Cognitive inhibition in older high-lethality suicide attempters

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Background: People who attempt suicide often display cognitive impairments, particularly poor cognitive control. Could poor cognitive control contribute to high suicide rates in old age? A component of cognitive control, cognitive inhibition—active suppression of task-irrelevant processing—is very sensitive to aging and has been linked to attempted suicide. We investigated cognitive inhibition in older high-lethality suicide attempters, closely resembling suicide victims, as well as low-lethality attempters, and control groups with and without depression and suicidal ideation.

Methods: A total of 102 participants aged 60 years and older (17 psychiatrically healthy control subjects, 38 depressed control subjects, 16 suicide ideators, 14 low-lethality suicide attempters, and 17 high-lethality suicide attempters) underwent comprehensive clinical and cognitive assessments. They completed the Delis–Kaplan Executive Function System Color-Word Interference Test, a validated modification of the Stroop test.

Results: High-lethality suicide attempters demonstrated a distinct pattern of cognitive inhibition deficits. Compared with psychiatrically healthy control subjects and suicide ideators, high-lethality attempters took longer to complete inhibition trials, even after accounting for potential confounding factors (age, education, Mini mental state examination score, information processing speed, and accuracy). Compared with non-suicidal depressed and healthy control subjects, low-lethality suicide attempters committed more uncorrected errors; however, this difference was not specific to the inhibition condition.

Conclusions: Older suicide attempters are a cognitively heterogeneous group. Poor cognitive control in high-lethality attempters may undermine their ability to solve real-life problems, precipitating a catastrophic accumulation of stressors. Meanwhile, low-lethality attempters' poor performance may reflect a careless approach to the task or faulty monitoring. Copyright © 2014 John Wiley & Sons, Ltd.

Introduction

It is becoming increasingly clear that individuals who attempt suicide or die by suicide have a predisposition for this behavior (Mann, 2003; Turecki *et al.*, 2012)—a reduced ability to adapt to stressors, leading them to suicidal ideas and acts. In addition to impulsive aggression (McGirr and Turecki, 2007) and persistent hopelessness (Beck *et al.*, 1985; Szanto *et al.*, 1998), several studies have now reported impairments in cognitive domains such as attentional/cognitive control,

episodic memory, working memory, and language fluency (Keilp *et al.*, 2001; Raust *et al.*, 2007; Richard-Devantoy *et al.*, 2012; Keilp *et al.*, 2013) as well as in decision-making (Jollant *et al.*, 2005; Dombrovski *et al.*, 2010; Clark *et al.*, 2011). Cognitive impairments may be particularly prominent in older suicide attempters (Erlangsen *et al.*, 2008; Dombrovski *et al.*, 2008a; Dombrovski *et al.*, 2010; Gujral *et al.*, 2013; McGirr *et al.*, 2012). Age-related decline in cognitive control (Amieva *et al.*, 2004; Drag *et al.*, 2010) may be among the factors contributing to the increasing suicide

rates in old age (Erlangsen *et al.*, 2008; Dombrovski *et al.*, 2008b).

Cognitive control enables us to flexibly adapt our behavior to meet current demands (Barch *et al.*, 2009) especially in the face of ambiguous, complex, and/or changing environments (Botvinick *et al.*, 2001). Thus, deficient cognitive control has been hypothesized to reduce one's ability to respond adaptively to stressors, increasing the likelihood of seeing suicide as the only obvious solution in vulnerable individuals. Cognitive control is a general ability that underlies performance on tests of task switching, cognitive inhibition, error detection, response conflict and cognitive flexibility (Miller and Cohen, 2001). Cognitive inhibition, a major component of cognitive control and an active suppression process that limits the processing of irrelevant stimuli for the on-going task (Shallice and Burgess, 1991), is very sensitive to aging (Hasher *et al.*, 1999). Aging most notably affects shifting, updating, and inhibition functions (Miyake *et al.*, 2000), nonautomatic controlled inhibition processes (Darowski *et al.*, 2008), as well as decision-making (Eppinger *et al.*, 2012), and cognitive control (Tisserand *et al.*, 2004).

Suicide attempts vary in medical severity, from acts that cause no medical damage to those that would have been fatal without rescue. There is increasing evidence that the cognitive and broader biological profile of those individuals who make serious (high medical lethality) versus low-medical lethality suicide attempts are different (Keilp *et al.*, 2001; Oquendo *et al.*, 2003; Dombrovski *et al.*, 2011b; McGirr *et al.*, 2012). We have previously reported a deficit in cognitive inhibition in older depressed suicide attempters compared with depressed and healthy subjects (Richard-Devantoy *et al.*, 2012). However, this study did not take into account the heterogeneity of suicidal behavior, nor investigated whether those who contemplated suicide but did not exhibit suicidal behavior differ in cognitive control. It is unclear whether cognitive control deficits specifically characterize only those who carry out serious attempts (those with high medical lethality attempts) and whether they are also present in those who currently contemplate suicide (Marzuk *et al.*, 2005) or carry out low lethality attempts.

Depression is the most common mental disorder in those who die by suicide or attempt suicide (Conwell *et al.*, 1996; Szanto *et al.*, 2001; Waern *et al.*, 2003). It remains unclear to what extent the cognitive control profile of older suicide attempters is qualitatively different from that of other patients with late-life depression. The aim of this study was to examine cognitive inhibition ability in older adults who had serious (near fatal) and low lethality suicide attempts and to compare them with similarly depressed nonsuicidal individuals (with no lifetime history of suicide attempt or suicidal ideation) and to those who contemplated suicide but never tried to kill themselves. We hypothesized that both groups of suicide attempters would show a deficit in cognitive inhibition in comparison with the other groups and that high-lethality attempters would show the most pronounced deficit.

Materials and methods

Population sample

Four groups of participants aged 60 years and older ($n = 102$) were recruited: (i) 31 depressed patients with a history of suicide attempt (14 low-lethality suicide attempters and 17 high-lethality suicide attempters) and current suicidal ideation; (ii) 16 depressed patients with current suicidal ideation with a specific plan but with no lifetime history of a suicide attempt; (iii) 38 depressed control subjects with no lifetime history of a suicide attempt or ideation; and (iv) 17 psychiatrically healthy control subjects with no history of any Axis I disorder or a suicide attempt.

Suicide attempters, suicide ideators, and nonsuicidal depressed control subjects were all diagnosed with major depression without psychotic features by the Structured Clinical Interview for Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition Axis I Disorders (First *et al.*, 2002). Depressed patients and control subjects were all fluent in English, with a Mini mental state examination (MMSE) (Folstein and Mc Hugh, 1975) score of ≥24. Exclusion criteria were bipolar disorder, schizophrenia, schizoaffective disorder, electroconvulsive therapy in the previous 6 months, and neurologic disorders including stroke, epilepsy, brain tumor or brain injury, and sensory disorders that precluded participating in cognitive assessment. All participants provided written informed consent. The University of Pittsburgh Institutional Review Board approved the study.

Our study was conducted at a university psychogeriatric inpatient unit and a specialty outpatient research clinic for late-life depression. Because we aimed to capture cognitive control in a state similar to a suicidal crisis, we assessed participants with major depression during an acute depressive episode. Participants were assessed within 2 weeks of inpatient admission or at the beginning of outpatient treatment. Depressed participants continued to receive psychotropic medications as clinically indicated. We ensured that none were intoxicated or had withdrawal symptoms at the time of assessment.

Neuropsychological assessment was overseen by an experienced neuropsychologist (M. A. B.) and took place in one to two sessions over 1–3 days. Assessors were blind to clinical history and mood ratings. Suicide attempters had a self-directed injurious act with a clear intent to end one's own life (O'Carroll *et al.*, 1996). To capture a state close to the suicidal crisis, all of these participants were required to have suicidal ideation with a specific plan at the time of study enrollment. These participants displayed a high level of suicidal intent during their attempts and expressed severe suicidal ideation. A psychiatrist (K. S. or A. Y. D.) verified suicide attempt history using a clinical interview, medical records, and information from relatives.

Clinical assessment

Depression severity was measured with the 17-item Hamilton Rating Scale for Depression (Hamilton, 1960). Burden of physical illness was assessed with the Cumulative Illness Rating Scale adapted for geriatrics (Miller *et al.*, 1992).

Medical seriousness of attempts was assessed using the Beck Lethality Scale (BLS) (Beck *et al.*, 1975). For participants with multiple attempts, data for the most serious attempt are presented. High-lethality attempts required a medical intervention, resulting in coma, need for resuscitation, unstable vital signs, penetrating wounds of abdomen or chest, third-degree burns, or major bleeding, as defined by a score of 4 on the BLS. None had experienced head injuries directly related to attempt, however, to avoid including attempters who may have suffered brain damage and cognitive dysfunction as a result of the attempt we identified those with potential anoxic-ischemic or toxic brain injury, based on the BLS, medical records and the clinical interview. Past suicidal behavior was also characterized using the Suicide Intent Scale (Beck *et al.*, 1974). This instrument characterizes several dimensions related to the suicide attempt with 18 items coded on a three-point scale.

Neuropsychological assessment

We used the Delis–Kaplan Executive Function System (DKEFS) (Delis *et al.*, 2001) Color-Word Interference Test (CWIT), which consists of four conditions: color naming, word reading, inhibition, and inhibition/switching.

In the CWIT color naming condition, the participant is asked to name the colors of a series of red, green, and blue squares as quickly as possible without

making mistakes. In the second task condition, which is the word reading trial, the participant is presented with a page containing the words "red," "green," and "blue" printed in black ink. The participant is asked to read the words aloud as quickly as possible without making mistakes. Then, in the inhibition condition based on the Stroop procedure (Stroop, 1935), the participant is presented with a page containing the words "red," "green," and "blue" printed incongruently in red, green, or blue ink. The participant is asked to say the color of the ink in which each word is printed. Last is the inhibition/switching condition, in which the participant is presented with a page containing the words "red," "green," and "blue" written in red, green, or blue ink. Half of these words are enclosed within boxes. The participant is asked to say the color of the ink in which each word is printed (as in the third trial) but to read the word aloud (and not name the ink color) when a word appears inside a box.

Performance is measured by completion time and error rates on each of the four conditions. In addition, color naming and word reading times may be summed for a composite score representing component functions. Finally, multiple studies have demonstrated that cognitive control impairments in late-life depression are largely mediated by slowed information processing speed (Butters *et al.*, 2000; Butters *et al.*, 2004a; Sheline *et al.*, 2006). Thus, we controlled for information processing speed in our analyses to isolate inhibition impairments that distinguish suicide attempters.

Analysis

All analyses were conducted with Statistical Package for the Social Sciences 20.0 (SPSS, Chicago, Illinois, USA). All statistical tests were two-sided. We first compared groups on demographic and clinical characteristics using analysis of variance (ANOVA) and chi-square tests. For these and all subsequent ANOVAs, we examined *post hoc* contrasts using the Tukey's honestly significant difference test.

We used the general linear model to test the influence of different variables on performance of the DKEFS-CWIT inhibition total time to completion. Then, we used a linear regression model to test the association between the history of high-lethality suicide attempt and inhibition test scores, adjusting for age, global cognitive performance (MMSE score), severity of depression, information processing speed (CWIT naming total time to completion), and CWIT accuracy (measured by uncorrected errors), separately. Then,

we used a linear regression model to test the association between group status and DKEFS-CWIT inhibition total time to completion adjusting for age, MMSE score, information processing speed, and CWIT performances, together. Finally, as the distribution of the number of errors was zero-inflated, we used a generalized linear model with a negative binomial log link (which afforded the best fit for the distribution) to examine uncorrected, self-corrected, and total errors. DKEFS naming total time to completion was used as an information processing speed measure.

Results

Demographic and clinical characteristics

The five groups were similar in age, gender, and MMSE scores (Table 1). The four depressed groups did not differ significantly in the severity of depressive symptoms, psychotropic exposure, prevalence of lifetime or current substance use disorders, or burden of medical illness. The suicidal intent of high-lethality and low-lethality suicide attempters was similar.

Cognitive inhibition

As we hypothesized that both groups of suicide attempters would show a deficit in cognitive inhibition in comparison with the other groups and that high-lethality attempters would show the most pronounced deficit, we first compared attempters' performance with controls, and then, we separated the attempter group on the basis of the medical severity of the attempt. Compared with healthy and depressed control subjects, suicide attempters demonstrated a higher rate of DKEFS-CWIT inhibition uncorrected (Wald $\chi^2(3) = 14.8$, $p = 0.002$) but not self-corrected errors (Wald $\chi^2(3) = 3.7$, $p = 0.29$, both controlling for age and education) and took more time to complete the DKEFS-CWIT inhibition condition (F(3, 96) = 4.9, $p = 0.003$, $\eta_p^2 = 0.134$, controlling for age and education).

Cognitive inhibition in high-lethality and low-lethality attempters

High-lethality suicide attempters demonstrated a distinct pattern of cognitive inhibition deficits (Figure 1). The groups differed in time taken to complete the inhibition condition of the task (F(4, 97) = 3.93, $p = 0.005$; $\eta_p^2 = 0.081$), with high lethality attempters displaying poorer performance compared to depressed and healthy

Table 1 Demographic and clinical characteristics

	High-lethality suicide attempters (n = 17) HSA	Low-lethality suicide attempters (n = 14) LSA	Ideators (n = 16) SI	Depressed controls (n = 38) D	Healthy controls (n = 17) HC	F or χ^2	p	Post hoc Tukey HSD
Females, n (%)	4 (23.5)	6 (42.9)	9 (56.3)	23 (60.5)	11 (64.7)	8.3	0.08	
White, n (%)	17 (100)	12 (85.7)	15 (93.8)	33 (86.8)	12 (70.6)	7.4	0.11	
Age, mean ± SD	69.3 ± 6.5	64.4 ± 3.5	67.4 ± 7.4	67.8 ± 6.1	71.4 ± 10.2	2.1	0.08	
Education (years), mean ± SD	13.0 ± 3.5	14.3 ± 2.7	14.8 ± 3.1	14.6 ± 2.4	15.1 ± 1.8	1.5	0.19	
MMSE, mean ± SD	27.5 ± 1.8	28.5 ± 1.7	28.7 ± 1.2	28.6 ± 1.9	28.9 ± 1.8	1.2	0.19	
HAMD-17, mean ± SD	11.2 ± 7.9	17.3 ± 6.7	16.4 ± 6.6	15.7 ± 5.5	2.3 ± 2.2	18.7	<**0.001**	HSA, LSA, SI, D > HC
Suicide Ideation Scale, mean ± SD	17.2 ± 12.0	18.4 ± 12.7	11.4 ± 8.5	—	—	26.7	<**0.001**	HSA, LSA, SI > D
Suicide Intent Scale, mean ± SD	16.4 ± 4.8	18.1 ± 6.3	—	—	—	0.67	0.42	
Medical illness burden (CIRSG), mean ± SD	9.8 ± 4.4	8.9 ± 3.3	9.6 ± 5.7	10.8 ± 3.3	—	0.83	0.48	
Lifetime substance use disorders, n (%)	5 (31.3)	3 (25)	1 (7.1)	3 (8.8)	—	10.9	0.08	

HAMD-17 items, Hamilton Depression Inventory 17-items; CIRSG, Cumulative Illness Rating Scale-Geriatrics; MMSE, Mini mental state examination; HSA, High-Lethality Suicide Attempters; LSA, low-lethality suicide attempters; SI, suicide ideators; D, depressed controls; HC, healthy controls.
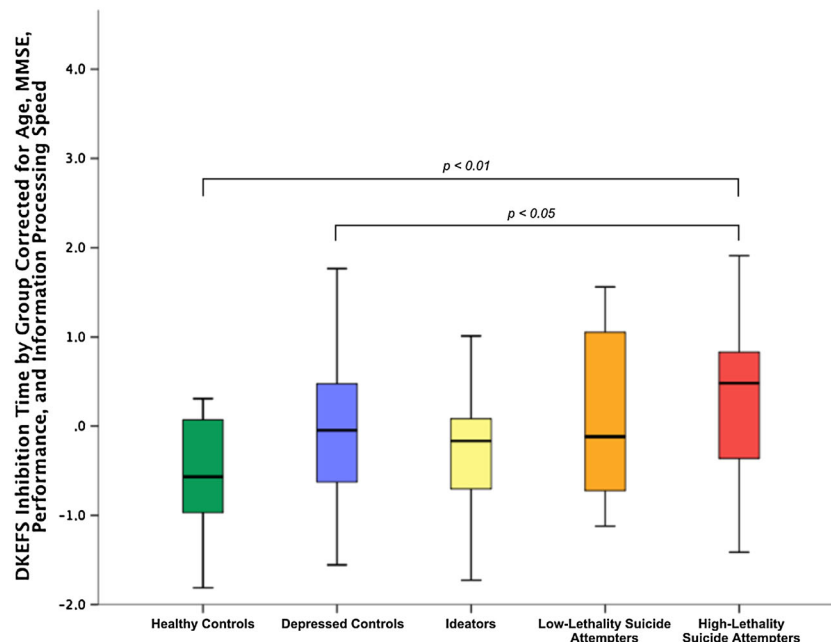
Figure 1 DKEFS inhibition time by group corrected for age, MMSE, accuracy and information processing speed.

control subjects, and suicide ideators. Compared with depressed control subjects, low-lethality attempters demonstrated an increased rate of DKEFS-CWIT uncorrected errors (Wald $\chi^2(4) = 17.5$, $p = 0.002$, controlling for age and education). No significant difference was found between low-lethality and high-lethality suicide attempters on any of the DKEFS-CWIT inhibition variables. Finally, the groups differed in time to execute the DKEFS-CWIT naming condition ($F(4, 97) = 4.3$, $p = 0.003$, $\eta_p^2 = 0.154$), with high lethality attempters displaying poorer performance compared with healthy and depressed control subjects. We found no significant differences between groups in other DKEFS-CWIT conditions: word-reading, color-naming, and inhibition-switching.

Compared with patients with high-lethality suicide attempts, ideators and healthy control subjects were faster in the inhibition condition, even after controlling for age, MMSE score, information speed processing, and accuracy (Table 2). This difference remained after taking into account the severity of depression.

Finally, group differences in inhibition self-corrected errors were diminished when accuracy in the color-naming condition was taken into account, indicating that low-lethality attempters' poor performance was not specific for the inhibition condition (Table 3).

Discussion

In the present study, high-lethality suicide attempters displayed impaired cognitive inhibition when compared

with depressed control subjects, healthy control subjects, and suicide ideators. High-lethality attempters took longer to complete the inhibition condition of the task compared with all other groups, except low-lethality attempters, who demonstrated an intermediate performance. This difference remained after taking into account possible confounders including education, global cognitive performance, and information processing speed. Interestingly, low-lethality suicide attempters tended to make more uncorrected errors in all conditions, suggesting a careless approach to the task or a lack of monitoring. These results indicate that people with a history of attempted suicide display a considerable cognitive heterogeneity, which can be parsed to some extent by grouping them into high-lethality versus low-lethality attempters (Keilp et al., 2001; Dombrovski et al., 2011a; McGirr et al., 2012). Finally, we found no differences between groups for DKEFS-CWIT inhibition-switching, which it is not surprising in view of low sensitivity of this condition to individual differences in cognitive control ability (Lippa and Davis, 2010).

There is accumulating evidence that people vulnerable to suicide display deficits in various aspects of cognitive control. We have previously reported that, in an overlapping sample of older people with depression, a history of high-lethality attempts predicted poor performance on the Wisconsin Card Sort (McGirr et al., 2012). In a US study of younger adults, Keilp and colleagues (Keilp et al., 2013) found an impairment in Stroop performance in suicide attempters compared

Table 2 Group differences in DKEFS total time to completion by condition, with high-lethality suicide attempters as a reference group (n = 102)

Independent variable	Model 1: age-corrected					Model 2: age, MMSE, and information processing speed-corrected*					Model 3: age, MMSE, information processing speed, and accuracy-corrected*,**				
	Standardized coefficient	P-value	η_p^2	Post hoc	Model R²	Standardized coefficient	P-value	η_p^2	Post hoc	Model R²	Standardized coefficient	P-value	η_p^2	Post hoc	Model R²
Inhibition total time to completion															
Group	0.37	**<0.001**	**0.173**	**HSA > SI, D, HC**	0.276	0.18	**0.019**	**0.084**	**HSA > SI, HC**	0.521	0.18	**0.025**	**0.081**	**HSA > SI, HC**	0.521
Age	0.42	<0.001	0.172	—		0.27	<0.001	0.118	—		0.27	0.001	0.112	—	
MMSE	—	—	—	—		−0.10	0.15	0.017	—		−0.10	0.18	0.013	—	
Color naming time to completion	—	—	—	—		0.5	<0.001	0.321	—		0.50	<0.001	0.318	—	
Uncorrected errors	—	—	—	—		—	—	—	—		0.02	0.76	0.003	—	
Inhibition-switching total time to completion															
Group	0.26	**0.006**	**0.083**	**HSA > D, HC**	0.165	0.05	0.47	0.020	**NS**	0.530	0.04	0.58	0.014	**NS**	0.547
Age	0.34	0.001	0.107	—		0.15	0.038	0.049	—		0.16	0.028	0.053	—	
MMSE	—	—	—	—		−0.20	0.006	0.082	—		−0.18	0.014	0.064	—	
Color naming time to completion	—	—	—	—		0.59	<0.001	0.392	—		0.57	<0.001	0.383	—	
Uncorrected errors	—	—	—	—		—	—	—	—		0.13	0.063	0.034	—	

HSA, high-lethality suicide attempters; LSA, low-lethality suicide attempters; SI, suicide ideators; D, depressed control subjects; HC, healthy control subjects; NS, non significant; η_p^2, partial eta squared.

*N = 100 (One healthy control and one low-lethality suicide attempter were missing the MMSE score).

**Gender and education did not explain significant variance in any of the models.

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Table 3 Group differences in DKEFS inhibition errors, with high-lethality suicide attempters as a reference group ($n = 100$)

Independent variable	Model 1: age-corrected					Model 2: age-, and MMSE-corrected**					Model 3: age, MMSE, and color-naming accuracy-corrected**,***				
	χ^2****	P-value	η_p^2	Post hoc	AIC	χ^2	P-value	η_p^2	Post hoc	AIC	χ^2	P-value	η_p^2	Post hoc	AIC
Inhibition self-corrected errors															
Group	9.5	0.050	**0.123**	HSA > D, SI, HC	346	5.3	0.26	0.089	NS	343	7.0	0.14	0.093	NS	337
Age	0.8	0.38	0.006	—		0.22	0.64	0.002	—		0.0	0.83	0.004	—	
MMSE	—	—				5.0	0.026	0.083	—		4.8	0.029	0.086	—	
Color-naming self-corrected errors	—	—		—		—	—		—		6.3	0.012	0.004	—	
Inhibition uncorrected errors															
Group	21.4	<0.001	**0.116**	LSA > D, HC HSA > D	245	18.1	0.001	**0.126**	LSA > HC, D	239	9.3	0.055	0.122	NS	235
Age	6.3	0.012	0.032	—		4.2	0.039	0.026	—		3.1	0.077	0.020	—	
MMSE	—	—		—		9.1	0.003	0.077	—		5.9	0.016	0.071	—	
Color-naming uncorrected errors	—	—		—		—	—		—		4.6	0.031	0.005	—	

HSA, high-lethality suicide attempters; LSA, low-lethality suicide attempters; SI, suicide ideators; D, depressed control subjects; HC, healthy control subjects; NS: Non significant; η_p^2, partial eta squared.

*Generalized linear model using a negative binomial log link.

**Two participants with missing MMSE scores were excluded from every model to compare fits.

***Gender and time to completion did not explain additional variance in any of the models. Any variance explained by education was absorbed by the MMSE.

****df: group, 4; continuous predictors, 1.

with both patients and healthy control subjects. Our finding of a high uncorrected error rate in low-lethality attempters parallels that of Brazilian study by Malloy-Diniz and colleagues (Malloy-Diniz *et al.*, 2009) who reported a positive correlation between the number of suicide attempts and the number of errors on the Stroop test in younger bipolar I patients. Findings, however, are mixed with respect to the motor component of cognitive inhibition, captured by the Go/No-Go test (Raust *et al.*, 2007; Richard-Devantoy *et al.*, 2012; Keilp *et al.*, 2013). The only previous study of cognitive inhibition in older suicide attempters (Richard-Devantoy *et al.*, 2012) had found significant impairments in access to relevant information and deletion of irrelevant information in comparison with both depressed and healthy control groups. That study, however, lacked the power to subdivide suicide attempters according to lethality of suicide attempt, nor did it include a comparison group of suicide ideators. The intermediate performance of suicide ideators in the current sample suggests a dose–response relationship between cognitive control deficits and the progression of the suicidal process. This dose–response relationship, however, was lacking in our previous analysis of a screening measure of cognitive control, EXIT25, in a larger, overlapping sample of older adults (Gujral *et al.*, 2013), where suicide ideators performed as poorly as suicide attempters.

How exactly do cognitive control deficits contribute to suicidal behavior? Cognitive control can be thought of as the ability to organize information in a way that helps achieve the best outcome. It underlies certain (but not all) aspects of decision-making, which in turn appears impaired in younger (Jollant *et al.*, 2005) and older (Dombrovski *et al.*, 2010; Dombrovski *et al.*, 2011a) suicide attempters. Decisions that involve uncertainty, options with multiple features, and changes over time place particularly high demands on cognitive control (Walton *et al.*, 2010)(Dombrovski *et al.*, under review). Because the suicidal process involves the following: (i) a catastrophic accumulation of stressors (Mathew and Nanoo, 2013), such as widowhood (Erlangsen *et al.*, 2004) and physical illness (Juurlink *et al.*, 2004); (ii) an inability to find alternative solutions (Pollock and Williams, 2001; Pollock and Williams, 2004); and (iii) the disregard for the tragic consequences of suicide (Baumeister, 1990; Williams and Pollock, 2001), future experiments need to elucidate the contribution of poor cognitive control to these failures of real-life problem-solving and decision-making. We propose the hypothesis that the inability to find and implement alternative solutions in a suicidal crisis is the most direct consequence of cognitive control deficit.

Deficits of cognitive inhibition in suicidal older patients may be related to the dysfunction of the lateral prefronto-parietal network (Harrison *et al.*, 2005; Alichniewicz *et al.*, 2013; Coderre and van Heuven, 2013). Cognitive control abilities in general depend on the associative cortices comprising the lateral frontoparietal and cinguloopercular networks (Milham *et al.*, 2002) (Dombrovski *et al.*, under review). Studies have implicated that the dorsolateral prefrontal cortex is crucial in working memory processes and in the ability to inhibit responses (McDowd *et al.*, 1995; Kane and Engle, 2002). Indeed, initial results from FDG-PET (Sublette *et al.*, 2013) and fMRI studies (Jollant *et al.*, 2011) point to frontoparietal and cinguloopercular alterations in attempted suicide. FDG-PET studies have found lower regional cerebral metabolic rates of glucose in right dorsolateral prefrontal regions of suicide attempters compared with depressed nonsuicidal subjects (Sublette *et al.*, 2013). Deficits in cognitive control and the putative frontoparietal and cinguloopercular alterations in attempted suicide appear distinct from impairments in value-based decision-making paralleled by paralimbic and particularly ventromedial prefrontal cortex dysfunction (Noonan *et al.*, 2010; Glascher *et al.*, 2012) and anterior cingulate cortex (Glascher *et al.*, 2012). These latter deficits are illustrated by our recent findings of paralimbic and particularly ventromedial prefrontal cortex disruptions during value-based decision-making in older suicide attempters, which correlated with high impulsivity, a neglect of decision-relevant information, and poorly planned suicide attempts (Dombrovski *et al.*, 2013). Thus, we would argue for the existence of two independent vulnerability pathways, marked by cognitive control/frontoparietal versus value/paralimbic dysfunction. The first pathway, illustrated by the current behavioral findings, may involve an inability to find and implement alternative solutions in a crisis, and can be further probed by cognitive control tasks and paradigms involving uncertainty. The second, "value/paralimbic" pathway, may involve impulsivity, a low threshold for suicidal acts, and a disregard of deterrents, and can be probed by paradigms that involve value comparisons, such as gambling or intertemporal choice tasks. .

It has also been shown that alterations of cognitive inhibition in depressed older patients were associated with poor antidepressant response (Butters *et al.*, 2004b; Alexopoulos *et al.*, 2005; Murphy and Alexopoulos, 2006; Alexopoulos *et al.*, 2009). Early identification of inhibition impairments would not only facilitate recognition of individuals at risk of suicide (especially high-lethality attempters) but also inform compensatory therapeutic approaches (Alexopoulos *et al.*, 2009).

Limitations

Our findings are limited by a case–control design and retrospective assessment of suicidal behavior. Another limitation is the relatively modest group size, as we dichotomized the group of suicide attempters on the basis of lethality. Although the design dissociates the role of major depression, it does not identify whether the deficits in cognitive control are stable or state-dependent.

Conclusion

Clinicians need useful predictors of late-life suicide attempts (Alexopoulos *et al.*, 2009), above and beyond correlates of depression. The consistency with which cognitive control deficits are implicated in suicidal behavior across samples and age groups highlights their potential clinical predictive utility. Of all facets of cognitive control, poor cognitive inhibition shows perhaps the strongest association with suicidal behavior. Finally, an understanding of cognitive vulnerability to suicide could guide clinicians in developing remedial and compensatory interventions for older people at risk (Kiosses *et al.*, 2010; McLennan and Mathias, 2010).

Conflict of interest

Meryl Butters has received remuneration from GlaxoSmithKline for performing neuropsychological assessment services. No other author declares that they have no conflicts of interest.

Key points

- Cognitive control was impaired in older suicide attempters.
- Older high-lethality suicide attempters displayed an exaggerated Stroop effect, even after accounting for a number of possible confounders.
- Low-lethality, but not high-lethality, suicide attempters committed more uncorrected errors across conditions, suggesting a careless approach to the task.
- Inhibition deficits in high-lethality attempters may undermine their ability to solve real-life problems, precipitating a catastrophic accumulation of unresolved problems culminating in a suicidal crisis.

Acknowledgement

Author contributions

K. S. and A. D. obtained funding. K. S., A. D., and M. B. designed the study and oversaw subject recruitment and data collection. S. R. D. performed the statistical analyses with statistical review by A. D. S. R.D. drafted the manuscript, which was edited and finalized by A. D., M. B., J. K., and K. S.

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