The Association Between Suicide Risk and Affective Temperaments in First-Episode and Neuroleptic-Naïve Major Depressive Disorder

Lu Yin
Peking University HuiLongGuan Clinical Medical School
Ting-Ting Wang
Bengbu Medical College
Yan-Yan Wei
Peking University HuiLongGuan Clinical Medical School
Li-Gang Zhang
Peking University HuiLongGuan Clinical Medical School
Shuang-Jiang Zhou
Peking University HuiLongGuan Clinical Medical School
Li-Ye Zhang
Peking University HuiLongGuan Clinical Medical School
Jian-Jin Yu
Peking University HuiLongGuan Clinical Medical School
Hong-Juan Li
Peking University HuiLongGuan Clinical Medical School
Jing-Xu Chen (chenjx1110@163.com)
Peking University HuiLongGuan Clinical Medical School

Research Article

Keywords: suicide risk, temperament, depression, first-episode, neuroleptic naïve, TEMPS-A

Posted Date: October 15th, 2021

DOI: https://doi.org/10.21203/rs.3.rs-934338/v1

Abstract

Background

Suicide risk is associated with depression. Affective temperaments may play a role in this risk. We explored the relationship between affective temperaments and suicide and identified some traits that can predict suicide risk in depression.

Methods

We analyzed the results of Temperament Evaluation of the Memphis, Pisa, Paris, and San Diego Auto-questionnaire (TEMPS-A) in 284 participants recruited from a psychiatric clinic and the community in Beijing and compared the subscale scores (cyclothymic, dysthymic, anxious, irritable and hyperthymic) among major depressive disorder (MDD) versus the general population as well as depressive patients with versus without suicide risk, using student's test, Chi-square test, rank sum test, multivariable regression modeling and receiver operating characteristic (ROC) analysis.

Results

The incidence of suicidal risk in depressive subjects was 47.62% (80/168). Being unmarried (P<0.001), unemployment (P=0.007) and temperaments of dysthymic, cyclothymic, anxious, and irritable scores (all P<0.05) were significantly more prevalent in depressive patients than in the general population. A young age (P<0.001), female sex (P=0.037), being unmarried (P=0.001), more severe depression (P<0.001), and dysthymic, anxious and cyclothymic temperament (all P<0.05) were significantly more prevalent in depressive disorder patients with suicide risk than in those without suicide risk. The logistic regression analysis showed that younger age (OR=0.937, 95% CI 0.905~0.970), female sex (OR=2.606, 95% CI 1.142~5.948), more severe depression (OR=1.145, 95% CI 1.063~1.234), cyclothymic temperament (OR=1.275, 95% CI 1.102~1.475) and dysthymic temperament (OR=1.265, 95% CI 1.037~1.542) were all independently associated with high suicidal risk in first-episode major depressive patients (P<0.05). By ROC analysis, the area under the compound factor (age, sex, HAMD score without the 3rd item, cyclothymic and dysthymic temperament) was 0.853 (95% CI 0.790~0.903).

Conclusion

The suicide rate in first-episode neuroleptic-naïve major depressive disorder (MDD) subjects was higher than we thought. Temperament traits differ between the general population and those with major depressive disorder. Major depressive disorder subjects with much more severe depressive symptoms and cyclothymic or dysthymic temperament were at high risk of suicide. Compound factors (age, sex, HAMD score without the 3rd item, cyclothymic and dysthymic temperament score) could be predictors of suicide risk in the clinic.

1. Introduction

Suicide, the act of intentionally injuring oneself at the will of death, including attempt, preparation, ideation and plan, is a challenging and complex public health problem for all countries [1]. According to WHO website data, close to 800,000 people die by suicide worldwide each year [2]. The latest data from the United States referenced 44,965 people dead of suicide in 2016; meanwhile, that number in China was 9 per 100,000 population (approximately 126,000 people) and ranking 13 in all-cause mortality in 2017[3]. There are many reasons people commit suicide, such as physical diseases, mental disorders, life stress or events. Suicide can occur at any time of life, but in young people aged 15 to 29, it ranks second among causes of death[4]. Studies on factors leading to suicide have been undertaken for decades. The dimensions include but are not limited to genes, neuroanatomy, biochemistry, the environment, nutrition, physical and mental diseases, mainly depression and alcohol abuse[2, 5–9], but suicide prevention remains an area of uncertainty and needs further research[10].

Suicide prevention should focus on mental disorders, especially major depressive disorder (MDD). According to a cross-sectional epidemiological nationwide study conducted during 2013-2015 in China, the lifetime prevalence of mood disorder was 7.4%[11], and the lifetime prevalence of suicidal ideation, plan and attempt were 53.1%, 17.5% and 23.7%, respectively[12], which were much higher than those in the Chinese general population (3.1%, 0.9% and 1.0%)[13].

Temperament describes individual differences in behavior regulated based on biology[14]. It derives from the original theory of Hippocrates and Galen about chemical imbalance and modern studies of neurochemistry and psychiatry[14]. Temperament traits are diverse among different populations, and there have been some independent studies on depressive patients and the general population[15–17], but there is still a lack of comparative studies between them.

In China, the majority of first-episode depressive patients will present to primary care, with problems other than mood disorder[18]. Due to the low recognition rate, many self-harm patients could not wait to perform their suicide act before they went to psychiatric clinics, which still lacks data but provides much news. For the purpose of suicide prevention, we need to find a relationship between suicide and temperament. Two studies evaluated participants from the general population and patients with depressive disorder assessed by the Temperament Evaluation of the Memphis, Pisa, Paris, and San Diego Auto-questionnaire (TEMPS-A) and showed that cyclothymic, irritable, and especially dysthymic temperaments might be important factors in self-harm in adolescents[19]. In depressive patients, cyclothymic and dysthymic temperaments were associated with suicide acts in bipolar disorder compared with major depressive disorder[20]. These studies are the basis of our further research on temperament traits in first-episode neuroleptic-naïve major depressive disorder. We know that temperament cannot solely predict suicide risk in either the general population or depressive disorders, but we hope to sketch features associated with a high suicide rate and find some common characteristics, as either a theoretical foundation or practical guidance, for clinicians.

2. Methods

2.1 Subjects

All subjects were recruited from February 2018 to September 2019 in the outpatient clinic of Beijing HuiLongGuan Hospital, affiliated with the Clinical Medical College of Peking University, China. All participants provided written informed consent that was approved by the institutional review board of the Beijing HuiLongGuan Hospital, Peking University. The inclusion criteria were age 18–60 years, Han ethnicity, first episode, naïve drug use, educational level above junior middle school and major depressive disorder diagnosed by the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5) on the consensus of two independent senior psychiatrists titled with associate chief physician or above. Patients were excluded if they had an organic mental disorder, substance use disorder, mental retardation, neurological illness, psychotic disorder or were pregnant or breastfeeding.

The healthy controls were enrolled from the community near the hospital according to the criteria of Han Chinese individuals without any personal or family history of mental illness. The exclusion criteria were the same as those for the patient group.

2.2 Instruments

Major depressive disorder was diagnosed by the Chinese version of the Mini International Neuropsychiatric Interview (M.I.N.I.), Version 5.0[21], a short-structured interview including six questions on suicidality, which is a useful tool for assessing suicide risk[22–24]. The suicide risk section scores ranged from 0 to 33. As in our previous study, patients with a score <6 were classified as having nonsuicidal risk, and those with a score ≥6 were classified as having suicide risk[9]. The 17-item Hamilton Depression Rating Scale (HAMD-17) was used to assess the severity of depressive symptoms[25]. The third (suicidal) item was excluded when evaluating the association between suicide risk and severity of depression. Considering the rating consistency and reliability of our study, five psychiatrists attended a training session on the use of the M.I.N.I. and HAMD-17.

Effective temperaments were evaluated by the short version of the Temperament Evaluation of the Memphis, Pisa, Paris, and San Diego Auto-questionnaire (TEMPS-A)[26, 27]. The TEMPS-A is a self-report questionnaire containing 39 items measuring five affective temperament tendencies of people: dysthymia, cyclothymia, hyperthymia, anxiety, and irritation. Every subject received a “Z-score” on each of the five temperament dimensions. The dominant temperament is generated from the comparison of the five

Z-scores. The range around one Z-score (Z1) of the mean (mean±1 SD) is considered the “standard” score, “mild deviation” is the interval between Z1 and Z2 (mean±2 SD) and “moderate deviation” is the Z-score equal to or above Z2 (mean±2 SD).

2.3 Statistical analysis

Data are presented as the means ± standard deviations, proportions or medians. Preliminary tests of association used standard bivariate comparisons based on analysis of variance methods or rank-sum tests for continuous data and contingency tables for categorical data. Multiple comparisons between suicidal and nonsuicidal risk depressive patients and healthy controls were tested by the Kruskal-Wallis H test, and the resulting P-values were adjusted. The Mann–Whitney U test was used for continuous variables (including the total score of temperament dimensions). All factors statistically significant in preliminary tests were put into logistic regression modeling, and the alpha level was set at 5%. Factors supported by logistic regression modeling were included in receiver operating characteristic (ROC) analyses to compute the area under the curve (AUC) as a percentage. Analyses were performed using the commercial software SPSS version 20.0.

3. Results

3.1 Demographic characteristics of major depressive disorder (MDD) patients and healthy controls (HCs)

There were significant differences in marital status (OR=4.300, 95% CI 2.580~7.166) and vocational status (OR=3.144, 95% CI 1.311~7.398) (Table 1). Scores for both groups on dysthymic, cyclothymic, anxious, and irritable temperaments were significantly different (all P<0.001). Compared with healthy people, the depressive patients had higher scores on all temperaments except hyperthymic, especially on dysthymic (U=1859.50, z=11.74) and cyclothymic temperaments (U=2728.00, z=10.32) (Table 2). Scores of hyperthymic temperament for healthy individuals (mean rank=136.40) and first-episode MDD patients (mean rank=146.71) were not significantly different (P=0.290) using an exact sampling distribution for U (Table 2).

Table 1
Comparisons of demographic characteristics between MDD patients and HCs.

Variables	MDD	HCs	Statistic	OR	95%CI		*P*-value
	(N=168)	(N=116)	(*t* or x^2)		lower	upper	
Age (years), Mean (SD)	30.40(12.50)	32.15(9.46)	1.27	1.014	0.993	1.035	0.205
Gender, n (%)			0.01	1.031	0.630	1.685	0.904
Male	62(36.90)	42(36.21)					
Female	106(63.10)	74(63.79)					
Education, n (%)			0.39	0.847	0.502	1.429	0.533
High school and below (< 12 years)	45(26.79)	35(30.17)					
Above high school (≧ 12 years)	123(73.21)	81(69.83)					
Marital status, n (%)			32.96	4.300	2.580	7.166	<0.001*
Married	62(36.90)	83(71.55)					
Unmarried	106(63.10)	33(28.45)					
Vocational status, n (%)			7.18	3.114	1.311	7.398	0.007*
On the job	140(83.33)	109(93.97)					
Unemployment	28(16.67)	7(6.03)					
MDD: Major depressive disorder; HCs: Healthy controls							
* statistically significant							

Table 2
Comparisons of TEMPS-A between MDD and HCs.

Variables	MDD (N=168)				HCs (N=116)				Statistic U	Statistic z	*P*-value
	mean rank	Median	95% CI		mean rank	Median	95% CI				
Dysthymic temperament	189.43	5	4.26	4.93	74.53	0	0.61	1.20	1859.50	11.74	<0.001*
Cyclothymic temperament	184.07	7	6.40	7.30	82.29	1	1.80	2.85	2728.00	10.32	<0.001*
Anxious temperament	177.59	2	1.55	1.90	91.68	0	0.32	0.59	3849.00	9.06	<0.001*
Irritable temperament	163.70	2	1.64	2.18	111.79	0	0.62	1.10	6182.00	5.46	<0.001*
Hyperthymic temperament	146.71	2	2.08	2.73	136.40	2	1.79	2.61	9036.00	1.06	0.290
MDD: Major depressive disorder; HCs: Healthy controls											
* statistically significant											

3.2 Demographic and temperament characteristics of suicidal and nonsuicidal MDD

Comparing the differences between suicidal and nonsuicidal subgroups of the first-episode neuroleptic-naïve MDD, the younger the current age, the higher the risk of suicide (OR=1.070, 95%CI 1.037~1.104), suicidal risk depressive patients (SR-P) saw doctors at an age of 25.79±10.51 years, and the nonsuicidal risk depressive patients (NSR-P) saw doctors at 34.6±10.51 years. Females had a significantly higher risk of suicide than males (OR=0.507, 95% CI 0.267~0.963), and the constituent ratio of females in the suicide group was 71.25%. Unmarried people (76.25%) had a significantly higher risk of suicide than married people (OR=3.068, 95% CI 1.581~5.955). People with higher HAMD scores had a significantly higher suicide risk (OR=0.873, 95% CI 0.823~0.925). However, employment and educational level were not significant suicide risk factors in first-episode neuroleptic-naïve MDD. The median illness durations of suicidal and nonsuicidal patients were 6.5 and 6 months, respectively, and the differences were not significant (Z=0.89, P=0.374) (all P>0.05) (Table 3).

Upon comparing the differences in temperament scores in suicidal, nonsuicidal, and healthy control subgroups in all five affective temperament groups, the distribution of scores was not the same (Fig. 1). Scores for cyclothymic temperament (H=121.932, P<0.001), dysthymic temperament (H=150.393, P<0.001), irritable temperament (H=35.430, P<0.001), and anxious temperament (H=92.437, P<0.001) were significantly different. The median scores for dysthymic temperament were 6 (n=80) in the suicidal group, 4 (n=88) in the nonsuicidal group, and 0 (n=116) in the healthy control group. The median score of the whole was 3 (n=284). When Bonferroni correction was performed on statistical significance level of the pairwise comparison, the distributions of dysthymic temperament, cyclothymic and anxious scores between three subgroups were all statistically significant (all P<0.005) (Fig. 1), and irritable temperament showed no significant difference between the suicidal and the nonsuicidal subgroups (Z=2.381, adjusted P=0.052) (Table 4). The differences in the three subgroups in the hyperthymic temperament group were not significant (H=4.59, P=0.101). The scoring directions of the three subgroups in all temperaments were suicidal risk group > nonsuicidal risk group > healthy control group, except in hyperthymic temperament patients (Table 4) (Fig. 1).

Table 3
Comparisons of demographic and clinical characteristics between the suicidal and nonsuicidal groups

Variables	NSR-P	SR-P	Statistic	OR	95%CI		*P*-value
	(N=88)	(N=80)	(*t* or x^2or z)		lower	upper	
Age(years), mean (SD)[a]	34.60(12.73)	25.79(10.51)	4.91	1.070	1.037	1.104	<0.001*
Gender, n (%)			4.36	0.507	0.267	0.963	0.037*
Male	39 (44.31)	23 (28.75)					
Female	49 (55.68)	57 (71.25)					
Education, n (%)			0.30	1.211	0.611	2.398	0.584
High school and below (< 12 years)	22 (25.00)	23 (28.75)					
Above high school (≧ 12 years)	66 (75.00)	57 (71.25)					
Marital status, n (%)			11.35	3.068	1.581	5.955	0.001*
Married	43 (48.86)	19 (23.75)					
Unmarried	45 (51.14)	61 (76.25)					
Vocational status, n (%)			0.31	0.794	0.350	1.800	0.580
On the job	72 (81.82)	68 (85.00)					
Unemployment	16 (18.18)	12 (15.00)					
Duration of illness (months), median [b]	6.00	6.50	0.89	-	-	-	0.374
HAMD total scores, mean (SD) [a]	20.83(6.42)	25.61(6.61)	5.23	0.873	0.823	0.925	<0.001*
HAMD scores without item 3, mean (SD) [a,c]	19.89(5.02)	24.00(6.42)	4.60	0.883	0.833	0.936	<0.001*

SR: suicidal risk patient, NSR-P: nonsuicidal risk patient.

* statistically significant

[a] *t* tests; [b] rank sum tests

[c] third (suicide) item was removed from the total HAMD score.

Table 4. Comparisons of TEMPS-A subscales among the SR, NSR, and HC groups

	Statistic z			Post hoc tests adj. sig.			Mean rank	Median	Statistic H	*P*-value
	SR	NSR	HC	SR	NSR	HC				
Cyclothymic								5	121.93	<0.001*
SR	-	3.93	10.76	-	<0.001*	<0.001*	210.02	8		
NSR		-	6.77		-	<0.001*	160.49	6		
HC			-			-	62.29	1		
Dysthymic								3	150.39	<0.001*
SR	-	3.53	11.72	-	<0.001*	<0.001*	212.61	6		
NSR		-	8.19		-	<0.001*	168.36	4		
HC			-			-	74.53	0		
Hyperthymic								2	4.59	0.101
SR	-	-	-	-	-	-	-	1		
NSR	-	-	-	-	-	-	-	2		
HC	-	-	-	-	-	-	-	2		
Irritable								1	35.43	<0.001*
SR	-	2.38	5.86	-	0.052	<0.001*	178.89	2		
NSR		-	3.42		-	0.002*	149.90	1		
HC			-			-	111.79	0		
Anxious								1	92.44	<0.001*
SR	-	3.22	9.32	-	0.004*	<0.001*	198.05	2		
NSR		-	6.06		-	<0.001*	158.99	1		
HC			-			-	91.68	0		
SR: suicide risk; NSR: nonsuicide risk; and HC: healthy control.										
[a] Difference among three groups, Kruskal–Wallis test, P<0.001, Bonferroni correction: 0.05/5 tests=0.01.										

3.3 Multivariable logistic regression modeling and ROC

Factors preliminarily associated with suicide risk among depressive disorders were further tested by multivariable logistic regression modeling. The HAMD scale includes suicide items, so we subtracted the item-3 score from the HAMD summary score. The logistic regression modeling was statistically significant (x^2=72.846, P<0.001). The final factors independently associated with suicide risk were current age (OR=0.937, 95%CI 0.905~0.970), gender (OR=2.606, 95%CI 1.142~5.948), HAMD score without the 3rd item (OR=1.145, 95%CI 1.063~1.234), and cyclothymic (OR=1.275, 95%CI 1.102~1.475) and dysthymic temperaments (OR=1.265, 95%CI 1.037~1.542) (Table 5).

We used age, gender, HAMD score without the 3rd item, and cyclothymic and dysthymic temperament factors, which were significantly associated with suicide, in the multivariable regression modeling for ROC analysis. The independent five factors in the modeling were combined to obtain a predicted component score. The computed AUC was 85.3% (95% CI 0.790-0.903), well above a chance association (50.0%). The optimal differentiation of patients with versus without suicidal risk was associated with the presence prediction value, optimally yielding a sensitivity of 87.5% and a specificity of 68.18% (Fig. 2).

Table 5
Factors associated with suicidal risk in MDD: multivariate logistic regression analysis

Variates	*β*	OR	95%CI		*P-value*
			Lower	Upper	
Age	-0.065	0.937	0.905	0.970	<0.001
Gender (female/male)	0.958	2.606	1.142	5.948	0.023
HAMD score without the 3rd item [a]	0.136	1.145	1.063	1.234	<0.001
Cyclothymic temperament	0.243	1.275	1.102	1.475	0.001
Dysthymic temperament	0.235	1.265	1.037	1.542	0.020

[a] third(suicide) item was removed from the total HAMD score.

4. Discussion

To the best of our knowledge, this is the first study exploring the associations of temperament, depressive symptoms and suicide risk among first-episode neuroleptic-naïve MDD patients. In these subjects, we obtained the following: (1) suicide rate; (2) temperament trait differences from healthy controls; (3) cyclothymic and dysthymic temperament, as well as sex, age, and severe depression, were independent risk factors for suicide risk; and (4) the compound predictor for suicide risk in first-episode neuroleptic-naïve MDD.

Many studies have shown that depressive episode frequency is closely related to suicidal risk[8, 28, 29]. A higher episode frequency means a higher suicide rate. In this study, we found that the suicide rate of first-episode neuroleptic-naïve MDD was as high as 47.62%, close to previous studies of major depressive disorder from 47–69%[30–32], meaning that nearly half of the depressive patients had suicidal ideation or attempted suicide during their first major depressive episode.

Approximately 20% of the general population has a certain type of emotional temperament[16]. Generally, females are prone to be dysthymic, cyclothymic and anxious temperament, while males are prone to be hyperthymic and irritable temperament; some specific affective temperaments have a higher suicidal risk[16]. In this study, the direction of temperament in healthy controls was hyperthymic > irritable > anxious >cyclothymic >dysthymic, and in MDD, it was dysthymic > cyclothymic > anxious > irritable > hyperthymic, which is evidence that more females than males suffer from depression. This study tried to identify suicide risk factors for temperament in first-episode depressive patients. Compared with the healthy controls, the first-episode MDD patients scored significantly different on dysthymic, cyclothymic, anxious and irritable temperaments, and the significant difference direction was dysthymic > cyclothymic > anxious > irritable.

We compared the temperament differences between suicidal and nonsuicidal risk in depressive patients. As expected, cyclothymic and dysthymic temperaments were associated with a greater risk of suicide. The five factors significantly and independently differentiated patients with versus without suicidal risk based on multivariable logistic regression modeling: female sex, current age, dysthymic and cyclothymic temperament and higher HAMD score. The compound predictor of the five sets a model of high suicide risk. The final factors/features of suicide-risk patients were the same as the clinical impressions, and young females with severe major depressive disorder always complained of hopelessness. Their characteristics may include cyclothymia or dysthymia before the depressive episode. People with cyclothymic temperament traits show instability in mood, thoughts, and behaviors, while mood instability usually leads to suicidal behavior, and quickly changing mood stations enhance suicidal ideation and attempts[16]. Depressive patients with cyclothymic temperament traits are probably developing bipolar disorder[33] and high rates of suicide and hospitalization[20, 34], which might be the final outcome for cyclothymic temperament trait depressive disorder patients.

Many previous studies have examined the demographic characteristics of suicide risk factors in depressive disorder patients. As expected, the onset age was strongly associated with suicide, which is also supported by other studies[27, 35]. Early onset age (especially <18 years) of depression is associated with an increasing rate of converting to bipolar disorder[36], which is a high risk factor for suicide[20, 37]. Subjects of this study were people with a current age over 18 years, and the mean illness duration was 6-6.5 months; we did not obtain the suicide rate of younger adolescents, which still needs further research. Other demographic suicide risk factors in MDD included female sex (71.25%) and unmarried status (76.25%), in accordance with previous observations[20, 38]. We found that a greater suicide risk was more associated with female sex, which was also confirmed in other studies[17, 39]. However, men may have more violent suicide attempts than women, and lethal action makes their suicide death rate higher than in women[37], which also needs further study. Our study showed that unmarried or unemployed persons are a population significantly suffering from depression, and unmarried people have significantly higher instances of thoughts or actions of suicide.

In our study, first-episode depression was detected in the subjects by the HAMD. As the disease progresses, the final diagnosis might be unipolar disorder, bipolar disorder or other mental diseases accompanied by affective symptoms. We found that HAMD scores that removed the 3rd (suicide) item could still predict suicidal risk in major depressive disorders. This means that the total HAMD-17 score, in addition to the 3rd (suicide) item, is closely linked to suicide risk[40, 41]. Particularly of note, the standardized HAMD scale predicting suicide may result in approximately 30% false positives[42], which is inevitable.

Serotonin is a neurotransmitter involved in many brain and body functions. Impaired serotonergic function is involved in the development of suicide behavior and was proven decades ago[43]. Some studies on genes showed that depression and suicide were at the same gene locus[6, 44–46], other than a causal relationship. They found that the S allele in the serotonin transporter-linked polymorphic region (5-HTTLPR) may associate with affective temperament, especially cyclothymic temperament[47]. Sarmiento-Hernández's study showed that the S-allele and the SS genotypes of 5-HTTLPR were associated with suicide attempts[48]. They provide a theoretical basis for the relationship between cyclothymic temperament and suicide. If the suicide risk and temperament are genetic phenotypes and share the same locus, is interference difficult? Other studies have shown that affective temperaments may change to some degree, and people could exhibit one type of character trait during puberty and deviate when they grow up[49]. They provide the basis that temperament is changeable throughout a person's life[50]. Japanese researcher Inoue studied the influence of ambient temperature on temperament[51], which makes us believe that the final outcome could be intervened.

5. Limitations

Several important limitations should be considered. First, our study had a cross-sectional design, and the factors associated with suicide should not be considered direct risk factors or "causes". Second, the self-report scale may cause recall bias. Third, the single site of observation may cause selection bias, and some high suicide risk patients did not ask doctors for help. Finally, due to cultural background differences, the results may not be suitable for other populations or ethnicities.

6. Conclusions

The findings of study support that there are temperament differences between the general population and depressive patients. People with cyclothymic or dysthymic temperament traits have higher suicide risk than those with other temperament traits. Younger females with cyclothymic and dysthymic temperament combined with higher HAMD scores may elevate the identification rate of suicide.

Declarations

Ethics approval and consent to participate

Study was approved by and carried out in accordance with the Ethics Committee of Beijing HuiLongGuan Hospital. Informed consent was obtained from participants/legal guardians of participants involved in the study.

Consent for publication

All authors have agreed to the submission of the final manuscript.

Human identity revealing data is used in the study-Not applicable.

Availability of data and materials

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

Competing interests

The authors declare that they have no conflict of interests.

Funding

This study was supported by Beijing Council of Science and Technology (Z171100001017001), The Capital Health Research and Development of Special (2018-3-2132). The funding bodies played no role in the design of the study and collection, analysis, and interpretation of data and in writing the manuscript.

Authors' contributions

Lu Yin: Conceptualization, Data curation, Formal analysis, Writing - original draft.

Ting-Ting Wang: Conceptualization, Methodology, Validation, Investigation, Writing - original draft.

Yan-Yan Wei and Li-Gang Zhang: Funding acquisition, Conceptualization, Supervision, Validation.

Shuang-Jiang Zhou: Investigation, Methodology, Supervision, Validation.

Jian-Jin Yu: Investigation, Methodology, Supervision.

Li-Ye Zhang: Investigation, Methodology, Supervision.

Hong-Juan Li: Investigation, Methodology.

Jing-Xu Chen: Study design.

Acknowledgements

The authors would like to thank Hong-Mei Chen, Hong-Jie Min, Ran Li□Ning Wang and Hai-Ting Xu for all of their hard work and significant contributions to the study.

Authors' information

[a] Peking University Hui-Long-Guan Clinical Medical School, Beijing Hui-Long-Guan Hospital, Beijing, 100096, China

[b] Bengbu Medical College, 233000, Bengbu, China

References

1. Dengsen Yang XL, Yonxin Xu: **Hsiang-ya Psychiatry**, First edn. Beijing, China: Science Press; 2015.
2. **WHO suicide data** [https://www.who.int/teams/mental-health-and-substance-use/suicide-data]
3. Zhou M, Wang H, Zeng X, Yin P, Zhu J, Chen W, Li X, Wang L, Wang L, Liu Y *et al*: **Mortality, morbidity, and risk factors in China and its provinces, 1990-2017: a systematic analysis for the Global Burden of Disease Study 2017**. *Lancet* 2019, **394**(10204):1145–1158.

4. S S, A F: **WHO launches the first world suicide report**. *The lancet Psychiatry* 2014, **1**(4):255–256.
5. Preti A: **Animal model and neurobiology of suicide**. *Prog Neuropsychopharmacol Biol Psychiatry* 2011, **35**(4):818–830.
6. Zubenko GS, Maher BS, Hughes HB, 3rd, Zubenko WN, Scott Stiffler J, Marazita ML: **Genome-wide linkage survey for genetic loci that affect the risk of suicide attempts in families with recurrent, early-onset, major depression**. *Am J Med Genet B Neuropsychiatr Genet* 2004, **129B**(1):47–54.
7. Crump C, Sundquist K, Sundquist J, Winkleby MA: **Sociodemographic, psychiatric and somatic risk factors for suicide: a Swedish national cohort study**. *Psychol Med* 2014, **44**(2):279–289.
8. Morris DW, Trivedi MH, Husain MM, Fava M, Budhwar N, Wisniewski SR, Miyahara S, Gollan JK, Davis LL, Daly EJ *et al*: **Indicators of pretreatment suicidal ideation in adults with major depressive disorder**. *Acta Psychiatr Scand* 2010, **121**(6):480–484.
9. Chen JX, Feng JH, Zhang LG, Liu Y, Yang FD, Wang SL, Tan YL, Su YA: **Association of serum uric acid levels with suicide risk in female patients with major depressive disorder: a comparative cross-sectional study**. *BMC Psychiatry* 2020, **20**(1):477.
10. The L: **Suicide prevention: creating a safer culture**. *Lancet* 2016, **388**(10055):1955.
11. Huang Y, Wang Y, Wang H, Liu Z, Yu X, Yan J, Yu Y, Kou C, Xu X, Lu J *et al*: **Prevalence of mental disorders in China: a cross-sectional epidemiological study**. *Lancet Psychiatry* 2019, **6**(3):211–224.
12. Dong M, Wang SB, Li Y, Xu DD, Ungvari GS, Ng CH, Chow IHI, Xiang YT: **Prevalence of suicidal behaviors in patients with major depressive disorder in China: A comprehensive meta-analysis**. *J Affect Disord* 2018, **225**:32–39.
13. Lee S, Fung SC, Tsang A, Liu ZR, Huang YQ, He YL, Zhang MY, Shen YC, Nock MK, Kessler RC: **Lifetime prevalence of suicide ideation, plan, and attempt in metropolitan China**. *Acta Psychiatr Scand* 2007, **116**(6):429–437.
14. Zentner M, Shiner, R. (ed.): **Handbook of temperament**. New York, NY: Guilford Publications; 2012.
15. Pompili M, Baldessarini RJ, Innamorati M, Vazquez GH, Rihmer Z, Gonda X, Forte A, Lamis DA, Erbuto D, Serafini G *et al*: **Temperaments in psychotic and major affective disorders**. *J Affect Disord* 2018, **225**:195–200.
16. Rihmer A, Rozsa S, Rihmer Z, Gonda X, Akiskal KK, Akiskal HS: **Affective temperaments, as measured by TEMPS-A, among nonviolent suicide attempters**. *J Affect Disord* 2009, **116**(1-2):18–22.
17. Kringlen E, Torgersen S, Cramer V: **A Norwegian psychiatric epidemiological study**. *Am J Psychiatry* 2001, **158**(7):1091–1098.
18. Tao W, Yulong C, Yanru L: **A survey of 5754 cases of depression with somatic symptoms as the first symptom in digestive clinic of general hospital**. *World Chin J Dig*, **08**:108–110.
19. Guerreiro DF, Sampaio D, Rihmer Z, Gonda X, Figueira ML: **Affective temperaments and self-harm in adolescents: a cross-sectional study from a community sample**. *J Affect Disord* 2013, **151**(3):891–898.
20. Baldessarini RJ, Tondo L, Pinna M, Nunez N, Vazquez GH: **Suicidal risk factors in major affective disorders**. *Br J Psychiatry* 2019:1–6.
21. Si TMSL DW, Su YA, Chen JX, Dong WT, Kong QM, Zang WH: **Evaluation of the reliability and validity of Chinese version of the mini-international neuropsychiatric interview in patients with mental disorders**. *Chin Ment Health J* 2009, **23**(7):493–503.
22. Reas DL, Pedersen G, Karterud S, Ro O: **Self-harm and suicidal behavior in borderline personality disorder with and without bulimia nervosa**. *J Consult Clin Psychol* 2015, **83**(3):643–648.
23. Jung YE, Kim MD: **Lifetime suicidal attempts and current suicidal risk in aging survivors of the Jeju April 3 incident**. *J Affect Disord* 2018, **225**:1–3.
24. Csorba J, Dinya E, Plener P, Nagy E, Pali E: **Clinical diagnoses, characteristics of risk behaviour, differences between suicidal and non-suicidal subgroups of Hungarian adolescent outpatients practising self-injury**. *Eur Child Adolesc Psychiatry* 2009, **18**(5):309–320.
25. Zheng YP, Zhao JP, Phillips M, Liu JB, Cai MF, Sun SQ, Huang MF: **Validity and reliability of the Chinese Hamilton Depression Rating Scale**. *Br J Psychiatry* 1988, **152**:660–664.
26. Akiskal HS, Mendlowicz MV, Jean-Louis G, Rapaport MH, Kelsoe JR, Gillin JC, Smith TL: **TEMPS-A: validation of a short version of a self-rated instrument designed to measure variations in temperament**. *J Affect Disord* 2005, **85**(1-2):45–52.

27. Chengmei Y, Jia H, Zezhi L: **[Reliability and validity of the Chinese short version of the Temperament Evaluation of Memphis, Pisa, Paris and San Diego-Auto Questionnaire (TEMPS-A)]**. *Chin Mental Health J* 2014, **028**(002):151–155.
28. Wiener CD, de Mello Ferreira S, Pedrotti Moreira F, Bittencourt G, de Oliveira JF, Lopez Molina M, Jansen K, de Mattos Souza LD, Rizzato Lara D, Portela LV *et al*: **Serum levels of nerve growth factor (NGF) in patients with major depression disorder and suicide risk**. *J Affect Disord* 2015, **184**:245–248.
29. Chen L, Liu YH, Zheng QW, Xiang YT, Duan YP, Yang FD, Wang G, Fang YR, Lu Z, Yang HC *et al*: **Suicide risk in major affective disorder: results from a national survey in China**. *J Affect Disord* 2014, **155**:174–179.
30. Li H, Luo X, Ke X, Dai Q, Zheng W, Zhang C, Cassidy RM, Soares JC, Zhang X, Ning Y: **Major depressive disorder and suicide risk among adult outpatients at several general hospitals in a Chinese Han population**. *PLoS One* 2017, **12**(10):e0186143.
31. Asnis GM, Friedman TA, Sanderson WC, Kaplan ML, van Praag HM, Harkavy-Friedman JM: **Suicidal behaviors in adult psychiatric outpatients, I: Description and prevalence**. *Am J Psychiatry* 1993, **150**(1):108–112.
32. Sokero TP, Melartin TK, Rytsala HJ, Leskela US, Lestela-Mielonen PS, Isometsa ET: **Suicidal ideation and attempts among psychiatric patients with major depressive disorder**. *J Clin Psychiatry* 2003, **64**(9):1094–1100.
33. Morishita C, Kameyama R, Toda H, Masuya J, Ichiki M, Kusumi I, Inoue T: **Utility of TEMPS-A in differentiation between major depressive disorder, bipolar I disorder, and bipolar II disorder**. *PLoS One* 2020, **15**(5):e0232459.
34. Pompili M, Rihmer Z, Akiskal HS, Innamorati M, Iliceto P, Akiskal KK, Lester D, Narciso V, Ferracuti S, Tatarelli R *et al*: **Temperament and personality dimensions in suicidal and nonsuicidal psychiatric inpatients**. *Psychopathology* 2008, **41**(5):313–321.
35. Thompson AH: **Younger onset of depression is associated with greater suicidal intent**. *Soc Psychiatry Psychiatr Epidemiol* 2008, **43**(7):538–544.
36. James A, Wotton CJ, Duffy A, Hoang U, Goldacre M: **Conversion from depression to bipolar disorder in a cohort of young people in England, 1999-2011: A national record linkage study**. *J Affect Disord* 2015, **185**:123–128.
37. Rosso G, Albert U, Bramante S, Aragno E, Quarato F, Di Salvo G, Maina G: **Correlates of violent suicide attempts in patients with bipolar disorder**. *Compr Psychiatry* 2020, **96**:152136.
38. Bornheimer LA: **Suicidal Ideation in First-Episode Psychosis (FEP): Examination of Symptoms of Depression and Psychosis Among Individuals in an Early Phase of Treatment**. *Suicide Life Threat Behav* 2019, **49**(2):423–431.
39. Bernal M, Haro JM, Bernert S, Brugha T, de Graaf R, Bruffaerts R, Lepine JP, de Girolamo G, Vilagut G, Gasquet I *et al*: **Risk factors for suicidality in Europe: results from the ESEMED study**. *J Affect Disord* 2007, **101**(1-3):27–34.
40. Zhu Y, Zhang H, Shi S, Gao J, Li Y, Tao M, Zhang K, Wang X, Gao C, Yang L *et al*: **Suicidal risk factors of recurrent major depression in Han Chinese women**. *PLoS One* 2013, **8**(11):e80030.
41. Eikelenboom M, Smit JH, Beekman AT, Penninx BW: **Do depression and anxiety converge or diverge in their association with suicidality?** *J Psychiatr Res* 2012, **46**(5):608–615.
42. Maris RW: **Suicide**. *Lancet* 2002, **360**(9329):319–326.
43. Stanley M, Mann JJ: **Increased serotonin-2 binding sites in frontal cortex of suicide victims**. *Lancet* 1983, **1**(8318):214–216.
44. Thornton LM, Welch E, Munn-Chernoff MA, Lichtenstein P, Bulik CM: **Anorexia Nervosa, Major Depression, and Suicide Attempts: Shared Genetic Factors**. *Suicide Life Threat Behav* 2016, **46**(5):525–534.
45. Bozorgmehr A, Alizadeh F, Ofogh SN, Hamzekalayi MRA, Herati S, Moradkhani A, Shahbazi A, Ghadirivasfi M: **What do the genetic association data say about the high risk of suicide in people with depression? A novel network-based approach to find common molecular basis for depression and suicidal behavior and related therapeutic targets**. *J Affect Disord* 2018, **229**:463–468.
46. Levey DF, Polimanti R, Cheng Z, Zhou H, Nunez YZ, Jain S, He F, Sun X, Ursano RJ, Kessler RC *et al*: **Genetic associations with suicide attempt severity and genetic overlap with major depression**. *Transl Psychiatry* 2019, **9**(1):22.
47. Gonda X, Fountoulakis KN, Rihmer Z, Lazary J, Laszik A, Akiskal KK, Akiskal HS, Bagdy G: **Towards a genetically validated new affective temperament scale: a delineation of the temperament phenotype of 5-HTTLPR using the TEMPS-A**. *J Affect Disord* 2009, **112**(1-3):19–29.

48. Sarmiento-Hernandez EI, Ulloa-Flores RE, Camarena-Medellin B, Sanabrais-Jimenez MA, Aguilar-Garcia A, Hernandez-Munoz S: **Association between 5-HTTLPR polymorphism, suicide attempt and comorbidity in Mexican adolescents with major depressive disorder**. *Actas Esp Psiquiatr* 2019, **47**(1):1–6.
49. Zorzetti R, Pereira LD, Lara DR, de Araujo RMF: **Low affective temperament consistency during development: Results from a large retrospective study**. *J Affect Disord* 2019, **248**:180–184.
50. Trofimova I, Christiansen J: **Coupling of Temperament with Mental Illness in Four Age Groups**. *Psychol Rep* 2016, **118**(2):387–412.
51. Inoue T, Kohno K, Baba H, Takeshima M, Honma H, Nakai Y, Suzuki T, Hatano K, Arai H, Matsubara S *et al*: **Does temperature or sunshine mediate the effect of latitude on affective temperaments? A study of 5 regions in Japan**. *J Affect Disord* 2015, **172**:141–145.

Figures

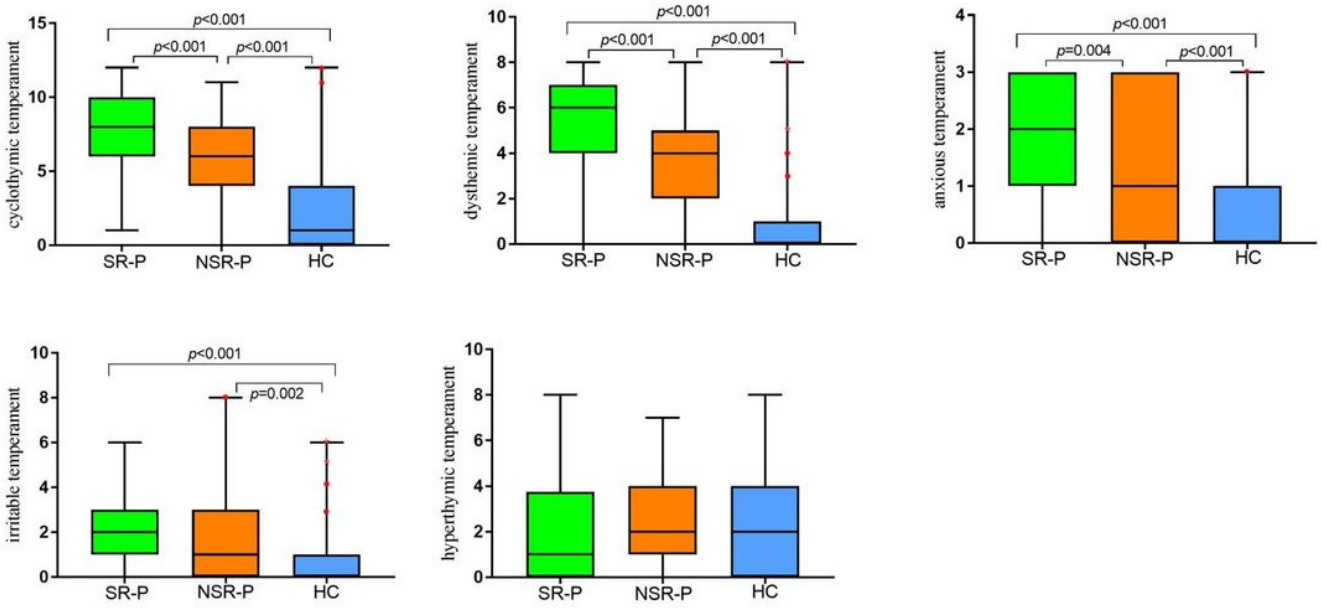

Figure 1

Box plots of the TEMPS-A subscales across the groups of FND-P and healthy controls. The solid lines show the medians, and the boxes show the interquartile ranges. Outlier (●) means cases with values between 1.5 and 3 box lengths from the upper or lower edge of the box. Asterisk (*) means cases with values more than 3 box lengths from the upper or lower edge of the box. The box length is the interquartile range. SR: suicide risk; NSR: none-suicide risk; and HC: healthy control. P-value is adjusted by Bonferroni correction.

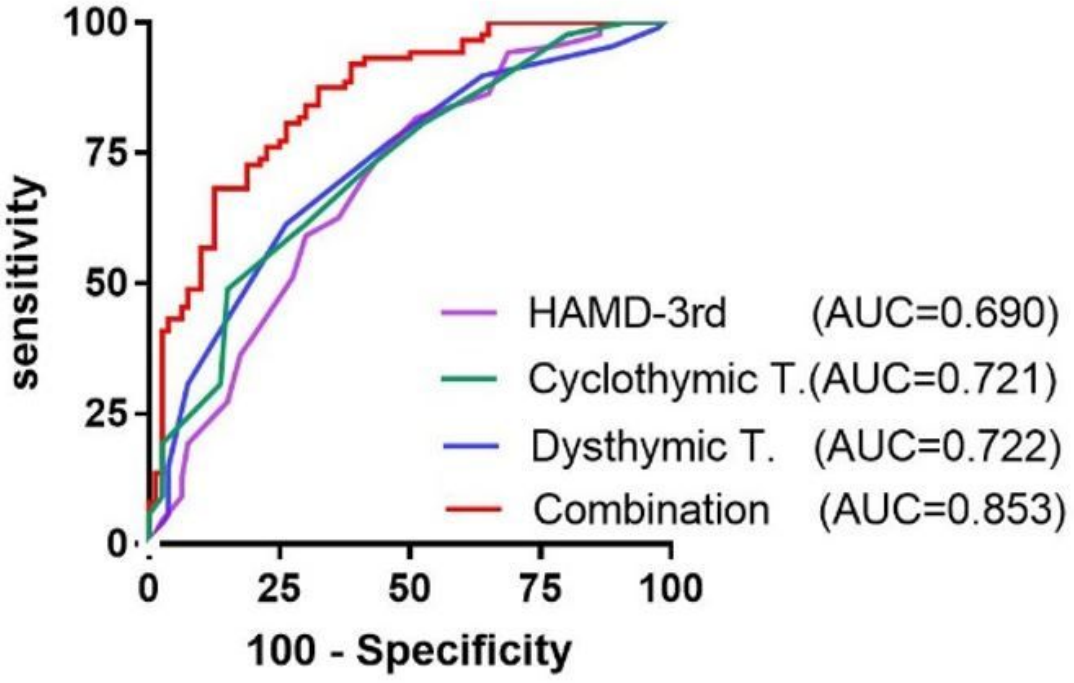

Figure 2

ROC curves for the prediction of the incidence of suicide in the first episode of major depressive disorder. Red curve, model including age, gender, HAMD score without the 3rd item, cyclothymic and dysthymic temperament, AUC=0.853 (95%CI, 0.790~0.903). Youden index sensitivity 87.50%, specificity 68.18%.