



## The association between immune markers and recent suicide attempts in patients with serious mental illness: A pilot study



Faith Dickerson<sup>a,\*</sup>, Maria Adamos<sup>a</sup>, Emily Katsafanas<sup>a</sup>, Sunil Khushalani<sup>a</sup>, Andrea Origoni<sup>a</sup>, Christina Savage<sup>a</sup>, Lucy Schweinfurth<sup>a</sup>, Cassie Stallings<sup>a</sup>, Kevin Sweeney<sup>a</sup>, Armin Alaedini<sup>b</sup>, Melanie Uhde<sup>b</sup>, Emily Severance<sup>c</sup>, Holly C. Wilcox<sup>d</sup>, Robert Yolken<sup>c</sup>

<sup>a</sup> Stanley Research Program, Sheppard Pratt Health System, Baltimore, MD, USA

<sup>b</sup> Department of Medicine, Columbia University, New York, NY, USA

<sup>c</sup> Stanley Neurovirology Laboratory, Johns Hopkins School of Medicine, Baltimore, MD, USA

<sup>d</sup> Department of Psychiatry and Behavioral Sciences, Johns Hopkins School of Medicine, Baltimore, MD, USA

### ARTICLE INFO

#### Keywords:

Suicide  
Attempted  
Biomarkers  
Inflammation  
Gastrointestinal

### ABSTRACT

Previous studies have identified elevations in markers of gastrointestinal inflammation in schizophrenia and mood disorders but studies have not measured the association between these markers and recent suicide attempts. We assessed 210 patients receiving treatment for schizophrenia, bipolar disorder, or major depression. We employed the Columbia Suicide Severity Rating Scale to identify recent and lifetime suicide attempts (actual, aborted, and interrupted). Psychiatric participants and a control group of 72 individuals without a psychiatric disorder had a blood sample drawn from which were measured specific markers of gastrointestinal inflammation and also C-Reactive protein (CRP). A total of 20 (10%) of psychiatric participants had a suicide attempt in the previous one month and 95 (45%) an attempt during their lifetime but not in the previous one month. The recent attempters had significantly elevated levels of antibodies to yeast mannan from *Saccharomyces cerevisiae* (ASCA), the food antigen gliadin, and bacterial lipopolysaccharide (LPS) compared with the non-psychiatric group when adjusting for demographic and clinical variables. These markers were not elevated in individuals with a past, but not recent, suicide attempt history. Our study indicates that there is evidence of gastrointestinal inflammation in some individuals who have had a recent suicide attempt.

### 1. Introduction

Psychological autopsy and epidemiological studies indicate that more than 90% of people who die by suicide have a diagnosable psychiatric illness, particularly major depression, bipolar disorder, or schizophrenia (Cavanagh et al., 2003; Nordentoft et al., 2011). Genetic factors, independent of those associated with psychiatric disorders, may also play a role in suicide but genes of large effect have yet to be identified (Mullins et al., 2014). The ability to predict suicide attempts based on clinical factors remains limited (Zalsman et al., 2016). Currently available biomarkers also have limited predictive value (Oquendo et al., 2014). The identification of blood-based markers would provide for more personalized methods for the assessment and treatment, and ultimately prevention, of suicide attempts.

Many individuals with schizophrenia and mood disorders have evidence of immune activation suggesting that immune dysregulation may be part of the etiopathology of these disorders (Gibney and

Drexhage, 2013; Haapakoski et al., 2016; Leboyer et al., 2016; Severance et al., 2015). Studies by our group and others indicate that the gastrointestinal tract is often the primary source of this immune activation as evidenced by increased levels of markers of gastrointestinal inflammation in individuals with serious mental illness (Kiecolt-Glaser et al., 2015; Petra et al., 2015; Severance et al., 2015). These markers have varying degrees of prevalence and intercorrelations (Severance et al., 2013, 2014). Furthermore, increased rates of suicide and suicide attempts have been found in some populations of individuals with celiac disease (Ludvigsson et al., 2011) or inflammatory bowel diseases (Gradus et al., 2010).

Several of these immune markers have been the focus of our recent investigations. Gliadin is a component of gluten, found in wheat and related cereals. Antibody response to dietary gliadin is associated with celiac disease, an immune-mediated enteropathy, and with non-celiac wheat sensitivity (Uhde et al., 2016) and is thought to indicate intestinal inflammation and/or intestinal barrier dysfunction. We have

\* Corresponding author.

E-mail address: [fdickerson@sheppardpratt.org](mailto:fdickerson@sheppardpratt.org) (F. Dickerson).

found increased levels of antibodies to gliadin in individuals with schizophrenia (Dickerson et al., 2010) and with bipolar disorder (Dickerson et al., 2011) and in individuals with acute mania during a hospital stay (Dickerson et al., 2012); in the latter study the levels of immune markers were lower 6 months after hospital discharge. We also have studied the antibody response to yeast mannans represented by antibodies to *Saccharomyces cerevisiae* (ASCA), a commensal organism present in some foods and in the intestinal tract of many individuals (Severance et al., 2014). Elevated ASCA levels are associated with increased intestinal inflammation (Kaul et al., 2012). We have previously found increased levels of ASCA in individuals with mood disorders (Severance et al., 2014).

Results from other investigators indicate that inflammation may be associated not only with a proclivity for a psychiatric disorder, but specifically with suicidal behavior. Studies have found an association between a suicide attempt history and the level of cytokines such as IL-6 which are cell signaling molecules involved in the immune response and which can arise from inflammation from many sources, including the gastrointestinal tract (Black and Miller, 2015; Courtet et al., 2016; Gananca et al., 2016; O'Donovan et al., 2013). An association between elevated antibodies to *Toxoplasma gondii*, an apicomplexan parasite, and suicide attempts has also been reported (Arling et al., 2009). In a recent study, we found that individuals with serious mental illness who had a lifetime history of a suicide attempt had elevated levels of IgM class antibodies to *Toxoplasma gondii* and Cytomegalovirus (CMV); we also found an association between the levels of these antibodies and the number of suicide attempts (Dickerson et al., 2016b).

There has been little study of the association between markers of gastrointestinal inflammation and recent suicide attempts. In addition, most studies of biological markers and suicide attempts have focused on a lifetime history of suicide attempts rather than recent attempts; a study of the latter may be more informative about state-based immune dysregulation that could signal an acute period of elevated risk. The purpose of this study was to examine the association between levels of markers of gastrointestinal inflammation and a recent suicide attempt in individuals with schizophrenia, bipolar disorder or major depressive disorder in comparison with non-psychiatric controls.

## 2. Methods

### 2.1. Sample

The study sample consisted of individuals with schizophrenia, bipolar disorder, or major depressive disorder as well as non-psychiatric controls who were recruited consecutively in the period May 2014 to November 2016. These individuals were enrolled in ongoing studies of the role of infections and the immune response in individuals with serious psychiatric disorders (Dickerson et al., 2016a). We recently reported on an earlier and smaller version of this cohort in a study of lifetime suicide attempts (Dickerson et al., 2016b).

The inclusion criterion for individuals with schizophrenia was a current diagnosis of schizophrenia, schizophreniform disorder, or schizoaffective disorder. The inclusion criterion for individuals with bipolar disorder was a diagnosis of bipolar disorder including bipolar I disorder, bipolar II disorder, or bipolar disorder not otherwise specified, and for major depressive disorder, single or recurrent major depression. Participants were recruited from inpatient, day hospital, and outpatient programs of Sheppard Pratt Health System and from affiliated psychiatric agencies. The diagnosis of each psychiatric participant was established by the research team including a board-certified psychiatrist and based on the Structured Clinical Interview for DSM-IV Axis I Disorders and available medical records.

The non-psychiatric controls were recruited from posted announcements in community settings in the same geographic area as the health system where the psychiatric participants were recruited (Dickerson et al., 2014a). These individuals were screened to rule out the presence

of a current or past psychiatric disorder with the Structured Clinical Interview for DSM-IV Axis I Disorders, Non-patient Edition (First et al., 1998). Participants were not asked directly if they had a history of a suicide attempt.

All participants met the following additional criteria: age 18–65 (the controls were age 20–60); proficient in English; absence of any history of intravenous substance abuse; absence of intellectual disability; absence of HIV infection; absence of serious medical disorder that would affect cognitive functioning; absence of a primary diagnosis of alcohol or substance use disorder over the past 3 months.

The studies were approved by the Institutional Review Boards of the Sheppard Pratt Health System and the Johns Hopkins Medical Institutions following established guidelines. All participants provided written informed consent after the study procedures were explained.

### 2.2. Measure of suicide attempt history

All psychiatric participants were assessed by trained raters on the Columbia Suicide Severity Rating Scale (C-SSRS) (Posner et al., 2011). Per the C-SSRS, a suicide attempt was defined as a potentially self-injurious act carried out with at least some wish to die as a result of the act: an actual attempt, an aborted attempt, or an interrupted attempt. Participants were assessed as to the occurrence of an attempt over their lifetime and also in the previous one month. Psychiatric participants were categorized into one of three groups: those who had made a suicide attempt in the past one month; those who had made a suicide attempt during their lifetime but not in the past one month, and those who had no lifetime history of a suicide attempt.

### 2.3. Demographic and clinical variables

All participants were asked about demographic variables including maternal education as a proxy for pre-morbid socioeconomic status, their current cigarette smoking status and were evaluated on a cognitive battery, the Repeatable Battery for the Assessment of Neuropsychological Status (RBANS) (Randolph et al., 1998).

Psychiatric participants were interviewed and rated on the Brief Psychiatric Rating Scale (BPRS) (Overall and Gorham, 1962). They were also interviewed about their recent and past use of alcohol and drugs and classified in one of 3 groups: no history, past history only, or recent history (in the last 3 months). Current medications received were recorded from clinical charts and participant self-report and it was noted whether each participant was receiving the following types of medication at the time of the study visit: second generation antipsychotic, lithium, anticonvulsant mood stabilizer, antidepressant medication.

### 2.4. Plasma collection and measurement of immune markers

Each participant had a blood sample obtained using standard venipuncture methods. Plasma was separated from the blood and was stored at  $-70^{\circ}\text{C}$  until testing. In almost all cases blood samples were collected on the same day that the interview measures were completed.

Levels of IgA antibody to yeast mannan from *Saccharomyces cerevisiae* (ASCA) were determined by the enzyme-linked immunosorbent assay (ELISA), according to the assay kit manufacturer's protocol (IBL America, Minneapolis, MN). IgG antibody to gliadin and levels of C-Reactive protein was measured by ELISA as previously described (Severance et al., 2014). IgA antibody to bacterial lipopolysaccharide (LPS) was measured by ELISA, as follows. Wells of 96-well Maxisorp round-bottom polystyrene plates (Nunc, Roskilde, Denmark) were coated with  $50\ \mu\text{L}/\text{well}$  of a  $.01\ \text{mg}/\text{mL}$  solution of LPS from *E. coli* O111:B4, *Pseudomonas aeruginosa*, and *Klebsiella pneumoniae* (Sigma-Aldrich, St. Louis, MO) in  $.1\ \text{M}$  carbonate buffer (pH 9.6) or left uncoated to serve as controls. After incubation at  $37^{\circ}\text{C}$  for 1 h, all wells were washed and blocked by incubation with 1% bovine serum

Download English Version:

<https://daneshyari.com/en/article/4933169>

Download Persian Version:

<https://daneshyari.com/article/4933169>

[Daneshyari.com](https://daneshyari.com)