.17 | 0.244   |
| SCWT(total)                 | 179.4(28.7)      | 177.3(31.5)         | 0.32  | 0.753   | 177.7(30.3)  | 179.4(29.6)   | -0.26 | 0.797   |

Note: BD(bipolar Disorder); TMT-A (the Trail Making Test-A); SDMT (Symbol Digit Modalities Test); HVLT-R (Hopkins Verbal Learning Tests-Revised); BVMT-R (Brief Visuospatial Memory Test-Revised); and SCWT (Stroop Color-Word Test).

**Associations between total FAST scores, neurocognitive measures and other clinical variables in stratified sampling.**

We examined the correlation between FAST scores and neurocognitive measures and other variables across the BD subtypes. Our results showed that the correlations between FAST scores and neurocognitive measures were similar in the BD-I group and BD-II group. We found that FAST total scores, interpersonal relationships and occupational functioning were negatively associated with higher scores on the Symbol Digit Modalities Test and Hopkins Verbal Learning Tests-Revised in both BD subtypes. In addition, leisure time was moderately correlated with scores on the Brief Visuospatial Memory Test-Revised, and financial issues were moderately correlated with scores on the Hopkins Verbal Learning Tests-Revised in the BD-I group (See Figs. 1, 2).
We also analyzed the correlation between FAST scores and neurocognitive measures and other variables across the employed and unemployed group. As it was statistically significantly different between the employed/unemployed, we used education level as a control variable in the partial correlation analysis. In the employed group, we found that the autonomy domain was negatively related to Stroop Color-Word Test scores and occupational functioning; financial issues was negatively correlated with the Hopkins Verbal Learning Test-Revised scores and with interpersonal relationships; and leisure time was correlated with scores on the Symbol Digit Modalities Test and Brief Visuospatial Memory Test-Revised. The FAST total score was negatively associated with higher scores on the Symbol Digit Modalities Test, Hopkins Verbal Learning Test-Revised, Brief Visuospatial Memory Test-Revised and Stroop Color-Word Test (see Fig. 3).

In the unemployed group, we found that only occupational functioning and cognitive functioning were related to scores on the Symbol Digit Modalities Test. No associations were found between FAST total scores or specific domains and the neurocognitive measures (see Fig. 4).

Discussion

This preliminary study examined the associations between clinical symptoms, social function and neurocognitive function among 81 euthymic BD patients stratified by occupational status (employed/unemployed) and subgroups of DSM-IV BD (BD-I and BD-II). In line with earlier findings (DelBello et al., 2007; Wingo et al., 2010), our findings showed that employed BD patients displayed greater social functioning (autonomy, occupational functioning, and interpersonal relationships) and performed better in verbal learning and processing speed than unemployed patients, indicating that employed BD patients could develop stronger social functions and some neurocognitive functions. In a previous cluster analysis study with euthymic BD patients, the group with lower functioning, measured by FAST scores, showed the highest unemployment rate, which indicated the main areas of functional loss in autonomy, occupational functioning, cognition and interpersonal relationships (Solé et al., 2018). This is basically consistent with our findings. Some studies reported that employed BD patients showed greater neurocognitive functioning measured by the Assessment of Neuropsychological Status (RBANS), especially in the verbal memory domain (Dickerson et al., 2004). Another study clearly showed that BD patients who have jobs may show better executive function than those without jobs (Altshuler et al., 2007), which is consistent with our results.

Further correlation analysis under stratification showed that social function outcomes had close ties with neurocognitive function among employed BD patients. There was a stronger correlation between neurocognitive function and the occupational and interpersonal relationship domains in the FAST, followed by the financial issues and autonomy domains. Verbal learning measures were predominantly associated with the occupational domain of the FAST in the employed group. Previous studies have demonstrated a strong correlation between verbal learning ability and occupational status (Dickerson et al., 2004), and our results confirmed this association. In addition, processing speed was also significantly correlated with the leisure time and interpersonal relationship domains in employed BD patients. We considered that employed person is more likely to participate in social activity, to facilitate self-management, and to promote learning and information-processing capacity. Many papers (Andreou et al., 2013; Bonnin et al., 2014; Bora, 2018; Duarte et al., 2016; Konstantakopoulos et al., 2016; Sanchez-Moreno et al., 2018; Szmulewicz et al., 2018) have reported that social functional impairment could be associated with neurocognitive measures. Remarkably the measures of processing speed, visual memory and verbal learning were powerful determinants of functional impairment in these studies, consistent with our
findings for the employed group. Bearden et al. also evidenced that baseline cognitive impairment across multiple domains, particularly working memory and speed of processing, were significantly associated with concurrent occupational function impairment (Bearden et al., 2011). Jaeger et al. found that baseline attention and speed of processing domains could predict functional outcomes (including occupational function) over a 12-month period (Jaeger et al., 2007). Most jobs require relatively strong abilities in the areas of learning, memory and processing speed. Thus, the improvement of these functions may benefit occupational performance. Unfortunately, we found that the correlation between neurocognitive function and social function significantly weakened in the unemployed group compared with the employed group (see Figs. 3 and 4), demonstrating the poorer association between social function and neurocognition in unemployed BD patients. We presume that occupational status may be a core factor in promoting overall functional development in euthymic bipolar patients.

Our findings also testified the neurocognitive differences between the BD subtypes. There were no differences in neurocognitive measures between the BD subtypes, which is in line with earlier findings (Dittmann et al., 2008). Dittmann and his colleagues evaluated psychomotor speed, working memory, verbal learning, visual / constructional abilities and executive functions in euthymic bipolar patients by using the Repeatable Battery for the Assessment of Neuropsychological Status (RBANS) (Randolph et al, 1998) and the Trail Making Test (TMT) A and B (Lezak et al., 2004, Lu and Bigler., 2000). They also concluded that patients with both BD subtypes had similar levels of neurocognitive deficits. Similarly, another meta-analysis reported that neurocognitive differences between clinical BD subtypes were very subtle and not significant (Bora, 2018). However, some studies have obtained different conclusions; for example, one study indicated that BD I patients performed worse than BD II patients in all areas of cognitive function except for working memory (Schenkel et al, 2012). Another meta-analysis revealed that BD-II patients may present deficits in working memory and executive function, and more than half of the studies showed worse verbal memory. This moderate difference between BD subtypes may be complicated due to residual symptoms, number of episodes, age at illness onset, etc. (Solé et al, 2011).

Furthermore, significant differences in FAST scores and its six domains between the BD subtypes showed that BD-I patients had excellent total functioning, especially in occupational functioning and interpersonal relationships. Our findings are consistent with previous studies that showed that BD-I patients had better social function than BD-II patients did (Vinberg et al., 2017; Kupka et al., 2007; Vieta, 2010). We considered that BD-I patients with mania were more likely to seek opportunities for social activity and interpersonal communication. In contrast, Dell’Osso and his colleagues found that bipolar patients with remitted BD and BD-I had significantly lower GAF scores than those with BD-II (Dell’Osso et al., 2007). The reasons for the discrepancy in functional outcomes may be related to functioning measures, duration of illness, education levels, and pre-disease cognitive performance (Chen, et al., 2019; Baune, et al., 2015). Besides, our correlation analyses did not suggest functional differences between the BD subtypes, indicating the same associations between processing speed and occupational functioning and interpersonal relationships both in the BD-I and BD-II patients (Duarte et al., 2016). We speculate that both BD-I and BD-II patients may exhibit similar functional impairments even in euthymia.

Our results did not show significant differences in demographic characteristics, clinical measures or social or neurocognitive functioning measures between genders. Some studies have reported that male patients could show poorer social and neurocognitive functional outcomes than female patients (Sanchez-Moreno et al., 2018; Vaskinn et al., 2011), but Bücker et al. reported that males had better working memory and sustained attention than females (Bücker et al, 2014). Further study is needed to verify this gender difference in total functioning based on a larger sample size.
Several limitations of this study should be taken into consideration. First, cognitive functional assessments are scarce and do not reflect all dimensions of neurocognitive functioning in BD patients. The outcomes with no significant differences in neurocognitive measures between BD subtypes need to be tested using full-scale instruments in future research. Second, although occupational status can be viewed as an advantage of this study, current occupational status does not reflect the quality or stability of job performance, which is a particularly important area for understanding functional recovery and deserves further clarification. In addition, some studies have pointed out that the definition of occupation may influence the final assessment results (Duarte et al., 2016; Kozma et al., 2010). A prior study defined employment as including fulfilling domestic responsibilities at home or attending school (Altshuler et al., 2007), thus this association between total functioning and occupational status should be cautiously elucidated. Third, the possible effects of psychotropic medications on social function and neurocognitive function should be considered, and typical antipsychotics and partial mood stabilizers could hinder total functioning performance (Dias et al., 2012). Finally, the sample size was not sufficient, which could reduce the statistical power when conducting comparison and correlation analysis.

**Conclusions**

In summary, our findings mainly revealed that employed BD patients may present better social and neurocognitive functions, and stronger associations between social functioning and neurocognitive functioning were found in employed BD patients than in unemployed BD patients. Moreover, euthymic BD-I patients may perform better occupational functioning and interpersonal relationships compared to those of euthymic BD-II patients. However, no differences in neurocognitive impairments were found between the BD subtypes. This preliminary finding indicated that occupational status may be an important determinant that contributes to functional recovery in euthymic BD patients.

**List Of Abbreviations**

BD: bipolar disorder

HDRS-17: 17-item Hamilton Depression Rating Scale

YMRS: Young Mania Rating Scale

FAST: Functioning Assessment Short Test

MCCB: The MATRICS Consensus Cognitive Battery

TMT-A: Trail Making Test-A

SDMT: Symbol Digit Modalities Test

HVLT-R: Hopkins Verbal Learning Tests-Revised

BVMT-R: Brief Visuospatial Memory Test-Revised

SCWT: Stroop Color-Word Test
Declarations

Ethics approval and consent to participate

We received approval from the Ethics Committee of Tianjin Anding Hospital. Written informed consent was obtained from all participants. All methods were carried out in accordance with relevant guidelines and regulations.

Consent for publication

Not applicable

Availability of data and materials

The datasets used and analysed during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors of this paper report no conflicts of interest in connection with this manuscript.

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Authors' contributions

Yong Zhang: Conceptualization, Methodology, Resources. Xinyu Liu: Data curation, Formal analysis, Writing-Original draft preparation. Xiaojuan Ma: Supervision, Project administration. Wenchen Wang: Data curation, Investigation, Formal analysis. Jian Zhang: Data curation. Xia Sun: Data curation, Software. All authors contributed to and have approved the final manuscript.

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