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Findings of P_{300}-like and CNV-like potentials in rat model of depression following repeatedly forced swim stress ☆

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ABSTRACT

The aim of this study was to explore whether there were abnormalities of CNV-like and P_{300}-like potentials in stressed rats following repeatedly forced swim stress. Forty male rats were randomly divided into 4 groups: the control groups (Control-1 and Control-2) and the stressed groups (Stress-1 and Stress-2). Rats in stressed groups were administered to repeatedly forced swim 7 or 14 days respectively. Body weight gain, saccharin preference test and open field test were performed. After being anesthetized with urethane, P_{300}-like potentials were evoked by the oddball auditory stimulation and CNV-like potentials were elicited by condition-test stimulus. Results of behavioral tests displayed less body weights and less saccharine solution intake in stressed rats and significant effects of stress on the number of crossing squares, the duration of rearing and the number of grooming in open field test. Prolonged P3 latencies and decreased P3 amplitudes of P_{300}-like potentials were found in the stressed rats. CNV amplitudes were lower in the stressed rats than those in control. Moreover, there were significant correlations between parameters of ERPs (including P3 latency, amplitude and CNV amplitude) and a serial of behavioral traits. This study provides an important evidence of changes of CNV-like and P_{300}-like potentials in depressed rats following repeatedly forced swim stress. Based on this study, ERPs should be taken into consideration and applied as the useful tools in the research work of depressed animal models.

1. Introduction

Depression is considered as a stress-related disorder underscoring the role of stress as a key determinant in disease etiology. Stress model is one of the most suitable animal models for depression accordingly (Henn and Vollmayr, 2005; Vollmayr and Henn, 2003). Among the stress models of depression, the forced swim stress is a putative animal model of depression which emulates the behavioral despair paradigm of depression (Porsolt et al., 1978). In addition, most human depression disorders are induced by chronic stress. In the study we administrated repeatedly forced swim stress to establish animal model of depression.

Depression is characterized by depressed mood, loss of interest, feelings of worthlessness, disturbed sleep or appetite, low energy, poor concentration and suicidal ideations (Fava and Kendler, 2000), which can be partially reproduced and evaluated in animals models by the observation of a series of behavioral traits, such as open field test, saccharin preference test and maze test et al. (Deussing, 2006). Event related potentials (ERPs) can partially and sensitively reflect the state of mood and cognitive function of depressed patients (Cavanagh and Geisler, 2006; Dietrich et al., 2000; Schrijvers et al., 2008). However, up to date, there is rare experimental evidence that the ERPs are used as test facility to appraise the animal models of depression.

P_{300} is known as a tool for evaluating brain function in major depression for several decades (Diner et al., 1985; Kaya et al., 2007; Nandrino et al., 2004; Neuhaus et al., 2007; Santosh et al., 1994). Variations of some components of P_{300} are sensitive index for detecting the impairment of executive and affective processes in depression (Hansenne et al., 2000; Karaaslan et al., 2003; Sumich et al., 2006; Vandoolaeghe et al., 1998). The contingent negative variation (CNV) is a slow negative shift in the electroencephalogram which is a tool to evaluate a serial of complicated psychomotility (Jonkman, 2006; Leuthold et al., 2004; Macar and Besson, 1985; Walter, 1965). It is widely accepted that the CNV waveform is correlated with cognitive functions (such as alertness and arousal) and influenced by emotional state. For example, attention dysfunction or depression decreased the CNV amplitude, on the contrary, great CNV was produced by high level of arousal (Ashton et al., 1994; Boudarene and Timsit-Berthier, 1997; Carretie et al., 2004; Kropp et al., 2001).

Previous reports have demonstrated that CNV-like and P_{300}-like waveforms could be obtained by 'passive' procedure in rats (Ebenezer, 1986; Nakamura et al., 1993; Rucker et al., 1986; Takeuchi et al., 1999). The 'passive' procedure of ERPs is especially suitable for the empirical

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study in anesthetized rats because of the convenient application and the exclusion of perturbation of autonomic activities of animals (Ebenezer, 1986; O'Brien, 1982; Rucker et al., 1986). Although the interference of anesthetized state might decrease the amplitudes of ERPs, some studies have found that the ERPs latencies and scalp distribution were similar with those in human (Ebenezer, 1986; O'Brien, 1982). In recent years, although there were few articles related P_{300} and CNV in rats carried out under anesthesia state, some original articles about mismatch negativity (MMN) in anesthetized rats found that anesthetized rats could respond to auditory stimulus and anesthesia state did not hamper the occurring of MMN (Eriksson and Villa, 2005; Lazar and Metherate, 2003; Tikhonravov et al., 2008). In addition, ERPs could be recorded in some comatose patients in clinical electrophysiology detection (Daltrozzo et al., 2007; Gott et al., 1991; Kane et al., 1996). Therefore, we presumed that CNV-like and P_{300}-like potentials in anesthetized rats could also be recorded.

The aims of the study were to investigate the variances of CNV-like and P_{300}-like potentials in stress-related depression animals and establish whether there was a relationship between ERPs and behavioral traits in depressed animals following repeatedly forced swim stress.

2. Materials and methods

2.1. Animals

Male Sprague–Dawley rats weighing 160–180 g at the beginning of the experiments were obtained from the Medical Laboratory Animal Center, Chengdu University of Traditional Chinese Medicine. The procedure of the studies was conducted according to the guidelines for the care and use of laboratory animals approved by the Chinese government. Forty rats were randomly divided into 4 groups with 10 rats in each group: the control groups (7 days group marked as Control-1 and 14 days group marked as Control-2) and the stressed groups (7 days group marked as Stress-1 and 14 days group marked as Stress-2). All rats were housed singly under controlled temperature (21 ± 1 C) and maintained on a 12 h light/dark cycle (with light on, 08:00 am–20:00 pm) with food and water available ad libitum. They were acclimated to 5 min of handling once a day for 7 consecutive days (control phase) before being used in experiment. Behavioral traits of all rats were observed and measured by body weighing, saccharine preference test and open field test.

2.2. Stress procedure

Stressed group rats were individually subjected to forced swim stress which was performed for 5 min between 08:00 am and 10:00 am in a blue, opaque and round plastic cylinder (50 cm height, 30 cm diameter) filled with 30 cm depth of water (10 ± 0.5 °C) for 7 (Stress-1 group) or 14 (Stress-2 group) consecutive days (Qi et al., 2006). All stressed group rats were alternate in order each day and the water was changed as 2 rats were done. Control group animals were left undisturbed in the home cages except for the necessary administration such as regular cage cleaning and weighing.

2.3. Behavioral tests

2.3.1. Body weight gain

All rats were weighed on the 1st day of handling, at the end of control phase (baseline) and on the next day of the last forced swim stress (Stress-1, Control-1, 8th day; Stress-2, Control-2, 15th day, respectively). Body weight gain was calculated as a percentage of individual body weight on baseline (the ratio of body weight gain).

2.3.2. Saccharin preference test

The habituation of drinking saccharin was performed during the control phase. Rats were provided a free choice between two bottles during habituation and test. One bottle contained water and the other contained 1% saccharin solution. To avoid the possible effects of side preference in drinking, the position of the bottles was switched after 12 h. We measured the consumption of water and saccharin solution of rats by weighing the bottles during 24 h time window starting from 08:00 am on the last day of control phase (baseline) and 10:30 am on the last-stressed day. To prevent the confounding influence on the saccharin preference test, the animals were not deprived of water or food throughout entire experiment (Harris et al., 1997). The saccharin preference was calculated as saccharin intake/total (saccharin + water) intake.

2.3.3. Open field test

The recording of open field test was performed between 08:30 am and 10:30 am on the last day of control phase (baseline), then on the 8th (Stress-1, Control-1) and 15th day (Stress-2, Control-2) respectively after weighed. Each animal was placed in the centre of the open field (76 cm square chamber, 40-cm-high walls, light of 40 lx. with its floor divided into 25 equal squares) for 5 min in a quiet room (Zheng et al., 2006). The number of crossing squares (also named locomotor, at least three paws in a square), the number of rearing (also named explorer activity, posture sustained with hind-paws on the floor) and the times of grooming (including washing or mouthing of forelimbs, hind-paws, face, body and genitals) were counted manually for 5 min (Wang et al., 2008). The square chamber was cleaned each time after testing a rat.

2.4. ERPs recording

ERPs were recorded with the 4-channel Electromyography/Evoked potential system (Nihon Kohden, Japan). Rats were anesthetized with one dose of urethane (1.2 g/kg, i.p., Sigma Chemical Company). It was considered to be anesthetized successfully that the rats had no response to pinching of the tail. Needle electrodes were placed in the scalp muscle of skull fonticulus minor of median suture (recording), apex nasi(reference), and tail (ground). The rectal temperature of all rats was maintained at 37 ± 1 °C throughout the experiment.

2.4.1. P_{300}-like potentials

The P_{300}-like waveforms were evoked with the 'oddball' paradigm (O'Brien, 1982).Twenty deviant sounds (2000-Hz frequency, 95-dB sound pressure level, 100-ms duration, 10-ms rise and fall times) were randomly presented in 80 standard sounds (1000-Hz frequency, 60-dB sound pressure level, 100-ms duration, 10-ms rise and fall times) with a stimulation rate of 0.5 Hz. The data of 20 trials of P_{300} signals were averaged, and filtered with a band filter from 0.01 Hz–30 Hz. The sensitivity was 10 μV/Div, and analysis time was 100 ms/Div.

The peak latencies of N1, N2, P3 subcomponents were measured with the marks in the evoked potential system. Considering the stability of wave N1, the amplitude of wave P3 was defined the voltage from the peak of wave N1 to the trough of wave P3.

2.4.2. CNV-like potentials

Intersession intervals between P_{300} and CNV were at least 10 min. CNV-like potentials were recorded by condition-test stimulus (S1–S2): an electrical stimulus (50-Hz stimulating rate, 30-mA current intensity, 0.1-ms pulse duration, 1-s stimulating duration) to a footplate after an auditory stimulus (2000-Hz frequency, 105-dB sound pressure level, 100-ms duration, 10-ms rise and fall times). The interval of S1–S2 was 2 s and intertrial intervals of 30 trials varied randomly from 5 to 10 s. Before recording, ten training trials were given for habituation. The data of 30 trials of CNV signals were averaged, and filtered with a band filter from 0.01 Hz–30 Hz, and sensitivity was 20 μV/Div, and analysis time was 500 ms/Div.

The baseline was defined by a cursor when the voltage showed 0.00 μV. The onset latency (OL) of expectancy wave (A point) in CNV was