Journal of Affective Disorders 145 (2013) 264–269

Contents lists available at SciVerse ScienceDirect

Journal of Affective Disorders

journal homepage: www.elsevier.com/locate/jad

Brief report

Neurocognitive alterations in first degree relatives of suicide completers

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ARTICLE INFO

Article history:
Received 10 March 2012
Received in revised form
8 May 2012
Accepted 30 May 2012
Available online 25 July 2012

Keywords:
Suicide
Family study
Relatives
Wisconsin card sorting test
Neurocognitive function

ABSTRACT

Background: Suicide aggregates within families and the relatives of suicide completers are at an increased risk for suicide. Though neurocognitive changes are gaining increasing attention as part of the vulnerability for suicide, the literature on neurocognitive alterations among suicide relatives as possible endophenotypes of suicide is sparse.
Method: Normothymic first-degree relatives ($n=14$) of suicide completers without personal histories of suicide attempts were compared to individuals without family histories of suicide ($n=14$) matched for age-, sex- and education. Participants completed the Wisconsin card sorting test, a well validated test of cognitive control in a changing environment.
Results: First-degree relatives of suicide completers made significantly more perseverative errors and have a lower level of conceptual responses than comparison subjects.
Conclusion: Alterations found in first-degree relatives of suicide completers suggest a decreased responsiveness to changing, yet unambiguous, conditions. These neurocognitive impairments are similar to deficits observed among individuals engaging in suicide attempts. Neurocognitive impairments revealed by the Wisconsin card sorting test may represent a neurocognitive endophenotype of suicide.

1. Introduction

Suicide is a major public health concern. Research efforts have made clear that suicide is a complex behaviour that is the result of several interacting vulnerabilities including biological, environmental, and societal factors (McGirr and Turecki, 2007). In addition, it is increasingly clear that some individuals carry a vulnerability to suicidal behaviour rendering them more likely to engage in suicidal behavior if confronted with negative life events (Mann, 2003). Understanding this vulnerability is a major challenge with great opportunity with respect to improving prevention.

Suicide aggregates in families (Brent et al., 1996, 2002; Johnson et al., 1998; Kim et al., 2005; McGirr et al., 2009), and adoption studies suggest that this is attributable to a significant heritable contribution estimated to be 45% (Statham et al., 1998). Accordingly first degree relatives are at a 3–5 fold risk increase for suicidal behaviour (Baldessarini and Hennen, 2004; Brent et al., 2002; Kim et al., 2005; Tidemalm et al., 2011). The search for endophenotypes (Gottesman and Gould, 2003), or traits that mediate the relationship between genes and suicide, represents a great potential for screening, as well as modification and intervention. Studying the relatives of suicide completers provides a unique opportunity to explore transmissible traits that may predispose individuals to suicide.

There has been growing research interest in neurocognitive alterations associated with suicidal risk, and in their potential as endophenotypes of suicide (Courtet et al., 2011; Mann et al., 2009). Cognitive functions are clearly relevant in suicidal behaviour, for incorrect appraisal of the environment or failure to adapt in the face of a changing environment may result in an increased risk for suicide (Jollant et al., 2011). Indeed, a growing neuropsychological and neuroimaging literature suggests that suicide attempters display dysfunction in a variety of cognitive domains, including decision-making (Jollant et al., 2005, 2010; Malloy-Diniz et al., 2009), reversal learning (Dombrovski et al., 2010, 2011), deterministic learning (Keilp et al., 2001; McGirr et al., 2012), problem solving (Grover et al., 2009; Schotte et al., 1990), attention (Keilp et al., 2008) or sensitivity to the social environment (Jollant et al., 2008). Evidence is also growing that a greater degree of cognitive impairment is observed with increasing severity of suicidal behaviour (Keilp et al., 2001; McGirr et al., 2012).

Despite interest in cognitive function as putative endophenotypes, limited data exists on cognitive function among the relatives of suicide completers. We have previously reported a

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http://dx.doi.org/10.1016/j.jad.2012.05.062

family study among first degree relatives of suicide completers in which executive function was assessed at baseline and then following a standardized laboratory psychosocial stress paradigm (McGirr et al., 2010). The relatives of suicide completers exhibited a blunted stress response that was associated with a disruption in cognitive inhibition. This preliminary and, to our knowledge, only neurocognitive study of relatives of suicide completers suggests that neurocognitive alterations, in addition to pathological personality traits (McGirr et al., 2009), may be transmitted in families.

The Wisconsin cart sorting test (WCST) is a well-known and validated task of executive function and rule learning in a changing, yet unambiguous, environment. Several studies suggest that deficits in WCST performance are observed among suicide attempters. In this study, we hypothesized that first degree relatives of suicide completers' performance would be significantly lower on the WCST in comparison to individuals with no personal or family history of suicidal acts.

2. Methods

2.1. Participants

Through collaboration with the Quebec's Coroner's Office, we are able to characterize representative suicides from the Montreal region. We recruited 14 relatives of suicide completers without personal histories of suicidal behaviour, none of whom currently met criteria for psychopathology, including depressive disorders, anxiety disorders and substance disorders. Proband suicide completers ($n=11$; 36.36% female, 63.63% male; 45.00 ± 7.07 years of age) all died in the context of a major depressive episode, with $n=6$ (54.54%) also meeting criteria for substance dependence, $n=1$ (9.09%) for borderline personality disorder, and $n=2$ (18.18%) for anti-social personality disorder. Suicide methods included hanging ($n=5$, 45.45%), gunshot ($n=1$, 9.09%), carbon monoxide ($n=1$, 9.09%) and drug overdose ($n=3$, 27.27%).

Age-, sex-, and education-matched healthy controls ($n=14$), were identified through advertisements in local newspapers. Controls were retained for the current study only after semi-structured interviews detailed below confirmed the absence of personal or family history of suicidal behaviour, and current psychopathology. Exclusion criteria further included cerebrovascular incidents, chronic obstructive pulmonary disease, as well as diagnoses of dementia or mild cognitive impairment. Head injury was screened for, and patients excluded if evidence of post-concussive symptomatology was confirmed on history.

This sample's neurocognitive function conceptual reasoning subsection of the WAIS-III, the continuous performance test, the trail making test, the stroop test, and the verbal fluency test have been previously reported (McGirr et al., 2010). No differences were noted between suicide relatives and comparison subjects prior to the psychosocial stressor. Diurnal variation of cortisol and alpha-amylase were characterized on successive days, which confirmed the absence of dysregulation of the hypothalamic-pituitary-adrenal axis or sympathetic tone (McGirr et al., 2010).

The study was approved by the Research Ethics Board of the Douglas University Mental Health Institute; suicide family members and controls signed informed consent forms.

3. Assessments

All subjects provided demographic information and underwent psychiatric assessment prior to coming to the laboratory to perform neuropsychological testing. Axis I&II Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) psychiatric disorders were assessed using the Structured Clinical Interview for DSM-IV (SCID) Axis I (Spitzer et al., 1992) and Axis II disorders (First et al., 1995), and were eligible if these schedules revealed the absence of current psychopathology. Participants also completed the Beck Depression Inventory (BDI) and Beck Anxiety Inventory (BAI). All participants were currently normothymic.

Participants completed a computerized 128-card version of the Wisconsin card sorting test (Resources, 2003). This test involves matching a card to one of four decks on the basis of either color, shape, or number of shapes displayed on the card. Feedback is provided after each card is assigned. After ten correct assignments, the rule is changed ('set-shifting') without the participant being informed, and feedback provided accordingly. The test provides psychometric data with respect to total errors (sum of perseverative and non-perseverative errors), perseverative errors (associated with continuing to choose according to the previous rule), non-perseverative errors, and conceptual responses (insight into abstract rules). Administration of the WCST occurred 30 min prior to the reported salivary baseline previously characterized in this sample reported (McGirr et al., 2010).

4. Statistical analyses

We performed analyses using the SPSS statistical package version 19 (SPSS Inc., Chicago, IL). Data distributions were checked for normality. Student-t test was employed for normally distributed variables, while Mann–Whitney test was employed for non-normally distributed data. Significance was set at $\alpha \leq 0.05$.

5. Results

There were no significant differences with respect to demographic, depressive or anxious symptomatology were identified (Table 1). Suicide relatives were significantly more likely than control participants to have had a depressive disorder in the past, but were currently normothymic.

With respect to the WCST, analyses are illustrated in Fig. 1. Non-normality was identified for perseverative and nonperseverative errors. Relatives of suicide completers had significantly lower levels of conceptual level responses ($t(26)=2.04$, $p=.050$) and marginally significantly greater percentage of perseverative errors (Mann–Whitney $U=140.00$, $p=.053$). No statistically different impairments were identified with respect to total errors ($t(26)=1.77$, $p=.088$) or non-perseverative errors (Mann–Whitney $U=127.50$, $p=.175$).

6. Discussion

In this study, we characterized first-degree relatives' neurocognitive function using the WCST, a well-established and validated neuropsychological test. Our analyses suggest that normothymic first-degree relatives of suicide completers exhibit deficits in cognitive control as evidenced by an increased level of perseverative errors and decreased level of conceptual responses. We previously showed, in the same population, alterations in cognitive inhibition following a social stress test (McGirr et al., 2010). Together, our data suggest a set of neurocognitive alterations in healthy first-degree relatives of suicide completers even in the absence of a personal history of suicidal behaviour. As these neurocognitive impairments have previously been reported in suicide attempters, this preliminary evidence suggests that they