A Little Bit About Me:

For the past two years, I have been conducting research with the Aftercare Research Program at UCLA's Semel Institute for Neuroscience and Human Behavior. This program involves treatment and research for patients with schizophrenia, specifically focusing on improving cognitive functioning. Research has been such a significant part of my UCLA experience, and it was very important to me that my capstone project reflected this. I wanted to use my research experience to ask the questions I was interested in, conduct the research, and do the data analysis to come to a conclusion. This capstone is the perfect culmination of my undergraduate experience and allowed me to focus on an incredibly fascinating and complex diagnosis: schizophrenia. Looking back on this experience, it is evident how much I have grown as a researcher and a writer.

The Honors Scholars program played a large role in my development as a student, researcher, and writer. As a freshman, UCLA's size and course selection was daunting. From the start, the Honors Scholars program gave me a community and the courage to embrace everything UCLA had to offer. I decided to become involved in research after taking HNRS:50, a course that pushed me to explore different opportunities at UCLA. Over COVID, this program gave me the structure and guidance I needed to confidently map out and succeed in my courses despite the atypical online course format. It also fostered my love of learning; the program encouraged me to take courses outside of my major requirements. I took courses I would have never considered taking and discovered a newfound appreciation for Neil Gaiman, modern art, and Daniel Yergin. I would not be the person I am today with this program.

I am incredibly grateful to the Honors Scholars program and my counselor Angel for his patience, guidance, and kindness. Angel is such a grounding force; I cannot accurately capture how lucky I feel to have had him in my corner throughout my entire UCLA experience.

Advised by Dr. Subtonik, Semel Institute for Neuroscience and Human Behavior

Schizophrenia, Symptoms, and Suicide

1. INTRODUCTION

With suicide rates among the general population steadily increasing, scientists and medical professionals have dedicated their research to addressing this public health crisis (CDC). Even more alarming are the suicide rates among patients diagnosed with mental illnesses like anxiety, depression, or schizophrenia. Historically, suicide has been heavily associated with mental disorders like depression and anxiety. A recent systemic review and meta-analysis revealed that suicide is more likely in patients with a major depressive disorder than in the general population (Cai 2021). Anxiety disorders are also associated with suicide (Nepo 2010). However, a 5-year study found that the highest rates of suicidality are among patients diagnosed with schizophrenia, higher than in patients with a primary diagnosis of anxiety or depression (Sartorius 1986).

Schizophrenia is a mental disorder characterized by an impaired grasp of reality (Insel 2010). Patients with schizophrenia have a higher level of suicidality risk compared to the general population (Sher 2019). Indeed, between 20-50% of schizophrenia patients attempt suicide in their lifetime with 10% of patients dying by suicide (Sher 2019).

Notably, suicidality in schizophrenia patients with comorbid diagnoses of depression and anxiety has been investigated. One study found that the majority of patients with schizophrenia examined were also diagnosed with anxiety disorders (Huppert & Smith 2005). This common comorbid diagnosis is particularly important as patients diagnosed with both an anxiety disorder and a mood disorder, like schizophrenia, have a significantly higher suicidality risk than patients with only one diagnosis (Sareem et al. 2005). Regardless, patients with a comorbid or primary diagnosis of schizophrenia are at a higher risk of suicide.

Suicide can be understood as a spectrum, ranging from suicide ideation to suicide plan to suicide attempt to death by suicide (Bai 2021). While suicide ideation, suicide plan, and suicide attempt are all linked to a higher likelihood of death by suicide, there are distinct factors and motivations specific to every stage. Thus, the symptoms associated with each stage must be examined independently.

The continuum begins with suicide ideation, suicidal and morbid thoughts (Bai 2021). Suicide ideation is more common in patients with schizophrenia than in the general population; a meta-analysis and systematic review found that the prevalence of suicide ideation among people with schizophrenia is 29.9%, compared to 9.2% in the general population (Klonsky 2016) (Bai 2021).

The reasons behind suicide ideation are complex, and a systematic review found that severe psychiatric symptoms are risk factors for suicide ideation among people with schizophrenia (Bai 2021). A different systematic review identified a link between different psychiatric symptoms like depression and hallucinations and suicide ideation (Hor 2010). Multiple systematic reviews have reliably identified depressive symptoms in patients as predictors of suicide ideation (Bai 2021; Fang 2021). Moreover, a separate one-week study using experiential sampling found that while depressive symptoms did predict suicide ideation in patients with psychosis, feelings of anxiety, guilt, and hostility did not predict suicide ideation (Palmier-Claus 2013). Indeed, the link between positive symptoms and the increased likelihood of suicide ideation is not clear. Although one study found that there was no significant connection between positive symptoms and suicide ideation among 120 patients with schizophrenia, there are multiple studies that have found that positive symptoms are linked to suicide ideation (Hocaoglu 2009; Nath; Andriopoulos et al. 2010). Moreover, one study examined the severity of guilt feelings upon hospital admission over the course of 15 days and found that guilt feelings predicted suicide ideation (Kontaxakis 2004). A cross-sectional study also found that both guilt and hallucinations were related to a 6% increase in the likelihood of experiencing suicide ideation (Grover 2022). Also, one study examined the link between unusual thought content and suicide ideation in 110 patients with schizophrenia over the course of a month, finding that unusual thoughts contributed to the presence and intensity of suicide ideation (Freeman et al. 2019). Although the amount of literature focusing on suicide ideation in patients with schizophrenia is increasing, it still pales in comparison to the volume of research focusing on suicide attempts.

The likelihood that a patient attempts suicide after experiencing suicide ideation is not fully understood. This is clearly demonstrated in the findings of a meta-analysis conducted by Chapman et al. 2014. Overall, the meta-analysis determined an odds ratio of 6.49, indicating that a patient with schizophrenia and suicide ideation was 6.49x more likely to attempt suicide than patients without suicide ideation (Chapman et al. 2014). However, the studies examined in the meta-analysis had a wide range of results; one cohort study in Denmark determined an odds ratio as low as 0.55 compared to a high ratio of 81 in a case-control study in Japan (Chapman 2014). Similarly, a meta-analysis determined a suicide attempt odds ratio of 5.8 for patients with schizophrenia and suicide ideation (Hubers et al. 2018).

Although neurotic symptoms like depression, anxiety, and guilt are commonly associated with suicide in nonpsychotic patients, there are a number of psychiatric symptoms related to a suicide attempt in patients with schizophrenia. There is evidence that hostility, anxiety, depression, guilt, unusual thought content, hallucinatory behavior, and emotional withdrawal are elevated in patients with schizophrenia experiencing suicidality (Drake et al. 1985); (Berardelli et al. 2021); (Palmier Claus 2013); (Weissman et al. 2006); (Vertriglio 2016).

Depressive symptoms are usually associated with suicide risk in patients with schizophrenia and mood disorders (Drake et al. 1985) (Kaschow 2011). One retrospective study focusing on the hospital records of 104 patients diagnosed with schizophrenia found that they were more likely than controls to attempt suicide when exhibiting depressive symptoms (Drake et al. 1985). Moreover, treatment of depressive symptoms using anti-depressants reduces suicide risk (Kaschow 2011). Furthermore, a systematic review and meta-analysis have shown

that suicide attempts are 2.11x more likely in patients experiencing psychosis and depression (Gournellis 2018). This symptom is particularly important to study as over 50% of patients who die by suicide also exhibited depressive symptoms just prior to death (Berardelli 2021).

Moreover, anxiety symptoms in patients with schizophrenia have also been connected to greater suicidality risk (Berardelli et al. 2021). With 65% of patients with schizophrenia also exhibiting anxiety symptoms, the relationship between anxiety symptoms and suicide deserves greater attention (Berardelli 2021). Patients with psychosis were also more likely to attempt suicide during periods of anxiety (Hocaoglu 2009).

The next neurotic symptom associated with suicidality is guilt. The conclusions of the research on guilt and suicidality are mixed. Although one cross-sectional analysis found that guilt had the strongest association with suicide attempts, a different study found that guilt was not associated with greater suicidality (Palmier-Claus 2013) (Grover 2022).

Although less research has been devoted to unusual thought content and hallucinatory behavior, there is still research that links these psychiatric symptoms with suicidality. Hostility or aggressive behavior is commonly associated with schizophrenia (Perlini 2018). One study identified hostility as a prominent symptom in people who attempted suicide, often with a history of hostile relationships (Weissman et al 2006). Moreover, elevated levels of lifetime suicide risk were linked to observed hostility during hospital admission for patients with schizophrenia (Pompili 2007). Additionally, a narrative review found that hallucinations and unusual thought content were both risk factors for suicide (Vertriglio 2016). A separate systematic review found that hallucinations and delusions increased suicidality risk (Hor 2010). Furthermore, a cross-sectional analysis found that positive symptoms were related to a 4% increase in the likelihood of a suicide attempt (Grover 2022).

It is important to note that the associations between positive symptoms and suicidality are controversial. Although Hor & Taylor 2010, Grover et al. 2022, and Vertriglio et al. 2016 found an association between positive symptoms like hallucinations and unusual thought content and suicidality, Hawton et al. 2005 had different conclusions, they did not find significant associations between positive symptoms and suicidality. In fact, Hawton et al. 2005 found that hallucinations decreased suicidality risk. Thus, researchers acknowledge that there is disagreement on the relationship between positive symptoms, specifically delusions and hallucinations, and suicidality (Hocaoglu 2009).

AIMS AND HYPOTHESIS:

Using our knowledge of past research on risk factors for suicide among patients with schizophrenia, we want to extend our understanding using data from participants in the Aftercare Research Program. The 24-item Expanded Brief Psychiatric Rating Scale (BPRS) was used to rate a wide array of psychiatric symptoms, including suicidality. These symptoms include guilt, anxiety, depression, hostility, unusual thought content, hallucinatory behavior, and emotional withdrawal (Overall & Gorham 1962). This will deepen our understanding of suicidality and provide a valuable resource for clinicians in the future.

Based on previous clinical findings in the literature, we predict that severe levels of guilt, anxiety, depression, hostility, unusual thought content, hallucinatory behavior, and emotional withdrawal will be associated with suicidality.

2. METHODS

2.1 Participants:

This study examined 82 patients recruited from Los Angeles psychiatric hospitals, practices, and clinics. All members of the study were enrolled in a psychiatric treatment program located at the UCLA Aftercare Research Program. The study participants were examined during the time period from March 16, 2005, to September 27, 2012. During their time at UCLA Aftercare, research participants normally attended 1 - 2 clinic visits per week. The UCLA Institutional Review Board approved this study with written informed consent from all participants.

2.2 Study Inclusion and Exclusion Criteria:

In order to be included in the study, all participants received a diagnosis of (1) a psychotic illness with the first major psychotic episode within the past 2 years, and (2) a diagnosis of DSM-IV of schizophrenia, schizoaffective disorder, depressed type, or schizophreniform disorder.

2.3 Measures:

2.3.1 Symptoms Assessment:

The Brief Psychiatric Rating Scale (BPRS) was used to assess different psychiatric symptoms among patients (Zanello et al, 2013). The BPRS measures 24 different symptoms and follows a numerical rating scale of one (not present) to seven (very severe). The BPRS was administered to patients every two weeks by a trained examiner. For the purposes of our study, the symptoms examined included: guilt, anxiety, depression, hostility, unusual thought content, hallucinatory behavior, emotional withdrawal, and suicidality.

Using a semi-structured interview, patients were rated by a trained BPRS administrator. A rating of 6 or 7 indicated high levels of symptomatology. For example, in evaluating suicidality, ratings of 6 or 7 indicated suicide severe ideation or suicide attempt. Moreover, a symptom was recorded whenever the patient had a rating of 6 or 7 within the six-month time frame, not necessarily at the same time they had a suicidality rating of 6 or 7. In this way, we were able to use cut-off scores to divide patients experiencing symptoms into two groups: "high" and "low/none".

2.3.2 Statistical/Correlational Analysis:

Chi-Square tests with p-values below 0.05 determined significance.

3. RESULTS

Symptom	Chi-Square Value (χ 2)	P-Value	Sensitivit y (%)	Specificit y (%)
Guilt	4.9	0.027	7.1	100.0
Anxiety	100	0.0002	21.4	98.5
Depression	25.9	< 0.001	35.7	100.0
Hostility	4.9	0.027	7.1	100.0
Unusual Thought				
Content	37.6	< 0.001	64.3	97.1
Hallucination s	10.8	0.001	67.1	91.2

	Low Suicide	High Suicide
Low Guilt	68	13
High Guilt	0	1

 $(\chi 2 (1) = 4.9, p = 0.3)$, Sensitivity = 7.1%, Specificity = 100.0%

	Low Suicide	High Suicide
Low Anxiety	67	11
High Anxiety	1	3

$$\chi 2 (1) = 10.0$$
, p = 0.0002, Sensitivity = 21.4%, Specificity = 98.5%

	Low Suicide	High Suicide
Low Depression	68	9
High Depression	0	5

$$\chi^2$$
 (1) = 25.9, p <0.001), Sensitivity = 35.7%, Specificity = 100.0%

Low	Suicide	High Suicide
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Low Hostility	68	13
High Hostility	0	1

 $(\chi 2 (1) = 4.9, p = 0.027)$, Sensitivity = 7.14%, Specificity = 100.0%

	Low Suicide	High Suicide
Low Unusual Thoughts	66	5
High Unusual Thoughts	2	9

 $(\chi 2 (1) = 37.6, p < 0.001)$, Sensitivity = 64.3%, Specificity = 97.1%

	Low Suicide	High Suicide
Low Hallucinations	62	8
High Hallucinations	6	6

$$(\chi 2 (1) = 10.8, p = 0.001)$$
, Sensitivity = 42.9%, Specificity = 97.2%

Out of the 82 patients, 14 (17.1 %) were rated as a 6 or 7 on suicidality on the BPRS. A 6 or a 7 indicates severe levels of suicidality. The remaining 68 (82.9%) of the 82 patients did not experience high levels of suicidality over the course of 6 months.

Looking at sensitivity, unusual thought content and hallucinations had the highest levels at 64.3% and 42.9%. All tests had very high specificity.

Notably, patients with a depression rating of 6 or 7 over the course of six months on the BPRS had a 36% risk of undergoing suicidal thoughts or attempting suicide. Additionally, three (21%) of the 14 patients who reported high levels of anxiety over the course of six months, also had a rating of 6 or 7 on suicidality.

4. DISCUSSION

The main goal of our study was to examine psychotic and neurotic symptoms in relation to suicidality. Although we found that typical predictors of suicide such as severe levels of anxiety, depression, and hostility were all independently associated with suicidality, the symptoms with the strongest relationships to suicidality were unusual thought content and hallucinations. Indeed, the usual neurotic predictors of suicide in the general population and individuals with an affective disorder were not as applicable to patients with schizophrenia. In

fact, researchers have acknowledged that the risk factors specific to schizophrenia are likely to be different than suicide risk factors in the general population (Hor & Taylor 2010).

We found a relationship between depressive symptoms and suicidality, which is consistent with the findings of Hor & Taylor 2010, Bai et al, 2021, Fang, Kaschow et al. 2011, Drake & Cotton 1986, Hawton et al. 2005, and Gournellis et al. 2018. However, we found that depressive symptoms were a weak predictor of suicidality. The weaker association between depression to suicidality could be explained by the results of a study conducted by Young et al. 1998. Their study tracked mood variability among 96 patients over the course of a year and found that although depression occurred concurrently with suicidality it was not a predictor of suicidality (Young et al, 1998). Thus, although our results also concur that depressive symptoms have a relationship with suicidality, it is a weak predictor.

Our findings on anxiety and suicidality lined up with some of the available literature by Berardelli et al 2021, Goodwin et al. 2002, and Hocaoglu & Babuc 2009, showing that high levels of anxiety and suicidality were related. However, although the relationship was highly significant, the sensitivity was weak. Research conducted by Palmier-Claus et al. 2014 and Young et al. 1998 found no connection between anxiety and suicidality in patients with schizophrenia. Indeed, neurotic symptoms like depression, anxiety, and guilt greatly impact mood variability and have a past history of being associated with deaths by suicide in the general population but the current findings suggest that they are not as relevant in the context of schizophrenia as severe psychotic symptoms (Peters et al 2018).

Interestingly, our results indicate a higher risk of suicidality when severe levels of psychotic symptoms like hallucinations and unusual thought content have occurred. These were the two key predictors with the highest sensitivity. These results make sense, as experiencing psychiatric symptoms, especially severe ones, can be very distressing for patients. Patients might feel that killing themselves is the only way to escape the hallucinations. Experiencing unusual thought content can contribute to a patient's mental instability and cause them to abandon medication treatment out of fear and panic (Pompili 2007). The subsequent panic and lack of medication adherence can contribute to future suicidality (Pompili 2007). In fact, a systematic review conducted by Hor & Taylor 2010 compiled the results of 10 studies examining psychotic symptoms and suicidality in patients with schizophrenia and found that unusual thought content and hallucinations were particularly associated with suicidality (Hor & Taylor 2010). Moreover, patients with command hallucinations may even be experiencing hallucinations that encourage the patient to attempt suicide. In a study examining 106 patients with schizophrenia, clinicians found that not only were command hallucinations often underreported but also played an important role in future suicide attempts, particularly for past patients that had previously attempted suicide (Zisook et al. 2005). This data adds clarity to the exploration of clinical predictors of suicide.

There were several other limitations to our study. Firstly, we categorized symptoms into "severe" and "not severe" which simplified the range of our findings. Additionally, the low base rate of some symptoms at the severe level made the calculation of sensitivity unreliable. Moreover, we did not examine correlations with a full range of symptoms, instead choosing to focus on each symptom individually. Next, the sample size was small for some categories; for

example, we only had one patient with high levels of guilt. This reduced the predictive power of symptoms with low base rates of severe levels. Another limitation of our study was the time frame. Our study did not investigate the temporal significance of our variables with suicidality and instead examined the association between suicidality and all symptoms within a 6-month time frame. However, our study closely parallels everyday clinical practice wherein patients are seen more infrequently. Our results are more generalizable to typical schizophrenia treatment. Lastly, past research has identified demographic characteristics like gender, age, occupation, and living situation as powerful predictors of suicide attempts (Sher and Kahn 2019). Another powerful predictor is previous suicide attempts and social factors like recent rejections (Sher and Kahn 2019). Our study did not include these factors. In the future, there is potential to incorporate these characteristics into our analysis. Moreover, it would be valuable to include medication adherence in future work to gain a larger understanding of preventative factors in suicide.

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