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Auditory top-down control and affective theory of mind in schizophrenia with and without hallucinations

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ABSTRACT

Social cognitive impairments may represent a core feature of schizophrenia and above all are a strong predictor of positive psychotic symptoms. Previous studies could show that reduced inhibitory top-down control contributes to deficits in theory of mind abilities and is involved in the genesis of hallucinations. The current study aimed to investigate the relationship between auditory inhibition, affective theory of mind and the experience of hallucinations in patients with schizophrenia. In the present study, 20 in-patients with schizophrenia and 20 healthy controls completed a social cognition task (the Reading the Mind in the Eyes Test) and an inhibitory top-down Dichotic Listening Test. Schizophrenia patients with greater severity of hallucinations showed impaired affective theory of mind as well as impaired inhibitory top-down control. More dysfunctional top-down inhibition was associated with poorer affective theory of mind performance, and seemed to mediate the association between impairment to affective theory of mind and severity of hallucinations. The findings support the idea of impaired theory of mind as a trait marker of schizophrenia. In addition, dysfunctional top-down inhibition may give rise to hallucinations and may further impair affective theory of mind skills in schizophrenia.

1. Introduction

Deficits in social interactions are one of the key features of schizophrenia (Fletcher and Frith, 2009; Nitzburg et al., 2015). It is well established that poor ability to attribute mental states (e.g., beliefs, emotions, intentions) to oneself and to others (theory of mind, ToM; Frith, 1992) causes unsuccessful social interactions and social functioning (Brüne, 2005), and impaired ToM was frequently shown in schizophrenia (Hirao et al., 2008; Irani et al., 2006; Kelemen et al., 2005; Kington et al., 2000; Lam et al., 2014; Russell, 2000; Scherzer et al., 2012; for meta-analyses see Bora et al., 2009; Chung et al., 2014; Sprong et al., 2007). Several studies showed that impaired ToM skills were associated with the severity of psychotic symptoms (Bora et al., 2009; Guastella et al., 2013; but see Abdel-Hamid et al., 2009; Urbach et al., 2013), especially with delusions and hallucinations (Corcoran et al., 1995; Frith, 1992; Harrington et al., 2005a; Jardri et al., 2014; for a critical review see Harrington et al., 2005b).

To date, the majority of research on ToM in schizophrenia focused on cognitive ToM (referring to inferences about beliefs and knowledge; Abu-Akel and Shamay-Tsoory, 2011), while research on affective ToM (referring to inferences about emotions; Baron-Cohen et al., 2001), has been relatively sparse (for a meta-analysis see Chung et al., 2014). The Reading the Mind in the Eyes Test is a well-established test of affective ToM, requiring the ability to recognize a complex affective state in other people's eyes (see Hirao et al., 2008; Vellante et al., 2013). Recently, Wang et al. (2015) pointed to the importance of inhibitory control to ToM functions in remitted patients with schizophrenia. Furthermore, a dual-task experiment of Bull et al. (2008) in which reduced affective ToM performance during an inhibition task was observed suggested even greater involvement of inhibitory control in affective compared to cognitive ToM. The authors claimed that good performance on the Reading the Mind in the Eyes Test may require inhibition of social and personal features (e.g., gender, age, facial features) attributed to the faces (see also Mahy et al., 2014). Since the occurrence of hallucinations was additionally associated with impaired inhibitory top-down control (Bozikas et al., 2014; Ford and Mathalon, 2004; Hugdahl et al., 2013) the current study aimed to investigate the connections between auditory inhibition, affective ToM and the experience of hallucinations in patients with schizophrenia.

The Dichotic Listening Test provides a reliable instrument for the separate measurement of bottom-up and top-down processes by administering two different instructions (non-forced condition, forced-left condition). A typical finding in the non-forced condition (bottom-up) is a clear right ear advantage (Hugdahl and Andersson, 1986; Kimura,

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1967), which several authors found to be reduced in schizophrenia (for meta-analysis see Ocklenburg et al., 2013; for review see Ocklenburg et al., 2015). Modulation of the right ear advantage is at the core of the forced-left condition, where participants have to shift their attention to the left ear and inhibit the bottom-up information from the right ear. Performance on the forced-left condition is supposed to represent top-down inhibitory control and adequate monitoring of incoming auditory information.

It was expected that performance on the affective ToM task as well as on the forced-left condition of the Dichotic Listening Test would be impaired in patients with schizophrenia, particularly in those with greater severity of hallucinations. In order to achieve adequate affective ToM performance, it is important to monitor emotions and stereotypies evoked by the stimuli (e.g., gender, age) and to inhibit interferences between one's own perspective and the perspective of the other (for a similar argumentation see Bull et al., 2008). Thus, an association between the performances on the forced-left condition of the Dichotic Listening Test (requiring auditory monitoring and inhibitory skills), and the affective ToM test was expected. Due to the proposed close association between auditory top-down control, affective ToM, and hallucinations, the relationship between affective ToM and hallucinations may be mediated by reduced inhibitory top-down control.

2. Methods

2.1. Participants

Twenty patients with an ICD-diagnosis of schizophrenia/schizoaffective disorder (paranoid (F20.0), $n = 4$; catatonia (F20.2), $n = 1$; undifferentiated (F20.3), $n = 1$; residual (F20.5), $n = 8$; schizoaffective (F25), $n = 1$; psychotic disorder (F23), $n = 5$) and 20 age, sex and educational level matched healthy controls with no history of substance abuse or other medical, psychiatric, or neurological disorders participated in the study (Table 1). Patients were recruited from two hospitals in Graz ($n = 12$) and Hall ($n = 8$), Austria. Schizophrenia symptoms were assessed using the Positive and Negative Syndrome Scale (PANSS; Kay et al., 1987). Patients were divided into a group with "high" (PANSS P3 > 3; $n = 7$) and a group with "low" hallucinatory behavior (PANSS P3 ≤ 3; $n = 13$; see Hugdahl et al., 2013). All patients received antipsychotic drugs (typical antipsychotics, $n = 1$; atypical antipsychotics $n = 18$; both, $n = 1$). The chlorpromazine equivalents were calculated according to a systematic review of methods (Patel et al., 2013) using linear equations (Andreasen et al., 2010). Participants did not have any hearing difficulties. All participants signed informed consent, and the study was approved by the Ethical Committee of the University of Graz.

2.2. Tasks

2.2.1. ToM task

A computerized version of the Reading the Mind in the Eyes Test (RMIE; Baron-Cohen et al., 2001) was used. The participants were asked to decide for each of 36 pairs of eyes which of four adjectives best matched the mental state of the person on the photograph. The four words were marked with different colours, which could be selected with respective buttons on the keyboard. Stimuli were presented without time limit and in random order. A glossary of all difficult adjective descriptors was presented, and their meanings were explained.

2.2.2. Auditory top-down inhibition task

During the Dichotic Listening Test (Hugdahl, 2009; Hugdahl and Andersson, 1986), the listener is presented with two different consonant–vowel stimuli at the same time (ba, da, pa, ta, ga, ka), one in the right and one in the left ear. Participants were instructed to report on each trial which syllable they perceived. After the dichotic stimulus and a stimulus-free interval (500 ms), the 6 consonant–vowel stimuli were presented on the screen. Participants were required to select the syllable they had perceived using the computer mouse (5000 ms). After an inter-trial interval of 4500 ms, the next trial started.

The dichotic stimuli were presented in three separate blocks with different instructions (Hugdahl, 2009). The participants were either instructed to report on each trial which syllable they perceived, without being informed that there were two different syllables presented at the same time (non-forced condition, NF), or to pay their attention to and report the stimulus from the right ear (forced-right condition, FR), or from the left ear (forced-left condition, FL). While the forced-right condition refers to non-inhibitory attention, the forced-left condition involves a conflict between bottom-up and top-down processes, with the bottom-up process favoring a right-ear response and the top-down process pushing for a left-ear response. Thus, the manipulation allows to study the ability to exert top-down inhibitory control over the bottom-up right-ear-advantage effect. Testing started with the non-forced condition followed by the forced conditions in counterbalanced order. The blocks consisted of 36 trials each, whereby 6 trials were homonyms and not relevant for the index calculation. The order of syllables was randomized (for a similar procedure see Kompus et al., 2012; Thomsen et al., 2004).

For each condition, a laterality index (LQ_{NF}, LQ_{FL}, LQ_{FR}) was calculated ($LQ = (\text{left ear} - \text{right ear}) / (\text{left ear} + \text{right ear}) * 100$), where positive scores indicate more left ear answers. To gain an index of auditory top-down control, residualized change scores were calculated by regressing the LQ_{FL} scores on the LQ_{NF}. Higher scores indicate increased auditory inhibition skills (for a similar approach see Westerhausen et al., 2015). An analogous score was calculated for LQ_{FR}.

Table 1
Demographic and clinical variables.

	Patients ($n = 20$) (high ($n = 7$)/low ($n = 13$) hallucinatory behavior)	Controls ($n = 20$)	t/χ^2	df	p
Age (M ± SD)	37.7 ± 15.3 (44.4 ± 15.1 / 34.0 ± 14.7)	38.3 ± 13.7	0.1	38	0.89
Sex (M/F)	16/4 (7/0 / 9/4)	12/8	1.9	1	0.17
Handedness (R/L)	15/5 (5/2 / 10/3)	18/2	1.6	1	0.21
Education (CS/HS)	11/9 (3/4 / 8/5)	13/7	0.4	1	0.52
Verbal intelligence (M ± SD)	27.0 ± 6.6 (25.4 ± 5.6 / 27.8 ± 7.2)	29.1 ± 5.0	1.1	38	0.27
Duration of illness (yrs, M ± SD)	12.5 ± 12.3 (19.1 ± 11.8 / 8.9 ± 11.5)				
PANSS Positive (M ± SD)	21.5 ± 9.9 (30.4 ± 7.9 / 16.7 ± 7.2)				
PANSS Negative (M ± SD)	21.9 ± 10.3 (28.4 ± 11.5 / 18.4 ± 7.9)				
PANSS P3 (M ± SD)	2.7 ± 1.8 (4.7 ± 0.8 / 1.6 ± 1.0)				
APD dose (CPZ equivalents, M ± SD)	440 ± 225 (568 ± 256 / 371 ± 181)				

Note. APD = antipsychotic drug; CPZ = chlorpromazine; CS = compulsory school; F = female; L = left; M = male; PANSS P3 = hallucinatory behavior item of the Positive and Negative Syndrome Scale; R = right. Scores of groups with high ($n = 7$, PANNS P3 > 3) / low ($n = 13$) hallucinatory behavior are given in parentheses.