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Decision-making in unipolar or bipolar suicide attempters

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ABSTRACT

Objective: Disadvantageous decision-making (mainly measured by the Iowa Gambling Task) has been demonstrated in patients with suicidal behavior compared to controls. We, therefore, aimed at clarifying the qualitative and quantitative relationship between decision-making and the risk of suicidal behavior in unipolar and bipolar disorders respectively, as well as establishing the strength of this relationship.

Methods: (1) We conducted a cross-sectional study comparing IGT performances between 141 unipolar suicide attempters and 57 bipolar suicide attempters. (2) We conducted a systematic review and a meta-analysis of studies comparing IGT performances in patients with vs. without a history of suicidal acts in bipolar and unipolar disorder, together and separately.

Results: (1) Among suicide attempters, bipolar and unipolar groups performed similarly ($t(195) = -0.7$; $p = 0.48$). Unipolar non-attempters performed better IGT than unipolar suicide attempters ($t(221) = 3.1$; $p = 0.002$), only in female gender, whereas performances were similar in bipolar patients whatever the history of suicide attempt ($t(77) = -0.3$; $p = 0.7$).

(2) A meta-analysis of 10 studies confirmed significantly impaired decision-making with a moderate effect-size (-0.38 (95% CI $[-0.61 - -0.16]$; $z = -3.3$; $p = 0.001$) in unipolar disorder and ($g = -0.4$ (95% CI $[-0.75 - -0.05]$; $z = -2.2$; $p < 0.026$) in bipolar disorder suicide attempters compared to unipolar and bipolar non-attempters, respectively.

Limitations: It was not possible to analyse according to the level of lethality attempt.

Conclusion: Overall, a strong significant association was found between decision-making and the risk of suicidal behavior in unipolar disorder and bipolar disorder. However, further neuropsychological studies need to analyse separately unipolar and bipolar disorder and to study gender differences.

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1. Introduction

The stress-diathesis model postulates a vulnerability to suicidal acts with genetic and early developmental components (including childhood abuse) interacting with proximal stressful events e.g. social negative events like marital conflict or job loss, depression or alcohol abuse (Mann, 2003a). This lower ability to respond adequately to stress is also highlighted by numerous studies showing deficient cognitive functioning, notably disadvantageous decision-making (Richard-Devantoy et al., 2013b; Courtet et al., 2011a) or reduced cognitive inhibition (Richard-Devantoy et al., 2012a). Decision-making impairment and deficient cognitive control were viewed to contribute to suicidal behavior

synergistically, yet independently (Richard-Devantoy et al., 2013c).

Impaired decision-making was found in euthymic patients with a history of mood disorder and a past history of suicidal acts (notably those who used a violent mean) in comparison to euthymic patients with a history of mood disorder without history of suicidal act and healthy controls (Jollant et al., 2007b, 2010, 2005). Decision-making deficit has been found in normothymic patients, at distance from their suicidal act, and in comparison to patient controls suggesting it represents a cognitive trait-marker of suicide vulnerability. Suicide attempters tend to choose options with higher immediate reward but long-term loss over options with lower reward but long-term gain, an impairment related to lateral orbitofrontal cortex dysfunction in this population (Jollant et al., 2010). This result in middle-aged patients has been replicated in studies with patients suffering from depressive (Westheide et al., 2008) or bipolar disorder (Malloy-Diniz et al., 2009; Martino et al., 2010) but not by others studies (Adida et al., 2011; Gilbert et al., 2011; Gorlyn et al., 2013). Interestingly, decision-making deficit was also found in both adolescent (Dougherty et al., 2009; Mathias

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et al., 2011; Oldershaw et al., 2009; Ackerman et al., 2014; Bridge et al., 2012) and elderly (Clark et al., 2011a; Dombrovski et al., 2010, 2011) suicide attempters, suggesting that disadvantageous decision-making could be a factor of cognitive vulnerability to suicidal behaviors across the lifespan. Decision-making impairment in suicide attempters was further correlated to the likelihood of interpersonal difficulties, a well-known trigger of suicidal acts, and with genetic variants related to suicidal behaviors (Jollant et al., 2007a, 2007b). These findings point toward decision-making deficit being at the interface of genes and the (social) environment. Decision-making deficit could also be a potential endophenotype of suicidal behaviors, although to date, there is a lack of information regarding stability of performance over time, and deficits in healthy relatives (Courtet et al., 2011b).

One frequently raised question relates to the possibility that impaired decision-making in suicide attempters may act as a transdiagnostic trait or may depend on the nature of the associated psychiatric disorder (Lopez-Castroman et al., 2014). Impaired decision-making seems to be a vulnerability trait of suicidal behavior in mood disorders, but we may wonder if this actually the case in both unipolar and bipolar disorders. Indeed, such a differential effect has already been described. For instance, impulsivity is viewed as a major vulnerability trait of suicidal behavior in patients with mood disorders (Oquendo et al., 2004), but some found that it discriminated suicide attempters in unipolar but not in bipolar patients (Raja and Azzoni, 2004). Whereas impulsivity helped to distinguish major depressive disorder's subjects without a history of suicide attempt from those with such a history, this was not the case in bipolar disorder subjects where no difference in impulsive traits was observed between bipolar without and with history of suicide attempts (Perroud et al., 2011). At the cognitive level, Iowa Gambling Task (IGT) scores was found to be significantly different between suicide attempters and non-attempters in mood disorders (Richard-Devantoy et al., 2013b), but no studies have examined IGT performances between unipolar and bipolar patients according to their suicidal status. In the perspective to develop therapeutic interventions targeting cognitive abilities, it is necessary to shed light on the intimate mechanisms of neurocognitive vulnerability in suicide attempters. In sum, it is not clear if decision-making impairment may be more differentially associated to the risk of suicidal act in unipolar and bipolar disorders, respectively.

To answer this question, we simultaneously run two approaches: (1) we tested decision-making in unipolar and in bipolar suicide attempters separately and in non suicide attempters, and then made for the first time the direct comparison between unipolar versus bipolar attempters, and (2) we conducted a systematic review and a meta-analysis of studies comparing IGT performances in patients with vs. without a history of suicidal acts in unipolar and bipolar disorders, together and separately. We, therefore, aimed at clarifying the qualitative and quantitative relationship between decision-making and the risk of suicidal behavior in unipolar and bipolar disorders, respectively, as well as establishing the strength of this relationship.

2. Methods and material

2.1. Cross-sectional study

2.1.1. Population and clinical assessment

Three hundred and three patients with a unipolar ($n=224$) or bipolar ($n=79$) disorder were recruited, and divided into two groups: (1) 198 euthymic patients with a history of a serious suicide attempt and mood disorders ($n=141$ with unipolar disorder and $n=57$ with bipolar disorder); (2) 105 euthymic patient

controls with a history of mood disorders ($n=83$ with unipolar disorder and $n=22$ with bipolar disorder) but without a history of suicidal act. Finally, 37 healthy controls with no history of depression or suicide attempt, and with no current psychopharmacological treatment were recruited.

All participants were French natives and written informed consent was obtained from all of them. This study was conducted at Montpellier University Hospital, France and has been approved by the local Ethics Committee (CPP Sud Méditerranée IV, CHU Montpellier).

A suicide attempt was defined as a self-directed injurious act with a clear intent to end one's own life (Mann, 2003a). All patients were euthymic at the time of evaluation, with a 21-item Hamilton Depression Rating Scale score (Hamilton, 1960) below 12 and no current diagnosis of a major depressive episode according to DSM-IV criteria. Patients with neurological disorders, a history of brain injury or a history of electroconvulsive therapy in the last 2 years were not included.

Psychiatric diagnoses were carried out according to the DSM-IV criteria. The MINI 5.0.0 (Sheehan et al., 1998) was used together with any other available information.

2.1.2. Neuropsychological assessment

The cognitive battery included measures of verbal IQ with the French version of the National Adult Reading Test (NART) (Mackinnon et al., 1999) and decision-making with the computerized version of the Iowa Gambling Task (IGT) described elsewhere (Bechara et al., 1999). For the IGT, a net score (total number of safe minus risky choices, so the higher the score the better the performance) was calculated for the whole task but also for the first 50 choices (roughly corresponding to *decision-making under ambiguity* during which participants have to gain experience; IGT1-50) and the last 50 choices (corresponding to *decision-making under risk* when many participants have acquired a certain understanding of the underlying contingencies; IGT51-100).

2.1.3. Statistical analysis

The Shapiro-Wilk's test showed a normal distribution for most of the scores, so parametric tests were used. *T*-Test of Student was used to compare quantitative variables. A Chi-square test was used to compare qualitative variables. Spearman's correlation tests were also used. A conservative p -value=0.01 was used taking into account multiple comparisons. All analyses were performed using SPSS 21.0 (SPSS, Inc., Chicago, IL).

2.2. Meta-analysis

2.2.1. Data sources

An English and French systematic literature search of MEDLINE, Embase, and PsycInfo databases was performed for human studies published from January 1st, 1960 to March 31st, 2015. The Medical Subject Heading (MeSH) term "suicide" was combined with the MeSH terms "Cognition", "Neuropsychology", "Neuropsychological Tests", "Executive Function", "Decision Making", "Prefrontal Cortex", and with the Title and Abstract (TIAB) terms "neuropsychological functions", "executive functioning", and "executive performance". An iterative process was used to ensure that all relevant articles were obtained. A further hand search of the bibliographical references of the selected papers and existing reviews was conducted to identify additional potential studies.

2.2.2. Study selection

Abstract selection was based on the Strengthening the Reporting of Observational studies in Epidemiology (STROBE) checklist, which describes items that should be included in reports of cohort studies. Abstracts identified through the literature search

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