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Awareness of the Unaware: Anosognosia as a Comorbidity in Mental Health Conditions

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AWARENESS OF THE UNAWARE: ANSOGNOSIA AS A COMORBIDITY IN
MENTAL HEALTH CONDITIONS

by

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for the Honors in the Major Program in Nursing
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ABSTRACT

AWARENESS OF THE UNAWARE: ANOSOGNOSIA AS A COMORBIDITY IN MENTAL HEALTH CONDITIONS

Integrative Literature Review

The primary purpose of this integrative review of the literature is to describe healthcare provider's recognition of anosognosia in individuals with comorbid mental health disorders, as a differentiating diagnosis needing preeminent early intervention. The secondary purpose is to examine how anosognosia influences outcomes in the population of individuals with severe mental illness. It is expected that early recognition by clinicians and implementation of additional interventions to address anosognosia as the most influential comorbidity of schizophrenia, will decrease exacerbations and improve treatment and patient outcomes. A literature review exploring clinician's acknowledgement of anosognosia was performed using various databases. Search terms included: Anosognosia, Lack of Insight, Denial of Illness, and Schizophrenia. The data was conformed into tables and synthesized the relationships to identify consistent findings as well as gaps in the current literature. Initial review of the articles retrieved 73 articles relevant to the topic and 18 articles that met inclusion criteria. The studies suggest that mental health conditions with anosognosia have increased rates of adverse outcomes. Anosognosia is a difficult disorder to identify. While many studies have explored the biological basis of anosognosia, the studies performed on safety with mental illness fail to acknowledge anosognosia as a co-morbid condition. Evaluation and clinical guidelines remain inconsistent with research to support the need for recognition of this co-morbidity.

DEDICATIONS

I would like to thank everyone in my life that has pushed me and been there to support me through my darkest times.

To Dad, thank you for always motivating me to be the best version of myself, and raising me to always strive for something greater. I love you! You are my best friend, and my number one cheerleader, thank you for always being there for me.

To Lorri, you are a truly amazing person, thank you for your love and encouragement and for bringing me into your family. And to my Nanny, without you I'm not sure how my life would have turned out. Thank you for giving me my childhood.

Lastly,

To my Mother, not a day goes by that I don't miss you. Everything I do, is dedicated to you.

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INTRODUCTION

Anosognosia, or the literal translation “Without Disease Knowledge”, has commonly been referred to as a lack of insight into one’s disease. Anosognosia has been recognized in a broad range of health conditions such as dementia, hemiplegia, and Huntington’s Disease, but is considered one of the cardinal clinical manifestations found in, 60-81% of all persons diagnosed with schizophrenia (World Health Organization, 2020). In individuals with schizophrenia, anosognosia is one of the most prevalent and influential attributes leading to adverse and inconsistent treatment outcomes of schizophrenia, including: Noncompliance to medication adherence, remission of psychological symptoms, impaired community function, risk of violence to self and others, and increased frequency of involuntary commitment to an acute mental health facility.

In addition, the federal Healthcare Cost and Utilization Project, has found schizophrenia to be the third leading causes of hospital readmissions in the United States, only behind renal failure and ulcerative colitis (Fingar, K.R. et al., 2017). Anosognosia is a co-morbidity that carries heavy influence on the potential for positive outcomes in the treatment and management of schizophrenia, yet this complex construct has not been subjected to critical scrutiny or adequately addressed. Understanding the multifaceted phenomenon of anosognosia in the presence of related mental health conditions can improve the identification and treatment, and ultimate outcomes in quality of life, for people with anosognosia and co-morbid mental health conditions.

PROBLEM STATEMENT

Psychiatric diagnoses are typically descriptive and are subject to scrutiny based on the clinical manifestations of the condition. There is currently no singular blood test or brain scan that can confidently diagnose a mental illness. Psychiatric mental health clinicians perform a series of exams and look to the DSM-V for diagnostic categories and dimensions as a pathway of assessment for underlying psychological conditions. Anosognosia is listed as an adjuvant clinical manifestations of schizophrenia in the DSM-V, however, at present time there is not a standardized diagnostic screening or plan of treatment for individuals with anosognosia as a comorbid condition with schizophrenia. This makes it exceedingly difficult to manage individuals that have disbelief in the accuracy of their diagnosis or the day-to-day consequence associated with their illness.

The early detection of anosognosia and the pathological nature of the early stages of schizophrenia, are mainstay for reducing the duration of untreated psychosis. Reduction of the time an individual spends in a state of psychosis is exceptionally important because active psychosis is indicative of disease progression. Longer duration of untreated psychosis is associated with more severe symptoms when admitted to an acute care facility or mental health unit, poor prognosis, risk of violence, elevated risk for suicide, and more frequent relapses with involuntary commitment (Dell’Osso, Glick, Baldwin, & Altamura, 2013).

At present time, reducing psychosis for the majority of individuals can only be achieved with consistent drug therapy adherence. The concept of insight into an individual’s mental health condition is the leading predictor of medication adherence, and primary reason for discontinuation of antipsychotic medication (Zhou, Rosenheck, Mohamed, 2017). When individuals do not have acceptance or acknowledgement of their illness, they are less likely to

seek out care or pay for drug therapy. Challenges in the care of a person with anosognosia and a combined mental health disorders occur when the individual's preferences or beliefs, are at odds with the standard of care for their primary condition. Once correlations between anosognosia and poor treatment outcomes are established, clinician's will be better prepared to implement additional interventions to guide treatment adherence and improved physiologic and psychological outcomes for this group of individuals.

Anosognosia is a multifaceted phenomenon and planning for an appropriate treatment plan needs to take into account the individual's inability to recognize their illness, and failure to construct an adaptive narrative account of the challenges posed by having a psychiatric condition. An inability to reflect on the past and plan for the future makes the diagnosis of anosognosia in a mental health condition a key factor when determining treatment and drug therapy. Poor insight can directly influence difficulty in making sense of positive and negative clinical manifestations of psychiatric conditions (Osatuke, Ciesla, Kasckow, Zisook & Mohamed, 2008). For example, individuals with schizophrenia may have temporary delusions, however, individuals with schizophrenia and anosognosia are more likely to preserve positive symptoms as their reality, which can influence all decisions thereafter based off of fabricated knowledge.

When determining an individual's decisional capacity, three primary domains emerge as the most important and predictive results to show functional competency and vulnerability enhancement. The three primary domains affected by anosognosia are as follows: 1) Executive functioning, memory, and insight, 2) Decisional capability for health care treatment and other daily decisions involved in the comprehension of the nature of the information about the condition, and 3) The understanding of application to one's own condition, and the ability to

process and critically understand the information provided (Jeste, Depp, & Palmer, 2006). People who suffer from anosognosia will have an impaired ability to make well-informed decisions about health care and are more likely to suffer poor outcomes such as financial loss and increased risk for exacerbations of their mental health condition.

With contradicting evidence and a complex history, anosognosia is currently measured and treated as a multifactorial anomaly that stems from psychological, neuropsychological, and organic components. Increased admissions to acute care facilities, crisis stabilization units, and correctional facilities can result from lack of recognition for this co-morbidity, resulting in under treatment of the condition.

PURPOSE

The primary purpose of this integrative review of the literature is to examine how anosognosia influences outcomes in the population of individuals with severe mental illness. The secondary purpose is to describe healthcare provider's recognition of anosognosia in individuals with comorbid mental health disorders, as a differentiating diagnosis needing preeminent early intervention. It is expected that early recognition by clinicians and implementation of additional interventions to address anosognosia as the most influential comorbidity of schizophrenia, will decrease exacerbations and improve treatment and patient outcomes.

BACKGROUND

The investigation into anosognosia clinically requires a carefully operationalized, working knowledge definition, as well as a systematic method of measuring and quantifying the level of insight one has into their illness. While this remains a challenge, mental health clinicians have defined the concept of “insight” as an individual’s ability to understand the conceptual elements as the following: Awareness to having an illness; Recognizing the signs and symptoms while accrediting consequences and deficit to the illness; and, The ability to appreciate and understand the need for treatment. “Insight,” is thus recognizable as a multifactorial construct measured on a continuum, rather than an “all or none” phenomenon (David, 1990).

Recognition of “anosognosia,” as its own terminology is not a clearly defined concept across the mental health continuum. Little distinction has been made between anosognosia, lack of insight, and denial of illness, as these terms have often been used interchangeably to describe the neurological and psychological phenomena of anosognosia. The term, ‘denial’, is distinguished as a reflection of a healthy perpetual defense mechanism, rather than a pathological avoidance of reality. The consistency and magnitude to which denial is attributed to healthy functioning in an individual, suggests that it is a psychological base of coping (Haan & Harder, 1992). Individuals experiencing denial have information of illness cognitively and consciously available to them, but dismiss it in an attempt to protect against distress and preserve emotional wellbeing. By contrast, those with anosognosia do not have the information of illness available to them to contemplate over. More than denial, the term ‘anosognosia’ is defined as a deficit of self-awareness related to unawareness of neurological defects regardless of compelling evidence, adjoined with the use of confabulation to explain any threats indicating illness. It is therefore pertinent to acknowledge that these individuals are unable to fathom their illness themselves

when being screened for psychiatric illness. Understanding the dissimilarity between anosognosia and denial will not only aid in the standardization of terminology and accuracy for future research, but will also help mental health practitioners recognize the gravity of this diagnosis, rather than seeing it as a symptom of a larger disease.

Assessment of Anosognosia

In an attempt to quantify and measure such a complex construct, several instruments currently exist to measure the level of insight one has into their illness. Among these various tools, the Scale to Assess Unawareness into Mental Disorder (SUMD) is one of the most widely used instruments taking into account the wide psychometric properties of the illness. Presented as an interview derived from Amador's complex model of insight, the SUMD distinguishes the processes of awareness and attribution through a 74 piece questionnaire assessing: Awareness of having a mental disorder, recognition of signs and symptoms and explanations of the cause of these signs and symptoms (Amador et. Al, 1994). Consider question 2 on the SUMD, "awareness of the achieved effects of medication." This questions the individual's beliefs regarding the effects of medication and explicitly associates medication compliance with one's level of insight. Medication compliance is thus built in as a beneficial assumption for patients, into the very instrument used by clinicians to assess for anosognosia. Unfortunately, although the SUMD has proven to be the most reliable tool when assessing insight, the extensive length of this test makes it commonly used solely in studies and not in clinical settings.

In addition to the SUMD, there are several self-administered validation tools that are present among extensive literature such as the Beck Cognitive Insight Scale (BCIS). This exam measures the extent to which an individual recognizes their illness and need for treatment by

evaluating patients' self-reflectiveness and self-certainty of their experiences. One's self-reflectiveness includes items measuring the ability to have objectivity and openness to feedback, and the latter measures one's certainty about their beliefs and judgment (Beck, A.T, 2004). These subscales are useful when determining an individual's willingness and capacity to entertain corrective feedback about delusional beliefs and thinking. The overall estimate of the composite cognitive insight index score is then measured taking the score of self-certainty and subtracting it from the self-reflectiveness subscale. This index was found to significantly correlate with the Awareness of Having a Mental Disorder item on the SUMD (Riggs, S., Grant, P., Perivoliotis, D., & Beck, A.T., 2012).

While these are the current tools that psychiatric professionals use to determine the extent of insight an individual has insight into their disease, the measurement tools are not purposefully designed to thoroughly evaluate the multidimensional nature of the clinical phenomenon of anosognosia. Development of a standardized tool to diagnose and measure anosognosia would not only aid in clinicians identification of these individuals, but would also allow for reliability and standardization of research results.

Theory of Organic Abnormalities as a Factor of Anosognosia

Although still in its clinical incipiency, anosognosia was originally a term coined by renowned psychologist Joseph Babinski, with regards to a lack of insight into specifically, left hemiplegia. The concept of anosognosia reflects on the idea that focal lesions and diffuse brain damage caused individuals with left hemiplegia to have unawareness of the paralysis that affected them. As expressed by Xavier Amador, individuals exhibiting poor insight into schizophrenia remarkably parallel the same characteristics expressed by individuals with

neurological disorders. As seen in 10-18% of stroke victims with hemiparesis, these individuals present with a severe lack of awareness into their illness, deny illness despite conflicting evidence, use confabulations in order to explain observations made by others, and have a compulsion to prove their self-concept (Amador & Paul-Oudouard, 2000). Since the acceptance of this parallelism, many studies have been conducted in an attempt to examine the areas of the brain responsible for causing impairment of insight.

Theories have often framed schizophrenia as disorder resulting from a disruption in neural connectivity leading to impaired communication between areas of the brain. The advancement of neuroimaging techniques have provided researchers with the ability to see an unparalleled window into the changes of the brain seen in schizophrenia that are associated with structural abnormalities including neutrophil loss and reduced gray matter volumes in the prefrontal cortex. The diagnosis of schizophrenia is now accepted as a hypo-functionality of the prefrontal cortex, which is critically responsible for short-term memory, auditory processing, episodic memory and decision-making. Anosognosia, as a complex construct of insight and recognition, is also mediated by brain regions at a higher hierarchical level of thought processing. One study performed by Shad, Muddasani, and Keshavan, measured specific prefrontal sub-regions in individuals with schizophrenia, using voxel-based morphometry, an MRI technique used to investigate focal differences in brain anatomy. In this study, researchers utilized the SUMD (Scale to Assess Unawareness in Mental Disorder) assessment tool to quantify the insight function in 14 subjects, and compare their level of insight to the dorsolateral and orbitofrontal regions in the prefrontal cortex. The findings from this study resulted in an inverse relationship between the volume of the dorsolateral region and awareness of symptoms (Shad et. Al, 2006). The dorsolateral region of the brain being most commonly associated with

executive functions including: The working memory, selective attention, and self-monitoring. The results from this study are further validated from a study performed in the Netherlands asking 47 individuals with schizophrenia and 21 normal controls, to think about themselves while being assessed by a functional MRI. The individuals with anosognosia showed significantly lower activation in several areas of the brain as compared to the individuals that had high scores of insight when assessed using the Beck Cognitive Insight Scale.

It would be ideal to merit the same neurologic disturbances for both psychiatric and neurological individuals causing the underlying the problem of lack of insight. However, since the biological basis of neural activity and thought processing areas of the brain are not fully understood for individuals with anosognosia as a comorbid condition with other mental health disorders, treatment for mental health disorders is often reactive rather than proactive, leading to exacerbation's of the disorder and admission to a facility.

SIGNIFICANCE

The development of the operationalized definition of anosognosia in conjunction with new clinical measurement tools for insight, have allowed clinicians to better recognize that persons with severe mental illness are a heterogeneous group. A large percentage of individuals with serious mental illnesses are able to recognize their condition, and are willing to participate in treatment. These are the individuals that show fewer problems with substance abuse, violence, and have the most potential for recovery. Alternatively, individuals that have anosognosia, have presented throughout literature with poor treatment compliance, increased risks for violence and increased risks for suicide. With the developing ability to recognize individuals with anosognosia, additional steps should be taken to implement a standardized diagnostic tool, classify anosognosia as a subtype diagnosis, implement early interventions, and treatments to thereby improve safety and prevent poor outcomes.

METHODS

For this thesis, research articles were identified, systematically analyzed, and synthesized in order to gain a better understanding of the current literature on anosognosia in the presence of co-morbid mental health conditions, the populations healthcare needs, and effect on individual treatment outcomes and admissions to acute care facilities or crisis stabilizations units. Databases that were used to search for articles included Cumulative Index to Nursing and Allied Health Literature (CINAHL), Educational Resources Information Center (ERIC), Elton B. Stephens Co. Host (Ebsco Host), Medical Literature On-line (Medline), and Psychological Information Database (PsychINFO). Searches used a combination of the following terms: anosognosia, lack of insight, denial of illness, treatment adherence, violence, suicide, hospitalization, and schizophrenia. Inclusion criteria were peer-reviewed articles and publications written in the English language that were available from 2000-2020. While the focus of this study is on practices in the United States, international articles written in the English language will be included. Exclusion criteria included articles published in a language other than English and dates outside of the specified publication date, articles without evidence of anosognosia as a significant comorbidity of an existing mental health disorder, and lack of evidentiary support for admission to a facility directly due to anosognosia.

Each article will be evaluated and critiqued for relevance to the topic and its application in individuals with anosognosia and clinical practice. Subsequently, all of the articles will be synthesized to identify consistent findings as well as the gaps in the current literature. An evidence table will be developed to highlight findings for each article and will be included in the review for this thesis.

This literature search yielded 3,902 results for the key terms “anosognosia,” “lack of insight” and “schizophrenia.” After exclusion criteria were applied, 1,746 results articles were eliminated. The remaining 2,156 articles were reduced again to include only the key terms “anosognosia” and “schizophrenia” and this yielded 209 results. Another pooling of terms was used for “anosognosia,” and “treatment” or “adherence” or “suicide” or “violence” and “schizophrenia” yielding 73 results when exclusion criteria were applied. The remaining articles will be reviewed for relevance and additional studies from references were included in the literature review.

RESULTS

Disparities in Outcomes and Need for Early Intervention

The analysis of the literature review revealed a common health-related theme among individuals that have anosognosia, specifically, the greater potential for negative outcomes due lack of treatment compliance. Individuals with severe mental disorders are at heightened risk for hospitalizations, risk of violence to self or others, and suicide, either due to anosognosia or poor treatment compliance. Each of these potential negative outcomes are examined in greater detail in the next section of this paper.

Treatment Adherence and Insight

Among the research included in the table of evidence, six of the studies are focused around the correlation between an individual's level of insight, and their compliance to prescribed treatment plans. All of these studies are similar in that they assess individuals that have a DSM diagnosis of schizophrenia. Three of the studies: (Kamali, M., Kelly, B.D., Clarke, M., Browne, S., Gervin, M., Kinsella, A., Lane, A., Larkin, C., O'Callaghan, E. (2006) and (Coldham EL, Addington J, Addington D. 2002) and (Novak-Grubic, V. & Tavcar, R. (2002) assessed the correlates of treatment adherence in patients that were admitted into an acute care facility during their first episode of psychosis. The sample subjects of these studies were assessed at baseline and then followed up six months, to one year later. Data collected at follow up appointments were different for each of these three studies, however, the Positive and Negative Symptom Severity scale (PANSS) was consistently used in order to measure the subject's levels of insight. (Kamali et. al, 2006) found that of the (N=60) individuals, one third exhibited poor insight at baseline and were found to be non-adherent to medication within the first 6 months of discharge. This study yielded similar results to (Coldham et. al, 2002), which

found non-adherent individuals to have significantly poorer insight at both assessments. Lastly, the study conducted by (Novak-Grubic et. al., 2002) aimed to assess the predictors of noncompliance and outcomes for male individuals following their first episode of psychosis. This study concluded that lack of insight was one of the leading predictors for non-compliance to treatment. In addition, outcomes for the treatment compliant group were notably favorable with relapse rates significantly lower than the non-adherent group. These results should be used to establish a strategy that emphasizes special attention paid to compliance-promoting interventions, in order to decrease readmissions to acute care facilities.

In addition to these studies, Hassan, A.E., Elnabawy, A., Eldeeb, M., & Essa, A. (2019), and Mohamed, S., Rosenheck, R., McEvoy, J., Swartz, M., Stroup, S., Lieberman, J.A. (2009), further validate poor insight as the greatest predictor for lack of treatment adherence with data collected from a combined sample size of (N=421). The study findings by Mohamed et. al, (2009) went further to suggest that higher levels of insight are associated with lower symptom severity, and better community function. Contrariwise, these results can infer that the overall course of illness is highly influenced by the presence of anosognosia as a co-morbidity. Lastly, Tessier, A., Boyer, L., Husky, M., Baylé, F., Llorca, P., & Misdrahi, D. (2017), used a cross-sectional study to assess the relationships between individual's self-reported medication adherence, insight, and therapeutic alliances, with several other measures. Results showed that treatment adherence can be enhanced by increasing one's level of insight through therapeutic alliance with a psychiatrist. Thus, continuous follow-ups and consistency with office visits would be most beneficial for those with anosognosia to promote compliance with treatment plans and medications.

Overall, the studies focusing on outcomes following first episode of psychosis, can concluded that identifying the subgroup of individuals with anosognosia can predict poor treatment adherence behaviors in the future. The studies that were analyzed for this review reinforce a need for specialized continuous interventions for the subtype of individuals with anosognosia in order to promote compliance.

Negative Outcomes

The research discussed has substantial evidence to demonstrate anosognosia as a pivotal comorbidity affecting patient's non-adherence to treatment. However, it is crucial to recognize the importance of remaining adherent to treatment, as adherence is the leading predictor for determining individuals' with mental illness' outcomes. Four studies from the table of evidence investigate correlations to unwanted hospitalization for individuals with schizophrenia. In a retrospective study conducted by Weiden, Kozma, Grogg, and Locklear (2004), (N=4,325) individuals were assessed for adherence to antipsychotic medications in relation to unwanted admissions to psychiatric facilities. Their results yielded that individuals reporting adherence of MPR (medication possession ratio) greater than 70% are less likely to be hospitalized, as compared with noncompliant individuals. Overall, the risk for hospitalization increased from an Odds Ratio of 2.81 (if non-compliant for only eleven days) to 3.96 times more likely for hospitalization, if there is a gap in medication greater than 30 days. These results suggest that the longer an individual goes un-medicated, the more presumable it is the individual will be hospitalized. These results are further validated by a study conducted by Morken, Widen, and Grawe (2008), which assess the outcomes associated with treatment adherence. Results from this study show that non-adherence to either oral or depot antipsychotic medication, are associated

with an Odds Ratio (OR) of 10.27 for having a psychotic relapse, and a 4.00 OR for readmission to a hospital (Morken et al., 2008). Both Morken, et. al, and Weiden, et. al, conclude there is nearly a four-fold chance of using hospital services if the individual is non-adherent to medication.

Proper ability for clinicians to identify anosognosia as comorbidity and further interventions to increase treatment adherence are paramount for potential beneficial impacts on the mental health and criminal justice delivery systems. Ascher-Svanum, Faries, Zhu, Ernst, Swartz, and Swanson (2006), prospectively examined the relationships between adherence with antipsychotic medications and functional outcomes among (N=1,906) individuals with a DSMIV diagnosis of schizophrenia. The outcomes measured included: Psychiatric hospitalizations, use of emergency psychiatric services, arrests, violence, victimizations, poorer mental functioning, poorer life satisfaction, greater substance use, and more alcohol-related problems. Using interviews in six month intervals for three years, Ascher-Syanum et. al's findings highlighted that non-adherence in the first year significantly predicted poorer functional outcomes in the following two years.

From these results, it can loosely be assumed that early interventions would significantly influence the potential for positive outcomes in the individuals' future years. Interventions to ensure compliance in the early stages following discharge can decrease unwanted admission to facilities, and decrease periods of time spent in psychosis. Longer durations of untreated psychosis is associated with more severe symptoms when admitted to an acute care facility or mental health unit, poor prognosis, risk of violence, elevated risk for suicide, and more frequent relapses with involuntary commitment (Dell'Osso, Glick, Baldwin, & Altamura, 2013).

Insight and Violence

Another common theme that emerged in the research was the incidences of violence among persons with anosognosia in their severe and persistent mental illness. It is important to note that most individuals with serious mental illness are not dangerous and more likely will be victims of perpetrators of violent acts. Nonetheless, individuals with anosognosia are at heightened risk for violent behavior when their symptoms remain untreated, especially with psychosis and paranoia (Treatment Advocacy Center, 2016). Four studies from the table of evidence examine schizophrenia and its correlation to violence as an outcome. The leading factors contributing to violent acts being: Non-adherence to medication, as well as presence of anosognosia. Ascher-Svanum et al. found within the measured functional outcomes, non-adherent patients were more than twice (10.8% versus 4.8%; $p < 0.001$) as likely to engage in violent activities and be arrested, than the control sample of adherent patients (Ascher-Svanum et al, 2006). Similar measures were used by Elbogen, Van Dorn, Swanson, Swartz, and Monahan (2006), who sampled (N=1,011) outpatients from five US cities, assessing attitude towards medication adherence and physically assaultive behavior, over a six month time span. The results were cross-examined using logistic regression for correlations between violence and attitude towards perceived treatment need. Those who became physically assaultive were significantly more likely to be non-adherent to treatment ($p < 0.001$), more severely ill, and abusing substances. The findings from this study provide empirical support for the assertion that adherence to medications is associated with reduced violence in patients with severe mental disorders.

Upon closer examination of violent acts committed by individuals with severe mental illness, two studies from the table of evidence examine the extent to which anosognosia is a

factor. Lincoln and Hodgins (2008), examined (N=209) individuals that had previously been admitted to a hospital, on average, 8.5 times. A chi square test was used to test the association between the PANSS-insight ratings and history of physically aggressive behavior, over the last two years. Results showed that significantly more patients with low or no insight, when compared with those with good insight, behaved aggressively in the second and third follow-up periods (Lincoln, et. al, 2008). Consistent with these results, Buckley, Hrouda, Friedman, Noffsinger, Resnick, and Camlin-Shingler (2004) also found that the violent individuals from their sample group had marked deficits in insight (71% scoring 4 [moderate deficit] or more, and 12.5% scoring 7 on the PNSS, with significantly greater deficits than nonviolent patients on both the PNSS and SUMD) (Buckley et. al, 2004). Identification of anosognosia in individuals with schizophrenia would therefore enhance clinician's violence risk assessment in psychiatric practice settings.

Suicide

As the second leading cause of death in Americans aged 15-24 years old, suicide is becoming a strong vector of concern. Not coincidentally this is the age group in which most young people leave for college, join the military, and experience a first episode of major mental illness. Of the suicides reported to the CDC in 2018, more than 54% of them did not have a known mental health condition. As a preventable cause of death, addressing the known risk factors can help decrease the risk for suicide among individuals with serious mental illness. These influential factors include: Depressive symptoms, substance abuse, awareness of illness, and a history of violent behavior (Treatment Advocacy Center, 2016).

Three studies from the table of evidence examine suicide as a negative outcome for individuals with a potential diagnosis of anosognosia in their mental illness. Findings from a study conducted by Verma, Srivastava, Singh, Bhatia, and Deshpande (2016), (N=175) suggest that there is a triangular relationship between individuals with good insight, better executive functioning, and suicide attempts at some point during the illness (Verma, et. al, 2016). While this study suggests that individuals who lack anosognosia are more likely to commit suicide, this study fails to incorporate the level of treatment compliance within the sample. As results from the studies in the table of evidence have shown, treatment adherence maintains a huge influence on outcomes. For example, a suicide and mental illness study based in Kentucky found that out of (N=28) individuals only 2 persons who had killed themselves had evidence of their antipsychotic medications in their blood. Therefore, 93% of the sample was left untreated or had not been adherent with their medications (Shields, Hunsaker, & Hunsaker, 2007).

Moreover, another study taking into account the level of treatment adherence was conducted by Barrett, Mork, Færden, Nesvåg, Agartz, Andreassen, and Melle, (2015). This study investigated the relationship between suicidality and insight, in individuals that had been adherent to treatment for more than 52 weeks following their first episode of psychosis. Barrett et. al, yielded results exhibiting patients who gained insight over their first year in treatment, were, to a lesser degree, suicidal at one year follow-up. (Barrett et. al., 2015). Overall, the status of one's adherence to medication poses great implications for the consequent course of illness.

DISCUSSION AND KNOWLEDGE GAPS

The literature review supports that there is an imperative need for clinicians to recognize and treat anosognosia as a unique co-morbidity in mental illness needing additional interventions following clinical guidelines. An overarching finding among studies is that individuals with anosognosia are particularly at risk for lack of treatment adherence. Without compliance to medication, these individuals will experience increased potential for negative outcomes, such as: Unwanted admissions to psychiatric facilities, violence, and risks for suicide. The literature synthesis highlights the need for a standardized diagnostic tool, early intervention, as well as the need for a contingency plan when planning treatment.

Of the literature that has been reviewed for this study, there is a lack of continuity when it comes to evaluating the sample populations for anosognosia, and the methods used to reevaluate these individuals. While the use of the Positive and Negative Symptom Severity Scale (PANSS), was the predominate tool used, only one item out of thirty in the PANSS is used to assess the level of insight. As a tool used for measuring sensitivity to treatment changes, this tool should be used for assessing overall responsiveness to medications, rather than assessing for, and measuring changes in level of insight for individuals with anosognosia. The use of the PANSS tool, rather than tools used specifically for measuring insight, such as the Scale to Assess Unawareness in Mental Disorder (SUMD), or Beck Cognitive Insight Scale, can have implications for the criteria and methods used in samples of future studies. Standardization of the tool used to assess for anosognosia in individuals with schizophrenia allows for validity and reliability when comparing research.

Throughout the literature, there was consistently a gap in treatment behavior of the samples of individuals with anosognosia. In numerous studies the sample population was being

monitored for adherence to medications, alternatively, some studies failed to monitor whether or not the population was being adherent to medication regimes. This difference in the sample's behavior can lead to concomitants in individual outcomes. Collectively, samples should mirror behavior in treatment adherence, in order to produce standardized results for measuring outcomes in individuals with anosognosia.

Another issue alluded in the literature is the limited number of studies that differentiate treatments plans for individuals with anosognosia, versus the typical treatment for someone with schizophrenia. Clinicians should make a distinction between diagnoses, as the subtype of schizophrenia with anosognosia, should portend non-compliance as the biggest outcome predictor. While much of the current research has been into reactive measures to increase treatment compliance, future research should be proactive in testing interventions increase compliance in these individuals with anosognosia. With enough research to assume individuals with anosognosia are more likely to have poor compliance, investigation into structured outpatient treatment plans following discharge would be more beneficial moving forward.

IMPLICATIONS

While there exists several tools for measuring one's insight into their illness, standardization of a diagnostic tool to test for anosognosia would allow clinicians to better identify this co-morbidity in individuals with severe mental illness. In addition to improving clinicians' recognition of this disorder, standardization would also allow for greater reliability and validity of research into optimal treatment plans for individuals with anosognosia. Current research into the use of an abbreviated version of the Scale to Assess Unawareness in Mental Disorder (SUMD) shows promising results as a dependable tool to be used in clinical practice when identifying anosognosia as a co-morbidity. As a recognized diagnosis with heavy influence on re-hospitalization, violence, and suicide, clinicians should reclassify patients with anosognosia into a high-risk category following evaluation.

Unsurprisingly, lack of fully developed clinical guidelines for anosognosia as a comorbidity in mental illness, can be rationalized by the absence of a standardized diagnostic tool. Currently, clinical practice guidelines exist within medicine to serve as a framework for clinical decisions and support the best evidence based practices for improved patient outcomes. The American Psychiatric Association failed to acknowledge anosognosia as a comorbid condition in the Practice Guideline (December 2019) for Treatment of Patients with Schizophrenia as well as the Practice Guideline (August 2015) for Psychiatric Evaluation (American Psychiatric Association, 2020). Currently, Treatment Guidelines from the American Psychiatric Association project to be updated in the Summer of 2020. This update should include anosognosia as a potential comorbidity, and should be included in the initial evaluation of all individuals with a potential diagnosis of schizophrenia. The required screening for anosognosia during the first evaluation would require the clinician to subtype the diagnosis of schizophrenia

as “with/without anosognosia”. Such a requirement would drastically change treatment plans and hospital discharge plans, allowing for advanced planning and tailored treatment regimes for these individuals.

As a high-risk category of individuals, additional measures should be taken to ensure that they are compliant to medication and treatment regimes. In our current health care system in America medical decisions are based off of liberty and autonomy. Just as all Americans, people living with mental health conditions have the right to make decisions about their lives, including their medical treatments. In a system that governs psychiatric patients through their freedom of will, the logic of anosognosia introduces the intractable dilemma: Can a person make an informed choice to refuse treatment, if the symptoms of the illness impair awareness of the illness itself? This durable link between psychiatry and the law must align with a common understanding of anosognosia and it’s relation to compliance behaviors.

It is estimated that schizophrenia only affects 1.1% of the population in the United States of America. Despite this relatively low prevalence, schizophrenia is associated with substantial economic burden in the United States. Tax payer’s estimated economic costs to manage individuals with schizophrenia totaled to over \$155.7 billion in 2013 (Cloutier, et. al, 2016). This total equivalates an average excess annual cost of over \$44,733 per person with schizophrenia. In comparison, at a cost of \$327 billion dollars annually to manage an estimated 88 million adults with pre-diabetes, diabetes has become the most expensive chronic disease in the U.S (American Diabetes Association, 2020). Nevertheless, the overall economic burden to manage an individual with schizophrenia is more than twice the cost to manage an individual with diabetes annually. With high expenses, investigations into the driving forces of expenses for individuals with

Schizophrenia, are needed in order to target areas of focus for treating these individuals more effectively.

Since it is not uncommon that individuals with anosognosia will resist treatment, a structured environment with monitoring is needed to ensure compliance to medications. Of the studies that have tested, certain interventions such as Mandatory Outpatient Treatment is noted to have positive effects on individuals with anosognosia that have resisted treatment. Up to 75% of individuals with this court order have said MOT has helped them regain control of their lives, 81% have said that MOT helped them get and stay well, and 90% of individuals have said MOT has made them more likely to keep appointments and take medication (Treatment Advocacy Center, 2020). With repeated results of improvement with adherence and positive outcomes, MOT should become a guideline for treating individuals with anosognosia.

Anosognosia is a common comorbidity in schizophrenia and should be evaluated by all clinicians. With the ability to promote better patient outcomes through early recognition of this comorbidity, the inclusion of anosognosia should be included into the American Psychiatric Association's clinical guidelines and evaluations for patients with schizophrenia. It can be loosely correlated that early recognition of this disorder will allow for reduced hospitalizations, increased treatment adherence, and decreased risks of violence to self and others. Research into the best proactive treatment measures is increasingly important for potentially good outcomes, and should be the focus of future research. Successful efforts should permit early disease recognition with aggressive and structured treatment programs.

TABLE OF EVIDENCE

Author(s) Year Location	Study Design and Purpose	Sample Size	Intervention Protocol	Screening Measures	Outcome Measures	Key Findings and Limitations
<p>Ascher-Svanum, H., Faries, D.E., Zhu, B., Ernst, F.R., Swartz, M.S. & Swanson, J.W. (2006). Medication adherence and long-term functional outcomes in the treatment of schizophrenia in usual care. <i>J Clin Psychiatry</i>, 67(3), 453-60.</p>	<p>prospectively examined the relationships between adherence with any antipsychotic medication and functional outcomes among schizophrenia patients</p>	<p>N=1906</p>	<p>Assessed outcome measures over a three year period in patients with the DSM IV diagnosis of schizophrenia</p>	<p>1906 participants with DSM-IV diagnoses of schizophrenia or schizoaffective or schizophreniform disorder in a multi-site, 3-year, prospective, naturalistic study conducted in the United States between July 1997 and September 2003. Outcome measures were assessed at 6-month intervals using systematic medical record abstraction and structured interview of patients.</p>	<p>Outcomes included: psychiatric hospitalizations, use of emergency psychiatric services, arrests, violence, victimizations, poorer mental functioning, poorer life satisfaction, greater substance use, and more alcohol-related problems</p>	<p>Nonadherence was associated with poorer functional outcomes.</p> <p>Nonadherence in the first year predicted significantly poorer outcomes in the following 2 years.</p> <p>Findings highlight the importance of adherence with antipsychotic medication in the long-term treatment of schizophrenia and its potential beneficial impact on the mental health and criminal justice delivery systems.</p>
<p>Barrett, E. A., Mork, E., Færden, A., Nesvåg, R., Agartz, I., Andreassen, O.</p>	<p>aim of the present study was to investigate predictors of suicidality in patients with</p>	<p>N=146 individuals with first episode psychosis that had</p>	<p>The patients were interviewed as soon as possible after treatment</p>	<p>Suicide attempts and depressive episodes were recorded in the SCID-I</p>	<p>the following variables were dichotomised : depressive episodes, suicide</p>	<p>The opposite effects of insight at baseline versus insight at follow-up on</p>

<p>A., & Melle, I. (2015). The development of insight and its relationship with suicidality over one year follow-up in patients with first episode psychosis. <i>Schizophrenia Research, 162</i>(1-3), 97-102.</p>	<p>first episode of psychosis (FEP) over one year, focusing on the relationship between insight and suicidality.</p>	<p>been adherent to treatment for 52 weeks</p>	<p>starts (baseline) and again after 12 months (follow-up) by trained psychologists or psychiatrists .</p>	<p>interview Current suicidality was assessed at baseline and follow-up by item 8 on the Calgary Depression Scale for Schizophrenia (CDSS) Severity of positive and negative symptoms for the last week was assessed with PANSS</p>	<p>attempts, hospital admissions (all into no incident = 0, ≥ 1 incident(s) = 1), and PANSS depression (item G6) (scores 1 and 2 = 0, scores $\geq 3 = 1$) for the regression analyses. Independent variables were removed from subsequent analyses if they did not have a statistically significant contribution. In a final model, the interaction between Insight (baseline) \times Insight (follow-up) was entered in a fourth block.</p>	<p>suicidality at follow-up could also reflect patients' <i>change</i> in insight. Patients with stable levels of insight across baseline and follow-up did not differ in risk for suicidality at follow-up. However, patients who gained insight over their first year in treatment were to a lesser degree suicidal at one year follow-up, whilst patients who lost insight were to a stronger degree suicidal at one year follow-up.</p>
<p>Buckley, P.F., Hrouda, D.R., Friedman, L., Noffsinger, S.G., Resnick, P.J., & Camlin-Shingler, K. (2004). Insight and its relationship to violent behavior</p>	<p>To research the interrelationship between lack of insight and illness attributes in patients with schizophrenia who commit violent acts.</p>	<p>N=115</p>	<p>One hundred fifteen violent patients with schizophrenia in a jail or court psychiatric clinic were evaluated on measures of</p>	<p>DSM-IV diagnosis of schizophrenia (N=77) or schizoaffective disorder (N=38) who had committed violent acts Insight into</p>	<p>Violent and nonviolent groups were compared on measures of symptoms, cognition, functioning, and insight by using Mann-Whitney</p>	<p>Violent patients had marked deficits in insight (71% scoring 4 [moderate deficit] or more and 12.5% scoring 7 on the PNSS</p>

<p>in patients with schizophrenia. <i>American Journal of Psychiatry</i>, 161, 1712–1714.</p>			<p>symptoms, illness severity, insight into illness, and the legal consequences of their illness (“forensic insight”). A sample of nonviolent patients served as a comparison group.</p>	<p>illness was assessed with the PNSS and the SUMD</p> <p>Insight into legal complications of illness (“forensic insight”) was assessed in the violent cohort on three items (concern about becoming ill, relationship of illness to crime, and acceptance of responsibility for crime) on the Eisner Scale, a scale developed to evaluate the discharge readiness of forensic patients</p> <p>Additional data were collected from patient interviews and reviews of clinical records and forensic and collateral source documents.</p>	<p>nonparametric tests. Relationships between Positive and Negative Syndrome Scale insight scores, Positive and Negative Syndrome Scale to Assess Unawareness of Mental Disorder items, and Eisner Scale items were examined by using Spearman’s correlations.</p>	<p>with significantly greater deficits than nonviolent patients on both the PNSS and SUMD</p> <p>Those who had been violent scored significantly lower ($p < 0.001$) on awareness of mental disorder, awareness of effect of medications and awareness of social consequences of mental disorders when compared to the nonviolent individuals.</p> <p>Limitations: Difficulty obtaining a sample population.</p>
<p>Carpenter WT, Strauss JS, Bartko JJ. (1973). Flexible system for the diagnosis of schizophrenia:</p>	<p>This study was designed as a pilot study to lay the scientific ground work for future studies</p>	<p>n=1,202</p>	<p>Patients were between the ages of 15-44, from 9 different</p>	<p>The individuals that were a part of this study were assessed by</p>	<p>A one-way analysis of variance was used to determine the association</p>	<p>Poor insight was a symptom that was found in 85% of this</p>

<p>Report from the WHO International Pilot Study of Schizophrenia. <i>Science</i>, 182, 1275-1278.</p>	<p>done on the signs and symptoms for diagnosis of individuals with schizophrenia.</p>		<p>countries, and had recently been hospitalized with the diagnosis of schizophrenia from the DSM-II</p>	<p>the researchers within 2 weeks of admission to the hospital using the Present State Examination (PSE) to determine symptoms.</p>	<p>between each sign and symptom and the outcome data provided at the 5-year follow up.</p>	<p>sample. More interestingly, researchers concluded that presenting signs and symptoms were not good at predicting prognosis. As a result the researchers suggest using a past medical history or markers of chronicity to be used when diagnosing schizophrenia. Limitations: There was a loss of patients in between the 2 year follow up and the 5 year follow up.</p>
<p>Coldham, E.L., Addington, J. & Addington, D. (2002). Medication adherence of individuals with a first episode of psychosis, <i>Acta Psychiatr Scand</i>, 106, 286-290.</p>	<p>The purpose of this study was to determine rates of adherence to antipsychotic medication in first episode patients and the correlates of adherence in this group.</p>	<p>n=143</p>	<p>Outpatient at baseline, 1-y follow-up</p>	<p>Insight: was measured using the PANSS</p>	<p>Outcome was measured through the individual's adherence to treatment at the 1 year follow up</p>	<p>The nonadherent group had significant poorer insight at both assessments. In a logistic regression analyses, controlling for age, family involvement,</p>

						<p>premorbid functioning, and cannabis use, insight was not significant.</p> <p>Limitations: N/A</p>
<p>Elbogen, E.B., Van Dorn, R.A., Swanson, J.W., Swartz, M.S., Monahan, J. (2006). Treatment engagement and violence risk in mental disorders. <i>British Journal of Psychiatry</i>, 189, 354–360.</p>	<p>Cross sectional study</p> <p>In five US sites, 1,011 outpatients with severe psychiatric disorders were assessed for attitude towards medication adherence and physically assaultive behavior over a six month time span. Those who became physically assaultive were significantly more likely to be non-adherent to treatment ($p < 0.001$), more severely ill and abusing substances.</p>	<p>N=1011</p>	<p>200 outpatients from publicly funded mental health treatment programmes were sampled from 5 states. They were assessed for previous acts of violence and then attitude towards treatment adherence. These results were cross examined for correlations between attitude and violence</p>	<p>1. The MacArthur Community Violence Interview was used to assess individuals level of violence</p> <p>2. perceived treatment effectiveness, which was measured using the Consumer Satisfaction Questionnaire</p> <p>3. perceived treatment benefit was measured using questions from the National Institute of Mental Health Epidemiologic Catchment Area (ECA)s</p>	<p>logistic regression to examine the associations between participants' demographic and clinical characteristics and the likelihood of engaging in any physically assaultive behaviour, in addition to other aggressive acts and violence in the past 6 months.</p>	<p>19.7% engaged in any form of violence. The findings provide empirical support for the assertion that perceived treatment need is associated with reduced levels of violence among patients with mental disorders. The results suggest clinical consideration of patients' perceptions of treatment benefit can help enhance violence risk assessment in psychiatric practice settings.</p> <p>Limitations: Did not include level of insight or anosognosia ... BCIS should have</p>

						been used as it also assesses one's attitude towards treatment.
Gharabawi, G.M., Lasser, R.A., Bossie, C.A., Zhu, Y., & Amador, X. (2006). Insight and its relationship to clinical outcomes in patients with schizophrenia or schizoaffective disorder receiving long-acting risperidone. <i>Int Clin Psychopharmacol</i> , 21(4), 233-40.	This study assessed the correlation between the use of long acting anti-psychotic medication and patient's level of insight, and perceived quality of life	N=614 schizophrenia or schizoaffective disorder	First assessment at enrollment in a risperidone treatment trial, followed by assessments at weeks 12, 24, 48, and 50.	Insight was measured using the PANSS Clinical Global Impressions-Severity (CGI-S); and the Medical Outcomes Study Short-form 36-item Health Survey (SF-36) (patient-rated quality of life)	Patient's symptoms assessed using : PANSS total and 3 factors: negative symptoms, anxiety/depressive symptoms, and disorganized thought	Long-acting risperidone was associated with improvements in insight, symptom domains, clinical status and quality of life measures. Associations were noted between patient-rated quality of life and specific symptom domains, but not insight. Patients improved significantly on PANSS total from baseline to end point, regardless of baseline insight. Patients with severe lack of insight at baseline had the highest overall level of symptoms at baseline and follow-up. Limitations: This study did not

						include overall patient functionality improvement
Hassan, A.E., Elnabawy, A., Eldeeb, M., & Essa, A. (2019). Assessment of impact of insight on medication adherence in schizophrenic patients. <i>The Egyptian Journal of Hospital Medicine</i> , 74(4), 885.	The aim of this study was to study the relation between insight and medication adherence and other factors that may affect both of them.	n=50 schizophrenic outpatients "DSM 5" aged > 18 years old who were attending the hospital for regular follow up were included in this study.	Patients' insight was measured by the Schedule for Assessment of Insight-Expanded Version (SAI--E) The degree of medication adherence was measured by using Medication Adherence Rating Scale (MARS).	Degree of insight in our patients was evaluated and assessed by the Expanded Version of the Schedule of Assessment of insight (SAI-E). We found that the mean value was 11.92 [+ or -] 5.6 indicating poor insight in majority of our patients.	Outcome was measured on patient adherence to treatment	Insight and adherence were found to be closely related, low insight was associated with poor adherence in patients with schizophrenia. Moreover, these results should be used to establish a strategy for improving the prognosis of chronic schizophrenia Limitations: N/A
Kamali, M., Kelly, B.D., Clarke, M., Browne, S., Gervin, M., Kinsella, A., Lane, A., Larkin, C. & O'Callaghan, E. (2006). A prospective evaluation of adherence to medication in first episode schizophrenia. <i>Eur Psychiatry</i> , 21(29)–33.	Longitudinal study Inpatient at baseline, 6-mo follow-up	n=60 First-episode schizophrenia or schizophreniform disorder (SCID)	Patients were assessed for baseline level of insight, then reassessed 6 months later for medication adherence and level of insight.	Insight was measured using the PNSS	Outcome was measured through compliance interview at 6 month follow up for original hospitalization	One third of patients with schizophrenia were non-adherent with medication within six months of their first episode of illness. High levels of positive symptoms at baseline, lack of insight at baseline, alcohol misuse at

						<p>baseline and previous drug misuse predict non-adherence</p> <p>These results indicate that an identifiable subgroup of patients with first episode schizophrenia is at high risk of early non-adherence to medication.</p> <p>Reduced insight is the best predictor of non-adherence in patients who do not misuse alcohol or other drugs.</p> <p>Limitations: This study was conducted in a Dublin psychiatric hospital</p>
<p>Lincoln, T.M. & Hodgins, S. (2008). Is lack of insight associated with physically aggressive behavior among people with schizophrenia living in the community? <i>The Journal of Nervous and</i></p>	<p>This study was done to examine if lack of insight is related to physically aggressive behavior toward others among persons with schizophrenia, after controlling for known predictors such</p>	<p>N=209</p> <p>On average, patients had been admitted to a psychiatric hospital 8.5 times with a mean length of the last hospital stay at 34.6</p>	<p>Patients with schizophrenia were followed for 2 years after discharge. At discharge, psychopathy traits, insight and symptoms</p>	<p>PANSS-insight ratings were used for categorizing patients as having at least some insight (ratings 1-3) or low or no insight (ratings 4-7).</p>	<p><i>Chi square</i> tests were calculated to test for an association between aggressive behavior and insight for each follow-up period. Significantly more patients</p>	<p>Taken together, 27 (15.9%) patients engaged in aggressive behavior at least once during the 2-year follow-up period: 9 incidents were</p>

<p><i>Mental Disease, 196(1), 62-66.</i></p>	<p>as psychopathy traits, and positive symptoms.</p>	<p>months</p>	<p>were assessed. At the beginning of each six-month period, insight and symptoms were assessed, whereas aggressive behavior, reported by patients and collateral informants, was assessed at the end of each period.</p>	<p>Aggressive behavior was assessed using the MacArthur Community Violence Instrument which includes: throwing something at someone, pushing, shoving, grabbing, slapping, kicking, biting, choking, ect.</p>	<p>with low or no insight when compared with those with good insight behaved aggressively in the second and third follow-up periods.</p>	<p>reported in the first period, 12 in the second, 14 in the third, and 11 in the fourth period. The results demonstrate that among individuals with schizophrenia, aggressive behavior was more strongly associated with high scores for psychopathy traits and positive symptoms than with lack of insight.</p> <p>Limitations: Length of stay in the hospital exceeds that of American hospitals... participants were taken from 4 sites: Canada (36%), Germany (26%), Finland (26%), and Sweden (12%). This study also failed to mention the extent to which patients were</p>
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						adherent to medication which may be the factor playing to decreased levels of violence
Mohamed, S., Rosenheck, R., McEvoy, J., Swartz, M., Stroup, S. & Lieberman, J.A. (2009). Cross-sectional and longitudinal relationships between insight and attitudes toward medication and clinical outcomes in chronic schizophrenia. <i>Schizophr Bull.</i> , 35(2):336-46.	Cross sectional and longitudinal study between the relationship of insight and medication adherence	n=371	Clinical Antipsychotic Trial of Intervention Effectiveness (CATIE) was a large 18-month follow-up study pharmacotherapy of people with schizophrenia.	Insight was measured using the Insight and Treatment Attitudes Questionnaire and attitudes toward medication by the Drug Attitude Inventory.	Medication adherence was assessed by the treating psychiatrist. Bivariate correlations and mixed model regression analyses were used to test the relationship of insight and medication attitudes to outcomes at baseline and during the follow-up period. Regression models were used to evaluate the relationship between change in insight and medication attitudes and changes outcomes.	Higher levels of insight at baseline were significantly associated with lower levels of schizophrenia symptoms at follow-up while more positive medication attitudes were significantly associated with both lower symptom levels and better community functioning Limitations: Phase 1 of the CATIE recruited 1493 patients with schizophrenia at 57 clinical sites in the United States. Broad inclusion and minimal exclusion criteria were used, allowing the enrollment of

						patients with coexisting conditions. of the 1460 persons included in the trial, 1089 did not complete the trial.
Morken G., Widen J., & Grawe R. (2008) Non-adherence to antipsychotic medication, relapse and rehospitalisation in recent-onset schizophrenia. <i>BMC Psychiatry</i> , 8,32.	RCT The aims of this study were to describe outcome with respect to persistent psychotic symptoms, relapse of positive symptoms, hospital admissions, and application of treatment by coercion among patients with recent onset schizophrenia being adherent and non-adherent to antipsychotic medication.	N=50	The patients were clinically stable at study entry and had less than 2 years duration of psychotic symptoms. Outcomes for poor and good adherence were compared over a 24-month follow-up period.	Registration of antipsychotic medication adherence was based on patient interviews. These were done by monthly for two years. Information on adherence was also gathered from therapists, carers, plasma assays, and patient records. Global Assessment of Functioning (GAF) assessed overall functioning at 0, 12 and 24 months.	Good adherence to antipsychotic medication was defined as less than one month without medication.	The Odds Ratio (OR) of having a psychotic relapse was 10.27 and the OR of being admitted to hospital was 4.00 among non-adherent patients.
Novak-Grubic, V. & Tavcar, R. (2002). Predictors	This study aimed to assess predictors of	N=56	1 year follow up from	Insight was measured using the	Outcomes were	Thirty patients (53.6%)

<p>of noncompliance in males with first-episode schizophrenia, schizophreniform and schizoaffective disorder. <i>Eur Psychiatry</i>, 17, 148-154.</p>	<p>noncompliance in male patients with first-episode schizophrenia, schizophreniform and schizoaffective disorder in a naturalistic setting.</p>		<p>discharge of psychiatric facility</p>	<p>PNSS</p>	<p>measured with attendance of appointments and medication compliance assessed as self-report and/or reports from key-relatives</p>	<p>dropped out of treatment in the first year and 21 of them relapsed. With the Cox survival analysis three predictors of noncompliance were found: diagnosis of schizophrenia versus the other two diagnoses, positive symptoms at admission, and lack of insight at discharge.</p> <p>In compliant patients, the relapse rate was low, and therefore special attention and compliance-promoting interventions in first-episode patients are needed.</p> <p>Limitations: many patients withdrew from the study, the reasons why, were not listed here.</p>
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<p>Shad MU, Muddasani S, Keshavan MS. (2006). Prefrontal subregions and dimension of insight in first episode schizophrenia: a pilot study. <i>Psychiatry Res</i>, 146(1), 35–42.</p>	<p>This study examined the relationship between specific prefrontal subregions and the awareness and attributional dimensions of insight in schizophrenia. This study examined the correlation between insight dimensions of awareness and attribution of symptoms and dorsolateral prefrontal cortex (DLPFC) and orbitofrontal cortex (OFC) volume</p>	<p>n=35</p>	<p>Subjects were determined to have schizophrenia by diagnosis through the DSM.</p>	<p>14 subjects with first-episode, antipsychotic-naïve (FEAN) schizophrenia. In addition, 21 healthy subjects provided control data for volumetric assessments</p>	<p>Insight was assessed with Scale to Assess Unawareness of Mental Disorders. Morphometric assessments were adjusted for intra-cranial volume and were conducted by trained raters blind to clinical information using BRAINS-2.</p>	<p>The findings from this study resulted in an inverse relationship between the volume of the dorsolateral region and awareness of symptoms. The dorsolateral region of the brain being most commonly associated with executive functions including: The working memory, selective attention, and self-monitoring.</p> <p>Limitations: The sample size in this study is small.</p>
<p>Tessier, A., Boyer, L., Husky, M., Baylé, F., Llorca, P., & Misdrahi, D. (2017). “Medication adherence in schizophrenia: The role of insight, therapeutic alliance and perceived trauma associated with psychiatric care.”</p>	<p>Cohort study assessed the relationship regarding symptomatology, self-reported adherence with medication, insight, medication side-effects, therapeutic alliance and perceived trauma related</p>	<p>n=72</p>	<p>a diagnosis of schizophrenia or schizoaffective disorder according to DSM-IV-TR criteria (2) at least 18 years old, (3) able to understand the protocol, and (4) fluent</p>	<p>The severity of one’s insight and psychopathology was assessed by the PANSS, which comprises three different subscales (positive, negative and general psychopathol</p>	<p>Adherence to medication was self-reported.</p>	<p>Medication non-adherence concerns 50% of schizophrenic patients.</p> <p>Adherence could be enhanced by reducing perceived trauma or increasing insight.</p>

<p>Psychiatry Research, 257, 315-321.</p>	<p>to psychiatric treatment.</p>		<p>French speaker. Exclusion criteria included traumatic head injury, any past or present major medical or neurological illness and mental retardation.</p>	<p>ogy).</p>		<p>The present study articulates the need for mental health clinicians to be sensitive to patients' perception of traumatic experiences related to psychiatric treatment and to be aware of the importance of therapeutic relationship in treating patients with schizophrenia.</p> <p>Limitations: As this assessment reflected the endorsement of a single item, it may have been subject to recall bias or influenced by the participant's mental state. Third, insight was evaluated using the BIS scale (Birchwood et al., 1994). This self-report insight scale (BIS) is a quick and reliable measure</p>
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						exploring insight in a multidimensional concept which include the subjective impression of patient facing to clinical symptoms.
<p>Van der Meer, L., De Vos, A.E., Stiekema, A.P., Pijnenborg, G.H., Van Tol, M.J., Nolen, W.A., David, A.S., & Aleman, A. (2013). Insight in schizophrenia: Involvement of self-reflection networks? <i>Schizophrenia Bulletin</i>, 39(6), 1288—1295.</p>	<p>The current study aims to investigate the neural correlates of self-reflective processing and its relationship with insight in schizophrenia.</p>	<p>N=47 (shizo). N=21 (controls)</p>	<p>Forty-seven schizophrenic patients and 21 healthy controls performed a self-reflection task in a functional magnetic resonance imaging (fMRI) scanner. The tasks comprised a self-reflection, close other-reflection, and a semantic (baseline) condition. Insight scores were obtained with the (Beck Cognitive Insight Scale [BCIS]).</p>	<p>A total of 47 patients with a diagnosis of schizophrenia participated in the study (35 male, 12 female). Patients were inpatients as well as outpatients, and were recruited from several mental health institutions in the North of the Netherlands. Clinicians screened their caseload and selected patients based on three questions of the multidimensional construct of insight to estimate insight level and to ensure that both patients with</p>	<p>In the scanner, task instructions were once more presented on the screen. The self-reflection task contained 180 sentences, subdivided into three main conditions (self, other, and semantic) of 60 sentences each. Total task duration was 15 minutes long.</p>	<p>Better insight was associated with greater response in the inferior frontal gyrus, anterior insula, and inferior parietal lobule during self-reflection. In addition, better cognitive insight was associated with higher activation in ventromedial prefrontal cortex during self-reflection.</p>

				good and with poor insight would be selected.		
Verma, D., Srivastava, M.K., Singh, S.K., Bhatia, T. & Deshpande, S.N. (2016). Lifetime suicide intent, executive function and insight in schizophrenia and schizoaffective disorders. <i>Schizophr. Res.</i> , 178, 12–16.	This study was investigating the triangular relationship between suicide intent, insight and cognitive competence in schizophrenia.	N=175 DSM-IV TR diagnoses of schizophrenia or schizoaffective disorder	All the subjects were interviewed on Beck's cognitive insight scale and tested on the Trail Making Test. All the subjects who had lifetime history of suicide attempt were interviewed on Pierce's suicide intent scale.	All the subjects were interviewed on Beck's cognitive insight scale and tested on the Trail Making Test. All the subjects who had lifetime history of suicide attempt were interviewed on Pierce's suicide intent scale.	N/A	Our study suggests that good insight and better executive functioning may be significantly correlated with suicide attempts at some time during the course of illness.
Weiden, P., Kozma, C., Grogg, A. & Locklear, J. (2004). Partial compliance and risk of rehospitalization among California Medicaid patients with schizophrenia. <i>Psychiatr Serv</i> 55, 886–891.	Retrospective Study The objective of this study was to evaluate the relationship between compliance with an antipsychotic medication regimen and risk of hospitalization in a cohort of California Medicaid patients with schizophrenia.	N=4,325 Outpatients for whom antipsychotics were prescribed for treatment of schizophrenia from 1999 to 2001.	Patients were followed for one year and had an average of 19.1 dispensing events.	DSM dx of schizophrenia. patients were also required to have at least one prescription in the six months before their index date.	Compliance behavior was estimated by using four different definitions: gaps in medication therapy, medication consistency and persistence, and a medication possession ratio.	Risk of hospitalization was significantly correlated with compliance. With all definitions, lower compliance was associated with a greater risk of hospitalization over and above any other risk factors for hospitalization. A gap of 11 to 30 days was

						associated with an OR of 2.81, and a gap of more than 30 days was associated with an OR of 3.96. Limitations: This study did not take into account the risk factor of lack of insight for these patients
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