**NEUROCOGNITIVE MEASURES OF PSYCHIATRIC PATIENTS DURING ACUTE ILLNESS**

by

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**ABSTRACT**

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Suicide is the tenth leading cause of death in the United States. Thus, identifying objective measures that predict suicidal behaviors is important. While examining decision-making, executive function, and learning and memory, previous research has found impairment in populations at risk for suicidal behavior. However, decision-making in response to stress in a population at risk for suicidal behavior has not been explored. In this study, we examine these neurocognitive measures in a sample of young adult psychiatric inpatients at the time of psychiatric hospitalization.

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The sample consists of psychiatric inpatients (n=13) and healthy controls (n=8). Participants completed the Cups Gambling Task (CGT) under neutral and stressful conditions, wherein the stressor was high frequency white noise played randomly in 12 of 45 trials. Participants also completed four tasks from the CANTAB suite: Motor Screening (MOT), One Touch Stockings of Cambridge (OTS), Stop Signal Task (SST), and Spatial Working Memory (SWM). T-tests were performed to examine differences on all outcome variables, and mixed models were performed on CGT variables. Effect size (ES) was calculated using Cohen’s d for all comparisons.

Inpatients chose fewer correct options on CGT for both the neutral (d=0.609, t(19)=1.17) and stressful (d=0.614, t(19)=1.37) conditions compared to controls. There were no differences in the total reward in the neutral condition (d=0.041, t(19)=0.091), however inpatients earned more in the stressful condition (d=0.458, t(19)=1.02) compared to controls. Mixed models showed that this increase was not significant with low ES (d=0.164). However, reaction time decreased between the neutral and stressful conditions (d=0.988 β=-391.84). Inpatient and control groups showed no difference in MOT ‘mean error’ (d=0.008, t(19)=0.986). Inpatients had greater ‘mean choices to correct’ (d=1.39, t(19)=3.71) compared to controls. There were no differences in SST ‘Delay 50%’ between patients and controls (d=0.199, t(19)=0.368). On SWM, inpatients had a greater ‘strategy score’ (d=1.32, t(19)=2.95) compared to controls.

Public Health Importance: Psychiatric inpatients at the time of acute illness showed poorer performance on behavioral tasks indicating decision making, spatial planning, and spatial working memory. Both inpatients and controls showed more impulsivity in decision-making under stressful conditions. Future studies are needed to examine these behavioral measures in a larger sample.

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# Introduction

## Epidemiology

Suicide is the 10th leading cause of death in the United States ([CDC, 2016](#_ENREF_1)). From 1999 to 2016 the suicide rate has increased by 3.4 per 100,000. Among males the per 100,000 rate increased from 17.1 to 21.8, or 27.%, from 1999. The female rate has risen from 4.0 to 6.2 per 100,000, a 55% increase ([CDC, 2017](#_ENREF_2" \o "CDC, 2017 #78)).

In 10-year age groups, the 5-14 year-old group has consistently had the lowest rate of any ten year category, but since 1999 the rate of suicide in this youth category has nearly doubled from 0.6 per 100,000 to 1.1 per 100,00. In the 10-year age groups, 5-14 has the largest percent increase from 1999 followed by 55-64, 53.3%, and 45-54, 41.7%. In terms of highest rate there have been major changes since 1999. The top three age ranges in ’99 were 85+, 75-84, and 35-44 and in 2016 the top three were 45-54, 85+, and 55-64. This increase in suicide among younger age groups can be seen fully in Figure 1 below.

These data are indicating that, now, much younger people are killing themselves. As suicide becomes more prevalent in younger people, it becomes more burdensome on society. While premature death is a tragedy at any age, we tend to consider the loss of a younger person to be costlier. To quantify the problem, studies have been done on the financial burden of suicide. One such study from 2016 estimated that, in 2013, the direct medical and indirect economic costs of suicide were over $53 billion ([Shepard, Gurewich, Lwin, Reed, & Silverman](#_ENREF_14)). From 2013 to 2016, the suicide rate increased by 0.9 per 100,000 which continues to drive the economic burden.



Figure 1. Suicide death rate per 100,000 among all 10-year age groups between the years 1999 and 2016 in the United States, data from CDC Wonder

## High Risk Groups

A meta-analysis done by Harris and Barraclough in 1997 shows data of six studies from the United States, the United Kingdom, and Sweden that show among all treatment group s and all psychiatric diagnoses there were 11.52 times as many deaths observed than expected by population standard. These elevated rates of suicide among individuals with history of mental illness is especially concerning as they are already a highly vulnerable population. A study done by Hjorthøj et al in 2013 shows that, in a Danish sample, the rate ratio (RR) of suicide increases at every level of psychiatric treatment. When the referent group is set as ‘No psychiatric treatment’, ‘Psychiatric medication only’ has a RR of 7.85, ‘At most outpatient treatment’ has a RR of 15.73 and ‘Psychiatric hospitalization’ has a RR of 94.40.

## predictors of suicide

According to a 2017 meta-analysis the self-report predictors of suicide death are not very effective at predicting suicide (FRANKLIN ET AL). These typical subjective predictors have not been satisfactory, in fact the over the last 50 years suicide prediction has not been improved despite much effort (FRANKLIN ET AL). Subjective predictors must be replaced with new predictive techniques and methods. Machine learning is one novel method used to predict suicide ideation (RYU ET AL). In their sample from the Korea National Health & Nutrition Examination Survey, Ryu et al. found that machine learning could predict suicide ideators with an accuracy of 82.1% using 15 variables in the model. This type of modeling, involving many factors becomes cumbersome. Neurocognitive measures are used in psychiatric study when participant self-report is not subjective enough and prone to biases, as is the situation with the topic of suicide. Neurocognitive measures are specific, objective, and they can be measured quickly using behavioral tasks. This makes these measures the best tool in solving the issue of subjectivity in predictive suicide research.

The neurocognitive measures that will be focused on here are in the domains of decision-making (DM) and executive function (EF). DM is the cognitive process resulting in one course of action chosen from a set of possible actions. EF can be defined as the self-management and control that an individual has over their working memory, cognitive flexibility, and inhibition. Deficits in DM and EF can greatly impair an individual’s daily functioning
(CITATION). Such deficits are seen in many common psychiatric diagnoses which are understood to have increased risk for suicide, such as bipolar disorder (Standardized Mortality Ratio = 1505), schizophrenia (SMR = 845), personality disorders (SMR = 708), and depression (SMR = 2035) (HARRIS AND BARRACLOUGH).

Given that psychiatric disorders with increased risk of suicide coincide with those that have impairments in these domains then the measure of DM and EF deficits may be an objective predictor of suicide regardless of diagnosis. DM is further complicated by the life stressors that occur when individuals are considering their decisions. Acute stress has been shown to have negative effects on DM including riskier, more disadvantageous choices (STARCKE ET AL).

## Literature Review

The literature review was conducted using the search terms “Executive Function” AND (Suicide OR Suicidal OR Suicidality) on Pubmed in October 2018. When articles were limited to full text available and human subjects, there were 74 results. The abstracts were read to limit studies to only those evaluating EF and DM in relation to suicide. There were 39 articles excluded for the following reasons: EF and DM or suicide included but not both (28), Drug study (4), Review paper (6), Case Study (1)

 Of the remaining 35 articles, six examined suicide in the context of major depressive disorder, five in schizophrenia, two each in bipolar disorder, traumatic brain injury, and epilepsy as well as one each in borderline personality disorder and dementia. The remaining 16 were in the contexts of multiple or non-specified disorders. These articles measured EF and DM after the onset of suicidality. These results can detail how the participants with suicidality are different from those participants without, they cannot describe if differences in EF are present prior to an attempt or if they are the result of an attempt.

 In general, the studies showed that DM and EF impairments are prominent among suicidal populations. Studies used a mix of interview measures and behavioral tasks to evaluate DM and EF. The Executive interview and brief psychiatric rating scale are among the scales used in evaluating DM and EF in these studies. The most common behavioral tasks are the Iowa Gambling Task, the Wisconsin Card Sorting Task, and the Stroop suicide task. Two studies used tasks from Cambridge cognition. There is not a consensus of the methods used to analyze DM and EF in the study of suicide.

There were four studies that indicated no relationship between EF and suicide ([Brenner et al., 2015](#_ENREF_1); [Glenn & Nock, 2014](#_ENREF_6); [Huber et al., 2012](#_ENREF_7); [Kasckow, Liu, & Phillips, 2012](#_ENREF_8); [McGirr et al., 2010](#_ENREF_12)), as well as two studies that indicated better EF in a suicide population ([Kim, Jayathilake, & Meltzer, 2003](#_ENREF_9); [Nangle et al., 2006](#_ENREF_13)). Both of those studies were in a population of individuals with psychotic disorders, which could indicate that there is a unique relationship between EF and suicidality in those individuals as compared to participants with mood disorders.

With these varying results in the relationship between DM and EF and suicidality, more research needs to be done with more diverse measures. Of all the studies, four of them tested psychiatric patients ([Dombrovski et al., 2008](#_ENREF_3); [Garcia Espinosa et al., 2010](#_ENREF_4); [Gilbert et al., 2011](#_ENREF_5); [Huber et al., 2012](#_ENREF_7)) and the remainder tested individuals who had history of mental illness and or suicidal behaviors. Further study needs to be done on individuals at time of hospitalization, rather than individuals with mental health history, since it is known that hospitalization is a vulnerable time.

 Another gap in the literature is that suicide studies are not done prospectively. There is an opportunity to study suicide before the attempt and or death happens. Psychiatric inpatients coming out of hospitalization are at highly elevated risk 12 months after discharge, which presents the question of how those people are objectively different from those that do not spend time in a psychiatric hospital. To understand the patient before and after suicide attempt could be beneficial to further prevention efforts.

 These studies also mostly do not examine stress in the context of DM and EF. One study examined functioning using a stress paradigm ([McGirr et al., 2010](#_ENREF_12)). McGirr et al. implemented the trier social stress test (TSST) to induce stress in their participants and DM and EF tests were administered before and after the TSST to observe how individuals at increased risk of suicide compared to controls. DM at time of stress needs to be better understood as DM in daily life is often within the context of stress.

## Public health significance

In the effort to stop the increase in suicide that the United States has experienced since 1999, predicting suicide accurately is becoming more pressing. The current suicide prediction measures are not working well enough and novel objective predictors are needed to establish suicide risk before the attempt. Neurocognitive deficits have been measured in individuals with all manner of mental illness, but there has not yet been a focus on all psychiatric inpatients regardless of primary diagnosis, even though this is proven to be a high suicide prevalence group.

# Objectives

The current study is designed to learn greater detail about the objective neurocognitive basis by which psychiatric inpatients and psychiatrically healthy controls differ. This will add to the existing literature which shows that individuals who have been hospitalized for psychiatric illness are at greater risk of dying from suicide compared to psychiatrically healthy counterparts and hopefully start in establishing what objective measures can be taken to assess suicide risk in a predictive fashion rather than the inconsistent self-report measures or individual history of suicidal ideation, thoughts, and behaviors that currently predict future suicide attempt. By being able to accurately assess future suicide risk, it may be easier to finally reverse the trend of increased suicide prevalence in the United States. Psychiatric inpatients will exhibit deficits in the major domains of DM and EF, particularly increased risky DM behaviors and reduced response inhibition, spatial planning and spatial memory when compared to psychiatrically healthy controls. Inpatient participants will also exhibit a more severe impairment in DM in the context of stress indicated by lower correct decisions.

# MEthods

Thirteen inpatients were recruited from Western Psychiatric Hospital. Patients heard about this study through their treatment teams and physicians after they were medically stable. To be recruited, patients had to be in their first hospitalization of the recruitment frame, January – April 2018. This means that if they were hospitalized twice in that window, and were missed for recruitment the first time, they would not be eligible the second. Patients had to be 18 years old and stable to participate in the study.

Eight control participants were recruited through the University of Pittsburgh Clinical and Translational Science Institute Research Participant Registry. The control participants were individuals with no prior personal history of psychiatric disorder and no family history of severe psychiatric illness, such as bipolar disorder or psychotic disorders. Controls also did not have a previous history of suicidal behavior, self-injury, and neither physical nor sexual abuse. Physical and sexual abuse were listed as exclusion criteria due to the biological testing that was conducted on the sample but was not used in the current study.

The study was approved by the institutional review board of the University of Pittsburgh and all participants provided written informed consent as well as compensated for their time.

In this study, participants were assessed only at baseline, which for inpatients was the time of their hospitalization. The participants were given five behavioral tasks to complete; the Cups Gambling Task (CGT) with a stressful and neutral condition; and four tasks from Cambridge Cognition’s Cambridge Neuropsychological Test Automated Battery (CANTAB). The CANTAB tasks have been used and published in a variety of research areas including schizophrenia, mood disorders, and cognition.

Levin’s CGT was created to assess risky DM in children ([Levin & Hart, 2003](#_ENREF_10)) and was later adapted to adults as well ([Levin, Hart, Weller, & Harshman, 2007](#_ENREF_11)). The CGT was administered on a laptop computer with headphones on during both the neutral and stressful conditions. The task requires the choice between taking a small guaranteed amount of money or a greater non-guaranteed amount of money. The non-guaranteed dollar amount is under one of multiple cups on the right side of the screen; the guaranteed amount of money under one cup on the left side of the screen. A countdown from three precedes each trial and the options are presented. In each trial of the task, there is a correct and incorrect answer dependent on the ratio of dollars to cups on each side of the screen. Each participant goes through 45 trials of each condition. The participants received 10% of the total money they earned during the task, up to $20. The stressful condition was administered with a high frequency white noise played through the headphones in 12 of the 45 trials. The total number of correct, total reward, and reaction time were the outcomes analyzed for each condition.

The four CANTAB tasks administered were the Motor Screening Task (MOT), One Touch Stockings of Cambridge (OTS), Stop Signal Task (SST), and Spatial Working Memory (SWM). These tasks were completed in the order presented above on an iPad.

The MOT is an introduction to the platform that the tasks are performed on. The task consists of colored crosses appearing on the screen which the participant must tap as quickly and accurately as possible. The task indicates sensorimotor or comprehension deficits which would otherwise invalidate data from the next tasks. The outcomes of this task are median and mean latency to selection, and mean error.

The OTS is a spatial planning test given to assess spatial planning and working memory. The task requires participants to select the number of moves it would take to make one set of balls in stockings look like a second set of stockings on the screen, moving one ball at a time. The participants choose the number from a multiple choice set along the bottom. To orient to the task, the participants tap the balls to move them in the first trial. Subsequently, the movements are done entirely in the participants’ head. The output variables of this task are mean choices to correct, mean latency to correct, and first choice correct.

The SST is a response inhibition test that measures an individual’s impulse control. The participants are required to tap the screen on whichever side an arrow points when it appears, unless the stop signal sounds, in which case the participant does not tap the screen. The trials are grouped into blocks of 16 with 12 go trials and 4 stop trials in each. This task yields reaction time (RT), mean correct RT on go, median correct RT on go, direction errors, proportion correct stops, and delay 50%. The delay 50% is the average delay time between arrow and stop signal at which the participants could stop from touching the screen.

The final task is SWM, which measures working memory. The test starts with a set of boxes on a screen. The participants must go through the set of boxes, by touching each, to find a token using process of elimination. Whenever a token is found, the participant starts the search again, looking for the next token until a token is found under every box in the set. Each token will be found under a different box so tapping a box whose token has already been found is considered an error. The task outcomes are mean error and strategy score. Strategy score increases when a participant alters their search pattern, a lower strategy score indicates a more reasoned approach to finding tokens.

All statistics were run in STATA 15 SE, licensed by the University of Pittsburgh, T-tests were used to analyze the CGT outputs for each condition between groups as well as a mixed regression to analyze effects of condition, group, and the interaction term condition x group on each outcome variable. CANTAB outcome variables were evaluated using t-tests. Effect size (ES) was calculated for all measures using Cohen’s d. For all ES calculation interpretation, the threshold for large is set at 0.80 and moderate at 0.40, any ES less than 0.40 was defined as small. Due to low sample size, significant differences are not expected except with large effect sizes.

# Results

Inpatient group mean age was 24.51, 6 of 13 were male and the most common psychiatric diagnoses in the sample were Depressive Disorders, Substance Use Disorder, and Stress Disorders. Control group mean age was 23.33, 3 of 8 were male and no member of the control group met for diagnosis of a psychiatric disorder. All diagnosis information can be seen in Table 1 below.

Table 1. Demographic and Diagnosis data by group

|  |  |  |
| --- | --- | --- |
|  | Control Group | Inpatient Group |
| N | 8 | 13 |
| Age – Mean (SD) | 23.33 (3.07) | 24.51 (4.46) |
| Male (%) | 3 (37.5) | 6 (46.2) |
| Bipolar Disorder | 0 | 2 |
| Depressive Disorder | 0 | 8 |
| Psychotic Disorder | 0 | 1 |
| Alcohol Use Disorder | 0 | 4 |
| Substance Use Disorder | 0 | 7 |
| Anxiety Disorder | 0 | 4 |
| Obsessive-Compulsive Disorder | 0 | 2 |
| Eating Disorder | 0 | 2 |
| Attention Deficit Hyperactive Disorder | 0 | 2 |
| Stress Disorder | 0 | 8 |

On the CGT, control participants made more total correct choices than inpatients in both the neutral condition (d = 0.609) and stressful condition (d = 0.614) (Table 2). The total reward was not different between groups in the neutral condition. In the stressful condition, the inpatients were earning a greater reward (d = 0.458). For both the neutral and stressful condition, differences in reaction time were small and not significant between inpatient and control groups. Inpatients were choosing the correct set of cups less often but made more money in the stressful condition.

We did further analysis on the CGT using mixed regression to show the levels of change between groups, between conditions, and in an interaction term (Table 3). Between conditions, there was a decrease in reaction time (d = 0.988). The differences in total correct and total reward were both not significant between the neutral and stressful condition. The total correct was less for inpatients vs. controls (d = 0.453), which confirms the result of the t-tests in the previous analysis. The total reward and reaction time both had non-significant differences between groups in the regression analysis. In the interaction term, the differences were not significant for total reward, total correct, and reaction time. These are concordant with the t-test results.

In the MOT, the inpatients had a longer mean (d = 0.719) and median (d = 0.643) latency to selection than controls. The mean error in this task was not different between each group. For the OTS, controls had lower mean choices to correct (d = 1.39, p = 0.002), a shorter latency to correct (d = 0.778), and a higher number of first choice correct (d = 1.3, p = 0.009) (Table 2).

On the SST, inpatients had a slower overall reaction time (d = 0.477) and mean correct reaction on go trials (d = 0.481), and a greater number of direction errors (d = 0.455). The inpatients’ proportion of correct stops was not different from controls. In the SWM task, the inpatients had more total errors (d = 1.17, p = 0.017) and a less successful strategy score (d = 1.3, p = 0.008) (Table 2).

Table 2 Results of two tailed T Tests for behavioral tasks performed by Control and Inpatient subjects

|  |
| --- |
|  |
|   | Measure  | Control (n=8) Mean (SD)  | Inpatient (n=13) Mean (SD) | T-Test df = 19 | p  | Effect Size Cohen's D |
|
|  **Cups Task Neutral Condition**  | Total Correct | 22 (9.89)  | 17.53 (5.29) | 1.17 | 0.268 | **0.609** |
| Total Reward | 80.5 (14.48) | 81.07 (13.89) | -0.091 | 0.929 | 0.041 |
| Reaction Time | 1807.72 (497.78) | 1701.24 (1025.76) | 0.273 | 0.788 | 0.122 |
|  **Cups Task Stress Condition**  | Total Correct | 24.25 (8.78) | 19.08 (8.21) | 1.37 | 0.188 | **0.614** |
| Total Reward | 86.5 (10.21) | 92.38 (14.15) | 1.0198 | 0.3206 | **0.458** |
| Reaction Time  | 1415.874 (551.67) | 1271.84 (668.66) | 0.51 | 0.616 | 0.229 |
| **One Touch Stockings of Cambridge** | Mean Choices to Correct | 1.05 (0.09) | 1.30 (0.22) | -3.71 | **0.002** | **1.39** |
| Mean Latency to Correct | 7835.39 ( 2660.65)  | 9638.39 (2092.108) | -1.73 | 0.099 | **0.778** |
| 1st Choice Correct | 19 (1.77)  | 15.85 (2.73)  | 2.89 | **0.009** | **1.3** |
| **Motor Screening**  | Mean Latency | 647.14 (88.82) | 733.07 (134.04) | -1.6 | 0.126 | **0.719** |
| Median Latency | 598.13 (117.20) | 689.23 (154.05)  | -1.43 | 0.168 | **0.643** |
| Mean Error | 9.71 (3.52) | 9.69 (3.01) | 0.0176 | 0.986 | 0.008 |
| **Stop Signal Task** | Delay 50%†  | 337.76 (241.25) | 370.5 (92.38) | -0.368 | 0.772 | 0.199 |
| Reaction Time  | 163.99 (45.49) | 181.73 (31.25) | -1.06 | 0.301 | **0.477** |
| Mean Correct RT on GO | 519.817 (203.15) | 771.76 (640.46) | -1.07 | 0.298 | **0.481** |
| Median Correct RT on Go | 501.75 (219.96) | 552.23(102.26) | -0.719 | 0.481 | 0.323 |
| Direction Errors | 1 (1.41) | 1.77 (1.83) | -1.0125 | 0.324 | **0.455** |
| Proportion Correct Stops | 0.538 (.195) | 0.5 (0.141) | 0.512 | 0.615 | 0.23 |
| **Spatial Working Memory** | Total Errors | 3.75 (6.25) | 13.38 (9.18)  | -2.61 | **0.017** | **1.17** |
| Strategy Score‡ | 12.375 (3.11) | 16.85 (3.1) | -2.95 | **0.008** | **1.32** |
| †The stop signal delay at which the subject was able to stop 50% of the time (lower is better)  |
| ‡The number of times a participant changes their search pattern (lower is better)  |
| significant p values (< 0.05) and moderate effect sizes ( >0.40) have been bolded  |

Table 3 Mixed Linear Regression of Condition and Inpatient status on behavioral tasks

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|   | Condition β (95% CI) p | Effect Size Cohen's d  | Inpatient β (95% CI) p | Effect Size Cohen's d  | ConditionxInpatient β (95% CI) p | Effect Size Cohen's d  |
|
|
| Total Correct | 2.25 (-1.55, 6.05) 0.246 | 0.364 | -4.46 (-10.59, 1.67) 0.154 | **0.4525** | -.711 (-5.54, 4.11) 0.773 | 0.089 |
|
| Total Reward | 6 (-9.38, 21.38) 0.444 | 0.236 | 0.58 (-11.25, 12.40) 0.924  | 0.031 | 5.30 (-14.24, 24.85) 0.595 | 0.164 |
|
| Reaction Tim*e* | **-391.84 (-659.80, -123.88) 0.004** | **0.988** | -106.48 (-834.79, 621.83) 0.774  | 0.089 | -37.55 (-378.12, 303.02) 0.829 | 0.068 |
|
| significant p values (< 0.05) and moderate effect sizes ( >0.40) have been bolded  |  |

# Discussion

These results indicate the neurocognitive differences between psychiatric inpatients and psychiatrically healthy controls. Inpatients at time of acute illness showed poorer performance on behavioral tasks within domains of DM and EF including risk in DM, spatial planning, and spatial working memory. These results indicate that individuals at time of acute illness are impaired in their ability to function at a level typical of psychiatrically healthy individuals.

Inpatients and controls both showed greater impulsivity of decision making under the stressful condition of the CGT in comparison to the neutral condition. This increase reaction time can be considered a learning effect, but the total reward does not increase between conditions to a meaningful degree.

The inpatients had greater reward than controls in the CGT even though they had fewer correct decisions. The risky decision making of the inpatients in this sample was resulting in larger reward at the end of the task, which is unexpected.

There were two CANTAB tasks each with two significant output variables, the OTS and SWM. These measures were OTS mean choices, OTS 1st choice correct, SWM total errors, and SWM strategy score. These results are highly statistically significant even with low sample size, so it can be said that the inpatient group’s spatial memory and spatial planning are impaired compared to the control group.

Validated, common behavioral tasks were used to get the most accurate and comparable data possible. The study is novel in the assessment of psychiatric inpatients and their stress response in time of psychiatric crisis. The use of a stressor in the CGT is better able to simulate the real-life situations in which people are forced to make difficult decisions under increased pressure. The sample size of the study is small, and the population is very young which reduces the overall generalizability of the findings.

The future research should focus on obtaining a larger sample size and a more representative sample of the age groups that are most represented in suicide statistics. Future research following inpatients from time of hospitalization through the first year after could give greater understanding of the DM and EF changes that happen within the 12 months following a hospitalization which have proven to be so prone to suicide.

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