Schizophrenia Research xxx (2017) xxx–xxx

Contents lists available at ScienceDirect

Schizophrenia Research

journal homepage: www.elsevier.com/locate/schres

Using wearable technology to detect the autonomic signature of illness severity in schizophrenia

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ARTICLE INFO

Article history:
Received 6 April 2017
Received in revised form 19 September 2017
Accepted 21 September 2017
Available online xxxx

Keywords:
Schizophrenia
Psychosis
Heart rate
Functioning
Mobile health
Digital technology

ABSTRACT

Introduction: Research suggests that people with schizophrenia have autonomic dysfunctions. These have been linked to functioning problems, symptoms and considered a risk factor for illness chronicity. The aim of this study is to introduce a new Mobile Health (mHealth) method using wearable technology to assessing autonomic activity in people's everyday life. We aim to evaluate the new method acceptability and characterise the association between schizophrenia illness features and autonomic abnormalities.
Method: Thirty participants with schizophrenia and 25 controls were asked to wear a mHealth device measuring autonomic activity and movements during their normal everyday life. Measures of device use acceptability were collected from all participants. Participants with schizophrenia were also assessed for symptoms and functioning levels. Measures of heart rate variability (HRV), electrodermal activity (EDA) and movement were collected by the device and groups were compared. Correlation between physiological measures, functioning, symptoms and medication levels were assessed in people with schizophrenia.
Results: The mHealth device method proved to be acceptable and produced reliable measures of autonomic activity and behaviour. Compared to controls, people with schizophrenia showed lower levels of HRV, movement and functioning. In people with schizophrenia illness severity, particularly positive symptoms, was associated with parasympathetic deregulation.
Conclusions: Autonomic abnormalities can be detected using wearable technology from people's everyday life. These are in line with previous research and support the notion that autonomic deregulation are relevant illness features for mental and physical health in schizophrenia. This method may be developed as a monitoring system for well-being and relapse prevention.

1. Introduction

People with schizophrenia experience a significant reduction in their functioning levels from illness onset (Cella et al., 2016; Reichenberg et al., 2014). Functioning problems are largely responsible for the long term consequences of the illness, poor life quality and much of the illness associated burden for sufferers, carers, the health care system and the society (Harvey, 2009; Jaaskelainen et al., 2013; Stouten et al., 2014). Much of the work done in this area has used interview based tools to assess the illness impact on social and occupational levels (Cella et al., 2016; Heinrichs et al., 2006; Schneider and Struening, 1983).

Challenges in the definition of functioning and its broad conceptualisation have made it difficult to study the biological markers associated with this illness feature. One exception is research in the field of autonomic nervous system activity. Since the 80s autonomic system dysfunction have been consistently linked to functioning difficulties in people with schizophrenia (Brekke et al., 1997; Ohman et al., 1989; Tarrier and Barrowclough, 1990). Despite not always converging in identifying a specific biological system, the majority of the evidence supports the notion that autonomic deregulation may be implicated in functioning problems (Fujibayashi et al., 2009). Several studies suggest that reduce vagal tone and heart rate variability (HRV) are found in people with schizophrenia, and to a lesser degree in unaffected relatives (e.g. Bar et al., 2005; Ieda et al., 2014; Moon et al., 2013) and this is associated with lower scores on the Global Assessment of Functioning (Khandoker et al., 2010), illness chronicity (Toichi et al., 1999) and both positive and negative symptoms severity (Boettger et al., 2006; Kim et al., 2004). A recent meta-analysis suggested that this feature should be considered an endophenotype of schizophrenia (Clamor et al., 2016). Less convergent are findings from studies investigating sympathetic regulation. Some studies found people with schizophrenia displaying elevated event related phasic and tonic electrodermal

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https://doi.org/10.1016/j.schres.2017.09.028
0920-9964/

activity, EDA, compared to controls (Zahn et al., 1997) while other studies found no differences (Castro et al., 2008; Hempel et al., 2005). Recently Montaquila et al. (2015) proposed that sympathetic deregulation in people with schizophrenia may be dependent on diminished parasympathetic activity and the consequent difficulties of the parasympathetic system to down-regulate sympathetic activity. This account may explain the incongruent sympathetic activation findings and explain why event-related activation is largely found in the normal range while there may be a selective difficulty in down-modulating this response. To date only a limited number of studies measured sympathetic and parasympathetic activity simultaneously and therefore this hypothesis has only partial empirical support.

Most of the studies available in the literature assess the relationship between autonomic activity and schizophrenia illness features using laboratory based paradigms. This method however does not allow assessing directly the relevance of autonomic events to functioning problems. Recent technological developments produced devices capable of recording autonomic activity from wearable devices. These are worn on such as regular cloths or watches and allow regular information gathering over extended time periods. This new prospect has made physiological research outside the laboratory accessible and allowed, for the first time, to study how autonomic deregulations contribute to mental health symptoms (Okruszek et al., 2016). This methodology is also beginning to be used for monitoring and prevention in neurological and cardiometabolic conditions (Corino et al., 2017; Picard et al., 2017; Sarkis et al., 2015).

The use of wearables and mobile health (mHealth) devices in people with schizophrenia may also be useful to support intervention to improve cardiometabolic health (Mitchell and De Hert, 2015). Recent research suggested that wearable devices may be useful to support weight loss and improve lifestyle in people with severe mental health condition (Naslund et al., 2016; Naslund et al., 2017).

This study has three aims. The first is to evaluate the acceptability and feasibility of the new mHealth technology in people with schizophrenia. The second is to compare sympathetic and parasympathetic activity between people with schizophrenia and healthy controls during everyday life. The third is to assess the association of possible autonomic abnormalities with functional difficulties and symptoms of schizophrenia.

2. Methods

2.1. Design

Cross-sectional comparing a group of people with schizophrenia with a control group.

2.2. Participants

Participants with schizophrenia were recruited from the National Health System, Community Mental Health Teams in South London (UK). Inclusion criteria were: (i) DSM-IV diagnosis of schizophrenia, (ii) aged 18–65, (iii) good command of English language. Exclusion criteria: (i) recent medication change (i.e. in the last month), (ii) poor literacy or learning disability, (iii) a DSM-IV diagnosis of substance dependence. Participants in the control group were healthy individuals recruited with advertisement from the local community to match the clinical group for age and gender. Inclusion criteria were set to allow appropriate group matching: age between 18 and 65 years, no history of DSM-IV diagnosis of schizophrenia or other mental disorder, no evidence of head injury/organic brain disorder, no learning disability and no diagnosis of substance dependence.

2.3. Measures

For all participants we collected demographic information (e.g. age, gender). For participants in the clinical group we collected information on their mental health history and current medication. Antipsychotic dosage was converted to chlorpromazine equivalents using guidelines form Woods (Woods, 2003).

2.4. Acceptability

The assessment acceptability was evaluated using an acceptability feedback questionnaire. The assessment questions were designed to be rated using a 7-point Likert scale. Questions enquired whether: i) the device disrupted participants' life; ii) stopped participants from doing usual activities; iii) it was embarrassing to wear the device around other people; iv) it was easy to remember to wear the device; v) it was enjoyable wearing the device as part of this study. This measure was used in a previous study involving people with schizophrenia and a similar mHealth device (Edwards et al., 2016).

2.5. Functioning

Functioning was assessed with the time use survey (Short, 2006). This is a semi-structured interview asking participants to retrospectively report the time spent in a variety of activities in the last month (e.g. work, education, socializing, sleep). Time spent in each activity is converted in number of hours per week. Time spent in structured activity is considered and index of function levels. Structured time includes activities such as work, volunteering, studying, socializing, travelling, hobbies, house chores, caring for others and looking after children. This measure was used in previous research with people with schizophrenia (Cella et al., 2016).

2.6. Symptoms

Symptom severity was measured using the Positive and Negative Syndrome Scale (PANSS) (Kay et al., 1987). This is a 30-item assessing symptom severity in the past week. For this study we considered five factors: Positive Symptoms (Pos), Negative Symptoms (Neg), Disorganised (Dis), Excited (Exc) and Negative Emotion Depressed (Emd) (Cella et al., 2014a; Wallwork et al., 2012).

2.7. Autonomic system

The measurement of the autonomic activation was conducted using a wearable device worn on the participant's wrist (i.e. Empatica E4) (Garbarino et al., 2014). The device has 3 sensors recording: i) *Electrodermal Activity (EDA)* via skin conductivity (this assesses overall responsiveness to external events by assessing sympathetic nervous system arousal); ii) *Blood volume pulse* with a photoplethysmography sensor. From this measure it is possible to extract time between heart beat peaks (inter-beat intervals IBI). From IBI data it is possible to extract hear rate variability (HRV); inter-beat intervals (RR); standard deviation of RR intervals (SDNN) and square root of the mean squared differences of successive RR intervals (RMSSD); iii) *Acceleration* (ACC) via a 3-axis accelerometer. Data from this sensor can be used to calculate activity levels.

2.8. Procedure

For the clinical group eligible participants who were considered suitable by their care team were approached and offered to take part in the study. Upon entering the study demographic and clinical information were collected from clinical records and during the initial assessment appointment all the study assessment measures were administered. Participates in the control group were screened for current and past

Please cite this article as: Cella, M., et al., Using wearable technology to detect the autonomic signature of illness severity in schizophrenia, Schizophr. Res. (2017), https://doi.org/10.1016/j.schres.2017.09.028