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Motivation and Social Withdrawal in Schizophrenia: Factors Related to Passive Social Withdrawal and Active Social Avoidance

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Motivation and Social Withdrawal in Schizophrenia: Factors Related to Passive Social Withdrawal and Active Social Avoidance

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Abstract

Schizophrenia is a disabling disorder and social withdrawal in schizophrenia is related to particularly adverse outcomes. Social withdrawal may be a result of “passive” motivation (disinterest or lack of drive to engage with others) or “active” motivation (fear, hostility, or distrust of others). The purpose of this study was to better understand passive social withdrawal and active social avoidance, by exploring their relationships with social abilities and social functioning outcomes. In addition, we explored whether the EEG frontal alpha asymmetry hypothesis, which has been previously linked to shyness and sociability, might contribute to our understanding of social withdrawal motivation.

This was a cross-sectional study that used regression models to evaluate the relationships between motivation to withdraw, social abilities, and social functioning outcomes. Electroencephalographic (EEG) recordings were also used to explore whether frontal alpha asymmetry is related to differences in symptoms. Overall, we found differences in passive and active withdrawal across predictors and functional outcomes. Passive social withdrawal substantially predicts social functioning and is distinct from the effects of social cognition and social competence. Active social avoidance is uniquely associated with cognitive bias. Finally, we describe a potential relationship between frontal alpha asymmetry and social withdrawal motivation, although our sample size was not large enough to make generalizations. Overall, this study suggests the importance of focusing specifically on motivation when treating social withdrawal and presents suggestions for future research and interventions.

Motivation and Social Withdrawal in Schizophrenia: Factors Relate to Passive Social Withdrawal and Active Social Avoidance

Introduction

Schizophrenia is a chronic and severe psychiatric disorder, shown to have a robust negative impact on individuals and on society as a whole. The disorder is related to a variety of adverse outcomes, including diminished quality of life, depression, impaired physical health, stigma, high risk of suicide, homelessness, and substance abuse (Millier, et al., 2014). The disorder also impacts society as a whole, including increased health care use and family/caregiver burden. In addition, due to the severity of the disorder and insufficient treatment options, schizophrenia puts a disproportionately high burden on the global economy (Ho, Andreasen, & Flaum, 1997; Insel, 2008; Chong, et al., 2016). Thus, a better understanding of the symptoms and functional outcomes associated with schizophrenia is needed in order to develop more effective treatments and to improve outcomes for people affected by the disorder.

The current understanding of schizophrenia is particularly lacking in regard to negative symptoms. Positive symptoms of the disorder, such as hallucinations and delusions, have received much attention in research literature and are typically addressed and managed with pharmacologic interventions. In contrast, negative symptoms, such as apathy, alogia, anhedonia, and social withdrawal are not effectively treated by any one form of treatment (Buckley, Harvey, Bowie, & Loebel, 2007; Sarkar, Hillner, & Velligan, 2015). Negative symptoms are particularly disabling for patients, as they are typically chronic, persist during periods of remission, and are related to overall poor functioning and quality of life (Fervaha, Foussias, Agid, & Remington, 2014;

Novick, Montgomery, Cheng, Moneta, & Haro, 2015). In addition, negative symptoms are not merely a by-product of hallucinations and delusions. The literature suggests that baseline functioning and treatment response may be more strongly related to negative symptoms than positive symptoms (Rabinowitz et al., ,2012). Due to the strong impact of negative symptomology and lack of treatment options, in 2006 the National Institute of Mental Health (NIMH) called for a research focus on negative symptoms, examining their etiology and treatment (Kirkpatrick, Fenton, Carpenter, & Marder, 2006). The NIMH MATRICS initiative (Measurement and Treatment Research to Improve Cognition in Schizophrenia) identified a need for a better understanding of negative symptoms in order to promote more effective treatments. In line with this need, the goal of this study is to gain a more thorough understanding of one commonly experienced negative symptom: social withdrawal.

Social Withdrawal in Schizophrenia

Social withdrawal has been identified as one of the most common negative symptoms in patients (Bobes, Arango, Garcia-Garcia, & Rejas, 2011) and is a predictor of adverse functional outcomes. Social withdrawal is often present early in the etiology of the disorder, is a predictor of later psychosis in children at a high-risk for the disorder (Matheson et al., 2013), and may contribute to the development and maintenance of positive symptoms (Cannon et al., 2016; Velthorst et al., 2009; Cannon et al., 2008, Johnstone, Ebmeier, Miller, Owens, & Lawrie, 2005). In addition, there is some evidence to suggest that the behavior of socially isolating may alter the expression of genes that contribute to the onset of later psychosis (Jiang, Rompala, Zhang, Cowell, & Nakazawa, 2013). Social withdrawal is also a particularly concerning symptom, because it reduces the likelihood and quality of treatment engagement (Kreyenbuhl, Nossol, & Dixon, 2009). Individuals with a tendency to withdraw socially are less likely to be physically present in therapy and to be engaged in therapeutic settings (Elis, Caponigro, & Kring, 2013). Thus, although various psychosocial and cognitive-based interventions may be effective in treating some symptoms of the disorder (Atkinson, Coia, Gilmour, & Harder, 1996; Lysaker et al., 2012; Elis, Caponigro, & Kring, 2013; Terzian et al., 2013; Morin & Franck, 2017; Ma et al., 2019), patients with social withdrawal often show high drop-out rates and poor treatment engagement. These reasons warrant further investigation of social withdrawal in schizophrenia, in order to better understand factors underlying this symptom and to devise more effective and personalized treatments for impaired social functioning (Harvey, Strassing, & Silberstein, 2019).

In a recent summary of social disability in schizophrenia, Green et al. (2018) described two sets of determinants of social withdrawal: ability and motivation. Ability refers to the "skills needed to interact with one's world," such as social cognition and nonsocial cognition (memory, attention, processing speed, etc.). On the other hand, social *motivation* refers to one's willingness or drive (or lack of) to approach or avoid social interaction. The following sections describe motivational differences in social withdrawal (passive versus active) and how social abilities may play a role in motivation. Finally, we explore how one hypothesis of neurophysiological functioning, the frontal alpha asymmetry hypothesis, may help inform this line of research.

Motivational Differences: Passive versus Active

It is important to consider motivational differences that may contribute to social withdrawal and functioning. In line with Gray's model of behavioral approach and avoidance (Gray, 1987), Reddy et al. (2014) hypothesized about two distinct motivational systems in schizophrenia that may result in social withdrawal: behavioral approach vs behavioral avoidance. Social withdrawal in schizophrenia may be a result of a *lack* of behavioral approach motivation, resulting in a general disinterest or reduced drive to engage in social activities. On the other hand, social withdrawal may also be the result of *heightened* behavioral avoidance, such that an individual actively avoids social activities out of fear, distrust or concern about hostile intentions of others. These two systems are neurologically distinct from one another (Insel, 2010; MacDonald & Macdonald, 2011) and varying interactions between the two motivational systems (reduced approach plus heightened avoidance) seem to result in the heterogeneity in social withdrawal observed in schizophrenia (Reddy et al., 2014). In general, severity of each of these motivational factors are related to greater severity of symptoms and worse overall functioning (Blanchard, Horan, & Brown, 2001; Horan & Blanchard, 2003; Horan, Kring, & Blanchard, 2006; Grant & Beck, 2010; Achim, et al., 2013).

One question that follows is whether these motivational distinctions are related to real differences in social functioning. Robertson et al. (2014) examined the relationship between motivational differences and real-world social functioning using the Positive and Negative Syndrome Scale (PANSS; Kay, Fiszbein, & Opler, 1987). The PANSS is a gold standard research assessment of symptom severity in schizophrenia, that includes two different items related to social withdrawal: passive/apathetic withdrawal and active social avoidance. "Passive/apathetic social withdrawal" refers to a diminished interest and initiative in social interactions, seeming to reflect reduced approach motivation. “Active social avoidance” is characterized by an intentional avoidance of social interaction, as a result of unwarranted fear, hostility, or distrust, which seems to reflect heightened avoidance motivation. They found that severity on each of these PANSS items significantly predicted real-world social functioning. However, passive/apathetic withdrawal was much more strongly related to adverse functioning, explaining 25% of the variance of social functioning, while active social avoidance only explained 3.5%. Similarly, Kalin et al. (2015) found that both passive and active social withdrawal predicted real-world social functioning, while passive was a relatively stronger predictor of functioning.

However, to assess real-world functioning outcomes, the above two studies used observer ratings based on a semi-structured interview with participants. This kind of assessment requires that the rater use clinical judgment to assign ratings about a person’s social functioning. Unfortunately, there are limitations to this kind of assessment. There appears to be a negative bias of mental health workers when it comes to patients’ functioning, such that observers/clinicians have a tendency to underestimate a person’s own social functioning and quality of life (Ofir-Eyal, Hasson-Ohayon, Bar-Khalifa, Kravetz, & Lysaker, 2017). On the other hand, there are also limitations to strict self-report measures, because of patient challenges with insight into their own symptoms and behaviors (Sabbag et al., 2012; Gould, Sabbag, Durand, Patterson, & Harvey, 2013; Harvey, Strassnig, & Silberstein, 2019). Given discrepancies found between observer rating scales and self-report measures, the present study aims to expand upon this research by including both self-report and observer-rated social functioning measures.

Social Abilities and Social Withdrawal

Another question to consider is whether an individual's social abilities are systematically related to differences in motivation for social withdrawal. Previous research has revealed a variety of ability-related factors that contribute to social withdrawal in schizophrenia (e.g. Lysaker et al., 2012; Marder & Galderisi, 2017; Green, Horan, & Lee, 2019). Researchers have hypothesized that deficits in aspects of social cognition and social competence make it challenging for individuals with schizophrenia to understand and interact effectively with others, leading to aversive or discouraging experiences during social interactions. These negative experiences may then cause an individual to either actively avoid most social interactions or experience decreased motivation and social disinterest (Quinlan, Roesch, & Granholm, 2014). Accordingly, there are social cognitive interventions aimed at targeting these predictors that show promising effects on symptoms (Kurtz & Richardson, 2012; Fiszdon & Reddy, 2012; Kurtz, Gagen, Rocha, Machado, & Penn, 2016), although the relationship between treatment benefits and real-world functioning has not been consistently demonstrated (Horan & Green, 2019; Green, Horan, & Lee, 2019).

Social competence, or one's ability to perform social activities, in part predicts social withdrawal and functioning (Kalin et al., 2015). However, the direction of this relationship is unclear. There is some evidence to suggest that poor social competence leads to negative social experiences, which contributes to social anxiety and a tendency to withdraw from others (Nemoto et al., 2019). Conversely, Sitzer, Twamley, Patterson,

& Jeste (2008) found that social skills performance and self-reported frequency of social contact were negatively related, such that patients with better social skills reported fewer social contacts. One possible explanation for this finding is that individuals with less social skills may be less aware of their social interactions and are thus less accurate in their self-reports. Another explanation is that individuals with greater social skills may have more insight into their symptoms and be more worried about how others perceive them. Since treatment for schizophrenia often involves social skills training in an effort to improve social competence (Kopelowicz, Liberman, & Zarate, 2006), it is important to understand whether social competence relates to one's motivation to withdraw (Granholm, Holden, & Worley, 2018).

Another category of predictors of social withdrawal in schizophrenia include aspects of social cognition. Social cognition refers to the specific mental processes underlying one's ability to perceive, understand, and interpret social information, including recognizing the thoughts and emotions of others, the ability to distinguish others' thoughts from one's own, and social attributional biases. While non-social neurocognition (e.g. memory, attention, processing speed) modestly predict social functioning outcomes, social cognitive abilities strongly predict social functioning outcomes (Green & Horan, 2010; Fett, Viechtbauer, Dominguez, Os, & Krabbendam, 2011; Lam, Raine, & Tee, 2014). *Emotion recognition*, or the ability to perceive and understand others' emotions, is often impaired in schizophrenia and related to adverse social interactions (Kohler et al., 2010), further increasing the tendency to social withdrawal. *Theory of mind*, or the ability to understand and form ideas about the mental states (e.g. thoughts, beliefs, and intentions) of oneself and others, is also often impaired in the disorder and related to adverse social functioning (Roncone et al., 2002; Kosmidis, Giannakou, Garyfallos, Kiosseoglou, & Bozikas, 2011; Green et al., 2012). Another predictor of social withdrawal includes *hostile attribution bias*, or the tendency to attribute hostile intentions of others in neutral social interactions (Buck, Browne, Gagen, & Penn, 2020; Hansen et al., 2009).

The literature suggests that motivation may play a mediating role in the relationship between cognitive abilities and real-world functioning (Thomas, Luther, Zullo, Beck, & Grant, 2017, Green, Horan, & Lee, 2019). However, previous studies looked at general motivation, and did not look separately at passive versus active motivational processes. A more nuanced understanding of the relationship between motivation and these related factors may help clinicians determine which patients will benefit most from social cognitive interventions. The present study aims to expand upon this line of research by examining relationships between social abilities and passive versus active social withdrawal motivation.

Depression, Motivation, and Withdrawal

It is also important to note that, although depression is typically associated with anhedonia and a tendency towards social withdrawal, there is evidence to show that depression does not fully account for the level of social withdrawal in schizophrenia (Marder & Galderisi, 2017). For example, Robertson et al. (2014) found that, although depressive symptom severity was a significant predictor, it only accounted for a modest 4% of the variance in social functioning. However, this current study included a measure of depressive symptom severity to check whether mood may impact the studied relationships.

Frontal Alpha Asymmetry Hypothesis of Social Withdrawal

In addition to the above mentioned cognitive and behavioral predictors of social withdrawal, are there neurophysiological differences related to passive and active motivations for social withdrawal? The search for neurophysiological markers related to specific symptoms may help to improve diagnostics and individualized treatment approaches (Green, Horan, & Lee, 2019). One possible marker of motivation and social withdrawal behaviors is frontal alpha asymmetry.

The EEG frontal alpha asymmetry hypothesis proposes that asymmetries in frontal activity during electroencephalographic (EEG) recordings are related to emotional and motivational tendencies. Davidson (1993) proposed that frontal EEG asymmetries reflect the activity of underlying brain systems related to motivational tendencies to approach and withdraw from stimuli. Relatively stronger right frontal activity is associated with greater emotional distress, fearfulness, and shyness, while greater left frontal activity is associated with extroversion and being socially outgoing (Schmidt, 1999). Since EEG alpha power is inversely related to brain activation, negative frontal asymmetry values reflect stronger relative right frontal activation (Davidson & Tomarken, 1989).

Previous studies suggest that frontal asymmetry is related to motivation. For example, Hughes, Yates, Morton, & Smillie (2015) used a behavioral task during EEG to test whether frontal asymmetry was related to an individual’s likelihood of choosing to complete a high-effort task when a high-reward was presented (Effort Expenditure for Rewards Task, EEfRT, Treadway, Buckholtz, Schwartzman, Lambert, & Zald, 2009). They found that relatively stronger left frontal activation was associated with increased willingness to pursue high rewards, even when additional effort was required. This suggested that alpha asymmetry may present a neurophysiological marker of approach motivation. Other research has attempted to link frontal alpha asymmetry to underlying brain networks related to motivation (Tops, Boksem, Quirin, Ijzerman, & Koole, 2014; Gorka, Phan, & Shankman, 2015; Tops, Quirin, Boksem, Maarten, & Koole, 2017). That line of research suggests that greater relative right frontal activation reflects aberrant functioning of brain networks that respond to stress in reactive ways. However, it is important to note that there is no known direct evidence that links frontal asymmetry to subcortical structures involved in effort-related decision making and motivation.

Relationships between clinical symptoms (e.g. anxiety, anhedonia, and withdrawal) and frontal EEG alpha asymmetry have been established across various clinical disorders, including schizophrenia, depression, and anxiety (Jetha, Schmidt, & Goldberg, 2009a; Kemp et al., 2010). Gordon, Palmer, & Cooper (2010) found a deficit in left frontal activity at rest, as indicated by greater left alpha power than controls in schizophrenia. Additionally, there is evidence to suggest that EEG alpha asymmetry is a stable trait in adult outpatients with schizophrenia (Jetha, Schmidt, & Goldberg, 2009b).

Another area of work has looked into the relationship between alpha asymmetry and social behaviors. Jetha, Schmidt, & Goldberg (2009a) explored the relationship between resting EEG frontal asymmetry, trait shyness, and trait sociability. They found that high trait shyness was associated with greater resting right frontal EEG activity, while greater trait sociability was associated with greater resting left frontal activity. However, this relationship has not been consistently found. Horan, Wynn, Mathis, Miller,

& Green (2014) found that, alpha asymmetry was not correlated with clinical symptom ratings, on either self-report measures of behavioral inhibition or with clinical symptom ratings. Their results suggested that schizophrenia is associated with frontal alpha asymmetry, though they did not support the hypothesis that this is a potential neurophysiological marker of social behaviors.

It is important to note that the relationship between frontal alpha asymmetry and social withdrawal might be explained by depressive symptoms. It has been hypothesized that anterior brain asymmetry is associated with emotions that are liked to withdrawal, such as fear and disgust (Tomarken, Davidson, Wheeler, & Doss, 1992; Gable, Reis, & Elliot, 2000). Bartolomeo, Erickson, Arnold, & Strauss (2019) found that frontal alpha asymmetry was inversely related to social motivation in youth at a clinical high risk for psychosis. However, this relationship was accounted for by mood symptoms. They suggested that depression in these individuals contributes to reduced approach motivation, leading to negative symptoms. However, Gordon, Palmer, & Cooper (2010) showed that the pattern of asymmetry found in schizophrenia is distinct from that found in depression.

Importantly, frontal alpha asymmetry may present a cortical-level marker of social withdrawal. For example, changes in frontal asymmetry predicted social symptom improvements following psychotherapeutic interventions (e.g. social anxiety symptoms following cognitive behavioral therapy, Moscovitch et al., 2011; reduced social isolation in autism spectrum disorder following social skills treatment, Van Hecke et al., 2015). Such findings present promising ideas for innovative treatments. Various interventions have been able to alter frontal alpha asymmetry using brain stimulation techniques. For example, repetitive transcranial magnetic stimulation aimed at changing EEG frontal asymmetry (by increasing left side activity or decreasing right side activity) results in improvements in depression (Loo & Mitchell, 2005) and anxiety (Pallanti & Bernardi, 2009). Neurofeedback training has been shown to be effective in changing frontal brain asymmetry, which further results in clinically significant improvements in self-reported emotional responses (Allen, Harmon-Jones, & Cavender, 2001; Harmon-Jones, Harmon-Jones, Fearn, Sigelman, & Johnson, 2008, Peeters et al., 2014, Lee et al., 2019; Quaedflieg et al., 2016; Mennella, Patron, & Palomba, 2017, Micoulaud-Franchi et al., 2019). Transcranial direct current stimulation (tDCS) is yet another noninvasive treatment option that targets cortical function and has shown promising results in treating symptoms of schizophrenia (Gupta, Kelley, Pelletier-Baldelli, & Mittal, 2018). If frontal alpha asymmetry is related to motivation and social withdrawal in schizophrenia, it may be a promising treatment target for individuals with treatment-resistant social withdrawal.

Thus, the present study aims to expand upon previous research to examine whether EEG frontal alpha asymmetry is systematically related to social withdrawal in schizophrenia. We propose that frontal alpha asymmetry may present a cortical-level marker of social withdrawal in the disorder and may be related specifically to motivation to withdraw.

Current Study Aims

The present study aimed to expand our understanding of social withdrawal in schizophrenia by distinguishing between motivational differences. First, we aimed to determine whether passive social withdrawal and active social avoidance are systematically related to differences in real-world social functioning. Based on previous findings (Robertson et al., 2014; Kalin et al., 2015), we hypothesized that severity of both passive and active motivations would be directly related to worse social functioning, and passive withdrawal would be a relatively stronger predictor of outcomes. We expanded upon previous literature by including two kinds of outcome measures: trained observer ratings on a clinical interview and patients' self-report ratings of social functioning.

Next, we aimed to examine whether previously established predictors of social functioning in schizophrenia are systematically related to motivational differences. Specifically, we looked at social competence and three aspects of social cognition (emotion recognition, theory of mind, and hostile attribution bias). We hypothesized that all of these factors would predict both passive withdrawal and active avoidance. We expected hostile attribution bias to be a strong predictor of active social avoidance, given the negative interpretations of others inherent in the definition of active social avoidance. Findings from this aim may help clinicians determine whether specific interventions (e.g. social skills, social cognitive training) may be beneficial for individuals.

Finally, we aimed to explore one possible neurophysiological correlate of motivation and social withdrawal. We tested the frontal alpha asymmetry hypothesis in relation to social withdrawal motivation in individuals with schizophrenia. We hypothesized that greater right frontal activation at rest would be directly related to heightened social withdrawal, both for passive and active reasons. Although a relationship between social functioning and frontal asymmetry has been previously studied, this would be the first study to explore this relationship between this possible biomarker and social withdrawal ratings on the PANSS (a gold standard symptom severity assessment).

Methods

Participants

Participants were recruited from an outpatient program for adults with schizophrenia (posted fliers, internet postings, and referrals from other participants and healthcare providers). Those who expressed interest went through an in-person or telephone screening with research personnel. Eligible participants were then invited to participate. Inclusion criteria were: (1) over the age of 18, (2) right-handedness (3) presence of DSM-IV diagnosis of schizophrenia or schizoaffective disorder, (4) no current alcohol or substance abuse or dependence, (5) ability to provide informed consent, (6) no past or present significant medical or neurological illness (e.g. seizures or head trauma), and (7) not pregnant.

Interview procedure

The interview and self-report portions of this study were part of a larger study that investigated commonalities and differences related to social processes between schizophrenia and autism spectrum disorders (Rabany et al., 2019). It was approved by the Institutional Review Board at Hartford Hospital. Eligible participants were scheduled for appointments with trained research assistants. Appointments typically lasted between six-to-eight hours long, depending on participant availability and research staff’s evaluation on how long the participant could remain attentive for testing. During an initial visit, participants were assessed for the presence of schizophrenia or schizoaffective disorder using the Structured Clinical Interview for DSM-IV Axis I disorder. Participants were administered self-report questionnaires, clinical interviews, and tasks assessing social cognition and social functioning.

Prior to administering the clinical interviews, all research assistants were trained in-depth on the interviews until they reliably scored with 90% agreement. All clinical interviews were completed with one research assistant. All interviews with participants were video-recorded and later scored by a second research assistant. Any discrepant scores were discussed by the trained research staff to meet consensus.

In addition to the clinical assessments above, a subsample of the participants (n=9) agreed to be enrolled in an additional study using a TMS-EEG paradigm to collect neurophysiological data. EEG data acquisition was a part of a larger study investigating cortical connectivity mechanisms underlying symptoms of schizophrenia using a TMS-EEG paradigm. Clinical data from the first study was matched with neurophysiological data from the second study to examine our third aim: whether neurological differences detected by EEG may help us understand differences in social withdrawal.

Measures

Social withdrawal motivation. The *Positive and Negative Syndrome Scale* (PANSS) (Kay, Fiszbein, & Opler, 1987) was designed specifically for use in Schizophrenia samples, to measure positive, negative, and global symptomology. The scale was administered and scored by a research assistant in interview format. We specifically used the following items for our study: passive/apathetic social withdrawal and active social avoidance. We used scores on these two items to map onto the similarly named constructs.

Social functioning outcomes. The *Social Functioning Scale* (SFS) (Birchwood, Smith, Cochrane, Wetton, & Copestake, 1990) was used to assess outcomes of social functioning. The assessment was administered as a self-report questionnaire. Items assess participant's ability to complete tasks related to social interactions, their recent engagement in social activities, and their vocational abilities. The SFS includes items designed to measure social withdrawal, in addition to general social functioning (van Der Wee et al., 2019). This tool was specifically designed for use in schizophrenia samples and has been shown to be reliable, valid, sensitive, and responsive to change.

The *Quality of Life Scale* (QLS) (Heinrichs, Hanlon, & Carpenter, 1984) was also specifically designed for use in Schizophrenia samples and is used to assess deficit symptoms related to areas of quality of life. The scale was administered and scored by a research assistant in interview format. Thus, this measure required that the trained rater make clinical judgments based on the participant's responses to the interview questions. For the purpose of assessing social functioning, we used the "Interpersonal Relations" category, which consists of 8 items related to interpersonal and social experiences, including household relations, friendships, acquaintances, social activities, social network, social initiative, social withdrawal, and sociosexual relations.

Social competence and social cognitive factors. The *Social Skills Performance Assessment (SSPA)* (Patterson, Moscona, Mckibbin, Davidson, & Jeste, 2001) was used to assess social competence during social interactions. Participants were engaged in a conversation with a trained interviewer, who was acting as a conversational partner, for two 3-minute role plays. The two role play scenarios included (1) greeting a new neighbor and (2) calling a landlord to request that they repair a leak.

Interviewers then rated participants on various dimensions, including fluency, clarity, focus, negotiation ability, persistence, and social appropriateness. Higher scores suggest greater social competence.

The *Bell-Lysaker Emotion Recognition Task* (BLERT) (Bryson, Bell, & Lysaker, 1997) was used to assess Emotion Recognition. Participants were presented with a series of 21 10-second video clips and asked to identify which emotional state the individual was expressing, including happiness, sadness, fear, disgust, surprise, anger, or no emotion. Performance on this test is designed to predict social functioning independent of neurocognition.

The *Hinting* task was used to assess theory of mind (Corcoran, Mercer, & Frith, 1995). Participants were orally presented with 10 short passages presenting an interaction and brief conversation between two characters. At the end of each passage, one of the characters leaves a hint about their intentions. Participants were then asked what the character really meant. A correct response would receive a score of 2. If they did not respond accurately, they were read a second hint and could receive a score of 1 if they respond correctly. Total scores range from 0-20.

The Ambiguous Intentions Hostility Questionnaire (AIHQ) (Combs, Penn, Wicher, & Waldheter, 2007) was used to assess hostile attribution bias. The AIHQ consists of second-person vignettes of negative social situations with an unknown cause (e.g. "you are walking by a group of young people who laugh as you pass by"). For each vignette, participants were asked to rate the following on a Likert scale: (1) the intentionality of the other's action, (2) how angry it would make the person feel, and (3) how much he or she would blame the other person. These three items were totaled for an overall "blame score", which suggests the participant's tendency to attributing hostile intentions of others in social situations (Buck et al., 2017). Higher scores suggest a greater tendency towards hostile attributions.

Depression. The *Beck Depression Inventory*, Second Edition (Beck, Steer, & Brown, 1996) was used to assess severity of depressive symptoms in the past two-week time period. This is an 11-item self-report inventory used to assess a range of depressive symptoms, including severity of cognitive, affective, and somatic symptoms of depression. Higher scores indicate more severe levels of symptoms.

EEG acquisition & processing

During EEG data collection participants were instructed to keep their eyes open and to fixate at the marked stable target, while trying to minimize the numbers of blinks. EEG was recorded using a 64-channel TMS-compatible EEG system, with direct current BrainAmp MR plus amplifiers (BrainAmp MR Plus Amplifier, Brain Product GmbH, Gilching, Germany). The amplifiers were powered by the BrainAmp PowerPack, an external rechargeable battery, which allowed for recording in direct current mode (BrainAmp PowerPack, Brain Product GmbH, Gilching, Germany). Direct current EEG data were recorded by Brain Vision Recorder software (Brain Vision Recorder, Brain Products GmbH, Gilching, Germany). The BrainAmp amplifier and their accessories fulfilled all applicable requirements of the Medical Devices Directive 93/42/EEC (Class IIa, Annex IX) and the IEC 60601 standards (Protection class I, EN 60601-1, Type BF) on essential performance, electrical safety, and electromagnetic compatibility.

In addition to sixty-two EEG channels, an electrooculography (EOG) channel was recorded for offline correction of eye movements, blinks, and micro-saccadic artifacts.

The EEG signals were online-referenced to the FCz electrode and grounded to the AFz electrode. All signals were hardware-filtered between 0.016 and 1000 Hz and sampled at 5000 Hz (Brain Vision Recorder, Brain Products GmbH, Gilching, Germany).

EEG data were preprocessed using BrainVision Analyzer 2.2 (Brain Products GmbH, 2019). Data was visually inspected for the presence of any obvious muscle artifacts or excessively noisy channels. We used topographic interpolation to remove and replace bad channels. Manual artifact correction and rejection procedure were performed. To reference to a neutral reference, we used the Reference Electrode Standardization Technique (REST) toolbox in MATLAB (The Mathworks, Inc., Natick, MA, USA) (Dong et al., 2017). REST is a method used to minimize potential effects of the EEG reference on signals by transforming average scalp points at a reference point at infinity thus resulting in a theoretical zero reference. The sampling rate was changed to 250 Hz and a 0.5- to 100-Hz band pass filter was applied. Independent component analyses (ICA) was used to remove ocular artifacts. ICA separates components of the EEG waveform by the kurtosis of their amplitude over time (Vigário, 1997). This technique allows for the isolation of pure eye activity in EEG recordings while minimizing data loss.

Clean single-trial EEG data were segmented into 2-second epochs. We performed steps to compute frontal alpha asymmetry that have been used across various previous studies (Allen, Coan, & Nazarian, 2004; Hughes, Yates, Morton, & Smilie, 2015; Pitchford & Arnell, 2019) using customized scripts in MATLAB. Hilbert transformation was used to extract amplitudes of each frequency of the alpha frequency range (8-13 Hz). Mean alpha power was computed from homologous frontal electrodes

F3 and F4, averaged across frequencies with outlier analyses that were performed with the criterion of standard deviation > 3. Mean number of data points used in the calculation = 28109 (patient n = 9; SD = 1883.92), mean percent rejection = 4.95% (SD<0.01). In order to calculate asymmetrical activity, alpha power values were first log transformed and a difference score summarized the relative activity at homologous right and left hemispheres: The log difference score [ln(Right) – ln (left)] provides a unidimensional scale (ranging -1 to +1) representing relative activity of the right and left frontal area. Because it is assumed that alpha power is inversely related to cortical activity (Laufs et al., 2003), greater alpha power values in the right side indicates less cortical activity in the right versus left.

Results

Descriptive statistics. A total of fifty-two patients participated. Demographic information for the sample is presented in *Table 1*. The sample was comprised of young adults (67% male), with ages ranged between 19-34 years of age. ANOVA was used to check for effects of demographic characteristics (age, sex, and race) on all other study variables. All results were not significant (p-values> 0.05) indicating that there is not enough evidence to suggest a relationship between demographic characteristics and outcome variables of interest.

Medications. All participants were prescribed atypical antipsychotics, and 11 patients were concurrently prescribed first generation antipsychotics. To test for effects of antipsychotic medication intake, bivariate correlations between chlorpromazine (CPZ) equivalent dose and all study variables were examined. None of the correlations were significant, indicating that our results are not likely due to effects of medication intake.

In addition, 22 participants were also prescribed a mood stabilizer or antidepressant. Independent samples t-tests were used to identify any differences in study variables based on whether a participant was prescribed mood stabilizers or antidepressants. There were significant differences in scores on the *Social Functioning Scale* (SFS) ($t(46) = -2.03$, $p=0.048$), indicating that participants taking antidepressant medications reported worse social functioning. All other results were null.

Depression scores on the BDI-II were not significantly correlated with any of the outcome variables. In addition, when analyses were run with depression as a covariate, it did not change any patterns of significance. BDI-II mean score was 11.2 (SD=8.6), indicating minimal to mild depressive symptom severity in the majority of participants.

Aim 1

We used multiple regression to evaluate whether passive withdrawal and active social avoidance are related to differences in social functioning.

Clinical interview ratings. Multiple regression was used to test a model for predicting patients' social functioning based on a clinical interview (Quality of Life Scale, Interpersonal Relations subscale) from their ratings on passive/apathetic withdrawal and active social avoidance. Tests to see if the data met the assumption of collinearity indicated that although the predictors were correlated, multicollinearity was not a cause for concern (passive/apathetic withdrawal, Tolerance=0.454, VIF=2.20; active social avoidance, Tolerance= 0.464, VIF= 2.154). The data met the assumption of independent errors (Durbin-Watson value= 2.46). The histogram of standardized residuals indicated that the data contained approximately normally distributed errors, as did the normal P-P plot of standardized residuals, which showed points that were not completely on the line, but close.

Results are shown in *Table 2*. After age, sex, and race were entered in a first step, passive withdrawal and active social avoidance were entered in a second step. The overall model was significant once passive withdrawal and active social avoidance were added ($F(5,38) = 5.059$, $\Delta R^2 = 0.336$, $p < 0.01$), accounting for 40% of the variance in social functioning. Only passive/apathetic social withdrawal individually predicted social functioning based on clinical interview ratings ($\beta = -0.512$, $t(38) = -0.564$, $p<0.01$), while active social withdrawal did not ($\beta = -0.136$, $t(38) = -0.739$, $p > 0.05$).

Self-report ratings. Multiple regression was also used to test a model for predicting patients' social functioning, as measured by patient self-report. As reported above, multicollinearity was not a concern. The data met the assumption of independent errors (Durbin-Watson value= 1.902). The histogram of standardized residuals indicated that the data contained approximately normally distributed errors, as did the normal P-P plot of standardized residuals, which showed points that were not completely on the line, but close.

Results are shown in Table 3. Age, sex, and race were entered as covariates as a first step. On the second step, passive withdrawal and active social avoidance were entered simultaneously. The overall model was not significant ($F(5,38) = 1.770$, $R^2 = 0.189$, $p > 0.05$), and neither passive nor active social withdrawal predicted social functioning on the self-report measure.

Based on the initial results showing that participants prescribed antidepressants had significantly lower social functioning scores, we also ran this model with antidepressant intake included. When we included mood medications as a covariate, none of the results significantly changed, except that prescription of mood stabilizer or antidepressant medication significantly predicted self-reported social functioning (β = -0.403, t(38) = -2.80, p < 0.01).

Aim 2

Next, we assessed whether abilities related to social functioning (social competence and aspects of social cognition) are systematically related to social withdrawal motivation. Multiple linear regression analyses were used to test models for predicting patients' social withdrawal motivation from performance on four social ability measures: Hinting (theory of mind), BLERT (emotion recognition), AIHQ blame bias (hostile attribution bias), and SSPA total score (social competence).

Predicting passive withdrawal. The outcome variable of the first model was passive/apathetic social withdrawal (Table 4). The overall model was not significant ($F(7,34) = 1.388$, $R^2 = 0.222$, $p > 0.05$), and none of the four factors significantly predicted passive withdrawal. Tests to see if the data met the assumption of collinearity indicated that multicollinearity was not a concern (Hinting, Tolerance=0.758, VIF=1.319; BLERT, Tolerance= 0.728, VIF= 1.374; AIHQ blame bias, Tolerance= 0.875, VIF= 1.143; SSPA, Tolerance= 0.935, VIF= 1.070). The data met the assumption of independent errors (Durbin-Watson value= 2.154). The histogram of standardized residuals indicated that the data contained approximately normally distributed errors, as did the normal P-P plot of standardized residuals, which showed points that were not completely on the line, but close.

The outcome of the second model was active social avoidance (Table 5). The overall model was also not significant ($F(7,34) = 1.843$, $R^2 = 0.275$, $p > 0.05$). The only factor that significantly predicted active social avoidance was hostile attribution bias ($\beta = 0.344$, $t(34) = 2.20$, $p < 0.05$). The other three factors (theory of mind, emotion recognition, and social competence) did not significantly predict active social avoidance. As reported above, multicollinearity was not a concern. The data met the assumption of independent errors (Durbin-Watson value= 1.904). The histogram of standardized residuals indicated that the data contained approximately normally distributed errors, as did the normal P-P plot of standardized residuals, which showed points that were not completely on the line, but close.

Aim 3

Finally, we evaluated whether frontal alpha asymmetry is related to differences in social withdrawal motivation and social functioning in individuals with schizophrenia. The sample used to evaluate this aim consisted of n=9 individuals diagnosed with schizophrenia. Average age was 26 years old (SD= 3.58). There were 7 males and 2 female participants. Participant races were White (n=5), Black (n=1), Asian (n=1) and not reported (n=2).

Assuming that alpha neural oscillation is inversely related to activation, higher scores indicate relatively greater relative left frontal activation, while lower scores indicate relatively greater right frontal activation at rest. Since negative frontal asymmetry values reflect stronger relative right frontal activation, and stronger right front activation is associated with emotional distress and trait shyness, we predicted that lower alpha asymmetry values would be associated with higher levels of social withdrawal. We expected alpha asymmetry values and social withdrawal to be inversely related.

Spearman correlations were used to evaluate the relationship between frontal alpha asymmetry scores and variables of interest, including passive/apathetic social withdrawal, active social avoidance, self-report social functioning (SFS), and interviewer rated social functioning (QLS). Results are shown in *Table 6.* Effect sizes suggest strong inverse relationships between resting frontal alpha asymmetry and (1) passive withdrawal, (2) active avoidance, and (2) observer-rated social functioning in our sample. However, none of the correlations were statistically significant, and thus we are not able to confidently make inferences about the population at-large.

Discussion

The purpose of this study was to gain a better understanding of social withdrawal in schizophrenia by exploring differences in motivation. We used a gold-standard assessment of symptom severity (PANSS; Kay, Fiszbein, & Opler, 1987) to measure differences in patient's motivation to withdraw. Differences in passive and active withdrawal were examined by exploring differences in ability-related predictors and in social functioning outcomes. In addition, we explored whether the EEG frontal alpha asymmetry hypothesis, which has been previously linked to trait shyness and sociability, might help improve our understanding of social withdrawal motivation. Overall, we found distinctions between passive and active withdrawal in both predictors and functional outcomes.

Relationships with social functioning outcomes

First, we examined whether passive social withdrawal and active social avoidance were related to differences in social functioning outcomes. A strength of this study was that we included outcome measures of both observer ratings during a clinical interview and patients' self-reports of social functioning. When social functioning was assessed using observer ratings following a clinical interview, passive withdrawal predicted social functioning, while active social avoidance did not. This is line with previous research showing the substantial impact of passively motivated social withdrawal on patient functioning (Robertson et al., 2014; Kalin et al., 2015). This highlights the importance of targeting passive motivations for withdrawal when aiming to improve patients' social functioning.

Further, our findings showed that neither passive nor active motivations for withdrawal predicted social functioning on a self-report measure. This may be a result of patients' limited insight into their own symptoms and behaviors (Sabbag et al., 2012; Gould, Sabbag, Durand, Patterson, & Harvey, 2013; Harvey, Strassnig, & Silberstein, 2019). However, it may also be the case that interviewers inaccurately estimate a patients' social functioning and quality of life (Ofir-Eyal, Hasson-Ohayon, Bar-Khalifa, Kravetz, & Lysaker, 2016). Social withdrawal may be especially challenging to treat when there are such discrepancies between observer and patient ratings. This discrepancy highlights the importance of mental health workers collaborating with patients to come to a common understanding of the patient's own functioning.

Relationships with social abilities

Next, we examined whether various social abilities, including social competence and aspects of social cognition (theory of mind, emotion recognition, and hostile attribution bias) predicted passive withdrawal and active social avoidance. When looking at active social avoidance, we found that only hostile attribution bias predicted active social avoidance. None of the other factors predicted active social avoidance. This suggests that addressing cognitive biases is an important intervention target in the treatment of active social avoidance.

When testing predictors of passive social withdrawal, none of the factors (social competence and aspects of social cognition) were systematically related to passive motivation for social withdrawal. This suggests that current interventions aimed at social functioning, including improving social competence, teaching social cognitive skills, and challenging cognitive biases may not be useful in targeting passive motivations social withdrawal. This may help explain why passive withdrawal is generally resistant to many interventions.

The finding that almost none of the ability-related factors predicted motivation was unexpected. This provided evidence that social ability and motivation are two distinct factors. Thus, both factors should be considered when treating social withdrawal. An individual with passive/apathetic social withdrawal, showing reduced social participation, may not necessarily benefit from social cognitive training without direct intervention of motivational deficits. Instead, they may benefit from motivation-related interventions such as developing personally meaningful goals and engaging in energizing activities prior to other more traditional social skills or cognitive remediation groups (Thomas, Luther, Zullo, Beck, & Grant, 2017). On the other hand, an individual showing primarily active social avoidance may benefit from cognitive-based interventions aimed at reducing hostile attribution bias.

Frontal EEG alpha asymmetry and social withdrawal

Finally, we examined whether the EEG frontal alpha asymmetry hypothesis might provide a cortical marker of social withdrawal in schizophrenia. According to tests of statistical significance, our data did not support the EEG frontal alpha asymmetry hypothesis. It is likely that our small sample size interfered with our ability to adequately test this hypothesis. Thus, we still explored this potential relationship by examining effect sizes, since effect size is independent of sample size. Effect sizes indicated large magnitude of relationships in this sample between alpha asymmetry and both passive withdrawal and active social avoidance. Frontal alpha asymmetry appeared inversely related to social withdrawal, such that stronger relative right frontal activation was associated with higher severity of both passive and active withdrawal. This finding is in line with previous research showing a similar direct relationship between shyness/introversion and greater resting right frontal EEG activity (Jetha, Schmidt, & Goldberg 2009a; Horan, Wynn, Mathis, Miller, & Green, 2014; Bartolomeo, Erickson, Arnold, & Strauss, 2019). The small sample size unfortunately limits our ability to generalize findings to the population at large and we would need to replicate these findings before we could confidently infer that these relationships are present in the population.

Evidence of a possible relationship between resting alpha asymmetry and withdrawal-related motivation is a promising area of future research. Techniques aimed at directly altering neurophysiology may provide useful interventions for treatment-resistant social withdrawal. If there is a true relationship between frontal resting alpha asymmetry and social withdrawal, then we would expect therapies that target restoration of frontal lobe function to improve symptoms (Gheza, Bakic, Baeken, De Raedt, & Pourtois, 2019). Such therapies might include repetitive transcranial magnetic stimulation aimed at changing EEG frontal asymmetry or neurofeedback training in combination with cognitive behavior therapy.

Limitations & future directions

Several limitations of this study should be noted. First, the sample size was relatively small, and crucially small in our third aim. In addition, we were likely not able to capture patients at the most severe end of social withdrawal severity. The requirements of extensive in-person participation for this study may have dissuaded patients with more severe social withdrawal from agreeing to participate. Thus, findings should only be generalized to individuals at an outpatient level with mild-to-moderate levels of withdrawal.

Additionally, all patients were prescribed antipsychotic medications and nearly half were on mood stabilizing or antidepressant medications. Although we checked for effects of medications in our analyses, it is important to acknowledge how long-term medication use may impact motivation and symptoms. Thus, findings may reflect treatment-related changes, rather than organic symptoms of schizophrenia. To better understand the natural consequences of social withdrawal in schizophrenia, future studies should include unmedicated individuals with first episode psychosis.

Finally, we used items from the PANSS to measure social withdrawal, because it is such a widely used and well-validated instrument in schizophrenia research. Unfortunately, the PANSS restricts symptom ratings to be measured on a discrete scale, even though the underlying constructs are believed to be a continuous variable and visual inspection of our data suggested that ratings of passive and active withdrawal fit a normal distribution. It may be useful to look at these questions using a continuous measure that is specifically designed to measure motivational differences in social withdrawal.

Conclusions

Our results demonstrate differences in motivation that have important implications for social functioning in schizophrenia. Differences in motivation to withdraw is a critical area to consider when evaluating and treating social withdrawal in patients. Passively motivated social withdrawal (i.e. an apathetic disinterest in others) substantially predicts social functioning and is distinct from the effects of social cognition and social competence. This highlights the need for interventions other than just social-cognitive and social-skills training when treating passive social withdrawal. Conversely, when social withdrawal is active (i.e. motivated by fear, hostility, or distrust of others), it is strongly associated with cognitive bias, and thus may respond better to cognitive-based interventions.

Finally, although we did not find a significant relationship between frontal alpha asymmetry and social withdrawal motivation, we propose that our preliminary results warrant further investigation with a larger sample. Given the treatment prospects around identifying cortical-level markers of symptoms, future research in this area would be promising.

Appendix

Table 1

Demographic Characteristics of Participants (N = 52)

Characteristic	*n*	%
Sex		
Male	35	67.3
Female	17	32.7
Race		
White	38	73.1
Black	7	13.5
Asian	2	3.8
American Indian/Alaskan Native	2	3.8
Not Reported	3	5.8
Age		
Mean (SD)	25.66	(3.58)

Table 2

Multiple Regression Predicting Social Functioning on a Clinical Interview Rating (n = 44)

Step	Predictor	β	r	R^2	R^2 *Change*	*F*
Step 1	Age	0.207	0.192			
	Sex	-0.151	-0.143			
	Race	-0.045	-0.055	0.064	0.064	0.909
Step 2	Age	0.181	0.192			
	Sex	0.010	-0.143			
	Race	-0.214	-0.055			
	PASW	**-0.512****	-0.564			
	ASA	-0.136	-0.481	0.400	0.336	**5.059****

**$p<0.01$

PASW, *Passive/Apathetic Social Withdrawal*; ASA, *Active Social Avoidance*

Table 3

Multiple Regression Predicting Social Functioning on a Self-Report Measure (n = 44)

Step	Predictor	β	R	R^2	R^2 *Change*	*F*
Step 1	Age	0.222	0.222			
	Sex	0.035	0.043			
	Race	-0.052	-0.032	0.052	0.052	0.738
Step 2	Age	0.191	0.222			
	Sex	0.133	0.043			
	Race	-0.149	-0.032			
	PASW	-0.103	-0.271			
	ASA	-0.311	-0.348	0.189	0.136	1.770

PASW, *Passive/Apathetic Social Withdrawal*; ASA, *Active Social Avoidance*

Table 4

Multiple Regression Predicting Passive/Apathetic Social Withdrawal (n = 41)

Step	Predictor	β	*r*	R^2	R^2 *Change*	*F*
Step 1	Age	0.035	0.060			
	Sex	0.184	0.141			
	Race	-0.252	-0.214	0.082	0.082	1.129
Step 2	Age	0.014	0.060			
	Sex	0.186	0.141			
	Race	-0.267	-0.214			
	SSPA	-0.153	-0.230			
	BLERT	-0.208	-0.221			
	Hinting	0.159	0.065			
	AIHQ_blame	0.232	0.201	0.222	0.140	1.388

BLERT, *Bell-Lysaker Emotion Recognition Task*; AIHQ, *Ambiguous Intentions Hostility Questionnaire*; SSPA, *Social Skills Performance Assessment*

Table 5

Multiple Regression Predicting Active Social Avoidance (n = 41)

Step	Predictor	β	*r*	R^2	R^2 *Change*	*F*
Step 1	Age	-0.037	-0.011			
	Sex	0.178	0.129			
	Race	-0.210	-0.175	0.060	0.060	0.810
Step 2	Age	-0.115	-0.011			
	Sex	0.190	0.129			
	Race	-0.290	-0.175			
	SSPA	0.080	-0.030			
	BLERT	-0.272	-0.214			
	Hinting	0.304	0.157			
	AIHQ_blame	**0.344***	**0.281**	0.275	0.215	1.843

**p<0.05*
BLERT, *Bell-Lysaker Emotion Recognition Task*; AIHQ, *Ambiguous Intentions Hostility Questionnaire*; SSPA, *Social Skills Performance Assessment*

Table 6

Spearman's correlations with resting frontal alpha asymmetry (n = 9)

Variable	ρ	sig
PASW	-0.594	p=0.120
ASA	-0.674	p=0.067
SFS	0.033	p=0.932
QLS interpersonal rel.	0.599	p=0.117

PASW, *Passive/Apathetic Social Withdrawal*; ASA, *Active Social Avoidance*; SFS, *Social Functioning Scale*; QLS, *Quality of Life Scale*

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