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Research paper

## Suicidal ideation and affect lability in single and multiple suicidal attempters with Major Depressive Disorder: An exploratory network analysis

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## ABSTRACT

**Introduction:** A better understanding of the specific contribution of risk factors to suicidal behavior could arise from analyzing suicidal ideation (SI) in clinical samples, and comparing single versus multiple suicide attempters through contemporary methods allowing complex and dynamical analyses of multiple and simultaneously interacting suicide risk factors.

**Method:** We explored associations among suicidal ideation (SI), affect lability and other suicide risk factors in 323 suicidal attempters diagnosed with major depressive disorder (MDD). We analyzed the network structure and centrality of the total sample, and compared single versus multiple attempters and subjects with low and high suicidal ideation.

**Results:** SI was connected with anxiety (trait) and hopelessness. Central nodes for global and specific groups were affect lability (from anxiety to depression), anxiety as a trait, and harm avoidance. We observed some specific differences between clinical profiles of repeaters and non-repeaters and significant network density between high and low SI.

**Limitations:** Because our cross-sectional design, we cannot establish casual relationships among variables. We only examined associations at group level but not at single subject level.

**Conclusions:** Affect lability (mainly the shifts from anxiety to depression) and trait anxiety were central in each estimated network. These symptoms might be suitable targets for early detecting and treating suicidal patients.

## Introduction

The complex interactions and the specific contribution of risk factors to suicidal behavior remain unclear (Franklin et al., 2017; Kessler et al., 2015; O'Connor and Portzky, 2018). A better understanding could arise from analyzing suicidal ideation (SI) in clinical samples (Wei et al., 2018) and comparing single versus multiple suicide attempters (Boisseau et al., 2013).

Literature shows that suicidal risk is higher for multiple attempters (Méndez-Bustos, et al., 2013; Miranda et al., 2008), that multiple attempts could be a behavioral marker of severe psychopathology (Forman et al., 2004), and suggests some differences in specific symptoms (i.e., depressed mood, anxiety) and risk factors (drug and alcohol use, traumatic events in childhood; borderline personality traits) (Choi et al., 2013; Kochanski et al., 2018; Park et al., 2018). Moreover, Menon et al. (2016) observed higher levels of hopelessness in re-

attempters, which, irrespective of depression, could be a relevant clinical marker.

SI could predict suicide behavior (Horwitz, et al., 2015) in adolescents and adult depressive patients (Kwon et al., 2016; Wei et al., 2017). Although prior findings shows that SI increases the risk for suicidal behavior, and that decreasing SI in suicide attempters might decrease future reattempts (Joo et al., 2016), its predictive power is controversial (McHugh et al., 2019). Multiple suicide attempters exhibit significantly greater variability in suicidal ideation levels than either non- or single attempters (Witte et al., 2005). The nature of this variability is not unclear, but it might be caused by individual differences in emotion regulation, also termed affect lability, regarded as a transdiagnostic factor useful to understand psychopathology (Broome et al., 2015) and suicidal thoughts (Bowen et al., 2015), and a distal factor for suicide (Witte, 2010). It could be a precursor of depressive episodes (Balbuena et al., 2016; Marwaha et al., 2015;

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Thompson et al., 2011), suicidality in mood disorders (Rihmer, 2007), depressive patients (Bowen et al., 2011; Neacsiu et al., 2018), anxiety disorders (Bowen et al., 2004), bipolar disorder (Ducasse et al., 2017) and post-traumatic stress disorder (Marwaha et al., 2013). Although affect lability has been associated with suicidal ideation, even in subjects with low levels of depression (Law et al., 2015), the specific pathways to suicide thoughts and acts are not truly understood. Literature recommends examining it in clinical and research contexts as promising approach to better understand mood disorders (Bowen et al., 2013) and suicidal thoughts (Peters et al., 2016). Instead of quantifying emotional states and how they are experienced by subjects, measures of affect lability are focused on emotional transitions between two specific (polarized) emotions (i.e., from normal mood to anxiety; or from anxiety to depression) (Contardi et al., 2018). This perspective is aligned with literature showing that psychopathology is highly dynamic and changeable (Nelson et al., 2017), and that psychiatric disorders, including depression, involves frequent changes in emotional intensity and severity (Baetz and Bowen, 2011).

The lack of specificity and the low capability to accurately predict suicide outcomes (Ribeiro et al., 2016), could be partially explained by some methodological constraints, such as using single or inaccurate predictors (de Beurs et al., 2017; Walsh et al., 2017). Improving the prediction of suicidal behavior could be enhanced through the usage of continuously distributed transdiagnostic symptoms (Bowen et al., 2013). This requires exploring methods aimed at simultaneously analyze interactions and reciprocal influences among suicide risk factors in specific samples (Franklin et al., 2017), such as the network analysis (Borsboom, 2017). It is a well suited method to study complex systems like symptoms (Borsboom and Cramer, 2013), and elements like affect states or cognitive processes (Fried et al., 2017; van Roekel et al., 2019), avoiding reductionism when studying psychopathology (Borsboom et al., 2018). Research analyzing SI through network methods is sparse and mainly conducted with general samples of adults (de Beurs et al., 2017) and adolescents (Núñez et al., 2018). Two studies have analyzed SI in suicide attempters. Shiratori et al. (2014) explored motives for suicide in a large and a wider age-range sample observing that depression and physical illness were the most relevant motives. de Beurs et al. (2017) examined associations between suicidal symptoms (Beck et al., 1979) and repeated suicidal behavior in adult patients, observing that the desire to for an active attempt was the most central suicidal symptom, without differences between repeaters and non-repeaters.

New insights on the ways in which suicidal ideation, psychiatric symptoms and other suicide risk factors might cluster into particular types of linked networks in suicide attempters could be added analyzing trait-dependent vulnerability factors, which might improve the identification of suicide risk and the prevention of suicidal behavior (van Heringen, 2012). In the light of the clinical stress x diathesis model of suicide (Man et al., 1999), in a sample of suicidal attempters with a primary diagnosis of MDD, we conducted a network analysis to explore associations among SI and distal suicide risk factors, such as personality traits (i.e. harm avoidance and impulsivity) (Ortin et al., 2012; Perroud et al., 2013; Klonsky and May, 2015), affect lability (Ducasse et al., 2017), suicide correlates (hopelessness) (Ribeiro et al., 2018), and psychiatric symptoms, mainly anxiety (Allan et al., 2014; Bentley et al., 2016; Capron et al., 2012). We additionally included history of aggression and impulsivity, two components of the diathesis for suicidal behavior (van Heringen, 2012). Whereas the former is a distal factor for suicide (Hawton and Heeringen, 2009), helpful to distinguish between suicide attempters and non-attempters in patients with MDD (Keilp et al., 2006), the latter has been found to be associated to suicide (Binnelly et al., 2015; Calati et al., 2008; López-Castroman et al., 2012) in patients with affective disorders (Camarena et al., 2014). Because the still controversial evidence on the association of these factors with suicide behavior (Gvion and Apter, 2011; Melhem et al., 2019; Perroud et al., 2013), new insights about its role

and relationships could be obtained by computing simultaneous interactions with other suicidal factors. First, we analyzed the general network structure of these associations and estimated network centrality indices as recommended by Epskamp et al. (2018) and Bringmann et al. (2019). Second, we compared the network structure and centrality indices between non-repeaters and repeaters and between subjects with high and low SI. Because the occurrence of negative connections, we followed recent suggestions (Robinaugh et al., 2016), and analyzed the influence of each node by using the expected influence metrics (Heeren et al., 2018). Because the high emotional disturbances in patients with MDD (Pe et al., 2014), given its influential role on suicidal ideation and the higher levels observed in depressed attempters (Neacsiu et al., 2018), we hypothesized that nodes assessing affect lability would be central in the overall network. Within the network frame, strongly connected networks of psychiatric symptoms might indicate higher vulnerability to mental disorders in adults with MDD (van Borkulo et al., 2015; Pe et al., 2014). Consequently, we expected to find a more densely connected network in patients with higher SI levels, which could suggest a higher suicidal risk.

## Method

### Participants

We analyzed 323 patients identified from a cohort of suicide attempters consecutively recruited in a specialized unit of Montpellier University Hospital between 1999 and 2012, who completed all the questionnaires included into the current analysis. All participants made their suicide attempts in the frame of an affective episode. Suicide attempts were defined as self-injury behaviors with a non-zero level of suicidal intent (Trémeau et al., 2005). Patients were 18 and over (mean age = 39,  $\pm$  13.52, women = 69.96%), French speaking. This study was approved by the local research ethics committee (CPP Sud Méditerranée, IV, CHRU Montpellier, France).

### Materials and Procedure

We obtained Axis I DSM-IV psychiatric diagnosis by the French version of the Diagnostic Interview for Genetic Studies (DIGS; Preisig et al., 1999) and the Mini International Neuropsychiatric Interview (MINI; Sheehan et al., 1998).

We assessed suicidal ideation by the Scale for Suicidal Ideation (SSI; Beck et al., 1979), a 19-item questionnaire designed to measure the intensity, pervasiveness, and characteristics of suicidal ideation in adults. It also assesses the risk of later suicide attempt in individuals who have thoughts, plans, and wishes to commit suicide. We addressed anxiety by the State-Trait Anxiety Inventory (STAI; Spielberger et al., 1983), a self-report questionnaire including separate measures of state (20 items) and trait (20 items) anxiety. We addressed hopelessness by the Beck Hopelessness Scale (Beck, 1988), a 20-item questionnaire assessing feelings about the future, loss of motivation, and expectations, frequently used as an indicator of suicidal risk in depressed people who have made suicide attempts. We assessed impulsivity by the Barrat Impulsiveness Scale (BIS 10; Patton et al., 1995), a 34-item self-report tool, addressing impulsive personality traits with a global score and the cognitive, motor and planning subscales. We measured personality traits by the Tridimensional Personality Questionnaire (TPQ; Cloninger, 1987). We analyzed two personality dimensions: Harm avoidance (HA), characterized by excessive worrying, pessimism, shyness, and being fearful, doubtful, and easily fatigued; and novelty seeking (NS), associated with exploratory activity in response to novel stimulation, impulsive decision making, extravagance in approach to reward cues, quick loss of temper, and avoidance of frustration. We used the total score of the Life History of Aggression (H\_AGR) Assessment (Coccaro et al., 1997). Finally, we assessed affect lability with the French version of the 54-items Affect Liability Scale (Ducasse et al.,

2017; Harvey et al., 1989). Participants are asked to describe their emotions with a 0-3 score. The items are grouped in six dimensions addressing transitions from normal mood to depression (ALS\_dep; 11 items), euphoria (ALS\_bip; 7 items), anxiety (ALS\_anx; 7 items) and anger (ALS\_ang; 7 items), from anxiety to depression (ALS\_anx\_dep; 8 items), and from depression to elation (ALS\_elation; 9 items). Because we analyzed patients diagnosed with major depressive disorder, and given the few available evidence about bipolar disorders coming from network analysis (Fried and Cramer et al., 2017), we excluded the subscales addressing transitions from normal mood to euphoria and from depression to elation.

#### Data analysis

Network estimation, node centrality and network stability, total sample

##### Network estimation

A network consists of the visualization of the associations between variables. We computed the polychoric correlations among the nodes (risk factors), as suggested by McNally et al. (2017). We did not include psychiatric diagnoses within the tested models. We estimated networks using Graphical Gaussian Model (GGM) (Epskamp et al., 2018), a suitable method to explore relationships when using large data sets, multiple variables and continuous data. Based on partial correlation coefficients (Costantini et al., 2015), GGM takes into account the whole data set to establish possible relationships between nodes simultaneously, controlling for all other nodes (Bhushan et al., 2019). It comprises a set of items or variables represented by circles and lines (edges) reflecting connections between nodes (the most thickness the more higher the connections between nodes). We eliminated spurious associations between nodes and excluded small associations from the graphs using the graphical LASSO (Least Absolute Shrinkage and Selection Operator; Friedman, et al., 2008) implemented in the R package q graph (Epskamp et al., 2012; 2018).

##### Node centrality

Within the network approach to psychopathology, and because nodes possess independent causal powers that influence other nodes (Heeren et al., 2018), addressing its capability to trigger the development of other nodes is crucial (Cramer and Borsboom, 2015). This could be done by computing centrality indices, which provide information about the importance of each node in a network (how connected and clinically relevant a symptom is in a network) (Fried et al., 2017). Because recent concerns on the suitability of using centrality indices when applying network analyses to psychopathology, in accordance with Bringmann et al. (2019), we only used the strength centrality index. The strength of a node is the sum of the absolute value of its connections with other nodes in the network and quantifies how well a node is directly connected to other nodes (Mullarkey et al., 2019). We estimated this index using the R qgraph package (Epskamp et al., 2012).

The standard centrality indices could not accurately capture the node's influence within a particular network (Bringmann et al., 2019; Everett and Borgatti, 2014). Therefore, we conducted an additional analysis to test this aspect. We used two new metrics addressing both the nature and strength of the cumulative influence of a node within a particular network (Robinaugh et al., 2016), which are particularly useful when negative connections are found (Heeren et al., 2018), as we observed when comparing both repeaters versus non-repeaters and low versus high SI levels. The one-step expected influence (EI1) addresses the node's influence with its immediate neighbors, and the two-step expected influence (EI2) addresses the immediate influence of a node within the network and the secondary influence on the network through its neighbors. These indices were computed with the R package networktools (Jones, 2018).

##### Network stability and accuracy

We computed the stability of the strength centrality index using the correlation stability coefficient (CS-coefficient), which quantifies the maximum proportion of cases that can be dropped to retain, with 95% certainty, a correlation with the original centrality of higher than (by default) 0.7. Values should be at least 0.25 for the centrality to be stable, and preferably above 0.5. Finally, we computed accuracy of edges in the networks by a non-parametric bootstrap method to calculate 95% confidence intervals of the edge weights. This addresses if the edges do significantly differ from one-another. To do this we used the R package bootnet (Epskamp et al., 2018).

##### Group comparisons

Before the network modeling, through *t*-test for independent groups, we compared subgroups (repeaters versus non-repeaters; high versus low SI (estimated by the median value)), in terms of suicidal risk factors and symptoms. Then, we compared the overall network structure, strength centrality index, relative importance and expected influence. We computed the overall network structure by the Network Comparison Test (NCT), a two-tailed permutation test calculating between-groups differences repeatedly (1000 times), using the R package NCT (van Borkulo, 2016). We used two main parameters: the global strength invariance (the weighted sum of absolute connections), and the edge invariance (the maximum difference in edge weights). The differences are considered significant at the threshold of .05 (van Borkulo et al., 2015).

#### Results

##### Sociodemographic and clinical characteristics

Sociodemographic and clinical data of participants are described in Table 1 (total sample and subgroups (high SI, Low SI, non-repeaters, and repeaters).

##### Estimated Network

As the graphical LASSO network shows, SI is connected to anxiety trait (ANX\_TR) and hopelessness (HOP) (Figure 1). The strength of these two connections is not significantly different (Supplementary figures 1a and 1b depict differences among edges and nodes respectively). The strongest connection is observed between ANX\_TR and anxiety state (ANX\_ST), which is significantly different from all network edges. The second strongest connection is represented by the link between two affect lability dimensions (ALS\_anxdep and ALS\_anx), which differs from almost every network connection, except from the within-domain connections of affect lability symptoms, such as occurs with the third strongest connection corresponding to the link between novelty seeking (NS) and impulsivity (IMP). Anxiety symptoms are connected to harm avoidance (HA), being the link with ANX\_TR slightly but significantly higher than the link observed for ANX\_ST. A weak link is observed between ANX\_TR and IMP. Both anxiety symptoms are linked to hopelessness (HOP) and also to affect lability symptoms through a node representing emotional shifts from anxiety to depression (ALS\_anxdep). HOP is also linked to both HA and IMP which are negatively and positively linked to NS, respectively. IMP is linked to every affect lability node, being the connection with the node representing the shift from normal mood to anger (ALS\_ang) slightly, but not significantly higher than the rest of the connections observed between these two groups of symptoms. Finally, a negative association is observed between NS and HA.

##### Strength centrality index

We explored the connectivity patterns of nodes by the strength centrality index, which characterize their relative importance within the network (Costantini et al., 2015). The item addressing affect lability (from anxiety to depression; ALS\_anxdep) showed the highest strength value, followed by anxiety as a trait (ANX\_TR), and two nodes

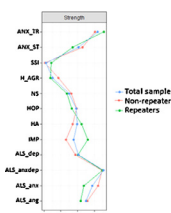
**Table 1**  
Sociodemographic and clinical characteristics (Mean (SD), or N (%))

Variable	Total Sample (N = 323)	High SSI (N = 160)	Low SSI (N = 163)	Non-repeaters (N = 134)	Repeaters (N = 189)
Age, years	39(13.52)	40.20(13.36)	37.82(13.61)	38.20(13.69)	39.57(13.41)
Female	226(70.00)	100(62.50)	126(77.30)	76(56.71)	150(79.36)
Education					
≤ 12 years of education	170(52.63)	85(53.12)	85 (52.14)	36(26.86.21)	74(39.15)
≥ 13 years of education	153(47.36)	75(46.87)	78(47.85)	98(73.13)	115(60.84)
Marital status					
Single	118(36.53)	55(34.37)	63(38.65)	49(36.56)	69(36.50)
Married	135(41.79)	70(43.75)	65(39.87)	61(45.52)	74(39.15)
Separated	19(5.88)	10(6.25)	9(5.52)	10(7.46)	9(4.76)
Divorced	42(13.00)	19(11.87)	23(14.11)	11(8.20)	31(16.40)
Widowed	9(2.78)	6(3.75)	3(1.84)	3(2.23)	6(3.17)
Diagnosis					
Major depressive disorder	323(100)	160(100)	163(100)	134(100)	189(100)
Anxiety disorder	221(68.42)	116(72.50)	105(64.41)	89(66.41)	132(69.84)
Eating disorders	59(18.26)	35(21.87)	24(14.72)	17(12.68)	42(22.22)
Schizophrenia	3(.92)	2(1.30)	1(.60)	0(0)	3(1.58)
Substance dependence/abuse disorder	32(9.9)	20(12.50)	12(7.4)	11(8.20)	21(11.11)
Alcohol use/abuse disorder	77(23.83)	47(29.40)	30(18.40)	22(16.41)	55(29.10)

addressing affect lability (from normal mood to anxiety (ALS\_anx), and from normal mood to anger (ALS\_ang) (Figure 2).

*Expected influence*

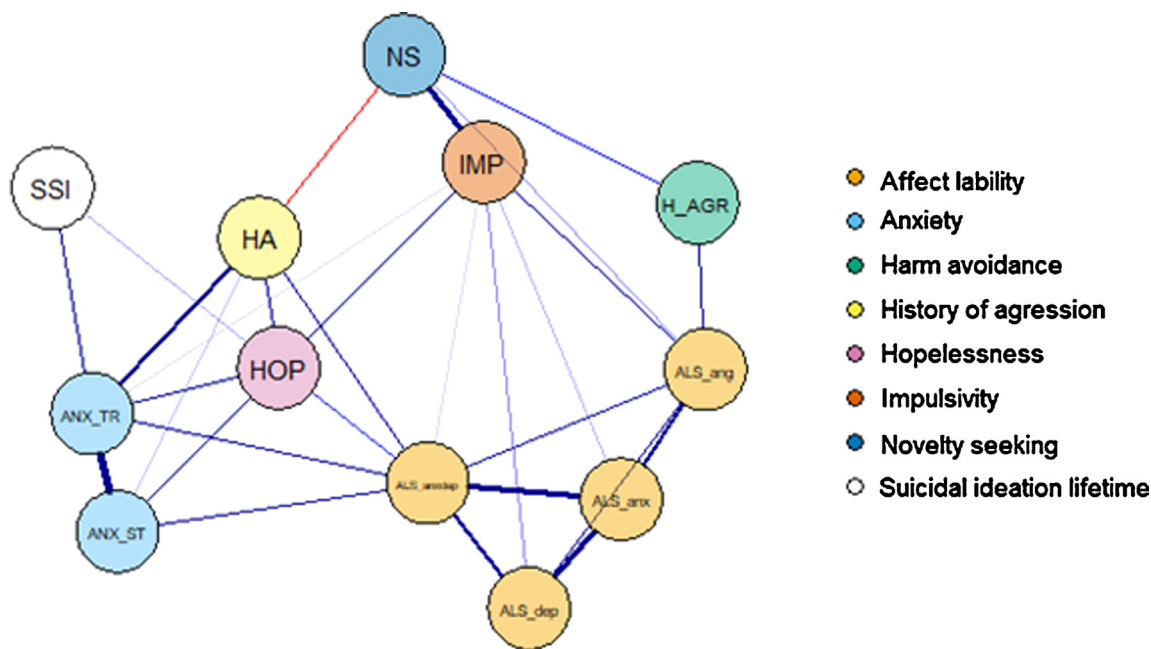
The expected influence analysis (Figure 3) revealed that the nodes with higher values were those addressing shifts from anxiety to depression (ALS\_anxdep) which showed the highest level, followed by the node reflecting changes from normal mood to anxiety (ALS\_anx) and from normal mood to depression (ALS\_dep). A second group of nodes was represented by an affect lability symptom (from normal mood to anger (ALS\_ang), anxiety as trait (ANX\_TR) and anxiety state (ANX\_ST), harm avoidance (HA), and hopelessness (HOP) which presented slight differences in their positions when EI1 and EI2 were compared. Finally, a third group of nodes (impulsivity (IMP), novelty seeking (NS), history of aggression (H\_AGR) and suicidal ideation (SSI) showed the lowest values in both EI1 and EI2.



**Figure 2.** Centrality indices of nodes per each item; total sample, non-repeaters and repeaters.

*Network stability and accuracy*

The centrality stability analysis of the strength centrality index was 0.749 (Supplementary Figure 2a). The edge-weight accuracy indicated that several edges were not meaningfully different from each other because their confidence intervals overlap, and that several nodes showed values significantly different from zero (Supplementary Figure



**Figure 1.** Representation of network model of suicidal ideation and psychopathology items. Two main components are depicted: the symptoms or nodes (circles), and the edges (lines linking the nodes). The edges represent the relationships between nodes (blue lines correspond to positive associations). The thickness of the edges represents the magnitude of the association between nodes.



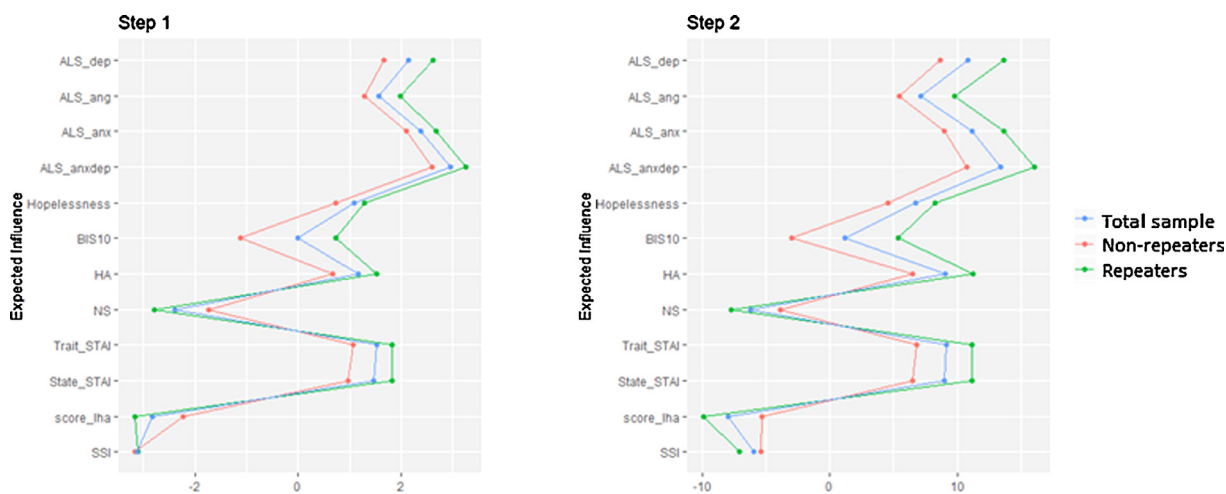


Figure 3. Expected influence; total sample, non-repeaters, repeaters. A) One-step; B) Two-step

2b).

Group comparisons

Repeaters versus non-repeaters

Repeaters shows higher levels of suicidal ideation, history of aggression, anxiety trait, novelty seeking, harm avoidance, impulsivity, hopelessness and affect lability (from anxiety to depression) (Supplementary Table 1).

The graphical LASSO networks (Supplementary Figure 3) shows some between-group differences (i.e., a more densely connected network in repeaters than non-repeaters (37 vs 25 edges respectively), a different connectivity pattern of SI (fewer connections in the non-repeaters network), and negative connections between SI and impulsivity and between anxiety trait and history of aggression in repeaters. These differences were not significant (global strength,  $p = .693$ ; edge invariance,  $p = .555$ ).

The analysis of the strength centrality index showed some different connectivity patterns for specific nodes (Figure 2). Repeaters subjects showed higher strength values in impulsivity and harm avoidance.

The expected influence analysis revealed similar patterns for single and multiple attempters. Nodes addressing affect lability (from anxiety to depression, from normal mood to anxiety, and from normal mood to depression) showed the highest levels of both EI1 and EI2, followed by anxiety (trait and state) and harm avoidance. Repeaters obtained higher values than non-repeater, mainly in impulsivity (EI1 and EI2), affect lability and anxiety symptoms (with clearer differences in EI2).

High versus low suicidal ideation. Participants with high SI showed higher levels of anxiety (trait and state), harm avoidance and hopelessness (Supplementary Table 2).

The graphical LASSO networks showed some between-group differences (Figure 4). We observed a more densely connected network in high SI than low SI. High SI showed more negative connections, mainly the history of aggression. This node presented different connectivity patterns (i.e. it was negatively associated to anxiety trait in low SI, but

to anxiety state, harm avoidance and affect lability (from anxiety to depression) in high SI. Moreover, positive connections were observed between this affect lability node and history of aggression in the low SI group). We additionally found different connectivity patterns for impulsivity. It was associated with anxiety trait in the group with high SI, but slightly associated with anxiety state in the group with low SI. Additionally, impulsivity was linked to affect lability (from normal mood to depression) in the high SI group but not in the low SI group. It was clearly associated with hopelessness in low SI, but weakly in high SI.

The analysis of centrality showed that in subjects with higher SI the strength values were higher for anxiety trait and lower for hopelessness (Figure 5). We observed mixed results for both harm avoidance (high strength centrality value in high SI) and anxiety state (slightly low strength value in high SI). Additionally, we observed some between-group differences for specific nodes. Hopelessness was higher in the group with lower SI, where affect lability (from anxiety to depression) showed higher strength values. In the high SI group, we observed higher strength values for anxiety as trait. These differences were significant for the edge invariance ( $p = .018$ ), and marginally significant for the global strength ( $p = .069$ ) (Supplementary Figure 4).

The expected influence analysis yielded similar patterns showing affect lability and anxiety as the most central nodes, which was particularly clear for high SI (Figure 6).

Discussion

We explored relationships between suicidal ideation, affect lability and other suicidal risk factors in suicide attempters diagnosed with MDD. The most central node was affect lability (from anxiety to depression). It was followed by two additional affect lability nodes (from normal mood to anxiety and from normal mood to anger), and anxiety trait. We found specific associations between SI and both anxiety as trait and hopelessness. Anxiety as trait obtained the second highest strength value, and was connected to anxiety as state, being this link the strongest edge observed within the network. Additionally, these two anxiety symptoms were connected to harm avoidance and hopelessness (also connected each other) and to the affect lability node with the highest centrality values (addressing shifts from anxiety to depression), which in turn was linked to the rest of the affect lability symptoms, probably serving as a “bridge” between them and other network nodes (i.e. history of aggression and impulsivity). These findings support previous research highlighting both affect lability (Peters et al., 2016) and anxiety symptoms (Kanwar et al., 2013) as central psychopathological aspects of suicidal behavior, suggesting that affect lability, mainly the node addressing shifts from anxiety to depression might play

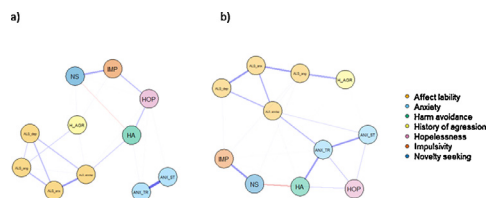


Figure 4. Representation of network model of suicidal ideation and psychopathology items. a) Low SI; b) High SI.

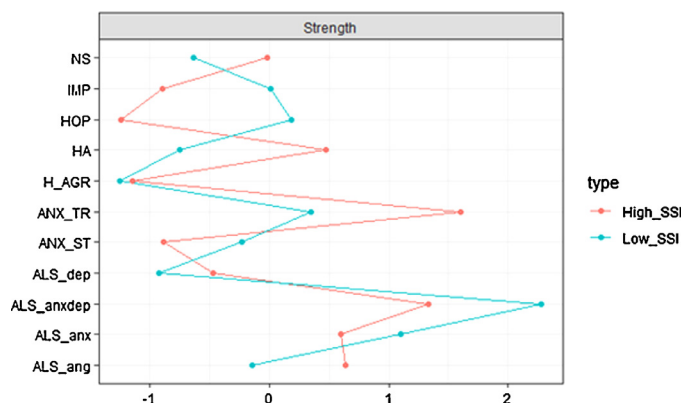


Figure 5. Strength centrality index of nodes per each item; High SI, Low SI.

a relevant role in the activation, persistence and remission of the network (Robinaugh et al., 2016). This is a hypothesis deserving further research by longitudinal designs.

When visually observed, some differences can be found between the networks of repeaters and non-repeaters. Whereas in repeaters SI was positively connected to anxiety as trait and hopelessness and negatively associated to impulsivity, in non-repeaters, it was only linked to anxiety as trait. Moreover, impulsivity in repeaters was connected to anxiety symptoms, which did not occur in non-repeaters. When examining centrality, overall the results were similar to the pattern observed in the global sample. However, there are some differences for impulsivity, which obtained higher strength values in repeaters, and for anxiety state and affect lability (from normal mood to anxiety), whose values were higher in non-repeaters. Accordingly, suicide attempts in repeaters would be more clearly associated with impulsivity, as previously reported (Boisseau et al., 2013). However, given the controversial role of impulsivity as predictor of higher suicidal risk (Anestis et al., 2014; van Heeringen, 2012), under the network frame, we argue that, instead of showing the influence of a single node, these results could reflect complex interactions related to global emotional regulation difficulties. This fits with Peters et al. (2016), who observed that impulsivity was a redundant factor to predict suicidal thoughts when including affect lability. Given the abovementioned differences, we tested between-group differences in network density. Our findings revealing no significant differences support prior results by de Beurs et al. (2017), who argued that, because both groups are suicide attempters (probably sharing a similar high suicidal risk), the network density should not be strongly different. Nevertheless, given our cross-sectional design, and because the lack of information about suicidal behavior of non-repeaters after this analysis, future studies are needed to test this hypothesis.

We compared the networks of groups with high versus low SI. We found that affect lability and anxiety as trait were central nodes, and we observed different symptomatic profiles. First, there were slightly different connectivity patterns for history of aggression and impulsivity.

Second, we observed different strength values, being anxiety trait and affect lability (from anxiety to depression) the central nodes in high SI and just the latter the central node in low SI. Third, we found clear between-group differences in anxiety trait and hopelessness which were higher and lower in high SI respectively. Fourth, the expected influence analysis showed that central nodes in high SI were affect lability symptoms (except shifting from normal mood to anger), anxiety symptoms, and harm avoidance, which differed from low SI, where the most central nodes were affect lability symptoms. We cannot rule out that the differences we found between low and high SI for the strength values might be explained by the symptomatic differences we observed between these groups. This could be applied to anxiety symptoms, but not for impulsivity and affect lability, which did not show group differences. Finally, we found a more densely connected network in patients with high SI, which might suggest a higher probability to future suicidal reattempts. However, because our cross-sectional design and the still controversial role of network density (Schworen et al., 2018), this is a hypothesis deserving further research.

Both affect lability and anxiety were important nodes in each estimated network. Although the evidence is still controversial concerning the role of central nodes as interventional targets (Bringmann et al., 2019), affect lability and anxiety might be suitable targets for specific interventions with suicidal patients, which should be carefully tested. The finding that affect lability (from anxiety to depression) is central in the network of MDD patients supports that failures to daily regulate negative emotions (Cohen et al., 2005) are prospective predictor of depressive illness, and a relevant aspect of MDD (Bylsma et al., 2011; Peeters et al., 2006; Thompson et al., 2012). Moreover, our findings are aligned with evidence revealing associations between affect lability and SI in different psychiatric disorders (Marwaha et al., 2013), and fit with Beard et al. (2016), who found that sad mood and worry (which mirrors anxiety, as suggested by Balbuena et al., (2016)), were the most central symptoms in adult psychiatric patients. Beside the affect lability, we found that anxiety as trait was also central and that SI was connected to the network mainly through this symptom. Previous studies have

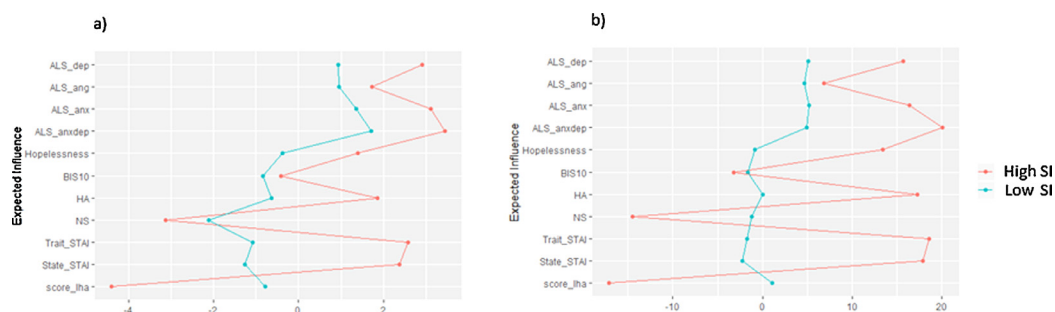


Figure 6. Expected influence; High SI, Low SI. A) One-step; B) Two-step

highlighted the relevance of anxiety as a risk factor for suicide ideation and suicide attempts (Nepon et al., 2010; Thibodeau et al., 2013), however its predictive power would be relatively weak when addressed in isolation (Bentley et al., 2016). Our findings support prior literature revealing that patients with SAD and comorbid depressive symptoms are at elevated risk for attempting suicide (Sareen et al., 2005). This in turn supports that the interaction between anxiety and depressive symptoms (comorbidity in the common cause perspective) could be a stronger risk factor than depression alone (Kanwar et al., 2013), as reported by Bowen et al. (2015a), who found that mixed anxiety-depression accounts for 17.8% of suicide attempts. Therefore, although the clinical relevance of centrality indices needs further clarification (Bringmann et al., 2019; van Borkulo et al., 2015), the present research adds new specific evidence showing that mood instability is an important symptom of MDD (Balbuena et al., 2016; Bowen et al., 2015; Marwaha et al., 2015), and a relevant risk factor for suicide (Peters et al., 2016). Moreover, our findings are aligned with previous literature highlighting affect lability (Peters et al., 2016) and anxiety (Kanwar et al., 2013) as relevant aspects when assessing and treating suicidal patients. Then, smartphones-based monitoring of affective lability may represent a valuable option for improving the real time detection of suicidal ideas, as reported by Thompson et al. (2014), who observed that an ecological momentary assessment of trajectories of affects predicted suicidal ideation with a high precision. Moreover, therapies such as mindfulness-based cognitive therapy (MBCT; Segal et al., 2002) have been shown to be effective in reducing risk for relapse and recurrence in unipolar depression (Chiesa and Serretti, 2011; Galante et al., 2013; Piet and Hougaard, 2011). MBCT has also shown promising results for affect regulation, weakening the association between depressive symptoms and suicidal ideation in depressed patients (Barnhofer et al., 2015). Finally, as reported by Keng and Tong (2016), trait-mindfulness has been negatively correlated to lability of negative emotions, independently of depression.

Some limitations to the present study deserve mention. The finding showing that shifting from anxiety to depression was the most central node suggests that anxiety lead to depression (Avenevoli et al., 2001; Kaufman and Charney, 2000). However, because the evidence revealing the opposite direction (Cramer et al., 2010), and given our cross-sectional design, we cannot disentangle how nodes trigger each other over time (Bos et al., 2017), and causal relationships among nodes cannot be inferred (Dablander et al., 2019). Additionally, centrality indices must be carefully interpreted when analyzing psychological networks (Bringmann et al., 2019). For instance, the most central nodes might not necessarily be the most important treatment targets (Rodebaugh et al., 2018). Moreover, we only examined associations at group level but not at single subject level (Fisher et al., 2018). Despite these limitations, network analysis remains as a useful approach to explore and obtain insights on patterns of associations across individuals using cross-sectional data (Bos et al., 2017). On the other side, we used self-report measures, and because the great number of items addressing the variables of interest, we collapsed them into single nodes. Therefore, we did not have enough variance to conduct correlational analyses between the node expected influence and variance in symptom severity rating. Consequently, our results coming from the expected influence analysis must be considered as both preliminary and exploratory ones. Despite this limitation, our exploratory study provides for the first time evidence about the simultaneous interactions among several components of diathesis for suicide in suicidal attempters coming from a specific psychiatric population. Further research using a larger sample is needed to test our preliminary findings, analyzing symptoms or suicidal factors individually. Our sample size is relatively small, but it is enough for a clinical study (Franklin et al., 2017), and the bootstrapped indices as well as results based on splitting the sample showed moderate stability and accuracy, making the results interpretable. Moreover, we used a suitable number of nodes, similar to the study by de Beurs et al. (2017). Concerning the clinical profile of

participants, although we just included patients mainly diagnosed with MDD, as frequently does occur with complex patients, comorbidities were also observed. Future studies should try to exclude this possible confounding factor.

In summary, our study provides additional evidence showing that affect lability and anxiety as trait would be central psychopathological factors for suicide behavior in suicide attempters with MDD. We observed some differences between the symptomatic profiles of repeaters and non-repeaters and also between high and low SI. Further longitudinal and large-scale studies focusing on these specific clinical profiles are needed to a deeper comprehension of the complex associations between suicidal behavior and psychological and affective symptoms.

## Contributors

Daniel Nunez did the literature searches, performed the network analyses, and wrote the manuscript.

José Luis Ulloa gave support for statistical analyses using the R software

Emilie Olié, Sebastien Guillaume and Adrian Alacreu-Crespo supervised inclusions and assessments, reviewed the manuscript and revised critically for intellectual content.

Philippe Courtet designed the study and directed its implementation, analysis and interpretation, including quality assurance and control.

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## Declarations of competing interest

None

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## Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.jad.2020.04.004.

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