Asian Journal of Psychiatry 5 (2012) 54–57

Contents lists available at SciVerse ScienceDirect

Asian Journal of Psychiatry

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

The study of acoustic startle reflex in male patients with chronic schizophrenia☆

Zhiren Wang [a,1,2], Yunlong Tan [a,1], Fude Yang [a,*], Wufang Zhang [b], Yizhuang Zou [a], Chongsheng Song [a], Yu Zhou [a], Yingli Li [a], Xiangyang Zhang [a,c], Dongfeng Zhou [b,**]

[a] Center for Biological Psychiatry, Beijing Hui-Long-Guan Hospital, Beijing 100096, PR China
[b] Institute of Mental Health, Peking University, Key Laboratory of Mental Health, Ministry of Health (Peking University), Beijing 100191, PR China
[c] Menninger Department of Psychiatry, Baylor College of Medicine, Houston, TX 77030, USA

ARTICLE INFO

Article history:
Received 3 November 2011
Received in revised form 4 December 2011
Accepted 19 December 2011

Keywords:
Schizophrenia
Startle reflex
Prepulse inhibition

ABSTRACT

Objective: To explore the deficits of acoustic startle reflex (ASR) that might exist in Chinese patients with schizophrenia and the effects of antipsychotics on ASR.
Methods: Participants included 25 male patients with chronic schizophrenia treated with typical antipsychotics (typical group), 25 who were treated with atypical antipsychotic clozapine (clozapine group) and 25 healthy male subjects (control group) matched for age and years of education. Startle reflex to acoustic stimuli were examined in all subjects from the three groups. At the same day of startle testing, psychopathological symptoms of the patients were assessed with the Positive and Negative Syndrome Scale (PANSS).
Results: (1) Startle response (SR) was significantly reduced in typical group as compared to control group [(553.6 ± 516.9) mV vs. (942.0 ± 447.3) mV, $P = 0.009$]. SR of clozapine group [(755.9 ± 439.4) mV] was greater than that of typical group and less than that of control group, but there was no significant difference between the clozapine group and the other two. (2) Habituation (HAB) of startle reflex in typical group was significantly lower than in control group [(17.8 ± 35.8)% vs. (44.9 ± 28.9)%, $P = 0.027$]. HAB of clozapine group [(22.9 ± 34.1)%] was higher than that of typical group and less than that of control group, but there was no significant difference between clozapine group and the other groups. (3) Compared with healthy controls, patients of typical group exhibited the significant reduction in prepulse inhibition (PPI) of startle reflex ($P = 0.024$) when prepulse interval (LI) was 120 ms. PPI of clozapine group was higher than typical group and less than control group, but no significant differences in PPI were found between clozapine group and the other groups. While LI was 30- or 120-ms, PPI among the three groups showed not significantly different ($P > 0.05$). (4) No significant relationship was found between PPI of different LIs and symptom scores assessed with PANSS in patients with schizophrenia ($P > 0.05$).
Conclusion: Our findings suggest impaired PPI in Chinese patients with schizophrenia; Atypical antipsychotic clozapine might partly improve disinhibition of startle reflex in schizophrenic patients.

1. Introduction

Core features of schizophrenia include cognitive and emotional disturbances that may be linked to a disruption in the normal processing and/or hierarchical organization of sensory and cognitive information. Furthermore, disturbances in perception, thought and language structure, and behavioral organization in schizophrenia may result from impaired automatic, preconscious inhibitory mechanisms that normally regulate the quantity and quality of sensory and cognitive information that reaches consciousness (Chen and Zhang, 2007).

One of the most common experimental paradigms used to investigate this abnormality is prepulse inhibition (PPI) of the startle response. PPI is usually defined as a reduction of the startle reflex due to weak sensory pre-stimulation and is thought to regulate sensory input by filtering out irrelevant or distracting stimuli to prevent sensory information overflow, allowing for selective and efficient processing of relevant information (Chen and Zhang, 2007).

Many studies (Braff et al., 2001a,b) have consistently demonstrated PPI deficits in schizophrenia, and PPI of ASR has been

☆ *Note*: The results of the survey were published in Chinese Journal of Psychiatry in Chinese (2010, 43, 135–139). The copyright of the paper belongs to Chinese Medicine Association. The data from the study can be published secondly in English authorized by Chinese Medicine Association.

* Corresponding author at: Institute of Mental Health, Peking University, Huayuan North Road 53, Haidian District, Beijing 100191, PR China. Tel.: +86 10 82801998; fax: +86 10 62028350.
** Corresponding author. Tel.: +86 10 62718210.
E-mail addresses: zhiren75@gmail.com (Z. Wang), yangfd200@126.com (F. Yang), zhoudf@bjmu.edu.cn (D. Zhou).
[1] These authors have contributed equally to this work.
[2] Psychiatric Research Center, Beijing Huilongguan Hospital, 100096 Peking, China.

1876-2018/$ – see front matter © 2012 Elsevier B.V. All rights reserved.
doi:10.1016/j.ajp.2011.12.010

considered a candidate endophenotype of schizophrenia (Braff and Light, 2005).

A recent study (Swerdlow et al., 2005) has suggested there may be an ethnic difference in PPI and the magnitude of the startle response between normal Caucasian and Asian subjects. Asians showed decreased ASR amplitude and increased PPI compared with Caucasians.

The general objective of the present study was to explore the deficits of acoustic startle reflex (ASR), including SR, HAB and PPI that might exist in Chinese patients with schizophrenia. In addition, several studies (Quednow et al., 2006; Wynn et al., 2007) suggested that antipsychotic medication, especially atypical antipsychotics, might improve PPI deficits in patients with schizophrenia, so the subjects of schizophrenia were divided with two groups (typical group and clozapine group) in order to further explore the effects of antipsychotics on ASR.

2. Subjects and methods

2.1. Subjects

Participants included 25 male patients with chronic schizophrenia (DSM-IV, American Psychiatric Association, 1994) treated with typical antipsychotics (typical group), 25 those treated with atypical antipsychotic clozapine (clozapine group) and 25 healthy male subjects (control group) matched for age and years of education. All subjects were right-handed Han Chinese being recruited at the same period from Beijing area and had no difficulty in hearing [exclusion for threshold $>$ 40 dB at 1000 Hz, Diagnotic Audiometer, AD229b, Denmark]. No participant had current alcohol or drug abuse, a positive history of alcohol and drug dependence in the last year or lifetime history of 5 years of alcohol or drug abuse/dependence, or any head injury. Subjects abstained from smoking for at least 30 min prior to startle testing, as acute smoking could potentially increase PPI (Meincke et al., 2004a). At the time of startle testing, symptom severity of the patients was assessed with the Positive and Negative Syndrome Scale (PANSS) (Si et al., 2004). In typical group, five patients were finally excluded from data analysis due to inadequate startle amplitude to pulse stimuli alone-"non-startle" (see exclusion criteria below, 3 patients) and refusal to cooperate (2 patients). 12 subjects were current smokers. In clozapine group, four patients were finally excluded from data analysis due to "non-startle", and 10 subjects were current smokers. In control group, three patients were finally excluded from data analysis due to "non-startle", and 13 subjects were current smokers.

There were no significant differences in age, years of education smoking status and the rate of non-startlers of ASR ($P > 0.05$). After being presented with a description of the study, all subjects gave signed informed consent to participate, which was approved by the Research Ethical Committee of Beijing Hui-long-guan Hospital.

2.2. Startle response measurement

Startle reflex to acoustic stimuli was measured by using a SR-HLAB startle response monitoring system for humans (SR-HLAB, San Diego Instruments, San Diego, CA, USA). Methodology for measuring PPI was similar to previous reports (Braff et al., 1992; Swerdlow et al., 2007). The room for the measurement was completely sound-proofed and electrically shielded. The subjects were seated comfortably on a couch. They were alert and instructed to stare at a fixed "*x*" target. Two 5 mm silver/silver chloride electrodes filled with gel were positioned below and lateral to the right eye over the orbicularis oculi, and a ground electrode was placed behind the right ear over the mastoid. All resistances were less than 10 kΩ. The acoustic startle response (eyeblink component) was measured via electromyography (EMG) of the right orbicularis oculi muscle. Recorded EMG activity was band-pass filtered (100–1000 Hz). Amplification was set at 10,000 (a 0.25 mV signal triggered a 2.5 V amplifier output) for all subjects. The system was set to record 250 1-ms readings starting at the onset of the startle (pulse alone) stimulus. All acoustic stimuli were delivered binaurally through headphones.

The test session included a total of 75 active and 16 no-stimulation trials, and began with a 2 min acclimation to white noise at a 70-dB sound pressure level that continued throughout the session. Startle stimuli were 40-ms noise bursts at a 115-dB sound pressure level. Prepulses were 20-ms noise bursts 15 dB higher than background, with onset at 30, 60, or 120 ms (ms) prior to pulse onset. Six startle stimuli (pulse-alone trials, PAs) were presented at the beginning (block 1, the first trial was excluded from data analysis) and five PAs were presented at the end (block 4) of the session, which were used to assess habituation. In blocks 2 and 3, each block consisted of eight PAs, eight trials of prepulse plus pulse at each of the 3 prepulse trial types and eight no-stimulation trials, all presented in a pseudorandom order (range of inter-trial intervals, 11–19 s; mean inter-trial interval, 15 s). In 16 no-stimulation trials, data were recorded without stimulus presentation to assess basal electromyographic activity (no significant main or interaction effects were noted). The entire session lasted approximately 23 min.

A software program (SR-HLAB Review Data) scored the signals automatically, offline according to software parameters derived from published literature (Braff et al., 1992). Subjects, whose ratio (mean pulse alone amplitude in the first block/mean amplitude of base line in the first block) was below 4.0 were excluded from subsequent analyses, which was similar to the criteria for "nonstartlers" established by Braff et al. (Braff et al., 1992). Peak latency (latency from stimulus to maximum blink amplitude) is defined as the point of maximal amplitude occurring within 150 ms from the pulse alone stimulus. Responses in which onset and peak latencies differed by more than 95 ms were considered to be artifactual (not generated by the stimulus) and were discarded. Trials were also discarded if excessive EMG activity was observed during the first 20 ms of recording. Less than 5% of the trials were discarded in both the schizophrenic and normal control groups using these parameters.

In this study, we obtained measures of (1) startle response to PAs in the first block, (2) habituation (%) of startle response during the session calculated by the formula ([1 − mean startle magnitude in block 4/mean startle magnitude in block 1] $\times$ 100), and (3) PPI (%) under the formula ([1 − (mean startle response with prepulse trials)/mean startle response to PAs in the blocks 2 and 3] $\times$ 100).

2.3. Statistical analysis

All statistical analyses were performed with the SPSS 13.0 (Chicago, IL, USA). *F* test and chi-square tests (Fisher's exact test when appropriate) were used to compare means and categorical proportions, respectively. PPI measures with differential parameters were examined with ANOVA, using repeated measures. Data were collapsed across blocks 2 and 3 for PPI analyses because no interactions and main effects of block were observed. Pearson's correlation was employed to see possible correlations between PPI and clinical characteristics. All *p*-values reported are two-tailed. Statistical significance was defined as $P < 0.05$.