Schizophrenia Research 107 (2009) 83–91

Contents lists available at ScienceDirect

Schizophrenia Research

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

Abnormal brain response during the auditory emotional processing in schizophrenic patients with chronic auditory hallucinations

Jee In Kang [a,b], Jae-Jin Kim [a,d,*], Jeong-Ho Seok [a], Ji Won Chun [a,d], Seung-Koo Lee [c], Hae-Jeong Park [c,d]

[a] Institute of Behavioral Science in Medicine, Yonsei University College of Medicine, Gwangju Gyeonggi, Republic of Korea
[b] Department of Psychiatry, Ilsan Hospital, National Health Insurance Corporation, Goyang Gyeonggi, Republic of Korea
[c] Department of Diagnostic Radiology, Yonsei University College of Medicine, Seoul, Republic of Korea
[d] Brain Korea 21 Project for Medical Science, Yonsei University College of Medicine, Seoul, Republic of Korea

ARTICLE INFO

Article history:
Received 21 September 2007
Received in revised form 11 August 2008
Accepted 12 August 2008
Available online 25 September 2008

Keywords:
Schizophrenia
Auditory hallucinations
Auditory emotional processing
Amygdala
Hippocampus

ABSTRACT

Objective: Few neuroimaging studies have been conducted regarding clinical associations between auditory hallucinations (AHs) and affective disturbances in patients with schizophrenia. This study aimed to elucidate the neurobiological basis of emotional disturbances in schizophrenic patients with persisting AHs.

Methods: Using functional magnetic resonance imaging (fMRI), the cortical responsiveness during the processing of laughing and crying sounds was measured and compared between 14 hallucinating schizophrenic patients, 14 nonhallucinating schizophrenic patients and 28 normal controls.

Results: The hallucinating patients showed differential neural activities in various areas including the amygdala, the hippocampus, the cingulate, the prefrontal cortex, and the parietal cortex, compared with the nonhallucinating patients and the normal controls. In particular, compared with the nonhallucinators, the hallucinators revealed reduced activation in the left amygdala and the bilateral hippocampus during the processing of crying sounds.

Conclusion: Our findings suggest that the persistence of AHs in schizophrenia may induce functional disturbances of the emotion-related interconnected neural networks, including reduced responsiveness in the amygdala and hippocampus to negative stimuli.

1. Introduction

Although auditory hallucinations (AHs) have been considered to be the major feature of the positive dimension opposed to negative symptoms of schizophrenia (Andreasen et al., 1995), they include heterogeneous phenomena and have an effect on other domains of mental functions due to their intrusiveness. Phenomenological research has confirmed the importance of the meaning and interpretation of hallucinating voices that patients with schizophrenia hear (Chadwick and Birchwood, 1994; Copolov et al., 2004; Morrison et al., 2004). Hallucinating voices tend to talk in various emotive tones, such as angry, frightening or pleasant (Nayani and David, 1996). Most patients with AHs experience adverse effects, such as emotional distress and feeling endangered (Miller et al., 1993), and patients with more frequent and long-lasting AHs experience them more derogatory and hostile in tone (Nayani and David, 1996).

Previous functional imaging studies have shown a significant activation in the limbic and paralimbic structures when patients with schizophrenia experience AHs (Silbersweig et al., 1995; Dierks et al., 1999; Shergill et al., 2000). For example, a PET study showed that AHs had associations with activation in the bilateral inferior frontal/insular, anterior cingulate and temporal cortex, the right side of the thalamus and the inferior colliculus, and the left side of the hippocampus and the

* Corresponding author. Department of Psychiatry and Diagnostic Radiology, Yongdong Severance Hospital, 612 Eonjuro, Gangnam-gu, Seoul, 135-720, Republic of Korea. Tel.: +82 2 2019 3341; fax: +82 2 3462 4304.
E-mail address: jaejkim@yonsei.ac.kr (J.-J. Kim).

0920-9964/$ – see front matter © 2008 Elsevier B.V. All rights reserved.
doi:10.1016/j.schres.2008.08.019

parahippocampal gyrus (Silbersweig et al., 1995). In an event-related fMRI study based on patients' own experience of AHs, bilateral amygdalar activation while hearing AHs was a remarkable finding (Dierks et al., 1999). These findings suggest that repetitive experiences of distressing AHs in patients with schizophrenia can result in changes of neural activity in the specific regions including the limbic system.

Here, a question can be raised. “How do patients with persisting AHs respond to real emotional stimuli?” A behavioral study reported that schizophrenic patients with AHs had impaired auditory affect perception, especially on a nonverbal affective stimuli requiring the recognition of environmental sounds, and they have increased liability for deficits in auditory affect perception (Rossell and Boundy, 2005). In addition, during the emotional prosodic processing using happy, sad and neutral voices, hallucinating patients had significant deficits, compared to nonhallucinating patients and normal controls (Shea et al., 2007). A recent fMRI study reported that patients with AHs showed abnormal increases in the frontal cortex, the insula, the cingulate, and the amygdala during the auditory processing of emotional words related to the hallucinatory experience (Sanjuan et al., 2007). These regions have been known to be neural structures underlying the emotional processing (Phan et al., 2002). Particularly, the amygdala reportedly plays an important role in processing affective information throughout various emotions and modalities including auditory stimuli (Sander and Scheich, 2001; Phan et al., 2002; Fecteau et al., 2007) and has a reciprocal connection with the prefrontal cortex, the temporal cortex, the insula, and the thalamus (Davis and Whalen, 2001; Das et al., 2005). Taken together, it can be predicted that the presence of AHs may have an influence on activity of the regions engaged in the auditory emotional processing.

This study was designed to investigate the neurobiological basis of emotional disturbances in patients with persisting AHs. Differential brain activation pattern during the auditory emotional processing was determined using laughing and crying sounds as task stimuli for the fMRI in schizophrenic patients with AHs (hallucinators), schizophrenic patients without AHs (nonhallucinators) and normal controls. Based on the previous finding of the involvement of the limbic system during AHs, we hypothesized that the persistence of AHs in patients with schizophrenia would result in functional changes of the emotion-related areas including the amygdala. We expected, therefore, that the hallucinators would show decreased hemodynamic response in the limbic system during the auditory emotional processing.

2. Methods

2.1. Subjects

Subjects consisted of fourteen hallucinators, 14 nonhallucinators and 28 normal controls. The patients were diagnosed using the structured clinical interview for the DSM-IV (SCID-IV) (First et al., 1997) and severity of their symptom was assessed using the positive and negative syndrome scale (PANSS) (Kay et al., 1986). The normal controls were screened for any current or lifetime history of a DSM-IV axis I disorder.

Table 1
Means ± SD of demographic variables for subjects

	Normal subjects (n = 28)	Hallucinators (n = 14)	Nonhallucinators (n = 14)	Significance
Age (years)	29.9 ± 2.9	29.5 ± 4.1	30.4 ± 3.7	N.S.
Sex (male/female)	14/14	7/7	7/7	N.S.
Education (years)	13.6 ± 2.0	12.1 ± 1.4	13.5 ± 2.2	0.04
Duration of illness (years)	–	9.1 ± 4.0	6.7 ± 3.3	N.S.
Auditory hallucination scale (AHS)				
AHS-6: amount of negative content(range 0–4)	–	2.2 ± 1.0	0	
AHS-7: degree of negative content (range 0–4)	–	2.8 ± 0.9	0	
AHS-11: uncontrollability of voices (range 0–4)	–	3.1 ± 0.9	0	
AHS-total (range 0–44)	–	23.3 ± 4.7	0	
PANSS				
Positive (range 7–49)	–	17.9 ± 2.2	13.8 ± 2.3	<0.01
P1: Delusion (range 1–7)		2.9 ± 0.7	2.7 ± 0.8	N.S.
P3: Hallucinatory behavior (range 1–7)		3.7 ± 0.5	1.0 ± 0.0	<0.01
Sum of P scores except for P3 (range 6–42)		14.1 ± 2.1	12.8 ± 2.3	N.S.
Negative (range 7–49)	–	17.3 ± 3.9	16.1 ± 1.7	N.S.
N1: Blunted effect (range 1–7)		2.6 ± 0.9	2.7 ± 0.6	N.S.
N2: Emotional withdrawal (range 1–7)		2.5 ± 0.7	2.4 ± 0.6	N.S.
N3: Poor rapport (range 1–7)		2.0 ± 0.4	1.9 ± 0.5	N.S.
N4: Passive social withdrawal (range 1–7)		2.5 ± 0.7	2.3 ± 0.5	N.S.
N5: Difficulty for abstract thinking (range 1–7)		2.8 ± 0.7	2.4 ± 0.6	N.S.
N6: Lack of spontaneity (range 1–7)		2.4 ± 0.6	1.9 ± 0.7	N.S.
N7: Stereotyped thinking (range 1–7)		2.6 ± 0.6	2.5 ± 0.9	N.S.
General (range 16–112)	–	35.4 ± 5.0	32.2 ± 4.3	N.S.
Total (range 30–210)		70.6 ± 8.4	62.1 ± 7.3	<0.01
Anhedonia total scores* (range 0–101)	21.5 ± 11.1	34.8 ± 10.1	39.5 ± 16.8	<0.01
Social anhedonia scale* (range 0–40)	8.9 ± 4.9	14.5 ± 3.8	16.8 ± 8.1	<0.01
Physical anhedonia scale * (range 0–61)	12.7 ± 7.3	20.3 ± 8.4	22.7 ± 10.3	<0.01
Chlorpromazine equivalent dose (mg)	–	701.8 ± 435.6	435.6 ± 299.6	N.S.

PANSS, positive and negative syndrome scale; N.S., not significant. *Scores were significantly different between schizophrenic patients and normal subjects, but there was no difference between the groups with AH and without AH.