Temperament, Character, and Suicide Attempts in Unipolar and Bipolar Mood Disorders

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ABSTRACT

Objective: Personality features may indicate risk for both mood disorders and suicidal acts. How dimensions of temperament and character predispose to suicide attempts remains unclear.

Method: Patients (n = 597) from 3 prospective cohort studies (Vantaa Depression Study [VDS], Jorvi Bipolar Study [JoBS], and Vantaa Primary Care Depression Study [PC-VDS]) were interviewed at baseline, at 18 months, and, in VDS and PC-VDS, at 5 years (1997–2003). Personality was measured with the Temperament and Character Inventory-Revised (TCI-R), and follow-up time spent in major depressive episodes (MDEs) as well as lifetime (total) and prospectively ascertained suicide attempts during the follow-up were documented.

Results: Overall, 219 patients had 718 lifetime suicide attempts; 88 patients had 242 suicide attempts during the prospective follow-up. The numbers of both the total and prospective suicide attempts were associated with low self-directedness (β = –0.266, $P = .004$, and β = –0.294, $P < .001$, respectively) and high self-transcendence (β = 0.287, $P = .002$, and β = 0.233, $P = .002$, respectively). Total suicide attempts were linked to high novelty seeking (β = 0.195, $P = .05$). Prospective, but not total, suicide attempts were associated with high harm avoidance (β = 0.322, $P < .001$, and β = 0.184, $P = .062$, respectively) and low reward dependence (β = –0.274, $P < .001$, and β = –0.134, $P = .196$, respectively), cooperativeness (β = –0.181, $P = .005$, and β = –0.096, $P = .326$, respectively), and novelty seeking (β = –0.137, $P = .047$). No association remained significant when only prospective suicide attempts during MDEs were included. After adjustment was made for total time spent in MDEs, only high persistence predicted suicide attempts (β = 0.190, $P < .05$). Formal mediation analyses of harm avoidance and self-directedness on prospectively ascertained suicide attempts indicated significant mediated effect through time at risk in MDEs, but no significant direct effect.

Conclusions: Among mood disorder patients, suicide attempt risk is associated with temperament and character dimensions. However, their influence on predisposition to suicide attempts is likely to be mainly indirect, mediated by more time spent in depressive episodes.

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Mood disorders are associated with high suicide risk. At least half of all suicides occur in people with mood disorders.[1] The lifetime risk of suicide among mood disorder patients is 5%–6%.[2] For suicide prevention, knowing risk factors is of utmost importance. Because the base rate of suicide is low, the search for risk factors has largely focused on suicide attempts as a proxy for suicide. The risk factors for suicide attempts and suicide are grossly similar, although those who commit suicide are more often male, have psychotic symptoms, and use more lethal methods.[3,4]

Social, psychological, and clinical risk factors for suicide attempts in mood disorders include younger age, hopelessness, poor perceived social support, impulsive-aggressive traits, and concurrent cluster B personality and substance use disorders (for reviews, see Isometsä[3] and Hawton et al[4]). Most likely, an interaction between multiple risk and protective factors predisposes one to suicidal behavior.[5] In a series of prospective studies,[6–9] we have shown that a major determinant, with consistently high population attributable fraction, is the time spent in high-risk illness phases. As compared to euthymia, major depressive phases and mixed episodes have shown a 25- and 65-fold increased incidence of suicide attempts, respectively.[8] Among mood disorder patients, suicidal acts in the absence of an illness episode are rare.[6–9]

Personality traits are known to predict risk of mood disorders in prospective studies.[10] Specifically, we have recently shown that temperament and character traits also predict future burden of depression.[11] Selected personality traits might also be useful indicators of risk for suicidal behavior.[12] Personality factors might increase the risk of suicide in mood disorders directly by moderating the impact of other risk factors on suicidal behavior during a suicidal crisis. Indirect causal pathways through a mediating factor could include predisposing to comorbid psychiatric, anxiety, or substance use disorders[13]; to psychotic symptoms[14]; or to poor social support[15] or increasing the time spent in high-risk mood states.[11]

In this study, we used Cloninger's unified biopsychosocial theory of personality,[16,17] which postulates 4 temperament and 3 character dimensions

Clinical Points

- Temperament and character predict suicidal acts, but their effect is mainly indirect.
- The influence of these traits on the risk of suicide attempts is largely mediated by longer time spent in depressive episodes, ie, high-risk states.
- Treatments that shorten and prevent major depressive episodes are credible measures in reducing risk for suicidal acts.
- Understanding the role of temperament and character in predisposing one to depressive episodes may be helpful in targeting treatment to patients at risk.

(see supplementary material at PSYCHIATRIST.COM). These dimensions are measured using a self-rating questionnaire, the latest version being the Temperament and Character Inventory-Revised (TCI-R).

Previous studies investigating the relationship between suicide attempt and TCI in mood disorders have been cross-sectional. In these studies, the presence of at least 1 lifetime suicide attempt has been associated consistently with high harm avoidance,[18–23] novelty seeking[20,23] or high self-transcendence,[24,25] and low self-directedness[18,20,24,25] or cooperativeness,[23] although negative reports[26] also exist. Overall, cross-sectional studies suggest that some personality dimensions are associated with risk of suicidal acts. However, the scarcity of prospective studies and inconsistent adjustment for confounders have prevented solid conclusions regarding the role of personality in risk for suicidal acts. To our knowledge, no prospective longitudinal study among mood disorder patients has specifically investigated the relationship between personality features and risk of suicide attempts. Moreover, a key predictor of accumulated risk for suicidal acts, the proportion of time a patient spends in major depressive episodes during follow-up,[6–9] has not been controlled for in any previous study.

Aims of the Study

We have previously reported that TCI dimensions predict vulnerability to mood disorders[27] and future burden of depression[11] and that time spent in major depressive and mixed episodes is a major determinant of overall risk for suicide attempts in mood disorders.[6–9] In this study, we hypothesized that, among patients with mood disorders, high harm avoidance, novelty seeking, and self-transcendence would increase the rate of suicide attempts, whereas high self-directedness and cooperativeness would decrease the rate. Furthermore, we hypothesized that these effects would be mediated through increased time spent in major depressive episodes.

To test these hypotheses, we investigated the relationship between temperament and character dimensions and (1) lifetime (total retrospective and prospective) suicide attempts and (2) prospectively evaluated new suicide attempts during follow-up. We also tested whether TCI dimensions act directly on the rate of suicide attempts or indirectly by increasing the duration of illness relative to chronological age (for lifetime suicide attempts) or, more specifically, the duration of major depressive episodes (prospectively evaluated suicide attempts). In final analyses of prospectively evaluated suicide attempts, we controlled for confounding sociodemographic and clinical risk factors and conducted formal tests of mediation effects.

METHOD

Patients were from 3 cohorts (the Jorvi Bipolar Study [JoBS],[28,29] the Vantaa Depression Study [VDS],[30,31] and the Vantaa Primary Care Depression Study [PC-VDS][32,33]) of collaborative research projects of the Department of Mental Health and Substance Use of the National Institutes of Health and Welfare, Helsinki, Finland (principal investigator: E.T.I.). The pertinent ethics committee approved the research protocols.

Detailed methodologies have been described elsewhere for JoBS,[28,29] VDS,[30,31] and PC-VDS.[32,33] A summary is provided in Table 1.

Screening and Baseline Evaluation

Patients were screened for bipolar disorder (JoBS), major depressive disorder (MDD) (VDS), or depressive disorder (PC-VDS) in an acute mood episode. The patients were fully informed about the study and written informed consent was obtained. Diagnoses were based on semistructured interviews (Table 1). In PC-VDS, two-thirds of the patients had MDD; the rest had dysthymia, current subsyndromal but lifetime MDD, or true minor depression. The final baseline cohorts consisted of 191 patients with *DSM-IV* bipolar I and II disorder (JoBS), 269 with MDD (VDS), and 137 with depressive disorder (PC-VDS). Interrater agreement in diagnostic interviews was excellent ($\kappa = 0.86–1.00$).[29,30,32]

Information was also gathered on demographic characteristics; current symptomatology was obtained using the 17-item Hamilton Depression Rating Scale (HDRS),[34] the 21-item Beck Depression Inventory (BDI),[35] the 21-item Beck Anxiety Inventory (BAI),[36] and the Young Mania Rating Scale (YMRS)[37]; and illness history was obtained using a retrospective life chart.

Follow-Up

After baseline assessments, patients were interviewed at 6 (JoBS and VDS) and at 18 (JoBS, VDS and PC-VDS) months and at 5 years (VDS and PC-VDS). Repeated interviews with the Structured Clinical Interview for *DSM-IV-TR* Axis I Disorders Research Version, Patient Edition (SCID-I/P) (with psychotic screen)[38] (JoBS and PC-VDS at all follow-up assessments, and VDS at 5 years); Schedules for Clinical Assessment in Neuropsychiatry (SCAN) 2.0[39] (VDS at 18 months); and Structured Clinical Interview for *DSM-IV* Axis II Personality Disorders (SCID-II) and all observer- and self-reported symptom scales were included at all follow-up assessments. Information on course of illness was then integrated into a prospective life chart based on *DSM-IV*

Table 1. Methods Used in the Jorvi Bipolar Study (JoBS), the Vantaa Depression Study (VDS), and the Vantaa Primary Care Depression Study (PC-VDS)

Phase	JoBS[28,29]	VDS[30,31]	PC-VDS[32,33]
Timing of screening	January 1, 2002, to February 28, 2003	February 1, 1997, to May 31, 1998	January 1, 2002, to December 31, 2002
Catchment area	Adjacent cities of Espoo, Kauniainen, and Kirkkonummi, Finland (population, 261,100 in 2002)	City of Vantaa, Finland (population, 169,000 in 1997)	Two districts in the city of Vantaa, Finland (population, 63,400 in 2002)
Setting	Department of Psychiatry, Jorvi Hospital, Helsinki University Central Hospital, Espoo, Finland	Department of Psychiatry of the Peijas Medical Care District, Helsinki University Central Hospital, Vantaa, Finland	Primary Health Care Organization of the City of Vantaa, Finland 3 Health centers 2 Maternity clinics served by 30 general practitioners with population-based responsibility
Target group	All psychiatric patients aged 18–59 y (1) seeking treatment, (2) referred to treatment, or (3) already in treatment with an acute deteriorating clinical state	All psychiatric patients aged 20–59 y (1) seeking treatment, (2) referred to treatment, or (3) already in treatment with an acute deteriorating clinical state	Consecutive primary care patients aged 20–59 y in general practitioners' waiting room
Exclusion from screening	*ICD-10* schizophrenia	*ICD-10* schizophrenia, bipolar I disorder	Poor general health status prohibiting completion of screening form
Screening procedure	(1) Mood Disorders Questionnaire, 7/13 items positive, or (2) clinical suspicion of bipolar disorder (n = 28)	(1) 5 Screening questions for depression from SCAN, 1 positive, or (2) Scale for Suicide Ideation, score ≥ 6	(1) PRIME-MD: 1 positive mood disorders item, and (2) telephone interview: 1 or more main symptoms of depression according to the SCID-I/P (w/psychotic screen)
Total screened, n	1,630	806	1,111 (8 refused)
Screened positive, n	546	703	402
Refusals, n	Screening, 46 (2.8% of all screened), Interview, 49 (9.0% of positive screens)	161 (22.9%)	37 (9.2%)
Diagnostic interview	After informed consent, *DSM-IV* (SCID-I/P and SCID-II)	After informed consent, *DSM-IV* (Axis I, SCAN) and *DSM-III-R* (SCID-II, modified to *DSM-IV*)	After informed consent *DSM-IV* (SCID-I/P and SCID-II)
Inclusion criteria	*DSM-IV* bipolar I or II disorder with a new depressive, manic, hypomanic, mixed, or depressive mixed episode of bipolar disorder	*DSM-IV* MDD with a new depressive episode	*DSM-IV* MDD with no current treatment in psychiatric care
Cohort, n	191 (65 inpatients, 126 outpatients)	269 (46 inpatients, 223 outpatients)	137 outpatients from primary car
6-mo follow-up, n (%)	176 (92.1)	229 (85.1)	…
18-mo follow-up			
Patients, n (%)	161 (84.3)	198 (73.6)	92 (67.2)
Participants vs nonparticipants	Somewhat older (mean [SD] = 39.0 [11.9] y vs 33.7 [12.1] y; $t_{189} = 2.711$; $P = .007$)		
Time for interview, mean ± SD, mo	19.8 ± 3.0		
5-y follow-up			
Patients, n (%)	…	182 (67.7)	112 (82.0)
Switch of diagnosis, n		Bipolar disorder, 29; schizophrenia, 1; schizoaffective disorder, 2	Bipolar disorder, 5
Participants vs nonparticipants		More often female (72.1% vs 55.6%, $\chi^2 = 6.581$, $P = .010$), married or cohabiting (75.6% vs 59.7%, $\chi^2 = 7.725$, $P = .005$), less alcohol dependence at baseline (39.5% vs 72.3%, $\chi^2 = 16.064$, $P < .001$)	No difference in age, gender, or baseline depression severity
Time for interview, mean ± SD, y		5.2	5.2
Diagnostic reliability at baseline	20 Videotaped diagnostic interviews; κ coefficient for bipolar disorder = 1.0	20 Videotaped diagnostic interviews; κ coefficient for current MDD = 0.86 (95% CI, 0.58–1.00); not tested for comorbidity	20 Videotaped diagnostic interviews; κ coefficient for current MDD = 1.0; not tested for comorbidity
Symptom assessment	YMRS, HDRS, BDI, BAI (baseline and 18 mo)	HDRS, BDI, BAI (baseline, 18 mo, and 5 y)	HDRS, BDI, BAI (baseline, 18 mo, and 5 y)
Personality assessment	TCI-R (baseline and 18 mo)	TCI-R (5 y)	TCI-R (baseline and 18 mo)
Internal consistencies of the scales	Cronbach α values for the scales used were good in patient cohorts at all time points (TCI-R [0.81–0.94], BDI [0.86–0.95], BAI [0.89–0.93], HDRS [0.70–0.88], and YMRS [JoBS: 0.59–0.88])		

Abbreviations: BAI = Beck Anxiety Inventory; BDI = Beck Depression Inventory; HDRS = Hamilton Depression Rating Scale; MDD = major depressive disorder; PRIME-MD = Primary Care Evaluation of Mental Disorders; SCAN = Schedules for Clinical Assessment in Neuropsychiatry, version 2.0; SCID-I/P = Structured Clinical Interview for *DSM-IV-TR* Axis I Disorders, Research Version, Patient Edition; SCID-II = Structured Clinical Interview for *DSM-IV* Axis II Personality Disorders; TCI-R = Temperament and Character Inventory-Revised; YMRS = Young Mania Rating Scale.

Table 2. Sociodemographic Characteristics, Current Symptomatology, and Personality Traits of Patients With or Without Lifetime Suicide Attempt

Characteristic	Patients With Lifetime Suicide Attempt (n = 219)		Patients Without Lifetime Suicide Attempt (n = 378)		χ^2	*P*
	n	%	n	%		
Gender						NS
Female	155	70.8	247	65.3		
Male	64	29.2	131	34.7		
Education[a]						NS
University or polytechnic	70	32.2	150	40.4		
Vocational	52	24.0	93	25.1		
None	95	43.8	138	37.2		
Marital status[b]					4.354	.037
Married or cohabiting	94	43.1	194	52.0		
Single	124	56.9	179	48.0		
Work status[c]						NS
Employed	147	68.1	259	69.4		
Unemployed	69	31.9	114	30.6		
Comorbid disorders evaluated at baseline						
Any anxiety disorder	125	57.1	171	45.2	7.775	.005
Alcohol dependence, current	33	15.1	38	10.1		NS
Any personality disorder current	121	55.3	150	39.7	13.559	< .001
Psychotic features, lifetime	82	37.4	62	16.4	33.541	< .001
	Mean	SD	Mean	SD	*t*	*P*
Age	38.8	12.2	41.2	12.4	2.241	.025
BDI, baseline	27.1	11.1	22.6	10.0	−5.166	< .001
BAI, baseline	24.2	12.5	19.4	11.3	−4.782	< .001
HDRS, baseline	16.0	7.3	13.1	5.9	−5.305	< .001
BDI, HDRS minimum[d]	18.2	12.9	11.6	10.2	−6.914	< .001
BAI, HDRS minimum[d]	17.8	12.7	12.0	10.2	−6.100	< .001
HDRS minimum	12.6	8.6	8.9	6.7	−5.829	< .001
TCI-R						
Harm avoidance[e]	107.5	20.9	105.2	18.6	1.271	NS
Novelty seeking[f]	107.2	18.8	101.6	16.6	3.405	.001
Reward dependence[g]	98.1	15.1	99.1	15.7	−0.642	NS
Persistence[g]	106.2	21.3	105.8	19.4	0.217	NS
Self-directedness[h]	129.3	22.7	136.7	19.5	−3.797	< .001
Cooperativeness[g]	128.4	19.6	131.9	16.8	−2.035	.042
Self-transcendence[e]	70.8	16.1	65.1	15.5	3.868	< .001
PSSS-R[i]	42.0	12.6	43.2	12.6		NS

[a]Missing data: 2/219, 7/378. [b]Missing data: 1/219, 5/378. [c]Missing data: 3/219, 5/378. [d]Indicates score at index interview conducted when the HDRS scores were at a minimum. [e]Missing data: 31/219, 86/378. [f]Missing data: 31/219, 87/378. [g]Missing data: 30/219, 87/378. [h]Missing data: 32/219, 87/378. [i]Missing data: 19/219, 33/378.

Abbreviations: BAI = Beck Anxiety Inventory, BDI = Beck Depression Inventory, HDRS = Hamilton Depression Rating Scale, NS = nonsignificant, PSSS-R = Perceived Social Support Scale-Revised, TCI-R = Dimensions of Temperament and Character Inventory-Revised.

criteria.[29,31,32,40] The current study's criteria for hypomania, except duration of at least 2 days, were the same as those in the *DSM-IV*. The sociodemographic characteristics of the patients are shown in Table 2.

Personality Assessment

Patients were instructed to think of the way they would typically act or feel when responding to the 240-item Temperament and Character Inventory-Revised.[41] The TCI-R was included in JoBS, at baseline and at 18-month follow-up in PC-VDS, and at 5-year follow-up in VDS.

Suicide Attempts

A *suicide attempt* was defined as a self-injurious behavior with nonfatal outcome accompanied by evidence that the person had at least some degree of intent to die.[6–9] At baseline, the information of previous suicide attempts was obtained by interviews and psychiatric records. The information regarding suicide attempts during follow-up was based on both patient interview and medical records. At follow-up, we assessed episodes of depression and suicide attempts independently by questioning patients first about their life events and mood and then about suicide attempts to avoid automatically attributing the disorders to each other, or the acts to the episode.

Study Design

We examined whether TCI-R dimensions predicted number of prospectively ascertained suicide attempts or were associated with number of lifetime (including prospective) attempts. To minimize the effect of mood, each patient's personality dimensions were determined at an index interview conducted when the HDRS scores (PC-VDS) or HDRS and YMRS scores (JoBS) were at a minimum or at 5-year follow-up (VDS). If HDRS and YMRS scores were at a minimum in different evaluations (n = 28), the time point when the patient was clinically healthier was chosen. In some cases (n = 28), only a single evaluation was available.

Statistical Methods

Poisson regression was applied in modeling the number of suicide attempts during the (participant-specific) time of exposure as a function of explanatory covariates.[42] Existence of overdispersal was first tested for by using a dispersion test in "AER" R-package version 1.2–1,[43] and quasi-Poisson models were used only in the presence of clear overdispersal. Regression estimates were computed by standard generalized linear modeling (glm-function) in R-software 64-bit Linux-version 2.15.3.[44] Formal tests of mediation[45] were conducted for the 2 dimensions with most robust effect on suicide attempt risk (harm avoidance and self-directedness). Methodological details of the Poisson regression are presented in the supplementary material.

Missing-data modeling was performed using multiple imputation by chained equations implemented with "mice" R package version 2.17.[46] Details of missing-data modeling along with imputed and nonimputed sensitivity analysis[47] are presented in the supplementary material. As a sensitivity analysis, we studied whether personality is differentially associated with having attempted suicide versus the number of attempts. The status outcome was modeled by using standard logistic regression models.[42]

Table 3. Quasi-Poisson Regression Coefficients for Temperament and Character Traits Predicting Lifetime Number of Suicide Attempts and Poisson Regression Coefficients When Predicting Number of New Suicide Attempts

	Lifetime Attempts[a]				New Attempts[b]			
Variable	Coefficient	SE	*P* Value	n[c]	Coefficient	SE	*P* Value	n[c]
Novelty seeking	0.195	0.099	**.050**	479	−0.137	0.069	**.047**	457
Harm avoidance	0.184	0.098	.062	480	0.322	0.071	**<.001**	458
Reward dependence	−0.134	0.103	.196	481	−0.274	0.072	**<.001**	459
Persistence	−0.136	0.097	.161	481	−0.008	0.070	.911	459
Self-directedness	−0.266	0.091	**.004**	479	−0.294	0.064	**<.001**	457
Cooperativeness	−0.096	0.098	.326	481	−0.181	0.065	**.005**	459
Self-transcendence	0.287	0.094	**.002**	480	0.223	0.072	**.002**	458
No. of previous attempts	…	…	…	…	0.122	0.032	**<.001**	555
Previous attempt	…	…	…	…	1.185	0.328	**<.001**	555
	New Attempts During MDE[d]				New Attempts, Multiple Imputation[b,e]			
Novelty seeking	0.020	0.101	.842	386	−0.143	0.083	.089	555
Harm avoidance	0.137	0.109	.210	386	0.320	0.084	**<.001**	555
Reward dependence	−0.111	0.105	.289	387	−0.249	0.087	**.005**	555
Persistence	−0.130	0.094	.169	387	−0.019	0.099	.851	555
Self-directedness	−0.132	0.108	.221	385	−0.295	0.079	**<.001**	555
Cooperativeness	−0.112	0.099	.261	387	−0.160	0.079	**.044**	555
Self-transcendence	−0.042	0.108	.696	386	0.194	0.095	**.042**	555
No. of previous attempts	0.110	0.027	**<.001**	452	0.122	0.032	**<.001**	555
Previous attempt	0.836	0.208	**<.001**	452	1.185	0.328	**<.001**	555

[a]Lifetime attempts were adjusted for sex and dataset (Vantaa Depression Study [VDS], Vantaa Primary Care Depression Study [PC-VDS], or Jorvi Bipolar Study [JoBS]) covariates.
[b]New suicide attempts were adjusted for age, sex, dataset, number of previous attempts, and an indicator for having had an attempt before the life-charted follow-up period. Age- and sex-adjusted coefficients for the latter 2 are also shown for comparison.
[c]Number of patients is shown per analysis, as different covariates had different amounts of missing values.
[d]The analysis for new suicide attempts was repeated using only new attempts during an MDE as the outcome (exposure was months in MDE, and patients without MDEs were excluded).
[e]Herein, missing-data modeling was used for bias correction, approximating the situation with 555 complete observations.
Abbreviations: MDE = major depressive episode, SE = standard error.

RESULTS

In total, 219 of the 597 patients (36.7%) had had 1 or more lifetime suicide attempts; 88 patients made 1 or more attempts during their prospective, life-charted follow-up period. The total number of lifetime suicide attempts in the sample was 718, with the mean being 1.20 (SD = 2.79). Altogether, 242 prospectively ascertained suicide attempts were observed during the participant-specific follow-up periods, with the mean rate being 0.018 attempts/mo (SD = 0.074).

Univariate Associations Between Personality Traits and Number of Lifetime and New Suicide Attempts

Table 3 shows which (standardized) personality traits were associated with number of lifetime suicide attempts, number of new suicide attempts, and number of new suicide attempts during a major depressive episode (MDE). All models for lifetime suicide attempts tested positive for overdispersal ($P < .01$), requiring the use of quasi-likelihood method (see Method), whereas models for prospective suicide attempts did not show significant overdispersal. Most associations were in the same direction for numbers of lifetime (total) and prospective suicide attempts, but novelty seeking was weakly positively associated with the number of lifetime suicide attempts and (weakly) negatively associated with the number of prospective suicide attempts.

For example, an increase of 2 SDs higher harm avoidance nearly doubled the monthly rate of suicide attempts compared to the population mean in harm avoidance ($\exp[0.322 \times 2\ \text{SD}] = 1.90$-fold rate; 1 SD implied $\exp[0.322] = 1.38$-fold rate). Effects on lifetime attempts are similarly reported but in terms of annual rates over lived years of life. While considerable in magnitude, the effects of personality were still modest in comparison to a previous suicide attempt, which implied a 3.27-fold increase in the expected participant-specific rate of new attempts. Missing-data modeling did not have a significant effect on the estimates, but restricting analysis to the periods during MDE did. All personality traits were nonsignificant predictors for the number of prospective suicide attempts occurring during MDEs (Table 3).

Duration of Illness and Time Spent in MDEs

Lifetime duration of illness, as assessed here, was not significantly related with the number of lifetime suicide attempts ($\beta = -0.030$, standard error [SE] = 0.384, $P = .938$). However, prospectively each month of MDE in the life chart increased the rate of new suicide attempts by 1.05-fold ($\beta = 0.049$, SE = 0.004, $P < .001$). That is, a year-long MDE was associated with a 1.80-fold rate of new suicide attempts.

The associations between personality traits and the number of lifetime suicide attempts were unaffected by adjustment for lifetime duration of illness (eg, self-directedness, $\beta = -0.276$ with $P = .004$; and self-transcendence, $\beta = 0.287$ with $P = .002$) or age-normalized duration of illness ($\beta = -0.277$ and 0.288, respectively). However, when we controlled for prospective time spent in MDEs, all associations between

Table 4. Regression-Coefficient Estimates for Prospectively Evaluated New Suicide Attempts With Various Adjustments and Sensitivity Analyses[a]

Variable	Novelty Seeking	Harm Avoidance	Reward Dependence	Persistence	Self-Directedness	Cooperativeness	Self-Transcendence
Original	−0.143	**0.320*** **	**−0.249** **	−0.019	**−0.295*** **	**−0.160***	**0.194***
Time spent in MDE	−0.102	−0.124	−0.094	**0.190***	−0.001	−0.048	0.149
BDI	−0.119	**0.210***	**−0.187***	−0.003	**−0.224** **	−0.117	**0.189***
BAI	−0.138	**0.245** **	**−0.218***	−0.004	**−0.231** **	−0.119	0.192
Psychotic symptoms	−0.150	**0.296*** **	**−0.279** **	−0.003	**−0.245** **	−0.130	0.138
Hopelessness	−0.121	**0.207***	−0.162	0.069	**−0.211***	−0.086	**0.232***
Social support	−0.090	**0.184***	−0.006	0.079	**0.196***	−0.074	**0.222***
Married	−0.122	**0.338*** **	**−0.221***	−0.052	**−0.294*** **	−0.151	0.162
Substance use	**−0.201***	**0.296*** **	**−0.245** **	−0.011	**−0.250** **	−0.122	0.176
All other traits	−0.181	0.094	−0.206	0.012	**−0.274***	0.106	0.178
Depressed only	0.049	**0.321***	−0.159	−0.264	**−0.473*** **	**−0.235***	0.258
Bipolar disorders only	**−0.383*** **	**0.298** **	**−0.350** **	**0.376*** **	0.009	−0.006	0.107
Bipolar I disorders only	**0.496** **	0.011	**−0.708*** **	0.016	**−0.432***	**−0.742*** **	0.179
Bipolar II disorders only	**−0.620*** **	**0.441*** **	−0.223	**0.691*** **	0.187	**0.345***	0.080
Logistic models	0.159	**0.328***	**−0.340***	−0.174	**−0.537*** **	**−0.323***	0.191

[a]The first row shows the original (multiply imputed) coefficients from Table 3 (n = 555) for comparison, whereas the other coefficients show how these change when adding the indicated covariate to the model: time spent in MDE = proportion of time in major depressive episode; BDI = Beck Depression Inventory; BAI = Beck Anxiety Inventory; psychotic symptoms (yes/no); hopelessness score; (perceived) social support score; married (yes/no); substance use (yes/no); then, all other personality traits adjusted were adjusted for. "Depressed only" shows the original estimates in the 379 patients from Vantaa and Vantaa Primary Care Depression Studies, whereas the "bipolar disorders only" shows the estimates in the 176 patients from Jorvi Bipolar Study. "Bipolar I disorder only" shows estimates in the 81 bipolar patients that are of the type I, whereas the "bipolar II disorders only" shows the same estimates for the 95 bipolar II disorder patients. Finally, "logistic coefficients" shows the original analysis but predicts the status of having made a new suicide attempt instead of the number of new attempts, adjusting for a possible attempt before the baseline and the number of such attempts.

*$P < .05$. **$P < .01$. ***$P < .001$.

Abbreviations: BAI = Beck Anxiety Inventory, BDI = Beck Depression Inventory, MDE = major depressive episode.

personality traits and the number of new suicide attempts lost significance (Table 4), with the exception of persistence, which became a statistically significant predictor of the number of new suicide attempts.

In general, adjusting for risk factors other than time spent in MDEs during follow-up did not explain associations between personality and number of new suicide attempts, although the effects of reward dependence may be mediated through perceived social support and hopelessness (Table 4). Adjusting for all other personality traits, however, attenuated all associations except that between self-directedness and new suicide attempts (Table 4). Sensitivity analyses between the cohorts are further discussed in the supplementary material.

Formal Analyses of Mediation

The direct and indirect effects of harm avoidance and self-directedness on prospectively ascertained suicide attempts indicated significant indirect mediated effect through time at risk in MDEs, but no significant direct effects (Figure 1). Details of the formal analyses are provided in the supplementary material.

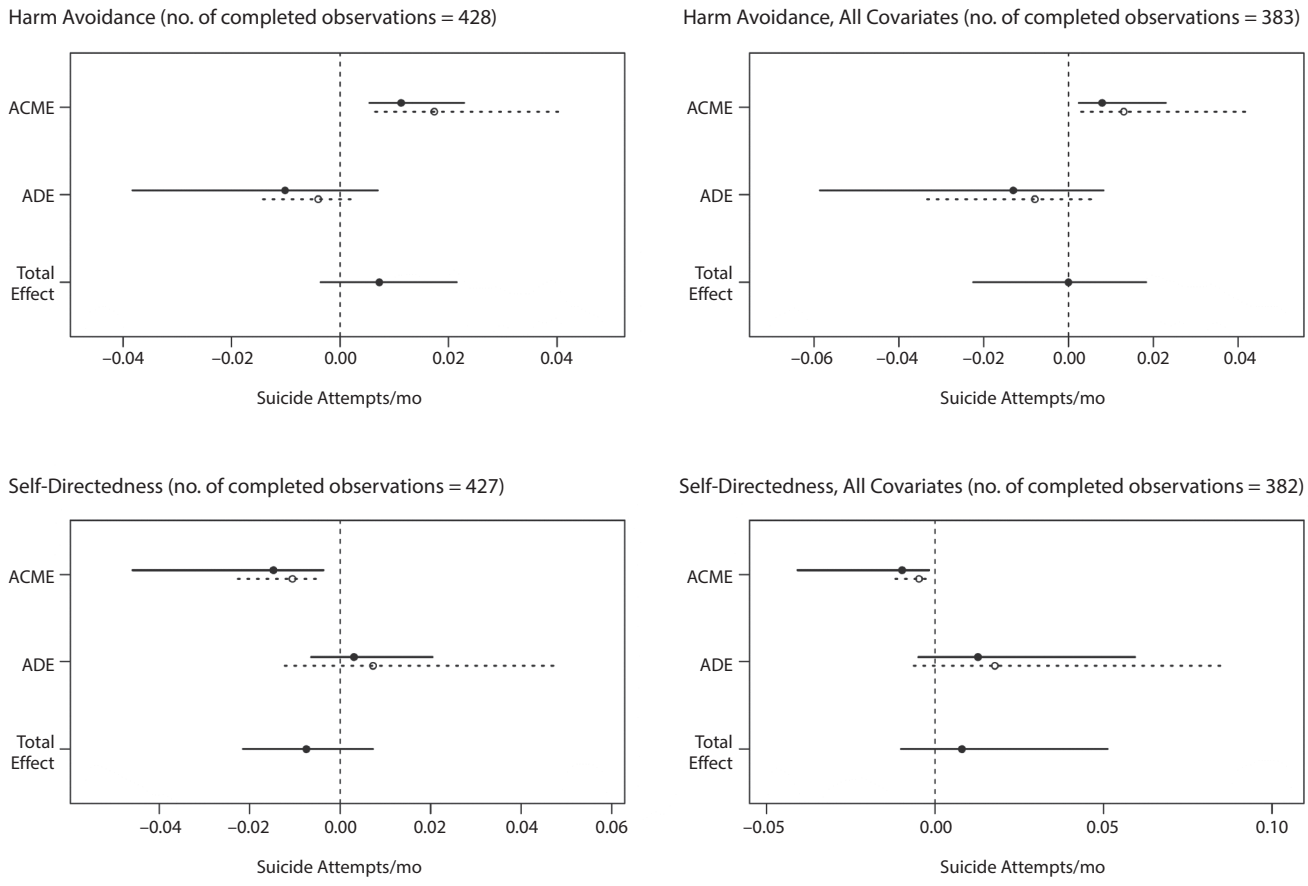
DISCUSSION

We investigated the relationship between temperament and character and suicide attempts in 3 prospectively studied mood disorder cohorts. In these regionally representative samples, the influence of individual temperament and character on suicide attempt risk was mediated by time spent in high-risk states, ie, MDEs. There was no evidence for a major moderating effect on risk for suicide attempts occurring during MDEs.

This study has numerous methodological strengths. It is the first to evaluate the effect of time at risk on suicidal behavior in conjunction with personality, made possible by use of graphic life charts. Information on suicide attempts was gathered both retrospectively and prospectively during the follow-up, with mostly consistent findings. The most important strength was availability of life charts with information on illness course and timing of suicide attempts, allowing testing of mediator and moderator hypotheses. The TCI-R was available at several evaluations, thus reducing the effect of current mood on self-assessment. Patients were assessed prospectively with semistructured interviews with excellent interrater reliability and both objective and subjective structured and semistructured measures. Information regarding all comorbid Axis I and II disorders at baseline was also available. We investigated a broad range of risk and protective factors from several domains, including Axis I and II comorbid disorders and symptoms, history of suicidal behavior, and psychosocial factors in the risk of suicide attempts. All cohorts employed similar methodology allowing valid comparisons and pooling of data.

Nevertheless, limitations exist. The lengths of follow-up differed, as the 5-year follow-up data from JoBS were not yet available. The data were therefore modeled in Poisson regressions via the standard offset, or length-of-exposure, term. Second, similarly to any retrospective study, depression might affect recall of previous suicide attempts. Third, it was only possible to investigate time spent in crudely classified risk states instead of detailed temporal tracking of individual specific risk states. Risk for attempts most likely covaries significantly with levels of depression, hopelessness, and possibly anxiety, none of which were measured on a daily basis. Thus, the observed gradient between symptom

Figure 1. Average Causal Mediation Effects (ACME) and Average Direct Effects (ADE) of Harm Avoidance and Self-Directedness Personality Traits on Patients' Rate of Suicide Attempts as a Result of Time Spent in Major Depressive Episodes (MDEs)[a]



[a]The panels on the left side show estimated effect of 1 SD difference in personality trait mediated through time spent in MDE (ACME) and directly "caused" by the trait (ADE). An interaction analysis examined whether these effects differ between those who are 1 SD above the mean in the trait (solid line) and those who are 1 SD below the mean (dotted line). Also, the total effect of the traits is shown. The panels on the right side adjust for possible confounding due to baseline depressive symptoms, anxiety symptoms, psychotic symptoms, hopelessness, perceived social support, marital status, and substance use. The number of complete observations per condition is shown in parentheses in the panel titles.

states[6–9] is most likely an underestimate. Fourth, as we modeled sample rates, the usual precautions apply for causal inferences at the individual level. Fifth, the study was naturalistic, and treatment was not controlled for. Treatment could influence the risk for suicide attempts by reducing the time ill and, perhaps, by modifying the risk in illness phases independent of the influence of mood. Sixth, we cannot exclude the possibility that some personality dimension, eg, impulsive or nonimpulsive aggressive traits,[48–51] not sufficiently captured by the dimensions of the TCI-R might have important moderating effects on risk for suicidal acts. Seventh, in the analyses, we controlled for numerous risk factors besides the time ill hypothesized to mediate effects of temperament and character. However, there are other risk factors, such as reasons for living, that were not measured. Eighth, while we controlled for most known confounders in the mediation analyses, the sequential ignorability assumption[45] cannot be explicitly tested; proof of causality remains unattainable. Finally, we investigated suicide attempts among patients with mood disorders, and generalizability of findings to completed suicides among them, or to suicidal behavior among other types of patients, requires further confirmation.

The associations of TCI-R dimensions with suicide attempts among patients with mood disorders were mostly consistent and expected. Like earlier studies[18–23] with mood disorder patients, our study found the rate of lifetime suicide attempts to be associated with high novelty seeking and also, as a trend, with high harm avoidance. Moreover, the rate of prospectively evaluated suicide attempts was also associated with high harm avoidance. Contrary to findings regarding lifetime suicide attempts in our study and from a birth cohort study,[52] the rate of prospective suicide attempts was associated with low novelty seeking, which was mostly due to patients with bipolar disorder. Reward dependence was negatively associated with the number of prospective suicide attempts. Most,[18–20,23–26] but not all,[21,22] former studies among mood disorder patients have found no association with lifetime suicide attempts and reward dependence; we found the possible effect of reward dependence to derive from its correlation with perceived social support. Prospectively evaluated suicide attempts were associated with high persistence in patients

with bipolar disorder which, after adjusting for the time spent in MDEs, resulted in a slight positive finding among all patients. This unexpected finding appears specific to bipolar disorder and requires an independent replication. The numbers of both lifetime and prospectively evaluated suicide attempts were associated with high self-transcendence and low self-directedness and cooperativeness. These findings are in accordance with most studies among mood disorder patients evaluating the association of lifetime suicide attempts with self-transcendence,[24,25] self-directedness,[18,20,24,25] and cooperativeness.[23] Of these traits, the role of self-directedness seems central, as only it persisted as independently significant when the effects of the traits were adjusted for each other (Table 4). Nevertheless, it appears that whatever the precise mechanisms through which these traits exert their influence, they must be indirect rather than direct or moderating effects on risk.

In a series of previous studies,[6–9] we have shown total time spent in mood episodes during follow-up to be a major determinant of risk for suicidal acts among patients with mood disorders. Here, we observed total duration of MDEs to covary with personality in explaining suicide attempt rates. When the effects of MDEs were parceled out, personality did not predict suicide attempts. The statistical analysis of mediation further supported indirect effects. Thus, most of the effects are likely to be mediated through time spent in high-risk states. It is noteworthy that none of the other risk factors we investigated seemed to have a similar mediating role. As we have shown,[11] analogous associations exist between the personality traits and prospectively evaluated low/dysphoric mood episodes in the general population. Thus, the mediating effect of mood states is a credible mechanism for explaining associations between personality and suicide attempts.

In conclusion, risk of suicide attempts among mood disorder patients is associated with temperament and character dimensions. However, these associations lose significance after adjusting for time spent in MDEs, and mediation analyses support indirect rather than direct effects. Thus, their influence on predisposition to suicide attempts is likely to be mainly indirect, mediated by increased time spent in depressive episodes.

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Supplementary Material

Article Title: Temperament, Character and Suicide Attempts in Unipolar and Bipolar Mood Disorders

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List of Supplementary Material for the article

Disclaimer

This Supplementary Material has been provided by the author(s) as an enhancement to the published article. It has been approved by peer review; however, it has undergone neither editing nor formatting by in-house editorial staff. The material is presented in the manner supplied by the author.

Supplementary material

1. Cloninger's unified biopsychosocial theory of personality

Cloninger's unified biopsychosocial theory of personality postulates four temperament and three character dimensions.[1, 2] The different temperament dimensions are defined in terms of basic stimulus-response characteristics, and character refers to individual differences in higher cognitive functions underlying a person's goals and values and voluntary rational processes. Novelty Seeking (NS) is thought to be related to the behavioral activation system, Harm Avoidance (HA) to the behavioral inhibition system, Reward Dependence (RD) to the behavioral maintenance system, and Persistence (P) to perseverance in behavior despite frustration and fatigue. Of the character dimensions, Self-directedness (SD) refers to an individual's ability to control, regulate and adapt their behavior in accord with chosen goals and values, Cooperativeness (C) to their tendency towards social tolerance, empathy, compassion and helpfulness, and Self-transcendence (ST) to their identification with nature and ability to accept ambiguity and uncertainty.

2. Sensitivity analyses between the cohorts

In interaction tests, the observed negative association between NS and the number of new suicide attempts (Table 3 in main manuscript) were mostly due to BD patients (Table 4 in the main manuscript), who showed a clear NS effect (β = -0.383) compared to depression patients (β = 0.049). BD patients also lacked the association between C and the number of new suicide attempts, or for SD and number of new attempts. That is, low SD was a strong predictor of the number of new suicide attempts in depression patients, but it was not associated with suicide attempt-rates in the BD patients (β = 0.009, p = n.s.). P mainly had an effect for BD patients (β = 0.376). In addition to differences between the depression patients and BD patients, there were also many significant interactions with personality traits in predicting the number of new suicide attempts in BD I *versus* BD II patients. Finally, we assessed (dimensionally) whether predicting the number of new suicide attempts yielded different implications than predicting (categorically) who makes an attempt. As the lower right coefficients of the Table 4 show, predictions are qualitatively similar for the number of new attempts and the attempter status (one or more attempts) outcomes. Imputation analysis did not reveal prominent missing-data effects (Table 3).

3. Poisson regression

As our primary approach, Poisson regression was applied in modeling the number of suicide attempts during the (participant-specific) time of exposure as a function of explanatory covariates.[3] Observed number of suicide attempts, y_i, for patient i was modeled as a Poisson distributed random variable. The participant-specific rate of attempt occurrences, λ_i, was modeled by a logarithmic link function: the natural log of λ_i was a sum of an exposure offset, a_i, a linear model on covariates (i.e., independent variables), and a normally distributed random-effect perturbation, ξ_i, for overdispersal modeling.[3] In sum, the model was

$$y_i \sim \text{Poisson}(\lambda_i),$$
$$\log(\lambda_i) = \log(a_i) + \Sigma_k \beta_k x_{i,k} + \xi_i,$$
$$\xi_i \sim \text{Normal}(0, \sigma^2),$$

where "~" signifies "distributed as". The offset, a_i, stands for the number of follow-up months (length of 'exposure') for the patient i when modeling new suicide attempts, for the patients age when modeling life-time attempts, and for the months in MDE when modeling new suicide attempts that occurred during MDE. Thus, $\lambda_i / a_i = E(Y|X_i)$, or in other words, the expected rate of suicide

attempts per unit time in patients with covariate values X_i. This way, exponential of a regression coefficient β_k for the covariate k, $\exp(\beta_k)$, directly yields a multiplicative coefficient for the expected rate of suicide attempts for those participants with covariate k one s.d. above the mean. Or if the covariate is dichotomous instead of a standardized z-score, $\exp(\beta_k)$ yields the multiplicative increase in patient i's suicide-attempt rate due to the group membership indicated by $x_{i,k} = 1$ (as opposed to a patient j with $x_{j,k} = 0$).

Standard Poisson regression model assumes equality of outcome mean and variance, and when this assumption is not satisfied, overdispersal is said to occur. In that case, parameter $\sigma^2 \neq 0$ captures the difference between mean and variance. Since the modeling of overdispersal (estimation of σ^2) decreases statistical power, however, existence of overdispersal was first tested for dispersiontest in "AER" R-package version 1.2-1[6]; if existing, σ^2 was estimated, and otherwise simply set to $\sigma^2 = 0$. Quasi-Poisson (overdispersal) or Poisson (no overdispersal) regression models were estimated using the standard Generalized Linear Modeling (glm-function) in R-software 64-bit Linux-version 2.15.3,[5]the former being a standard approximation for an explicit random effect (ξ_i) typically used in Bayesian framework.[3]

4. Multiple imputation

The following strategy, based on multiple imputation by chained equations"mice" R package version 2.17[6] was taken. Method of imputation was predictive mean matching. First, initial imputation model was created using "quickpred" function of mice for prediction selection, with default options.[6,7] Then predictors that lead to convergence problems or yielded bad imputations were further dropped from imputation model (e.g., long-tailed suicide-attempt distributions were ill-suited predictors and exposure time variable highly correlated with sample indicators). After a suitable and well-behaving imputation model was established, 35 imputation chains were initiated and then iterated for 30 iterations of mice-algorithm; standard regression estimates in the resulting 35 imputation data sets were pooled using moment-based statistics and an F reference distribution.[8] Table e1 summarizes variables in our data and their abbreviations in this supplement. Figure e1 summarizes the missing-data pattern. Figure e2 shows that distributions of imputed values satisfactorily captured those of the observed values. Ten mice iterations yielded satisfactory mixing of the 35 chains, as is typical,[6] but 30 iterations were run to be on the safe side. Variable selection only by quickpred was insufficient, however, but a good imputation model was achieved by excluding variables marked with star in Table s1 when predicting missing values.

Table e1. Variables and their abbreviations

sam1	Jorvi Bipolar Study patient
sam2*	Vantaa Depression Study patient
sam3	Primary-care Vantaa Depression Study patient
age	Age in years
sex	Gender indicator
y*	Number of new suicide attempts
ybl*	Number of previous suicide attempts
ns	Novelty seeking (personality trait)
ha	Harm avoidance (personality trait)
rd	Reward dependence (personality trait)
ps	Persistence (personality trait)
sd	Self-directedness (personality trait)
co	Cooperativeness (personality trait)
st	Self-transcendence (personality trait)
exposure*	Length of follow up in months
bdi*	Beck's Depression Inventory
bai*	Beck's Anxiety Inventory
hss*	Hopelessness score
pssup*	Perceived Social Support
msta	Marital status (married/not)
psys	Psychotic symptoms (yes/no)
subu	Substance use (yes/no)
mdet	Proportion of exposure under Major Depressive Disorder
jobs_bd1	Indicator for Type I Bipolar Disorder for JoBS patients (as opposed to Type II)
vds_bipo	Indicator for MDE turning to BD during VDS follow-up

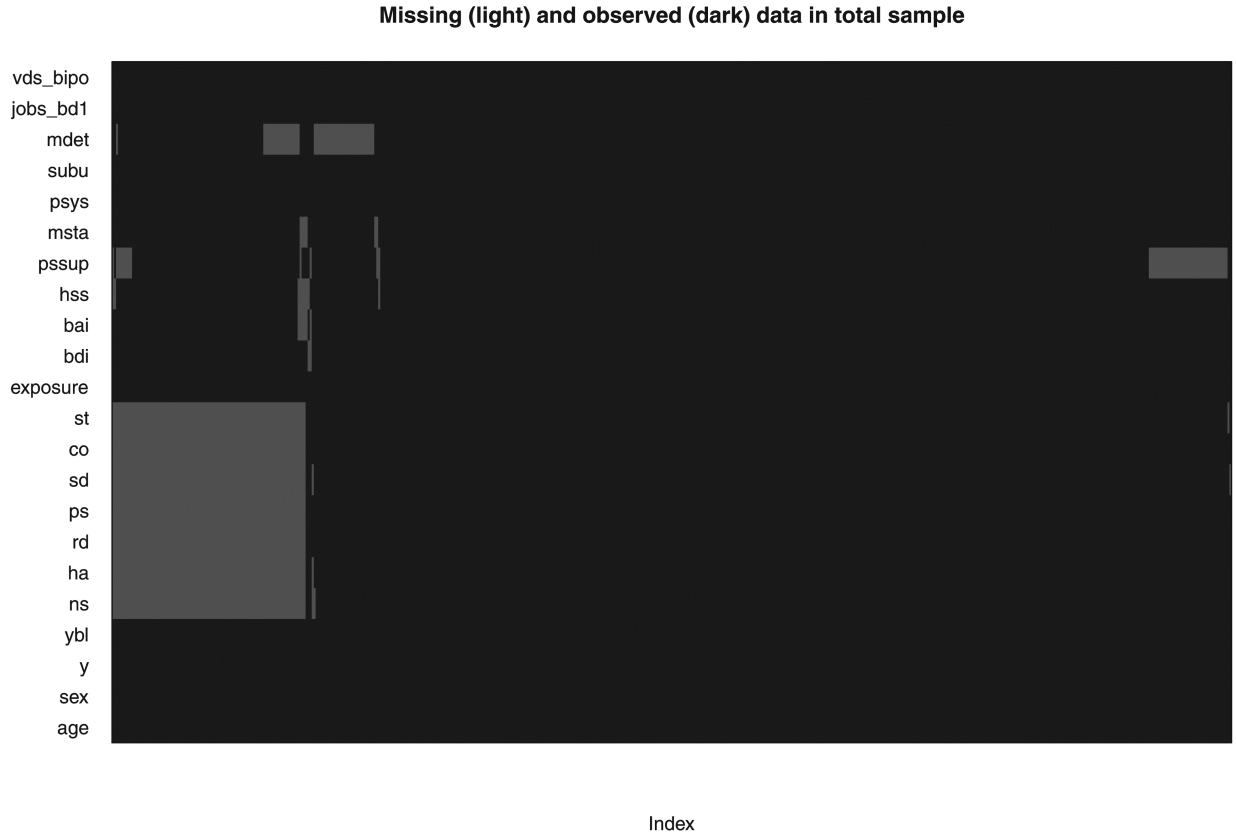

Figure e1. Clustered missing-data pattern.

Index/x-axis shows observations and y-axis variables; missing values are marked with light gray, whereas observed values with darker gray.

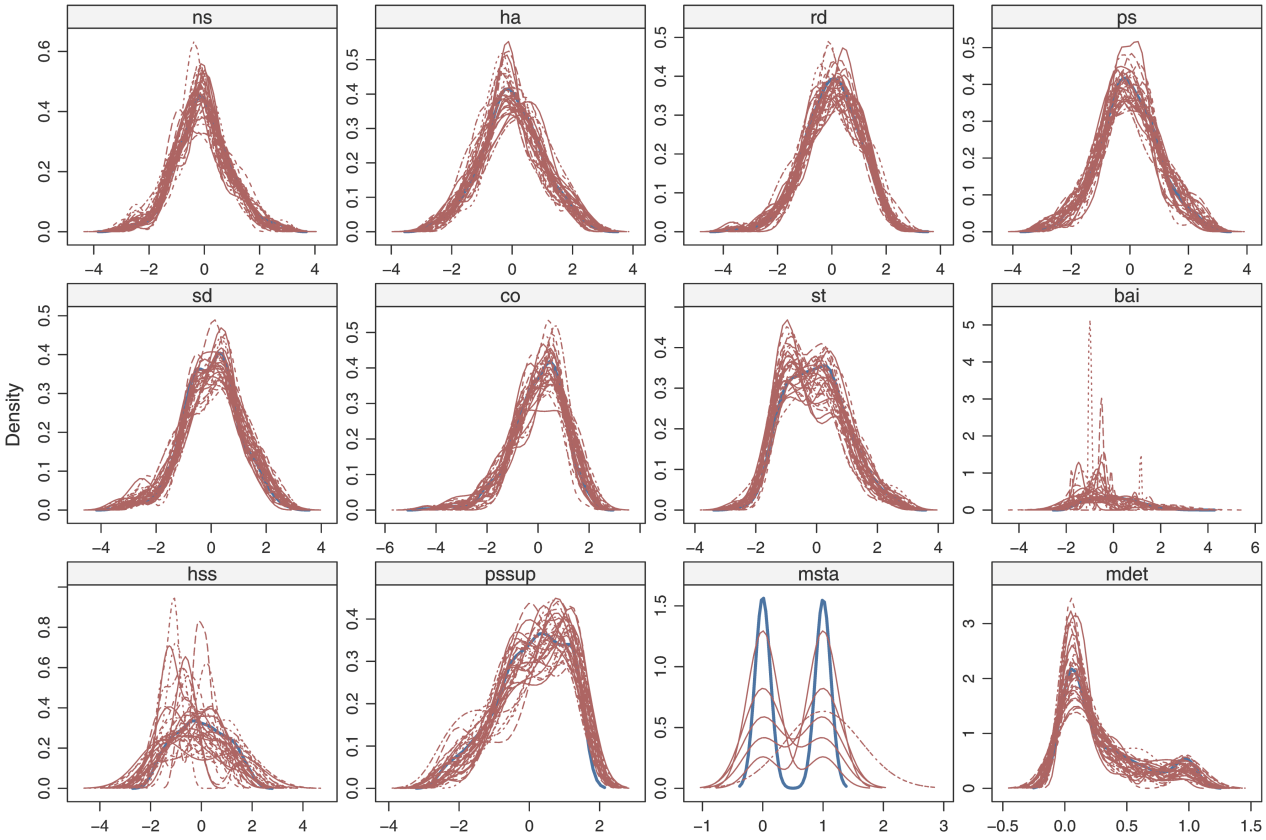

Figure e2. Density estimates of imputed (red) and observed (blue) values.
Densities of imputed values are separately shown for all the 35 chains, demonstrating good correspondence with observed distributions. Other variables than personality traits had so few missing values that single density estimates necessarily appear to vary, although good overall correspondence existed.

5. Formal analyses of mediation

For cases with a clear possibility that another variable mediates a personality trait's effects to new suicide attempts, we conducted a formal mediation analysis using a general approach to causal mediation analysis and version 4.4.2 of the "mediation" R package that implements it[9,10] (robust standard-error estimates and 1000 quasi-Bayesian simulations, linear regression model for mediating variable, and Poisson regression model for the outcome). Because it can be difficult to say whether a covariate should be thought as a confounder for personality, we studied both a minimal set of confounding covariates and all possible confounders. The minimal set contained age, sex, having had a previous suicide attempt, number of previous suicide attempts, and cohort indicators. All covariates contained the aforementioned plus baseline BDI and BAI, psychotic symptoms, hopelessness, perceived social support, marital status, and substance use (excluding the studied mediator, of course). For the mediating variable candidate, we estimated the Average Causal Mediation Effect (ACME), Average Direct Effect (ADE), and total effect for the personality trait in question. In text, we report just these estimates that assume no interaction between personality status and the mediator[9], with 95% confidence intervals, but in a Figure 1, we also show the mediated and direct effects separately by "treatment" status. That is, we study whether the mediating variable mediates effects of both high and low poles of the continuous personality traits or just one or other. The hypothetical high-pole "treatment" group was defined as the studied personality trait being 1 s.d. above the sample mean, *versus* the low-pole "control" group with the trait 1 s.d. below the mean. We also studied simple moderation by assessing statistical significance of interaction terms for selected variables and traits.

Upon examining the Table 4, one sees that both Harm avoidance and Self-directedness showed robust effects despite adjustments for other covariates than the time spent in MDE. Thus, these personality traits were selected for further mediation analyses that assess the possibility that their effects on suicide attempts were mediated by increased time spent in MDE. Indeed, 1 s.d. higher Harm avoidance were estimated to imply 0.014 more suicide attempts per month via the increased time spend in MDE (95% CI = 0.007 – 0.031, $p < 0.01$), and not at all due to direct effects of Harm avoidance (ADE = -0.007, CI = -0.027 – 0.005, $p = 0.30$). For Self-directedness, the ACME was -0.013 (CI = -0.034 – -0.005, $p < 0.01$) and ADE virtually non-existent, 0.005 (CI = -0.009 – 0.034, $p = 0.62$). Taking into account all the other covariates attenuated, but did not remove, these mediated effects, and the mediated effects were similar in both poles of the traits (Figure 1). No interaction (or "moderation") effects were observed for the time spent in MDE and Self-directedness ($p = 0.39$ for interaction term in Poisson regression), but Harm avoidance may have minor interactions with time spent in MDE ($p = 0.051$). The supplementary figure e3 shows how the canonical link function changed by the levels of standardized Harm avoidance and standardized (z-score of) months spent in MDE.

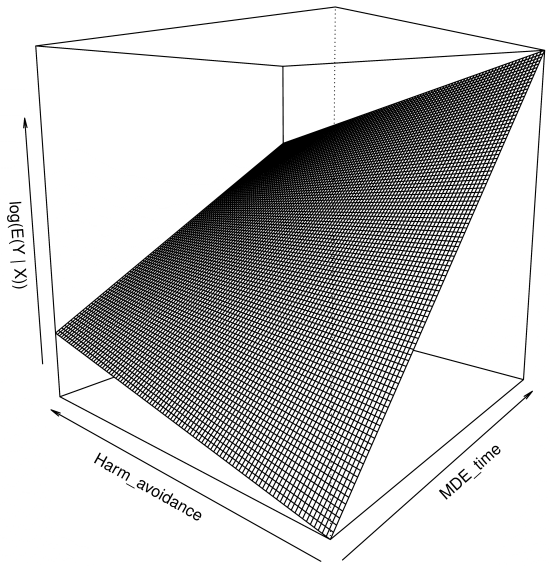

Figure e3 on moderation/interaction. MDE-time-by-Harm avoidance interaction.
A generalized linear (Poisson regression) model was estimated with the minimal set of covariates (see Methods) plus MDE-time, Harm avoidance, and their interaction term. The figure shows how the link function (log of suicide-attempt rate) changes by the joint levels of Harm avoidance and time spent in major depressive episodes (MDE). A borderline significant interaction was observed, with those low in Harm avoidance showing a stronger effect of MDE time on suicide-attempt rate compared to those high in Harm avoidance.

6. Supplementary material References

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