Better Together: Effects and Treatments of Loneliness and Social Isolation Across the Schizophrenia Spectrum

By

Laura Hieber Adery

Dissertation

Submitted to the Faculty of the

Graduate School of Vanderbilt University

in partial fulfillment of the requirements

for the degree of

DOCTOR OF PHILOSOPHY

in

Psychology

June 30, 2019

Nashville, Tennessee

Approved:

Dr. Sohee Park, Ph.D.

Dr. Andrew Tomarken, Ph.D.

Dr. Megan Saylor, Ph.D.

Dr. Bruce Compas, Ph.D.

DEDICATION

This dissertation is dedicated to the many amazing individuals in the Nashville community that volunteered their time and vulnerability to help progress our understanding of the illness they face. Without their openness and willingness to spend countless hours describing their experience or participating in research and, sometimes quite strange seeming, intervention activities, this work would not be possible. I also dedicate to anyone struggling with feeling alone, isolated and unsure where to turn or previously turned away for support. There is a place for all of us to belong, and I hope that this work inspires and presses the field forward toward inclusion efforts to improve well-being for all.

ACKNOWLEDGMENTS

This work has spanned my time in graduate school and has truly been a labor of love. I have many supporters, collaborators and general life cheerleaders to thank, without whom it surely would not have been possible.

Thank you foremost to my advisor, Dr. Sohee Park, for your wisdom, support, and commitment to creative and meaningful scientific investigations. Your passion for schizophrenia research is inspiring, and only surpassed by your compassion for those we aim to study and serve. The freedom and encouragement you grant to explore, ask questions and investigate from any angle of interest is unparalleled and an experience that has truly transformed me both as a researcher and a human.

Thank you to my committee members, Bruce Compas, Andy Tomarken and Meg Saylor. Each of you pivotally shaped the trajectory of my time in graduate school and provided functional support and mentorship that proved imperative to my arrival at this dissertation. Thank you each for your advice, time and belief in me.

Thank you to the members of the Park Clinical Neuroscience Laboratory, past and present; Joel Peterman, Taylor Benson, Rachel Aaron, Megan Ichinose and Lénie Torregrossa, who have been like a second family to share joys and to lean on for support throughout my graduate work. To Heathman Nichols, especially, for countless hours side by side with me keeping our choirs off the ground and for endless support when I second guessed my ideas. To Lindsey McIntosh, Channing Cochran, Matthew Snodgress and all the amazing undergraduate assistants in the lab- we would be literally nowhere without you! Thank you to each of the study participants who volunteered their time and energy to contribute to expanding our scientific knowledge. This work also would not have been possible without the generous financial support of the Lisa M Quesenberry Foundation, the Vanderbilt Curb Scholar program, Vanderbilt University and the NIMH.

I cannot express how deeply appreciative I am to my family and friends for supporting and cheering me along each step of the way. Thank you especially to my husband, Ruben, for listening to me explain my research countless times, loving me unconditionally, and not leaving me when writing made me a stress-monster!

You have all had a part in bringing this to fruition and I am in awe of what is possible through extraordinary social support.

TABLE OF CONTENTS

TABLE OF CONTENTS

LIST OF TABLES

Table Page

LIST OF FIGURES

Figure Page

CHAPTER I

Introduction

Individuals with schizophrenia are among the most socially isolated and stigmatized individuals in our society (Perry et al., 2011), and experience distressing differences in their perception of the world and self-identity (Maher, 1974). Mounting evidence suggests powerful detrimental effects of loneliness as a result of dissonance between desired and present social interaction across virtually all populations (Cacioppo & Cacioppo, 2018). Despite this, little is known about the influence of isolation and loneliness on social perception, severity of psychotic symptoms, or how to approach alleviation of this painful experience. First, key constructs are defined and the epidemic of loneliness is described. Next, evidence of the unique burden of loneliness and isolation on populations vulnerable to psychosis is provided. Then, current treatment of the loneliness epidemic is presented, and the importance of targeting individuals with psychosis more specifically is discussed. Finally, research questions are presented and the scope of this work is defined.

The Imperative of Human Connection

Humans are inherently social beings. This intrinsic need to belong comprises "a pervasive desire to form and maintain at least a minimum quantity of lasting, positive, and significant interpersonal relationships" (Baumeister & Leary, 1995). The strength and intensity of need for affiliation vary across individuals, but it is clear that for both physical and psychological survival and success, optimal levels of social connection and interactions are essential (Cacioppo et al., 2006, 2014; Holt-Lunstad et al., 2010; House et

al., 1988). Obtaining these basic needs for social connection necessarily involve “frequent, positive interactions with other people in an enduring context in which relatedness is associated with concerns for one another's welfare.” (Baumeister & Leary, 1995). In other words, social contact of a somewhat reciprocal and positive nature is essential for an individual to thrive. Previous research indicates that feelings of belongingness are key to inducing a sense of meaningfulness, and that in essence, belongingness is the source of meaning in life (Heine et al., 2006; Williams et al., 2002). Indeed, loneliness has been strongly negatively correlated with life satisfaction and a sense of purpose or meaning in life as well as availability of social network (Zysberg, 2012). I argue that loneliness is a powerful common denominator at the core of cascading damages to health, cutting at the physical and psychological cores that comprise a fulfilling life.

Stress is a necessary but not sufficient mechanism for inducing illness. It may be argued that social distress is the most potent form of stress. Social distress impacts our very source of meaning and threatens the quality of connection that is necessary for survival to even experience other stressors. The stress-buffering model proposes that social relationships protect against adverse effects of stressful life events (Cohen and Wills, 1985). When we lose touch with our community, we in turn lose touch with ourselves, the myriad of benefits gleaned from social relationship, and simple yet crucial reminders of our own humanity. Just as physical malnourishment has deleterious effects on our well-being, social malnourishment (whether determined in first years of life by environment, or later in life through environmental or self-imposed factors) may cause the self to wither away. This weakening occurs in a fashion that has proven to induce some of the most severe symptoms of psychopathology known; namely those of florid psychosis. In fact, social deprivation and distress prove so powerful that these effects may be acutely or chronically

induced even in otherwise healthy individuals, as will be discussed to some length in this manuscript.

To a large extent we understand our world through interacting with others (Echterhoff et al., 2009; Hardin & Higgins, 1996; Swann & Bosson, 2010) and we rely on others to confirm our conceptions of reality. Social distance or deprivation in any form can be seen to elicit undesirable effects. However, feelings of loneliness emphasize the fact that social species require not simply the presence of others but also the presence of significant others whom they can trust, inspire goals and purpose, with whom they can plan, interact, and work together to survive and prosper (Cacioppo & Patrick, 2008).

Indeed, social interactions recruit the neural circuitry that overlaps with the brain regions involved in the reward circuitry, including the ventral tegmental area (VTA) dopamine (DA) neurons and the nucleus accumbens (Gunaydin et al., 2014; Robinson et al., 2002). Conversely, the absence of social contact also triggers a strong desire or craving to seek social interaction. Socially excluded individuals display an enhanced memory for social events (Gardner et al., 2000), and individuals who endorse higher loneliness show increased attention toward social cues (Gardner et al., 2005; Pickett et al., 2004).

William James (1890) hypothesizes that social pain may be even worse than physical pain, writing "If no one turned round when we entered, answered when we spoke, or minded what we did, but if every person we met 'cut us dead,' and acted as if we were non-existing things, a kind of rage and impotent despair would ere long well up in us, from which the cruelest bodily tortures would be a relief." The intensity of distress associated with experiences of social separation have been taken as evidence demonstrating a link between physical and social pain (Eisenberger, 2012), and using aid for physical pain, such

as ibuprofen, has even been demonstrated to partially alleviate social pain (Novembre, 2014, DeWall et al., 2010).

The Construct of Loneliness

Richard Bach (1990), states, “The opposite of loneliness is not togetherness, it's intimacy”. This sentiment echoes the evidenced philosophy that physical presence of significant others in one’s social environment is not necessarily sufficient to foster conditions of well-being. Rather, one needs to feel adequately and intimately connected to avoid feeling lonely. While the particulars of an individual’s need for affiliation vary across a spectrum, absence of optimal intimacy yields similar results for all. Accordingly, a person’s subjective emotional and cognitive assessment of their social position, rather than the pure absence of social stimulation contributes uniquely to their experience, and perhaps the gravity of consequence, of isolation (Cacioppo et al., 2010, Macdonald, Hayes, & Baglioni, 2000).

Therefore, it may be that loneliness has a unique contribution of subjective distress across a spectrum of social involvement. Isolation leads to distress that may manifest in other forms, however the acute social pain of loneliness intensifies any experience of isolation to more dangerous degrees. Loneliness is a chronic, gnawing condition that induces distress and impedes life satisfaction and function. Loneliness has also been characterized as the aversive feelings of separateness, alienation, emptiness, rejection and perceived social isolation (Lynch & Convey, 1979, Sadler, 1978, Weiss, 1973). Perceived social isolation has often been used as an interchangeable term for loneliness (Cornwell & Waite, 2009, Hawkley & Capitanio, 2015, Cacioppo, Fowler, & Christakis, 2009), as subjective appraisal is inherent in the distress. The opposite of loneliness is ascribed as

belongingness or social embeddedness (de Jong Gierveld et al., 2016). Loneliness has been defined as "the unpleasant experience that occurs when a person's network of social relations is deficient in some important way, either quantitatively or qualitatively" (Peplau et al., 1978, Hawkley et al., 2008). This term thus can be applied to define situations in which the number of existing relationships is smaller than is considered desirable, as well as instances in which the quality or intimacy one desires has not been realized.

The Cognitive Discrepancy Model of loneliness developed by Peplau and Perlman (1981) implicates an incongruity between actual versus desired level of social involvement, contributing to feelings of loneliness and suggesting that it is not necessarily the amount of social involvement, but rather a dissatisfaction with the amount that causes this distress. The cognitive discrepancy model of loneliness represents an extension of earlier theoretical ideas developed by Thibaut and Kelley (1959), showing that satisfaction and attraction in relationships is based on an individual's internal Comparison Level. According to this model, individuals judge their interpersonal relationships against an internal standard or expectation. When this standard is met or exceeded, social satisfaction is achieved. However, when current social involvement is beneath this internal standard, dissatisfaction ensues, via loneliness. (Rokach, 2013). A proposed ''social monitoring system'' exists which weighs perceived information on an individual's current and desired level of social acceptance Gardner et al., 2005; Leary et al., 1995).

Epidemiology of Loneliness

Recently, loneliness has become regarded as somewhat of an epidemic, and deadlier than obesity, and with equivalent effect on health as alcoholism or smoking 15 cigarettes per day (Holt-Lunstad et al., 2015). Holt-Lunstad and colleagues found in this

meta-analysis of 218 studies collecting data on approximately four million people, that lonely people had a 50% increased risk of early death, compared to those with good social connections. Obesity as compared raised the chance of dying before the age of 70 by around 30%. Loneliness has been found to be a prevalent, common, and disconcerting social phenomenon overall (Cacioppo and Patrick, 2008). Recent estimates suggest that up to 32% of adults in the US experience loneliness and that up to 7% report feeling intense loneliness (Hawkley et al., 2010). There is also evidence that prevalence rates are rising (Cacioppo et al., 2015), estimated as about 11-17% in the 1970s (Peplau et al., 1978), and rising to estimates of up to over 40% in some recent estimates of healthy populations and indicated as an enduring form of distress (Edmondson, 2010; Perissinotto, Cenzer, & Covinsky, 2012, Stickley et al., 2013)

If the prevalence of loneliness in healthy people seems high, it is even more significantly elevated in those who are diagnosed with psychotic disorders. The majority of adults with psychosis (80%) were found to endorse loneliness over the past 12 months, ranking this as one of the top two anticipated challenges in the next 12 months (Stain et al., 2012, Morgan et al., 2014). Our own work in Study 1 demonstrates clearly that patients with schizophrenia experience severe loneliness, as measured by the UCLA Loneliness Scale. In fact, patients experienced higher levels of loneliness than their healthy control counterparts ($F(1,34) = 20.6955$, $p < .0001$), contradicting traditional accounts of social anhedonia in schizophrenia. Increased loneliness also corresponded to higher levels of positive symptoms overall in individuals with schizophrenia ($r_s = 0.5186$, $p = 0.0274$), as rated by the Scale for the Assessment of Positive Symptoms (SAPS: Andreasen, 1984). Troublingly, many people and even skilled clinicians may interpret the social withdrawal of individuals with schizophrenia as globally purposeful, attributable to social anhedonia,

however patients have been demonstrated to experience consummatory social pleasure despite heterogenous difficulty with anticipatory pleasure estimates (Gard et al, 2007).

Theorized Links of Loneliness to Psychosis

Schizophrenia is characterized by social withdrawal as well as hallucinations and delusions that are almost always social and emotional in nature. It is clear that loneliness is a major factor in the lessoned well-being and potential increase of symptomatology, and large studies have confirmed its' pervasiveness in the disorder, despite prior notions that negative symptoms such as social anhedonia and avolition exhibited by some individuals with schizophrenia were tantamount to justification of lack of attention to their social exclusion. Compared to non-clinical controls, patients with psychosis are up to six times more likely to experience loneliness and its consequences over the course of their entire life (Meltzer et al., 2013, Kimhy et al., 2006). The Australian National Survey of Psychosis showed the extent of loneliness in psychotic illness, with the majority (80.1%) of adults with a diagnosis of psychosis endorsing feeling lonely in the past 12 months (Stain et al., 2012) and loneliness being ranked as one of the greatest challenges (after financial concerns) to be faced in the year ahead (Morgan et al., 2014). In the second Australian National Survey of Psychosis this was replicated and extended, showing a higher percentage of individuals feeling lonely across all psychotic disorders compared to the general community ($p < 0.001$), where the majority of participants in this, 79.9%, reported feeling lonely in the past 12 months. (Badcock et al., 2015). Regression analysis on symptoms and loneliness determined that subjective thought disorder and loss of pleasure are significantly associated with loneliness, however no directionality could be determined in this study since only cross-sectional data was obtained (Badcock et al., 2015).

Overall, unfortunately patients have been found to have smaller friendship and family networks, and less social interaction, compared to the general population (Breger et al., 2006; Palumbo et al., 2015). The availability of friends and family to support patients is shown to predict hospital stay length as well as severity of psychotic symptoms (Hultman et al., 1996). Conversely, inclusive and supportive friendship and family networks are found to be associated with better outcomes and more efficient use of health services (Harvey et al., 2003; Marino et al., 2015). Severity of positive symptoms has also been linked specifically with fewer and less satisfying social relationships and high levels of loneliness in people with schizophrenia (Angell and Test, 2002).

The effects of isolation in bringing about anomalous pseudo-psychotic experiences has long been established and documented. Highly suggestive evidence of isolation as a potent social stressor, over and above simple effects of sensory restriction, are the psychoses found of solitary confinement and of language-isolated refugees. For example, there is psychiatric reference as early as 1912 of paranoid psychoses exhibited in prisoners in solitary confinement (Nitsche et al., 1912), as well as in the hard of hearing and in communication-deprived refugees (Ziskind, 1958). It has been demonstrated that the EEG recordings of subjects under distressing isolated conditions resemble those of persons with hallucinations produced by psychotogenic drugs (Heron et al., 1956).

In the Genetic and Psychosis (GAP) longitudinal study of a catchment area in southeast London from 2005-2010, weaker social support in childhood and adulthood was also found to be associated with greater risk of psychosis not only at first contact with psychiatric service (OR 9.03) but at 1 year prior to admission (OR 5.67) and at 5 years prior to admission (OR 2.68) (Stilo et al. 2013). First episode cases were also around nine times more likely than controls to report indicators of social separation at first presentation

(Stilo et al., 2016). In particular, they were five times more likely to live alone and to be single, as well as 12 times more likely to be unemployed (Stilo et al., 2016). These associations held at 1 year and 5 years pre-first episode, but odds ratios increased as time before onset decreased (Stilo et al., 2016). This may suggest that isolation both contributes and exacerbates developing prodromal symptoms and that social adversity, through negative emotional processes, might contribute to the occurrence and persistence of psychotic symptoms (Stilo et al., 2016, Freeman et al. 2002; Freeman & Garety, 2014).

Even in healthy individuals, greater loneliness has been found to lead to more negative evaluations of others and lack of interpersonal trust (Lamster et al., 2016). The tendency to endorse conspiracy theories has been proposed as an exaggeration of the processes involved in the search for meaning (Whitson and Galinsky, 2008). For example, researchers find that when individuals across the spectrum of health feel uncertain, or when they lack control over a situation, they are much more likely to endorse superstitious beliefs and conspiracy theories (Whitson and Galinsky, 2008, Stillman et al., 2009). Graeunner and Coman (2017) propose that social exclusion creates uncertainty and feelings of lack of control in individuals, motivating them to reestablish some perception of control by engaging in search for meaning.

Gradin and colleagues (2012) studied neural responses in patients with schizophrenia to social exclusion via activation in the medial prefrontal cortex (mPFC), which is implicated in emotional and social information processing. Participants were excluded using the Cyberball social ostracism task (Williams & Jarvis, 2006). Increasing social exclusion was found to increase activation in the mPFC in controls. In contrast patients failed to modulate mPFC responses with increasing exclusion. Furthermore, this blunted response to exclusion correlated with increased severity of positive symptoms.

(Gradin et al., 2012). These data demonstrate differing neural response to social exclusion in a highly excluded population, suggesting that perhaps overtime, response to such a social stressor becomes pseudo-adaptive, at the expense of other function.

Loneliness and Erosion of Identity

Schizophrenia has been referred to as an "I am" illness (Estroff, 1989), meaning that this disorder affects an individual's core identity, the qualities, characteristics and continuities that distinguish one person from another. Schizophrenia, it has been associated with fluidity and characterized by inconsistent autobiographical recall and changes in self-representation over time (Boulanger et al., 2013, Prebble et al., 2013, Raffard et al., 2010). The appreciation of a sense of self has been reported as deficient in this illness (Lysaker & Lysaker, 2010, Mishara et al., 2014, Parnas et al., 2014, Scharfetter, 2003). Persons with schizophrenia, when administered a standardized questionnaire about identity, endorsed items such as: "I didn't know who I was", "My ancestry changed", "I often had to look in the mirror", "I thought I had children", "I had to say repeatedly "I am who I am", "My body or parts of it changed", "My sex changed". They showed an imprecise awareness of the continuity over time of their body, personal history, and social function. (Scharfetter, 2003).

The disorder is also associated with the loss of a coherent sense of self, anomalous self-experience, and the blurring of the distinction between the self and other (Ferri et al., 2012; Parnas et al., 2002; Sass and Parnas, 2003; Hobson and Meyer, 2015). Just as immigrants have been reported to experience, changes of self may act as a way to blend in with a new environment, mark affiliation and discern distinction. When this goes awry, or exclusion prevents it, inadequate markers of identity may give rise to further dysfunction.

Bleuler's original depiction of a "split mind" in coining the term 'schizophrenia' may be interpreted as a split or loss of unity in mental life (Roccatagliata, 1991), perhaps to be seen in a functional light as a survival attempt at creating an 'other' to satisfy need for socialization.

Fineberg and colleagues (2015) used latent semantic analysis to examine first-person accounts of patients with schizophrenia, finding that patients used fewer first-person singular pronouns ('I'), and more third-person plural pronouns (e.g., 'they') compared to patients with mood disorders. This has also been replicated in findings by our lab, as well as the significant correlation between loneliness and word count (r_s= 0.61, $p< 0.05$) in a sample of narrative essays from participants with schizophrenia spectrum disorders.

McIntyre et al. (2016) propose that the Social Identity Approach may have important implications for mental health outcomes, and for psychosis in particular, as it is associated with a loss of contact with self and reality. Social Identity Theory posits that a person's sense of who they are, and self-image is based on their group membership, and that belonging to groups gives us a sense of social identity; a sense of belonging to the social world. (Tajfel & Turner, 1979). McIntyre et al. (2016) specifically showed that 'cultural disidentification', reduces feelings of belonging, and conversely that 'positive group membership identification' promotes a greater internal locus of control, in other words a more concrete 'self', in turn safeguarding mental health (Greenaway et al. 2015, Thoits, 1983).

These findings suggest that more precise and intense identification may reduce paranoid ideation, promoting internal locus of control. In fact, paranoid delusions are the symptom most sensitive to the effects of weak social identity. Patients experiencing paranoid delusions may think others are out to get them, at times to the extent of fearing for

their very lives. Paranoid beliefs are the most common symptom of first psychotic episode and are reported to be present in over 90% of patients (Moutoussis et al., 2007). Other groups have found an association between migrant groups, victims of social defeat, and greater positive syndrome- in particular, paranoid and manic symptoms (Westermeyer, 1989, Cantor-Graae & Selten, 2005).

Migrant groups and other socially defeated groups (such as those who have survived trauma) have a commonality of drastic changes in self-identity, in addition and in relation to their increased psychosis risk. 'Self' and 'Other' distinctions are argued to be functionally dependent, via a theory known as functional antagonism (Turner et al., 1987). Essentially, as the salience of one self-category increases, the salience of other categories consequently decreases (Turner et al. 1987). There is evidence that one's human identity may become less salient when interacting with animals that display human-like behaviors, and more salient during nonsocial inanimate observation, such as when watching the moon landing (Bora & Pantelis, 2013).

People who are at very high risk of psychosis, and who are experiencing the prodromal symptoms that typically precede a first episode of illness, may also lack the social cognitive skills that are required to maintain firm social identities, such as theory of mind skills (Bora & Pantelis, 2013). Loss of sense of self identification, separation from old or native groups, and exclusion or difficulty assimilating to new ones, produces a weakened self-identification as the defining characteristics fade and an individual in stuck in a limbo-like state, scanning for meaning and confirmation of sense of self. This scan for meaning combined with lack of social sensory input may lead to creation of anomalous compensatory symptoms, that while distressing, compensate a concrete reality and identity to cling to. Loneliness, as a social signal, motivates the self to reach out and extend

outwards, hoping for the attachment and social stimulation it craves, and as a byproduct weakening and dissolving the concrete self-boundary outwards for purposes of social survival.

The self-disturbances that occur so often in social isolation may be in part attributable to changes in sensory and multisensory function (Parnas et al., 2003, Nelson et al., 2009a), over-extended sense of presence (Blanke et al., 2014) and the loss of the self-other boundary (Nelson et al., 2009b; Thakkar et al., 2011; Michael and Park, 2016), which are all commonplace in schizophrenia and which without anchor of "other" may be symptoms of erosion of "self".

More recently, it has been suggested that weaker bodily self-representation may be a core component of the pathology of schizophrenia, and that this may be caused by inadequate body-related multisensory integration processes (Postmes et al., 2014), which manifests as a loss of implicit self-knowledge and self-other differentiation (Gallese and Ferri, 2014). Weaker and more variable sense of body boundary has also been demonstrated in patients with schizophrenia via the Pinocchio Illusion, bringing about a sensation that one's nose is growing in response to a tactile-proprioceptive manipulation (Michael and Park, 2016). Interestingly, this illusion is found to associate with social isolation regardless of diagnosis, suggesting that reduced self-other social interactions may contribute to disturbances of the bodily self across the psychosis spectrum (Michael and Park, 2016; Benson and Park, 2018).

Thakkar et al. (2011) used the Rubber Hand Illusion, which can be elicited by stroking an individual's unseen hand simultaneously with a visible dummy hand, bringing about the sense of ownership over the rubber hand in those susceptible to the illusion. Thakkar et al. (2011) found a stronger sense of this illusion in patients with schizophrenia

over healthy controls, demonstrated by self-report as well as measured proprioceptive drift. Furthermore, associations of severity of symptoms as assessed by the PANSS are observed with greater variability when judging the limits of peripersonal space (Delevoye-Turrell et al., 2011). Overall a more variable representation of the body, and reduced distinction between bodily self and other can be observed as a function of the lack of concrete social stimulation necessary for concretizing such distinction.

Even symptoms such as thought disturbance can be viewed as a phenomenon of self-disturbance, of less of definition of concrete individual perhaps due to weakened availability of context. Sterzer (2016) notes that the early Heidelberg School (Gruhle, Mayer-Gross, Beringer), which first named and defined the self-disturbances, proposed that thought insertion involves a disruption of the inner connectedness of thoughts and experiences, and a "becoming sensory" of those thoughts experienced as inserted.

Further deficits in social cognition found in individuals with schizophrenia demonstrate relationship to impaired self-identity. For example, biological motion processing is one of the most basic abilities in a repertoire of human social cognitive skills and has been emphasized as important for inferring the identity and social role of the other person ("social perception") (Troje, 2013). Biological motion is recognized as one of the two most prominent techniques to study processes associated with identification of social stimuli and their emotional value (Billeke and Aboitiz, 2013). A basic Biological Motion task measures the ability to distinguish biological from non-biological motion (Kim et al., 2005). In a meta-analysis of 14 biological motion experiments on patients with a mean illness duration of 10.2±6.2 years, individuals with schizophrenia (compared with healthy controls) exhibited moderate to large deficits during biological motion processing (Okruszek & Pilecka, 2017). This has further implications for social functioning and other

social cognitive tasks as well. For example, complex social cognitive abilities, including mentalizing (Kim et al., 2013) and empathic accuracy (Olbert et al., 2013) are impeded and show links to biological motion processing in patients. It may be suggested that aberrant visual processing of biological motion cues may be one of the mechanisms that underlie abnormal social cognitive development trajectories in patients with schizophrenia. (Okruszek & Pilecka, 2017). This lays important groundwork for the research outlined in Chapters II-III.

Review of Intervention Efforts

It has now become clear that addressing the etiology and neurological, biological and social consequences of loneliness and social defeat are of utmost importance in understanding and working to alleviate their contribution to illness in individuals suffering from psychosis spectrum. However, despite mounted evidence for the catastrophic and disturbing consequences of distressing social deprivation in the realm of psychosis, loneliness remains an overlooked facet for intervention in patients with schizophrenia. Lim and Gleason conducted a meta-analysis in 2014 and stated, “To date, there has been no published study that has developed an evidence-based loneliness intervention in individuals with psychosis”. A meta-analytic review of interventions aimed at reducing loneliness in a range of different populations surprisingly included only five studies with individuals with mental health symptoms, and none of the studies were specific to psychosis (Masi et al., 2010). However, in the 80.1% of participants with psychotic disorders who endorsed feelings of loneliness in the second Australian national survey of psychosis, 37% identified loneliness as a particular barrier to their recovery (Stain et al., 2012).

Lim and Gleason have noted that there are many psychosocial interventions for individuals with schizophrenia aimed at training in social skills (2014). However, many of these trainings are non-naturalistic and generally involve computer-based training rather than person to person interactions which may serve to decrease loneliness in particular. Results of these interventions show mixed efficacy, but generally have weak transfer of skills to everyday socialization and often low adherence (Kurtz & Richardson, 2011). The focus of existing loneliness interventions has been largely the elderly population, with some work conducted in individuals with depression or in healthy populations. Considerations for the work outlined in Chapters IV and V build upon this groundwork.

Thesis Aims: Characterizing the Effects and Alleviating the Distress of Isolation

Loneliness is thought to drastically impede well-being, but systematic investigations on the impact of loneliness on social-cognitive processing have not been previously tested. Interventions for lonely individuals dealing with the unique challenges of psychosis have been nonexistent, with the emphasis of remediation efforts placed solely on social skill acquisition.

The chapters that follow describe a body of research conducted to assess the influence of exclusion, isolation and chronic loneliness on social perception, and explore potential avenues of remediation for this social distress. In Chapter II, an examination of whether temporary passive isolation or active social exclusion affect social perception among neurotypical and socially saturated young adults is conducted. In Chapter III, systematic characterization of loneliness in socially vulnerable individuals with schizophrenia is established and perception of social stimuli is compared to neurotypical populations of the same age. In Chapter IV, plausible remediation of loneliness through an

exposure-based social inclusion group using the unique social bonding principles of singing is explored. In Chapter V, differential benefits of a novel, immersive and directive social skill-building intervention are examined. Together, this work aims to significantly expand the understanding of the importance of confronting loneliness and social exclusion across populations, more specifically characterize the particular deficits associated with isolation in vulnerable populations, and offer two novel possible intervention methods to reduce the detrimental effects in a relatively simple, enjoyable and cost-effective manner.

CHAPTER II

Study 1: Effects of Social Exclusion, Isolation and Loneliness on Social Perception in Healthy College Aged Populations

The adverse effects of unwanted social isolation – loneliness - for mental and physical health are well documented (Cacioppo et al, 2014; Cacioppo et al, 2015). These consequences are associated with neural abnormalities including reduced gray matter volume in brain regions implicated in social perception i.e., the posterior superior temporal sulcus (pSTS) (Kanai et al, 2012). It has been long been established that the superior temporal cortex is structurally and functionally compromised in schizophrenia (see Shenton et al, 1992), and multiple studies have reported reduced pSTS activation during visual social perception tasks in schizophrenia (e.g., Pinkham et al, 2008; Kim et al, 2011; Thakkar et al, 2014).

The prevalence of social impairments long before the onset of psychosis has been firmly demonstrated (Addington et al, 2008; Lee et al, 2015), and empirical evidence points to undesired social deprivation or isolation as a major risk factor for psychosis. Moreover, past studies indicate that social isolation and exclusion can lead to adverse psychiatric outcome including increased risk for psychosis and exacerbation of psychotic symptoms (Tan and Ang, 2001; Hoffman 2007; Selten et al, 2013). For example, a retrospective study of military personnel found that the most robust prodromal predictor of psychosis was social isolation (Tan & Ang, 2001). In a longitudinal population-wide study of Israeli males, impairments in social activity constituted the most acute, pervasive deficit social isolation, recognizable up to 15 years before first hospitalization for schizophrenia

(Velthorst et al, 2016). Adverse consequences of impoverished social environment have also been observed in rodents; social withdrawal during rearing produces deficits such as impaired prepulse inhibition and neuronal hyperexcitability comparable to that exhibited in individuals with schizophrenia (Cai et al., 2007)

Hoffman (2007) noted that prior to first onset of auditory hallucinations, over 70% of respondents experienced social isolation. To explain this relationship between social isolation and hallucinations, Hoffman (2007) hypothesized that, similar to the cortical reorganization that occurs after limb amputation resulting in Phantom Limb syndrome, isolation for a vulnerable individual can lead to compensatory hyperactivity of the brain regions associated with social cognition, which then elicits hallucinations and delusions that are highly social in nature. Such experiences, and their perceptual nature, could plausibly impair social functioning, and as social perception is at the root of social function, the interconnection of social stimulation in one's environment and interpretation of stimuli is likely. Moreover, the Social Defeat hypothesis implicates social exclusion in the epidemiology of psychosis, citing major risk factors for development of schizophrenia such as migration, disadvantaged status, urban upbringing or trauma, which involve forms of extreme exclusion unlikely to be genetically coded (Selten et al. 2013, 2016). However, these putative relationships hitherto require empirical verification.

Study Aims

This study aimed to elucidate the relationship between social isolation and social perception within a typically developing and socially exposed population. We examine the potential independent detriments of acute isolation along with chronic, distressing perceived isolation via loneliness. Peplau & Perlman (1982) conceptualized loneliness as a

difference between one's perceived current level of social involvement and desired amount of social involvement. When these values are discrepant, feelings of loneliness ensue. Thus, the feeling of loneliness inherently implies a desire for social interaction, and to a greater extent than currently experienced. In the present study, we examined the effects of social exclusion on social perception in relation to psychosis-risk.

In Experiment 1, we manipulated social exclusion/inclusion in young, adult participants via a commonly used computerized ball-tossing game known as Cyberball (Williams & Jarvis, 2006) and subsequently presented point-light animations of human biological motion to assess the ease with which those participants could classify a given stimulus as living or nonliving In addition, we differentiated and examined objective social isolation as well as the subjective experience of loneliness, to determine the role of the component of personal distress.

In Experiment 2, we included a forced choice Biological Motion Recognition task and a Pure Isolation manipulation condition to clarify the role of active exclusion relative to simple isolation of an individual and to refine the perceptual task to assess performance accuracy. We hypothesized (1) that acute social isolation would influence how one perceives and classifies visually portrayed social stimuli and (2) that psychosis-proneness would be associated with increased endorsement of loneliness and decreased performance on a social perception task.

Experiment 1A: Effects of Acute Social Ostracism on Social Perception in Healthy College Aged Populations

Method

Participants

Sixty healthy participants were recruited from the Vanderbilt University student population and randomly assigned to one of three social manipulation conditions: 'Exclusion', 'Neutral' or 'Inclusion' (n = 20 each). All participants reported normal or corrected-to-normal vision. Inclusion criteria were as follows: no prior history of neurological or psychiatric disorder or current drug use. Demographic data are displayed in Table 1. There were no significant demographic differences among the three groups. The protocol for this study was approved by the Vanderbilt University Institutional Review Board. All participants gave written informed consent and were compensated with credit towards fulfillment of a psychology course research participation requirement. All participants were debriefed after the experiment about the social manipulation condition they received. Upon debriefing, three subjects were excluded from data analysis due to knowledge of the manipulation, resulting in N = 57 and group n = 19 for each condition.

Table 1.
Experiment 1A Demographic Data

	Exclusion Group (N=19)	Neutral Group (N=19)	Inclusion Group (N=19)
Age (years)	20.6 (2.1)	19.9 (1.2)	19.4 (2.5)
Sex	10M/9F	6M/13F	5M/14F

Procedure and Materials

Social Manipulation with the Cyberball game

Participants were randomly assigned to one of three conditions: Exclusion, Neutral or Inclusion. Subjects in the Exclusion and Inclusion conditions first participated in the Cyberball task, an open-source virtual ball-tossing game widely used in prior research to induce perceived ostracism, social exclusion and/or rejection (Williams, Cheung & Choi, 2000, Williams & Jarvis, 2006, Bernstein & Claypool, 2012). Participants were instructed that the aim of this task was to examine their mental visualization skills and that they would be playing with two other research participants playing the game online in real-time. Participants were instructed to visually imagine a scenario (e.g., scenery, distance between partners, temporal information etc.) in which they were playing catch with these two virtual participants. Participants were asked to pass the ball whenever they received it from one of the other two players, by clicking on the photo of the player to whom they wished to pass. In reality, these two other 'players' were cyber-confederates, and a computer algorithm determined the percentage of passes the participant would receive.

Each participant played 100 trials of ball tosses, which took about 10 minutes to complete. In the Exclusion condition, participants received equal ball tosses from the other players for the first six trials (33%, pseudo-randomly generated), after which they received no further tosses, which meant that they were conspicuously excluded from the ball game for most of the experiment and, thus, were relegated to being outsiders consigned to watching the other two individuals playing together. In the Inclusion condition, participants received ball tosses equally for the duration of the task (33%, pseudo-randomly generated). Participants in the Neutral condition did not play the Cyberball game and, instead, completed a paper and pencil questionnaire inquiring about dream behavior, with the

questionnaire lasting ten minutes. Post-experiment validity checks were administered to ensure that all participants were naïve to the Cyberball manipulation, resulting in the exclusion of three subjects.

Biological Motion Task

Immediately following this social manipulation, participants were given a task using point-light displays of biological motion sequences (see Figure 1). Biological motion is recognized as one of the two most prominent techniques to study processes associated with identification of social stimuli (Billeke and Aboitiz, 2013). Biological motion animations consisted of 12 dots denoting the locations of the head, torso and joints (elbows, wrists, knees, and ankles) of a human body engaged in one of 25 distinct and familiar activities: 5 walking (stairway walking, climbing, crossing a small object, and 2 plain walking with different viewing angle), 4 jumping (standing jump, leaping, rope-jumping, and high-jumping), 4 kicking (toward front, side, and 2 soccer kicking), 2 running (plain and turning around), 6 throwing (3 overhead and 3 under-throwing), and 3 crouching). Each stimulus was displayed for 1s and participants were asked to classify the sequence as "human activity" or "non-human motion" by pressing one of two keys.

Task difficulty was manipulated by adaptively 'scrambling' each animation (Figure 1, see also Kim, Park, & Blake, 2011 for details). Briefly, the adaptively scrambled motion from a biological motion was created as follows: Initially, the starting frame of a biological motion was taken, and the dot positions of 100% scrambled motion were created by spatially randomizing the initial position of each dot. Next, intermediate locations were generated between biological motion sequence and its corresponding 100% scrambled sequences to create a certain percent scrambled motion. For instance, an intermediate

position that divides the distance between position of 'head' dot and its moved position when scrambled with the ratio of 15:85 can be located. 15% spatially scrambled motion can be created when 15% intermediate locations for all the other dots are taken. In the same way, it is possible to create any % scrambled motion sequence in which the motion trajectory of each dot is identical to that of its corresponding biological motion. Therefore, this method of scrambling quantifies the degradation of biological motion.

The task began with a 100% biological motion trial. After each response, an adaptive staircase procedure was used to vary the degree of degradation (i.e., 'scrambling') presented on each trial based on the participant's response on the previous trial, the aim being to determine the degree of degradation that yields judgments of 'human motion' on 50% of trials. Initially, the degree of scrambling was changed in steps of 10%, but after the 6^{th} reversal in responses this change value was reduced to 5%, and after the twelfth reversal the staircase procedure was terminated. The threshold level of scrambling was determined by the % degree of scrambling at which a participant's endorsement of biological motion oscillated between "Yes" and "No" for six consecutive trials. Thus, the final % of scramble at which the participant reliably endorsed perception of biological motion defined that individual's threshold for that particular animation stimulus. These animation thresholds were averaged across the 25 animation stimuli to yield a global measure of biological motion classification threshold per participant. In addition to collecting threshold measures, we recorded reaction times (RT) for each trial, measured by the time to response from the offset of stimuli presentation, and averaged this across total trials for a global measure of each participant's speed with which she classified an animation to represent biological motion (human movement).

Figure 1.
Point-Light Biological Motion Displays At Varying Degrees Of 'Scramble'

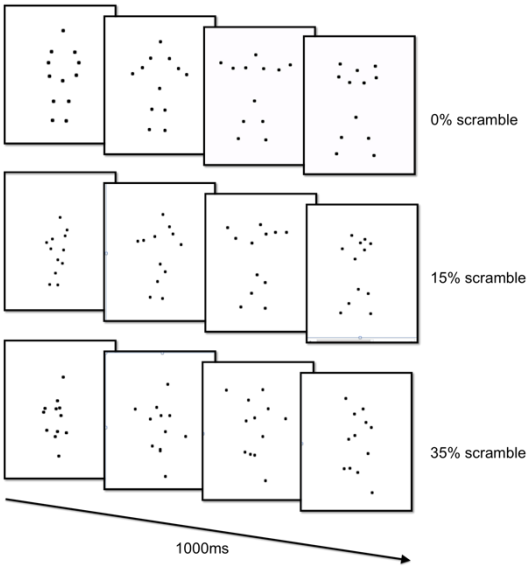


Fig 1. Example frames of the biological motion animation paradigm depicted at 0% scramble, or "pure motion", at 15% and at 35%. Participants viewed animations sequentially with smaller sequential intervals of scrambling, as described above.

Self-Report Measures

Following the biological motion classification task, two self-report measures were administered. One was the UCLA Loneliness Scale (Russell, 1996) that assesses subjective feelings of loneliness and perceived social isolation. This measure has been shown to be highly reliable in measuring a participant's subjective social distress via loneliness over a 1-year period, both in internal consistency (α: 0.89-0.94) and test-retest reliability (r=0.73) (Russell, 1996). The other measure was the Prodromal Questionnaire-Brief (PQ-B) that assesses the presence of attenuated psychotic symptoms and the degree of distress (PQB-Distress) associated with these behavioral signs (Ising et al., 2012).

Results

The results of the BM Classification task are presented in Figure 2 and in Table 2. Average biological motion classification thresholds were compared across the three acute social manipulation groups. The main effect of group was statistically significant ($F(2,57)= 4.8$, $p < 0.01$), with *t*-tests showing a significant difference between the Exclusion group and the Inclusion ($t(36) = 2.82$, $p = 0.0071$,) and between the Exclusion and Neutral groups ($t(36) = 2.59$, $p = 0.0128$). There was no significant difference between the Inclusion and Neutral groups ($p = 0.98$). See Figure 2.

Figure 2.
Effects of Social Manipulation on Biological Motion Classification Threshold

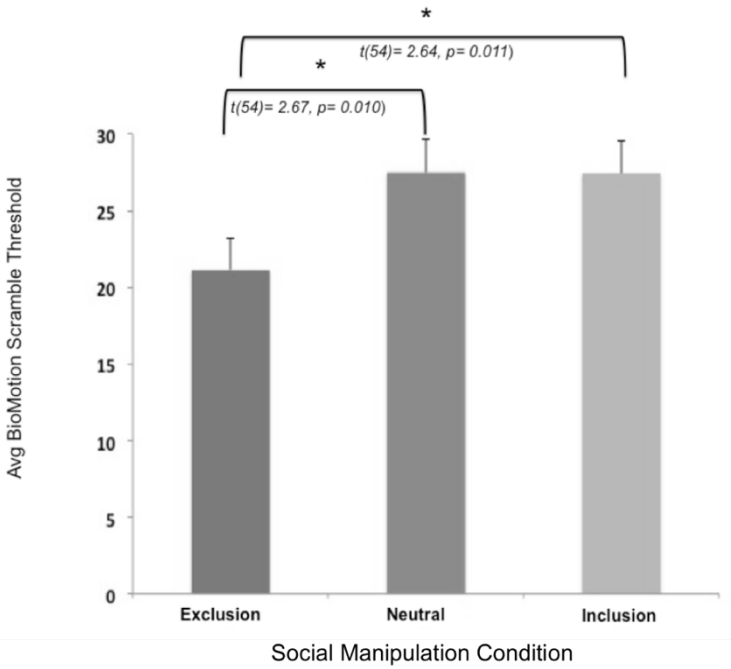


Fig 2. Significant difference in interpretation of social stimuli was found between the Excluded experimental group and Neutral groups, as well as between Excluded and Included groups. Error bars are across observers. No significant difference was found between Neutral and Inclusion conditions.

Table 2.
Group Differences on Measures Collected Post-Social Manipulation

	Exclusion	Neutral	Inclusion	Statistical test
BM threshold %	20.65 (6.4)	27.15 (6.89)	27.09 (8.94)	$p < 0.01$
BM RT (ms)	650 (220)	680 (280)	720 (260)	n.s.
UCLA Loneliness	20.1 (11.9)	16.8 (11.5)	22.1 (10.1)	n.s.
PQ-B	5.1 (3.6)	4.4 (3.1)	4.9 (4.5)	n.s.
PQ-B Distress	1.1 (1.8)	0.57 (1.0)	1.6 (2.5)	n.s.

There were no significant group differences in UCLA Loneliness scores ($F(2,57)= 1.08$, $p = 0.34$) or PQ-B scores ($F(2,57)= 0.19$, $p = 0.82$). However, regardless of social manipulation, increased Loneliness was positively correlated with increased PQ-B ($\rho = 0.57$, $p < 0.0001$) and PQ-B Distress levels ($\rho = 0.56$, $p < 0.0001$). Subjective Loneliness was not found to be directly associated with BM perception threshold ($\rho = -0.13$, $p = 0.386$). PQ-B Distress however, was negatively correlated with BM perception threshold ($\rho = -0.29$, $p < 0.05$).

Within the Exclusion group, there was a trend toward a significant correlation between loneliness and PQ-B Distress ($\rho = 0.48$, $p = .07$). However, no significant association between measures of chronic loneliness and performance on the social perception task was found in this population. In the Neutral group, there was a positive correlation between Loneliness and higher PQ-B scores ($\rho = 0.77$, $p < 0.001$) and a trend toward significant correlation between loneliness and PQ-B Distress ($\rho =0.45$, $p = .09$). In

the Inclusion group, there were positive correlations between PQ-B and Loneliness ratings ($\rho = 0.53$, $p < 0.01$), between PQ-B Distress and Loneliness ($\rho = 0.61$, $p < 0.005$), and between reaction time (ms) and Loneliness ($\rho = 0.52$, $p < 0.05$). Tables 3.A-C present these group-specific findings, using Bonferonni correction to control the family error rate.

Table 3.
Correlations between Biological Motion Threshold, Loneliness and Prodromal Scores

	BM Threshold	Loneliness	PQ-B	PQ-B Distress
BM Threshold	1.00			
Loneliness	–0.13	1.00		
PQ-B	–0.21	0.57***	1.00	
PQ-B Distress	–0.29*	0.56***	0.63***	1.00

*p < .05 **p < .001 ***p < .0001

Tables 4.A,B,C
Correlations between BM, Loneliness and Measures of Prodromal Risk By Group

A. Exclusion					
	BM Threshold	BM RT	Loneliness	PQ-B	PQ-B Distress
BM Threshold	1.00	1.00			
Loneliness	–0.25	0.28	1.00		
PQ-B	–0.23	–0.007	0.29	1.00	
PQ-B Distress	–0.31	–0.30	0.48	0.61*	1.00

B. Neutral					
	BM Threshold	BM RT	Loneliness	PQ-B	PQ-B Distress
BM Threshold	1.00	1.00			
Loneliness	0.05	–0.10	1.00		
PQ-B	–0.12	0.18	0.77**	1.00	
PQ-B Distress	–0.22	–0.22	0.45	0.33	1.00

C. Inclusion					
	BM Threshold	BM RT	Loneliness	PQ-B	PQ-B Distress
BM Threshold	1.00	1.00			
Loneliness	0.004	0.52*	1.00		
PQ-B	–0.12	0.27	0.53*	1.00	
PQ-B Distress	–0.34	0.37	0.61**	0.76***	1.00

*p < .05 **p < .001 ***p < .0001

Discussion

Results from Experiment 1A indicate that an acute episode of social isolation can significantly alter one's judgments about the visual portrayal of human activity in PL animations After just ten minutes of ostracism during a VR game, participants in the Exclusion group showed significantly altered judgments of BM compared to those comprising the Neutral and Inclusion groups, which did not differ from one another. This suggests that lack of social stimulation, via isolation and exclusion may be a potential

mechanism by which social perception is detrimentally altered. Compounded across time and at higher rates, this isolation could result in much more severe social perceptual difficulties. In Experiment 1A, higher endorsement of feelings of loneliness, the distress manifested by desire for more social interaction than acquired, was strongly associated with risk for psychosis across our sample, though not significantly altered between manipulation groups. These findings perhaps indicate that a more stable, pervasive condition such as loneliness might contribute more significantly to psychosis-risk than an acute manipulation of social isolation. This is supported by the observed relationship between distress level regarding prodromal symptoms and reduced perceptual acuity in the biological motion task, but not between biological motion classification and overall endorsement of prodromal symptoms. It would appear from this preliminary investigation that distress is the crucial feature linking these factors.

Interestingly, higher levels of loneliness were associated with slower reaction times in the Inclusion group. This finding indicates that loneliness may alter not only social perception but contribute to a slowing of processing speed for social stimuli as well. Indeed, prior research into social exclusion has demonstrated similar deficits on timed cognitive task performance, with effects found to be specific to social exclusion scenarios rather than broadly the result of hearing bad news (Baumeister et al., 2002). It is possible that exclusion from social groups triggers emotional distress that preoccupies the self-regulation system and reduces resources for executive control processes, producing a short-term impairment of cognitive functioning. Over time, and with chronic exposure, this reduction of resources due to social distress may result in a more pervasive slowing in processing speed, as well as cognitive impairment. However, the specific relationship of distress (exclusion) was not parsed from objective experience of being isolated from social

stimulation in this study, and thus Experiment 1B sought to clarify this relationship. Additionally, the Biological Motion judgment task simply required a subjective judgment about whether a given animation was human or non-human and, therefore, was not an objective measure of perceptual accuracy. This limitation thus precludes specific conclusions about the directionality of altered judgment of BM in the Excluded group. Experiment 1B was designed to clarify the quality of this alteration of perception by adopting a forced choice Recognition task to determine objective accuracy of judgments across groups. Finally, Experiment 1A included a measure of global loneliness but not a measure of objective social contact, meaning that we were unable to parse the distinct contributions of social distress from social isolation. Experiment 1B sought to remedy this limitation.

Experiment 1B. Differential Effects of Acute Social Exclusion and Passive Social Isolation

Method

Participants

Sixty additional healthy participants were recruited from the Vanderbilt University student population and randomly assigned to one of three social manipulation conditions: 'Exclusion', 'Neutral' or 'Isolation' (n = 20 per condition). Because Inclusion and Neutral groups were found to have no significant differences in this population in Experiment 1, the Inclusion group was removed for Experiment 2. Sample size was estimated to obtain power (1−β) at 0.80. All participants reported normal or corrected-to-normal vision and inclusion criteria remained consistent with Experiment 1. Demographic data are displayed in Table 4. There were no significant demographic differences among the three groups. As before, participants were compensated with credit towards fulfillment of a psychology course research participation requirement. All participants were debriefed after the experiment about the social manipulation condition they received, and data was excluded for participants with knowledge of the manipulation.

Table 5.
Experiment 1B Demographic Data

	Exclusion Group (N=20)	Neutral Group (N=20)	Isolation Group (N=20)
Age (years)	19.6 (1.2)	20.2 (1.3)	19.5 (0.9)
Sex	6M/14F	7M/13F	6M/14F

Procedure and Materials

Social Manipulation

Participants were randomly assigned to one of three conditions, however in Experiment 2 the conditions utilized were: Exclusion, Neutral or Isolation. Subjects in the Exclusion condition first participated in the Cyberball task, following the protocol from Experiment 1. Participants in the Neutral condition completed a paper and pencil questionnaire. In the Isolation condition, participants were instructed that a heart rate monitor would record their resting heart rate while sitting comfortably and quietly. The testing room was designed to have no environmental social stimuli and participants were asked to turn off all electronic devices. Participants in the Isolation condition were then left alone in the testing room for 10 minutes and a sound machine was used to ensure absence of outside social noise.

Biological Motion Tasks

Immediately following this social manipulation, participants were given the same staircased classification task using point-light displays of biological motion sequences from Experiment 1. Following this task, a 2-alternative-forced-choice biological motion 'Recognition' task was introduced. This task included 150 fixed trials presented randomly without replacement for each participant. This included 50 trials of biological motion sequences with 0% induced noise, or 'pure biological motion', 50 trials at 25% induced noise—the average 'threshold' point found in Experiment 1 and reported by other studies measuring this limit—and 50 trials with 100% induced noise, or 'pure noise' cases. Participants were instructed again to select 'yes' or 'no' on the keyboard indicating whether they believed each trial looked 'human' or 'not human'. In addition to collecting

accuracy measures, we recorded reaction times (RT) for each trial, defined as the time to response from the offset of stimuli presentation, and averaged this across total trials for a global measure of each participant's speed with which she/he classified an animation to represent biological motion (human movement).

Self-Report Measures

Following the classification and detection biological motion tasks, the UCLA Loneliness Scale and Prodromal Questionnaire-Brief (PQ-B) were again administered. Additionally, a measure of the pure quantity of social engagement over the past month was collected using a modified version of the Multipurpose Household Survey (Fiorillo & Sabatini, 2011).

Results

The results of the BM task are presented in Table 2 and in Figure 2. Average biological motion classification thresholds were compared across the Exclusion, Isolation and Neutral social manipulation groups. We replicated a statistically significant main effect of group ($F(2,57)= 3.15$, $p < 0.05$), with *t*-tests showing significant differences in perceptual discrimination between the Exclusion and the Isolation conditions ($t(36) = 2.21$, $p = 0.02$,) and between the Exclusion and Neutral ($t(36) = 1.77$, $p = 0.04$). There was in fact no significant difference found between the Isolation and Neutral groups ($p = 0.57$). See Figure 3.

Figure 3.
Effects of Social Manipulation on Biological Motion Classification Threshold

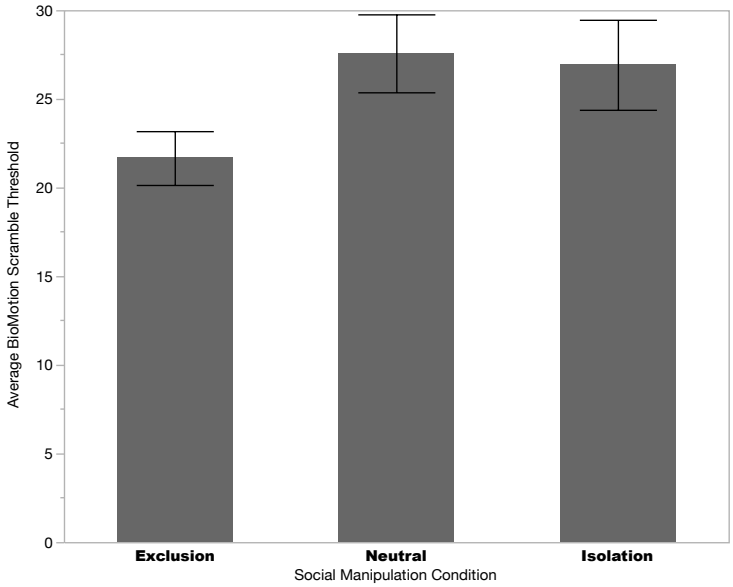


Fig 3. Significant difference in interpretation of social stimuli was found between the Excluded experimental group and Neutral groups, as well as between Excluded and Isolated groups. Error bars are across observers. No significant difference was found between Neutral and Isolation conditions.

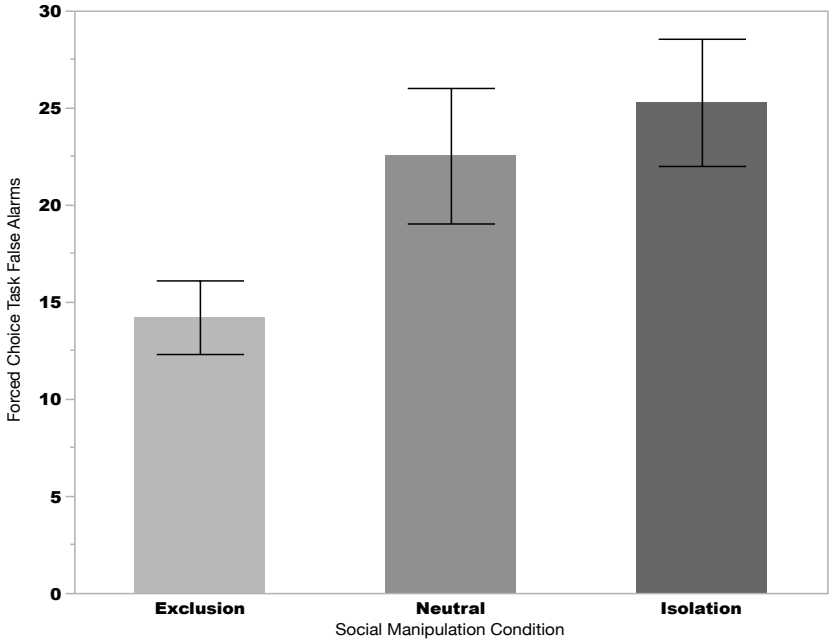
Table 6.
Group Differences on Measures Collected Post-Social Manipulation

	Exclusion	Neutral	Isolation	Statistical test
BM threshold %	21.67 (2.05)	27.57 (2.16)	26.92 (2.10)	$p < 0.05$
BM RT (ms)	668 (50)	586 (53)	695 (52)	n.s.
UCLA Loneliness	20.9 (2.5)	19.5 (2.6)	21.0 (2.6)	n.s.
Social Quantity	11.2 (3.1)	11.9 (3.4)	11.3 (3.3)	n.s.
PQ-B	3.2 (.79)	4.4 (.84)	4.2 (.82)	n.s.
PQ-B Distress	0.1 (.78)	0.7 (.83)	1.5 (0.80)	n.s.

There were no significant group differences in UCLA Loneliness scores, Social Quantity or Prodromal symptom endorsement. However, regardless of social manipulation, increased Loneliness was again found to be positively correlated with increased PQ-B ($\rho = 0.55$, $p < 0.001$). As in Experiment 1, we did not find a relationship between subjective Loneliness and BM perception threshold ($\rho = -0.13$, $p = 0.386$). We did not find a significant relationship between PQ-B Distress and BM threshold, as PQ-B endorsement was minimal.

In the second, forced choice Recognition task, we again found group differences after social manipulation. Average False Alarms (endorsing biological motion where it is ambiguous or not present) were compared across the Exclusion, Isolation and Neutral social manipulation groups and a statistically significant main effect of group was found ($F(2,57)= 4.01$, $p < 0.05$), with *t*-tests showing significant differences in perceptual discrimination between the Exclusion and the Isolation conditions ($t(36) = 2.09$, $p = 0.02$,) and between the Exclusion and Neutral ($t(36) = 2.92$, $p = 0.006$). No significant difference was found between Isolation and Neutral manipulation conditions on False Alarm rate ($t(36) = 0.57$, $p = 0.56$). See Figure 4. D' was calculated revealing no significant differences, driven by a high average Hit rate which also did not differ significantly. No relationship was found between Recognition task abilities and Loneliness scores. However, a trend relationship between scarcer daily social interaction and more frequent endorsement of biological motion in random noise was observed ($\rho = - 0.24$, $p = 0.06$).

Figure 4.
Effects of Social Manipulation on Biological Motion False Alarm Rate



Discussion

Results from Experiment 1B replicated the findings from Experiment 1A in that an acute episode of social isolation significantly altered one's judgments about the visual portrayal of human activity in PL animations. Participants in the Exclusion group again showed significantly altered judgments of BM compared to those comprising the Neutral group. Attempts to clarify contributing factors to this alteration by including a pure Isolation group indicate that the Isolation group and Neutral groups differ from one another on measures of social perceptual discrimination. This suggests that acute social defeat and exclusion compared to simple absence of social stimulation may be more important in altering social perception in an, on-average, highly socially saturated population. As in Experiment 1A, distress levels on the PQ-B and average subjective loneliness were very low in this student population. Despite this, brief exclusion altered social perception.

Compounded exclusion and defeat in vulnerable populations could be implicated in some of the severe social perceptual difficulties seen. Higher loneliness was associated with higher psychosis risk and distress, as replicated from Experiment 1A. However, objective social quantity appeared to influence social perception more strongly in this population. This would perhaps indicate that in a highly socially saturated college-aged population, chronic absence of social stimuli may ultimately affect perceptual differences, despite nonsignificant effects of acute isolation. In populations with chronic loneliness combined with an absence or scarcity of social perceptual input, data suggests that social perception may be significantly altered.

Conclusions

We sought to empirically test whether isolation and loneliness have a significant effect on basic visual social perception. We found that an acute social defeat manipulation via Cyberball altered subsequent processing of biological motion. Indeed, even just ten minutes of social exclusion could influence perception and speed of social information processing. Moreover, social distress (loneliness) and symptomatic distress (PQ-B Distress) seemed to be important for the relationship between social isolation and social perception. Findings indicate that loneliness is indeed strongly associated with higher risk for psychosis and higher distress regarding symptoms of prodromal psychosis. This suggests that social exclusion may lead to a wide range of abnormal experiences including perceptual aberrations, not just emotional problems. Thus, loneliness and isolation (i.e., reduction of social stimulation in general) may reduce one's ability to detect social information when it is in fact present.

There are caveats. Potential effects of induced social isolation on social perception were explored in college undergraduates, a group with inherently rich social interaction potential. Despite this, an acute ten-minute manipulation of social defeat experience was able to significantly alter social perceptual judgments, over and above effects of pure acute social isolation. In this population, quantity of social experience appeared to trend towards influence of social perception while subjective quality of social experience showed no relationship. Nonetheless, psychosis-risk and social distress were relatively low, suggesting that the influence of these more stable and chronic factors may not have been as prominent or easy to detect.

In addition, these results are not likely to be representative of less socially ensconced individuals (e.g., those with active psychosis or schizophrenia). We expect a dampening of the salience of an acute social manipulation in a population with more chronic social exclusion and loneliness prior to study enrollment. Having demonstrated significant alteration of social perception after exclusion in young adults with no history of psychosis, Study 2 set forth to investigate the contributions of social isolation and loneliness to social information processing in more socially isolated and vulnerable populations with schizophrenia as well as neurotypical counterparts of the same age.

CHAPTER III

Study 2: Social Exclusion, Loneliness and Social Perception in Patients with Schizophrenia and Age Matched Healthy Participants

Study Aims

The major aim of Study 2 was to characterize the prevalence of loneliness in a sample of patients with schizophrenia as compared to an age matched sample of healthy adults from the same community. A second aim was to investigate the relationship between social engagement and clinical symptoms or schizotypal quality in these populations. We thirdly aimed to determine the strength of association between social engagement, feelings of loneliness and social-perceptual inference.

We expected that consistent with existing literature, participants with schizophrenia would endorse significantly higher loneliness than exhibited by community controls. We further hypothesized that patients would endorse significantly lower quantitative social inclusion than their matched counterparts. We predicted that those who experienced greater loneliness would also experience greater prevalence of positive psychotic symptoms, based on aforementioned theories implicating absence of social input in greater spurious social meaning-making (Hoffman, 2007). Based on this framework, we predicted no such relationship would be found with negative symptoms of schizophrenia. In matched controls, we predicted a similar pattern in that higher reported loneliness would be associated with greater endorsed schizotypal symptoms, and particularly with greater reported distress over these endorsed experiences. Finally, we predicted that across groups,

social task inference patterns would be influenced by the social distress of loneliness, but not by pure quantity of reported social engagement.

Method

Participants

Individuals between the ages of 30-65 years old, living in the metro-Nashville area were recruited for the current study. The Structured Clinical Interview for DSM-IV and DSM-5 Disorders-Research Versions (SCID-IV or SCID-5-RV, First et al., 2002, First et al., 2015) were used to confirm appropriate diagnoses. The Institutional Review Board of Vanderbilt University approved study protocols and written informed consent was collected from each participant. All participants were compensated for their time at a rate of $20/hour, and travel and/or parking expenses were reimbursed.

Twenty-seven medicated outpatients with schizophrenia were recruited from private psychiatric or community rehabilitation facilities in Nashville, TN. Exclusion criteria for this group included alcohol or substance abuse within past 6 months, history of brain injury or neurological disease, or IQ>70. Medication information was collected to calculate standardized chlorpromazine equivalent dose (CPZ) values (CPZ-EQ, Andreasen et al., 2010).

Twenty-two healthy control participants were recruited from the metro-Nashville community and matched to the patient group on age, sex, race, handedness and IQ, as assessed by the National Adult Reading Test (NART). Exclusion criteria for healthy participants included past or present DSM-5 disorders, family history of a psychotic disorder, current or past substance use within six months prior to testing, IQ<70 and any presence of neurological disorder.

Table 7.
Participant Demographic Information

	Community Control (N=22)	Individuals with SZ (N=27)
Characteristic	Mean (SD)	Mean (SD)
M/F	11/11	13/14
Age (years)	44.33 (8.7)	47.9 (9.9)
Education (years)	13.11 (1.94)	13.19 (1.97)
Medication (mg/day)[a]	----	285.41 (242.48)
Estimated IQ[b]	107.22 (7.27)	101.37 (9.9)
Handedness[c]	80.95 (40.95)	77.77 (42.73)

[a] All patients were medicated. Antipsychotic dosage was converted to chlorpromazine (CPZ) equivalent (Andreasen et al., 2010). [b] Estimated from the National Adult Reading Test, Revised (NART-R; Blair & Spreen, 1989). [c] Edinburgh Handedness Inventory (Oldfield, 1971). Scores range from -100 (completely left-handed) to +100 (completely right-handed).

Pilot

Patients with schizophrenia were recruited and randomly assigned to receive exclusion, inclusion or neutral Cyberball social treatment, as designed in Study 1A. A sample of 22 patients (Exclusion=7, Neutral=7, Inclusion=8) completed Study 1A procedures. Analyses of this pilot data revealed that acute social manipulation (Cyberball) had no significant or trend-level effects on social performance in patients with schizophrenia. However, chronic loneliness rates were indicative of performance differences on biological motion tasks. Very high loneliness was reported on average by patients in this pilot, consistent with previous findings. Due to the chronic nature of isolation already reported to be regularly experienced by the sample, it is logical that an acute 10-minute social manipulation did not have the magnitude of impact on social inference in this population as in our heavily socially ensconced college-aged sample. This

is consistent with previous imaging literature demonstrating blunted neural response to social exclusion in this highly excluded population (Gradin et al., 2012). Study efforts were subsequently consolidated to elucidate the impact of chronic loneliness and isolation, rather than laboratory manipulations, on social performance in patients with schizophrenia as compared to healthy matched controls.

Procedure and Materials

All patients with schizophrenia and healthy control participants completed the forced-choice biological motion Recognition task described in Study 1B and the UCLA Loneliness scale, and Social Quantity self-report questionnaires. Matched control participants were administered the PQ-B and the Schizotypal Personality Questionnaire (SPQ; Raine, 1991). Participants with schizophrenia were interviewed with the Brief Psychiatric Rating Scale (BPRS; Overall & Gorham, 1962), the Scale for the Assessment of Positive Symptoms (SAPS; Andreasen, 1984), and the Scale for the Assessment of Negative symptoms (SANS; Andreasen, 1983). All clinical interviews were administered to patients by either an advanced clinical graduate student or a trained research assistant with consistently demonstrated interrater reliability.

Clinical Assessment Measures

Schizotypal Personality Questionnaire. The SPQ is a 74-item self-report questionnaire designed to assess schizotypal personality traits based on DSM-III schizotypal personality disorder criteria (APA, 1980). The SPQ is widely used and has been shown to have excellent psychometric properties (e.g., Wuthrich & Bates, 2006). Example items include “I am an odd, unusual person” and “Do you sometimes feel that

other people are watching you?". Items are binary scored with 1 point awarded to each True response and 0 awarded to False. Scores over 41 on the SPQ are considered "high" and scores under 12 are considered "low", based on the top and bottom 10% cutoff scores on the distribution of SPQ scores (Raine, 1991).

Brief Psychiatric Rating Scale. The BPRS is a clinical rating scale designed to quantify levels of a broad range of psychiatric symptoms, including depression, anxiety, hallucinations and unusual behavior. Each of 24 symptoms is rated with a 1-7 score for severity, with scores ranging from 0-144.

Scale for the Assessment of Positive Symptoms. The SAPS is a clinical rating scale designed to quantify levels of positive symptom severity in patients with schizophrenia. The scale is divided into four domains, Hallucinations, Delusions, Bizarre Behavior and Positive Formal Thought Disorder with between five and thirteen sub symptoms. Each symptom is rated for severity on a scale of 0-5. Scores on the SAPS range from 0-173.

Scale for the Assessment of Negative Symptoms. The SANS is a clinical rating scale designed to quantify levels of negative symptoms in patients with schizophrenia. The scale is divided into four domains, Affective Flattening or Blunting, Alogia, Avolition-Apathy, Anhedonia-Asociality and Attention. Each domain contains between five and eight symptoms rated for severity on a scale of 0-5. Scores on the SANS range from 0-129.

Results

Social Profiles and Clinical Symptoms

A one way analysis of variance showed that the effect of group on loneliness was significant, $F(1,46) = 13.24$, $p = .0007$, indicating a significant difference between loneliness endorsed by participants with schizophrenia ($M = 30.07$) and matched

community controls (M = 15.38), such that individuals with schizophrenia endorsed an average of about twice the severity of loneliness than controls (see Figure 5). Individuals with schizophrenia also exhibited significantly lower quantitative averages of social engagement (M = 6.4) as compared to controls (M = 10) over the past month ($F(1,46) = 7.60$, $p = .008$, see Figure 6). A trending but non-significant relationship was found between loneliness and psychiatric symptoms in participants with schizophrenia (BPRS $\rho = 0.35$, $p = 0.07$), but not with specifically positive (SAPS $\rho = 0.15$, $p = 0.42$) or negative (SANS $\rho = 0.23$, $p = 0.24$) symptoms. In healthy controls, however, we find significant relationships between higher endorsed loneliness and greater schizotypal traits (SPQ $\rho = 0.47$, $p = 0.02$), in particular in the Cognitive ($\rho = 0.45$, $p = 0.04$), and Interpersonal ($\rho = 0.44$, $p = 0.04$) domains. Distress over prodromal symptoms was not found to be associated with loneliness, however the mean endorsement of PQ-B items was just 2.9, and the rating of distress by community controls was -1.04, indicating that any of the few anomalous experiences they endorsed was on average, pleasant and not distressing. Multiple regression analysis was used to test if loneliness or social isolation significantly predicted participants' symptoms but proved insignificant for explaining variance in symptom severity from endorsement of either qualitative or quantitative social duress.

Figure 5.
Loneliness Severity in Individuals with Schizophrenia Compared to Matched Community Members

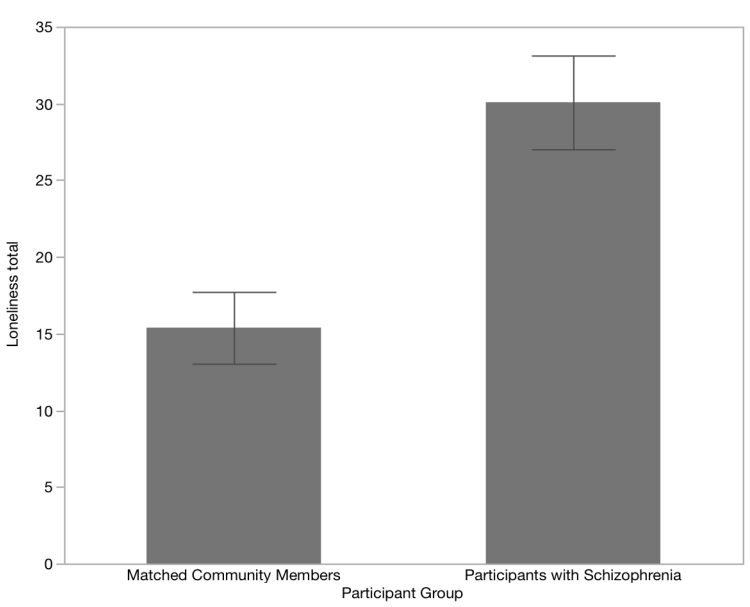
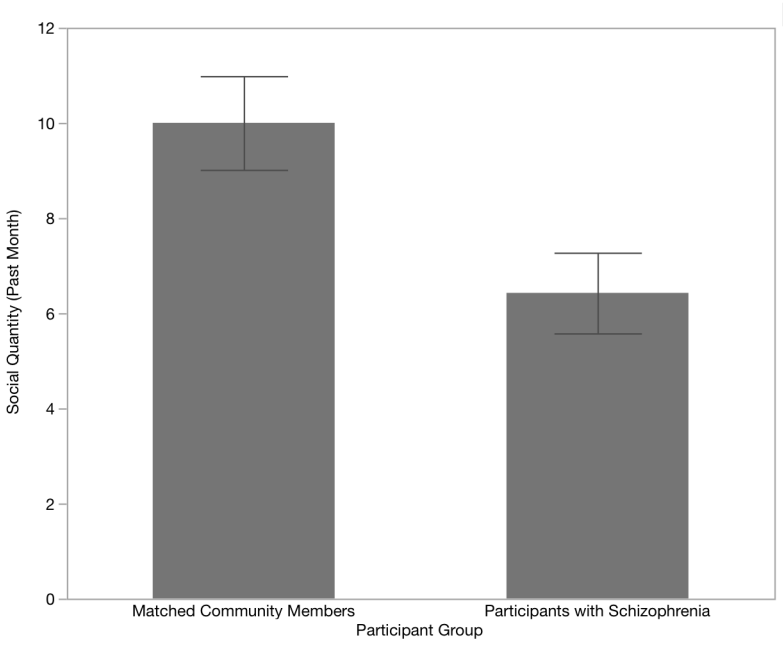


Figure 6.
Social Opportunity in Individuals with Schizophrenia Compared to Matched Community Members

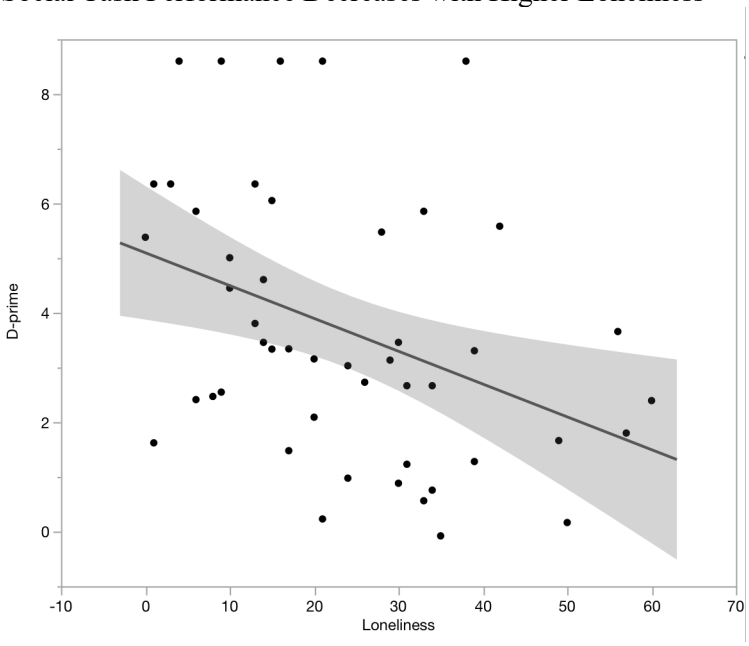


Social Inference Task

Analysis of the Biological Motion Recognition task revealed that healthy controls had significantly higher average rates of correct Hits compared to individuals with schizophrenia ($F(1,46) = 5.56$, $p = .02$), meaning that controls accurately identified displays of human motion more consistently than those with schizophrenia. Simple linear regression demonstrated that higher loneliness significantly predicted lower Hit accuracy across the sample ($\beta = -0.20$, $SE = 0.06$, $p < .001$) and explained a significant proportion of the variance in hit accuracy ($R^2 = 0.21$, $F(1, 46) = 11.93$, $p = 0.001$). No relationship was found between social engagement quantity and Hit accuracy.

No significant difference in rates of False Alarms at 25% induced noise was observed between groups. At 100% noise (true False Positive), individuals with schizophrenia demonstrated significantly higher rates of endorsement of biological motion than controls ($F(1,46) = 11.64$, $p = .0007$), meaning that on average, individuals with schizophrenia more frequently believed that there was a human characteristic in trials of random noise. In individuals with schizophrenia, a significant relationship between social engagement and reaction time on the 100% noise trials existed ($\beta = 0.09$, $SE = 0.03$, $p < .007$), such that higher social exposure predicted longer time needed to decide whether a pure noise trial included human motion or not ($R^2 = .25$, $F(1, 25) = 8.37$, $p = 0.007$, $p < .007$). Taking overall task performance together, using the metric D', greater loneliness significantly predicted poorer social inference task performance ($\beta = -0.06$, $SE = 0.02$, $R^2 = .15$, $F(1, 46) = 7.79$, $p = 0.007$, see Figure 7).

Figure 7.
Social Task Performance Decreases with Higher Loneliness



Discussion

As predicted, we replicated previous findings that individuals with schizophrenia experience significant loneliness, and demonstrated that, in fact, this population experiences loneliness at a rate of almost twice that of age-matched healthy counterparts. Overall, all participants endorsed at least one point of loneliness, suggesting that experience of loneliness indeed prevails across health status.

Quantitatively, individuals with schizophrenia also endorsed significantly diminished social activity, at about half the frequency when compared to healthy community peers. Interestingly, only trend level associations existed between loneliness and clinical symptoms of schizophrenia. Notably, the sample participating were all well-medicated with very low positive symptoms overall, which may have weakened the ability to detect any existing relationship to social distress symptoms. However, in unmedicated healthy controls, greater loneliness was associated with higher SPQ scores. Though

directionality of this effect was not determined, a pattern of higher social distress when experiencing traits on the psychosis spectrum is evident, despite these prodromal events being categorized on average in this sample as pleasant, not distressing.

Individuals with schizophrenia also experienced more difficulty correctly recognizing both the presence or absence of human motion in this study. Loneliness accounted for a portion of the variance of task performance, suggesting that chronic distressing separation from others does impede perceptual processing of social stimuli. Social engagement may serve as a protective factor, as those in the patient group with higher social quantity were more likely to spend more time deciphering trials of pure noise, suggesting less conviction of the accuracy of spurious perceptions.

Conclusions

Examination of the social distress and social engagement of middle-aged individuals experiencing chronic schizophrenia demonstrates the dearth of social support perceived and available to these vulnerable individuals. Even healthy mid-aged adults with no psychiatric conditions endorse experiences of loneliness, calling attention to the pervasive nature of unsatisfactory social quality, and starkly outlining the risk for those who are currently stigmatized, ostracized and isolated such as individuals with psychosis. We demonstrate evidence that chronic loneliness and weak social engagement indeed shows relationship to poorer social perception performance on a basic level, which may only extrapolate in higher order social function, thus potentially perpetuating the cycle. Having established the prevalence of this condition and highlighted potential deficits that may result, we next determined to address this adversity by creating and testing a novel social inclusion intervention, as outlined in Chapter IV.

CHAPTER IV

Study 3: Effects of a Choral Social Inclusion Intervention on Loneliness and Social Impairment for Individuals Across Psychosis Spectrum

Rationale and Study Aims

Music and group singing have been shown to beneficially alter the brain, through reduction of cortisol and increased oxytocin, improved sense of well-being and diminished feelings of loneliness and depression in healthy and aging populations (e.g., Loersch & Arbuckle, 2013, Clift & Hancox, 2010, Grape et al., 2003, Kreutz et al., 2004, Vickoff et al., 2013). Group singing particularly has been demonstrated to have a unique "ice-breaker effect" promoting faster group cohesion (Pearce et al., 2015). Humming has previously been reported to diminish auditory hallucinations in SZ, utilizing the same fronto-temporal regions and output systems (Green & Kinsbourne, 1990), however no group singing intervention has been implemented in populations with psychosis to date.

Thus, the purpose of this study was to examine the effects of a novel and naturalistic inclusive choral group intervention in individuals with schizophrenia, aimed to determine the efficacy of such an intervention on endorsement of loneliness and distress, on symptom ratings, and on performance on social detection via biological motion detection tasks. Inherent in the study design, the group also served as repeated social exposures and facilitated rehearsal of social interaction skills. We hypothesized that group members would display diminished loneliness, increased perceived well-being and ability to cope with stressors after eight sessions of group. A secondary hypothesis was that this increase in consistent social exposure would improve social inference as measured by biological motion recognition and Cogstate testing at the conclusion of the eight weeks.

Method

Participants

Twenty-one individuals with schizophrenia were recruited from the community and a local mental rehabilitation center in two group waves. Diagnoses were confirmed using the SCID-5-RV (First, 2015) and medical records. Eligibility requirements included IQ ≥ 70, no history of head injury or neurological disorder, and no history of illicit drug use in the year prior to the study. Musical ability and experience were not used as eligibility requirements for participation, and this was emphasized to all recruited group members. All participants were compensated for their time during baseline and post-intervention testing at a rate of $20/hr and compensated for travel expenses. Group participants were also rewarded a $2.00 bonus for completing check-in surveys at each choral session.

Seventeen individuals were retained through post-intervention testing. One participant dropped out after pre-testing due to transportation issues. Two participants became unable to attend groups after session 2 and session 4 due to work and treatment obligations. The final participant lost to follow up did attend one session but decided she would not like to continue due to self-consciousness of a nature related to her delusional symptom content. Data analyses reported reflecting pre-to-post intervention differences include only those participants who completed all time points. See Table 8 for pre- and post-intervention demographics, and Table 9 for retention and attendance.

Table 8.
Participant Demographic Information

	Pre-Intervention (N=21)	Post-Intervention (N=17)
M/F	10/11	7/10
Age (years)	48.33 (10.4)	48.05 (10.6)
Medication (mg/day)[a]	244.64 (256.21)	251.48 (241.32)
Estimated IQ[b]	95.82 (8.07)	94.9 (8.2)

Table 9.
Session Attendance

Total Number of Sessions Attended	Number of Participants
8 *(all sessions)*	7
7	4
6	2
5	4

Procedure and Materials

Pre-Intervention Testing

Baseline function and assessment values were obtained for all participants over the course of two weeks prior to intervention. Group 1 pre-testing was conducted in a research laboratory at Vanderbilt University. Group 2 pre-testing was conducted in a small conference room at the Park Center, a nonprofit rehabilitation agency for individuals with severe mental illness in Nashville, TN. Initial clinical symptoms were measured using the BPRS, SAPS, and SANS. Loneliness was measured using the UCLA Loneliness Scale. Average social engagement quantity over the past one month was collected. Participants completed the forced choice biological motion Recognition task as described in Studies 1-3. In addition, participants completed a computerized cognitive test of social emotional processing taken from the CogState Schizophrenia Battery (Piertzak et al, 2009). The Positive and Negative Affect Schedule (PANAS; Watson et al., 1988) was also administered to assess participant affect over the past week, and the Perceived Stress Scale (PSS; Cohen et al., 1983) was collected to assess perceived ability to cope over the past month.

CogState Social Emotional Task. CogState is a computerized, standardized program designed to assess cognitive function across populations. The cognitive test selected from the CogState Schizophrenia battery is designed to assess subjects with schizophrenia in both the acute and chronic stages. Moderate to large correlations are observed between CogState and the standard Measurement and Treatment Research to Improve Cognition in Schizophrenia (MATRICS) are observed (rs = .56–.79, Piertzak et al., 2009).

CogState has been found to have minimal practice effects after initial familiarization, no have ceiling or floor effects and has good test-retest reliability (e.g., Falleti et al., 2006, Maruff el al., 2009, Fredrickson et al., 2010). Other benefits include the brief amount of time required to administer tests and ease of explanation of tests and test administration. In this task, four avatar emotion faces are displayed with one "odd-man out" amongst them and participants are asked to tap the face that does not match as quickly and accurately as possible. The primary outcome measure is accuracy of performance.

Positive and Negative Affect Schedule (Watson et al., 1988). The PANAS is a 20-item self-report measure of current affect, with ten positive items (e.g., Enthusiastic, Inspired, Proud) and ten negative (Afraid, Hostile, Distressed). Each item employs a Likert-like 5-point scale from 'very slightly or not at all' (0) to 'extremely' (5). Scores range between 10 and 50 for Positive and for Negative. Reliability and validity are reported to be moderately good (Positive α = 0.86 to 0.90; Negative α = 0.84 to 0.87, Watson 1988).

Perceived Stress Scale (Cohen et al., 1983). The PSS is a 10-item self-report measure of the degree to which a participant appraises various situations in their life as stressful. Example items from this questionnaire include, "In the last month, how often have you felt confident about your ability to handle your personal problems?" and "In the last month, how often have you felt difficulties were piling up so high that you could not

overcome them?".

Participants respond on a 5-point scale ranging from 0 (Never) to 4 (Very Often). Positive items are reverse scored, and ratings are simply summed across items for a final score. The authors indicate that scores of around 13 are considered "average", while scores of 20 or higher are considered "high stress". The PSS is found to be a better predictor of experienced level of stress than life-event scores, as it highlights appraisal of these events, not simple occurrence. When compared to a depression scales, the PSS was found to measure a different and independently predictive construct (Cohen et al., 1983). As a primary motivation of the present study was to decrease perceived and experienced distress, the PSS was chosen to capture the subjective appraisal of participants' perception of their abilities to manage daily life.

Choral Inclusion Intervention

Choral rehearsals were held for one hour each week, over a course of eight weeks. Group 1 was held at Wilson Hall on Vanderbilt University's campus. Group 2 was held at the Park Center. Sessions began and ended with five minutes of free socialization. Fifteen minutes were then allocated for physical and vocal warm-ups with emphasis on body and self-other awareness (e.g., exercises to stretch and move the body, vocal exercises focused on volume, emotional expression and 'blending' with others in the group by listening to neighbors in a circle and trying to match). Twenty-five minutes were spent learning and rehearsing choral music. Beginner choral pieces ("Weave Me A Poem", by Blickhan & Ode, 2011 and "Lift Every Voice", by Johnson & Johnson, 1905) were selected for low complexity and neutral-positive message from public domain and were taught aurally. Sheet music and printed lyric pages were also provided to each participant. An

undergraduate volunteer pianist accompanied Group 1, while Group 2 was accompanied by a paid local community pianist, due to the former pianist's availability constraints. The pianists did not assist in coordination or conducting and had minimal yet positive interface with group participants. During music learning and singing, participation, group cohesion, enjoyment and emotive rehearsal were emphasized, and exact mastery of the music was deemphasized. Participants completed a 'weekly check-in' sheet including the PANAS and social engagement quantity over the past one week as well as impressions and feedback from the session during the remaining 5-10 minutes of choir session, for which they received $2.00 bonus. This questionnaire was presented as optional, but resulting compliance was one-hundred percent

Post-Intervention

All pre-intervention measures were conducted at post-intervention sessions, in the same location and rooms as was conducted pre-intervention. Participants were tested as immediately as possible, and all post-tests were completed within two weeks following the intervention.

Results

Matched pairs analysis demonstrates that eight weeks of a social inclusion singing group significantly reduced reported loneliness in the sample ($t(16)= 2.09$, $p = 0.02$), with a mean difference score of 6.29 (pre M = 30.2, post M = 23.8, see Figure 8). QQ plots were examined to verify normality of distribution of change scores. Additionally, number of sessions attended was positively correlated with attenuated loneliness ($t(16) = 4.15$, $p= .01$), while no significant association was found between amounts of social interaction per week.

Significant differences were also demonstrated in psychiatric symptom measurements after intervention, with reduction in BPRS ($t(16)= 1.89$, $p = 0.03$, mean difference = 2.17) but no significant change in SAPS or SANS. BDI scores were also significantly reduced at post-intervention measurement ($t(16)= 2.02$, $p = 0.02$, mean difference = 2.05). Furthermore, we found significant increased positive affect, via the PANAS. These results were maintained when accounting for session time point, arousal type (positive or negative), specific words, and individual subjects. Post hoc Tukey HSD tests showed that change was significant from each pre-intervention, session 1 and session 2 to sessions 5, 6 and 7 respectively at $p < .05$ or less (see Figure 9). Decrease in Negative affect over sessions was modest, but non-significant. No difference was found in perceived ability to cope with stress following the intervention, as measured by the PSS, and this was not found to be significantly related to endorsed level of social stress via loneliness at any time point.

No significant improvements on accuracy or efficiency were found on social inference tasks. However, replicating Study 2, higher symptoms ratings on BPRS were found to be associated with greater endorsement of false alarms on the biological motion recognition task ($\rho = 0.32$, $p = 0.04$). Higher loneliness was also inversely related to Hit rate on this task, such that lonelier individuals less accurately identified social motion ($\rho = - 0.57$, $p = 0.0007$). CogState social emotional performance did not significantly improve, though accuracy increased nonsignificantly (pre M = 81%, post M = 84%).

Figure 8.
Loneliness Is Significantly Reduced Pre To Post Intervention

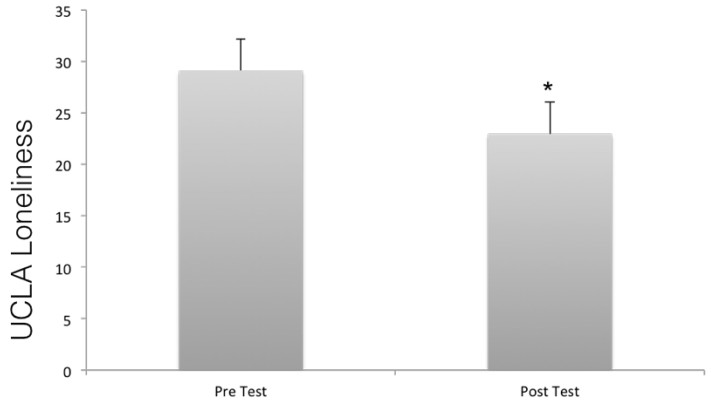


Figure 9.
Positive Mood Is Significantly Increased Over Intervention Time Points

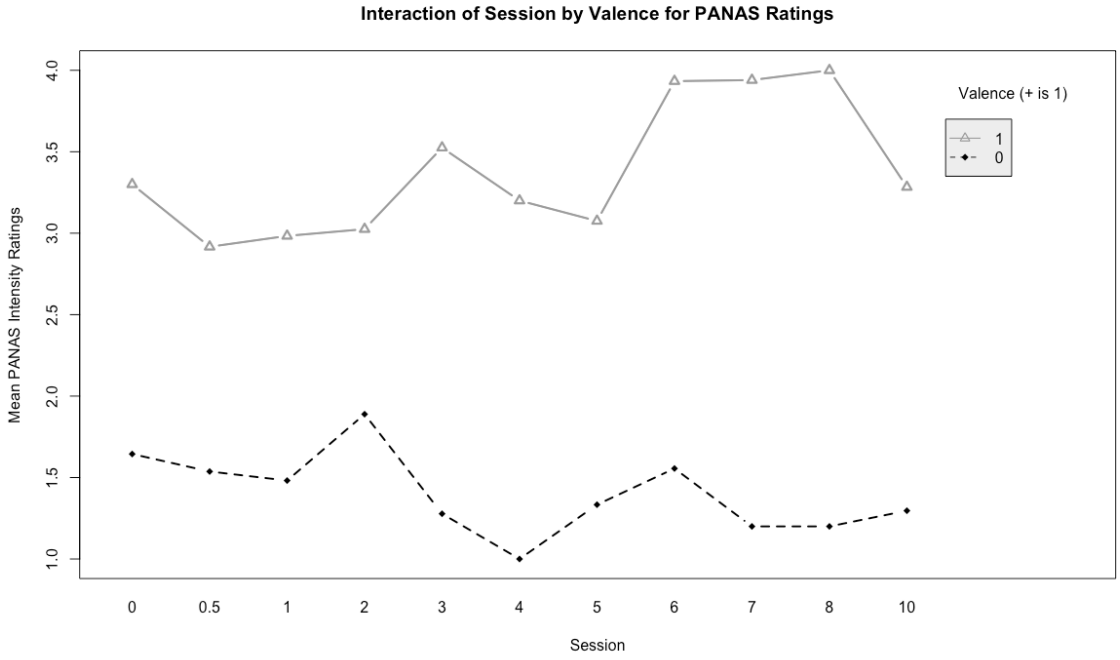


Fig 3. Positive affect (coded '1') significantly improves from session 0 (pre-intervention), sessions 1 and 2 to sessions 5, 6 and 7. Session 10 (post-intervention) shows a drop-off after two weeks post-group. Negative affect (coded '0') shows modest but non-significant decrease from pre to post intervention.

Discussion

To date, this is the first intervention study targeting and successfully reducing loneliness in individuals with schizophrenia. The social bonding principles of group singing may have allowed for more rapid sense of belonging and significant reduction of loneliness than other group therapy efforts. A dose dependent relationship suggests that participants who attended more total sessions benefitted most in relief of social distress. Despite no significant change in reported quantity of social engagement week to week, the quality of belonging improved greatly, suggesting that efforts need not be time-intensive to create a meaningful impact for socially isolated individuals. The group was also perceived as enjoyable, and affect was improved over the course of intervention. This enjoyability of the activities may contribute to the positive effects on clinical symptoms, and demonstrates that choral singing can be both clinically effective and pleasant to engage in for participants.

Conducting this study posed several challenges that may create limitations. Transportation once per week for ten weeks (including Pre and Post sessions) was a challenge for some participants, leading two initially recruited participants to drop out before intervention began. Some participants found maneuvering the CogState program to be challenging because of physical limitations or low familiarity with computer tools, which impeded their physical performance and may have impacted scoring. Lastly, due to the number of variables within the choir intervention itself, specificity of the 'active ingredients' that created success in diminishing loneliness and clinical symptoms was not determined by this study. Future work may assess specific contributions to hone in on a parsimonious intervention. In addition, further investigations may assess more specifically for improvements in frequency or quality of social interaction.

Conclusions

This study examined the efficacy of a novel, low-burden social intervention in patients suffering from psychosis. We hypothesized that group singing would be beneficial in improving social, perceptual and affective impairments of those experiencing auditory hallucinations. We demonstrated that an 8-week choral intervention can significantly reduce endorsed loneliness and clinical symptoms and improve affect, as assessed by PANAS. A protective relationship was found between the number of choir sessions a participant attended and expressed loneliness at post-testing. However, despite these improvements no significant improvement of social perception or positive symptoms was gained by this social exposure intervention.

Given the well-studied benefits of music, inherently concentrated social interaction and inclusion factors the group, this study provides a novel model for inexpensive and simplistic intervention available for implementation in individuals with schizophrenia and across the mental health spectrum. This program may serve as a safe opportunity to practice social skills in a group setting for highly isolated individuals. Participants resoundingly rated the intervention very highly on qualitative survey questions, suggesting that this exposure is not only effective but also enjoyable for participants.

Of course, singing together will not cure neuropsychiatric disorders but we believe this study provides compelling preliminary evidence for including music making as an adjunct treatment for relief of social distress. As social cognition performance remained unstirred by this intervention effort, we next initiated exploration of a novel immersive social skills training program to determine whether naturalistic social exposure and interactive training combined might improve outcomes in both social stress and social inference, as detailed in Chapter V.

CHAPTER V

Study 4: Effects of a Virtual Reality Social Training Intervention on Loneliness and Social Cognition for Individuals with Schizophrenia

Rationale and Study Aims

Having demonstrated that a social inclusion intervention is effective for reducing loneliness, but not improving social inference, we lastly sought to examine the efficacy of a novel socialization training intervention in both decreasing feelings of loneliness and improving social cognitive function in individuals with schizophrenia.

We aimed to do so with a novel, skill-based and adaptive virtual reality (VR) simulated social training intervention, in collaboration with the Robotics and Autonomous Systems Lab, under the direction of Dr. Nilanjan Sarkar at Vanderbilt University (see Bekele et al, 2016). While many behavioral training programs currently exist, such as Social Skills Training (SST) (Kreyenbuhl et al., 2010; Swartz et al., 2007), many of these psychosocial interventions yield only modest effect sizes for achieved social outcome (Kopelowicz et al., 2006; Pfammatter et al., 2006). Interventions that target social cognition, involving training of specific cognitive and emotional processes thought to underlie social interactions such as emotion recognition and theory-of-mind, have proven more effective (Kopelowicz et al., 2006: Kurtz and Mueser, 2008; Granholm et al., 2005; Lindenmayer et al., 2013; Penn et al., 2007). However, low generalizability, modest treatment effects and low compliance present challenges to implementation of existing methods (Kurtz and Mueser, 2008).

Despite these practical shortcomings, broad consensus on effective strategies for improving social functioning involve structured didactic procedures with concrete goals, role-playing, and rehearsal (Bellack, 2004). For efficient learning it is also important to

provide targeted feedback and rapid reinforcement, which allow for dynamic adjustments of task difficulty based on performance. Social learning occurs when the patient's goals and capacity are well calibrated so that errors are minimized, and targeted behaviors are reinforced (Swartz et al., 2010). Since all forms of learning involve mental simulation, imitation, and repetition in a wide variety of situations (Park et al., 2008; Matthews et al., 2012; Mazza et al., 2010), role-playing exercises in multiple contexts can help generalization. Lastly, optimal arousal and attention are indispensable for engaging the individual and facilitating learning (e.g., Corrigan et al., 1990; Nakamura and Csikszentmihalyi, 2002).

The advantages of incorporating VR into social intervention include flexibility, controllability, and virtually limitless creation of stimuli, while remaining low-burden, cost efficient, and safe (Strickland, 1997). VR provides opportunities for simulation and adaptive rehearsal, essential to practicing new skills across multiple contexts. This also promotes generalization of skills to real world application (Strickland, 1997; Mitchell et al., 2007). While we do not believe VR can replace interpersonal interactions, the controllable complexity of VR allows the user to navigate realistic social interactions across multiple scenarios with minimal distraction, confusion or distress, providing a safe "training ground" for skills, in environments they will encounter in their real daily lives (Moore et al., 2000; Tartaro et al., 2007; Standen et al., 2005).

Previously, VR has been shown to enhance medication adherence (Kurtz et al., 2006) and help individuals cope with auditory hallucinations (Craig et al., 2017; Du Sert et al, 2018). Furthermore, a randomized clinical trial of VR for vocational training found significant improvement in cognition, work outcome, and work-related self-efficacy after just ten, 30-minute VR sessions across five weeks (Tsang and Man, 2013). Park et al.

(2011) found in a larger, randomized controlled trial of SST with VR role-playing that individuals with schizophrenia in the VR training group exhibited greater improvement in conversational skills and assertiveness than a group that received SST with traditional role-playing.

Based on this prior literature, we hypothesized that 10 sessions of social simulation exercises in a low-stress setting (i.e. playing a social video game on the non-immersive VR platform) would improve social functioning in individuals with schizophrenia by improving deficits in social cognition. We hypothesize that through training and feedback, combined with inherent increased social engagement of the protocol, patients with schizophrenia would demonstrate significant improvement on measures of social cognitive accuracy, endorse decreased clinical symptoms, perceived alienation and loneliness, and report increased social engagement within their natural environments.

Specifically, we hypothesized that we would see an improvement in clinical symptoms measured by BPRS, SAPS and SANS scores after 10 sessions of social engagement and skill training. We hypothesized improvement in CogState Social Emotional task performance from baseline to post-test, but no significant improvement on Maze Learning, Identification or Two-Back tasks. Additionally, we expected that participants would demonstrate improvement on the BLERT and Eyes social emotion recognition and mental state inference tasks. We hypothesized that loneliness could be reduced from baseline by this intervention, as increased skill knowledge could be applied to self-initiated reduction of social distress, and because the nature of the study involved frequent positive socialization with team members and study avatars. We hypothesized that we may see translational effects of the training via greater reported social engagement quantity and higher social functioning as measured by the SFS.

Method

Participants

Individuals from the community who met DSM-5 criteria for schizophrenia and were taking antipsychotic medication were recruited from the Nashville Metro area. Inclusion criteria included a diagnosis of schizophrenia and continuous medication throughout the course of the study. Exclusion criteria included no history of head injury or neurological disorders, no history of substance use or alcohol abuse in the past six months, and an IQ $\geq$ 70. Diagnosis was confirmed by SCID-5-RV interviews conducted by masters'-level clinical psychologists who were blind to previous participant symptom and assessment scores. Participants were paid $20 per hour and compensated for travel expenses. See Table 10 for demographic and clinical summary.

Eighteen participants were assessed at baseline and began training. One participant dropped out after the fourth session due to increasing work demands. One participant completed 10 sessions of training but did not return for the post-treatment assessment. Therefore, 16 patients successfully completed the full study protocol, including initial pre-intervention assessment, 10 sessions of VR social skills training, and post-intervention assessment.

Table 10.
Participant Demographic Information

	SZ-PRE (*N*=18)	SZ-Completed (*N*=16)
M/F	10/8	9/7
Age (years)	48.78 (7.42)	48.63 (6.98)
Education (years)	13.11 (1.94)	13.19 (1.97)
Medication (CPZ mg/day)	285.41 (254.84)	260.44 (242.48)
Estimated IQ	102.02 (8.71)	102.69 (8.81)
Handedness	68.06 (40.95)	66.56 (42.73)

Procedure and Materials

Pre- and Post-Intervention Testing

All participants completed a pre-training baseline assessment of intellectual functioning, social engagement and clinical symptoms. Baseline measures included the UCLA Loneliness scale, social engagement quantity measure, SAPS, SANS, BPRS, and the CogState Schizophrenia Battery, as described in Study 3. Additional baseline and post-intervention measures included the Bell Lysaker Emotion Recognition Task (BLERT; Bryson, Bell & Lysaker, 1997), Social Functioning Scale (SFS; Birchwood et al., 1990), and theory of mind task assessing ability to infer the internal emotion states of others, called Reading the Mind in the Eyes (Eyes; Baron-Cohen et al., 2001). Participants completed post-training assessment within two weeks of their final training session. At the post-training visit, the above measures were reassessed, and participants completed a training satisfaction survey.

Additional Assessment Measures

Bell Lysaker Emotion Recognition Task (Bryson et al, 1997). The BLERT measures recognition of seven emotional states (happiness, sadness, fear, disgust, surprise, anger, or neutral) through prosody. Participants are shown in 2121 randomly presented videos of the upper body of a Caucasian male actor reciting the same few sentences through each emotional state, providing facial, auditory and movement cues. Performance is indexed as the total number of correctly identified emotions (ranging from 0 to 21).

Social Functioning Scale (Birchwood et al., 1990). The SFS is a 79-item scale used to assess social function in schizophrenia. Seven categories of social function are assessed including social engagement, interpersonal communication, activities of daily living,

recreation, social activities, competence at independent living and occupation/employment. Raw subscale scores are converted to scaled scores with a mean of 100 and SD of 15, and T-scale scores may then be compared to a normed sample. This scale has been shown to be adequately reliable and sensitive in measuring these domains of social function (Birchwood et al., 1990).

Reading the Mind in the Eyes Task (Baron-Cohen et al., 2001). The Eyes task assesses mental state attribution and complex facial emotion recognition from photographs depicting solely the eye region of the face. Subjects must infer the mental states of others from the images of their eyes, or exercise theory of mind, a skill that facilitates social intelligence and empathy. A series of 36 images are presented, and participants are asked to choose which best fits the state depicted from four presented emotion terms. The emotional terms presented are considered complex mental states (e.g., playful, comforting, irritated or bored) in contrast to basic emotions (e.g., happy, sad, angry or surprised). A glossary of all the mental state terms is available for participants to consult in any case where they are unsure of a word. Validity testing indicates no significant correlation between IQ and the Eyes Test, suggesting this measure is independent of general (nonsocial) intelligence (Baron-Cohen et al., 2001).

Virtual Reality Social Training

The goal of this VR program was to enhance social skills in an engaging, naturalistic and low-burden environment (for further detail, see Bekele et al., 2016; Bekele et al., 2013). Social interaction difficulty was also varied to promote skill training and reflect the natural variety of social demands in real life. In the physical world, micro-level, non-verbal social skills such as eye contact, facial expression, social distance and gesture

must be modified according to the demands of social situations (Spence, 2003). Such micro-level skills must then be integrated with appropriate macro-level strategies, such as starting conversations, greeting people, and requesting help or information. Our VR task promotes use of both micro and macro-level social skills by requiring participants to engage avatars via eye contact, assess avatar facial expressions and body language, initiate conversations and predict and perspective-take the emotions and reactions of others, all within diverse social contexts.

Avatars conveyed facial expressions and utilized pre-recorded human speech to ensure that the tone of voice and prosody was akin to what one would encounter in a real-life social interaction. Participants responded to the avatar using a keyboard to select from text-based menus superimposed on the scene that provided structured statements from which a subject could choose to initiate or continue an interaction. Additionally, a game-narrator provided verbal instructions for general game navigation and training feedback following conversational selections. Notably, there were no negative consequences in the game context (e.g., no loss of points), making it a low-stakes training program.

The content of the VR training was created to exercise an important aspect of SST curriculum that focuses on starting a conversation with an unfamiliar person in order to make requests or ask for information. Each training session requires a participant to complete 12 social "missions". A mission (e.g., "Find out the avatar's favorite TV show") involves the user approaching and interacting with a new person (an avatar) across three naturalistic social environments (a grocery store, café, or bus stop, see Figure 10A-D) through variable sequences of conversations. The participant chooses a mission from four available options and may move freely about the virtual space to explore and identify an avatar to engage.

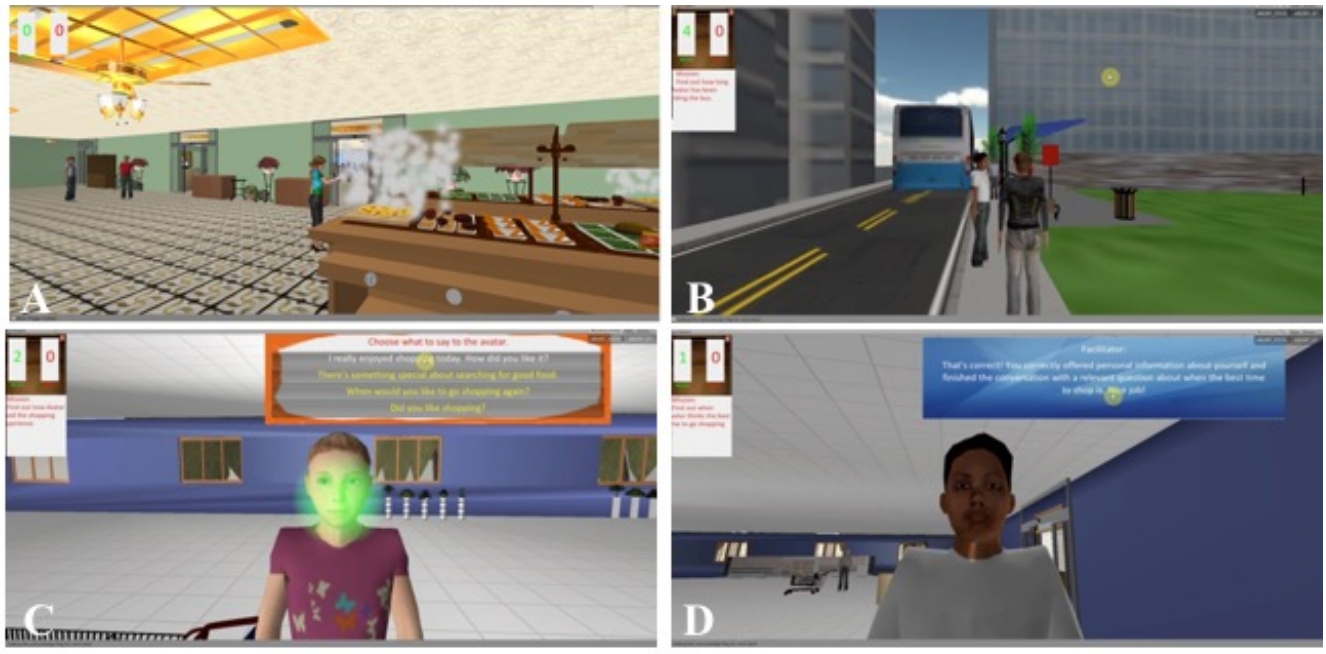
Upon approaching an avatar, the participant must fixate on the avatar's face to remove a transparent green mask occluding the face, encouraging eye contact and appropriate social distance. Participants then choose from a list of four conversational options presented on the screen to address their mission (e.g., "How did you start watching comedies?", "Comedies are a lot of fun", "What's your favorite one?" or "Nice! I really enjoy Friends. What's your favorite TV show?"). If participants choose an incorrect response (e.g., "What's your favorite one?"), dynamic audio feedback is provided by the narrator to inform the participant why the response was not ideal, and participants are instructed to select again (e.g., "Very good try. This question might get you the information you are trying to learn, but remember to offer information about yourself. Try again."). This real time feedback is provided to the participant after each response made, allowing for strategy updates, and in-vivo learning opportunities.

Social missions also vary by level of difficulty, determined by the number of conversational inquiries and responses required for mission completion. For an 'easy' scenario, a participant can interact with the avatar with minimal effort (i.e., mission is completed by one appropriate social inquiry). A 'medium' level of difficulty requires the participant to link two appropriate social bids together to attain a goal, such as joining a table occupied by strangers. For 'difficult' level interactions, the social goal may be attained only after the participant links several appropriate social bids together. Missions are considered unsuccessful if the participant chooses more than two incorrect conversational responses during an interaction, and a new mission must be selected.

Each session, participants completed four Easy, four Medium and finally four Hard missions sequentially to reach twelve successful missions. Mission environments were varied by session. After five training sessions, naturalistic environmental background noise

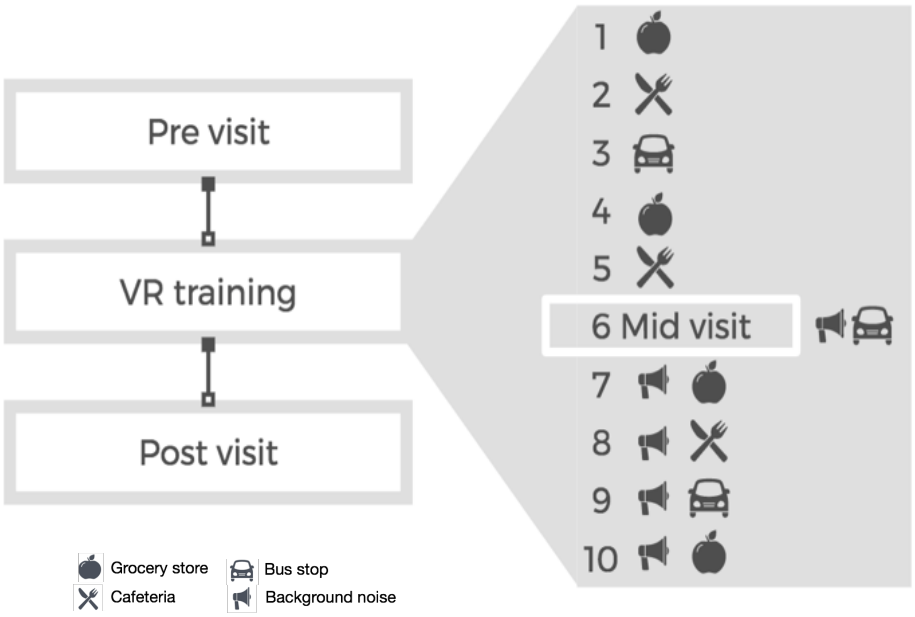
was added to the VR environments to increase mission difficulty. See Figure 11 for the outline of this training design. This scaffolded approach to mission difficulty, both across and within missions and training sessions, minimizes risk of repeated negative feedback that may lead to participant disengagement. There was also no time limit to complete a mission, nor the full set of twelve missions per session.

Figure 10A-D.
Virtual Reality Training Scenario Examples



A) Exploring the virtual environment in the café. Completed mission score is statically depicted on the left-hand side of screens. **B**) Scene from Bus Stop virtual environment. Current mission target appears statically on the left-hand side of screen after a mission is chosen. **C)** Multiple choice conversation initiation in Grocery Store environment. Green mask is removed after appropriate social gaze. **D)** Response choice feedback is provided after participant conversational selection and avatar response.

Figure 11.
Training Design



Results

Overall psychiatric symptom severity as measured by the BPRS was significantly improved from baseline to post-intervention training, $t(15) = -2.76$, $p = 0.006$ ($M_D = -4.27$, $SE = 1.54$). Negative symptom severity assessed by SANS also significantly decreased from baseline to post-training, $t(15) = 2.98$, $p = 0.004$ ($M_D = 9.22$, $SE = 3.1$, see Figure 12). No improvement of positive symptoms was observed from pre- to post-training.

Examination of CogState performance revealed non-significant improvement on the Social Emotional Cognition task. In fact, there was no observed improvement across CogState tasks. There was also no significant change on Eyes mental state attribution task performance from baseline to post-training. However, performance on the BLERT emotion recognition was seen to significantly improve from baseline to post-training, $t(15) = 2.98$, $p = 0.01$ ($M_D = 1.55$, $SE = 0.62$). In particular, when assessing negative verse positive

emotion trials, significant improvement was seen on identification of negative emotion states from baseline to post-training, $t(15) = 2.11$, $p = 0.02$ ($M_D = 0.72$, $SE = 0.34$, see Figure 13).

There was a non-significant, trend-level reduction of loneliness ($p = 0.056$, $M_D = 3.8$) and reported quantity of social engagement was not significantly affected by the social training regimen. One subscale of the SFS, Interpersonal Communication, was observed to modestly yet significantly improve from baseline to post-training, $t(15) = 1.82$, $p = 0.04$ ($M_D = 0.61$, $SE = 0.33$, see Figure 14). Additional improvement was seen in reduction of errors made during Social Missions across first to last training sessions and mission difficulty levels of VR social engagement. (Easy: $t(15) = -7.93$ $p < 0.0001$, $M_D = -4.4$, $SE = 0.51$; Medium: $t(15) = -4.40$, $p = 0.0004$, $M_D = -4.94$, $SE = 1.0$; Hard: $t(15) = -6.88$, $p < 0.0001$, $M_D = 5.05$, $SE = 0.69$. See Figure 14).

Figure 12.
Clinical Symptom Improvement Following Training

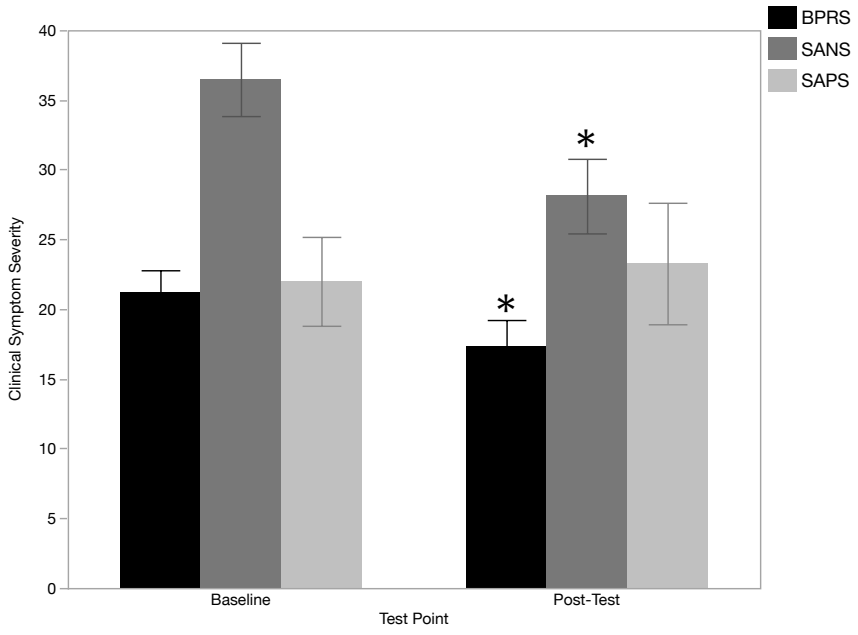


Figure 13.
BLERT Emotion Recognition Improvement Following Training

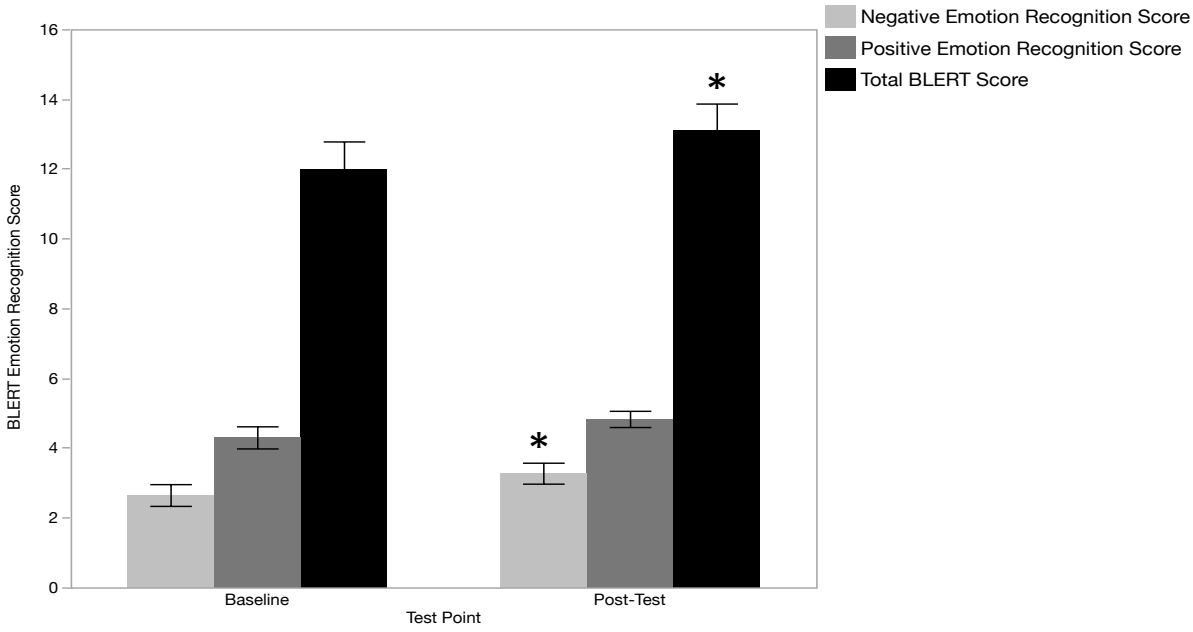


Figure 14.
Social Functioning Scales: Improvement in Interpersonal Communication After Training

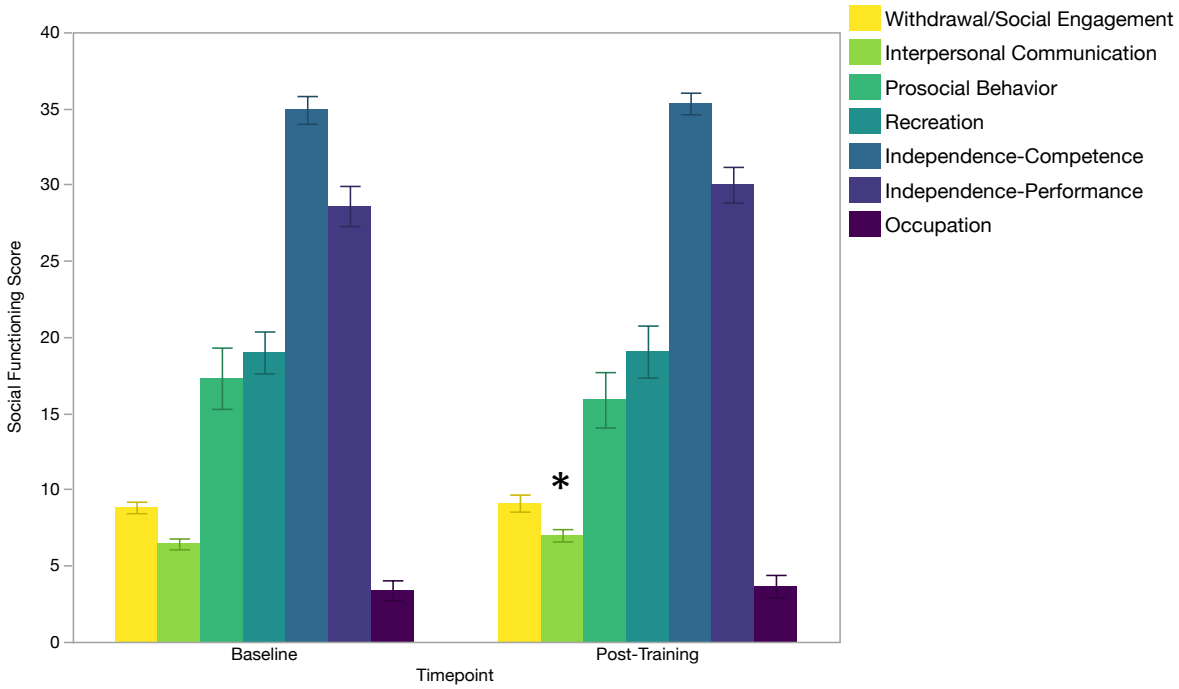
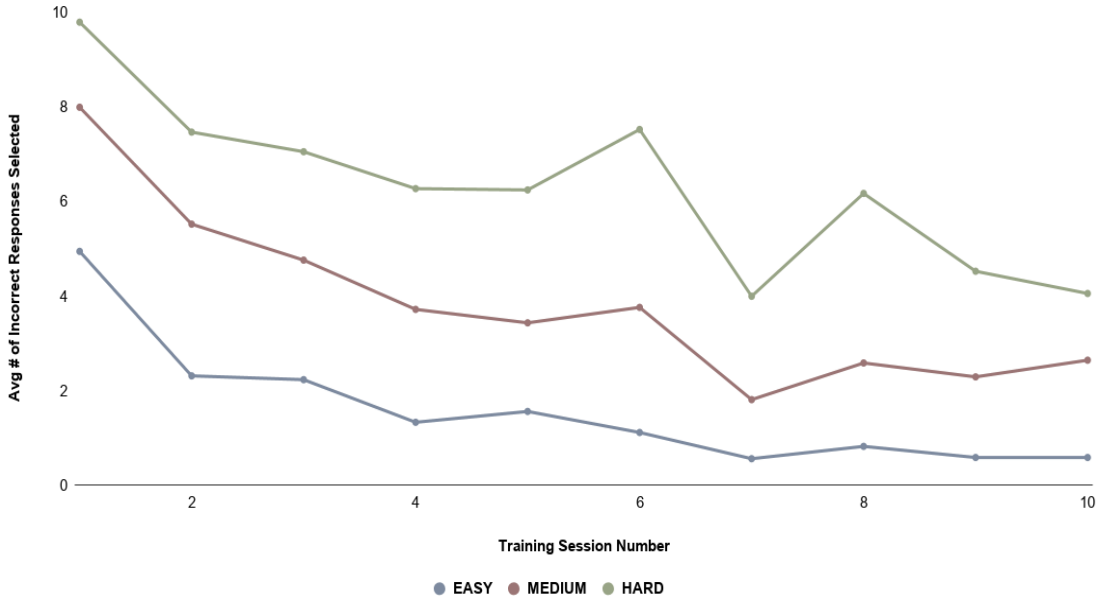


Figure 15.
Errors in Social Conversation Decreased Over Training Sessions Across Difficulty Level



Discussion

The reduction in clinical symptoms, and particularly negative symptoms, following ten weeks of novel VR social interaction training is very promising, as current pharmacological treatments have a limited impact on negative symptoms (Fusar-Polli et al, 2015). Currently available psychosocial interventions demonstrate only moderate or highly heterogeneous efficacy (Lutgens et al., 2017, Remington et al., 2016), with the exception of the Social Skills Training (SST), which seems to reduce both negative symptoms and improve social functioning (Granholm and Harvey, 2018; Turner et al, 2018). Importantly, though a primary aim of our intervention was to improve social skills, reducing negative symptoms represents a reduction of distress and may be a crucial gateway towards translation of these skills. For example, without reducing anhedonia or apathy, the participant may never have an opportunity to practice the skills acquired.

Improvement observed in emotion recognition accuracy on the BLERT task provides optimism regarding the translational benefit of our training task, which did not directly train participants to identify emotion states, but rather required appropriate steering of conversation based on an Avatar's reactions. It is especially notable that significant benefit was seen in the accuracy of discrimination between negative emotions, as this may translate to beneficial reduction of misattribution of hostile intent from others, a major symptom of psychosis. We expected to see improvements across social cognition tasks, however no traction was made on CogState measures. This may be related to the lack of synchronicity between the basic, concrete design of these tests and the more naturalistic, conversational ambition of our training task. Additionally, although CogState has been found to have no significant practice effects when testing interval is at least one month apart (Falleti et al., 2006), it is possible that gaining familiarity with how to maneuver the computer for some participants may aid and improve their second attempt at post-test to some degree.

Loneliness was seen to change nominally, though non-significantly. Though participants were socially included by study trainers prior to and after training sessions, the amount of time engaged with other humans was drastically less than in the Social Inclusion intervention outlined in Study 3. Participants interacted with virtual Avatars for a significant portion of time each session, which improved social skills, however perhaps these interactions were not as meaningful as training or conversation from engaged humans on specifically reducing social distress and perceived alienation. Social Engagement did not change subsequent to training, however increased performance on SFS Interpersonal Communication suggests that perhaps while frequency was not influenced, comfortability or confidence within currently available social interactions was improved. Follow-up

testing may also reveal more significant improvements or increased frequency of interaction. Inquiring about proportion of self-initiated socialization may also be an important addition to the assessment of improvements. Participants clearly improved on the training itself, making fewer errors in conversation consistently and significantly by session 10. Participants also reported high enjoyability of the training, crucial in determining the success of the intervention.

There are limitations to this interpretation. First, this small-sample pilot study had no control group, precluding our ability to differentiate specific from nonspecific treatment effects. It is also possible that coming to the laboratory twice a week for five weeks and interacting with the experimenters may have contributed significantly to improvements in symptoms. It will be important in future trials to compare the participants who complete VR social training to those who also come in to the laboratory twice a week but participate in a control task for this reason.

Conclusions

This study examined the efficacy of a novel, naturalistic social skills training program for individuals with schizophrenia. We hypothesized that practicing natural conversation in realistic environments would be beneficial in improving social inference, reducing social distress and increasing social engagement. We demonstrated that a 10-session training intervention was effective in reducing negative symptoms, which may prove as barriers to socialization for many participants. We saw significantly improve social inference in some domains, but not at all, and low impact on feelings of loneliness. Though improvements in quantitative social engagement were not observed, increased interpersonal communication scores suggests improvement in qualitative social

engagement, and further follow-up testing may elucidate latent or compounding socialization benefits. In other words, this training program may not cure, but help to 'get the ball rolling', in a population starting from fairly low engagement and comfort with socialization skills generally. Combined with other therapeutic measures, or perhaps in-vivo conversation "booster sessions" to practice translation of skills, this program may be a cost-effective and enjoyable adjunct treatment for any socially-depleted individuals.

CHAPTER VI

General Discussion

Previous research indicates that individuals higher on the psychosis spectrum perform worse at social cognition and social perception tasks. Our own research indicates that individuals higher on the psychosis spectrum also endorse higher levels of social distress via social isolation and loneliness. This body of work aimed to elucidate the relationship between social distress and social performance, and to develop treatments to enhance the abilities of those most affected bsy strengthening social bonds and skills in naturalistic and enjoyable domains.

In Study 1A we demonstrated that even acute social exclusion can alter subsequent social perception in a neurotypical college aged sample. Randomly assigned groups of demographically matched participants were excluded using only virtual representations of peers playing a simple game of catch. After just ten minutes of this treatment, those excluded from game play had significantly different perception and identification of human stimuli immediately following the game. While dosage was not systematically explored in this study, the effects of ten minutes of virtual ostracism provide serious implications for the potential effects of real life ostracism, exclusion and even common forms of active social defeat such as bullying. These experiences often last far longer than ten minutes and with repeated ‘hits’ to the system, it is plausible that subsequent social perception may be continuously and potentially permanently augmented. These effects were demonstrated in individuals with no psychiatric history, calling question to the role of resiliency for any individual when the protective factor of social support is removed.

Furthermore, we saw that even in this healthy sample, individuals who were

lonelier were more likely to endorse having had a greater number of psychosis-like experiences. Some of these experiences include "things that you see appear different from the way they usually do", "familiar surroundings sometimes seem strange, confusing, threatening or unreal to you" or you've "seen things that other people can't see or don't seem to see?". In other words, many of the perceptual anomalies that are assessed and flagged as indicative of risk for psychosis involve the same processes we see to be augmented after exclusion in Study 1A. Conceptualizing loneliness as a consecutive amount of isolation 'hits', perceived or believed, that becomes chronic overtime, it is possible to imagine how these more consistent, frequent and severe perceptual changes may begin to occur in everyday life.

In Study 1B, we replicate differences found after exclusion, but clarify that in socially ensconced individuals, acute social isolation may not be aversive, and in fact may be a pleasant or neutral experience with little impact on social perception. This was demonstrated by asking participants to sit quietly in a room devoid of social stimuli. Though participants were not told this would last ten minutes, participants knew this was the beginning of their experimental session and likely would predict this 'baseline measure' to be brief. It may be that the anticipation of this time period ending allowed participants to feel peaceful about their seclusion. It may be that using heartbeat monitoring as a decoy during this social seclusion gave the participants motivation to monitor their own breath or heartbeat, creating a moment of mindfulness which may also cause their seclusion to be perceived as pleasant or less stressful. Perhaps these individuals also welcomed a brief, innocuous reprieve from the inundation of social stimuli they experience as a byproduct of living and studying on an insular college campus. Overall, results from Study 1A+B suggest that consistent social support may be protective against detriments of purely

seclusionary social isolation, but that brief social ostracism and exclusion have the power to augment social perception significantly even in healthy individuals. Students whose symptom profile more closely matched that of someone suffering psychosis were also significantly more likely to endorse experience of chronic feelings of loneliness.

Study 2 examined the relationship between social rejection and perceptual performance further along the psychosis spectrum in patients with schizophrenia, as compared to typical age matched adults. We first demonstrated opposing patterns of perceptual impact in chronically socially isolated individuals, such that acute exclusion did not impact performance that was already significantly differentially altered from matched controls. Individuals with schizophrenia were found to be both much lonelier and much less socially engaged than their counterparts. In fact, our patient group endorsed about twice as severe chronic loneliness as their matched counterparts, as well as only half the quantity of monthly social engagement. It is likely that persistent social exclusion influences social perception such that short term manipulations do not significantly impact already augmented performance. Consistent with Study 1, healthy participants who exhibited more schizotypal traits were also lonelier. In patients, a trend level relationship was seen between psychiatric symptoms and loneliness. One reason for this may be that within our low sample number, all participants were chronically medicated to treat and diminish endorsed symptoms, while loneliness appeared more consistently pervasive across the population. Due to the clear evidence of differences in social satisfaction, social inclusion and accuracy on social perception, we questioned whether any intervention may be effective for alleviating these patterns of social deficit.

In Study 3, we examined a novel social inclusion choir intervention for efficacy in addressing these issues. Group singing proved to be quite a parsimonious activity for

promoting inclusion with a myriad of other documented benefits in other populations. In particular, faster group cohesion and the opportunity for mimicry and theory of mind rehearsal were ideal. Additionally, the natural paced breathing required for sustaining tones may beneficially impact vagal tone and provide opportunity for mindfulness and meditative practice. Our results demonstrate that choral social inclusion is an effective intervention for reducing loneliness and increasing perceived well-being and positive affect.

The feasibility and acceptability for this intervention were also quite high, with participants reporting high satisfaction and enjoyment of the group. Singing as a group also requires very few additional supplies or supports, making this low-cost, low-burden intervention accessible for implementation across a wide variety of settings and resource availability. It may be beneficial to conduct future investigations determining which component of group singing contributed most specifically to reduction of loneliness, or whether the combined techniques are necessary for this effect. However, this intervention included fairly standard components to a traditional choral group singing session, and thus joining an existing choir that would welcome members who are traditionally outcast from society may be equally beneficial for improving social distress. Importantly, social perceptual performance was not seen to be significantly enhanced by this treatment. Thus, it does not appear that augmentation of loneliness can also directly improve the social perception performance, at least in short term application.

Finally, we tested a novel naturalistic social inclusion VR training program to determine whether applied skills training would be beneficial for both improving social skills and reducing social distress. This training method is unique in the use of realistic virtual scenarios that mimic environments frequented by our population of interest. This was designed to enhance both the approachability and translational benefit of the training.

We also included gentle but direct feedback after every social encounter, ensuring in the moment direction on the specific social skills deficits exhibited by an individual participant. We found that this training technique had benefits for decreasing clinical symptom severity as well as improved social cognitive performance, however it was less effective for reducing loneliness. Some nonsignificant decrease in loneliness was found, which may be due to the inherent increased frequency of social interaction and positive support from staff at training sessions. Though VR offers many benefits as an avenue for providing personalized training and feedback, it seems clear that it cannot completely replace face-to-face interaction with real human beings. Social functioning was seen to have selective improvement specifically in interpersonal communication. This is punctuated by anecdotal report by participants that they experienced increased confidence in ability to converse with others. Real world social function was not globally improved, however post-intervention testing was conducted within two weeks of final training sessions. Thus, it is possible that further trickle-down effects may be seen with continued follow-up or more regularly training and exposure. It is possible that a combined effort of rigorous VR social skills training with additional booster sessions of social inclusion group as a place to practice trained skills and engage with others may be the most parsimonious adjunct therapy.

Through this combined work, we elucidate active social distress and related impairments, and offer two low-burden naturalistic intervention techniques to offset the immense social distress and impedance not currently aided by psychotropic medication or therapy in this population. It is our hope that these findings will further the literature on loneliness and the schizophrenia spectrum, and spark further creative endeavors to provide support and diminish distress in vulnerable populations.

REFERENCES

Addington, J., Penn, D., Woods, S. W., Addington, D., & Perkins, D. O. (2008). Social functioning in individuals at clinical high risk for psychosis. *Schizophrenia Research, 99*(1-3), 119-124. doi:10.1016/j.schres.2007.10.001

Andreasen, N. C. (1984). *Scale for the assessment of positive symptoms (SAPS)*. Iowa City: University of Iowa. doi:10.1037/t12696-000

Andreasen, N. C. (1984). *Scale for the assessment of negative symptoms (SANS)*. Iowa City: University of Iowa. doi:10.1037/t48377-000

Andreasen, N. C., Pressler, M., Nopoulos, P., Miller, D., & Ho, B. (2010). Antipsychotic dose equivalents and dose-years: A standardized method for comparing exposure to different drugs. *Biological Psychiatry, 67*(3), 255-262. doi:10.1016/j.biopsych.2009.08.040

Angell, B., & Test, M. A. (2002). The relationship of clinical factors and environmental opportunities to social functioning in young adults with schizophrenia. *Schizophrenia Bulletin, 28*(2), 259-271. doi:10.1093/oxfordjournals.schbul.a006936

Bach, R. (1990). *Jonathan Livingston Seagull*. New York: Avon Books.

Badcock, J. C., Shah, S., Mackinnon, A., Stain, H. J., Galletly, C., Jablensky, A., & Morgan, V. A. (2015). Loneliness in psychotic disorders and its association with cognitive function and symptom profile. *Schizophrenia Research, 169*(1-3), 268-273. doi:10.1016/j.schres.2015.10.027

Baron-Cohen, S., Wheelwright, S., Hill, J., Raste, Y., & Plumb, I. (2001). The "reading the mind in the eyes" test revised version: A study with normal adults, and adults with asperger syndrome or high-functioning autism. *Journal of Child Psychology and Psychiatry, 42*(2), 241-251. doi:10.1017/s0021963001006643

Baumeister, R. F., & Leary, M. R. (1995). The need to belong: Desire for interpersonal attachments as a fundamental human motivation. *Psychological Bulletin, 117*(3), 497-529. doi:10.1037//0033-2909.117.3.497

Baumeister, R. F., Twenge, J. M., & Nuss, C. K. (2002). Effects of social exclusion on cognitive processes: Anticipated aloneness reduces intelligent thought. *Journal of Personality and Social Psychology, 83*(4), 817-827. doi:10.1037/0022-3514.83.4.817

Bekele, E., Bian, D., Peterman, J., Park, S., & Sarkar, N. (2016). Design of a virtual reality system for affect analysis in facial expressions (VR-SAAFE); Application to schizophrenia. *IEEE Transactions on Neural Systems and Rehabilitation Engineering, 25*(6), 739-749. doi:10.1109/tnsre.2016.2591556

Bekele, E., Zheng, Z., Swanson, A., Crittendon, J., Warren, Z., & Sarkar, N. (2013). Understanding how adolescents with autism respond to facial expressions in virtual reality environments. *IEEE Transactions on Visualization and Computer Graphics, 19*(4), 711-720. doi:10.1109/tvcg.2013.42

Bellack, A. S. (2004). *Social skills training for schizophrenia: A step-by-step guide*. New York: Guilford Press.

Benson, T. L., & Park, S. (2018). Increased plasticity of bodily self-experience in individuals who may carry latent liability for schizophrenia. *Schizophrenia Research*. doi:10.1016/j.schres.2018.05.004

Bernstein, M. J., & Claypool, H. M. (2012). Not all social exclusions are created equal: Emotional distress following social exclusion is moderated by exclusion paradigm. *Social Influence, 7*(2), 113-130. doi:10.1080/15534510.2012.664326

Billeke, P., & Aboitiz, F. (2013). Social cognition in schizophrenia: From social stimuli processing to social engagement. *Frontiers in Psychiatry, 4*. doi:10.3389/fpsyt.2013.00004

Birchwood, M., Smith, J., Cochrane, R., Wetton, S., & Copestake, S. (1990). The social functioning scale the development and validation of a new scale of social adjustment for use in family intervention programmes with schizophrenic patients. *British Journal of Psychiatry, 157*(06), 853-859. doi:10.1192/bjp.157.6.853

Blanke, O., Pozeg, P., Hara, M., Heydrich, L., Serino, A., Yamamoto, A., . . . Rognini, G. (2014). Neurological and robot-controlled induction of an apparition. *Current Biology, 24*(22), 2681-2686. doi:10.1016/j.cub.2014.09.049

Blickhan, T. & Ode, E. (2011). *Weave me a poem* (Song, Key Bb.). National Endowment for the Arts.

Bora, E., & Pantelis, C. (2013). Theory of mind impairments in first-episode psychosis, individuals at ultra-high risk for psychosis and in first-degree relatives of schizophrenia: Systematic review and meta-analysis. *Schizophrenia Research, 144*(1-3), 31-36. doi:10.1016/j.schres.2012.12.013

Boulanger, M., Dethier, M., Gendre, F., & Blairy, S. (2013). Identity in schizophrenia: A study of trait self-knowledge. *Psychiatry Research, 209*(3), 367-374. doi:10.1016/j.psychres.2013.04.002

Breger, G., Fraser, R., Carbone, S., & McGorry, P. (2006). Emerging psychosis in young people - Part 1 - Key issues for detection and assessment. *Australian Family Physician*, *35*(315-312).

Bryson, G., Bell, M., & Lysaker, P. (1997). Affect recognition in schizophrenia: A function of global impairment of a specific cognitive deficit. *Schizophrenia Research, 24*(1-2), 98-99. doi:10.1016/s0920-9964(97)82268-2

Cacioppo, J. T., Hughes, M. E., Waite, L. J., Hawkley, L. C., & Thisted, R. A. (2006). Loneliness as a specific risk factor for depressive symptoms: Cross-sectional and longitudinal analyses. *Psychology and Aging, 21*(1), 140-151. doi:10.1037/0882-7974.21.1.140

Cacioppo, J. T., & Patrick, W. (2008). *Loneliness: Human nature and the need for social connection*. New York: WW Norton & Company.

Cacioppo, J. T., Fowler, J. H., & Christakis, N. A. (2009). Alone in the crowd: The structure and spread of loneliness in a large social network. *Journal of Personality and Social Psychology, 96*(6), 977. doi:10.2139/ssrn.1319108

Cacioppo, J. T., Hawkley, L. C., & Thisted, R. A. (2010). Perceived social isolation makes me sad: 5-year cross-lagged analyses of loneliness and depressive symptomatology in the Chicago Health, Aging, and Social Relations Study. *Psychology and Aging, 25*(2), 453-463. doi:10.1037/a0017216

Cacioppo, J. T., Cacioppo, S., & Boomsma, D. I. (2014). Evolutionary mechanisms for loneliness. *Cognition and Emotion, 28*(1), 3-21. doi:10.1080/02699931.2013.837379

Cacioppo, J. T., & Cacioppo, S. (2018). The growing problem of loneliness. *The Lancet, 391*(10119), 426. doi:10.1016/s0140-6736(18)30142-9

Cacioppo, S., Capitanio, J. P., & Cacioppo, J. T. (2014). Toward a neurology of loneliness. *Psychological Bulletin, 140*(6), 1464-1504. doi:10.1037/a0037618

Cacioppo, S., Grippo, A. J., London, S., Goossens, L., & Cacioppo, J. T. (2015). Loneliness: Clinical import and interventions. *Perspectives on Psychological Science, 10*(2), 238-249. doi:10.1177/1745691615570616

Cai, X., Wei, D., Gallagher, S. E., Bagal, A., Mei, Y., Kao, J. P., . . . Tang, C. (2007). Hyperexcitability of distal dendrites in hippocampal pyramidal cells after chronic partial deafferentation. *Journal of Neuroscience, 27*(1), 59-68. doi:10.1523/jneurosci.4502-06.2007

Cantor-Graae, E., & Selten, J. (2005). Schizophrenia and migration: A meta-analysis and review. *American Journal of Psychiatry, 162*(1), 12-24. doi:10.1176/appi.ajp.162.1.12

Clift, S., Hancox, G., Morrison, I., Hess, B., Kreutz, G., & Stewart, D. (2010). Choral singing and psychological wellbeing: Quantitative and qualitative findings from English choirs in a cross-national survey. *Journal of Applied Arts & Health, 1*(1), 19-34. doi:10.1386/jaah.1.1.19/1

Cohen, S., Kamarck, T., & Mermelstein, R. (1983). A global measure of perceived stress. *Journal of Health and Social Behavior, 24*(4), 385. doi:10.2307/2136404

Cohen, S., & Wills, T. A. (1985). Stress, social support, and the buffering hypothesis. *Psychological Bulletin, 98*(2), 310-357. doi:10.1037//0033-2909.98.2.310

Cornwell, E. Y., & Waite, L. J. (2009). Social disconnectedness, perceived isolation, and health among older adults. *Journal of Health and Social Behavior, 50*(1), 31-48. doi:10.1177/002214650905000103

Corrigan, P. W., Liberman, R. P., & Engel, J. D. (1990). From noncompliance to collaboration in the treatment of schizophrenia. *Psychiatric Services, 41*(11), 1203-1211. doi:10.1176/ps.41.11.1203

Craig, T. K., Rus-Calafell, M., Ward, T., Leff, J. P., Huckvale, M., Howarth, E., . . . Garety, P. A. (2017). AVATAR therapy for auditory verbal hallucinations in people with psychosis: A single-blind, randomised controlled trial. *The Lancet Psychiatry, 5*(1), 31-40. doi:10.1016/s2215-0366(17)30427-3

De Jong Gierveld, J., Van Tilburg, T., & Dykstra, P. (2016). Social isolation and loneliness. *Encyclopedia of Mental Health,* 175-178. doi:10.1016/b978-0-12-397045-9.00118-x

Delevoye-Turrell, Y., Vienne, C., & Coello, Y. (2011). Space boundaries in schizophrenia. *Social Psychology, 42*(3), 193-204. doi:10.1027/1864-9335/a000063

Dewall, C. N., Macdonald, G., Webster, G. D., Masten, C. L., Baumeister, R. F., Powell, C., . . . Eisenberger, N. I. (2010). Acetaminophen reduces social pain. *Psychological Science, 21*(7), 931-937. doi:10.1177/0956797610374741

Du Sert, O. P., Potvin, S., Lipp, O., Dellazizzo, L., Laurelli, M., Breton, R., . . . Dumais, A. (2018). Virtual reality therapy for refractory auditory verbal hallucinations in schizophrenia: A pilot clinical trial. *Schizophrenia Research, 197*, 176-181. doi:10.1016/j.schres.2018.02.031

Echterhoff, G., Higgins, E. T., & Levine, J. M. (2009). Shared reality: Experiencing commonality with others inner states about the world. *Perspectives on Psychological Science, 4*(5), 496-521. doi:10.1111/j.1745-6924.2009.01161.x

Edmondson B. (2010). All the lonely people. *AARP: The Magazine*, *83*.

Eisenberger, N. I. (2012). The pain of social disconnection: Examining the shared neural underpinnings of physical and social pain. *Nature Reviews Neuroscience, 13*(6), 421-434. doi:10.1038/nrn3231

Estroff, S. E. (1989). Self, identity, and subjective experiences of schizophrenia: In search of the subject. *Schizophrenia Bulletin, 15*(2), 189-196. doi:10.1093/schbul/15.2.189

Falleti, M. G., Maruff, P., Collie, A., & Darby, D. G. (2006). Practice effects associated with the repeated assessment of cognitive function using the cogstate battery at 10-minute, one week and one month test-retest intervals. *Journal of Clinical and Experimental Neuropsychology, 28*(7), 1095-1112. doi:10.1080/13803390500205718

Ferri, F., Frassinetti, F., Mastrangelo, F., Salone, A., Ferro, F. M., & Gallese, V. (2012). Bodily self and schizophrenia: The loss of implicit self-body knowledge. *Consciousness and Cognition, 21*(3), 1365-1374. doi:10.1016/j.concog.2012.05.001

Fineberg, S. K., Deutsch-Link, S., Ichinose, M., Mcguinness, T., Bessette, A. J., Chung, C. K., & Corlett, P. R. (2015). Word use in first-person accounts of schizophrenia. *British Journal of Psychiatry, 206*(01), 32-38. doi:10.1192/bjp.bp.113.140046

Fiorillo, D., & Sabatini, F. (2011). Quality and quantity: The role of social interactions in self-reported individual health. *Social Science & Medicine, 73*(11), 1644-1652. doi:10.1016/j.socscimed.2011.09.007

Fredrickson, J., Maruff, P., Woodward, M., Moore, L., Fredrickson, A., Sach, J., & Darby, D. (2010). Evaluation of the usability of a brief computerized cognitive screening test in older people for epidemiological studies. *Neuroepidemiology, 34*(2), 65-75. doi:10.1159/000264823

Freeman, D., & Garety, P. (2014). Advances in understanding and treating persecutory delusions: A review. *Social Psychiatry and Psychiatric Epidemiology, 49*(8), 1179-1189. doi:10.1007/s00127-014-0928-7

First, M. B., Spitzer, R. L., Gibbon, M., & Williams, J. B. (2002). *Structured clinical interview for DSM-IV-TR axis I disorders, research version, patient edition*. SCID-I/P.

First, M. B., Williams, J. B. W., Karg, R. S., & Spitzer, R. L. (2015). Structured clinical interview for DSM-5—Research version. *Arlington, VA: American Psychiatric Association*.

Fusar-Poli, P., Papanastasiou, E., Stahl, D., Rocchetti, M., Carpenter, W., Shergill, S., & Mcguire, P. (2014). Treatments of negative symptoms in schizophrenia: Meta-analysis of 168 randomized placebo-controlled trials. *Schizophrenia Bulletin, 41*(4), 892-899. doi:10.1093/schbul/sbu170

Gallese, V., & Ferri, F. (2014). Psychopathology of the bodily self and the brain: The case of schizophrenia. *Psychopathology, 47*(6), 357-364. doi:10.1159/000365638

Gard, D.E., Kring, A.M., Gard, M.G., Horan, W.P., & Green, M.F. (2007). Anhedonia in schizophrenia: distinctions between anticipatory and consummatory pleasure. *Schizophrenia Research, 93*, 253–260.

Gardner, W. L., Pickett, C. L., & Brewer, M. B. (2000). Social exclusion and selective memory: How the need to belong influences memory for social events. *Personality and Social Psychology Bulletin, 26*(4), 486-496. doi:10.1177/0146167200266007

Gardner, W. L., Pickett, C. L., & Knowles, M. (2005). Social snacking and shielding: Using social symbols, selves, and surrogates in the service of belonging needs. In K. D. Williams, J. P. Forgas, & W. von Hippel (Eds.), *The Social Outcast: Ostracism, Social Exclusion, Rejection, and Bullying* (pp. 227-242). New York: Psychology Press.

Garety, P., Bentall, R. P., & Freeman, D. (2008). Research evidence of the effectiveness of cognitive behavioural therapy for persecutory delusions. *Persecutory Delusions,* 329-350. doi:10.1093/med:psych/9780199206315.003.0016

Gradin, V. B., Waiter, G., Kumar, P., Stickle, C., Milders, M., Matthews, K., . . . Steele, J. D. (2012). Abnormal neural responses to social exclusion in schizophrenia. *PLoS ONE, 7*(8). doi:10.1371/journal.pone.0042608

Graeupner, D., & Coman, A. (2017). The dark side of meaning-making: How social exclusion leads to superstitious thinking. *Journal of Experimental Social Psychology, 69*, 218-222. doi:10.1016/j.jesp.2016.10.003

Granholm, E., & Harvey, P. D. (2018). Social skills training for negative symptoms of schizophrenia. *Schizophrenia Bulletin, 44*(3), 472-474. doi:10.1093/schbul/sbx184

Granholm, E., McQuaid, J. R., McClure, F. S., Auslander, L. A., Perivoliotis, D., Pedrelli, P., ... & Jeste, D. V. (2005). A randomized, controlled trial of cognitive behavioral social skills training for middle-aged and older outpatients with chronic schizophrenia. *American Journal of Psychiatry*, *162*(3), 520-529. doi: 10.1176/appi.ajp.162.3.520.

Grape, C., Sandgren, M., Hansson, L., Ericson, M., & Theorell, T. (2003). Does singing promote well-being?: An empirical study of professional and amateur singers during a singing lesson. *Integrative Physiological & Behavioral Science, 38*(1), 65-74. doi:10.1007/bf02734261

Green, M. F., & Kinsbourne, M. (1990). Subvocal activity and auditory hallucinations: Clues for behavioral treatments? *Schizophrenia Bulletin, 16*(4), 617-625. doi:10.1093/schbul/16.4.617

Greenaway, K. H., Haslam, S. A., Cruwys, T., Branscombe, N. R., Ysseldyk, R., & Heldreth, C. (2015). From "we" to "me": Group identification enhances perceived personal control with consequences for health and well-being. *Journal of Personality and Social Psychology, 109*(1), 53-74. doi: 10.1037/pspi0000019

Gunaydin, L., Grosenick, L., Finkelstein, J., Kauvar, I., Fenno, L., Adhikari, A., . . . Deisseroth, K. (2014). Natural neural projection dynamics underlying social behavior. *Cell, 157*(7), 1535-1551. doi:10.1016/j.cell.2014.05.017

Hardin, C. D., & Higgins, E. T. (1996). Shared reality: How social verification makes the subjective objective. In R. M. Sorrentino & E. T. Higgins (Eds.), *Handbook of motivation and cognition. Handbook of motivation and cognition, Vol. 3. The interpersonal context* (pp. 28-84). New York, NY, US: Guilford Press.

Harvey, C., Evert, H., Herrman, H., & Trauer, T. (2003). The relationship between social networks and occupational and self-care functioning in people with psychosis. *Social Psychiatry and Psychiatric Epidemiology, 38*(4), 180-188. doi:10.1007/s00127-003-0617-4

Hawkley, L. C., Hughes, M. E., Waite, L. J., Masi, C. M., Thisted, R. A., & Cacioppo, J. T. (2008). From social structural factors to perceptions of relationship quality and loneliness: The Chicago Health, Aging, and Social Relations study. *The Journals of Gerontology Series B: Psychological Sciences and Social Sciences, 63*(6). doi:10.1093/geronb/63.6.s375

Hawkley, L. C., & Capitanio, J. P. (2015). Perceived social isolation, evolutionary fitness and health outcomes: A lifespan approach. *Philosophical Transactions of the Royal Society B: Biological Sciences, 370*(1669), 20140114-20140114. doi:10.1098/rstb.2014.0114

Hawkley, L. C., & Cacioppo, J. T. (2010). Loneliness matters: A theoretical and empirical review of consequences and mechanisms. *Annals of Behavioral Medicine, 40*(2), 218-227. doi:10.1007/s12160-010-9210-8

Heine, S. J., Proulx, T., & Vohs, K. D. (2006). The meaning maintenance model: On the coherence of social motivations. *Personality and Social Psychology Review, 10*(2), 88-110. doi:10.1207/s15327957pspr1002_1

Heron, W., Doane, B. K., & Scott, T. H. (1956). Visual disturbances after prolonged perceptual isolation. *Canadian Journal of Psychology/Revue Canadienne De Psychologie, 10*(1), 13-18. doi:10.1037/h0083650

Hobson, R. P., & Meyer, J. A. (2005). Foundations for self and other: A study in autism. *Developmental Science, 8*(6), 481-491. doi:10.1111/j.1467-7687.2005.00439.x

Hoffman, R. E. (2007). A social deafferentation hypothesis for induction of active schizophrenia. *Schizophrenia Bulletin, 33*(5), 1066-1070. doi:10.1093/schbul/sbm079

Holt-Lunstad, J., Smith, T. B., & Layton, J. B. (2010). Social relationships and mortality risk: a meta-analytic review. *PLoS Medicine*, *7*(7), e1000316. doi: 10.1371/journal.pmed.1000316

Holt-Lunstad, J., Smith, T. B., Baker, M., Harris, T., & Stephenson, D. (2015). Loneliness and social isolation as risk factors for mortality. *Perspectives on Psychological Science, 10*(2), 227-237. doi:10.1177/1745691614568352

House, J., Landis, K., & Umberson, D. (1988). Social relationships and health. *Science, 241*(4865), 540-545. doi:10.1126/science.3399889

Hultman, C. M., Öhman, A., Öhlund, L. S., Wieselgren, I., & Öst, L. (1996). Electrodermal activity and social network as predictors of outcome of episodes in schizophrenia. *Journal of Abnormal Psychology, 105*(4), 626-636. doi:10.1037//0021-843x.105.4.626

Ising, H. K., Veling, W., Loewy, R. L., Rietveld, M. W., Rietdijk, J., Dragt, S., . . . Gaag, M. V. (2012). The validity of the 16-item version of the prodromal questionnaire (PQ-16) to screen for ultra high risk of developing psychosis in the general help-seeking population. *Schizophrenia Bulletin, 38*(6), 1288-1296. doi:10.1093/schbul/sbs068

James, W. (1890). *The principles of psychology*. New York: H. Holt and Company.

Johnson, J. W., & Johnson, J. R. (. R. (2018). *Lift every voice and sing* (Song, Key Ab.). Edward B. Marks Music Corporation.

Kanai, R., Bahrami, B., Duchaine, B., Janik, A., Banissy, M., & Rees, G. (2012). Brain structure links loneliness to social perception. *Current Biology, 22*(20), 1975-1979. doi:10.1016/j.cub.2012.08.045

Kim, J., Doop, M. L., Blake, R., & Park, S. (2005). Impaired visual recognition of biological motion in schizophrenia. *Schizophrenia Research, 77*(2-3), 299-307. doi:10.1016/j.schres.2005.04.006

Kim, J., Park, S., & Blake, R. (2011). Perception of biological motion in schizophrenia and healthy individuals: A behavioral and fMRI study. *PLoS ONE, 6*(5). doi:10.1371/journal.pone.0019971

Kim, J., Norton, D., Mcbain, R., Ongur, D., & Chen, Y. (2013). Deficient biological motion perception in schizophrenia: Results from a motion noise paradigm. *Frontiers in Psychology, 4*. doi:10.3389/fpsyg.2013.00391

Kimhy, D., Delespaul, P., Corcoran, C., Ahn, H., Yale, S., & Malaspina, D. (2006). Computerized experience sampling method (ESMc): Assessing feasibility and validity among individuals with schizophrenia. *Journal of Psychiatric Research, 40*(3), 221-230. doi:10.1016/j.jpsychires.2005.09.007

Kopelowicz, A., Liberman, R., & Zarate, R. (2006). Recent advances in social skills training for schizophrenia. *Schizophrenia Bulletin, 32*, S12-S23. doi:10.1093/schbul/sbl023

Kreutz, G., Bongard, S., Rohrmann, S., Hodapp, V., & Grebe, D. (2004). Effects of choir singing or listening on secretory immunoglobulin a, cortisol, and emotional state. *Journal of Behavioral Medicine, 27*(6), 623-635. doi:10.1007/s10865-004-0006-9

Kreyenbuhl, J., Buchanan, R. W., Dickerson, F. B., & Dixon, L. B. (2009). The schizophrenia patient outcomes research team (PORT): Updated treatment recommendations 2009. *Schizophrenia Bulletin, 36*(1), 94-103. doi:10.1093/schbul/sbp130

Kurtz, M. M., Baker, E., Pearlson, G. D., & Astur, R. S. (2006). A virtual reality apartment as a measure of medication management skills in patients with schizophrenia: A pilot study. *Schizophrenia Bulletin, 33*(5), 1162-1170. doi:10.1093/schbul/sbl039

Kurtz, M. M., & Richardson, C. L. (2011). Social cognitive training for schizophrenia: a meta-analytic investigation of controlled research. *Schizophrenia Bulletin, 38*(5), 1092-1104. doi:10.1093/schbul/sbr036

Kurtz, M., & Mueser, K. (2008). A meta-analysis of controlled research on social skills training for schizophrenia. *Schizophrenia Research, 98*, 56-57. doi:10.1016/j.schres.2007.12.124

Lamster, F., Lincoln, T. M., Nittel, C. M., Rief, W., & Mehl, S. (2017). The lonely road to paranoia. A path-analytic investigation of loneliness and paranoia. *Comprehensive Psychiatry, 74*, 35-43. doi:10.1016/j.comppsych.2016.12.007

Leary, M. R., Tambor, E. S., Terdal, S. K., & Downs, D. L. (1995). Self-esteem as an interpersonal monitor: The sociometer hypothesis. *Journal of Personality and Social Psychology, 68*(3), 518-530. doi: 10.1037/0022-3514.68.3.518

Lee, T. Y., Hong, S. B., Shin, N. Y., & Kwon, J. S. (2015). Social cognitive functioning in prodromal psychosis: a meta-analysis. *Schizophrenia Research*, *164*(1), 28-34. doi: 10.1016/j.schres.2015.02.008

Lim, M. H., & Gleeson, J. F. (2014). Social connectedness across the psychosis spectrum: Current issues and future directions for interventions in loneliness. *Frontiers in Psychiatry, 5*. doi:10.3389/fpsyt.2014.00154

Lindenmayer, J., Mcgurk, S. R., Khan, A., Kaushik, S., Thanju, A., Hoffman, L., . . . Herrmann, E. (2012). Improving social cognition in schizophrenia: A pilot intervention combining computerized social cognition training with cognitive remediation. *Schizophrenia Bulletin, 39*(3), 507-517. doi:10.1093/schbul/sbs120

Loersch, C., & Arbuckle, N. L. (2013). Unraveling the mystery of music: Music as an evolved group process. *Journal of Personality and Social Psychology, 105*(5), 777-798. doi:10.1037/a0033691

Lutgens, D., Gariepy, G., & Malla, A. (2017). Psychological and psychosocial interventions for negative symptoms in psychosis: Systematic review and meta-analysis. *British Journal of Psychiatry, 210*(05), 324-332. doi:10.1192/bjp.bp.116.197103

Lynch, J. J., & Convey, W. H. (1979). Loneliness, disease, and death: Altemative approaches. *Psychosomatics, 20*(10), 702-708. doi:10.1016/s0033-3182(79)73751-0

Lysaker, P. H., & Lysaker, J. T. (2010). Schizophrenia and Alterations in Self-experience: A Comparison of 6 Perspectives. *Schizophrenia Bulletin, 36*(2), 331-340. doi:10.1093/schbul/sbn077

Macdonald, E. (2000). The quantity and quality of the social networks of young people with early psychosis compared with closely matched controls. *Schizophrenia Research, 46*(1), 25-30. doi:10.1016/s0920-9964(00)00024-4

Maher, B. A. (1974). Delusional thinking and perceptual disorder. *Journal of Individual Psychology, 30*(1), 98-113.

Marino, L., Nossel, I., Choi, J. C., Nuechterlein, K., Wang, Y., Essock, S., . . . Dixon, L. (2015). The RAISE connection program for early psychosis. *The Journal of Nervous and Mental Disease, 203*(5), 365-371. doi:10.1097/nmd.0000000000000293

Maruff, P., Thomas, E., Cysique, L., Brew, B., Collie, A., Snyder, P., & Pietrzak, R. H. (2009). Validity of the cogstate brief battery: Relationship to standardized tests and sensitivity to cognitive impairment in mild traumatic brain injury, schizophrenia, and AIDS dementia complex. *Archives of Clinical Neuropsychology, 24*(2), 165-178. doi:10.1093/arclin/acp010

Masi, C. M., Chen, H., Hawkley, L. C., & Cacioppo, J. T. (2011). A meta-analysis of interventions to reduce loneliness. *Personality and Social Psychology Review, 15*(3), 219-266. doi:10.1177/1088868310377394

Matthews, N., Gold, B. J., Sekuler, R., & Park, S. (2012). Gesture imitation in schizophrenia. *Schizophrenia Bulletin, 39*(1), 94-101. doi:10.1093/schbul/sbr062

Mazza, M., Lucci, G., Pacitti, F., Pino, M. C., Mariano, M., Casacchia, M., & Roncone, R. (2010). Could schizophrenic subjects improve their social cognition abilities only with observation and imitation of social situations? *Neuropsychological Rehabilitation, 20*(5), 675-703. doi:10.1080/09602011.2010.486284

Mcintyre, J. C., Elahi, A., & Bentall, R. P. (2016). Social identity and psychosis: Explaining elevated rates of psychosis in migrant populations. *Social and Personality Psychology Compass, 10*(11), 619-633. doi:10.1111/spc3.12273

Meltzer, H., Bebbington, P., Dennis, M. S., Jenkins, R., Mcmanus, S., & Brugha, T. S. (2013). Feelings of loneliness among adults with mental disorder. *Social Psychiatry and Psychiatric Epidemiology, 48*(1), 5-13. doi:10.1007/s00127-014-0977-y

Michael, J., & Park, S. (2016). Anomalous bodily experiences and perceived social isolation in schizophrenia: An extension of the Social Deafferentation Hypothesis. *Schizophrenia Research, 176*(2-3), 392-397. doi:10.1016/j.schres.2016.06.013

Mishara, A. L., Lysaker, P. H., & Schwartz, M. A. (2013). Self-disturbances in schizophrenia: history, phenomenology, and relevant findings from research on metacognition. *Schizophrenia Bulletin, 40*(1), 5-12. doi:10.1093/schbul/sbt169

Mitchell, P., Parsons, S., & Leonard, A. (2007). Using virtual environments for teaching social understanding to 6 adolescents with autistic spectrum disorders. *Journal of Autism and Developmental Disorders, 37*(3), 589-600. doi:10.1007/s10803-006-0189-8

Moore, D., Mcgrath, P., & Thorpe, J. (2000). Computer-aided learning for people with autism – a framework for research and development. *Innovations in Education and Training International, 37*(3), 218-228. doi:10.1080/13558000050138452

Morgan, V. A., Mcgrath, J. J., Jablensky, A., Badcock, J. C., Waterreus, A., Bush, R., . . . Mackinnon, A. (2014). Psychosis prevalence and physical, metabolic and cognitive co-morbidity: Data from the second Australian national survey of psychosis. *Psychological Medicine, 44*(10), 2163-2176. doi:10.1017/s0033291713002973

Moutoussis, M., Williams, J., Dayan, P., & Bentall, R. P. (2007). Persecutory delusions and the conditioned avoidance paradigm: Towards an integration of the psychology and biology of paranoia. *Cognitive Neuropsychiatry, 12*(6), 495-510. doi:10.1080/13546800701566686

Nakamura, J., & Csikszentmihalyi, M. (2002). The concept of flow. In C. R. Snyder & S. J. Lopez (Eds.), *Handbook of positive psychology* (pp. 89-105). New York, NY, US: Oxford University Press.

Nelson, B., Fornito, A., Harrison, B., Yücel, M., Sass, L., Yung, A., . . . Mcgorry, P. (2009a). A disturbed sense of self in the psychosis prodrome: Linking phenomenology and neurobiology. *Neuroscience & Biobehavioral Reviews, 33*(6), 807-817. doi:10.1016/j.neubiorev.2009.01.002

Nelson, B., Sass, L. A., Thompson, A., Yung, A. R., Francey, S. M., Amminger, G. P., & Mcgorry, P. D. (2009b). Does disturbance of self underlie social cognition deficits in schizophrenia and other psychotic disorders? *Early Intervention in Psychiatry, 3*(2), 83-93. doi:10.1111/j.1751-7893.2009.00112.x

Nitsche, P. H., Willmanns, K., Barnes, F. M., & Glueck, B. (1912). The history of the prison psychoses. *Journal of Nervous and Mental Disease, 13.*

Novembre, G., Zanon, M., & Silani, G. (2014). Empathy for social exclusion involves the sensory-discriminative component of pain: A within-subject fMRI study. *Social Cognitive and Affective Neuroscience, 10*(2), 153-164. doi:10.1093/scan/nsu038

Okruszek, Ł, & Pilecka, I. (2017). Biological motion processing in schizophrenia – Systematic review and meta-analysis. *Schizophrenia Research, 190*, 3-10. doi:10.1016/j.schres.2017.03.013

Olbert, C. M., Penn, D. L., Kern, R. S., Lee, J., Horan, W. P., Reise, S. P., . . . Green, M. F. (2013). Adapting social neuroscience measures for schizophrenia clinical trials, part 3: Fathoming external validity. *Schizophrenia Bulletin, 39*(6), 1211-1218. doi:10.1093/schbul/sbt130

Overall, J. E., & Gorham, D. R. (1962). The brief psychiatric rating scale. *Psychological reports*, *10*(3), 799-812. doi:10.2466/pr0.1962.10.3.799

Palumbo, C., Volpe, U., Matanov, A., Priebe, S., & Giacco, D. (2015). Social networks of patients with psychosis: A systematic review. *BMC Research Notes, 8*(1). doi:10.1186/s13104-015-1528-7

Park, K., Ku, J., Choi, S., Jang, H., Park, J., Kim, S. I., & Kim, J. (2011). A virtual reality application in role-plays of social skills training for schizophrenia: A randomized, controlled trial. *Psychiatry Research, 189*(2), 166-172. doi:10.1016/j.psychres.2011.04.003

Park, S., Matthews, N., & Gibson, C. (2008). Imitation, simulation, and schizophrenia. *Schizophrenia Bulletin*, *34*(4), 698–707. doi: 10.1093/schbul/sbn048

Parnas, J., Bovet, P., & Zahavi, D. (2002). Schizophrenic autism: clinical phenomenology and pathogenetic implications. *World Psychiatry*, *1*(3), 131–136.

Parnas, J., Handest, P., Saebye, D., & Jansson, L. (2003). Anomalies of subjective experience in schizophrenia and psychotic bipolar illness. *Acta Psychiatrica Scandinavica, 108*(2), 126-133. doi:10.1034/j.1600-0447.2003.00105.x

Parnas, J., & Henriksen, M. G. (2014). Disordered self in the schizophrenia spectrum. *Harvard Review of Psychiatry, 22*(5), 251-265. doi:10.1097/hrp.0000000000000040

Pearce, E., Launay, J., & Dunbar, R. I. (2015). The ice-breaker effect: Singing mediates fast social bonding. *Royal Society Open Science, 2*(10), 150221. doi:10.1098/rsos.150221

Penn, D. L., Roberts, D. L., Combs, D., & Sterne, A. (2007). Best practices: The development of the social cognition and interaction training program for schizophrenia spectrum disorders. *Psychiatric Services, 58*(4), 449-451. doi:10.1176/appi.ps.58.4.449

Peplau, L. A., Russell, D., & Heim, M. (1978). *Loneliness: A bibliography of research and theory*. Washington, D.C.: American Psychological Association.

Perissinotto, C. M., Cenzer, I. S., & Covinsky, K. E. (2012). Loneliness in older persons: A predictor of functional decline and death. *Archives of Internal Medicine, 172*(14), 1078-1084. doi:10.1001/archinternmed.2012.1993

Perlman, D., & Peplau, L.A. (1982). Theoretical approaches to loneliness. In L.A. Peplau & D. Perlman (Eds.), *Loneliness: A sourcebook of current theory, research, and therapy* (pp. 123–134). New York: Wiley Interscience.

Perry, Y., Henry, J. D., Sethi, N., & Grisham, J. R. (2011). The pain persists: How social exclusion affects individuals with schizophrenia. *British Journal of Clinical Psychology, 50*(4), 339-349. doi:10.1348/014466510x523490

Pfammatter, M. (2006). Efficacy of psychological therapy in schizophrenia: Conclusions from meta-analyses. *Schizophrenia Bulletin, 32*, S64-S80. doi:10.1093/schbul/sbl030

Pickett, C. L., Gardner, W. L., & Knowles, M. (2004). Getting a cue: The need to belong and enhanced sensitivity to social cues. *Personality and Social Psychology Bulletin, 30*(9), 1095-1107. doi:10.1177/0146167203262085

Pietrzak, R. H., Olver, J., Norman, T., Piskulic, D., Maruff, P., & Snyder, P. J. (2009). A comparison of the cogstate schizophrenia battery and the measurement and treatment research to improve cognition in schizophrenia (MATRICS) battery in assessing cognitive impairment in chronic schizophrenia. *Journal of Clinical and Experimental Neuropsychology, 31*(7), 848-859. doi:10.1080/13803390802592458

Pinkham, A. E., Hopfinger, J. B., Pelphrey, K. A., Piven, J., & Penn, D. L. (2008). Neural bases for impaired social cognition in schizophrenia and autism spectrum disorders. *Schizophrenia Research, 99*(1), 164-175. doi:10.1016/j.schres.2007.10.024

Postmes, L., Sno, H., Goedhart, S., Stel, J. V., Heering, H., & Haan, L. D. (2014). Schizophrenia as a self-disorder due to perceptual incoherence. *Schizophrenia Research, 152*(1), 41-50. doi:10.1016/j.schres.2013.07.027

Prebble, S. C., Addis, D. R., & Tippett, L. J. (2013). Autobiographical memory and sense of self. *Psychological Bulletin, 139*(4), 815-840. doi:10.1037/a0030146

Raffard, S., D'Argembeau, A., Lardi, C., Bayard, S., Boulenger, J., & Linden, M. V. (2010). Narrative identity in schizophrenia. *Consciousness and Cognition, 19*(1), 328-340. doi:10.1016/j.concog.2009.10.005

Raine, A. (1991). The SPQ: a scale for the assessment of schizotypal personality based on DSM-III-R criteria. *Schizophrenia Bulletin, 17*(4), 555-564. doi:10.1093/schbul/17.4.555

Remington, G., Foussias, G., Fervaha, G., Agid, O., Takeuchi, H., Lee, J., & Hahn, M. (2016). Treating negative symptoms in schizophrenia: An update. *Current Treatment Options in Psychiatry, 3*(2), 133-150. doi:10.1007/s40501-016-0075-8

Robinson, D. L., Heien, M. L., & Wightman, R. M. (2002). Frequency of dopamine concentration transients increases in dorsal and ventral striatum of male rats during introduction of conspecifics. *The Journal of Neuroscience, 22*(23), 10477-10486. doi:10.1523/jneurosci.22-23-10477.2002

Roccatagliata, G. (1991). Classical concepts of schizophrenia. In G. J. Howells (Ed.), *The concept of schizophrenia: Historical perspectives.* (pp. 1-27). Washington, D.C.: American Psychiatric Press.

Rokach, A. (2013). *Loneliness updated: Recent research on loneliness and how it affects our lives*. London: Routledge.

Russell, D. W. (1996). UCLA Loneliness Scale (Version 3): Reliability, validity, and factor structure. *Journal of Personality Assessment, 66*(1), 20-40. doi:10.1207/s15327752jpa6601_2

Sadler, W. A. (1978). Dimensions in the problem of loneliness: A phenomenological approach in social psychology. *Journal of Phenomenological Psychology, 9*(1), 157-187. doi:10.1163/156916278x00078

Sass, L. A., & Parnas, J. (2003). Schizophrenia, consciousness, and the self. *Schizophrenia Bulletin, 29*(3), 427-444. doi:10.1093/oxfordjournals.schbul.a007017

Scharfetter, C. (2003). The self-experience of schizophrenics. *The Self in Neuroscience and Psychiatry,* 272-290. doi:10.1017/cbo9780511543708.014

Selten, J., Ven, E. V., Rutten, B. P., & Cantor-Graae, E. (2013). The social defeat hypothesis of schizophrenia: An update. *Schizophrenia Bulletin, 39*(6), 1180-1186. doi:10.1093/schbul/sbt134

Selten, J., Os, J. V., & Cantor-Graae, E. (2016). The social defeat hypothesis of schizophrenia: Issues of measurement and reverse causality. *World Psychiatry, 15*(3), 294-295. doi:10.1002/wps.20369

Shenton, M. E., Kikinis, R., Jolesz, F. A., Pollak, S. D., Lemay, M., Wible, C. G., . . . Mccarley, R. W. (1992). Abnormalities of the left temporal lobe and thought disorder in schizophrenia: A quantitative magnetic resonance imaging study. *New England Journal of Medicine, 327*(9), 604-612. doi:10.1056/nejm199208273270905

Spence, S. H. (2003). Social skills training with children and young people: Theory, evidence and practice. *Child and Adolescent Mental Health, 8*(2), 84-96. doi:10.1111/1475-3588.00051

Stain, H. J., Galletly, C. A., Clark, S., Wilson, J., Killen, E. A., Anthes, L., . . . Harvey, C. (2012). Understanding the social costs of psychosis: The experience of adults affected by psychosis identified within the second Australian national survey of psychosis. *Australian & New Zealand Journal of Psychiatry, 46*(9), 879-889. doi:10.1177/0004867412449060

Standen, P. J., & Brown, D. J. (2005). Virtual reality in the rehabilitation of people with intellectual disabilities. *CyberPsychology & Behavior, 8*(3), 272-282. doi:10.1089/cpb.2005.8.283

Sterzer, P., Mishara, A. L., Voss, M., & Heinz, A. (2016). Thought Insertion as a Self-Disturbance: An Integration of Predictive Coding and Phenomenological Approaches. *Frontiers in Human Neuroscience, 10*, 502. doi:10.3389/fnhum.2016.00502

Stickley, A., Koyanagi, A., Roberts, B., Richardson, E., Abbott, P., Tumanov, S., & Mckee, M. (2013). Loneliness: Its Correlates and Association with Health Behaviours and Outcomes in Nine Countries of the Former Soviet Union. *PLoS ONE, 8*(7), E67978. doi:10.1371/journal.pone.0067978

Stilo, S. A., Di Forti, M., Mondelli, V., Falcone, A. M., Russo, M., O'Connor, J., … Morgan, C. (2013). Social Disadvantage: Cause or Consequence of Impending Psychosis? *Schizophrenia Bulletin*, *39*(6), 1288–1295. doi: 10.1093/schbul/sbs112

Stilo, S. A., Gayer-Anderson, C., Beards, S., Hubbard, K., Onyejiaka, A., Bourque, F., ... & Murray, R. (2016). Is there a cumulative effect of social disadvantage on risk of psychosis?. *European Psychiatry*, *33*, S311. doi: 10.1016/j.eurpsy.2016.01.675

Strickland, D. (1997). Virtual reality for the treatment of autism. *Studies in Health Technology and Informatics*, 81-86. doi: 10.3233/978-1-60750-888-5-81.

Swann, W. B., Jr., & Bosson, J. K. (2010). Self and identity. In D. T. Gilbert, S. T. Fiske, & G. Lindzey (Eds.), *Handbook of Social Psychology* (pp. 589–628) (5th ed). Hoboken, NJ: John Wiley & Sons.

Stillman, T. F., Baumeister, R. F., Lambert, N. M., Crescioni, A. W., Dewall, C. N., & Fincham, F. D. (2009). Alone and without purpose: Life loses meaning following social exclusion. *Journal of Experimental Social Psychology, 45*(4), 686-694. doi:10.1016/j.jesp.2009.03.007

Swartz, M., Perkins, D. O., Stroup, T. S., Davis, S. M., Capuano, G., Rosenheck, R. A., . . . Lieberman, J. A. (2007). Effects of antipsychotic medications on psychosocial functioning in patients with chronic schizophrenia: Findings from the NIMH CATIE study. *American Journal of Psychiatry, 164*(3), 428-436. doi:10.1176/appi.ajp.164.3.428

Swartz, R. J., Costa, A. L., Beyer, B. K., Reagan, R., & B., K. (2010). *Thinking-Based Learning: Promoting Quality Student Achievement In The 21st Century*. New York: Teachers College Press.

Tajfel, H., & Turner, J. C. (1979). An integrative theory of intergroup conflict. In W. G. Austin & S. Worchel (Eds.), *The Social Psychology of Intergroup Relations* (pp. 33-37). Monterey, CA: Brooks/Cole.

Tan, H., Ang, Y., Tan, H., & Ang, Y. (2001). First-episode psychosis in the military: A comparative study of prodromal symptoms. *Australian & New Zealand Journal of Psychiatry, 35*(4), 512-519. doi:10.1046/j.1440-1614.2001.00912.

Tartaro, A., & Cassell, J. (2007). Using virtual peer technology as an intervention for children with autism. In J. Lazar (Ed.), *Towards Universal Usability: Designing Computer Interfaces for Diverse User Populations* (pp. 231-262). New York: John Wiley & Sons.

Thakkar, K. N., Nichols, H. S., Mcintosh, L. G., & Park, S. (2011). Disturbances in body ownership in schizophrenia: Evidence from the rubber hand illusion and case study of a spontaneous out-of-body experience. *PLoS ONE, 6*(10), E27089. doi:10.1371/journal.pone.0027089

Thakkar, K. N., Peterman, J. S., & Park, S. (2014). Altered brain activation during action imitation and observation in schizophrenia: A translational approach for studying social dysfunction. *American Journal of Psychiatry, 171*(5), 539-548. doi:10.1176/appi.ajp.2013.13040498

Thoits, P. A. (1983). Multiple identities and psychological well-being: A reformulation and test of the social isolation hypothesis. *American Sociological Review, 48*(2), 174-187. doi:10.2307/2095103

Thibaut, J. W., & Kelley, H. H. (1959). *The Social Psychology of Groups*. Oxford, England: John Wiley.

Troje, N. F. (2013). What is biological motion? Definition, stimuli, and paradigms. In M. D. Rutherford & V. A. Kuhlmeier (Eds.), *Social perception: Detection and interpretation of animacy, agency, and intention* (pp. 13-36). Cambridge, MA, US: MIT Press

Tsang, M. M., & Man, D. W. (2013). A virtual reality-based vocational training system (VRVTS) for people with schizophrenia in vocational rehabilitation. *Schizophrenia Research, 144*(1-3), 51-62. doi:10.1016/j.schres.2012.12.024

Turner, J. C., Hogg, M. A., Oakes, P. J., Reicher, S. D., & Wetherell, M. S. (1987). *Rediscovering the social group: A self-categorization theory*. Cambridge, MA, US: Basil Blackwell.

Turner, D. T., Mcglanaghy, E., Cuijpers, P., Gaag, M. V., Karyotaki, E., & Macbeth, A. (2018). A Meta-analysis of social skills training and related interventions for psychosis. *Schizophrenia Bulletin, 44*(3), 475-491. doi:10.1093/schbul/sbx146

Velthorst, E., Reichenberg, A., Kapra, O., Goldberg, S., Fromer, M., Fruchter, E., . . . Weiser, M. (2016). Developmental trajectories of impaired community functioning in schizophrenia. *JAMA Psychiatry, 73*(1), 48. doi:10.1001/jamapsychiatry.2015.2253

Vickhoff, B., Malmgren, H., Åström, R., Nyberg, G. F., Ekström, S., Engwall, M., . . . Jörnsten, R. (2013). Music structure determines heart rate variability of singers. *Frontiers in Psychology, 4*, 334. doi:10.3389/fpsyg.2013.00599

Watson, D., Clark, L. A., & Tellegen, A. (1988). Development and validation of brief measures of positive and negative affect: The PANAS scales. *Journal of Personality and Social Psychology, 54*(6), 1063-1070. doi:10.1037//0022-3514.54.6.1063

Weiss, R. S. (1973). *Loneliness: The experience of emotional and social isolation*. Cambridge, MA: The MIT Press.

Westermeyer, J. (1989). Psychiatric epidemiology across cultures: Current issues and trends. *Transcultural Psychiatric Research Review, 26*(1), 5-25. doi:10.1177/136346158902600101

Whitson, J. A., & Galinsky, A. D. (2008). Lacking control increases illusory pattern perception. *Science, 322*(5898), 115-117. doi:10.1126/science.1159845

Williams, K. D., Cheung, C. K., & Choi, W. (2000). Cyberostracism: Effects of being ignored over the internet. *Journal of Personality and Social Psychology, 79*(5), 748-762. doi:10.1037//0022-3514.79.5.748

Williams, K. D., Govan, C. L., Croker, V., Tynan, D., Cruickshank, M., & Lam, A. (2002). Investigations into differences between social- and cyberostracism. *Group Dynamics: Theory, Research, and Practice, 6*(1), 65-77. doi:10.1037//1089-2699.6.1.65

Williams, K. D., & Jarvis, B. (2006). Cyberball: A program for use in research on interpersonal ostracism and acceptance. *Behavior Research Methods, 38*(1), 174-180. doi:10.3758/bf03192765

Wuthrich, V., & Bates, T. C. (2005). Reliability and validity of two Likert versions of the Schizotypal Personality Questionnaire (SPQ). *Personality and Individual Differences, 38*(7), 1543-1548. doi:10.1016/j.paid.2004.09.017

Ziskind, E. (1958). Isolation stress in medical and mental illness. *Journal of the American Medical Association, 168*(11), 1427-1431. doi:10.1001/jama.1958.03000110001001

Zysberg, L. (2012). Loneliness and emotional intelligence. *The Journal of Psychology, 146*(1-2), 37-46. doi:10.1080/00223980.2011.574746