

Abnormal regional homogeneity in young adult suicide attempters with no diagnosable psychiatric disorder: A resting state functional magnetic imaging study



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ARTICLE INFO

Article history:

Received 9 September 2013

Received in revised form

1 April 2014

Accepted 15 October 2014

Available online 6 November 2014

Keywords:

Attempted suicide

Impulsive behavior

fMRI

Cerebral cortex

Hippocampus

Cerebellum

ABSTRACT

Many young adults who attempt suicide have no discernible mental illness, suggesting an etiology distinct from other psychiatric disorders. Neurological anomalies associated with a history of suicidal behavior may predict future risk. In the present study, we explored changes in neural circuit organization associated with suicidal behavior by comparing local synchronization of resting-state functional magnetic resonance imaging signals in suicide attempters without a psychiatric diagnosis (SA group, 19.84 ± 1.61 years, $n=19$) with those in healthy controls (HC group, 20.30 ± 1.72 years, $n=20$) using regional homogeneity (ReHo) analysis. The SA group exhibited significantly lower mean ReHo in the left (L) fusiform and supraorbital inferior frontal gyri, L hippocampus, bilateral parahippocampal and middle frontal gyri, right (R) angular gyrus, and cerebellar lobules RVIII, RII, and LVI compared with the HC group. Conversely, in the SA group, ReHo was higher in the R supraorbital middle frontal gyrus, R inferior parietal lobe, and L precuneus. The SA group also had significantly higher total Barratt Impulsiveness Scale scores compared with the HC group. Local functional connectivity is altered in multiple regions of the cerebral cortex, limbic system, and cerebellum of suicidal young adults. Elucidating the functional deficits associated with these ReHo changes may clarify the pathophysiological mechanisms of suicidal behavior and assist in identifying high-risk individuals.

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1. Introduction

Suicide is the second leading cause of death among 15–34 year olds in China, and it is estimated to become the leading cause of death for Chinese youth by 2020 (Phillips et al., 2002). Suicidal behavior is a complex phenomenon that has been studied from the perspective of behavioral and cognitive psychology, psychiatry, sociology, and neurobiology, but it is still impossible to predict suicide attempts. While patients with psychiatric disorders such as major depressive disorder (MDD) and schizophrenia are at increased risk for suicide, the vast majority of these patients never attempt to end their own lives. This indicates that there are predispositions to suicidal behavior independent of mental disorder. The stress-diathesis model of suicidal behavior (Mann et al., 1999) proposes that suicide risk is determined by both psychiatric

illness and a trait-related propensity for suicidal behavior independent of psychiatric diagnosis (Mann, 2003). Indeed, genetic studies on suicidal behavior (Baldessarini and Hennen, 2004; Brent and Mann, 2005; Mann et al., 2009) have demonstrated that heritability is independent of psychiatric diagnosis. Thus, suicidal behavior may be a separate nosological entity with an underlying neurobiological basis distinct from any associated psychiatric illness.

A previous study reported that 40% of suicide completers under the age of 16 did not have a psychiatric diagnosis (Spirito and Esposito-Smythers, 2006). Suicide in young adults without diagnosed psychiatric disorders appears to be a relatively impulsive act (Marttunen et al., 1998), and the influence of acute psychosocial stressors has been emphasized (Borowsky et al., 2001). Interpersonal conflicts, separation, rejection, and humiliation are the most commonly reported precipitants for suicide in adolescents and young adults. Nonetheless, the vast majority of adolescents and young adults who experience such traumas do not attempt suicide, again suggesting that there are other factors contributing

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to suicide, such as the underlying neurobiology of suicide itself. Identifying the neural correlates of suicidal behavior may facilitate earlier intervention and prevention.

Functional magnetic resonance imaging (fMRI) is a non-invasive method to measure spontaneous brain activity, such as low-frequency fluctuations in blood oxygen level-Dependent (BOLD) signals, and to identify unique neural activation patterns associated with specific cognitive processes and disease states. Most prior studies on aberrant neural activity patterns in suicide attempters were conducted using task-based BOLD fMRI (Jollant et al., 2008). Resting state fMRI (R-fMRI) can provide complementary information to that provided by task-based imaging (Carter et al., 2012), and has several critical advantages for certain imaging applications. First, task-independent fMRI can reveal unexpected changes in functional connectivity by imaging resting activity in multiple spatially distributed and functionally heterogeneous circuits simultaneously (i.e., circuits not engaged by specific tasks). Second, R-fMRI is most appropriate for examination of the so-called default circuit (Buckner et al., 2008; Whitfield-Gabrieli and Ford, 2012). Third, result variability due to individual differences in subject performance is obviated by R-fMRI.

Regional homogeneity (ReHo) is a relatively new analytic method in which Kendall's coefficient of concordance (KCC) is used to measure the similarity of the BOLD signal times series between neighboring voxels (Zang et al., 2004). By measuring the temporal relationships between BOLD changes, ReHo can reveal anomalies in local functional synchronization over time that are unique to patients that have attempted or will eventually attempt suicide. In fact, such analysis has revealed unique ReHo patterns in other psychiatric disorders, indicating aberrant connectivity between brain regions (Liu et al., 2006; Yuan et al., 2008; Paakki et al., 2010; Li et al., 2012). The goal of the current study was to

identify functional brain connectivity patterns unique to young adult suicide attempters.

2. Methods

2.1. Subjects

Nineteen young Han Chinese adults (age: 19.84 ± 1.61 years, all right-handed, 9 males and 10 females) with a history of at least one suicide attempt but without definitive psychiatric diagnoses were recruited as the suicide attempter (SA) group. A suicide attempt was defined as a self-injurious act with some degree of intent to die. Subjects were assessed by two trained psychiatrists, one to rule out psychiatric disorders using the Structured Clinical Interview for DSM-IV (SCID) and the other to confirm the lifetime absence of psychiatric and neurological illness. Fig. 1 presents a flow chart of the selection process for SA without psychiatric disorders. Table 1 provides detailed demographic information, such as age, level of education, and age at first suicide attempt. Twenty right-handed age- and sex ratio-matched Han Chinese control subjects were recruited from the local community (HC, age: 20.30 ± 1.72 years, 12 males and 8 females). Control subjects had no history of suicide attempts or psychiatric illnesses according DSM-IV criteria as confirmed by psychiatric interviews. Additional exclusion criteria for both groups were current or resolved neurological illness, history of severe traumatic brain injury; psychiatric disorders or suicide among first degree relatives; heart, liver, or kidney disease, diabetes or other serious physical illnesses; history of substance dependence or abuse (alcohol, cocaine and other drugs); any contraindication to MRI; or refusal to continue participation in the study. In addition, before the investigation, we established criteria for minimal image quality (see Section 2.2).

All subjects gave written informed consent before the experiment, and all were paid after the R-fMRI study, which was approved by the Ethics Committee of the First Affiliated Hospital of Chongqing Medical University, China (Approval no.: 2012 [24]).

Additional psychometric tests administered to participants included the Hamilton Anxiety Rating Scale (HARS) (Hamilton, 1959), Hamilton Depression Rating Scale (HDRS) (Hamilton, 1960), Suicide Attitude Questionnaire (SAQ) (Xie et al., 2012), and Barratt Impulsiveness Scale 11 (BIS-11) (Chao-Gan and Yu-Feng, 2010).

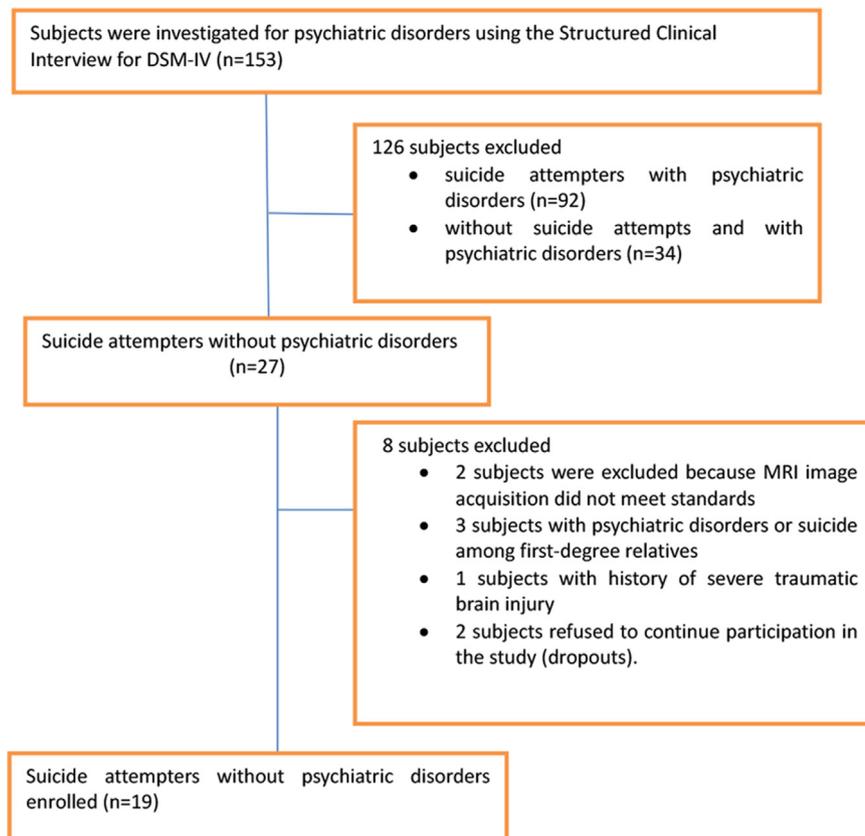


Fig. 1. Flow chart of the selection process for suicide attempters without psychiatric disorders (SA group).

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