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Review

Insights to the schizophrenia continuum: A systematic review of saccadic eye movements in schizotypy and biological relatives of schizophrenia patients☆

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ABSTRACT

Myles, J.B., S. Rossell, A. Phillipou, Thomas, E and C. Gurvich. A systematic review of saccadic eye movements across the schizophrenia continuum: Characterisation, pathophysiology and genetic associations. NEUROSCI BIOBEHAV REV 21(1) XXX–XXX, 2015.

One of the cognitive hallmarks of schizophrenia is impaired eye movements, particularly for the antisaccade task. Less saccade research has been conducted in relation to the broader schizophrenia continuum, that is, people with high schizotypy or first-degree relatives of people with schizophrenia. This systematic review sought to identify, collate and appraise prosaccade, antisaccade and memory-guided saccade studies involving behavioural, neuroimaging and genetic data published between 1980 and September 2016 in individuals with high schizotypy and first-degree relatives. A systematic literature search was conducted, using Ovid MEDLINE, PsycINFO, PubMed and SCOPUS databases. Of 913 references screened, 18 schizotypy, 29 family studies and two schizotypy and relatives articles studies were eligible for inclusion. Antisaccade error rate was the most consistent deficit found for high schizotypy. Relatives had intermediate antisaccade error rates between patients and healthy controls. Results from the limited genetic and neuroimaging studies echoed schizophrenia findings. Confounds were also identified. It was concluded that future research is required to refine the saccade endophenotype and to expand genetic and neuroimaging research.

Contents

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1. Introduction

Schizophrenia is a psychiatric disorder that can encompass a range of unusual behaviours, disorganised thoughts and distortions in the individual's perception and interpretation of reality. Schizophrenia has traditionally been viewed as a discrete disorder, where a person either meets diagnostic criteria, or they do not. More recently, schizophrenia has been conceptualised as a continuum, where subtle emotional, social and personal impairments, and mild perceptual alterations, unusual thoughts and eccentric behaviour are present in the healthy general population. This subclinical portion of the continuum has been referred to as schizotypy (Ettinger et al., 2014).

While schizotypy was first conceptualised as a distinct personality structure which leaves the person vulnerable to developing schizophrenia (Meehl, 1989), the weight of evidence now supports a continuum where schizotypy symptoms are present to varying degrees across the general population (Claridge and Beech, 1995). People with high levels of schizotypy sit closer to schizophrenia on the continuum in terms of symptoms, and are considered to be at a higher risk of developing psychosis than people with low schizotypy (Rawlings et al., 2008). This fully dimensional approach has received theoretical support in the literature, with studies identifying the same underlying factors found in schizophrenia, such as positive symptoms (e.g. delusions, hallucinations), negative symptoms (e.g. reduced pleasure or flat affect) and cognitive symptoms (Nelson et al., 2013). It is worth noting that in some literature, the cognitive factor is also referred to as "disorganised", reflecting the disorganised nature of thought and behaviour that can be associated with impaired cognition. Furthermore, schizotypy has been shown to have similar but attenuated cognitive and neurophysiological deficits to schizophrenia (Ettinger et al., 2014), as well as similar underlying genetic components, and environmental influences such as birth complications, childhood trauma and urban living (Nelson et al., 2013). Despite the often heated debate by the proponents of each model [see Beauchaine et al. (2008), and for a response Rawlings et al. (2008)] the weight of evidence appears to support the fully dimensional model of schizotypy (Mason and Claridge, 2006), which has been adopted by most studies.

It is also worth noting that the term schizotypy does not refer to schizotypal personality disorder (SPD). While there is a degree of similarity between the two concepts, SPD refers to a discrete disorder marked by clinical levels of acute distress due to pervasive social and interpersonal deficits, as well as perceptual distortions and eccentric behaviour (American Psychiatric Association, 2013), whereas schizotypy refers to sub-clinical symptoms of schizophrenia. Thus, while most people diagnosed with SPD may have high levels of schizotypy, not all people with high schizotypy will have SPD (Ettinger et al., 2014).

Schizotypy is a rapidly growing area of research. While the study of schizotypy is interesting in its own right (e.g. as a dimension of personality), schizotypy also offers a number of advantages for studying schizophrenia liability with the opportunity to control for many of the confounding factors associated with schizophrenia, such as hospitalisation, social isolation, medication/illicit drug use and health complications (Ettinger et al., 2014). Given the complexity and heterogeneity inherent in both schizotypy and schizophrenia (Greenwood et al., 2013), endophenotypes are often employed to simplify the process of studying genetic liability.

1.1. Endophenotypes

Endophenotypes are intermediate phenotypes that lie between the disease and the underlying molecular genetic background. Thus, by studying the endophenotype, insight can be gained into the disease while bypassing the need to look at psychopathology which may fluctuate within and between individuals (Tan et al., 2009). Consistent with the suggested criteria for the identification of endophenotypic markers, allied phenotypes should be (a) associated with illness, (b) heritable, (c) state-independent, (d) co-segregated with illness within families, and (e) also found in unaffected relatives at a higher rate than in the general population (Gottesman and Gould, 2003). Eye movement deficits, particularly in relation to the antisaccade task, have been proposed as a valid schizophrenia endophenotype useful for genetic studies (Radant et al., 2015).

While eye movements in schizophrenia have been extensively studied, saccadic performance has not been adequately analysed in those individuals who lie on the broader schizophrenia continuum, nor in unaffected relatives of people with schizophrenia. In order to refine the saccadic phenotype for future genetic studies, a clear understanding of saccadic performance in the broader schizophrenia continuum and for first-degree relatives is required. In this paper we provide an overview of the use of saccadic eye movements as a research tool, followed by a systematic review of saccadic eye movement studies in schizotypy and biological relatives.

1.2. Saccadic paradigms

Ocular motor dysfunction is one of the most replicated findings in schizophrenia. The first reported study in this area was performed over a century ago (Diefendorf and Dodge, 1908), with