Social approach and avoidance behaviour for negative emotions is modulated by endogenous oxytocin and paranoia in schizophrenia

Elliot C. Brown [a,*], Cumhur Tas [b,c], Duygu Kuzu [d], Aysen Esen-Danaci [e], Karin Roelofs [f], Martin Brüne [c]

[a] Maryland Psychiatric Research Centre, University of Maryland School of Medicine, Baltimore, MD, USA
[b] Department of Psychology, Üsküdar University, Istanbul, Turkey
[c] Research Department of Cognitive Neuropsychiatry and Psychiatric Preventive Medicine, LWL University Hospital, Ruhr University Bochum, Germany
[d] Department of Psychology, Arel University, Istanbul, Turkey
[e] Department of Psychiatry, Celal Bayar University, Manisa, Turkey
[f] Behavioural Science Institute and Donders Institute for Brain, Cognition and Behaviour, Radboud University Nijmegen, The Netherlands

ARTICLE INFO

ABSTRACT

Patients with schizophrenia suffer from dysfunctional social behaviour. Social approach and avoidance (AA) has been associated with motor responses, as the affective valence and gaze direction of facial stimuli can bias push and pull motor tendencies. The aim of this study was to investigate the role of endogenous oxytocin in social AA behaviour in schizophrenia. Basal plasma oxytocin levels were collected from 28 patients who were then given a joystick-based Approach-Avoidance Task (AAT). Reaction times were recorded and AAT effect scores calculated for responses to happy and angry faces, which either had direct or averted gaze. Individual differences in basal oxytocin had a significant relationship with AAT responses, and patients with higher levels of oxytocin tended to avoid angry faces more. Furthermore, greater avoidance of angry faces was correlated with more severe psychotic (positive and general) symptoms and greater paranoia. This suggests that the endogenous effects of oxytocin may be specific to the interpretation of negative threatening emotions in schizophrenia patients, and also provides evidence that psychotic symptoms and paranoia can impact on social AA behaviour by heightening threat avoidance.

© 2014 Elsevier Ireland Ltd. All rights reserved.

1. Introduction

The term "schizophrenia" refers to a group of mental disorders characterised primarily by negative and positive psychotic symptoms but are also marked with impairments in social behaviour. With regard to the motivational drives underlying social interaction, it has been hypothesised that many signs and symptoms associated with schizophrenia can be understood in the context of dysregulated social approach and avoidance (i.e. fight–flight) behaviour (Brüne, 2008), an interpretation that has received at least partial support through studies using ethological observation of patients' nonverbal behaviour (Annen et al., 2012; Geerts and Brune, 2009). Paranoia stemming from persecutory delusions is also a common feature in schizophrenia, which has been related to impairments in social perception, leading to misinterpretations of social stimuli and an increased sensitivity to social threat leading to greater social avoidance (Bentall et al., 1995; 2001). More recently, much work has focused on the underlying neurobiological factors related to dysfunctional social behaviour, with one popular chemical of interest being oxytocin. However, little work has been done to investigate social approach and avoidance behaviours in schizophrenia, nor how this may be affected by underlying neurobiological or psychopathological features of the illness.

Social approach and avoidance behaviour is directly related to the emotional valence of social stimuli (Roelofs et al., 2005). For example, approach and avoidance (AA) movements can create attitudinal biases, in which arm flexion induces more positive affective ratings of valenced stimuli, whereas arm extension induces more negative affective ratings (Cacioppo et al., 1993; Centerbar and Clore, 2006). A joystick-based task has been previously used to explore motor responses to social approach and avoidance behaviour (AAT; Rinck and Becker, 2007), whereby subjects either pull the joystick towards themselves, or push it away when presented positive or negative emotional faces. By comparing reaction times for different emotional faces, people tend to have faster congruent responses (i.e. pull (/approach) happy and push (/avoid) angry) than incongruent responses (i.e. pull-angry and push-happy). This low-level difference

* Corresponding author at: Maryland Psychiatric Research Centre (MPRC), Department of Psychiatry, University of Maryland School of Medicine, 55 Wade Avenue, P.O. Box 21247, Baltimore, MD 21228, USA.
E-mail address: elliot.c.brown@gmail.com (E.C. Brown).

seen in motor responses is thought to reflect associations between social AA behaviour and the processing of emotional valence.

Different pathological conditions, particularly those with impairments in social behaviour, have been shown to exhibit abnormalities in approach and avoidance responses on the AAT. For example, socially anxious individuals have a greater tendency to avoid angry faces (Heuer et al., 2007) when compared to socially non-anxious participants. In contrast, individuals with high levels of psychopathy demonstrate a lack of avoidance to angry faces (Louise von Borries et al., 2012). Gaze direction is an important factor in regulating social interaction and has also been found to modulate responses on the AAT, with direct gaze inducing a greater tendency to avoid angry faces in socially anxious people as compared to averted gaze (Roelofs et al., 2010), as those faces more directly communicate threat towards the perceiver (Adams and Kleck., 2005). In the case of schizophrenia, there is evidence to suggest that paranoid patients misinterpret gaze direction, which may lead to the perpetuation of persecutory delusions and feelings of paranoia (Rosse et al., 1994). Paranoid patients have also been found to take longer to make judgements about gaze direction (Franck et al., 2002), make more errors in gaze discrimination (Russell et al., 2001) and also misinterpret averted gaze as being directed towards them (Hooker and Park, 2005).

The neuropeptide oxytocin has been extensively investigated in terms of its role in social behaviour (McCall and Singer, 2012), and as a potential therapeutic tool for enhancing prosocial behaviour (e.g. Yamasue et al., 2012). There have been some suggestions that oxytocin can enhance the salience of social cues, increasing the affective valence, and thus also the attention towards social stimuli (Averbeck, 2010; Tabak, 2013), which is also indicated by an increase in amygdala activity (Gamer et al., 2010). Studies have found that oxytocin also modulates tendencies for social AA with one example showing that the administration of intranasal oxytocin in healthy people can induce a decrease in aversion specifically to angry faces (Evans et al., 2010). Kemp and Guastella (2010) suggest that oxytocin can increase approach-related behaviour and decrease withdrawal. Indeed a recent study showed that oxytocin administration induces a shift from threat avoidance to threat approach on the AAT (Radke et al., 2013).

People with schizophrenia seem to have a general tendency for avoiding negative social situations (Liddle, 1987). In particular, pathological threat beliefs in schizophrenia have been suggested to play a central role in the initiation and conditioning of avoidant mechanisms (Moutoussis et al., 2007), which are likely to be inclusive of social avoidance behaviours. Evans et al. (2011) presented participants with happy and angry faces in an associative learning task and found that people with schizophrenia, when compared to healthy controls, had a greater aversion to angry faces, even when choosing an angry face led to positive feedback. However, the possible implications of the variation in psychotic paranoid thoughts on these findings were not taken into account in that study. Furthermore, some recent studies have explored endogenous levels of oxytocin in schizophrenia, demonstrating negative correlations between plasma/central oxytocin and negative symptoms such as social and emotional withdrawal (Rubin et al. 2010; Sasayama et al., 2012). Most research investigating the effects of oxytocin in schizophrenia have focused on social cognitive domains but have not addressed the effect on social AA behaviours.

The overall aim of this study was to investigate social AA responses in a group of patients with schizophrenia, and how gaze direction impacted on these responses. More specifically, we tested whether endogenous oxytocin levels would have a relationship with social AA responses for positive and negative emotions. We also explored the possible effects of symptom severity and

paranoia on social AA. It was hypothesised that basal oxytocin, symptom severity and paranoia in schizophrenia would have an influence on the AA responses to negative and positive emotional social stimuli, and that differences in eye gaze may also play a role in this effect. Here we use schizophrenia as a model disorder to investigate the role of oxytocin and pathological threat beliefs (i.e. paranoia) in social behaviour, in terms of social AA. Due to the potential impairments in emotion recognition known in schizophrenia (Mandal et al., 1998), we also controlled for facial emotion recognition abilities.

2. Methods

2.1. Participants

Twenty-eight right-handed participants (15 male) diagnosed with schizophrenia were recruited from the Psychosis Unit of the Psychiatry Department at Celal Bayar Hospital University, with a mean age of 33.62 years (S.D.=8.61) and 11.56 years (S.D.=3.86) of education. Diagnosis was confirmed with the DSM-IV SCID and all participants were outpatients and considered as clinically stable (i.e., there was no psychiatric hospitalization in the past 6 months, and antipsychotic medication had been stable for the past 6 months) and had a mean number of 2.15 (S.D.=1.57) hospitalisations. Mean duration of illness of the group was 12.19 years (S.D.=6.43). Psychotic symptomatology of all participants was assessed with the Positive and Negative Syndrome Scale (PANSS (Kay et al., 1987)). The PANSS is a 30-item semi-structured interview designed to assess five symptom categories associated with schizophrenia: positive symptoms (i.e., hallucinations and delusions), negative symptoms (i.e., avolition and anhedonia), cognitive symptoms (i.e., thought disorder), hostility, and depression. A qualified and PANSS-trained psychiatrist assigned a score from 1 to 7 for each item, with higher scores indicating more severe psychopathology. For the whole group, the PANSS positive mean score was 12.56 (S.D.=3.58), PANSS negative mean was 16.63 (S.D.=5.50) and PANSS general was 27.26 (S.D.=7.98). All patients were taking atypical antipsychotic medication and therefore chlorpromazine equivalents were calculated for all patients to check for medication effects. The group mean chlorpromazine equivalent was 429.63 (S.D.=273.25). Importantly, none of the female participants were taking oral contraception, and no significant differences in basal oxytocin levels were found between male and female patients ($F(1,27)=2.69$, $p=0.114$). The study received ethical approval from the local ethics committee at Celal Bayar University, Manisa, Turkey.

2.2. Tasks

2.2.1. The Approach-Avoidance Task (AAT)

The stimuli used in the AAT task were based on a previous set of photographs of faces used in other AAT tasks (Roelofs et al., 2010), which had been selected from Ekman and Friesen (1976) and Karolinska Institute databases (Lundqvist et al., 1998). All photographs had been cropped to the hairline and were in black and white. Four different male and four female actors were used with half of the faces expressing anger and the other half expressing happiness. The eye gaze of the faces had been modified (Roelofs et al. 2010) resulting in half of the faces having a direct gaze and the other half having an averted gaze. This resulted in a total of 32 different stimuli (8 actors × 2 emotions × 2 gaze directions). The task was structured in four blocks: two experimental blocks, and two practice blocks preceding each experimental block. There were 24 trials in each practice block, making a total of 48 practice trials. Each stimulus was presented thrice in a pseudo-random order in the experimental block making a total of 192 experimental trials, with 96 in each block.

Participants were seated in front of the computer screen and a joystick was fixed to the table between the participant and the screen. The task was self-paced so participants triggered the onset of stimulus presentation by pressing the fire button on the joystick. A blank (black) screen was presented between each trial, and at stimulus onset, pictures appeared in the centre of the screen. In one practice/main block, participants were asked to push the joystick away from themselves when they saw an angry face and pull the joystick towards themselves when they saw a happy face ("congruent" condition). In the other practice/main block, participants were asked to do the opposite and pull the joystick towards themselves whenever an angry face was presented and to push the joystick away from themselves when a happy face was presented ("incongruent" condition). The order of the congruent and incongruent blocks was counterbalanced across participants. When the joystick was pushed during stimulus presentation, the face would shrink, getting smaller and smaller till it disappeared, and when the joystick was pulled, the face would zoom in until it disappeared after the maximum size was reached. Participants were asked to respond as quickly as possible, but also to be as accurate as possible. Initiation response times (RTs) (i.e. the first deviation