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Modulation of brain network parameters associated with subclinical psychotic symptoms

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ABSTRACT

Objective: Static deficits in small-world properties of brain networks have been described in clinical psychosis, but task-related modulation of network properties has been scarcely studied. Our aim was to assess the modulation of those properties and its association with subclinical psychosis and cognition in the general population.
Method: Closeness centrality and small-worldness were compared between pre-stimulus baseline and response windows of an odd-ball task in 200 healthy individuals. The correlation between modulation of network parameters and clinical (scores in the Community Assessment of Psychological Experiences) and cognitive measures (performance in the dimensions included in the Brief Assessment of Cognition in Schizophrenia battery) was analyzed, as well as between these measures and the corresponding network parameters during baseline and response windows during task performance.
Results: In the theta band, closeness centrality decreased and small-worldness increased in the response window. Centrality and small-worldness modulation were, respectively, directly and inversely associated with subclinical symptoms.
Conclusions: A widespread modulation of network properties in theta band was observed, with a transient increase of small-worldness during the response window, compatible with a transiently more integrated cortical activity associated to cognition. This supports the relevance of electroencephalography to study of normal and altered cognition and its substrates. A relative deficit in the ability to reorganize brain networks may contribute to subclinical psychotic symptoms.

1. Introduction

Psychosis may exist in a continuum from subclinical psychotic experiences to clinical syndromes (DeRosse and Karlsgodt, 2015). The cerebral underpinnings of the psychotic syndrome are largely unknown, but connectivity anomalies in the brain network have been proposed to play a role in psychosis (Friston, 1998; van den Heuvel and Sporns, 2011), with different reported findings (Pettersson-Yeo et al., 2011). Recent developments in brain imaging allow in-vivo assessments of connectivity in the cerebral network, both structural (i.e., tractography using magnetic resonance, MRI) and functional (i.e., by means of functional MRI or magnetoencephalography). Most studies of this kind to date assessed connectivity between a priori defined regions of interest. However, the global structural and functional properties of this network can be assessed using analyses based on graph theory. Such global assessments of brain connectivity are of particular interest in psychosis because of the widespread cortical involvement in higher cognitive functions (Dehaene and Changeux, 2011). Network properties relevant for the cerebral function include local clustering (related to local specialization) and average distance between nodes in the network (associated to global integration). Graph analysis is thus useful to estimate the global efficiency of the brain networks by means of balancing

Abbreviations: EEG, electroencephalogram; CAPE, Community Assessment of Psychic Experiences; BACS, Brief Assessment in Cognition in Schizophrenia Scale; WST, Wisconsin Card Sorting Test; CC, closeness centrality; SW, small-worldness; CLC, clustering coefficient; PL, path length; DMN, default mode network.

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distance and clustering between nodes (Bullmore and Sporns, 2009; Stam and Reijneveld, 2007).

Among the possible network structures, small-world is characterized by a high clustering coefficient and a small average distance between nodes, which allows an optimum balance between local specialization and global integration (Watts and Strogatz, 1998). Several studies described small-world features in the human brain (Bechtel, 2013), which have been associated with global cognitive capacities (Langer et al., 2012) and other psychological features (Kitzbichler et al., 2011). A deficit of small-world properties in brain networks has been associated with clinical psychosis (Shim et al., 2014), but some influence of treatment might contribute to that deficit in this population. Therefore, in order to overcome this problem and improving our current knowledge about the role of disconnectivity in the psychotic syndrome, a possible approach would be to assess the relation between disconnectivity and psychosis in a population never exposed to the effect of antipsychotics. Considering the prevalence of subclinical psychotic symptoms in the general population (Rössler et al., 2015) and their reported association with cognition (Blanchard et al., 2010) and risk for severe mental disorders (Linscott and van Os, 2013), it seems appropriate to explore a possible association between network properties, cognition and subclinical psychotic symptoms in that population, which would be not influenced by previous exposure to medication.

To the best of our knowledge, no such assessments have been reported, although previous studies suggest a relation between subclinical symptoms and cerebral disconnectivity. In this regard, a recent study has shown white matter differences in adolescents with psychotic experiences (O'Hanlon et al., 2015). Moreover, another study using functional MRI in subjects with non-clinical psychosis showed decreased connectivity between regions of the default mode network and frontal regions, as well as increased connectivity compared to controls within regions of frontal control networks (Orr et al., 2014). Abnormalities in fronto-temporal connectivity have also been reported in individuals at risk of mental disorders (Fusar-Poli et al., 2012). Nevertheless, none of these studies assessed global properties of the cerebral network.

In this context, the dynamic modulation of these network properties may be of special interest, since the formation of transitory synaptic assemblies underlying cognitive processing may be reflected in the modulation of network properties from resting to active task conditions (Singer, 2013). For this purpose, large temporal resolution would be required, given the fast changes in neural activity observed in the cortex during cognition. The electroencephalogram (EEG) appears then as a suitable tool, since it is able to measure electrical activity of neuronal assemblies in the order of hundreds of milliseconds (Mulert et al., 2008). However, to date, graph analyses have been usually performed in one condition. Only a few studies evaluated the task-related modulation of small-world properties using EEG. According to a recent EEG study, a network reconfiguration takes place during the active phase of an odd-ball task, which supports a global workspace as a precondition for cognition (Bola and Sabel, 2015). In this context, it seems worthy to explore the modulation of small-world properties in the human brain with EEG, as well as its relation to cognition.

Therefore, the aims of the present research are twofold: (i) to assess the changes in the modulation of brain functional networks in the general population during a cognitive task; and (ii) to study the possible association of network modulation with subclinical psychotic symptoms and cognitive performance. Given the aforementioned small-world properties of functional connectivity in the human brain and its role in cognitive capacities, we hypothesized that small-world parameters would increase from the basal to the active condition in a cognitive test. Moreover, we expected that lesser modulation would be associated to larger scores in subclinical symptoms and/or poorer cognitive performance. To this end, EEG was recorded when the subjects underwent a 3-tone odd-ball task, since performance in this task could be expected to be good and it has been extensively used in previous studies on psychosis (Bramon et al., 2004).

2. Materials and methods

2.1. Participants

Two-hundred healthy volunteers (aged 18 to 61 years) were recruited by means of public announcements. A small economic compensation was offered for displacement expenses. Each participant underwent a semi-structured interview to exclude psychiatric diagnoses. They were not screened for subclinical psychotic experiences prior to recruitment. Exclusion criteria included: (i) previous neurological diseases; (ii) head trauma and loss of consciousness; (iii) family antecedents of psychoses; (iv) current psychiatric disorders; (v) substance abuse or use of psychoactive drugs; and (vi) intelligent quotient (IQ) below 70. Education level was scored as degreed or non-degreed, whereas employment status as currently studying/working, unemployed or retired. Demographic data are summarized in Table 1.

Writing consent was obtained from each participant after they were informed on the nature of the study. The ethical committee of the three hospitals involved in the recruitment of participants (i.e., University Hospitals of Alava, Salamanca and Valladolid) endorsed the study according to The Code of Ethics of the World Medical Association.

2.2. Clinical and cognitive assessment

To score subclinical psychotic-like symptoms, all subjects completed the Spanish version of the Community Assessment of Psychic Experiences (CAPE) (Fonseca-Pedrero et al., 2012). Through 42 questions, this self-administered instrument scores the frequency and associated

Table 1
Demographic data, cognitive data and subclinical psychotic symptoms scores. Data are presented as percentage or mean and standard deviation (SD). BACS verbal memory score corresponds to the sum of the five recall attempts. BACS verbal fluency results from pooling letter and category fluency scores. CAPE score are shown as total sum for frequency and distress of each subscale.

Demographic data				
Age mean (SD) (years)				27.01 (8.35)
Male/female (%)				45.32%/54.68%
Secondary education/undergrad-graduate (%)				54.18%/45.82%
Employed/unemployed (%)				86.56%/13.44%
Cognitive data (BACS)		Mean	SD	Range
Verbal memory		54.31	8.63	23–74
Working memory		22.26	3.76	12–28
Motor speed		67.92	14.77	24–97
Verbal fluency		23.67	9.06	13–41
Processing speed		66.71	12.44	23–104
Executive function		19.29	14.89	10–20
Cognitive data (WCST)		Mean	SD	Range
WCST percent of perseverative errors		10.26	5.77	4–31.25
WCST completed categories		5.65	1.01	0–6
Cognitive data (WAIS-III)		Mean	SD	Range
Total IQ		110.08	11.95	75–139
Cognitive data (CAPE)		Mean	SD	Range
CAPE positive	Frequency	25.05	3.60	20–41
	Distress	7.40	5.48	0–26
CAPE negative	Frequency	22.06	4.36	14–38
	Distress	14.94	8.77	0–38
CAPE depressive	Frequency	12.89	2.43	8–22
	Distress	10.66	6.09	0–30
CAPE total	Frequency	60.01	8.55	44–90
	Distress	33.01	17.75	3–81