

Gender modulation of psychopathological dimensions associated to suicidality

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Summary. Objectives. The dimensional approach to psychopathology has been proposed to reliably evaluate suicidality. Potential gender modulation of psychopathological dimensions associated to suicide attempts was investigated. **Methods.** 91 subjects who committed a near-lethal suicide (SA group) and 374 who did not (nSA group) were recruited in a Psychiatric Intensive Care Unit regardless of their categorical diagnosis. The Hamilton Depression Rating Scale (HAM-D), the Brief Psychiatric Rating Scale – Expanded version (BPRS-E) and the Scale for Rapid Dimensional Evaluation (SVARAD) were administered at the admission. A Factorial Multivariate ANOVA was conducted according to General Linear Model: Sex and Suicidality were input as fixed factors, HAM-D, BPRS-E and SVARAD scores as dependent variables. **Results.** Men with SA (MSA) displayed significant lower scores in SVARAD Activation dimension compared to women with SA (FSA) ($p=0.049$), men without SA (MnSA) ($p<0.001$) and women without SA (FnSA) ($p<0.001$). Both SA groups displayed significant higher scores compared to nSA groups in regard of Depression item (BPRS-E) ($p<0.001$). The MSA group displayed significant lower scores in Psychomotor agitation (HAM-D) compared to FSA ($p=0.044$), MnSA ($p<0.001$) and FnSA ($p<0.001$). **Conclusions.** By means of multifactorial statistics sex resulted a moderator of the relation between activation/agitation and suicidality, despite categorical diagnosis.

Key words. Agitation, gender impact, psychopathological dimensions, sex variable, suicidality, suicide attempts.

Modulazione della variabile di genere sulle dimensioni psicopatologiche associate alla suicidalità.

Riassunto. Obiettivi. L'approccio dimensionale alla psicopatologia appare utile per una valutazione affidabile della suicidalità. Abbiamo indagato la potenziale modulazione che la variabile di genere può assumere sulle dimensioni psicopatologiche associate ai tentativi di suicidio. **Metodi.** A prescindere dalla loro diagnosi categoriale, sono stati reclutati 91 soggetti con un mancato suicidio (gruppo SA) e 374 senza (gruppo nSA), ricoverati presso il Servizio Psichiatrico di Diagnosi e Cura del Policlinico Umberto I di Roma. I partecipanti all'ingresso nel servizio sono stati valutati mediante le seguenti scale psicometriche: Hamilton Depression Rating Scale (HAM-D), Brief Psychiatric Rating Scale – Expanded version (BPRS-E) e Scale for Rapid Dimensional Evaluation (SVARAD). È stata implementata un'ANOVA multivariata fattoriale secondo il modello lineare generale: genere e suicidalità sono stati inseriti come variabili indipendenti, i punteggi alle scale HAM-D, BPRS-E e SVARAD come variabili dipendenti. **Risultati.** Gli uomini con tentativo di suicidio (MSA) hanno mostrato punteggi significativamente più bassi all'item Attivazione della scala SVARAD in confronto alle donne con tentativo di suicidio (FSA) ($p=0.049$), agli uomini senza tentativo di suicidio (MnSA) ($p<0.001$) e alle donne senza tentativo di suicidio (FnSA) ($p=0.049$). I soggetti con tentativo di suicidio (SA) hanno mostrato punteggi significativamente più alti in confronto ai soggetti senza tentativo di suicidio (nSA) all'item Depressione della scala BPRS-E ($p<0.001$). Il gruppo MSA ha mostrato punteggi significativamente più bassi all'item Agitazione psicomotoria della scala HAM-D in confronto ai gruppi FSA ($p=0.044$), MnSA ($p<0.001$) e FnSA ($p<0.001$). **Discussione e conclusione.** Per mezzo di un'analisi statistica multifattoriale la variabile di genere è risultata un moderatore della relazione tra la dimensione attivazione/agitazione e la suicidalità, a prescindere dalla diagnosi categoriale.

Parole chiave. Agitazione, dimensioni psicopatologiche, modulazione del genere, suicidalità, tentativi di suicidio, variabile di genere.

Introduction

Suicide represents a global public health concern being the first cause of death due to non-natural reasons with almost 800.000 deaths per year worldwide: an age-standardized suicide rate of over 10 per 100.000 population and higher suicide rates in men than in women have been reported¹. In the WHO European region alone, 1.4% of the total number of de-

aths is attributable to suicide². Importantly, for every adult who dies by suicide there are more than 20 others that attempt it¹.

Besides socioeconomic, environmental and cultural factors which have been repeatedly described³⁻⁵, specific clinical factors appear tightly related to a higher incidence of suicide attempts. A history of previous suicide attempt⁶ represents the most important predictors of suicide, therefore it would be helpful to shed light on psychopathological description of suicide attempts. In

addition, factors clearly associated to suicide ideation as psychiatric disorders, depression and hopelessness, do not directly correlate with the progression from ideation to attempt⁷. Different theories within the ideation-to-action framework as the Interpersonal Theory⁸ have been advanced, positing that the acquired capability for suicide significantly underlies suicide attempts⁹. Stressful life events¹⁰, lower parental support¹¹ and history of emotional abuse¹² have been associated to suicide attempters rather than suicide ideators. Moreover, young adults who recently attempted suicide showed a lower quality of life (QoL)¹³ compared to matched controls who did not¹⁴, displaying higher rates of depressive and borderline symptoms as hopelessness and non-suicidal self-injury (NSSI) compared to lifetime attempters and suicide ideators¹⁵.

A higher incidence of completed suicide among men compared to women has been highlighted^{16,17}: paradoxically, women show a higher incidence of suicidal attempts¹⁸⁻²⁰, likely explained by addressing differences in suicide methodology among genders^{21,22}. A gender variance differently influencing suicide risk factors has been described¹⁷ with women generally more vulnerable than men²³: current substance use disorders and hostility have been associated with increased suicide risk and self-harm among women²⁴. On the other hand, men are more at risk when not in a relationship, unemployed or receiving a low income²⁵. Menon et al. found that men who attempted suicide displayed higher baseline levels of aggressiveness compared to women, with more past episodes of violence²⁶. Anger has been previously investigated^{27,28} but no differences among genders concerning self-directed violence have been reported²⁹.

Suicide has received an increased attention by health operators and researchers aiming at identifying psycho-diagnostic and mediational factors that may represent potential reliable predictors of suicide risk³⁰. Although symptoms and signs are useful in defining mental disorders at risk for suicide as mood disorders³¹, the categorical approach does not appear reliable enough in providing effective prevention strategies^{32,33} or predicting time and ways in which people at risk will accomplish their intentions. Bearing this in mind, a dimensional approach aimed at defining specific state elements seems more helpful in profiling those individuals at high risk for suicide^{34,35}.

Psychopathological dimensions may be intended as clinical entities involving a set of co-varying and interdependent symptoms and signs; each clinical presentation, regardless of its categorical and descriptive classification, could be described based on the relative weight assumed by symptoms cohorts of specific psychopathological dimensions³⁶. Specific psychopathological dimensions have been associated to suicidality³⁷. Anger, irritability, aggressiveness, and hostility are deeply involved in depression, in

particular the unipolar type³⁸, but a direct link with suicide risk has not yet been established²⁸. Psychomotor activation, both iatrogenic³⁹ or not⁴⁰, and impulsivity^{37,41,42} have been thoroughly described as a serious risk factor for suicide and suicidal ideation. Psychological pain with its three described subscales (pain arousal, painful feelings and pain avoidance) are referred as more accurate predictors of suicide attempts than evaluation of depression, impulsivity, hopelessness and acquired capability for suicide⁴³⁻⁴⁵. However, in literature there is a lack of unanimous agreement about potential influence of the sex variable on the attitude toward suicidal behaviors: although it has been observed that gender acts over suicidal risk⁴⁶, there is no clear evidence whether psychopathological dimensions associated with suicide attempts specifically vary in regard of the sex variable.

AIM OF THE STUDY

The present study sought to investigate among patients admitted in a Psychiatric Intensive Care Unit (PICU) whether specific psychopathological dimensions are significantly associated with suicide attempts compared to non-suicidal inpatients with other acute mental issues. Secondly, the potential sex modulation on these dimensions has been investigated.

Materials and methods

SUBJECTS

All inpatients aged 18 or more were admitted in the PICU of Policlinico Umberto I Hospital in Rome from January 1st 2018 and January 31st 2019 and consecutively enrolled regardless of their categorical diagnosis. They were subsequently divided into 2 different groups based on suicide attempt (SA group, N=91 and nSA group, N=374) as the reason for hospitalization. Patients in the SA group committed a *near-lethal suicide*, intended as an attempt that would have been fatal had it not been for the provision of rapid and effective emergency treatment⁴⁷, and were admitted in the PICU from the emergency room, orthopedics or intensive care units. Out of the 465 patients whose data were then analyzed, 390 were hospitalized on a voluntary basis and signed free, informed consent, whereas 66 were on a Compulsory Medical Treatment (CMT) upon admission but revolved into voluntary hospitalization in the forthcoming days. For 9 patients this information was not available. The study adopted the Principles of Human Rights, as issued by the World Medical Association at the 18th WMA General Assembly, Helsinki, Finland, June 1964 and subsequently amended by the 64th WMA General Assembly, Fortaleza, Brazil, in October 2013.

The research protocol has been reviewed and approved by the Ethics Committee of the Umberto I University Hospital, Rome, Italy prior to enrolment.

ASSESSMENT

All data were anonymized. Socio-demographic variables, including age, occupation, working status, social status, civil status and education were collected retrospectively from medical records. Patients' symptomatology has been assessed by ward trained clinicians within three days of admission, at the first valid clinical interview. The following psychometric tools were administered: The 24 item Brief Psychiatry Rating Scale - expanded version (BPRS-E)⁴⁸ which is widely used and well validated, including additional items enhancing the stability and the thoroughness of the scale⁴⁹; the Italian version of the 21-item Hamilton Depression Rating Scale (HAM-D) to assess depressive symptoms⁵⁰; finally, for dimensional assessment of patients' psychopathology, the Italian Scale Rapid Dimensional Assessment Scale (SVARAD)^{51,52} was administered. This tool is an observer-rated scale consisting of 10 items, each one based on a 5-point scale with the score ranging from 0 ("not present") to 4 ("extremely severe"). This tool proved to be reliable and valid in clinical practice, even when time for evaluation is limited (emergency settings)³⁶. The SVARAD measures ten dimensions, alongside with their detailed description and accurate reference points for severity graduation: *Apprehension/Fear*, concerning the state of anxiety, anguish, fear, and the perception of imminent threat; *Sadness/Demoralization*, about distrust in oneself and one's own abilities, anhedonia and pessimism; *Anger/Aggressiveness*, including feelings of frustration, irritability and anger up to verbal or physical violence; *Obsessiveness*, investigating doubtfulness, rigidity, meticulousness, and perfectionism, up to rituals and compulsions and obsessions; *Apathy*, concerning indifference, detachment, and blunted affect; *Impulsivity*, or the tendency to suddenly act in ways that are improper or potentially harmful to oneself or others; *Reality Distortion*, considered as the difficulty in distinguishing between reality and fantasy, along with the tendency to attribute unusual and unshared meanings to events or experiences up to delusions or hallucinations; *Thought Disorganization*, about the disruption of logical organization of thought and impaired communicative functions; *Somatic Preoccupation/Somatization*, about the polarization on one's own body and health; *Activation*, involving increased motor activity, accelerated thought, disinhibition, feelings of hyperenergy up to euphoria or irritability^{36,52}.

STATISTICAL ANALYSIS

For descriptive statistics t-test and Pearson's Chi-square test were employed. Administration of phar-

macological treatment was analyzed in all samples. Clorpromazine Equivalents and Diazepam Equivalents⁵³ were calculated in order to assess a quantitative difference in drug assumption between men and women in SA group. A Factorial Multivariate ANOVA was conducted according to General Linear Model. Sex (Male/Female) and Suicidality (SA/nSA) were included as fixed factors. SVARAD, BPRS-E and HAM-D items were included as dependent variables. Pairwise comparisons were corrected with Bonferroni method. A One-way ANOVA was conducted for items whose scores resulted significant at the factor's interaction analysis, in order to investigate differences between samples divided based on sex variable: men with suicidal attempts (MSA), men without (MnSA), women with suicidal attempts (FSA) and women without (FnSA). Post-hoc statistics were corrected for multiple comparisons according to Bonferroni method. The software used for statistical analysis is IBM SPSS (Statistical Package for Social Science) Statistics 25 (2020).

Results

Analyses were conducted on 465 inpatients out of 501 initially recruited, due to missing data: 19,5% committed a suicide attempt and 80,5% did not. There was no difference in sex and age between the two groups (table 1). There were proportionally more patients receiving a CMT in the nSA group ($p=0.008$). Analyses of demographic variables showed a significantly higher proportion of employed subjects in the SA group ($p<0.05$) and a significant higher proportion of unemployed subjects in the nSA group ($p<0.05$). A significant higher proportion of unmarried subjects was observed in the nSA group ($p<0.05$). Importantly, statistics may have been affected by the occurrence of several missing data (table 1). No significant differences were found between groups concerning social status and education.

No significant differences were observed between the SA and the nSA groups concerning assumption of different treatments ($\chi^2=19.641$, $p=0.142$) (table 2). FSA group has been treated with more CPZ equivalents (459.1 ± 351.2 mg) compared to MSA group (331.8 ± 286.5 mg), although this finding did not reach statistical significance ($t=1.858$, $p=0.066$). FSA group has been treated with more Diazepam equivalents (58.9 ± 194.1 mg) compared to MSA group (52.2 ± 160.8 mg); this finding did not reach statistical significance as well ($t=0.176$, $p=0.861$).

SVARAD

Test Between Subjects of Factorial ANOVA showed an effect of sex variable only on the SVARAD item

Table 1. Sample's clinical and socio-demographic data. For 9 subjects' data for Voluntary Hospitalization (VH) and Compulsory Medical Treatment (CMT) were not available. For 86 subjects' data about Working Status were not available. For 52 subjects' data about Social Status were missing. For 51 subjects data about Civil Status were missing. For 72 subjects data about title of Education were missing.

	SA (n=91)	nSA (n=374)	Statistics	p
Age	43,6 ± 14,4	42,3 ± 14,3	t = 0.775	0.439
Sex				
Male	40 (44,0%)	183 (48,9%)	$\chi^2= 0.726$	0.394
Female	51 (56,0%)	191 (51,1%)		
CMT	5 (5,6%)	61 (16,6%)	$\chi^2= 14.343$	<0.001*
VH	84 (94,4%)	306 (83,4%)		
Working status				
Employed	42 (51,2%)	99 (31,4%)		
Unemployed	32 (39,0%)	196 (62,2%)		
Student	8 (9,8%)	20 (6,3%)		
Social status				
Alone	27 (33,8%)	96 (28,8%)	$\chi^2= 1.355$	0.716
Family of origin	22 (27,5%)	110 (33,0%)		
Own family	23 (28,7%)	89 (26,7%)		
Other	8 (10%)	38 (82,6%)		
Civil status				
Unmarried	38 (45,8%)	214 (64,7%)	$\chi^2= 10.262$	0.036*
Married	22 (26,5%)	58 (17,5%)		
Separated/Divorced	16 (19,3%)	44 (13,3%)		
Cohabitant	2 (2,4%)	5 (1,5%)		
Widower	5 (6,0%)	10 (3,0%)		
Education				
Primary-Middle school	22 (26,5%)	130 (42%)	$\chi^2= 6.716$	0.082
High school	46 (55,4%)	135 (43,5%)		
Graduation	15 (18,1%)	45 (14,5%)		

Activation. Pairwise Comparisons showed a higher mean score in item Activation for women compared to men.

Suicidality showed an impact on several SVARAD items: Sadness/Demoralization; Apathy; Impulsivity; Distortion of Reality; Thought Disorganization; Activation. Pairwise Comparisons showed higher mean scores in items Sadness/Demoralization, Apathy and Impulsivity for the SA group compared to the nSA group. Instead, scores of the items Reality Distortion, Thought Disorganization and Activation resulted higher for the nSA group compared to the SA group (table 3).

When the interaction Sex*Suicidality was consi-

dered, the only item Activation showed significant results. The Plot (figure 1) representing this result shows how the MSA group displays significant lower scores in Activation compared to all others groups: FSA (p=0.049); MnSA (p<0.001); FnSA p<0.001).

BPRS-E

Test Between Subjects of Factorial ANOVA showed an effect of Suicidality in the following BPRS-E items: Depression, Suicidality, Guilt, Hostility, Elevated Mood, Grandiosity, Suspiciousness, Hallucinations,

Table 2. Different patterns of pharmacological treatment frequencies for the whole sample.

AP+AC+BDZ	54.6% (N=254)
AP+AC	16.1% (N=75)
AP+BDZ	9.2% (N=43)
AP+AC+AD+BDZ	6.0% (N=28)
AP only	3.7% (N=17)
AP+AC+AD	2.2% (N=10)
AC only	1.3% (N=6)
AP+AD+BDZ	1.1% (N=5)
Other	4.3% (N=20)
Missing	1.5% (N=7)

AP= antipsychotics; AC= anticonvulsants; AD= antidepressants; BDZ= benzodiazepines.

Unusual Thoughts Content, Bizarre Behavior, Self-neglect, Conceptual Disorganization, Blunted Affect, Motor Retardation, Tension, Uncooperativeness, Excitement, Distractibility, Motor Hyperactivity.

Pairwise Comparisons showed higher score for the SA group in the following BPRS-E items: Depression, Suicidality, Guilt, Motor Retardation. Instead, lower scores for the SA group compared to the nSA group were observed in the following BRPS-E items: Hostility, Elevated Mood, Grandiosity, Suspiciousness, Hallucinations, Unusual Thoughts Content, Bizarre Behavior, Self-neglect, Conceptual disorganization, Blunted Affect, Tension, Uncooperativeness, Excitement, Distractibility, Motor Hyperactivity.

Sex variable showed a significant impact on item Elevation Mood in regard to which Pairwise Comparisons showed women to display higher scores compared to men.

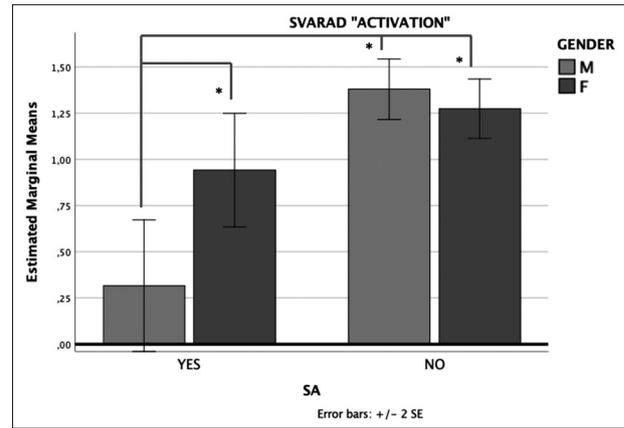


Figure 1. Significant differences (*) among the four groups (MSA, FSA, MnSA, FnSA) for the SVARAD item Activation, which resulted significantly modulated from both factors Gender and Suicidality. For statistical data see text and tables.

When the interaction Sex*Suicidality was considered, Depression, Hostility and Uncooperativeness items showed significant scores (table 4).

The MSA and FSA groups display significant higher scores compared to both MnSA and FnSA ($p < 0,001$) groups in regard of Depression item.

The MSA group displays significant lower scores in the item Hostility compared to MnSA ($p = 0,001$) and FnSA ($p = 0,006$) groups.

HAM-D

Gender variable showed a significant impact on Diurnal Variation item. Pairwise Comparisons showed women to display higher scores in this item compared to men. When the interaction Sex*Suicidality was considered, significant results were observed in regard of the Psychomotor Agitation item (table 5).

Table 3. SVARAD Factorial Anova, Test Between Subjects statistics.

Single factor	Dependent variable	F	p	Partial Eta Squared
Sex	Activation	3.940	0.048	0.009
Suicidality	Sadness/Demoralization	58.266	<0.001	0.115
	Apathy	6.069	0.014	0.013
	Impulsivity	41.890	<0.001	0.085
	Distortion of reality	50.873	<0.001	0.102
	Thought disorganization	49.414	<0.001	0.099
Sex*Suicidality	Activation	28.477	<0.001	0.060
	Activation	7.798	0.005	0.017

Table 4. BPRS-E Factorial Anova, Test Between Subjects statistics.

Factor	Dependent variable	F	p	Partial Eta Squared
Sex	Elevation mood	3.985	0.047	0.009
Suicidality	Depression	60.924	<0.001	0.123
	Suicidality	258.716	<0.001	0.372
	Guilt	33.607	<0.001	0.072
	Hostility	14.176	<0.001	0.031
	Mood elevation	17.086	<0.001	0.038
	Grandiosity	15.497	<0.001	0.034
	Suspiciousness	39.447	<0.001	0.083
	Hallucinations	6.513	0.011	0.015
	Unusual thought content	38.134	<0.001	0.080
	Bizarre behavior	25.380	<0.001	0.055
	Self-neglect	17.503	<0.001	0.039
	Conceptual disorganization	35.926	<0.001	0.076
	Blunted affect	5.122	0.024	0.012
	Motor retardation	3.971	0.047	0.009
	Tension	8.959	0.003	0.020
	Uncooperativeness	8.326	0.004	0.019
	Excitement	23.286	<0.001	0.051
	Distractibility	18.749	<0.001	0.041
	Hyperactivity	25.811	<0.001	0.056
Sex*Suicidality	Depression	4.554	0.033	0.010
	Hostility	5.723	0.017	0.013
	Uncooperativeness	4.585	0.033	0.010

The MSA group displays significant lower scores in the Psychomotor Agitation item compared to all the other groups: FSA ($p=0,044$), MnSA ($p<0,001$) and FnSA ($p<0,001$). Moreover, the FSA group showed significant lower scores respect to MnSA ($p=0,011$) as well.

Discussion

This study aimed at assessing specific psychopathological dimensions associated with suicide attempts in order to investigate whether these dimensions were influenced by sex variable. The core result of the study is that men with SA appear less activated than women. To our knowledge, this is the first study to report low rates of activation in men with SA compared to women, based on a dimensional approach. Our decision to exclude the categorical diagnosis from the analysis could be debatable. Besides our

aim was exactly to identify the psychopathological variables regardless of nosology: our analyses were conducted on a real-world sample consisting of a significant number of inpatients who were hospitalized in a PICU due to their clinical conditions, avoiding any categorical approach to the diagnosis. Our analysis evidenced that several items of the employed scales in turn describing specific psychopathological dimensions are related to suicide attempts: a number of items of SVARAD (table 3), BPRS-E (table 4) and HAM-D (table 5) scales resulted significantly associated to suicide attempts, partially in line with literature^{37,41,42}.

In respect of SVARAD, the main finding was that Activation resulted to be influenced by the interaction Sex*Suicidality. Indeed, the evidence that men with SA appear less activated in respect to women with SA and both nSA groups suggests a gender modulation on Activation item. Secondly, no significant

Table 5. HAM-D Factorial Anova, Test Between Subjects statistics.

Factor	Dependent variable	F	p	Partial Eta Squared
Sex	Diurnal variation	5,252	0,022	0,012
Suicidality	Depressed mood	41,475	<0,001	0,086
	Feelings of guilt	35,355	<0,001	0,074
	Suicide	399,440	<0,001	0,474
	Late insomnia	3,889	0,049	0,009
	Psychomotor agitation	35,911	<0,001	0,075
	Insight	50,735	<0,001	0,103
	Paranoia	40,011	<0,001	0,083
	Sex*Suicidality	Psychomotor agitation	9,420	0,002

gender modulation was found concerning the role of Impulsivity in suicidality which has nevertheless been confirmed, as already known from literature^{41,42}.

In respect of BPRS-E, when the interaction Sex*Suicidality was considered, analyses showed that SA groups had significant higher scores compared to nSA groups in Depression item. Therefore, a significant role of Suicidality in the interaction Sex*Suicidality may be hypothesized, determining such a significant finding. Moreover, the interaction Sex*Suicidality showed a significant gender modulation on Hostility and Uncooperativeness items insofar as men with SA appeared more collaborating than both the nSA groups. The rate of involuntary hospitalization resulted significantly higher among patients without SA and this may partially explain higher rates in Hostility and Uncooperativeness items among patients hospitalized against their will because of their acute psychiatric conditions. Considering Elevation Mood item scores, women with SA seemed more prone to mood elevation than men although the latter have been more frequently associated to mixed mood episodes when experiencing suicidal ideation⁵⁴.

In respect of HAM-D, when the interaction Sex*Suicidality was considered, results suggested a significant gender modulation on Psychomotor Agitation item insofar as males with SA displayed lower scores compared to all the other groups; no significant differences in agitation rates between men and women without SA were found. A greater sensitivity of women to environmental factors and stressors may be suggested by the results of Diurnal Variation item.

Starting from a dimensional approach that deliberately has disregarded any categorical characterization of recruited inpatients, our findings suggest the existence of a sex modulation on activation and agitation states with respect to suicide attempts. Indeed, our core result was that men with SA appeared

less activated than women, as evidenced by scores in Activation (SVARAD) and Psychomotor Agitation (HAM-D) items which might refer to a common dimensional psychopathological state. Noteworthy, a moderate association between agitation and suicidal behavior has been previously described⁵⁵ with in particular the mention of a significant association between higher agitation rates and increased suicide risk in men⁵⁶. As already mentioned, anger and aggressiveness are tightly associated to unipolar depression although the evidence of a direct link with suicide is still lacking²⁸. Over than 80% of suicide deaths among inpatients samples were characterized by an agitated state^{57,58}, intended as an acute state of psychological and physiological over arousal involving motor and psychic agitation, intense inner tension or crowded thoughts⁵⁹. As well known, the sex variable has been considered an established risk factor for suicide⁶⁰ and previous data suggest that men are associated to a greater predisposition toward agitated depression with restlessness and racing thoughts⁶⁰⁻⁶² and increased suicide risk. This hypothesis seems further being confirmed by the evidence of a higher incidence of suicide deaths in the frame of mixed mood episodes compared to unipolar ones⁶³⁻⁶⁵.

However, it is necessary to underline that previous studies did not consider sex variable as a moderator of agitation, as we did by means of multifactorial statistics. Moreover, the potential association between agitation, sex modulation and increased suicidality has been previously investigated specifically among samples of patients categorically diagnosed with mood disorders, particularly of bipolar - spectrum. Of note, our study methodology consisted of a dimensional approach, applying a structural analyses of psychopathological dimensions associated to suicide attempt, regardless of narrow nosologic characterizations. Interestingly, such an evaluation in the emergency room showed a strong predictive po-

wer of patients' psychiatric hospitalization⁶⁶. Therefore, our results may be partially not in line with previous data likely due to the dimensional analysis we have employed. In particular, we avoided investigating potential correlations between suicide attempts and mixed mood episodes with related symptoms, as previously done in literature^{54,67}.

Although evidence is accumulating that externalizing symptoms (e.g. irritability, anger, substance misuse, risk taking, impulsivity) in men's depression are associated to suicide risk⁶⁸, we found that men who attempted near-lethal suicide showed low rates of psychomotor activation and agitation, considering a dimensional approach transversely to any categorical diagnosis. Likely, these attempts still arise from aversive affective feelings and pathological experiences as hopelessness and mental ache, as already described^{17,69,70}. However, these findings would require further investigations in order to deepen whether such a phenomenon may be due to a gender-specific response bias in rating symptoms' severity or to real gender differences in clinical features, as it has been already suggested⁷¹ addressing diagnostic criteria and screening tools inefficiency^{72,73}. On the other hand, women with SA did not show such low rates of psychomotor activation.

Moreover, our findings showed that no significant differences were found between SA and nSA groups concerning the pharmacological treatments. Instead, women with SA appeared to have been treated with more considerable therapies (clorpromazine and benzodiazepine equivalents) compared to men, although without reaching statistical significance. Such a result seems to furtherly suggest the presence of lower rates of activation and psychomotor agitation in men with SA compared to women, thus requiring lower dosages of pharmacological interventions.

In women, a greater tendency toward psychiatric assessment and diagnosis has been proposed⁷⁴. Women at risk of suicide seem to receive more likely a psychiatric diagnosis by clinicians, as already described in literature⁷⁵. On the other hand, men receive less psychiatric approaches being more likely hospitalized in a psychiatric ward when their suicidal purposes appear tightly attributable to a severe psychiatric condition. These findings may suggest that other factors influencing suicide attempts are particularly important for women, as showed by scores in Diurnal variation item (HAM-D). As already advanced, a "diathesis stress model" may operate in women⁷⁶: they would be somehow more predisposed to develop depressive symptoms and social and environmental factors would tightly modulate that predisposition, potentially influencing suicide attempts.

The present work consists of a retrospective observational study: although strongly suggesting, our results do not allow to infer that the specific psychopatholo-

gical dimensions associated with suicide attempts represent valid predictors of suicide, according to our analysis. Longitudinal studies are required in order to describe potential risk predictors. The lack of categorical diagnosis of recruited patients does not permit correlations between nosologic diagnosis and psychopathological dimensions aiming at strengthening our considerations. Starting from an observational study, we are aware that at least part of the observed effect could be attributed to the Hawthorne effect or/and to the regression toward the mean. However, our study design involved a clinical assessment of patients' psychopathological states, expressly regardless of any categorical diagnosis. Further studies are needed aiming at deepening such correlations. Finally, we cannot rule out a selection bias since we recruited only patients with symptoms of a significant burden attending an academic inpatients clinic. However, we may argue that individuals experiencing suicidal ideation rarely do not reach specialized clinical assistance and hence an understatement of such critical states should have been reduced.

Conclusions

What has emerged from our study is that specific psychopathological dimensions are associated to suicide attempts. Of note, men hospitalized for SA appeared less activated compared to women with and without SA, who showed higher rates in Activation (SVARAD) and Psychomotor agitation (HAM-D) items. Starting from these results, the potential gender modulation on psychopathological dimensions associated to suicide attempts should be taken into account during clinical practice in order to implement early intervention strategies and prompt effective therapies. Overall, these considerations strongly support the need of a dimensional approach to psychopathology with the aim of treating suicide attempters by means of tailored interventions.

Author's contribution: all authors listed gave final approval of the version to be published and agreed to be accountable for all aspects of the work. In particular, Tommaso Accinni developed the study design, organized the work and wrote the article. Marianna Frascarelli was involved in study development and made statistical analysis. Sofia Vecchioni developed the study design and collected medical data. Lorenzo Tarsitani critically revised the manuscript. Massimo Biondi and Massimo Pasquini conceived the publication and revised the manuscript.

Data Availability Statement: raw data were generated at the Department of Human Neurosciences, Sapienza University of Rome. Derived data supporting the findings of this study are available from the corresponding author on request.

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References

1. Organización Mundial de la Salud (OMS). Suicide in the world: Global Health Estimates. World Heal Organ 2019; 32.
2. Pompili M, O'Connor RC, Van Heeringen K. Suicide prevention in the european region. *Crisis* 2020; 41: S8-20.
3. Bachmann S. Epidemiology of suicide and the psychiatric perspective. *Int J Environ Res Public Health* 2018; 15: 1425.
4. Tarolla E, Caredda M, Tarsitani L, Maraone A, Biondi M. Predictive factors for further suicide attempts in individuals presenting to an emergency service for an attempted suicide. A one-year longitudinal study. *Riv Psichiatr* 2015; 50: 28-33.
5. Scicchitano C, Caredda M, Tarolla E, et al. Predictive factors for further suicidal behaviour after a suicide attempt: preliminary results. *Riv Psichiatr* 2008; 43: 160-5.
6. Bostwick JM, Pabbati C, Geske JR, McKean AJ. Suicide attempt as a risk factor for completed suicide: even more lethal than we knew. *Am J Psychiatry* 2016; 173: 1094-100.
7. May AM, Klonsky ED. What distinguishes suicide attempters from suicide ideators? A meta-analysis of potential factors. *Clin Psychol Sci Pract* 2016; 23: 5-20.
8. Klonsky ED, May AM, Saffer BY. Suicide, suicide attempts, and suicidal ideation. *Annu Rev Clin Psychol* 2016; 12: 307-30.
9. Klonsky DE, Qiu T, Saffer BY. Recent advances in differentiating suicide attempters from suicide ideators *Curr Opin Psychiatry* 2017; 30: 15-20.
10. McFeeters D, Boyda D, O'Neill S. Patterns of stressful life events: distinguishing suicide ideators from suicide attempters. *J Affect Disord* 2015; 175: 192-8.
11. Saffer BY, Glenn CR, David Klonsky E. Clarifying the relationship of parental bonding to suicide ideation and attempts. *Suicide Life Threat Behav* 2015; 45: 518-28.
12. de Araújo RME, Lara DR. More than words: the association of childhood emotional abuse and suicidal behavior. *Eur Psychiatry* 2016; 37: 14-21.
13. Bastiaansen D, Koot HM, Ferdinand RF. Determinants of quality of life in children with psychiatric disorders. *Qual Life Res* 2005; 14: 1599-612.
14. Suresh Kumar P, George B. Life events, social support, coping strategies, and quality of life in attempted suicide: a casecontrol study. *Indian J Psychiatry* 2013; 55: 46-51.
15. Pérez S, Marco JH, García-Alandete J. Psychopathological differences between suicide ideators and suicide attempters in patients with mental disorders. *Clin Psychol Psychother* 2017; 24: 1002-13.
16. Giustini M, Settimi L, Vignally P, Davanzo F. Confronto di fonti informative per la sorveglianza dei suicidi e dei tentati suicidi in Italia. Istituto Superiore di Sanità. *Bollettino Epidemiologico Nazionale* 2008.
17. Miranda-Mendizabal A, Castellví P, Parés-Badell O, et al. Gender differences in suicidal behavior in adolescents and young adults: systematic review and meta-analysis of longitudinal studies. *Int J Public Health* 2019; 64: 265-83.
18. Canetto SS, Sakinofsky I. The gender paradox in suicide. *Suicide Life Threat Behav* 1998; 28: 1-23.
19. Schrijvers DL, Bollen J, Sabbe BGC. The gender paradox in suicidal behavior and its impact on the suicidal process. *J Affect Disord* 2012; 138: 19-26.
20. Freeman A, Mergl R, Kohls E, et al. A cross-national study on gender differences in suicide intent. *BMC Psychiatry* 2017; 17: 234.
21. Cibis A, Mergl R, Bramesfeld A, et al. Preference of lethal methods is not the only cause for higher suicide rates in males. *J Affect Disord* 2012; 136: 9-16.
22. Vörös V, Osváth P, Fekete S. Gender differences in suicidal behavior. *Neuropsychopharmacol Hung* 2004; 6: 65-71.
23. Sun L, Zhang J. Gender differences among medically serious suicide attempters aged 15-54 years in rural China. *Psychiatry Res* 2017; 252: 57-62.
24. Bohnert KM, Ilgen MA, Louzon S, McCarthy JF, Katz IR. Substance use disorders and the risk of suicide mortality among men and women in the US Veterans Health Administration. *Addiction* 2017; 112: 1193-201.
25. Qin P, Agerbo E, Mortensen PB. Suicide risk in relation to socioeconomic, demographic, psychiatric, and familial factors: a national register-based study of all suicides in Denmark, 1981-1997. *Am J Psychiatry* 2003; 160: 765-72.
26. Menon V, Sarker S, Kattimani S. Association between personality factors and suicide intent in attempted suicide: gender as a possible mediator? *Personal Ment Health* 2015; 9: 220-6.
27. Wilks CR, Morland LA, Dillon KH, et al. Anger, social support, and suicide risk in U.S. military veterans. *J Psychiatr Res* 2019; 109: 139-44.
28. Picardi A, Morosini P, Gaetano P, Pasquini M, Biondi M. Higher levels of anger and aggressiveness in major depressive disorder than in anxiety and somatoform disorders. *J Clin Psychiatry* 2004; 65: 442-3.
29. Sadeh N, Javdani S, Finy MS, Verona E. Gender differences in emotional risk for self- and other-directed violence among externalizing adults. *J Consult Clin Psychol* 2011; 79: 106-17.
30. Erbuto D, Innamorati M, Lamis DA, et al. Mediators in the association between affective temperaments and suicide risk among psychiatric inpatients. *Psychiatry* 2018; 81: 240-57.
31. Alonso J, Angermeyer MC, Bernert S, et al. Prevalence of mental disorders in Europe: results from the European Study of the Epidemiology of Mental Disorders (ESEMeD) project. *Acta Psychiatr Scand Suppl* 2004; 109: 21-7.
32. Siddaway AP, Holm-Denoma J, Witte TK, Ruscio J. Reexamining the latent structure of suicidal thoughts using taxometric analysis: implications for testing ideation to action theoretical models of suicidal thoughts and behavior. *Psychol Assess* 2021; 33: 243-54.
33. Liu RT, Jones RN, Spirito A. Is adolescent suicidal ideation continuous or categorical? A taxometric analysis. *J Abnorm Child Psychol* 2015; 43: 1459-66.
34. Glenn CR, Cha CB, Kleiman EM, Nock MK. Understanding suicide risk within the Research Domain Criteria (RDoC) framework: insights, challenges, and future research considerations. *Clin Psychol Sci* 2017; 5: 568-92.
35. Glenn CR, Kleiman EM, Cha CB, Deming CA, Franklin JC, Nock MK. Understanding suicide risk within the Research Domain Criteria (RDoC) framework: a meta-analytic review. *Depress Anxiety* 2018; 35: 65-88.
36. Biondi M, Pasquini M, Picardi A. *Dimensional psychopathology*. Berlin: Springer International Publishing, 2018.
37. Gvion Y, Apter A. Aggression, impulsivity, and suicide behavior: a review of the literature. *Arch Suicide Res* 2011; 15: 93-112.
38. Pasquini M, Picardi A, Biondi M, Gaetano P, Morosini P. Relevance of anger and irritability in outpatients with major depressive disorder. *Psychopathology* 2004; 37: 155-60.
39. Sharma A, Guski LS, Freund N, Götzsche PC. Suicidality and aggression during antidepressant treatment: systematic review and meta-analyses based on clinical study reports. *BMJ* 2016; 352: i65.
40. Angst J, Angst F, Stassen HH. Suicide risk in patients with major depressive disorder. *Prim Care Companion J Clin Psychiatry* 1999; 1: 57.
41. Gvion Y, Horresh N, Levi-Belz Y, et al. Aggression-impulsivity, mental pain, and communication difficulties

- in medically serious and medically non-serious suicide attempters. *Compr Psychiatry* 2014; 55: 40-50.
42. Cáceda R, Durand D, Cortes E, et al. Impulsive choice and psychological pain in acutely suicidal depressed patients. *Psychosom Med* 2014; 76: 445-51.
 43. Sun X, Li H, Song W, Jiang S, Shen C, Wang X. ROC analysis of three-dimensional psychological pain in suicide ideation and suicide attempt among patients with major depressive disorder. *J Clin Psychol* 2020; 76: 210-27.
 44. Troister T, Holden RR. A two-year prospective study of psychache and its relationship to suicidality among high-risk undergraduates. *J Clin Psychol* 2012; 68: 1019-27.
 45. Troister T, D'Agata MT, Holden RR. Suicide risk screening: comparing the Beck Depression Inventory-II, Beck Hopelessness Scale, and Psychache Scale in undergraduates. *Psychol Assess* 2015; 27: 1500-6.
 46. Poreddi V, Thimmaiah R, Ramu R, et al. Gender differences related to attitudes toward suicide and suicidal behavior. *Community Ment Health J* 2016; 52: 228-32.
 47. Levi-Belz Y, Gvion Y, Apter A. The serious suicide attempts approach for understanding suicide: review of the psychological evidence. *Omega* 2020; 30222820981235.
 48. Overall JE, Gorham DR. The Brief Psychiatric Rating Scale. *Psychol Rep* 1962; 10: 799-812.
 49. Dazzi F, Shafer A, Lauriola M. Meta-analysis of the Brief Psychiatric Rating Scale - Expanded (BPRS-E) structure and arguments for a new version. *J Psychiatr Res* 2016; 81: 140-51.
 50. Hamilton M. A rating scale for depression. *J Neurol Neurosurg Psychiatry* 1960; 23: 56-62.
 51. Pancheri P, Picardi A, Gaetano P, et al. Validazione della scala per la valutazione rapida dimensionale SVARAD = Validation of the SVARAD, a rating scale for rapid assessment of psychopathological dimensions. *Riv Psichiatr* 1999; 34: 84-93.
 52. Biondi M, Gaetano P, Pasquini M, Picardi A. The SVARAD scale for rapid dimensional assessment: development and applications in research. In: Biondi M, Pasquini M, Picardi A (eds). *Dimensional psychopathology*. Berlin: Springer International Publishing, 2018.
 53. Woods SW. Chlorpromazine equivalent doses for the newer atypical antipsychotics. *J Clin Psychiatry* 2003; 64: 663-7.
 54. Sani G, Tondo L, Koukopoulos A, et al. Suicide in a large population of former psychiatric inpatients. *Psychiatry Clin Neurosci* 2011; 65: 286-95.
 55. Rogers ML, Ringer FB, Joiner TE. A meta-analytic review of the association between agitation and suicide attempts. *Clin Psychol Rev* 2016; 48: 1-6.
 56. Bryan CJ, Hirschfeld MJ, Palmer BA, Schak KM, Roberge EM, Lineberry TW. Gender differences in the association of agitation and suicide attempts among psychiatric inpatients. *Gen Hosp Psychiatry* 2014; 36: 726-31.
 57. Busch KA, Fawcett J, Jacobs DG. Clinical correlates of inpatient suicide. *J Clin Psychiatry* 2003; 64: 14-9.
 58. Hall RCW, Platt DE, Hall RCW. Suicide risk assessment: a review of risk factors for suicide in 100 patients who made severe suicide attempts: evaluation of suicide risk in a time of managed care. *Psychosomatics* 1999; 40: 18-27.
 59. Koukopoulos A, Koukopoulos A. Agitated depression as a mixed state and the problem of melancholia. *Psychiatr Clin North Am* 1999; 22: 547-64.
 60. Wen-Hung KUO, Gallo JJ, Tien AY. Incidence of suicide ideation and attempts in adults: the 13-year follow-up of a community sample in Baltimore, Maryland. *Psychol Med* 2001; 31: 1181-91.
 61. Dilsaver SC, Benazzi F, Rihmer Z, Akiskal KK, Akiskal HS. Gender, suicidality and bipolar mixed states in adolescents. *J Affect Disord* 2005; 87: 11-6.
 62. Benazzi F. Depression with racing thoughts. *Psychiatry Res* 2003; 120: 273-82.
 63. Dome P, Rihmer Z, Gonda X. Suicide risk in bipolar disorder: a brief review. *Medicina* 2019; 55: 403.
 64. Akiskal HS, Benazzi F. Psychopathologic correlates of suicidal ideation in major depressive outpatients: is it all due to unrecognized (bipolar) depressive mixed states? *Psychopathology* 2005; 38: 273-80.
 65. Rihmer Z, Pestaloty P. Bipolar II disorder and suicidal behavior. *Psychiatr Clin North Am* 1999; 22: 667-73.
 66. Dazzi F, Picardi A, Orso L, Biondi M. Predictors of inpatient psychiatric admission in patients presenting to the emergency department: the role of dimensional assessment. *Gen Hosp Psychiatry* 2015; 37: 587-94.
 67. Olgiati P, Serretti A, Colombo C. Retrospective analysis of psychomotor agitation, hypomanic symptoms, and suicidal ideation in unipolar depression. *Depress Anxiety* 2006; 23: 389-97.
 68. Rice SM, Kealy D, Oliffe JL, Ogrodniczuk JS. Male-type depression symptoms linked to broader psychopathology. *J Affect Disord* 2018; 235: 523-4.
 69. Oliffe JL, Rosnagel E, Seidler ZE, Kealy D, Ogrodniczuk JS, Rice SM. Men's depression and suicide. *Curr Psychiatry Rep* 2019; 21: 103.
 70. Rice SM, Kealy D, Oliffe JL, Treeby MS, Ogrodniczuk JS. Shame and guilt mediate the effects of alexithymia on distress and suicide-related behaviours among men. *Psychol Heal Med* 2020; 25: 17-24.
 71. Parker G, Fletcher K, Paterson A, Anderson J, Hong M. Gender differences in depression severity and symptoms across depressive sub-types. *J Affect Disord* 2014; 167: 351-7.
 72. Genuchi M. Anger and hostility as primary externalizing features of depression in college men. *Int J Mens Health* 2016; 14: 113-28.
 73. Martin LA, Neighbors HW, Griffith DM. The experience of symptoms of depression in men vs women: analysis of the national comorbidity survey replication. *JAMA Psychiatry* 2013; 70: 1100-6.
 74. Gradus JL, Rosellini AJ, Horváth-Puhó E, et al. Prediction of sex-specific suicide risk using machine learning and single-payer Health Care Registry Data from Denmark. *JAMA Psychiatry* 2020; 77: 25-34.
 75. Gomes AP, Soares ALG, Kieling C, Rohde LA, Gonçalves H. Mental disorders and suicide risk in emerging adulthood: the 1993 Pelotas birth cohort. *Rev Saude Publica* 2019; 53: 96.
 76. Parker G, Brotchie H. Gender differences in depression. *Int Rev Psychiatry* 2010; 22: 429-36.

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