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Objective assessment of exploratory behaviour in schizophrenia using wireless motion capture

Ishraq Siddiqui [a,b,*], Gary Remington [a,b,c], Paul J. Fletcher [c,d,e], Aristotle N. Voineskos [a,b,c], Jason W. Fong [a], Sarah Saperia [a], Gagan Fervaha [a,b], Susana Da Silva [a,b], Konstantine K. Zakzanis [f], George Foussias [a,b,c]

[a] Schizophrenia Division and Campbell Family Research Institute, Centre for Addiction and Mental Health, 250 College St., Toronto, Ontario M5T 1R8, Canada
[b] Institute of Medical Science, Faculty of Medicine, University of Toronto, Medical Sciences Building, 1 King's College Circle, Toronto, Ontario M5S 1A8, Canada
[c] Department of Psychiatry, University of Toronto, 250 College St., Toronto, Ontario M5T 1R8, Canada
[d] Preclinical Research and Campbell Family Mental Health Research Institute, Centre for Addiction and Mental Health, 250 College St., Toronto, Ontario M5T 1R8, Canada
[e] Department of Psychology, University of Toronto, Sidney Smith Hall, 100 St. George St., Toronto, Ontario M5S 3G3, Canada
[f] Department of Psychology, University of Toronto Scarborough, 1265 Military Trail, Toronto, Ontario M1C 1A4, Canada

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ABSTRACT

Motivation deficits are a prominent feature of schizophrenia and have substantial consequences for functional outcome. The impact of amotivation on exploratory behaviour has not been extensively assessed by entirely objective means. This study evaluated deficits in exploratory behaviour in an open-field setting using wireless motion capture. Twenty-one stable adult outpatients with schizophrenia and twenty matched healthy controls completed the Novelty Exploration Task, in which participants explored a novel environment containing familiar and uncommon objects. Objective motion data were used to index participants' locomotor activity and tendency for visual and tactile object exploration. Clinical assessments of positive and negative symptoms, apathy, cognition, depression, medication side-effects, and community functioning were also administered. Relationships between task performance and clinical measures were evaluated using Spearman correlations, and group differences were evaluated using multivariate analysis of covariance tests. Although locomotor activity and tactile exploration were similar between the schizophrenia and healthy control groups, schizophrenia participants exhibited reduced visual object exploration ($F(2,35) = 3.40$, $p = 0.045$). Further, schizophrenia participants' geometric pattern of locomotion, visual exploration, and tactile exploration were correlated with overall negative symptoms ($|\rho| = 0.46–0.64$, $p <= 0.039$) and apathy ($|\rho| = 0.49–0.62$, $p <= 0.028$), and both visual and tactile exploration were also correlated with community functioning ($|\rho| = 0.46–0.48$, $p <= 0.043$). The Novelty Exploration Task may be a valuable tool to quantify exploratory behaviour beyond what is captured through standard clinical instruments and human observer ratings. Findings from this initial study suggest that locomotor activity and object interaction tendencies are impacted by motivation, and reveal deficits specifically in visual exploration in schizophrenia.

1. Introduction

Exploratory behaviour consists of actions towards attaining information about the unfamiliar, which may be incentivized by novel stimuli (i.e., novelty exploration) (Barnett and Cowan, 1976), and forms an important aspect of motivated behaviour (Cathomas et al., 2015). Novelty exploration has been linked to motivation by the conceptualization of exploratory animal behaviour as fulfilling an innate "need" for sensory change (Hughes, 1997), and by the common neurobiological substrates of novelty and reward (Bunzeck et al., 2012; Düzel et al., 2010; Krebs et al., 2009).

Amotivation is one of the two negative symptom subdomains of schizophrenia (the other being diminished emotional expression) (Foussias and Remington, 2010; Messinger et al., 2011), and poses a persistent and critical burden on individuals' community functioning (Fervaha et al., 2015; Foussias et al., 2011). Objective task-based investigations have examined how specific aspects of motivation contribute to the disease state (Green et al., 2015; Horan et al., 2015; Reddy et al., 2015; Strauss et al., 2014). However, although exploratory behaviour is routinely evaluated in clinical measures of apathy, and forms one of five apathy subdomains (Cathomas et al., 2015), objective psychometric investigations of exploratory behaviour have been scarce.

* Corresponding author at: Centre for Addiction and Mental Health, 250 College Street, Toronto, ON M5T 1R8, Canada.
E-mail address: ishraq.siddiqui@camh.ca (I. Siddiqui).

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Investigations of exploratory behaviour in schizophrenia have typically been conducted in the context of personality traits (Peritogiannis, 2015), with inconsistent findings of novelty seeking deficits in patients compared to controls (Galindo et al., 2016; Jetha et al., 2013; Ohi et al., 2012). Such novelty seeking traits have not shown a consistent relationship with negative symptoms (Guillem et al., 2002; Hori et al., 2008; Ohi et al., 2012; Smith et al., 2008), beyond what may be accounted for by other personality-associated factors (Ritsner and Susser, 2004). Investigations using objective measures have focused on visual exploration, tracking eye movements as participants view stimuli such as faces (Bortolon et al., 2016; Delerue et al., 2010; Drusch et al., 2014; Streit et al., 1997), objects or figures (Delerue and Boucart, 2013, 2012; Obayashi et al., 2001; Suzuki et al., 2012), or scenery (Egaña et al., 2013; Sprenger et al., 2013). These studies have identified gaze patterns with more fixation and less shifting in schizophrenia patients compared to controls. Despite some suggestion that these abnormalities are related to negative symptoms (Sprenger et al., 2013) and motivation (Delerue and Boucart, 2012), the findings have been presented as deficits in information processing rather than motivation.

In contrast, the open-field test, in which a subject's behaviour can be observed within a wall-bound chamber, has been the standard for investigating locomotor and exploratory behaviour in non-human animals, including animal models of schizophrenia psychopathology (Bauer et al., 2011; Karl et al., 2007). A variant of the original rodent open-field test, in which the chamber contains nose-poke holes to more specifically examine exploratory behaviour (Darbra and Pallarès, 2010; Karl et al., 2007; Young et al., 2011), was adopted to develop the Human Behavioural Pattern Monitor (HBPM) using a translational approach (Perry et al., 2009). In the HBPM paradigm, subjects were left without instruction in a novel room containing objects to explore, and analyses of recorded behaviour revealed that schizophrenia participants exhibited a substantially different profile of exploration compared to healthy controls (Minassian et al., 2010; Perry et al., 2010, 2009). However, these HBPM studies have focused primarily on inpatient populations with acute mania or psychosis. It remains unclear how these findings apply to schizophrenia beyond acute psychosis.

To further our understanding of motivation deficits in schizophrenia, we developed the Novelty Exploration Task (NET), a novel task that allows for objective monitoring of participants' exploratory behaviours in an open-field setting. Although inspired by the HBPM, the NET and HBPM differ in several critical aspects. First, the objects in the NET environment are a mixture of common items and uncommon objects that are likely unfamiliar to participants, to provide an element of novelty beyond that of being in a new place. Further, all behavioural metrics are computed from objective motion capture data without reliance on observer ratings. Finally, gaze direction estimated from captured data allows quantification of visual exploration of objects not coinciding with tactile contact. The NET was administered to schizophrenia patients and healthy individuals to test the hypothesis that patients would exhibit diminished exploratory behaviour, characterized by atypical locomotion patterns and reduced object exploration. Additionally, in evaluating the NET's concurrent, discriminant, and predictive validity, we expected NET performance to correlate with clinical measures of negative symptoms, amotivation, and community functioning.

2. Methods

2.1. Participants

Twenty-one schizophrenia patients (SZ) recruited from outpatient clinics and 20 healthy control subjects (HC), group-matched for age and sex, completed the study. Participants were between 18 and 55 years old, with no history of active substance abuse or dependence in the past 3 months (except for nicotine) or neurological disease. SZ participants had a DSM-IV diagnosis of schizophrenia (and no other concurrent Axis I disorder) based on a structured diagnostic interview (Mini International Neuropsychiatric Inventory (MINI) (Sheehan et al., 1998)); were on a stable dose of antipsychotic medications for at least the preceding four weeks; were capable to consent to participate in the study; and were not experiencing significant akathisia (global item >2 on the Barnes Akathisia Rating Scale (Barnes, 1989)) or extrapyramidal symptoms (ratings >2 on >2 items on the Simpson Angus Rating Scale (SAS) (Simpson and Angus, 1970)). HC participants did not meet criteria for any Axis I disorder, and had no family history of schizophrenia or related psychotic disorder in a first-degree relative.

2.2. Clinical measures

All participants were administered the Apathy Evaluation Scale – clinical version (AES) (Marin et al., 1991), the Brief Assessment of Cognition in Schizophrenia (BACS) (Keefe et al., 2004), and the Personal and Social Performance Scale (PSP) (Morosini et al., 2000). BACS Symbol Coding *Z*-scores and composite Z-scores, each determined based on age and sex normative data, served as measures of attention and global neurocognition, respectively. Participants also completed the Social Functioning Scale (SFS) (Birchwood et al., 1990) as a more comprehensive measure of social functioning, with the mean of the scaled scores of the seven SFS subscales comprising a global measure of social functioning. SZ participants were additionally administered the Scales for the Assessment of Positive Symptoms and Negative Symptoms (SAPS and SANS) (Andreasen, 1984, 1982), the Calgary Depression Scale for Schizophrenia (CDSS) (Addington et al., 1990), and the SAS, to assess symptom severity, depression, and medication-induced motor side-effects, respectively. For the SANS, subdomain scores were calculated for Amotivation (the sum of Avolition-Apathy and Anhedonia-Asociality subscale items) and Diminished Expression (the sum of Affective Flattening subscale and Poverty of Speech items) (Foussias et al., 2009). Chlorpromazine dose equivalents were calculated for SZ participants' antipsychotic medications (Gardner et al., 2010).

2.3. NET design

Participants spent 15 min, in line with aforementioned investigations using the HBPM, in an unfamiliar office setting where their behaviour was recorded. The LIBERTY LATUS (Large Area Tracking Untethered System) (Polhemus Inc., Colchester, VT) was used to capture motion data, specifically the position and orientation of three wireless markers worn by participants: one on each wrist (estimating hand position), and one attached to a hat (estimating head position and orientation). The testing room contained five commonplace and five uncommon objects at specified positions, but no chair (Fig. 1).

Prior to the task, participants indicated level of fatigue, a potential factor in task performance, on a 4-point Likert scale. Subjects were then asked to wait in the room alone until the experimenter returned to resume the study. No further instructions were provided, and participants were not informed the task was ongoing or that data were being collected. If a subject attempted to exit the room, he/she was instructed to remain in the room and that the experimenter would return shortly. After 15 min, the experimenter returned and asked participants to rate each object for level of novelty and interest on a 5-point Likert scale. These individual ratings were summed to compute total scores for object novelty and interest, respectively.

2.4. NET data processing

The primary NET outcome measures, broadly categorized as locomotion and object interaction, were computed from marker data using MATLAB version R2013a/8.1.0.604 (The MathWorks, Inc., Natick, MA). Distance travelled and spatial *d* respectively indexed extent and complexity of locomotor activity. Spatial *d* is a scaling exponent representing the geometric structure of a travelled path, with values ranging from 1 (direct and linear) to 2 (highly circumscribed) (Paulus

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