The Effect of a single, minimal dose of Antipsychotic on the Drive to Engage in Social Roles

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Table of Contents

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Abstract

The motivation for individuals to engage in extraordinary social roles is an important factor contributing to the formation of psychotic symptoms. While antipsychotics are widely prescribed to treat psychotic symptoms, few studies have investigated their effects on the drive to engage in extraordinary social roles. Thus, the objective of the current study was to examine the effect of an atypical antipsychotic (olanzapine) on the drive to play extraordinary social roles relative to an antipsychotic-placebo. One hundred and five healthy individuals (antipsychotic-placebo, n = 51, mean age: 23.8 years, 52.9% male; 2.5 mg olanzapine, n=54, mean age: 23.07 years, 55.5% male) participated in this randomized, single-dose, open-label study. Participants in the active medication group were given olanzapine, while those in the antipsychotic-placebo group received an inert pill that was believed to be olanzapine. All participants were informed of the drug's adverse effects through the consent form at the beginning of the experiment. All participants were individually presented with hundreds of names of social roles in an experimental psychology conditions in two sessions. The task of the participant was to decide whether or not they would consider performing the role at any moment of their life. The findings revealed that participants who took olanzapine were significantly slower than those taking the antipsychotic-placebo at accepting all role types and at rejecting extraordinary favorable roles in the first session. In the second session, participants taking olanzapine (vs. antipsychotic-placebo) were significantly slower at accepting extraordinary roles but faster at rejecting both ordinary favorable and extraordinary unfavorable roles. Compared to the antipsychotic-placebo, participants taking olanzapine became significantly faster at accepting ordinary roles and at rejecting extraordinary roles. In

conclusion, a single, minimal dose of olanzapine influences the speed at which healthy participants make decisions about engaging in social roles as compared to an antipsychotic-placebo. Olanzapine (vs. antipsychotic-placebo) may therefore modify the drive to play social roles. The results found in this study may inform future studies of the effect of antipsychotics on the drive to engage in extraordinary social roles.

Résumé

La motivation des individus à s'engager dans des rôles sociaux extraordinaires est un facteur important contribuant à la formation de symptômes psychotiques. Alors que les antipsychotiques sont largement prescrits pour traiter les symptômes psychotiques, peu d'études ont étudié leurs effets sur la motivation de jouer des rôles sociaux extraordinaires. L'objectif de la présente étude était d'examiner l'effet d'un antipsychotique atypique (olanzapine) sur la motivation des rôles sociaux extraordinaires par rapport à un antipsychotique-placebo. Cent cinq individus en bonne santé (antipsychotique-placebo, n = 51, âge moyen: 23,8 ans, 52,9% d'hommes, 2,5 mg d'olanzapine, n = 54, âge moyen: 23,07 ans, 55,5% d'hommes) ont participé à cette étude. Les participants du groupe médicamenteux actif recevaient de l'olanzapine, tandis que ceux du groupe antipsychotique-placebo recevaient une pilule inerte que l'on croyait être l'olanzapine. Tous les participants ont été informés des effets indésirables du médicament au moyen du formulaire de consentement au début de l'expérience. Tous les participants ont été présentés individuellement avec des centaines de noms de rôles sociaux dans des conditions de psychologie expérimentale en deux sessions. La tâche du participant consistait à décider s'il envisagerait ou non d'assumer ce rôle à n'importe quel moment de sa vie. Les résultats ont révélé que les participants qui prenaient l'olanzapine étaient plus lents que ceux qui prenaient le antipsychotique-placebo à accepter tous les types de rôle et à rejeter les rôles favorables extraordinaires dans la première session. Au cours de la deuxième séance, les participants prenant de l'olanzapine (vs. antipsychotique-placebo) étaient plus lents à accepter des rôles extraordinaires, mais plus rapide à rejeter des rôles défavorables ordinaires et extraordinaires. Comparé à l'antipsychotique-placebo, les participants prenant de

l'olanzapine sont devenus plus rapides à accepter des rôles ordinaires et à rejeter des rôles extraordinaires. En conclusion, une seule dose minimale d'olanzapine influe la vitesse à laquelle les participants en bonne santé prennent des décisions concernant leur rôle social par rapport à un antipsychotique-placebo. L'olanzapine (vs. antipsychotique-placebo) peut donc modifier le désir pour jouer des rôles sociaux. Les résultats trouvés dans cette étude peuvent fournir de plus amples informations sur les effets des antipsychotiques sur le désir de jouer des rôles sociaux extraordinaires.

Introduction

Schizophrenia

Schizophrenia is a chronic and severe mental disorder that includes both positive and negative symptoms. The positive symptoms involve hallucinations, delusions, and disorganized thought/speech, while the negative symptoms include a lack of motivation, enjoyment, and social interactions. Approximately 1% percent of the worldwide population is diagnosed with schizophrenia and annual costs for the disease in the US range from $94 million to $102 billion (NIMH, 2016). Research has suggested that delayed access to mental health services and uncertainty over choosing the correct course of treatment in early psychosis and schizophrenia is associated with slower or less complete recovery, increased risk of relapse and poorer outcome in subsequent years (Bottlender et al., 2003; Harrigan et al., 2003). In recent years, the dopaminergic system has been shown to play a vital role in schizophrenia, with effective drug treatments targeting the dopaminergic system. While there is evidence suggesting that schizophrenia is related to excessive activity of dopaminergic neurons, which has spurred the development of antipsychotic drugs (Seeman & Lee, 1975; Meltzer & McGurk, 1999; Yilmaz et al., 2012), it is also known that there are a number of genetic and environmental risk factors for developing psychosis and schizophrenia (Miyamoto et al., 2005). Emerging research on the causes of psychosis has largely focused on the biological factors and cognitive processes that are associated with schizophrenia, but there remains uncertainty about how these factors fit together to cause the disorder (Tandon et al., 2008).

A body of literature suggests that schizophrenia is not a categorical psychiatric disorder that is either present or absent in an individual but rather a continuum between normality and

schizophrenia (Nelson et al, 2013; Cochrane, Petch, & Pickering, 2012; Lenzenweger, 2006). For instance, the schizotypal personality questionnaire (SPQ) (Raine, 1991; Johns & van Os, 2001) has been developed to assess schizophrenia-like symptoms in healthy individuals. Several studies have shown that high SPQ scorers perform worse as compared low-SPQ scorers in verbal IQ (Noguchi, Hori, & Kunugi, 2008), visuospatial (Daly, Afroz, & Walder, 2001) and executive cognitive tasks (Suhr & Spitznagel, 2001; Cochrane, Petch, & Pickering, 2012), with schizophrenia patients exhibiting pronounced deficits in these same tasks (Raine et al., 1994).

Furthermore, the quantification of schizotypal traits in healthy populations may represent an opportunity for examining the mechanisms of schizophrenia symptoms in a less confounded context. Although a patient' set of symptoms may induce long-term disability or disease, this is less likely to be the case in healthy populations. Studying healthy subjects therefore allows for interpretations independent of the problems often found in patient-based research (i.e., concomitant effects of medications, illness duration, and severity).

Psychosis

The essential clinical features of psychosis are defined in the most recent version of the American Psychiatric Association's (APA's) *Diagnostic and Statistical Manual of Mental Disorders (DSM-V)*, which stipulates that psychotic symptoms include the presence of delusions, hallucinations (without insight into their pathological nature), or both hallucinations without insight and delusions. Psychotic symptoms are also defined in terms of formal thought disorders such as disorganized thinking and illogicality, grossly disorganized behavior, and catatonia according to the DSM-V. The severity of a patient's hallucinations and delusions are often indicative of the degree to which they have lost touch with reality (Arciniegas, 2015).

While hallucinations refer to the occurrence of sensory experiences in the absence of a corresponding external or somatic stimulus, which are typically visual or auditory in nature, delusions are defined as false beliefs that are firmly maintained even though there is evidence that conclusively contradicts the belief. Although there are many different types of delusions (i.e., grandiose, erotomaniac, persecutory, jealous, somatic, mixed), the DSM-V divides them into two broad categories: ordinary and bizarre. Ordinary delusions involve a misinterpretation of everyday experiences that are understandable but not accepted by the person's culture or environment. For instance, a person who believes that conspirators are stealing money from his savings to fund a terrorist group despite being presented with bank statements is considered to have an ordinary persecutory delusion. Bizarre delusions are phenomena that are considered physically impossible according to established social norms (i.e., a person who believes that a stranger removed his internal organs and replaced them with someone else's).

Psychosis is the dominant characteristic of many mental illnesses such as schizophrenia and associated spectrum disorders, and a secondary feature of mood and substance use disorders. Recent data has also shown that psychosis may be relatively common in several developmental and degenerative neurological conditions (Vialta-Franch et al., 2013; Forsaa et al., 2010). In addition, substantial evidence from multiple longitudinal studies conducted in Europe and the U.S. has revealed that adolescents and young adults who first exhibit less severe but still troubling psychotic symptoms are much more likely (conversion rate of ~10-30% within two years) to develop psychotic disorders such as schizophrenia as compared to the general population (Ruhrmann et al., 2010; Woods et al., 2009; Cannon et al., 2008).

Antipsychotics & Motivation

The classic dopamine hypothesis suggests that overactive dopamine transmission is implicated in the pathogenesis of schizophrenia (Iversen & Iversen, 2007). The dopamine hypothesis garnered support from the findings of Creese & colleagues (1976) and Seaman & Lee (1975), showing that higher (vs. lower) doses of first-generation antipsychotics were related to the blockade of D2 receptors. Neuroleptics were also shown to specifically block dopaminergic (D2) receptors mainly in subcortical regions of the brain (Carlsson and Lindqvist, 1963).

Previous findings have revealed that the positive symptoms of schizophrenia may be related to excessive dopaminergic transmission in subcortical regions while negative symptoms may be associated with a deficit in cortical dopaminergic transmission (Weinberger, 1987), suggesting that dysregulation of dopaminergic transmission is responsible for the clinical symptoms of schizophrenia. However, Meltzer (1989) developed the serotonin-dopamine hypothesis, which implicated both serotonin and dopaminergic systems in the mechanism of action of antipsychotic drugs. The second-generation 'atypical' antipsychotics (i.e., olanzapine, risperidone, and quetiapine) were therefore developed to selectively induce a moderate level of subcortical mesolimbic dopamine blockade and a high level of serotonin receptor blockade as well as reduce the unwanted side effects that were observed in the previous generation of antipsychotics (Vallianatou, 2012; Keefe et al., 2007). At moderate doses, atypical antipsychotics such as olanzapine have been shown to occupy approximately 60-90% of D2 receptors with serotonin occupancy at approximately 90% (Kapur et al., 1999; Nyberg et al., 1999). While other neurotransmitter systems including adrenergic, cholinergic and

histaminergic have also been found to be involved in the mechanism of action of second-generation antipsychotics (Kuroki et al., 2008), the dopaminergic system remains a central target for improving psychotic symptoms according to several meta-analyses showing a strong association for antipsychotic D2 receptor occupancy and clinical outcomes of schizophrenia (Pani et al., 2007; Yilmaz et al., 2012).

Despite advances in the pharmacological properties of novel antipsychotics, investigations to date have yielded inconsistent findings about the effect of antipsychotics on improving symptoms of schizophrenia. Emerging evidence suggests that atypical antipsychotics do not significantly improve the negative symptoms of schizophrenia (Harvey et al., 2016; Moosavi et al., 2015). A previous systematic review by Campbell et al. (1999) found that olanzapine exerts a negligible effect on negative symptoms, while a meta-analysis by Carman & colleagues (1995) revealed that risperidone was only moderately effective in treating negative symptoms. A recent meta-analysis by Fusar-Poli et al. (2015) reported that atypical antipsychotics are similar to conventional antipsychotics in the treatment of negative symptoms, and that these newer medications produced clinically insignificant effects on negative symptoms. However, there is evidence showing that antipsychotics, relative to placebo, effectively reduce symptoms such as hallucinations, delusions, and suspiciousness, although side effects are still common (Buchanan et al., 2010). Dixon et al. (1995) found that atypical antipsychotics decrease psychotics symptoms in approximately 70% of patients with schizophrenia (Dixon et al., 1995), while a more recent study by Agid et al. (2008) reported a reduction of positive symptoms occurring just a few hours after the intake of an atypical neuroleptic. Some studies have also shown that atypical antipsychotics improve neurocognitive

deficits (Masand, 2005), and that enhancements in cognitive functioning often occur after switching patients from conventional to atypical antipsychotics (Hill et al., 2010). Specifically, the administration of single doses of either risperidone or olanzapine have been independently associated with a wide-range of cognitive improvements (Harvey et al., 2005). However, some meta-analyses have also reported mild to moderate cognitive impairments with atypical antipsychotics in schizophrenia at relatively low doses (Desamericq et. al., 2014; Woodward et al. 2005). Other studies have shown that poorer cognitive function is associated with higher doses of antipsychotics (Takeuchi et al., 2013; Kawai et al., 2006).

Recent findings suggest that motivational deficits are core symptoms of schizophrenia, which are related to poorer functional outcomes (Foussias et al., 2014). Graham et al. (2008) found that motivational deficits may even be present at the onset of psychosis. Their study reported that patients with first-episode psychosis taking low doses of antipsychotics reacted slower than healthy subjects on a reaction time test involving reward attribution, suggesting an effect of antipsychotics on brain reward mechanisms. The effect of antipsychotics on motivational processes in schizophrenia has also been widely studied, which has provided insights into the influence of antipsychotics on negative symptoms (Gard et al., 2009). Single-dose administration of an atypical antipsychotic has been shown to be associated with some improvements in motivation in schizophrenia (Park et al., 2012), although many studies have reported opposite findings (Artaloytia et. al, 2006; Saeedi et. al, 2006; Mas et al, 2013). There is also a need to investigate the effect of antipsychotics on motivational processes in individuals without underlying pathology (Veselinovic et al., 2012).

A major limitation in both antipsychotic and schizophrenia studies is the lack of a measure that specifically relates motivation to psychosis (Fervaha et al., 2015; Choi et. al., 2014). In most patient-based research, motivation is generally characterized by a patient's ability or willingness to engage in goal-directed activities relating to a sense of drive (i.e., general motivation) (Heinrichs et al., 1984; Nakagami et al., 2008; Yamada et al., 2010; Vohs et al., 2013). Measures of general motivation are also commonly used to assess the effect of antipsychotic treatment on motivation in patients with psychotic symptoms (Fervaha et al., 2015; Wolf et al., 2014). A recent meta-analysis by Najas-Garcia & colleagues (2018) found that ~61.49% of studies investigating the effects of antipsychotics on clinical symptoms of schizophrenia used standardized questionnaires to assess motivation, while the remaining studies used either behavioral tasks or brain imaging. Furthermore, these measures do not reflect the drive to play social roles, which has been shown to be an independent factor contributing to schizophrenia-like symptoms (Fernandez-Cruz et al., 2016).

The Drive to Play Social Roles

The drive to engage with other people is fundamental for humans to effectively function and behave in their social environment (Forgas et al., 2005). A social interaction involves the actual presence or behavior of individuals as well as the abstract beliefs or desires they hold about the people they are interacting with (Saxe & Kanwisher, 2003). This may be particularly relevant for individuals with psychotic symptoms, which often include a clear social content with illusory social agents of numerous types (Bell et al., 2017). For instance, illusory social roles may consist of a family member or a historical or religious figure, groups (i.e., the CIA),

supernatural or fictional figures (i.e., angels or TV characters), or idiosyncratic social agents who only seem to be recognized solely by the individual who experiences them.

Patients with psychotic symptoms normally adopt social roles that are either frequently or infrequently encountered in everyday life. The drive to play certain social roles may depend on behaviors and attitudes, which are organized into strategies. The will to engage in certain extraordinary, as opposed to ordinary roles, may be associated with conflicting cognitive strategies, since the behavioral schemas associated with extraordinary roles are often different from the schemas associated with the ordinary social roles, which most of us have enact in our everyday lives. The use of divergent cognitive strategies has been shown to reduce verbal IQ scores, lower academic performance, and reduce social skills (Noguchi, Hori, & Kunugi, 2008). In individuals with high-risk for psychosis, the use of divergent strategies has been linked to lower efficiency in accuracy and reaction time in cognitive tasks (Cochrane, Petch, & Pickering, 2012; Suhr & Spitznagel, 2001).

Social agent representation is also a prominent feature in persecutory delusions, which are commonly observed in psychosis (Ellersgaard et al., 2014). Green et al. (2006) found that persecutory delusions in psychiatric patients often involve the presence of single or multiple human persecutors, which the patient can identify with. Grandiose delusions are also defined as beliefs that contain some social special relationship to famous individuals (Suhail & Cochrane, 2002). Furthermore, auditory verbal hallucinations are often exhibited by psychotic patients that hear voices relating to specific individuals (Wilkinson & Bell, 2016). McCarthy-Jones et al. (2014) revealed that approximately 70% of patients with voices identified their voices with people they had encountered in their past. Evidence to date therefore suggests that

psychotic symptoms often include a well-defined social component mainly consisting of illusory social actors.

Furthermore, Fernandez-Cruz et al. (2016) found that the drive to perform extraordinary social roles was associated with schizophrenia-like symptoms in healthy subjects. The findings from this study revealed that individuals who accepted a greater number of extraordinary roles had higher SPQ scores. A specific subtype of roles (i.e., extraordinary unfavorable) were strongly correlated to scores on the SPQ. In addition, the study revealed that individuals who accepted a higher number of extraordinary roles took less time at accepting and more time at rejecting all role types, as compared to individuals who accepted a lower number of extraordinary roles. These results suggest that the delusions may represent a drive to play extraordinary roles, which could contribute to the onset or progression of psychotic symptoms.

Nocebo effect

A placebo effect is thought to generate a therapeutic response in patients being administered an active drug. Controlling for this effect allows researchers to account for a fraction of the drug's total therapeutic effect. In contrast, the nocebo phenomenon refers to any negative effects and/or distressing symptoms that occur after the administration of an inert intervention (i.e., chemically inactive substance) that the patient believes to be an active drug. Since patients taking active medications typically have adverse and non-specific effects, which are not direct consequences of the pharmacological effects of the drug (Barsky et al., 2002), the nocebo effect may account for a fraction of the drug's adverse effects. Furthermore, the nocebo effect often includes a negative expectation relating to disclosures of side effects from treatments in clinical or experimental settings. For instance, there is evidence that shows that

informing subjects of a medication's adverse effects may lead to the manifestation of that same adverse effect, regardless of the pharmacological properties of the drug (Mondaini et al., 2007). Enck et al. (2008) found that the adverse effects produced by negative expectations typically induce changes in normal physiological functioning.

Patients also have preexisting notions about a specific type of medication, which often influences their symptoms. Misunderstandings about the medication may engender anxiety, suspicions, and vulnerability, and other adverse effects, all of which may be not be attributable to the medication itself. In an antidepressant clinical trial, Rief et al. (2009) found that patients who believed that they would be receiving tricyclic (TCA) antidepressants (i.e., TCA placebos) reported more adverse effects than patients receiving selective serotonin reuptake (SSRI) placebos. While few studies have investigated the nocebo effect of antipsychotics, it may be particularly relevant to account for this effect considering that patients with psychosis may already have adopted a negative belief about their medication, which may further exacerbate their symptoms and lead to poor treatment adherence. These nonspecific side effects may therefore present further distress to patients with psychosis and impede clinical improvement of psychotic symptoms (Rief et al., 2011).

Research objectives

In the current study, we examined the effect of a single, minimal dose of the antipsychotic olanzapine on the drive to engage in social roles relative to an antipsychotic-placebo using a social roles task. The drive to engage in social roles was quantified by the number of social roles that participants either accepted and their reaction times for each social role category (Fernandez-Cruz et al., 2016). Our hypothesis was that olanzapine reduces the

overall drive to engage in extraordinary social roles. Accordingly, we predicted that olanzapine (vs. antipsychotic-placebo) decreases the number of extraordinary roles that participants engage in, since these roles have been shown to be associated with schizophrenia-like symptoms (Fernandez-Cruz et al., 2016). In addition, we predicted that olanzapine (vs. antipsychotic-placebo) makes individuals faster at rejecting the extraordinary roles and at accepting the ordinary roles.

Considering that many previous clinical studies have shown that single-doses of atypical antipsychotic drugs reduce the severity of psychotic symptoms in individuals with schizophrenia (Leucht et al., 2009; Tollefson et al., 1997; Beasley et al., 1996), our study was conducted in healthy subjects to eliminate the possibility that the effect of the antipsychotic on the drive to engage in social roles may be due to the alleviation of psychotic symptoms. We also controlled for the adverse effects associated with the negative representation of taking an antipsychotic medication (i.e., nocebo effect) in the present study by explicitly telling participants in the non-medicated group that they would be administered olanzapine, which involved the disclosure of known side effects.

Methods

Participants

One hundred and five right-handed healthy participants (48.57% males, 51.42% females) aged between 18 and 30 years (mean: 23.45 years) were recruited by advertisements in English and French online advertisements. Participants who answered these ads were asked what their mother tongue was. Only English and French were accepted. The rest of the procedure was carried in the language of the participants. They had to have normal or corrected-to-normal vision and were screened by online questionnaires at the lab. Participants were excluded for any history of DSM-IV Axis I psychiatric illnesses (except for depressive episodes that resolved at least two years ago), alcohol and drug abuse, neurological or medical conditions that compromise brain functioning, and history of head injury with loss of consciousness longer than 5 minutes.

Experimental Procedure

Participants were invited to the lab for one testing session. At their arrival in the lab, participants were asked to complete a battery of questionnaires (demographics, SPQ, anxiety levels, fatigue levels) administered in their preferred language (English or French). All participants were then asked to provide written consent after they had completed the informed consent document, which was approved by the Research and Ethics Board of the Douglas Mental Health University Institute. The consent form (see Appendix) stated that participants would be given 2.5 milligrams of the active medication olanzapine including the disclosure of the medication's side effects. No verbal information about the medication was given to the participants.

The subjects were seated comfortably in a dimly lit room and had to stare at a computer screen placed 70 cm from their eyes. Instructions and stimuli were, like the questionnaires, given in the participants' preferred language. After a brief practice run of the social roles task (see below), either a capsule containing 2.5mg of olanzapine or a capsule having an identical appearance but containing saccharose (i.e., placebo) was administered to participants. The emptiness of the mouth was checked after swallowing both capsules. Immediately after, the participant performed the social roles task (session 1). Participants were then given a one-hour lunch break. In the second session, the participant repeated the social roles task. A neurochemical effect at this minimal dose is known to occur after 1 hour according to the peak plasma concentration for olanzapine (Bhana & Perry, 2001; Bishara et al., 2013). The stimulus sequences used for these sessions were counterbalanced across subjects. In the debriefing session, participants were asked to provide feedback about the experiment and completed the fatigue and anxiety level questionnaire.

Social Roles Task

Before the experiment, a list of 401 names of social roles (see Supplementary Appendix) were rated on nine-point Likert scales by 42 independent young adult evaluators who were first given a definition of the criteria used. The 'extraordinariness' category had to be rated highly for social roles that would usually exceed human physical or mental capabilities. The 'unfavorability' category had to be rated highly for disadvantageous or inconvenient roles. The roles were presented in different random orders across these evaluators. Using median ratings, the set of roles was then split into four groups, one for each category combination: (1) ordinary favorable, (2) ordinary unfavorable, (3) extraordinary favorable, and (4) extraordinary

unfavorable roles. The first of these four groups comprised 107 stimuli, including roles such as jogger, piano teacher, social worker, nurse, and swimmer. The second comprised 92 stimuli, including roles such as vandal, pick pocket, homeless person, and drunk driver. The third comprised 97 stimuli, including roles such as astronaut, Zorro, Hercules, and Prophet. The fourth comprised 105 stimuli, including roles such as devil, bandit, vampire, and slave. There were no significant differences across these four ensembles between their mean numbers of letters and their mean frequencies of use as computed from Google books Ngram viewer figures. The set of 401 roles was divided into two subsets of roles balanced for the proportion of each of the four ensembles. In each session, one of these subsets was presented and the subsets were counterbalanced across sessions. The roles were randomly presented one at a time, for 500ms, in black writing on a white background at the center of a computer screen. Each role was immediately followed by a fixation cross that lasted for 500 ms. The participants were asked to decide as quickly and as accurately as possible whether they could consider themselves performing each role at any moment in their life. The answers were provided by pressing a 'Yes' or a 'No' button with the index and the middle finger, respectively, a correspondence that was counterbalanced across participants. Only responses that were between 300 and 2,500ms after the onset of the presentation of each role were included in the analysis. This was done to eliminate the responses of the trials that participants did not pay enough attention to or were too hesitant.

Questionnaires

1. *Demographics*

Participants were asked to give their age, gender and number of years of education. They were also asked to confirm that they were right-handed and had perfect or corrected-to-normal vision. Participants reported whether they were smokers and were asked about their alcohol, recreational drug use habits, and history of medical illness. Participants who did not meet inclusion criteria were excluded.

2. *SPQ*

Schizotypal personality traits were assessed using the schizotypal personality questionnaire (SPQ; Raine, 1991; Dumas et al., 1998 for French translation), which is based on the DSM III-TR criteria for schizotypal personality disorder. The validity of the whole SPQ has been demonstrated (Raine, 1991). Its clusters have been defined by a factor analysis (Raine et al., 1994) and has been used in previous studies to assess psychotic symptoms (Sommer et al., 2010; Salokangas et al., 2013). There are 74 items in this questionnaire with 9 subscales, which are organized into 3 clusters. The cognitive-perceptual cluster includes the 'Ideas of Reference', 'Odd Beliefs and Magical Thinking', and 'Unusual Perceptual Experience' subscales, while the interpersonal cluster includes the 'Excessive Social Anxiety', 'No Close Friends', 'Constricted Affect' and 'Suspiciousness' subscales. The third cluster is disorganization and consists of the 'Odd Speech' and 'Odd and Eccentric Behavior' subscales. A total score was derived by adding the scores for each cluster. This questionnaire was used to control for schizotypal traits across individuals.

3. *Anxiety*

Anxiety levels were assessed using the 20-item state trait anxiety inventory (STAI-A, Spielberger, 1983) questions. Each item was assessed on a 4-point likert scale. The total score was derived by adding the scores from each question. Total scores can range from 20 to 80, with higher scores reflecting more anxiety. This questionnaire was used to control for any reductions in anxiety possibly brought about by the antipsychotic.

4. *Fatigue*

The Fatigue Assessment Scale (FAS) is a 10-item general fatigue questionnaire to assess fatigue (Michielsen et al., 2004). Each item was assessed on a 5-point likert scale. The total score was derived by adding the scores from each question. Total scores can range from 10 to 50, with higher scores reflecting more fatigue. This questionnaire was used to control for any reductions in energy levels possibly brought about by the antipsychotic.

Analyses

The number of accepted roles in each of the four categories and reaction times corresponding to acceptance or rejection were analyzed. The mean number of accepted roles and mean reaction times for each of the four categories were calculated for both groups. Since the number of roles that participants rejected in each category is inversely proportional to the number that they accept, the mean number of rejected roles in each category was not analyzed. Mixed-model repeated measures analyses of variance (ANOVAs) were done separately for number of accepted roles and for reaction times. For role acceptance, session (session 1 vs. session 2), extraordinariness (extraordinary vs. ordinary roles), and favorability (favorable vs. unfavorable roles) were entered as within-subject factors, and drug group (olanzapine vs. placebo) was entered as the between-subject factors. For reaction times, an additional factor of decision (accepted vs. rejected) was included. Many additional analyses were done to find the source of the interactions found. We used the Greenhouse and Geisser (1959) procedure to compensate for heterogeneous variances.

Results

Sample Characteristics

Table 1 shows the demographic and clinical characteristics for all subjects, comparing those taking olanzapine and those taking the antipsychotic-placebo. No significance difference in mean age was observed between both groups. In addition, there was no significant difference in the mean number of years of study between both groups.

The repeated measures ANOVA on the STAI anxiety questionnaire revealed a significant drug x session x anxiety score interaction ($F(1,103)=12.04$, $p=0.042$). Follow-up analyses found that individuals who received placebo were significantly more anxious after the experiment as compared to before ($F(1,103)=8.45$, $p=0.028$). When we considered the olanzapine group, there was no significant difference in mean anxiety score between the pre- and post- experiment sessions. In the pre-experiment session, participants taking olanzapine were significantly more anxious than those taking placebo ($F(1,103)=34.51$, $p=0.037$). However, there was no significant difference in mean anxiety score between placebo and olanzapine groups for the post-experiment session.

We found a significant drug x session x fatigue interaction ($F(1,103)=5.93$, $p=0.03$). *Post hoc* analyses revealed that participants receiving olanzapine were significantly more fatigued after the experiment as compared to before ($F(1,103)=11.56$, $p=0.041$). However, there was no significant difference in mean fatigue score between pre- and post- experiment sessions for participants who received the antipsychotic-placebo. In the post-experiment session, participants taking olanzapine were significantly more fatigued as compared to the

antipsychotic-placebo group (F(1,103)=2.09, p=0.034). No significant difference in mean fatigue score was observed between olanzapine and placebo groups in the pre-experiment session.

There was no significant difference in the mean overall SPQ score between olanzapine and placebo groups. Independent sample t-test showed no significant differences between the antipsychotic-placebo and olanzapine groups in any of the side effects commonly associated with olanzapine.

Table 1. Demographic characteristics of participants taking either the antipsychotic-placebo or olanzapine.

	Antipsychotic-Placebo (N=51)	Olanzapine (N=54)
Mean age (SD)	23.8 (1.71)	23.07 (2.79)
%male (%female)	52.9 (47.05)	55.55 (44.44)
Mean number of years of study (SD)	15.1 (1.5)	14.9 (1.2)
Mean STAI-A anxiety score pre-experiment (SD)	38.07 (10.25)	47.944 (4.03)
Mean STAI-A anxiety score post-experiment (SD)	43.09 (12.16)	45.57 (8.09)
Mean fatigue score pre-experiment (SD)	26.92 (9.31)	25.01 (4.85)
Mean fatigue score post-experiment (SD)	25.96 (9.84)	28.24 (7.86)
Mean global SPQ score (SD)	22.74 (1.42)	21.68 (2.63)

Note. SD = Standard Deviation

Role acceptance

The results from the repeated measures ANOVA revealed that there were no significant differences between antipsychotic-placebo and olanzapine groups for the acceptance of each role type in neither the first (Figure 1a) nor second sessions (Figure 1b). Furthermore, no significant session x drug interaction was observed (Figure 2).

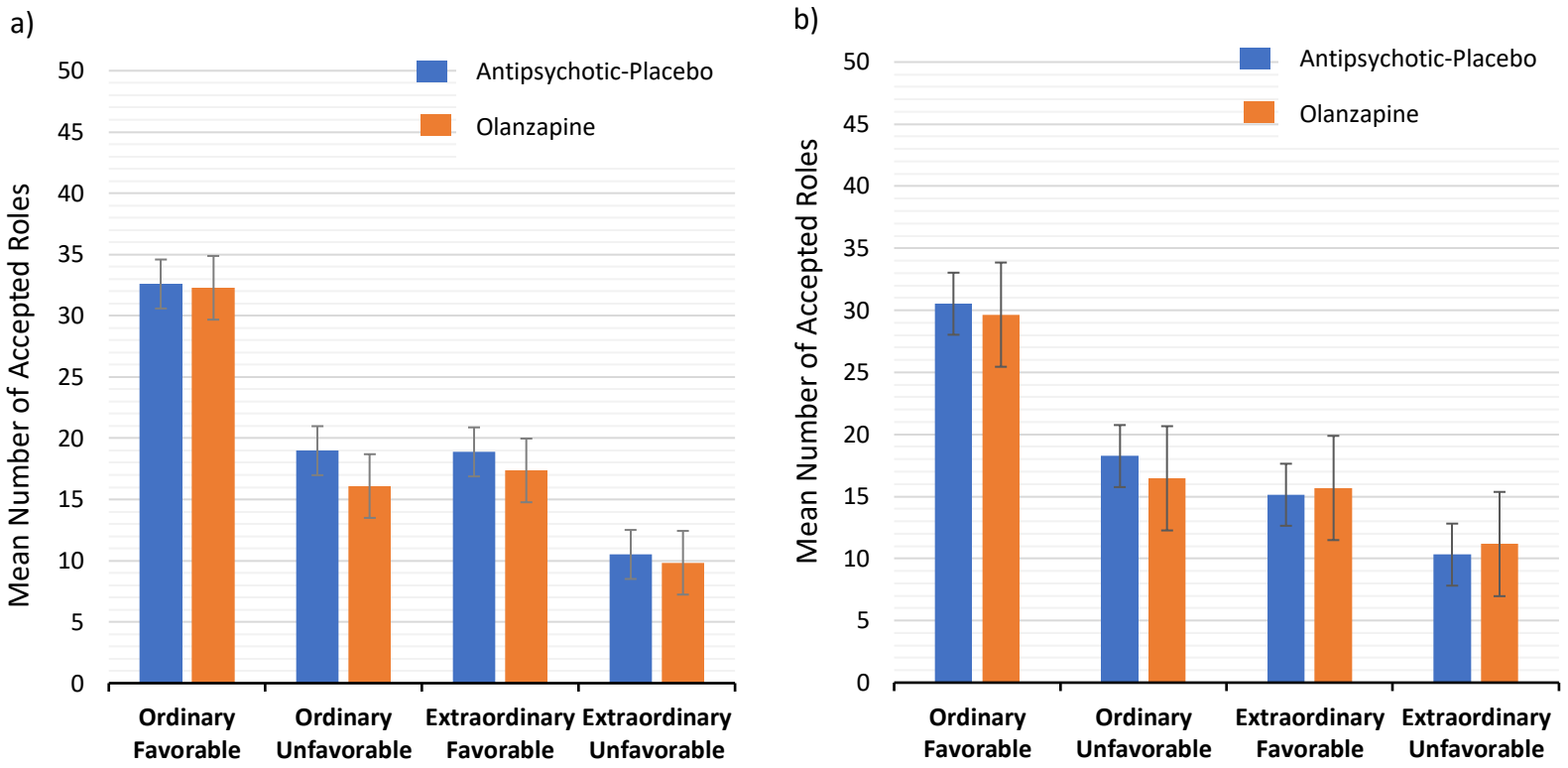

Figure 1. Mean number of social roles accepted in the a) first and b) second sessions in each category for antipsychotic-placebo and olanzapine groups. Standard errors are the vertical bars.

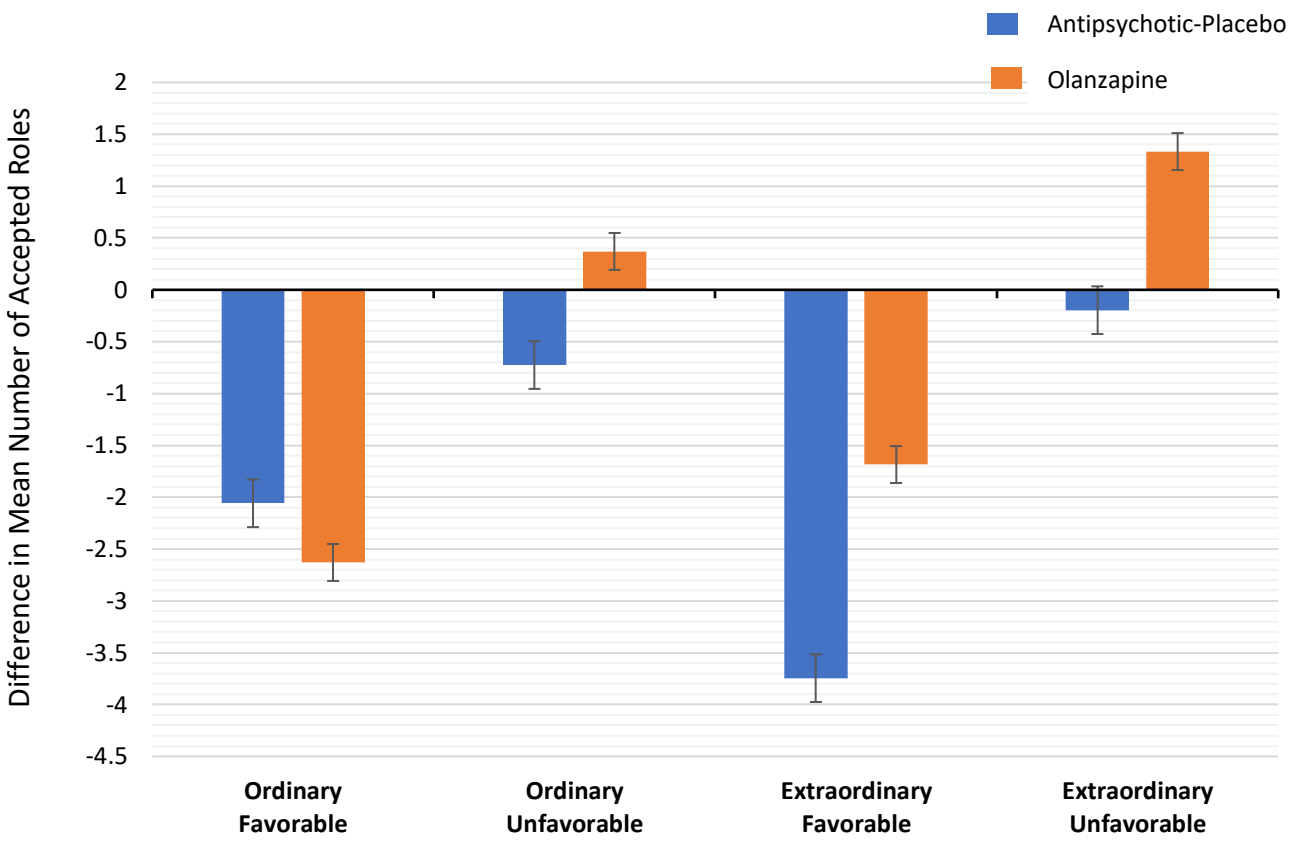

Figure 2. Mean difference (session 2 – session 1) in the number of accepted social roles in each category for antipsychotic-placebo and olanzapine groups. Standard errors are the vertical bars.

Reaction Times (RTs)

The results from the repeated measures ANOVA yielded a significant overall session x extraordinariness x favorability x decision x drug interaction ($F(1,103)=17.21$, $p=0.032$).

Acceptance RTs

In session 1, participants who were administered olanzapine were slower (M = 1030.51 ms, s.d. = 245) at accepting all role types (Figure 3a) than those who were administered the antipsychotic-placebo (M = 992.62 ms, s.d. = 267). This decision x drug interaction was significant ($F(1,103)=2.35$, $p=0.045$). Furthermore, we found a significant extraordinariness x favorability x decision x drug interaction ($F(1,103)=5.98$, $p=0.022$). Follow-up analyses revealed that participants on olanzapine were significantly slower at accepting each role type: ordinary favorable ($F(1,103)=2.44$, $p=0.042$), ordinary unfavorable ($F(1,103)=5.21$, $p=0.021$), extraordinary favorable ($F(1,103)=3.78$, $p=0.021$) and extraordinary unfavorable ($F(1,103)=4.69$, $p=0.0092$), as compared to those on the antipsychotic-placebo.

In session 2, participants taking olanzapine were slower (M = 1029.18 ms, s.d. = 283) at accepting extraordinary roles, regardless of favorability, than those taking the antipsychotic-placebo (M = 978.51 ms, s.d. = 263) (Figure 3b). This was revealed by a significant extraordinariness x decision x drug interaction ($F(1,103)=3.81$, $p=0.0021$). No significant favorability x decision x drug interaction was observed.

Figure 4 shows the difference (session 2 – session 1) in mean acceptance reaction times for each category of social roles for both antipsychotic-placebo and olanzapine groups. Our analysis revealed a significant session x extraordinariness x decision x drug interaction ($F(1,103)=6.44$, $p=0.033$). *Post hoc* analyses showed that for ordinary roles, regardless of

favorability, mean acceptance reaction times increased from session 1 (M = 991.69 ms, s.d. = 222) to session 2 (M = 997.67 ms, s.d. = 201) for individuals taking placebo, but significantly decreased from session 1 (M = 1025.34 ms, s.d. = 267) to session 2 (M = 985.81 ms, s.d. = 254) for individuals taking olanzapine ($F(1,103)=4.28$, $p=0.0088$).

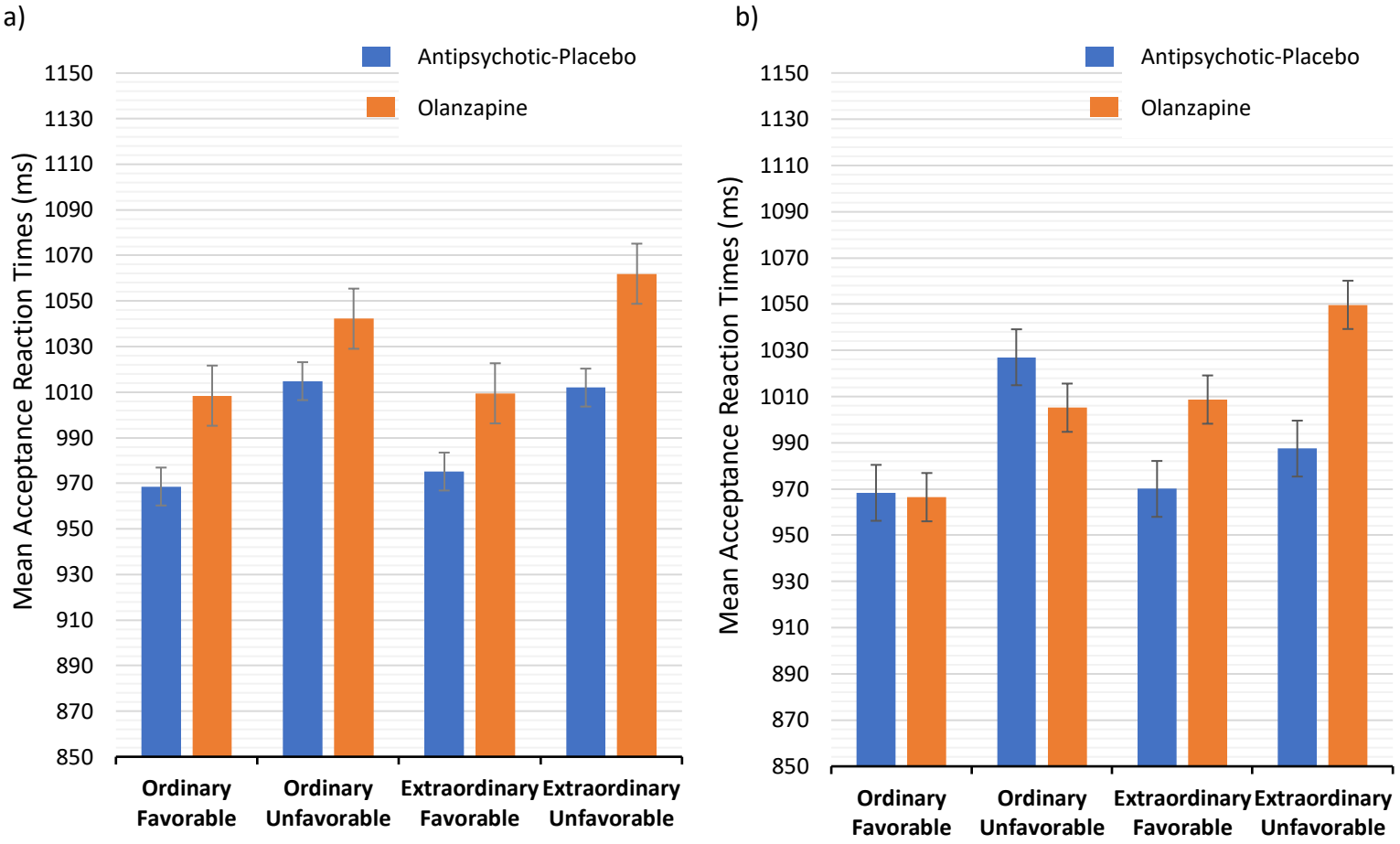

Figure 3. Mean reaction times (ms) for accepted social roles in the a) first and b) second sessions in each category for antipsychotic-placebo and olanzapine groups. Standard errors are the vertical bars.

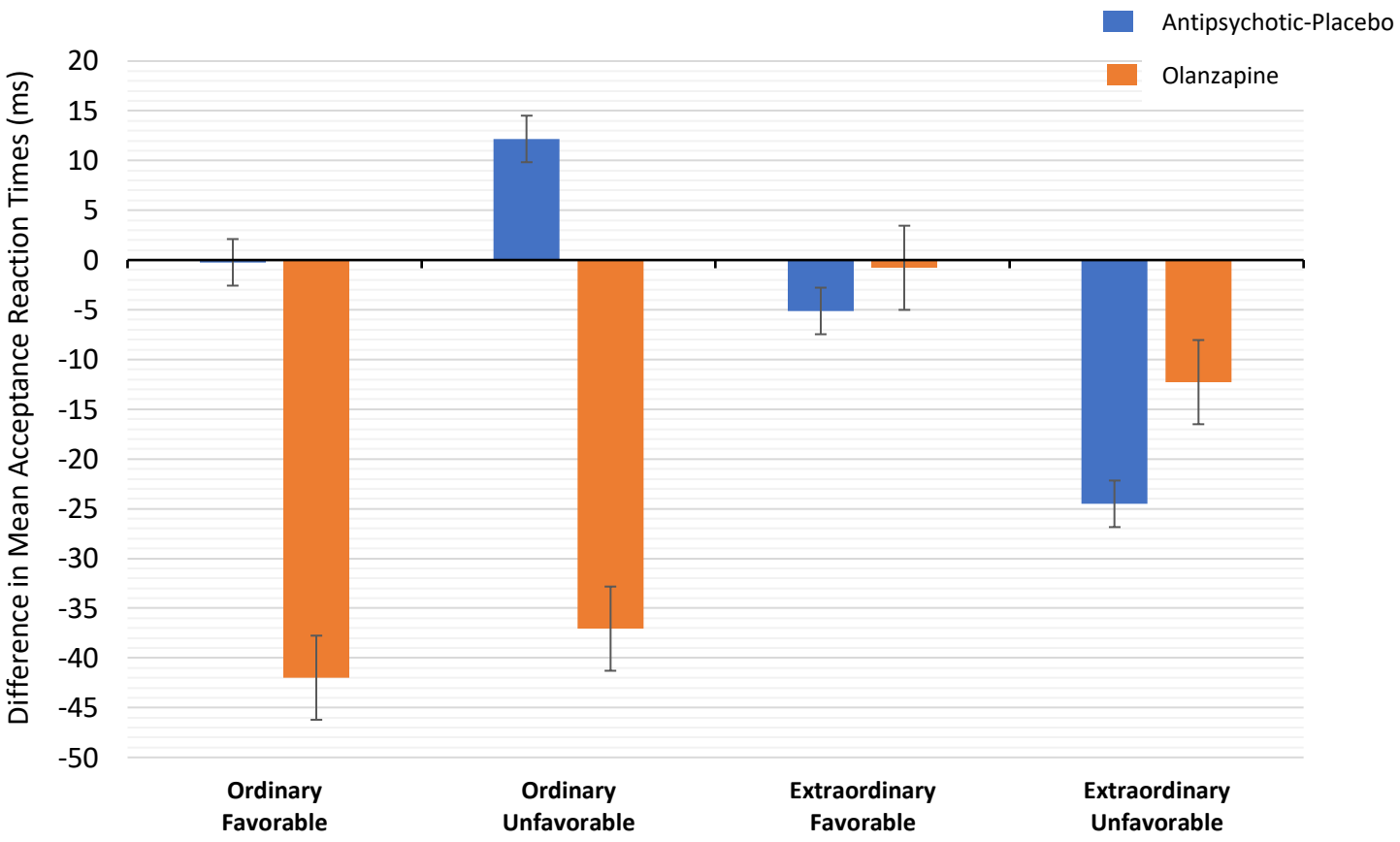

Figure 4. Mean difference (session 2 – session 1) in reaction times (ms) for accepted social roles in each category for antipsychotic-placebo and olanzapine groups. Standard errors are the vertical bars.

Rejection RTs

In session 1, the results from the repeated measures ANOVA revealed a significant extraordinariness x favorability x decision x drug ($F(1,103)=8.94$, $p=0.011$) interaction. Follow-up analyses found that participants on olanzapine were significantly slower (M = 1013.07 ms, s.d. = 322) at rejecting extraordinary favorable roles than the antipsychotic-placebo group (M = 962.83 ms, s.d. = 289; $F(1,103)=6.22$, $p=0.0067$) (Figure 5a).

In session 2, the repeated measures ANOVA yielded a significant extraordinariness x favorability x decision x drug ($F(1,103)=9.28$, $p=0.036$) interaction. *Post hoc* tests revealed that participants on olanzapine were significantly faster at rejecting both ordinary favorable (M = 981.32 ms, s.d. = 223 vs. M = 1020.57 ms, s.d. = 259; $F(1,103)=3.83$, $p=0.009$) and extraordinary unfavorable (M = 924.12 ms, s.d. = 255 vs. M = 961.84 ms, s.d. = 267; $F(1,103)=4.22$, $p=0.015$) roles, than the antipsychotic-placebo group (Figure 5b).

Figure 6 shows the difference (session 2 – session 1) in mean rejection reaction times for each category of social roles for both antipsychotic-placebo and olanzapine groups. The repeated measures ANOVA found a significant session x extraordinariness x decision x drug interaction ($F(1,103)=8.29$, $p=0.02$). *Post hoc* analyses showed that for extraordinary roles, regardless of favorability, mean rejection reaction times significantly decreased from session 1 (M = 966.31 ms, s.d. = 259) to session 2 (M = 948.64 ms, s.d. = 285) for individuals taking the antipsychotic-placebo ($F(1,103)=3.55$, $p=0.04$), and significantly decreased from session 1 (M = 999.13 ms, s.d. = 236) to session 2 (M = 918.25 ms, s.d. = 233) for individuals taking olanzapine ($F(1,103)=5.41$, $p=0.0062$).

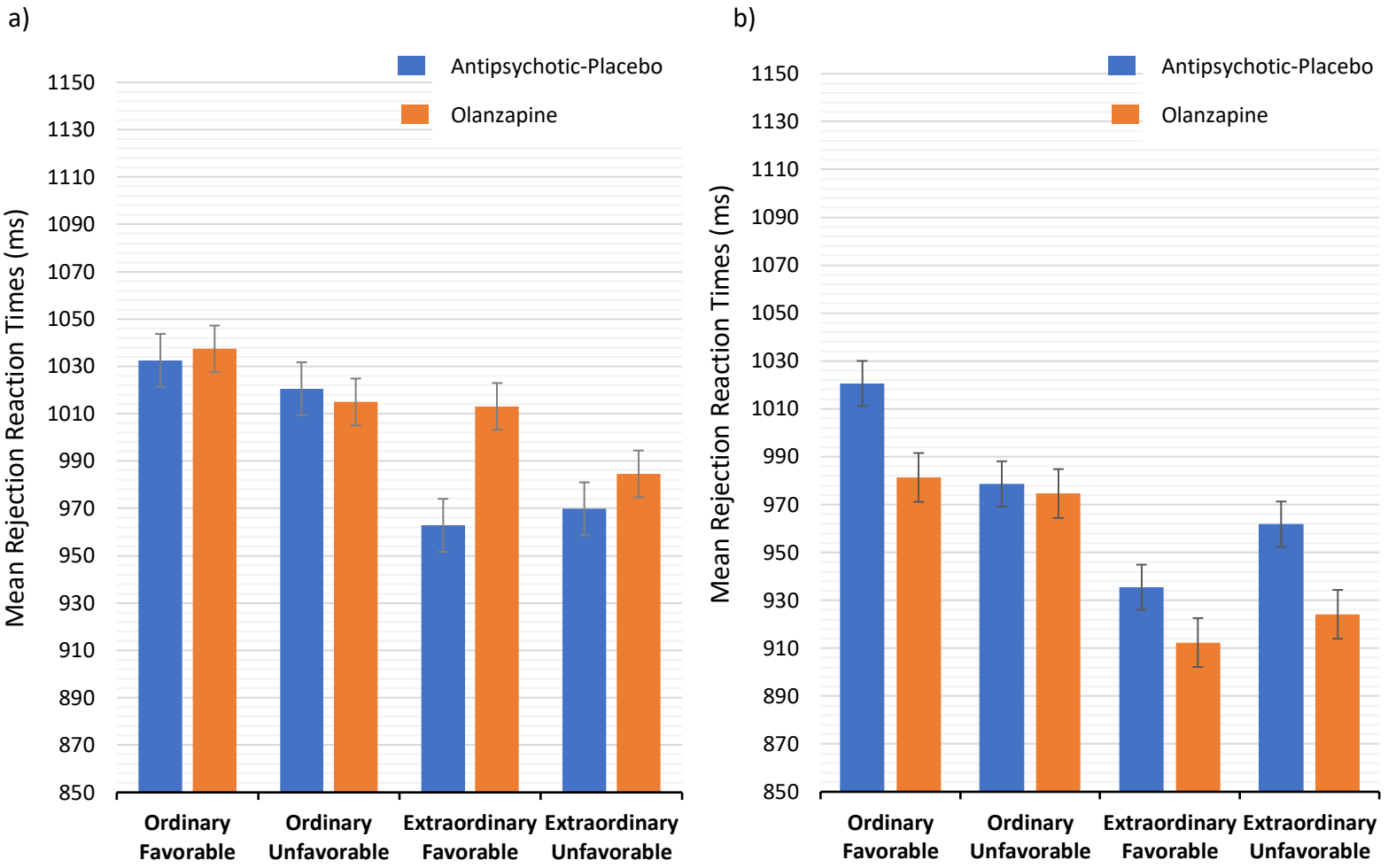

Figure 5. Mean reaction times (ms) for rejected social roles in the a) first and b) second sessions in each category for antipsychotic-placebo and olanzapine groups. Standard errors are the vertical bars.

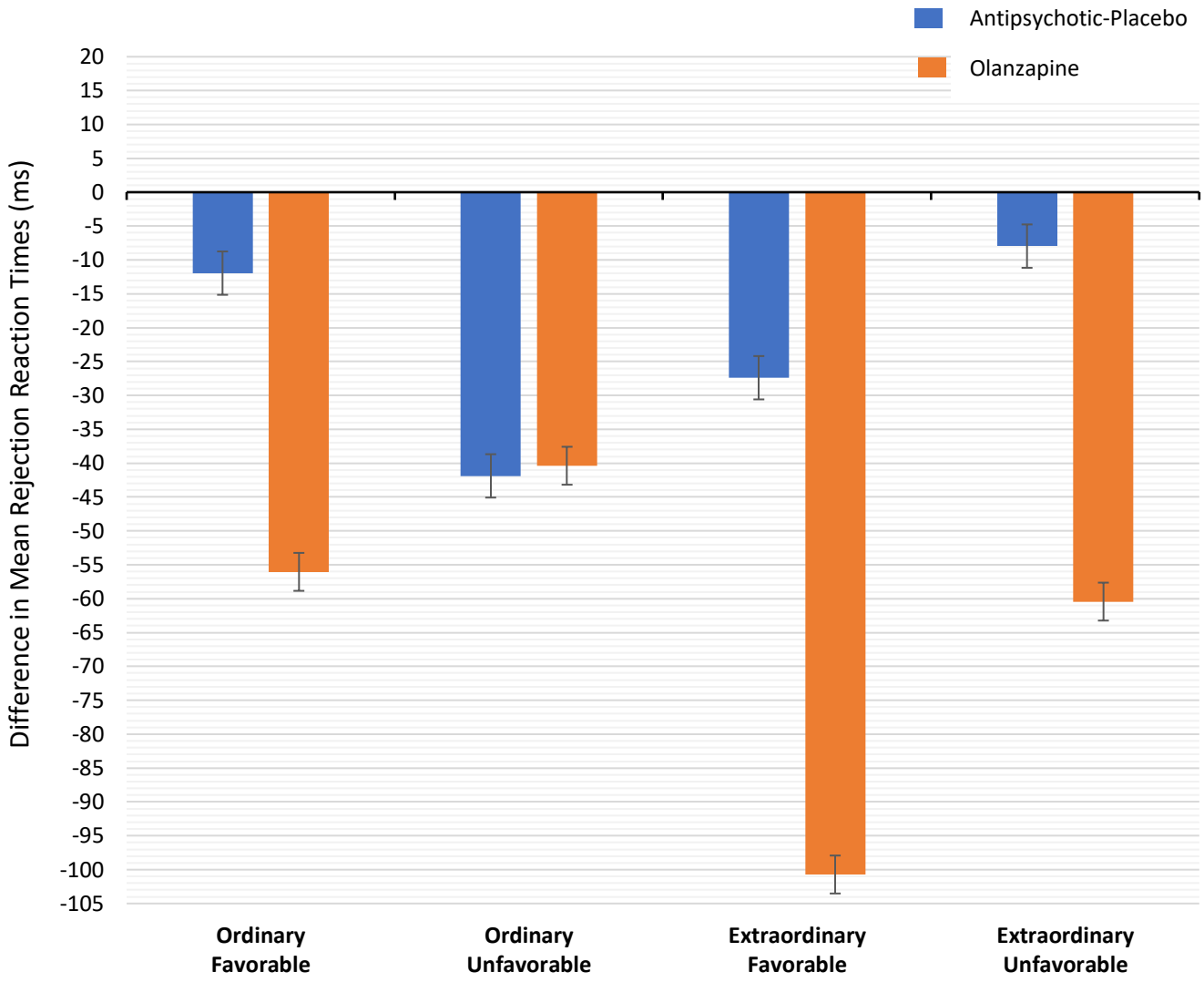

Figure 6. Mean difference (session 2 – session 1) in reaction times (ms) for rejected social roles in each category for antipsychotic-placebo and olanzapine groups. Standard errors are the vertical bars.

Discussion

The aim of the current study was to examine the effect of a single, minimal dose (2.5 mg) of olanzapine on the drive to play social roles. Healthy subjects were recruited to avoid confounding variables typically found in patients with schizophrenia (i.e., a patient's clinical symptoms, co-morbid diseases, concomitant medication, etc.). Furthermore, we controlled for the nocebo effect in the medicated group by telling participants in the non-medicated group that they were taking olanzapine, which included disclosure of the medication's negative side effects. The findings from our study revealed that olanzapine (vs. antipsychotic-placebo) modulates the speed at which individuals engage in roles but does not influence the number of roles that they accept. Overall, our results suggest that olanzapine may, in part, reduce the drive to engage in extraordinary social roles.

Contrary to our first prediction, no significant differences between antipsychotic-placebo and olanzapine groups were observed in the number of accepted extraordinary social roles. Furthermore, no significant differences between antipsychotic-placebo and olanzapine groups were observed in any social role category (see Figure 1), which suggests that the schemas associated with different categories of social roles are similar across both groups. A single low-dose of olanzapine therefore exerts a negligible effect on changing the set of pre-conceived notions that are associated with specific types of social roles (e.g., ordinary favorable). The schemas relating to social roles may arise from an individual's ability to subconsciously imitate the behaviors of family members, friends, and teachers, as well as characters portrayed in movies, television shows, books, and various other forms of media (van Baaren et al., 2004; Chartrand & van Baaren, 2009). Previous evidence strongly implicates the

role of the mirror neuron system in imitation behavior. Several studies have reported that mirror neurons are activated by both imitation and action observation (Iacoboni et al., 1999; Buccino et al., 2004; Rizzolatti and Craighero, 2004). A person's understanding of the objective or meaning of an observed action has also been shown to be associated with the mirror neuron system (Buccino et al., 2004; Gallese et al., 2004; Hamilton and Grafton, 2006; Bernier et al., 2007).

In line with our second prediction, olanzapine (vs. antipsychotic-placebo) influenced the time it took for participants to accept and reject different categories of social roles. Specifically, we found that individuals taking a single dose of olanzapine were slower at accepting extraordinary roles (see Figure 3b) and faster at rejecting both ordinary favorable and extraordinary unfavorable roles (see Figure 5b) in the second session (i.e., where the effect of the drug took place) than those taking the antipsychotic-placebo. This suggests that a single, low-dose of olanzapine has an effect on the degree to which individuals engage in social roles, which likely depends on how naturally rewarding social roles appear to participants (Krach et al., 2010). Furthermore, an individual's need to belong and be approved by important social groups may influence their desire to engage in social roles (Lery & Allen, 2010). Social exclusion and difficulties in maintaining social interactions may engender conflicting thoughts (Green, 1991), which have been shown to motivate individuals to create or maintain coherent beliefs, attitudes, and behaviors (Green, 1991).

Previous studies have found a relationship between motivational processes and speed of decision-making. A recent study by Avila et al. (2014) found that reaction times were decreased in decision-making tasks when the stimulus predicted significant behavioral

consequences such as reward or punishment. Further evidence has shown that performance speed on incentive-type tasks is modulated by reward expectation in human subjects (Mir et al., 2011). Prior studies have also shed light on the effect of antipsychotics on the speed of performance on decision-making tasks. Veselinović et al. (2012) found that reaction times were decreased in a decision-making task in healthy individuals taking low doses of antipsychotics (aripiprazole, halperidole, or reserpine) as compared to placebo. A study by Wang et al. (2013) showed that moderate doses of olanzapine (vs. placebo) improved processing speeds on two tasks (animal naming and digit symbol coding) in first-episode drug-naïve schizophrenic patients.

Our results revealed that participants on olanzapine became faster from the first to second sessions at accepting ordinary roles and at rejecting extraordinary roles, regardless of favorability, as compared to those on placebo (see Figures 4 & 6). It is possible that the changes in reaction times in the social roles task are due to multiple exposure to the test because of familiarity with stimuli. Developing strategies over time that alter performance might occur either as a task familiarity phenomenon or as a practice-related phenomenon. Participants may also have adopted a more cautious approach in the second session, which may have led to increases in reaction time. Furthermore, the findings from the current study suggest that individuals who were administered olanzapine were slower at accepting all social roles than those who were administered placebo in the first session of the experiment (see Figure 3a), where no drug effect should be observed. While the increases in RTs may be due to higher baseline anxiety levels in the olanzapine (vs. placebo) group, most studies examining the effect of anxiety on RTs have in large part suggested that decreases in RTs are observed with higher

levels of anxiety (Welford, 1980; Panayiatou et al., 2004). However, there is evidence that shows that highly anxious individuals may have found it harder to exert attentional control in decision-making tasks, resulting in slower RTs (Derakshan et al., 2009).

Our findings suggest that olanzapine may influence the pleasure-seeking drive that is associated with accepting or rejecting social roles. A hedonic, sensation-seeking drive is essential for humans to explore unfamiliar stimuli and acquire information to optimize choice behavior, which reduces uncertainty about their social environment (Reed, Mitchell, & Nokes, 1996). Recent studies have shown that humans intrinsically process novel and exciting stimuli as if they were themselves rewarding and pleasurable (Hazy, Frank, & O'Reilly, 2010; Kakade & Dayan, 2002). Participants who quickly accept social roles may be inspired to make decisions that satisfy a need for pleasure and novelty in their lives. Since subjects on olanzapine were slower at accepting extraordinary roles than the antipsychotic-placebo, it is possible that olanzapine made participants less willing to engage in novel choice opportunities. A previous study by Costa et al. (2014) showed that antipsychotics can change sensation seeking behavior during a decision-making task. While olanzapine has a known sedative effect, which could account for the slower reaction times observed in our study, participants taking olanzapine were also faster at rejecting both ordinary favorable and extraordinary unfavorable roles as compared to those on antipsychotic-placebo.

The observed changes in reaction times may also be related to olanzapine's effect on the incentive salience of social roles, which are considered a type of social reward. We suggest that olanzapine may dampen the salience of 'wanted' social roles (i.e., extraordinary), which may result in decreases in reaction times relative to the antipsychotic-placebo. Incentive

salience is frequently triggered by and assigned to a reward-related stimulus, and involves making a stimulus more “wanted” rather than hedonic (i.e., “liking” processes) (Berridge, 2007; Berridge & Robinson, 1998; Robinson & Berridge, 1993). Previous studies have provided support for the link between incentive salience and speed of decision-making, with decreases in reaction times reflecting more incentive salience for social rewards (Avila et al., 2014; Roesch et al., 2004). Since changes in reaction times are related to incentive salience, it may be that the motivational ‘wanting’ for social roles is reflected by the speed at which participants accept or reject social roles.

The effect of olanzapine on the incentive salience of social roles can be explained through the aberrant salience hypothesis (Kapur, 2003), which suggests that psychotic symptoms represent an aberrant state of incentive salience. The central notion of this hypothesis is that elevated levels of mesolimbic dopamine are responsible for the attribution of aberrant salience to stimuli. Furthermore, the aberrant salience hypothesis explains that antipsychotics permit the resolution of psychotic symptoms by reducing the salience of abnormal experiences, which strongly implicates the role of dopamine blockade in the mechanism of action of antipsychotics. While atypical antipsychotics are known to induce blockade of many neurotransmitter systems, there is strong evidence showing that olanzapine occupies approximately 60-90% of D2 receptors at low to moderate doses (Kapur et al., 1999; Nyberg et al., 1999). Atypical antipsychotics such as olanzapine may therefore decrease the aberrant salience associated with extraordinary roles, possibly through D2 receptor blockade.

The time it takes to either accept or reject stimuli in the social roles task may also reflect one's ability to form complex ideas about themselves. Bradford et al. (2015) showed that

individuals had significantly longer reaction times when attributing beliefs to other people as opposed to recognizing and attributing beliefs to oneself using a false-belief task, which allowed for direct comparison between self-oriented and other-oriented belief attribution. This suggests that participants may evaluate social roles in a manner that fits with their beliefs and view of themselves. However, when people do not act in accordance with their attitude or belief, cognitive dissonance may occur (Cooper, 2012; Brehm, 2007). According to cognitive dissonance theory, an inconsistency in the way individuals view themselves may lead to an uncomfortable feeling or state, suggesting that higher levels of dissonance are related to a more severe state of psychological discomfort (Kenworthy et al., 2011). As a result, individuals may be motivated to retrieve an acceptable state experience. This drive to reduce psychologically dissonant cognitions by modifying them to be consistent has been reported in many previous studies (Abelson, 1968; Aronson, 1968; Festinger, 1957).

Cognitive dissonance may have important implications for the formation and maintenance of delusions in individuals with schizophrenia. People who engage in extraordinary social roles (vs. ordinary roles) may believe that there is a large gap between who they are and who they want to be. This large discrepancy is generally present in individuals with persecutory delusions (Braver et al., 2014). Antipsychotics may therefore influence the drive to engage in social roles by reducing psychological dissonance in individuals with divergent and conflicting beliefs. Olanzapine may play a key role in motivating people to preserve an ordinary view of themselves while rejecting an extraordinary view of themselves, which would reduce the gap between how individuals perceive themselves and how they would like to be seen.

Limitations

Several limitations should be noted for the current study. First, acute administration of 2.5 mg of olanzapine may not significantly influence social role acceptance and reaction times. Future studies should examine the dose-response relationship of olanzapine on the drive to engage in extraordinary social roles. Second, olanzapine blood levels were not taken post drug administration, thus, important pharmacokinetic factors (e.g. concentration) could not be assessed. Third, the effect of olanzapine was assessed in healthy individuals with no psychotic symptoms. Patient populations could be used in future studies to investigate the effect of antipsychotics on their drive to engage in extraordinary social roles.

Conclusion

The current study found that a single, minimal dose of olanzapine modulates the speed at which participants accept or reject extraordinary social roles as compared to an antipsychotic-placebo. This may reflect the effect of the antipsychotic on an individual's desire to engage in extraordinary social roles. The drive to engage in extraordinary social roles may therefore represent a novel motivational construct that could be used to assess the effect of antipsychotics in individuals with psychosis. Examining the drive to engage in social roles in patient populations may also shed light on motivational processes that relate to the formation or maintenance of social interactions, which can improve a patient's sense of purpose and overall functional status. Future studies are needed to determine the effect of long-term antipsychotic use on the drive to play social roles in patient populations. Dose-response antipsychotic studies should also examine the relationship between the pharmacological effect of antipsychotic drugs and the drive to play social roles.

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Appendix

Social Roles and their Characteristics

		Mean ratings			
Stimulus number	Social Role Name	Arousal	Valence	Ordinariness	Favorability
1	Jesus	5.67	3.60	7.24	6.22
2	Harry Potter	4.40	3.23	6.73	6.83
3	knight	4.82	3.89	6.00	5.87
4	Buddha	6.35	3.42	6.80	7.17
5	ghostbuster	4.88	4.98	6.53	4.95
6	samurai	4.93	4.81	6.58	5.83
7	Peter Pan	5.35	3.34	6.97	6.70
8	Superman	4.41	2.81	7.43	7.34
9	fairy	4.97	3.12	6.77	6.78
10	Hindu God	5.74	4.43	6.97	5.82
11	prophet	5.09	4.26	7.12	6.10
12	Zeus	4.84	4.06	7.26	5.86
13	Einstein	4.72	2.34	8.00	7.84
14	mind reader	5.37	5.29	6.59	4.56
15	medieval king	4.57	4.93	5.81	5.06
16	God	4.96	3.90	8.22	5.89
17	mermaid	4.47	3.28	7.48	5.72
18	Joan of Arc	5.09	4.35	6.82	5.97
19	angel	5.30	3.14	7.45	7.23
20	elf	5.56	3.55	7.20	5.96
21	Gandhi	5.52	2.35	7.08	7.45
22	Noah	5.89	4.18	6.92	6.12
23	Napoleon	5.19	5.47	6.57	4.76
24	Robin Hood	4.63	2.76	6.34	6.61
25	Dalai Llama	6.25	2.71	7.01	7.07
26	Shakespeare	5.18	2.96	6.76	7.20
27	Hercules	4.25	3.42	7.21	6.87
28	Ironman	4.08	3.66	6.88	6.69
29	Santa Claus	5.89	2.74	6.87	6.85
30	Sigmund Freud	5.13	4.55	6.20	5.50
31	Batman	4.04	3.63	7.38	6.96
32	Brad Pitt	4.95	3.76	5.28	6.16
33	Angelina Jolie	4.92	3.69	5.61	5.88
34	Stephen Hawking	5.28	3.20	6.90	7.47

35	Madonna	5.05	4.10	5.93	5.79
36	Olympic athlete	4.35	3.33	6.38	7.28
37	Barack Obama	4.62	4.10	5.73	6.60
38	Bill Gates	5.58	3.89	6.77	6.21
39	Hillary Clinton	5.12	4.36	5.39	5.83
40	Moses	5.32	4.12	6.78	6.44
41	Pokémon trainer	5.27	3.99	6.35	5.74
42	Oprah Winfrey	5.67	4.26	5.79	5.84
43	Aladdin	5.11	3.13	6.34	6.21
44	Bono U2	4.97	4.21	5.58	5.89
45	Winston Churchill	5.49	4.37	5.98	6.18
46	Jay-Z	5.47	4.39	5.37	5.86
47	Kate Middleton	5.99	3.59	5.35	6.36
48	Prince William	5.88	4.16	5.18	5.58
49	Serena Williams	4.99	3.81	6.30	6.34
50	Queen Elizabeth II	5.99	4.08	5.89	5.54
51	Steve Jobs	5.35	3.93	6.73	6.86
52	Pierre Trudeau	5.60	4.46	5.94	5.67
53	Bob Marley	5.79	2.95	6.15	6.96
54	Spiderman	4.39	3.23	7.67	7.12
55	Che Guevara	4.38	4.60	6.17	5.81
56	Mark Zuckerberg	5.58	4.59	5.95	5.68
57	Charles Darwin	4.94	3.29	6.51	7.01
58	Gulliver	5.43	4.48	5.71	5.72
59	Cinderella	5.58	3.13	6.35	6.50
60	Marilyn Monroe	5.00	3.46	6.06	6.22
61	Princess Diana	5.62	3.38	5.61	6.18
62	Nelson Mandela	4.73	2.44	6.68	7.55
63	Cristiano Ronaldo	4.76	3.56	6.01	6.56
64	Michael Phelps	4.72	3.86	6.62	6.45
65	Zorro	4.99	3.97	6.65	6.26
66	Salvador Dali	4.73	3.61	6.32	6.46
67	Cupid	5.12	3.63	6.85	6.28
68	Bugs Bunny	5.14	2.75	6.16	6.75
69	Uncle Sam	5.75	5.35	5.18	4.66
70	wizard	4.28	4.10	7.29	6.30
71	Three Wise Men	5.96	4.12	5.72	5.98
72	Pied Piper	6.03	4.31	5.72	5.40
73	army general	5.13	5.54	5.26	4.82
74	FBI agent	4.41	5.11	6.03	5.56
75	sultan	5.61	4.85	5.79	5.43

76	ninja	4.51	4.70	6.62	5.59
77	Native Indian	5.81	3.88	4.77	6.25
78	tightrope walker	4.65	4.42	6.20	5.43
79	Pharaoh	5.14	4.91	6.85	5.30
80	satyr	5.24	5.03	6.10	5.10
81	faun	5.98	3.82	5.35	6.06
82	leprechaun	4.81	4.50	7.07	5.47
83	psychic	4.67	5.69	5.65	4.16
84	Alice in Wonderland	5.07	3.50	6.51	6.37
85	caveman	5.14	5.57	4.91	4.26
86	Invisible Man	4.89	4.77	7.81	5.16
87	werewolf	4.08	6.67	6.71	3.32
88	evil wizard	4.43	7.26	7.02	2.98
89	alien	4.29	6.02	7.18	4.61
90	centaur	4.93	4.50	6.88	5.54
91	Elephant Man	4.68	5.61	6.54	4.10
92	Frankenstein	4.43	6.18	6.86	3.95
93	Hades	4.39	6.75	6.60	3.42
94	Devil	4.11	8.18	6.94	2.58
95	mummy	4.60	5.49	6.40	5.04
96	hunchback	5.48	6.17	5.41	4.04
97	Captain Hook	4.95	5.34	6.00	4.42
98	slave	3.91	8.27	5.33	1.53
99	dwarf	6.17	4.55	5.69	4.76
100	ghost	3.98	6.62	7.20	3.33
101	Dr. Jekyll	5.45	5.63	6.08	4.63
102	evil clown	3.96	7.32	5.65	2.81
103	jester	4.98	4.37	5.22	5.63
104	vampire	4.07	6.80	7.48	2.92
105	Cyclops	4.59	6.39	7.00	4.18
106	The Joker	4.12	5.90	6.62	4.13
107	Medusa	4.36	6.77	6.87	3.27
108	Hitler	3.11	8.53	7.16	1.62
109	alien abductee	3.65	6.46	8.47	3.42
110	gladiator	4.09	5.86	6.33	4.99
111	Grim Reaper	4.36	6.66	6.24	2.91
112	cyborg	4.98	4.99	5.90	4.90
113	zombie	3.72	7.14	7.84	2.84
114	pirate	4.61	6.05	5.68	3.65
115	Darth Vader	4.83	6.37	6.35	3.87
116	witch	4.79	6.97	7.14	3.20

117	Green Goblin	4.47	6.26	6.72	3.71
118	leper	5.03	6.52	5.66	3.62
119	Kim Jong Il	4.08	6.94	5.92	3.22
120	Joseph Stalin	4.10	6.88	6.35	3.48
121	Bin Laden	4.00	8.63	6.10	1.54
122	Muammar Gaddafi	4.37	6.62	5.63	3.45
123	Hannibal Lecter	4.63	7.05	6.19	2.82
124	Cruella Devil	4.32	6.92	5.94	3.57
125	Sumo Wrestler	5.05	4.43	5.45	5.47
126	Sword Swallower	4.15	6.26	6.92	3.67
127	ogre	4.98	6.56	7.55	3.93
128	WWF Wrestler	4.23	5.33	5.54	4.45
129	muscleman	4.62	4.86	4.49	5.10
130	conjoined twins	4.59	5.78	6.96	4.11
131	contortionist	4.81	4.71	5.40	5.41
132	fire-eater	4.17	5.75	6.61	4.55
133	genocide victim	3.36	8.49	5.74	1.18
134	Ted Bundy	4.34	6.42	5.58	3.55
135	evil stepmother	3.81	8.29	5.17	2.13
136	sea witch	4.69	6.52	7.02	3.75
137	beekeeper	5.89	4.54	5.04	5.67
138	garbage man	6.50	5.66	2.84	5.04
139	KKK member	3.13	7.91	6.11	2.54
140	terrorist	3.09	8.86	6.21	1.38
141	cripple	5.10	7.04	4.52	3.30
142	tattooed man	5.21	4.90	3.77	4.40
143	weed smoker	5.80	5.19	3.05	4.33
144	convict	4.35	7.37	4.72	2.50
145	abusive guard	3.64	7.70	4.59	3.06
146	poor child	4.33	8.12	3.31	2.65
147	homeless person	4.79	7.50	3.75	2.87
148	burglar	4.04	7.28	4.94	2.88
149	rioter	4.32	6.21	4.38	3.70
150	rebels	4.54	5.58	5.00	4.76
151	child soldier	3.23	8.83	6.08	1.11
152	amputee	4.87	6.35	5.58	3.64
153	anorexic	4.20	7.75	4.60	2.64
154	goth	5.67	6.11	4.60	3.76
155	dictator	4.38	7.32	5.73	2.62
156	domestically abused	2.71	8.96	4.46	1.52
157	computer nerd	5.75	4.64	4.31	5.84

158	protestor	4.19	5.28	4.45	5.09
159	obese person	5.25	6.89	3.35	2.96
160	starving child	4.07	8.33	4.85	1.54
161	pregnant teen	4.95	6.60	4.25	2.92
162	suicidal person	2.98	7.60	5.28	1.65
163	carjacker	4.91	7.63	4.37	2.61
164	neo-Nazi	3.59	7.98	5.77	2.06
165	abused man	4.17	7.86	4.97	2.09
166	executioner	4.23	7.49	5.70	3.18
167	gangster	4.32	7.20	4.76	2.83
168	self-immolator	4.18	6.08	5.73	3.92
169	cleaning man	6.77	4.22	3.15	5.70
170	emo	5.44	6.68	4.88	3.28
171	grieving person	5.62	7.46	3.71	3.37
172	drunk driver	3.52	8.44	4.13	1.56
173	bullfighter	4.12	6.23	5.76	4.13
174	burn victim	3.64	8.47	5.23	1.75
175	Muslim extremists	3.62	7.44	5.80	2.55
176	pickpocket	4.50	7.65	4.29	2.72
177	punk	5.20	5.61	4.07	4.38
178	abused child	3.50	8.22	5.26	2.00
179	prostitute	4.69	6.64	4.26	3.24
180	losing boxer	4.89	6.19	4.14	3.78
181	heroin user	4.04	8.36	4.75	1.96
182	smoker	5.82	6.92	2.80	2.77
183	shoplifter	5.01	7.13	3.70	2.95
184	alcoholic	4.73	7.45	3.91	2.86
185	attacked woman	3.34	8.76	4.76	1.73
186	terminal patient	4.66	7.54	4.71	2.56
187	executed person	3.96	7.56	5.40	2.75
188	gang member	3.94	7.60	4.12	2.60
189	domestic abuser	2.84	8.59	4.40	1.14
190	gambler	5.40	6.33	3.39	3.23
191	transvestite	4.78	4.72	5.25	4.90
192	pubescent teen	5.18	6.25	2.75	4.10
193	blind	5.50	6.89	5.23	3.20
194	bully	3.88	7.65	3.27	2.17
195	child worker	5.18	6.61	4.42	3.34
196	murder victim	3.33	8.48	5.64	1.79
197	vandal	4.56	6.94	4.41	3.39
198	chauffeur	6.72	4.20	3.36	5.60

199	hillbilly	5.88	5.71	3.87	4.22
200	plowman	6.23	4.90	3.47	5.29
201	nomad	5.82	4.57	5.04	5.16
202	window washer	6.34	5.22	2.77	5.22
203	rapper	4.57	4.48	4.85	5.41
204	showgirl	4.67	4.53	4.41	4.89
205	plumber	6.41	4.54	3.62	5.75
206	old man	6.30	4.33	2.86	5.98
207	sick person	5.56	7.74	2.62	2.99
208	snake charmer	4.74	4.76	6.16	4.90
209	miner	5.39	5.90	4.69	4.56
210	lazy employee	6.42	6.79	2.52	3.10
211	sunburned person	5.11	6.70	3.46	3.57
212	shooter	3.91	7.48	5.29	2.96
213	armed robber	3.54	8.05	5.16	1.71
214	landmine detector	4.67	5.38	5.67	5.38
215	bandit	4.58	6.66	5.01	3.09
216	butcher	5.45	5.41	3.66	5.42
217	guitar player	5.82	2.69	4.40	6.97
218	teacher	5.84	3.10	4.15	6.94
219	skateboarder	5.55	4.35	4.24	5.25
220	student	5.79	2.94	2.29	7.07
221	public speaker	5.08	4.34	4.23	6.11
222	crane operator	5.97	5.03	4.17	5.41
223	working out	4.35	3.10	3.29	7.24
224	businessman	5.92	4.49	3.42	5.60
225	doctor	5.45	2.90	5.28	7.71
226	ballet dancer	5.86	3.21	5.40	6.60
227	shopper	6.13	4.43	1.79	5.20
228	pilot	5.29	3.24	5.63	6.73
229	fireman	4.59	3.47	5.57	7.42
230	chef	5.25	3.25	4.48	7.20
231	barista	6.15	3.51	3.79	5.58
232	librarian	7.24	3.36	3.33	6.75
233	gas pumper	7.51	5.50	2.43	4.60
234	computer gamer	5.86	5.11	3.84	5.12
235	astronaut	4.38	2.71	6.92	7.57
236	gardener	6.66	3.18	3.02	7.09
237	model	5.44	3.98	4.50	5.27
238	chess player	6.42	3.51	4.55	6.13
239	lab researcher	5.90	4.15	4.50	6.67

240	hairdresser	6.47	3.97	3.38	5.79
241	camper	6.36	3.75	3.24	6.02
242	golfer	6.59	4.15	3.52	5.81
243	bicyclist	5.84	3.02	3.83	7.06
244	veterinarian	5.79	3.29	4.63	7.05
245	dentist	5.95	4.40	4.14	6.22
246	sushi chef	5.72	3.12	4.65	6.53
247	hockey player	4.61	3.66	4.82	6.19
248	photographer	5.95	3.19	3.85	7.00
249	goalkeeper	5.96	4.19	4.22	6.58
250	yoga practitioner	6.56	2.96	4.10	6.52
251	music listener	6.43	2.19	3.01	7.32
252	toddler	5.21	2.84	2.56	6.64
253	driving	5.72	4.18	2.76	5.84
254	swimmer	5.63	3.42	4.35	6.43
255	celebrator	5.08	3.27	3.46	6.46
256	newlywed	4.72	3.16	3.80	6.80
257	schoolchild	6.08	3.35	2.70	6.63
258	in love	3.47	2.28	4.85	7.28
259	mother	5.42	2.30	4.45	8.45
260	lawyer	5.59	4.58	4.96	6.12
261	newspaper reader	6.50	3.48	2.93	6.47
262	construction worker	6.13	4.98	3.30	5.35
263	mountain climber	4.38	3.44	5.65	6.24
264	judo wrestler	5.08	4.37	5.31	5.62
265	baker	6.58	2.66	3.21	6.92
266	grandmother	6.14	2.20	3.99	7.79
267	grocery shopper	6.41	4.19	1.76	5.91
268	computer engineer	5.77	4.25	4.33	6.45
269	ice-skating	5.47	2.98	3.84	6.30
270	pregnant woman	4.89	3.69	3.61	6.38
271	motorcyclist	4.77	4.45	3.72	5.73
272	praying person	6.34	4.07	3.60	5.65
273	professor	5.34	3.49	5.02	6.84
274	football player	5.38	4.36	4.66	5.62
275	botanist	6.25	3.17	4.64	6.57
276	optometrist	6.56	3.99	3.92	6.00
277	disc jockey	4.54	3.91	4.33	6.04
278	singer	5.24	3.36	5.29	6.49
279	cheerleader	4.96	4.54	4.04	5.09
280	weightlifter	5.34	4.62	4.90	5.79

281	sailor	5.51	3.67	4.91	6.28
282	bartender	5.57	4.13	3.98	6.07
283	police officer	4.84	5.21	4.01	5.71
284	soldier	4.30	5.43	5.10	5.13
285	fisherman	6.37	4.17	3.84	6.16
286	trail biker	5.26	4.34	4.45	5.61
287	canoeist	6.40	3.52	4.12	6.24
288	scientist	5.41	3.81	5.61	7.05
289	marathon runner	5.46	3.79	5.60	6.72
290	tennis player	5.21	3.38	4.39	6.69
291	horse rider	5.36	3.33	4.18	6.28
292	flight hostess	5.80	3.64	3.49	6.55
293	politician	4.93	5.87	4.03	4.47
294	baseball player	5.83	4.43	4.65	5.84
295	gymnast	5.29	3.36	5.81	6.31
296	newborn baby	5.44	2.77	4.11	7.11
297	father	5.83	2.38	3.86	8.01
298	dog owner	6.10	3.13	2.51	6.51
299	waterpolo player	5.68	3.58	4.42	5.81
300	lacrosse player	5.20	4.48	4.41	5.27
301	painter	6.24	3.59	3.83	6.55
302	secretary	6.71	4.20	2.85	5.85
303	trumpeter	5.95	3.53	4.35	6.05
304	club dancer	5.03	4.39	3.37	4.87
305	security guard	5.70	4.97	3.46	5.59
306	skier	5.57	3.80	4.09	5.93
307	rower	5.80	4.00	4.22	5.90
308	boxer	4.60	5.03	4.79	5.12
309	bowler	6.45	4.00	3.52	5.55
310	farmer	6.14	3.57	4.16	6.95
311	violinist	6.20	2.69	5.03	6.85
312	basketball player	4.97	3.89	4.83	5.56
313	pole-vaulter	5.38	4.23	5.84	5.89
314	parachutist	4.37	4.29	6.06	5.75
315	motorcycle racer	4.61	4.23	5.17	5.28
316	lover	3.84	1.75	4.24	8.06
317	curler	6.48	4.00	3.95	5.45
318	jet skier	5.00	3.84	4.62	6.17
319	judge	5.49	5.25	4.90	5.97
320	diver	4.94	3.98	5.03	6.07
321	surfer	4.92	3.50	4.16	6.04

322	trophy winner	4.42	3.65	5.09	6.21
323	rafter	5.10	4.09	4.64	5.73
324	birthday girl	5.21	2.81	3.08	6.54
325	rock climber	4.49	3.59	5.33	5.88
326	zookeeper	5.87	3.64	4.73	6.13
327	sports fan	5.32	4.49	2.68	5.52
328	pharmacist	6.38	3.64	3.95	6.43
329	concertgoer	5.29	3.33	3.27	6.19
330	massage client	6.48	3.65	3.38	5.85
331	moviegoer	6.76	3.34	2.08	6.47
332	carpenter	6.35	3.81	3.68	6.29
333	restaurant customer	6.57	3.98	2.47	5.76
334	dancer	4.79	3.18	4.68	6.99
335	nature lover	5.90	2.78	4.06	7.57
336	piano teacher	6.41	3.14	4.35	6.74
337	jogger	5.80	3.35	3.25	6.20
338	sun tanning	5.72	4.98	2.98	3.95
339	piano student	6.83	3.30	4.10	6.83
340	snowboarder	5.16	4.28	4.25	6.11
341	texter	6.57	4.83	2.24	5.33
342	roller-skater	5.50	3.83	3.57	5.70
343	tree planter	5.67	3.08	4.00	6.96
344	mechanic	5.83	4.33	3.53	5.74
345	meditator	6.66	3.17	4.34	6.54
346	pub customer	5.56	4.47	2.58	5.58
347	celebrating Christmas	4.07	2.88	3.43	7.15
348	office worker	6.63	5.09	2.38	5.52
349	pool player	6.21	3.75	3.31	5.87
350	dog walker	6.87	3.20	2.60	6.47
351	sprinter	4.90	3.37	5.46	6.60
352	surgeon	5.36	3.47	5.74	7.02
353	jeweler	6.31	3.82	3.76	5.71
354	tourist	5.69	4.05	3.44	5.81
355	clown	5.39	5.25	4.82	4.76
356	shepherd	6.18	3.78	4.10	5.97
357	graduate	5.33	2.79	4.13	7.45
358	stockholder	5.46	4.93	3.61	5.43
359	detective	4.99	3.76	5.55	6.49
360	lawnmower	6.65	4.78	3.18	5.22
361	pilgrim	5.87	4.35	4.91	6.03
362	archer	5.13	3.81	5.28	5.78

363	paramedic	5.04	3.13	5.25	6.88
364	polo player	5.95	4.13	4.62	6.05
365	TV watcher	6.57	4.27	1.55	5.01
366	architect	5.99	2.86	4.96	7.02
367	forest ranger	5.38	3.54	4.68	6.31
368	cowboy	5.36	4.11	4.72	5.86
369	personal trainer	5.56	3.66	3.68	6.38
370	journalist	5.23	3.73	4.18	6.20
371	hiker	5.49	3.35	4.10	6.39
372	crossing guard	6.44	4.39	3.23	6.32
373	butterfly catcher	6.03	4.07	4.76	5.31
374	presenter	6.27	4.19	3.98	6.07
375	chemist	5.78	4.04	4.69	6.29
376	radio show host	5.48	3.65	4.39	6.37
377	nun	6.55	4.55	4.73	5.39
378	priest	6.03	5.11	5.16	4.91
379	social worker	5.98	3.33	4.69	6.90
380	astronomer	5.30	3.37	5.58	6.78
381	aircraft controller	5.91	3.87	4.99	6.85
382	archeologist	5.33	3.19	5.27	6.59
383	bus driver	6.86	4.51	3.08	5.85
384	train conductor	6.37	4.28	3.36	5.77
385	wine taster	6.26	3.53	3.91	6.42
386	manicurist	6.41	4.77	3.31	5.33
387	Nobel Peace Prize	4.20	1.73	6.98	7.87
388	movie director	4.69	3.05	5.67	6.85
389	traveler	5.00	2.98	4.23	6.92
390	storyteller	6.28	2.76	3.88	7.23
391	nurse	5.27	3.01	4.47	7.39
392	voter	6.14	3.74	2.85	6.62
393	writer	5.88	3.06	4.84	7.39
394	playing child	5.70	2.14	2.83	7.54
395	lifeguard	5.57	2.71	4.49	7.53
396	griller	6.08	4.38	3.58	5.41
397	bodysurfer	5.56	4.15	4.53	5.31
398	blogger	6.39	4.29	3.29	5.10
399	playing paintball	3.94	4.90	3.76	5.09
400	dinner host	6.16	3.15	3.23	6.19
401	X-ray technician	6.26	3.99	4.28	6.16

Note: Mean ratings computed from the scores of 42 independent evaluators on a 9-point Likert scale

Information and Consent Form for the Subject

Title of Research Study
Effects of Atypical Antipsychotics on an Electrophysiological Correlate of Delusion Proneness

Sponsorship
NARSAD: The Mental Health Research Association

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Prior to accepting to participate in this study, it is important to have read and understood the explanation of the proposed protocol. This form describes the goals, tests, benefits, risks, discomforts, and precautions that this study entails. It also describes your right to quit the study at any time. Any questions that you have will be addressed prior to your decision to participate in this medical research project.

Study Objectives
It is known that antipsychotic medications function to improve a number of psychotic symptoms. The exact mechanisms of this function remain incompletely understood. One possibility is that these medications facilitate, directly or indirectly, the mechanisms that allow us to understand unexpected information. By doing so, these medications could help patients with inaccurate beliefs (eg. delusions) to change their minds. Interestingly, a component of the electrical activity of the brain, termed the N400, reflects the efforts automatically deployed by the brain to understand unexpected information. As predicted, this component is smaller in patients with severe inaccurate beliefs, suggesting that their brains deploy less effort to process unexpected information. A recent study has demonstrated that even in healthy individuals, a smaller N400 accompanies the tendency towards delusional beliefs. The main goal of this study is to examine

the manner in which a low dose of an antipsychotic medication, olanzapine, influences this N400 measure and thus affects this tendency. Moreover, it includes a number of other tests that will be used to make sure that we are actually focusing on the tendency towards delusional belief rather than on another tendency.

Description of your participation in the study

Your participation in this study would involve one session of tests lasting 3 to 4 hours and taking place at the Douglas Hospital. It consists first of questionnaires that you will be requested to fill out. They include questions that aim to acquire general information such as your age, education, medical problems as well as questions related to personality characteristics, beliefs, and psychiatric symptoms. After filling the questionnaires having you will be sited at a computer terminal. A cap that includes small metal disks that capture the electrical activity of your brain will be placed on your head. Once this will be done, you will be given 2.5 milligrams of an active medication, olanzapine. You will then have to decide if the words appearing on the screen are names of animals or not. Then, names of social roles (ex: ''parent'') will appear and you will have to decide whether or not you would consider playing that role in your life. After a lunch break, you will have to make these decisions again (but this time, the medication will have had time to have its effect). The part of the experiment where you wear the cap is about 2 hours long.
A follow-up debriefing session will take place at the end of the experiment.

Risks and Discomforts

The procedure is not painful but may be slightly uncomfortable. The only risk involved in recording the electrical activity is the rare occurrence (1% of cases) of a local allergic reaction (rash) to the adhesive on the electrodes – this carries no danger to your health. If you experience such a reaction, the recording will be stopped.

Olanzapine is a drug that is widely used in clinical practice by thousands of patients and is approved by the Food and Drug Administration. The 2.5 milligram dose you will be taking is almost the lowest dose that is given to adults. There are several possible side-effects associated with this medication, although it is extremely unlikely that they could occur at the dose involved in this study. Also, note that all studies that examined side-effects looked at repeated administrations of the drug, rather than at single dose.

The adverse effects of this dose of olanzapine that you might experience are somnolence, dry mouth, light-headedness, constipation, increased appetite, stomach upset (nausea/indigestion), restlessness, sense of muscle weakness (with no actual loss of strength), insomnia, and muscle stiffness. However, mild drowsiness is the only adverse effect that is likely to occur.

Potential Benefits

We do not foresee any specific benefits for the subjects participating in this study. If our procedure uncovers something that suggests the possibility of a medical or psychiatric problem that requires further investigation, you will be informed and, if you wish, we will refer you to the appropriate service.

Voluntary Participation / Withdrawing from Study
You will be able to withdraw from the study at any point, without explanation, and without any negative consequences.

Confidentiality
The data obtained during this study will be analysed with the sole purpose of carrying out the stated research. Your information will be kept strictly confidential, and access to this information will be restricted to those directly involved in the study. All data pertaining to your file will be coded by number rather than by your name. None of the data pertaining to you will be transferred anywhere, unless you provide permission in writing.

Compensation for your participation
You will be compensated with $15/hour. If you decide to end your participation in the study before having finished the experiment, you will receive the monetary amount that corresponds to the activities in which you participated prior to stopping. You should expect to receive at least $45 for your participation.

Consent

I, (name)_____ accept to participate in the above-mentioned research study conducted by Dr. J. Bruno Debruille.

My participation in this research is voluntary.
I hereby declare that I have been explained and I understand the procedure and the reasons for this study.

Signature: _____ Date: _____

If you have any questions regarding the research or the procedure, you can contact: Dr. J. Bruno Debruille, at 514-761-6131, ext. 3410,. If you have any questions about your rights as a patient, or as a research subject, you can phone the Douglas Hospital Ombudsman at 761-6131, # 3287.