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Intact Alternation Performance in High Lethality Suicide Attempters

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Abstract

Suicide attempters often perform poorly on tasks linked to ventral prefrontal cortical (VPFC) function. Object alternation (OA) - a VPFC probe - has not been used in these studies. In this study, currently depressed medication-free past suicide attempters whose most severe attempt was of high (n=31) vs. low (n=64) lethality, 114 medication-free depressed non-attempters, and 86 non-patients completed a computerized OA task. Participants also completed comparison tasks assessing the discriminant validity of OA (Wisconsin Card Sort), its concurrent validity relative to tasks associated with past attempt status (computerized Stroop task, Buschke Selective Reminding Test), and its construct validity as a VPFC measure (Go-No Go and Iowa Gambling Task). Against expectations, high lethality suicide attempters - the majority of whom used non-violent methods in their attempts with some planning - outperformed other depressed groups on OA, with no group differences observed on Wisconsin Card Sort. Despite intact performance on OA, past attempters exhibited deficits on the Stroop and Buschke. OA performance was associated with performance on Go-No Go and Iowa Gambling, confirming that OA measures a similar construct. VPFC dysfunction may not be characteristic of all suicide attempters, especially those who make more carefully planned, non-violent - though potentially lethal - attempts.

Keywords

Neuropsychological; Depression; Affective Disorders; Object Alternation; Ventral Prefrontal Cortex

1. INTRODUCTION

Neural circuitry involving ventral prefrontal cortex is central to a number of neuropsychological models of suicidal behavior, for compelling reasons. Damage to ventral

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prefrontal, especially orbitofrontal, cortex can result in the type of impulsive aggressive behavior (Best et al., 2002) that is a significant risk factor for suicidal behavior in the context of psychiatric illness (Dumai et al., 2005; McGirr and Turecki, 2007; Gvion and Apter, 2011). Serotonin receptor and transporter abnormalities have been found in ventrolateral and orbitofrontal cortex in post-mortem studies of suicide completers (Arango, et al., 1997; Arango et al., 2002; Underwood et al., 2012). Deficits in language fluency and non-verbal design fluency, associated with left and right inferior prefrontal function respectively, have been found in past suicide attempters (Bartfai et al., 1990). In our own work, high lethality suicide attempters exhibited deficits in both language fluency and a secondary measure from the Wisconsin Card Sort (failure to maintain; Keilp et al., 2001) that is sensitive to ventral prefrontal dysfunction (Stuss, et al., 2000).

More recent studies have found deficits in suicide attempters on a variety of measures sensitive to VPFC dysfunction, including gambling tasks, impulse control tasks, and probabilistic reversal learning. The Iowa Gambling Task (Bechara et al., 1994; Bechara, 2007) is a decision-making task that is sensitive to damage in this cortical region (Bechara et al., 2000) and produces VPFC activation (Li et al., 2010; Lawrence et al., 2009). IGT deficits have been found in past attempters who have used violent methods in their attempts (Jollant et al., 2005), as well as in past attempters from mixed diagnostic groups (Jollant et al., 2007). IGT deficits have been found in attempters with suicidal ideation that persists after an attempt (Westheide et al., 2008), although IGT deficits have not been found in all studies of suicidal behavior (Legris et al., 2012; Gorlyn et al., 2013) or self-harm (Janis and Nock, 2009). Suicide attempters have performed poorly on impulse control tasks in a number of studies (Swann et al., 2005; Wu et al., 2009, Dougherty et al., 2009). Elderly suicide attempters have performed poorly on both the Cambridge Gambling Task (Clark et al., 2011) and probabilistic reversal learning (Dombrovski et al., 2010) – the latter well-validated in both human and animal studies with regard to their association with VPFC function (Clark et al., 2004).

One task sensitive to VPFC dysfunction that has not been used in studies of suicide attempters is Object Alternation (OA), a task requiring both mental flexibility and set maintenance for optimal performance. Given our own earlier findings (Keilp et al. 2001) and those of recent studies suggesting VPFC dysfunction in past suicide attempters, OA should - like other tasks sensitive to VPFC dysfunction - be impaired in past attempters.

The OA paradigm was first developed for use in primate lesion studies as an extension of the delayed match-to-sample and delayed alternation paradigms, and was specifically sensitive to VPFC damage in these primate studies (Pribram and Mishkin, 1956; Mishkin, 1969). The task involves baiting one of two distinct objects with a reward, and requiring the subject to learn that the reward will be moved to the opposite object, regardless of location, whenever reward is obtained. The original primate task was adapted for use in humans by Freedman and colleagues (Freedman et al., 1998), who found higher error rates in depressed subjects than healthy volunteers. Computerized versions of the task were later developed in various laboratories for use in both clinical (Blair et al., 2006; Gonzalez et al., 2008) and imaging (Zald et al., 2005) studies. Functional imaging studies have confirmed its association to VPFC function (Gold et al., 1996; Zald et al., 2005).

We had previously reported initial results from this study (71.0% of current samples; Keilp et al., 2013) and were surprised to find that the highest lethality attempters made fewer errors than lower lethality attempters, contrary to our initial hypotheses. This report is based on an expanded sample given the potential theoretical importance of this finding. It provides greater detail about object alternation performance via its various subscores, and examines its relationship to other measures that assess abstraction abilities, that differentiate past suicide attempters, and that are related to putative VPFC dysfunction. Medication-free, depressed individuals with and without a history of suicidal behavior – as well as a sample of healthy volunteers - were administered a computerized object alternation task as part of an extensive clinical assessment.

This assessment included the Wisconsin Card Sorting Task (WCST), an executive performance measure more closely associated with dorsolateral prefrontal dysfunction (Stuss et al., 2000). The WCST was included in order to examine the potential discriminant validity of OA with respect to suicidal behavior, following the rationale of Abbruzzese and colleagues (1997) who used these tasks to characterize differential deficits in schizophrenia (more impaired on WCST) and obsessive-compulsive disorder (more impaired on OA). A relative deficit in OA performance was expected based on studies cited above; few consistent differences in WCST performance have been found in past attempters (Jollant et al., 2011). In the original design for this study, then, we hypothesized that OA - and not standard measures from the WCST - would be associated with past suicide attempt.

To examine the possible concurrent validity of OA with respect to its sensitivity to suicidal behavior, OA performance was also compared to two tasks that have consistently discriminated past attempters in our studies - a computerized Stroop task and the Buschke Selective Reminding Test (Keilp et al., 2001; Keilp et al., 2008; Keilp et al. 2013; Richard-Devantoy et al., 2013). If OA deficits were characteristic of suicide attempters, we would also expect poor OA performance to be associated with these other deficits found in past attempters.

Finally, the construct validity of OA was examined by comparing performance on this task to that on other tasks associated with VPFC dysfunction, that were acquired in subgroups of the total sample. Presumably, all of these tasks are sensitive to dysfunction associated with VPFC, the broad “construct” of interest. OA performance was compared to performance on the Iowa Gambling Task and a Go-No Go task, both of which have been associated with VPFC function in both lesion and imaging studies (Zald and Andreotti, 2010).

Past attempters were divided for analyses into those who had made less vs. more lethal attempts, based on our earlier findings (Keilp et al., 2001) and our initial hypothesis that OA deficits would be most pronounced in those who had made the most severe past attempts.

2. METHODS

2.1. Subjects

Patients were 209 medication-free individuals in a major depressive episode (both unipolar and bipolar), including 114 who had never attempted suicide and 95 who had made at least

one suicide attempt (defined as a self-injurious act with intent to die). Non-patient comparison group included 84 healthy volunteers with no major psychiatric illness. Suicide attempter sample was divided into low lethality (n=64) and high lethality (n=31) past attempters. Lethality of past attempts was determined using Beck's rating of medical damage (Beck et al., 1975), which ranges from 0 (no injury) to 8 (death). Low lethality attempts were maximally rated 3 (minor injury requiring routine medical intervention); high lethality attempts were minimally rated 4 (injury requiring major medical intervention). At the time of assessment, all participants were free of major medical and neurological illnesses by history and medical exam.

2.2. Instruments

2.2.1. Clinical Assessment—The Structured Clinical Interview for DSM-IV, Axes I (SCID-I; Spitzer et al., 1990) and II (SCID-II; First et al., 1996) was used to establish diagnoses in patient subjects. The non-patient version of the SCID (SCID-NP; First et al., 1997) was used to rule out psychiatric diagnoses in healthy comparison subjects. Other clinical ratings have been described previously (Mann et al., 1999) and are listed in Table 1.

The Vocabulary subtest from the Wechsler Adult Intelligence Scale, 3rd revision (WAISIII; Wechsler, 1997) was used to estimate intellectual ability. The Columbia Suicide History (Oquendo, Halberstam et al., 2003) was used to characterize past suicidal behavior. Lethality of past suicide attempts was assessed via Beck's medical damage rating of physical injury resulting from an attempt [40]. Scale ranges from 0 (no physical damage) to 8 (death). Attempts rated 3 or below (maximally, mild physical injury requiring medical intervention) were designated as low lethality; those 4 and above (minimally, serious injury requiring medical intervention) were designated as high lethality.

2.2.2. Object Alternation Task—The OA task was presented on a Macintosh Powerbook laptop computer and programmed in PsyScope (Cohen et al., 1993). Two symbols, a red triangle and a blue circle, were presented simultaneously on a computer screen, with either the triangle on the left or the triangle on the right (side of presentation determined in a pseudo-random fashion). Subjects were instructed to select the object that they thought was correct on any given trial, and told there was a pattern to determining which item was correct on any given trial. Subjects responded by keypress to designate the location of the object they were selecting. Correct responses were reinforced with a computer beep; incorrect responses received a buzz. The subject's first response, to either symbol, was correct by default. Thereafter, the opposite figure that the subject responded to correctly was designated as correct on the next trial. To respond correctly on each trial, then, the subject was required to alternate between the objects from trial to trial, regardless of which side the alternate object was presented on. Once an object was designated as correct, it remained correct until selected by the subject. Intertrial interval was 500 msec. The test was stopped if the subject made 12 correct responses in a row (12 alternations without an error). If the subject did not complete the test to criterion, it was discontinued after 180 presentations of the stimuli. Subjects were scored on their ability to reach the criterion of 12 correct in a row, on the number of errors made, on the number of perseverative errors (errors following errors), and on failures to maintain a response set (achieving 5 or more correct

responses in a row and making an error before completing the test to criterion). Following Freedman and colleagues (1998), learning was characterized by calculating the number of errors for every set of 10 correct responses (in order to facilitate comparison across subjects, error scores for those who completed the test to criterion was set to zero for subsequent bins).

2.2.3. Wisconsin Card Sort—The Wisconsin Card Sort was administered to all subjects as a comparison measure, using the standard manual administration, to determine if deficits were specific to object alternation or affected abstraction abilities more globally. Abbruzzese and colleagues (1997) demonstrated that these tasks could be used to characterize differential deficits in schizophrenia (more impaired on WCST) and obsessive-compulsive disorder (more impaired on OA); a comparable strategy was employed here.

2.2.4. Computerized Stroop Task and Buschke Selective Reminding Test—Participants received an extensive battery of other neuropsychological measures, described elsewhere (Keilp et al., 2013). These tests included two measures that have consistently discriminated suicide attempters in our studies, a computerized Stroop task and the Buschke Selective Reminding task (Keilp et al., 2001; Keilp et al., 2008; Keilp et al., 2013). These measures were analyzed here to determine if suicide attempters' expected deficits on OA were accompanied by expected deficits on the Stroop and Buschke, and if OA performance was related to that on the Stroop and Buschke. An interference score for the Stroop task was computed based on the percent increase in reaction time between responses to colored non-word stimuli and incongruently-colored color names (see Keilp et al. 2005; Keilp et al., 2008). Buschke performance was characterized using the total recall score (Buschke and Fuld, 1974).

2.2.5. Go-No Go and Iowa Gambling Tasks—A subset of participants received a computerized Go-No Go task (Keilp et al., 2005) and the Iowa Gambling Task (IGT; Bechara et al., 1994), tasks that, like OA, are reputed to be sensitive to VPFC dysfunction. The Go-No Go task (Keilp et al., 2005) is a bimodal matching task requiring subjects to respond when stimuli appear in a specified visual location (top half of the screen) accompanied by the lower of two auditory beeps (200 Hz vs. 400 Hz). Performance was characterized in terms of the number of commission errors to incorrect location/tone pairings. The Iowa Gambling Task is the standard Macintosh version of the task, administered using standard instructions (which include informing subjects that some deck are better than others; Bechara, 2007). Performance was summarized in terms of the standard difference score, the difference between the number of selections from advantageous decks (C and D) minus selections from disadvantageous decks (A and B).

To evaluate the construct validity of OA, OA criterion attainment was compared to performance on both Go-No Go and the IGT. If these tests have common elements, OA criterion attainment should be associated with fewer commission errors on Go-No Go and a greater number of selections from better decks on IGT.

Given that Go-No Go and IGT were only administered to a subset of participants, they were not compared among attempter and non-attempter groups here. Group differences in our samples are described elsewhere (Keilp et al. 2013; Gorlyn et al. 2013).

2.3. Statistical Analyses

Demographic and clinical rating data were compared among groups using Analyses of Variance for continuous data and chi-squared analyses for categorical data. Subscores from OA and the WCST, as well as the Stroop Interference and Buschke SRT total recall score were first transformed into normatively-adjusted Z-scores (based on age, education, and sex) and then compared in the same manner (Keilp et al. 2005; Spreen and Strauss, 2006). Statistical comparisons of clinical groups were based on these Z-scores (to control influence of demographic factors); statistical comparisons of test scores were conducted on raw scores (to compare scaling on tests). A repeated measures Analysis of Variance was used to compare groups on errors per block of trials, with blocks defined as sets of 10 correct responses (see Figure 1.).

Student's t-tests were used to compare those who completed OA to criterion and those who did not on the Go-No Go and IGT summary scores.

Non-parametric correlations were computed between OA scores and clinical variables to examine its clinical correlates.

3. RESULTS

3.1. Demographic and Clinical Characteristics

Non-patients were younger than non-attempters, with attempter groups intermediate, but all groups were comparable in educational attainment and estimated intelligence (Table 1.). Depressed patient groups were all equally depressed, with comparable impulsiveness and cognitive complaint scores. Hopelessness was greatest in the low lethality group, with high lethality intermediate. Both attempter groups had elevated levels of suicidal ideation and hostility, and a higher percentage of individuals with borderline personality disorder than non-attempters. High lethality attempters had the greatest number of past depressive episodes, poorest global functioning scores, highest level of aggression, and greatest number of past substance abusers. Compared to low lethality attempters, high lethality attempters had more past attempts and a higher level of intent in their most recent and most lethal attempts. High lethality attempters also had the highest proportion of individuals with bipolar disorder.

Unipolar and bipolar subjects did not differ on any summary scores of OA or the WCST. Analysis of block-by-block error scores on OA revealed no difference across all blocks (group effect; $F[1,206]=0.10$, $p=0.75$), or in specific blocks (group by block effect: $F[7,1442]=0.38$, $p=0.92$).

3.2. Discriminant Validity

Non-patients and high lethality past attempters outperformed depressed non-attempters and low lethality attempters on all OA indices (Table 2.). High lethality attempters had the best

overall performance scores on this task, but were statistically comparable to non-patients. This was best reflected in the overall criterion attainment rate in high lethality attempters ($\chi^2=8.03$, $df=3$, $p=.045$), which was most pronounced in the unipolar patients (for unipolar alone; criterion rate in high lethality = 91.7%, in low lethality = 58.5%; in non-attempters=57.5%; $\chi^2=7.57$, $df=3$, $p=0.05$).

Block-by-block error scores for OA are depicted in Figure 1. Both non-patients and high lethality past attempters showed the lowest error rates across the test (group effect: $F[3,286]=3.10$, $p=0.03$). Interaction of group by block was not significant ($F[21,2002]=1.06$, $p=0.39$) indicating that the effect was relatively consistent across all blocks of trials.

WCST scores did not differ among the groups. Again, high lethality attempters had the best performance and low lethality attempters the worst, but these differences did not reach statistical significance. Although corresponding measures between the tasks were not well correlated (error scores $\rho=0.08$; perseverative error scores $\rho=0.12$; failure to maintain scores $\rho=0.10$; less than 2% shared variance for any pair of measures), OA criterion attainment was associated with better WCST performance on most WCST subscores (see Table 3.: category score, $t[288]=2.25$, $p=0.03$; error score, $t[288]=2.34$, $p=0.02$; percent error score, $t[288]=$, $p=0.04$ perseverative error score, $t[288]=2.55$, $p=0.01$; failure to maintain, $t[288]=2.18$, $p=0.03$), so that OA and WCST scores were not independent discriminators.

Analyses of all summary scores for both OA and WCST were repeated nonparametrically, with identical results.

3.3. Concurrent Validity

Other tests that we had previously found to distinguish past attempters continued to do so in this sample, despite the intact OA performance among high lethality attempters. On the Stroop and Buschke SRT, low and high lethality attempters were comparable, and, when pooled, performed significantly worse than both non-patients and depressed non-attempters (for Stroop Interference: $F[2,290]=4.51$, $p=.01$; for Buschke SRT total recall: $F[2,289]=6.47$, $p=.002$).

Those who completed OA to criterion did not differ in Stroop performance relative to those who did not complete OA to criterion (see Table 3.: $t[291]=0.56$, $p=0.57$). OA completers outperformed non-completers on Buschke total recall (Table 3.: $t[290]=2.68$, $p=0.008$), but this effect was more evident in non-patients (128.4 ± 13.2 vs. 122.4 ± 12.4 ; $t[82]=2.17$, $p=0.03$) than in patients themselves (122.2 ± 14.6 vs. 118.5 ± 17.6 ; $t[207]=1.73$, $p=0.09$). Concurrent validity for OA was not demonstrated.

3.4. Construct Validity

Among those who were administered the Go-No Go Task ($n=216$), subjects who completed OA to criterion ($n=138$; 36 non-patients, 102 depressed patients) made fewer errors than those who did not complete OA to criterion ($n=78$; 17 non-patients, 61 depressed; Table 3.: $t[214]=3.18$, $p=0.002$). Among those who completed the Iowa Gambling Task ($n=107$) those who completed OA to criterion ($n=71$; 26 non-patients, 45 depressed) had a significantly

greater number of net selections from good vs. bad decks than those who did not complete OA to criterion ($n=37$; 11 non-patients, 26 depressed; Table 3.: $t[106]=2.02$, $p=0.046$). As expected, OA completion was related to better performance on both tasks. Performance differences on these other putative VPFC tasks was not due to differences in basic estimated intelligence; the mean WAIS-III Vocabulary score in those who completed OA to criterion ($n=188$; 59 non-patients, 129 depressed) was comparable to that in participants who did not complete the test to criterion ($n=106$; 25 non-patients, 81 depressed; Table 3.: $t[292]=1.10$, $p=0.27$).

3.5. Clinical Correlates

Among all past attempters, those who completed the OA to criterion made more lifetime attempts (2.7 ± 2.0 vs. 1.9 ± 1.7 ; $t[93]=2.14$, $p=0.04$), had higher suicide intent scores (17.0 ± 5.7 vs. 14.3 ± 4.9 ; $t[89]=2.28$, $p=0.03$). Fewer failures to maintain on OA was associated with greater suicidal intent for both the maximum ($\rho=0.33$, $p=0.001$) and most recent ($\rho=0.32$, $p=0.002$) attempts. Better performers on this task appeared in this sample to have been at greatest risk for a serious attempt. In addition, the suicide intent scale contains factor-derived subscores for subjective intent and planning (Mieczkowski et al., 1993). Those completing OA to criterion showed comparable subjective intent relative to those who did not complete to criterion, but a trend toward higher planning ($p=0.06$). Those scoring above the 80th percentile in our distribution of planning scores (> 20), however, were significantly more likely to complete OA to criterion (85.0% vs. 60.3%; $\chi^2 [1]=4.25$, $p=0.039$).

4. DISCUSSION

Subjects who made the highest lethality past suicide attempts outperformed other depressed patient groups on the Object Alternation task, and were comparable to non-patients. Clinically, these high lethality attempters had more past episodes of depression, more past suicide attempts, and the highest percentage of past substance abuse, and were typical of other high lethality attempter samples. However, the percentage of those using a violent method in their most serious attempt was low.

Performance on OA was more sensitive to past attempt status than the WCST – though in the opposite direction expected. OA and WCST performance were correlated, however, and these measures did not function as independent discriminators. OA clearly did not reflect a deficit in past attempters, as did the Stroop and Buschke SRT, even though there was overlap between OA and SRT performance. Concurrent validity for OA as a measure of deficit in past suicide attempters was therefore not demonstrated. Despite the absence of OA deficits in past attempters in this study, however, OA appeared to be measuring a construct common to both the IGT and Go-No Go tasks, as expected given all three tasks' association with VPFC dysfunction (Zald and Andreotti, 2010).

Highly lethal suicide attempters were characterized by relative strengths as well as deficits. This is consistent with findings from Dombrovski and colleagues (2011), who found that elderly high lethality attempters outperformed other attempter and depressed groups on a delayed discounting task, showing normal range ability to defer reward. In a partially

overlapping sample, McGirr and colleagues (2012) found elevated error rates and lower conceptual attainment on the WCST. These results with respect to the WCST performance in high lethality attempters differ from those in our study, but again indicate that there may be various routes to serious suicide attempt, not all of which involve a global deficit in executive performance.

Ultimately, data here suggest that VPFC dysfunction may not be a general characteristic of suicide attempters, in contrast to studies that have found impairment on other tasks sensitive to it (Keilp et al., 2001; Jollant et al., 2005; Jollant et al., 2007; Westheide et al., 2008; Swann et al., 2005; Wu et al., 2009; Dougherty et al., 2009; Clark et al., 2011; Dombrovski et al., 2010; Richard-Devantoy et al., 2013).

There are limitations on the use of OA as a VPFC probe. OA is a complex task relying on distributed neural circuitry (Zald et al., 2005). It may be more sensitive to superior medial frontal lesions than to VPFC lesions (Fujiwara et al., 2008), and may selectively recruit regions of VPFC (i.e. ventrolateral PFC) that are independent of those paralimbic regions (ventromedial PFC) that have a greater involvement in emotional behaviors (Zald et al., 2005). Deficits on OA have been linked to global alterations in structural connectivity in normal aging (Lamar, 2013) as well as striatal dopamine denervation (Marie, 1999), in addition to VPFC lesions.

Moreover, OA differs procedurally from the gambling tasks, impulse control tasks, and reversal learning tasks that have typically been associated with VPFC dysfunction (Gold, et al., 1996; Zald and Andreotti, 2010). While OA contains an element of “reversal learning”, in the switch of reinforcement from object to object on successive reinforced trials, there is no requirement to establish a response set over multiple trials that then has to be changed. In addition, human reversal learning tasks typically have some probabilistic element (reinforcement for the large majority, but not all correct responses; Clark et al., 2004; Zald and Andreotti, 2010), and this inconsistency of outcome may be crucial to eliciting poor performance in suicide attempters.

Object alternation tasks differ from gambling and decision-making tasks because reward contingencies are not weighted, and do not involve consideration of gains vs. losses with each response. This uncertainty of reward may be a factor in eliciting a preference in suicide attempters for high positive payoffs despite the risk of higher losses (Dombrovsky et al., 2010; Jollant et al., 2011).

Object Alternation tasks differ from more straightforward impulse control tasks because the response rule must be discovered, not simply applied. Set maintenance is only relevant in the final stages of the task as performance approaches criterion performance. The VPFC appears to be engaged whenever such rules are established, but DLPFC may be more active in the process of establishing them (Bengsston et al., 2009).

Thus, procedural differences may account for suicide attempters' intact performance on OA. However, performance on the OA task was associated with the other putative VPFC measures administered in this study. Those who successfully completed Object Alternation to criterion made significantly more selections from profitable decks on the IGT and

significantly fewer commission errors on a computerized Go-No Go task. The overlap in what each of these tests measures was not explained by intelligence or general test taking ability. As we had previously reported, though, neither the IGT nor the Go-No Go task discriminated past attempters in the subsamples in which they were administered (Gorlyn et al., 2013; Keilp et al., 2013). These tests appear to be assessing a common construct, but not one relevant to past attempt status in the samples we have studied.

The lack of any suicide attempt-related differences on these tests suggests that unique characteristics of our sample affected our results. Participants in this study were more intelligent than the general population and relatively well-educated. However, other studies have examined similarly endowed attempters and found deficits on tasks such as the IGT (Jollant et al., 2005). A more critical difference in this sample is the high percentage of those who had used a non-violent method with a relatively high degree of planning in their most lethal attempt. Deficits on decision-making tasks such as the IGT are most pronounced in violent attempters (Jollant et al., op cit.). Though the high lethality attempters in this study reported a high intent to die, their use of non-violent methods suggests a degree of restraint that is likely to be associated with better executive function. While there is no doubt that severely depressed, highly impulsive individuals are at great risk for potentially lethal suicidal behavior (Gvion and Apter, 2011), there are other individuals with high intent to die and intact executive function who are also at great risk (Turecki, 2005). Planning during an index suicide attempt is associated with later mortality by suicide (Nimeus et al., 2002; Stefansson et al., 2012). Violent attempts appear to be associated with behaviors likely to cause more significant harm, but preconceived efforts to reduce discovery during an attempt appear to be associated with higher overall lethality (Beck and Steer, 1989; Misson et al., 2010). Therefore, models of suicidal behavior that are based exclusively on impulsiveness and violence will systematically mischaracterize a subgroup at considerable risk. Certain types of executive dysfunction may be associated with the form of suicidal behavior, then, but not with suicidal behavior itself. As noted above, some of the same subjects who did well on Object Alternation also performed poorly on the Stroop and Buschke SRT measures - tasks that may tap into a more widespread deficit in those who attempt any type of suicidal behavior.

This study is limited by its retrospective nature. Prospective studies are needed to examine the contribution of neurocognition to acute risk. As noted above, there is a paucity of attempters who used a violent method of attempt and had a high lethality outcome. Our current high lethality sample confirms that it is possible to make a very serious suicide attempt without exhibiting deficits on tasks purported to assess VPF functioning, but a comparison with more violent, high lethality attempters is needed.

Ultimately, this study highlights a central problem for characterizing neurocognitive risk factors for suicidal behavior: namely, reconciling various types of suicidal behavior in the search for underlying mechanisms. Suicidal behavior can include very lethal attempts vs. serial low lethality attempts, spontaneous attempts vs. more carefully planned and considered attempts, passive substance ingestion producing a high degree of sedation vs. violent attempts producing a high degree of physical disfigurement. The common underlying element is an action with a wish to die, but this wish can be expressed in myriad ways, and

is most likely influenced by state and trait factors that include neuropsychological integrity. Research samples in which any one type of attempt is overrepresented can easily distort our understanding of suicide risk. Systematic comparisons of the various methods and outcomes of suicide attempt are necessary.

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Object Alternation: Learning Curves (Errors every 10 correct)

Figure 1.

Object Alternation Learning Curves: Errors within each Block of the task. Blocks are defined as the number of trials required to make 10 correct responses (blocks can have different numbers of trials depending on the number of errors made, but will always contain ten correct responses). Errors are counted within each block to illustrate learning effects across the task. Decks) and Go-No Go Performance (Commission Errors). Those completing OA to criterion have significantly better performance on both tasks, in the form of more selections from better decks on the IGT and fewer commission errors on Go-No Go.

Table 1

Demographic and Clinical Rating Data

<u>Variable</u>	<u>p-value</u> ^I	<u>Contrast</u>	<u>Non-Patient Comparison</u>	<u>Depressed Non-Attempters</u>	<u>Low Lethality Attempters</u>	<u>High Lethality Attempters</u>
N		84	114	64	31	--
Age (yrs.)		32.5 ± 11.8	38.9 ± 11.7	35.6 ± 10.7	35.1 ± 11.3	0.002 C < NA
Education (yrs.)		15.7 ± 2.1	15.8 ± 2.7	15.2 ± 2.0	15.7 ± 2.5	0.37
WAIS-III Vocabulary (average scaled score)		14.0 ± 3.1	13.7 ± 2.7	13.1 ± 2.5	14.0 ± 3.0	0.27
Hamilton RSD (24-item)		1.5 ± 2.2	25.1 ± 7.5	26.9 ± 7.1	25.7 ± 8.1	<0.001 C < NA, LL, HL
Beck Depression Inventory		1.6 ± 2.3	27.0 ± 9.5	29.9 ± 10.6	28.9 ± 13.5	<0.001 C < NA, LL, HL
Global Assessment of Functioning (GAF)		89.4 ± 6.3	51.6 ± 10.6	48.1 ± 7.9	43.2 ± 11.3	<0.001 C < NA < LL < HL
Global Assessment of Functioning (GAF) without suicide item		89.4 ± 6.3	51.8 ± 10.7	48.2 ± 7.6	43.9 ± 12.1	<0.001 C < NA < LL < HL
Beck Hopelessness Scale		1.4 ± 1.5	11.7 ± 5.8	13.9 ± 5.3	12.5 ± 5.4	<0.001 C < NA, LL, HL NA < LL
Scale for Suicide Ideation (prior to enrollment)		0.0 ± 0.0	5.7 ± 7.0	13.8 ± 10.3	15.9 ± 10.2	<0.001 C < NA < LL, HL
Scale for Suicide Ideation (current)		0.0 ± 0.0	4.6 ± 6.0	9.0 ± 7.5	8.8 ± 9.9	<0.001 C < NA < LL, HL
Number Past Depressive Episodes	--		8.6 ± 13.0 [median=3]	12.3 ± 17.2 [median=4]	16.2 ± 18.7 [median=9]	0.04 NA < HL
Length Current Depressive Episode (wks)	--		156.5 ± 377.9 [median=20]	75.9 ± 174.0 [median=16]	63.5 ± 119.8 [median=15]	0.11
Barratt Impulsiveness Scale		38.8 ± 12.5	52.7 ± 17.9	56.5 ± 18.1	56.7 ± 22.5	<0.001 C < NA, LL, HL
Buss-Durkee Hostility Inventory		19.1 ± 9.0	32.6 ± 11.7	41.7 ± 11.2	37.8 ± 12.5	<0.001 C < NA < LL, HL
Brown-Goodwin Aggression History		15.6 ± 3.7	18.5 ± 4.6	21.6 ± 5.3	23.2 ± 6.3	<0.001 C < NA < LL < HL
Cognitive Failures		26.1 ± 11.9	52.4 ± 16.9	50.8 ± 16.5	51.9 ± 22.9	<0.001 C < NA, LL, HL
Number Previous Suicide Attempts	--	--	--	2.0 ± 1.8	3.3 ± 1.8	<0.001 LL < HL
Lethality of Most Recent Attempt	--	--	--	1.5 ± 1.2	4.7 ± 1.8	<0.001 LL < HL
Maximum Lethality of Attempt	--	--	--	1.9 ± 1.2	5.3 ± 1.2	<0.001 LL < HL
Suicide Intent Scale, Most Recent Attempt	--	--	--	14.3 ± 5.0	19.2 ± 4.7	<0.001 LL < HL
Suicide Intent Scale, Most Lethal Attempt	--	--	--	14.4 ± 5.0	20.0 ± 5.0	<0.001 LL < HL
Violent Attempt (Most Lethal)				23.4% (15)	9.7% (3)	0.11
Time since most recent attempt (months)				[median=8.9]	[median=8.9]	
Sex (% Female)		48.8% (41)	60.5% (69)	57.8% (37)	61.3% (19)	0.38
Axis I Diagnosis:	--					
% Unipolar			76.3% (87)	64.1% (41)	38.7% (12)	<0.001 NA, LL < HL
% Bipolar			23.7% (27)	35.9% (23)	61.3% (19)	
Axis II Diagnosis (% Borderline PD)			11.0% (12)	32.8% (21)	35.5% (11)	<0.001 NA < LL, HL

Variable p-value ^{<i>I</i>}	Contrast	Non-Patient Comparison	Depressed Non-Attempters	Low Lethality Attempters	High Lethality Attempters
Past Substance Abuse/Dependence	--	25.7% (29)	32.8% (21)	48.4% (15)	0.05 NA < HL
Post Traumatic Stress Disorder (Lifetime)		20.2% (23)	26.6% (17)	38.7% (12)	0.10

^{*I*} Omnibus ANOVA for continuous variables, chi-squared for categorical variables.

Table 2

Neuropsychological Performance Measures

<u>Variable p-value</u> ^I	<u>Contrast</u>	<u>Non-Patient Comparison</u>	<u>Depressed Non-Attempters</u>	<u>Low Lethality Attempters</u>	<u>High Lethality Attempters</u>
<u>Object Alternation</u>					
Completed to Criterion (%) ^I	70.2% (59)	57.9% (66)	57.8% (37)	80.6% (25)	0.04 C, HL > NA, LL
Errors ^I	0.01 ± 1.22 (42.0 ± 37.7)	-0.42 ± 1.14 (55.4 ± 35.2)	-0.39 ± 1.21 (54.5 ± 37.3)	0.16 ± 1.04 (37.7 ± 32.3)	0.01 C, HL > NA, LL
Percent Error (%)	0.26 ± 1.33 (37.2 ± 14.7)	-0.18 ± 1.10 (42.1 ± 12.2)	-0.16 ± 1.20 (41.9 ± 13.3)	0.17 ± 1.11 (38.2 ± 12.3)	0.04 C, HL > NA
Perseverative Errors	-0.11 ± 1.36 (20.7 ± 19.9)	-0.54 ± 1.26 (26.9 ± 18.4)	-0.52 ± 1.37 (26.6 ± 20.0)	0.06 ± 1.19 (18.2 ± 17.4)	0.03 C, HL > NA; HL > LL
Non-Perseverative Errors	0.11 ± 1.11 (21.4 ± 19.5)	-0.29 ± 1.06 (28.5 ± 18.6)	-0.25 ± 1.15 (27.8 ± 20.2)	0.22 ± 0.88 (19.5 ± 15.4)	0.01 C, HL > NA, LL
Failure to Maintain Set	0.06 ± 1.06 (1.3 ± 1.5)	-0.46 ± 1.43 (2.0 ± 2.0)	-0.46 ± 1.55 (2.0 ± 2.1)	0.28 ± 1.12 (1.0 ± 1.5)	0.004 C, HL > NA, LL
<u>Wisconsin Card Sort</u>					
Categories	-0.37 ± 0.74 (5.2 ± 1.6)	-0.34 ± 0.70 (5.3 ± 1.3)	-0.53 ± 0.84 (5.0 ± 1.7)	-0.14 ± 0.44 (5.7 ± 0.8)	0.10
Errors	-0.24 ± 1.09 (23.8 ± 20.0)	-0.29 ± 0.99 (23.1 ± 18.5)	-0.57 ± 1.15 (29.2 ± 21.6)	-0.10 ± 0.79 (19.5 ± 15.7)	0.13
Percent Error (%)	-0.22 ± 1.06 (22.3 ± 13.3)	-0.25 ± 0.96 (22.1 ± 12.6)	-0.54 ± 1.11 (26.7 ± 15.1)	-0.17 ± 0.84 (19.4 ± 10.5)	0.19
Perseverative Errors	-0.26 ± 1.26 (12.6 ± 10.8)	-0.36 ± 1.06 (12.7 ± 10.8)	-0.55 ± 1.31 (15.7 ± 12.8)	-0.15 ± 0.90 (10.2 ± 8.4)	0.37
Non-Perseverative Errors	-0.17 ± 1.06 (11.2 ± 10.6)	-0.20 ± 0.89 (10.4 ± 9.2)	-0.46 ± 0.96 (13.5 ± 10.9)	-0.11 ± 0.86 (9.3 ± 8.2)	0.22
Failure to Maintain Set	-0.16 ± 0.51 (0.6 ± 1.1)	-0.34 ± 0.69 (0.8 ± 1.2)	-0.34 ± 0.67 (0.8 ± 1.1)	-0.16 ± 0.52 (0.4 ± 0.9)	0.14
<u>Other Comparison Tasks</u>					
<u>Stroop</u>					
Interference (%)	0.07 ± 0.92 (24.9 ± 14.2)	-0.07 ± 1.27 (33.6 ± 22.0)	-0.41 ± 1.47 (36.3 ± 24.4)	-0.51 ± 1.19 (39.3 ± 23.1)	0.03 C > LL, HL
<u>Buschke SRT</u>					
Total Recall	0.08 ± 1.11 (126.6 ± 13.2)	-0.14 ± 1.36 (122.6 ± 16.5)	-0.47 ± 1.25 (120.0 ± 14.3)	-0.74 ± 1.43 (116.9 ± 15.7)	0.005 C > LL, HL; NA > HL

^I All continuous scores reported as normatively-corrected Z-scores. Raw scores are presented for each variable in parentheses.

Table 3

Object Alternation Criterion Attainment: Associations with Performance on Other Neuropsychological Tests

	Object Alternation Performance		
	Not to Criterion ¹	Complete to Criterion ¹	p-value ²
<u>Wisconsin Card Sort</u>			
Categories	-0.50 ± 0.81 (4.9 ± 1.7)	-0.30 ± 0.67 (5.4 ± 1.3)	0.03 *
Errors	-0.51 ± 1.14 (28.0 ± 21.5)	-0.21 ± 0.97 (22.3 ± 18.1)	0.02 *
Percent Error (%)	-0.46 ± 1.10 (25.6 ± 14.8)	-0.20 ± 0.96 (21.3 ± 12.2)	0.04 *
Perseverative Errors	-0.58 ± 1.23 (15.6 ± 13.0)	-0.22 ± 1.11 (11.7 ± 9.7)	0.01 *
Non-Perseverative Errors	-0.36 ± 1.00 (12.4 ± 10.3)	-0.17 ± 0.92 (10.6 ± 9.7)	0.10
Failure to Maintain Set	-0.38 ± 0.72 (0.8 ± 1.3)	-0.21 ± 0.56 (0.6 ± 1.0)	0.03 *
<u>Other Comparison Tasks</u>			
Stroop Interference (%)	-0.10 ± 1.14 (0.33 ± 0.21)	-0.18 ± 1.28 (0.32 ± 0.21)	0.57
Buschke SRT Total Recall	-0.49 ± 1.41 (119.4 ± 16.6)	-0.07 ± 1.22 (124.2 ± 14.5)	0.008 *
<u>Other Measures Linked to VPFC Function</u>			
Go-No Go Commission Errors (Ln transformed)	-0.49 ± 0.92 (2.10 ± 0.69)	-0.11 ± 0.89 (1.84 ± 0.67)	0.003 *
(Raw Go-No Go Commission Errors)	(9.2 ± 6.9)	(6.6 ± 5.0)	0.002 *
Iowa Gambling Test (IGT) Net Score	-0.60 ± 1.03 (3.7 ± 30.1)	-0.23 ± 0.83 (14.7 ± 25.1)	0.046 *
<u>Estimated IQ</u>			
WAIS-III Vocabulary Subtest (Scaled Score only)	13.5 ± 2.9	13.8 ± 2.8	.27

¹ All scores reported as normatively-corrected Z-scores (except WAIS-III Vocabulary). Raw scores are presented for each variable in parentheses.

² t-test for continuous variables

* p .05