Trajectories of suicidal ideation in depressed older adults undergoing antidepressant treatment

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ARTICLE INFO

ABSTRACT

Suicide is a public health concern in older adults. Recent cross sectional studies suggest that impairments in executive functioning, memory and attention are associated with suicidal ideation in older adults. It is unknown whether these neuropsychological features predict persistent suicidal ideation. We analyzed data from 468 individuals $\geq$ age 60 with major depression who received venlafaxine XR monotherapy for up to 16 weeks. We used latent class growth modeling to classify groups of individuals based on trajectories of suicidal ideation. We also examined whether cognitive dysfunction predicted suicidal ideation while controlling for time-dependent variables including depression severity, and age and education. The optimal model using a zero inflated Poisson link classified individuals into four groups, each with a distinct temporal trajectory of suicidal ideation: those with 'minimal suicidal ideation' across time points; those with 'low suicidal ideation'; those with 'rapidly decreasing suicidal ideation'; and those with 'high and persistent suicidal ideation'. Participants in the 'high and persistent suicidal ideation' group had worse scores relative to those in the "rapidly decreasing suicidal ideation" group on the Color-Word 'inhibition/switching' subtest from the Delis—Kaplan Executive Function Scale, worse attention index scores on the Repeatable Battery for the Assessment of Neuropsychological Status (RBANS) and worse total RBANS index scores. These findings suggest that individuals with poorer ability to switch between inhibitory and non-inhibitory responses as well as worse attention and worse overall cognitive status are more likely to have persistently higher levels of suicidal ideation.
Clinicaltrial.gov number: NCT00892047.

Published by Elsevier Ltd.

1. Introduction

Suicide in older adults is a serious public health concern (Conwell et al., 2011); suicide rates peak in individuals age 65 and older worldwide (WHO Mental Health Suicide Prevention [SUPRE] http://www.who.int/mentalhealth/prevention/suicide/ suicideprevent/en). Important risk factors for suicide in older adults include physical illness, financial problems, marital status, gender, chronic pain, race, loss of social ties, and social isolation (Juurlink et al., 2004; Sirey et al., 2008; Forkmann et al., 2012; Morrell et al., 1998; Barraclough, 1971). There is some evidence from cross sectional studies that certain cognitive deficits in older individuals increase their risk for suicidal behavior. In a cross-sectional study, King et al. (2000) assessed the role of executive functioning in late-life suicide in a small group of older adults using the Trail Making Test Part B. The findings suggested that there is a

greater decline in executive function in those who attempt suicide than in those who do not. In a subsequent cross sectional study, Dombrovski et al. (2008) reported that among older individuals with depression, those with suicidal ideation perform worse on measures of executive function, memory, and attention than those without suicidal ideation.

Gujral et al. (2013) examined global cognition and executive function as correlates of suicidal ideation and suicidal behavior in depressed older adults. Both suicide attempters and suicide ideators performed worse on the Executive Interview (EXIT; Royall et al., 1992) compared to non-suicidal depressed or non-psychiatric control subjects. The authors noted that suicide attempters and ideators and non-suicidal depressed subjects had similar total scores on the Dementia Rating Scale score and its Memory and Attention subscales. However, attempters and ideators were impaired with these measures relative to non-psychiatric control subjects. Thus, taken together, these cross-sectional studies suggest that executive dysfunction and other cognitive deficits may play a role in suicidal behavior in older individuals. However, little is known with regard to whether cognitive deficits can predict the course of suicidal ideation over time in adults. Furthermore, another important unanswered question is whether cognitive status can predict persistent suicidal ideation in depressed older adults during the course of antidepressant treatment.

The longitudinal course of suicidal ideation over time in older individuals treated with antidepressants has been examined in 2 studies by Szanto et al. (2003, 2007). The 2003 study used survival analysis to determine that while suicidality resolved in almost all older depressed patients with depression treatment, time to response was longer in those with higher suicide risk, i.e., those with a recent attempt or current suicidal ideation. In their 2007 study, the authors further classified elderly patients before and during 12 weeks of antidepressant treatment, as having 1) "non-suicidal", 2) "emergent", 3) "persistent", or 4) "resolved" suicidality. Their classification scheme was based on the temporal patterns of the scores on the suicide item of the Hamilton Depression Rating scale (Hamilton, 1960).

We analyzed data from an NIMH-sponsored clinical trial: "Incomplete Response in Late Life Depression: Getting to Remission" (IRL-GRey; Lenze et al., 2015). The primary aim of this study was to characterize the trajectories of change in suicidal ideation over time in individuals being treated for depression. To address this primary aim, we used latent class growth modelling to explore whether participants could be classified into distinct groups based on clinically meaningful trajectories of suicidal ideation. Our initial hypothesis stated that the latent class modelling approach would classify participants similar to the 4 groups which Szanto et al. (2007) noted, i.e., those with 1) "non-suicidal", 2) "emergent", 3) "persistent", or 4) "resolved" suicidality.

Our secondary aim was to examine if cognition was a marker of poorer prognosis. To our knowledge, no published studies to date have examined prospectively the impact of cognitive dysfunction on suicidal ideation over time in elderly depressed individuals. The studies of Szanto et al. (2007) compared factors which differed between patients with persistent suicidality and patients with resolving suicidality. They noticed that patients who had resolving suicidality were more likely to be on lithium while those with persistent suicidality were more likely to be on a second antidepressant. In our study, all patients were on venlafaxine XR monotherapy and no other therapeutic doses of secondary antidepressants and/or mood stabilizers; thus we wondered whether other factors such as cognitive dysfunction could have accounted for the differences. Given the recent cross sectional data suggesting that cognitive dysfunction in the elderly appears to be associated with suicidal behavior, we decided to extend those findings by examining whether the association of cognitive dysfunction and suicidal behavior occurs across time and if it could have distinguished groups with persistent suicidal ideation and resolving suicidal ideation. We hypothesized that trajectories of persistent suicidal ideation relative to trajectories of resolving suicidal ideation would be associated with: worse scores of executive function (hypothesis 2); worse subscale scores of the Repeatable Battery for the Assessment of Neuropsychological Status (RBANS) (hypothesis 3); and worse total RBANS scores (hypothesis 4).

2. Methods

We analyzed data from participants in the IRL-GRey study (Lenze et al., 2015), a clinical trial conducted at three academic sites (the University of Pittsburgh, the Centre for Addiction and Mental Health/University of Toronto, and Washington University). Data were collected between 7/2009 and 12/2014. In the current analysis, we included those who participated in the initial open treatment phase of the study (both those who completed the entire phase and those who dropped out). In this phase, individuals aged 60 and older with major depressive disorder were treated openly for up to 16 weeks with venlafaxine XR up to 300 mg/day. They were assessed at baseline, and at weeks one, two, four, six, eight, ten, and then finally at endpoint which was between weeks 12 and 16.

2.1. Depression, suicide, and neuropsychological measures

Scales focusing on suicidal ideation and depression were administered at each time point. In addition, neuropsychological assessments were administered at baseline. For this analysis, our primary measure of suicidal ideation was the Beck Scale for Suicidal Ideation (SSI; Beck et al, 1979, 1999; Brown et al., 2000). Time-dependent depressive symptoms were measured with the Montgomery Asberg Depression Rating Scale (MADRS; Montgomery and Asberg, 1979). To assess executive functions, three measures from the Delis–Kaplan Executive Function Scale (D–KEFS; Delis et al., 2001) were used: 1) Color-Word condition 3, called "inhibition" which assesses participants' ability to inhibit an automatic response (i.e., reading words); instead they must produce a response that requires more effort (i.e., naming the colors of the words); 2) Color-Word condition 4, called 'inhibition/switching' which measures both inhibition and set-shifting (i.e., cognitive flexibility); 3) the Trail Making comparison score (trails B/A ratio) which measures cognitive flexibility while controlling for fine motor speed. The DKFS Color Word Inhibition and Inhibition/Switching scores were used with permission from Pearson, Inc. Higher scores on the Color-Word 'inhibition' and 'inhibition/switching' test reflect better performance. The trails B/A ratio is calculated by dividing the number of seconds to complete condition 4 (which assesses cognitive flexibility) by the number of seconds to complete condition 5 (which assesses motor speed); this removes the 'speed' element from the test score so that cognitive flexibility can be ascertained independent of speed (Lezak et al., 2012). Higher scores on this score reflect worse performance.

We used the total score and subscale scores of the Repeatable Battery for the Assessment of Neuropsychological Status (RBANS) to characterize global cognitive performance (Duff et al., 2006). The RBANS was developed to assess neurocognitive status in older patients (Randolph et al., 1998). Its subscales assess five domains: immediate memory, delayed memory, language, attention, and visuospatial/constructional ability. The RBANS total score and subscale scores are standardized scores with a mean of 100 and standard deviation of 15. Higher scores reflect better performance.