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Original article

Physiological evidence of a deficit to enhance the empathic response in schizophrenia

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ABSTRACT

Empathy is crucial for maintaining effective social interactions. Research has identified both an early-emotional sharing and a late-cognitive component of empathy. Although considered a functionally vital social cognition process, empathy has scarcely been studied in schizophrenia (SZ). We used event-related potentials (ERPs) to study the temporal dynamics of empathic response in 19 patients with SZ and 18 matched healthy controls (HC) using an empathy for physical pain paradigm. Participants responded to pictures of hands in neutral and painful situations in an active empathic condition and one manipulated by task demands. Additionally, subjective ratings of the stimuli and empathic self-reports were collected. People with SZ had (1) decreased early-emotional ERP responses to pictures of others in pain; (2) decreased modulation by attention of late-cognitive ERP responses; (3) lower ratings of perspective taking and higher ratings of personal distress which were both related to decreased modulation of late-cognitive empathic responses; (4) a significant relationship between high affective overlap between somebody else's pain and their own pain and decreased modulation of late-cognitive empathic responses; (5) a distinct relationship between regulatory deficits in late-cognitive empathy and functioning. Patients had present but reduced early and late empathy-related ERPs. Patients also reported increased personal distress when faced with distress in others. The late ERP responses are thought to be associated with self-regulation and response modulation. The magnitude of these late responses was inversely associated with reported levels of personal distress in both patients and controls. Additionally, regulatory deficits in cognitive empathy were highly related with deficits in functioning. Decreased ability to regulate one's own emotional engagement and response to emotions of others may be an important source of distress and dysfunction in social situations for patients with schizophrenia.

1. Introduction

Empathy is a complex construct that overlaps with theory of mind (ToM), social perception, attributional bias and emotional processing. Social cognition research in schizophrenia (SZ) has thus far focused on these related constructs rather than empathy per se [19], despite evidence of the functional significance of decreased empathic capability [39,50].

Most definitions of empathy include "putting oneself into another person's shoes" on the basis of shared affect between self and other [10,31]. Current evidence suggests that two components mediate empathic response, a phylogenetically and ontogenetically early-emotional one, and a later cognitive response [42,43,46]. The early-emotional empathic response is automatically elicited by perception of another's emotional state (emotional contagion) and is associated with a neural network active both during perception of other people's pain and our own pain experience [12,32,42,49]. A recent meta-analysis of more than 32 studies that had investigated empathy for pain revealed that the anterior insula (bilateral) and the medial anterior cingulate cortex are largely associated with empathy for pain. They also found that the activation of these areas is also present during directly perceived pain [32]. The late-cognitive empathic component involves cognitive perspective taking and mentalizing [42]. The cognitive component can modulate the early-emotional empathic response through, for example, controlling attention or providing contextual qualities, like fairness or competitiveness [16,23,48]. Developmental studies suggest that these processes depend upon the ability to distinguish oneself from others, and then progress to

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Table 1
Demographic and clinical data.

	Healthy Control ($n = 18$)		Schizophrenia ($n = 19$)	
Gender	Male = 12	Female = 6	Male = 8	Female = 11
Ethnicity	African-American = 7	White = 11	African-American = 11	White = 8
	Mean	SD	Mean	SD
Clinical				
Age*	39.78	8.61	46.05	9.37
Subject's years of education*	15.61	2.59	13.42	2.12
Father's years of education	13.35	2.47	13.06	5.52
QLS[a,*]	108.88	14.54	61.00	19.08
PANSS				
Positive	N/A	N/A	17.47	6.27
Negative			17.73	5.98
General			29.78	10.99
Chlorpromazine Eq (md/day)[b]	N/A	N/A	657.6	532.6
Neurocognitive MCCB battery				
Speed of processing*	57.94	11.56	37.68	11.97
Attention and Vigilance*	52.06	11.28	37.84	13.98
Working memory*	55.72	9.06	41.00	13.46
Verbal learning*	48.89	10.01	35.95	8.70
Visual learning*	51.89	12.88	35.74	8.80
Reasoning and problem solving	52.33	8.79	46.63	10.06
Social Cognitive Index*	51.44	12.42	40.4	11.9
Empathy-IRI				
PT*	20.61	3.91	17.00	4.64
EC	20.06	5.08	19.00	4.73
PD*	8.94	4.77	12.26	4.69
FS	15.06	5.54	15.11	7.09

Clinical measures: QLS, Quality of Life scale PANSS, Positive and Negative Syndrome Scale, Neurocognitive measures: *MATRICS cognitive domains, MATRICS Consensus Cognitive Battery* (MCCB), T-scores; Empathy measure: IRI, Interpersonal Reactivity Index, overall subscales: PT = Perspective taking, EC = Empathic concern, PD = Personal distress, FS = Fantasy. One-way ANOVA were conducted for the clinical, neurocognitive and empathy measures and a Chi^2 for the demographic data.

* $P < 0.05$.

[a] Includes 17 healthy controls.

[b] Includes 16 patients.

higher cognitive processes, such as perspective taking [35]. The cognitive component of empathy has consistently been reported to be impaired in patients with SZ across behavioral [47] self-report [36] and fMRI studies [4]; however, the literature regarding the early-emotional empathic response is contradictory. Some studies suggest that this response is also decreased in patients [46] but other data suggests that it is preserved [21,47]. Recent meta-analyses report that patients with SZ are less facially expressive than healthy controls (HC) in response to emotionally evocative stimuli yet report experiencing equal or greater amounts of emotions [6,30]. Therefore, the experience of emotion appears to be preserved in patients with SZ [6,18,30,52] despite difficulties in reading other people's emotions [5].

In the current study, we used the temporal resolution of event-related potentials (ERPs) and an empathy for pain paradigm to evaluate automatic early-emotional and late-cognitive top-down empathic response in patients with SZ and HC. For this purpose, we investigated three early fronto-central components (N110, P180, N240) to assess the early response and three late parietal components (P3, early and Late Positive Potential; LPP) for the late one. These components were selected based on previous work using the same paradigm in healthy controls [13,16,35].

Participants viewed pictures of hands in painful or non-painful situations and were asked either to count the number of hands or indicate whether or not the situation was painful. Previous work in healthy subjects revealed an early ERP positivity greater to painful than neutral stimuli regardless of attention manipulations. However, this pain effect (PE), the difference in response to painful vs neutral stimuli, was greater when subjects attended to the painful aspect of the pictures than when they counted the number of hands [16,22]. We hypothesized that patients would show a preserved or enhanced early ERP response with an absence of differences in the early components between groups to the images of other's in pain. Previous studies show contradictive results in the early response in schizophrenia; however, all these empathy studies employed self-report measures to assess empathy. Studies employing more objective and naturalistic methods, such as the ERPs and Experience Sampling Method (ESM) revealed that patients experience negative emotions equally or more intensely than healthy controls [25,27,38,41,51]. Therefore, as ERPs measure objective immediate response to the stimuli, we predicted to find a preserved or enhanced empathic response in patients when compared with healthy controls. On the other hand, patients would show a decreased modulation of the PE by attention by means of decreased magnitude of the PE in the late components in the active empathic condition compared with healthy controls. We sought to investigate whether ERP responses elicited by painful stimuli correlated with self-report empathy ratings, subjective ratings of the stimuli and with overall quality of life. Additionally, we examined the relationship between the ERP responses and chlorpromazine equivalents just in the patient group.

2. Methods and materials

2.1. Participants and measures

Participants were 19 adult outpatients at a community mental health centre (Table 1) meeting DSM-IV [1] criteria for SZ or schizoaffective disorder, as assessed by the Structured Clinical Interview (SCID) [17] by a licensed clinical psychologist, and 18 HC screened for psychiatric disorders with the non-patient Edition of SCID [17]. The Yale Human Investigation Committee approved all procedures. After description of the study, subjects provided