Int J Clin Exp Med 2014;7(4):1110-1115
www.ijcem.com /ISSN:1940-5901/IJCEM1401060

Original Article

Study on the executive function of attention in depression patients based on SPECT technology

Xiaoyi Li[1,2], Hao Wu[3,4], Cen Lou[4,5], Baoping Xing[1,2], Enyan Yu[2]

[1]Department of Psychiatry and Mental Health, Tongde Hospital of Zhejiang Province, Hangzhou 310012, China; [2]The Mental Health Institute of Zhejiang Province, Hangzhou 310012, China; [3]Department of Psychiatry and Mental Health, Affiliated Sir Run Run Shaw Hospital, Medical School of Zhejiang University, Hangzhou 310016, China; [4]Sir Run Run Shaw Institute, Clinical Medicine of Zhejiang University, Hangzhou 310016, China; [5]Department of Nuclear Medicine, Sir Run Run Shaw Hospital, Zhejiang University School of Medicine, Hangzhou 310016, China

Received January 31, 2014; Accepted April 11, 2014; Epub April 15, 2014; Published April 30, 2014

Abstract: Objective: To investigate event-related potential in executive function of attention and characteristics of cerebral perfusion by 99mTc-ECD single-photon emission computed tomography (SPECT) in depression patients receiving the Oddball task. Methods: A total of 30 depression patients and 30 normal control subjects were selected to carry out the Oddball task. Event-related potential (ERP) technology combined with SPECT imaging technology was used to compare the reaction time, ERP-P300 latency and amplitude, and cerebral perfusion characteristics on sites of brain. Results: Compared with normal control group, when the Oddball task was performed, the reaction time or ERP-P300 latency was not significantly different in depression patients ($P > 0.05$), but P300 amplitude on F3 and F7 sites increased significantly ($t = 2.241$, 2.245, respectively; each $P < 0.05$). SPECT showed cerebral hypoperfusion in the right basal ganglia, left frontal lobe and temporal lobe of depression patients. Conclusion: During the Oddball task, the P300 amplitude on F3 and F7 sites increased significantly in depression patients, who also showed cerebral hypoperfusion in the right basal ganglia, left frontal lobe and temporal lobe. The result suggests that depression patients have brain region functional abnormalities involving attention execution and implicit memory processing during auditory channel information processing.

Keywords: Depression, event-related potentials, P300, executive function, tomography, emission-computed, single-photon

Introduction

Depression is a common disease with high morbidity. Patients often experience negative emotions and thinking disposition, feel obvious pain and bring heavy disease burden to the society [1]. Increasing studies have shown that depression patients have cognitive dysfunction, especially short-term memory, attention breadth and stability defect [2], and we assume that the abnormalities may be related to attention processing pattern and brain region function in depression patients. Functional magnetic resonance imaging (fMRI) has revealed that under functional tasks the activity in the right dorso-lateral prefrontal lobe, prefrontal cortex and anterior cingulate regions decreased in first-onset depression adolescents [3]. In order to investigate event-related points under executive function of attention and cerebral perfusion characteristics in depression patients, event-related potential (ERP) technology and single photon emission computed tomography (SPECT) were applied to detect P300 evoked potential and obtain simultaneous cerebral perfusion characteristics of depression patients conducting the Oddball task.

Subjects and methods

Subjects

Inclusion criteria of the depression group included: 1) The diagnosis complied with diagnostic criteria for depressive episode in *Chinese Classification and Diagnostic Criteria for Mental Disorders, 3rd edition (CCMD-3 and DSM-IV)*; 2) The age ranged from 18 to 60 years old and a

subject could be a male or a female; 3) HAMD-17 rating was ≥ 24 points; 4) A patient had not taken anti-depressant agents or other antipsychotic drugs; had not taken too much dopa preparation or dopa function regulators in the recent two years. Exclusion criterion was: patients who suffered from diseases of liver, gallbladder, heart, lung, kidney, intestine and other vital organs, or suffered from brain organic diseases should be excluded. Inclusion criteria of the normal control group included: 1) gender, age, education level and income basically matched with those in the patient group; 2) Physically and mentally healthy at entry; no abnormalities were found during physical examination; No any mental disorder meeting diagnostic criteria; 3) HAMD-17 rating was ≤ 7 points; 4) No history of special drug use and no history of special drug use within two weeks. A written informed consent was obtained from each subject.

Oddball task and 99mTc-ECD SPECT

The Oddball task was compiled by psychological-dedicated software E-Prime (Version 1.2.1.844) with 100 single tones, including 80% standard non-target stimulation with a sound intensity of 60 dB, a frequency (Spl) of 1000 Hz, a rise and fall time of 10 ms, a duration of 50 ms, and 20% target stimulation with a sound intensity of 60 dB, a frequency (Spl) of 1500 Hz, a rise and fall time of 10 ms, a duration of 50 ms.

The experiment was performed by professionals in a soundproof shielding cerebral electrophysiology room. The subject sat in a chair and first put on a 10-20 system standard electrode cap which matched with a 32-channel event-related brain potential system produced by Brain Product Company. A reference electrode was placed on the connecting line between bilateral mastoids, the forehead was connected to the ground, and the 32 channel cerebral electricity was recorded, while a recording electrode was placed 1.5 cm above the right eye to record the ocular electricity and ECG electrodes were placed to record ECG. Then the subject relaxed muscles, closed his or her eyes, and always kept a clear head and kept attention.

After the subject accepted binaural auditory Oddball stimulation task, standard non-target stimulation and target stimulation randomly alternated. The subject was urged to at once push response key "1" with the right index finger when he or she had heard the target stimulation. The interval of the stimulation task was 1200 ms or 1500 ms randomly. Before the official test started, the subject exercised the same procedure until the target stimulation occurred twice. After completion of the test, a vein indwelling needle was left for intravenously injecting cerebral perfusion imaging agent when event-related cognitive potential P300 was detected.

Five minutes after the venous needle was indwelled, cerebral perfusion imaging agent (marked with 99mTC) was slowly injected (micro pump) and P300 was simultaneously detected. 60 minutes after P300 detection, SPECT scanning was performed by using Millennium VG8 SPECT instrument with low-energy high-resolution collimators. 128 × 128 matrix brain tomography rotated for 360°, reconstruction was performed by the computer, and coronal, sagittal, and cross-sectional three-dimensional images were obtain by SPECT scanning.

SPECT image analysis

Corresponding irregular (ROI) interesting region in each layer of images was outlined, and the beginning was on right side and the mirror image was precisely copied to left side. On the third layer, the cerebellum was outlined; on the 6th layer, frontal and temporal lobes were outlined; on the 7th layer, cingulate gyri, basal ganglias and frontal lobes were outlined; on the 8th layer, the cingulate gyri, temporal lobes, thalami, prefrontal and occipital lobes were outlined; on the 10th layer, frontal lobes were outlined; on the 11th layer, frontal and parietal lobes were outlined. X-Ppert workstation computer dedicated software was used for semi-quantitative analysis, rCBF average per pixel count on bilateral occipital lobes was considered as reference value, rCBF radioactivity ratio (RAR) on each brain region was calculated, and RAR = average per pixel count on each brain region ROI/reference value [4].

ERP recording, collection and processing

During execution of the Oddball task, analysis and interception of latency, amplitude and reaction time were performed for P300 presented on each electrode site. The Brian Vision

Table 1. P300 latency and amplitude results on all sites during execution of Oddball auditory stimulation in the depression group and normal control group

Electrode site	Depression group		Normal controls		$t_{latency}$	$P_{latency}$	$t_{amplitude}$	$P_{amplitude}$
	Latency (ms)	Amplitude (μv)	Latency (ms)	Amplitude (μv)				
F3	337.64 ± 44.19	4.28 ± 2.98	331.69 ± 48.81	2.66 ± 2.04	0.370	0.714	2.241	0.032*
F4	338.91 ± 51.94	3.63 ± 2.55	342.00 ± 48.09	2.52 ± 1.41	-0.179	0.859	1.478	0.149
C3	353.23 ± 55.54	3.62 ± 2.38	340.47 ± 43.66	3.08 ± 2.28	0.799	0.429	0.735	0.466
C4	362.27 ± 68.09	3.39 ± 2.28	339.16 ± 43.50	3.69 ± 2.97	1.450	0.154	-0.390	0.699
P3	351.75 ± 49.10	5.19 ± 3.06	350.09 ± 48.19	5.25 ± 4.98	0.125	0.901	-0.053	0.958
P4	362.32 ± 59.53	5.94 ± 3.96	343.33 ± 49.82	5.62 ± 5.23	1.258	0.214	0.262	0.794
O1	363.17 ± 53.19	5.82 ± 3.58	340.76 ± 45.86	6.08 ± 5.99	1.556	0.126	-0.194	0.847
O2	364.69 ± 59.92	6.36 ± 4.15	336.18 ± 52.87	6.14 ± 6.43	1.769	0.083	0.147	0.884
F7	331.36 ± 57.99	6.88 ± 5.38	334.00 ± 44.99	5.02 ± 2.42	-0.161	0.873	2.245	0.031*
F8	344.96 ± 53.56	6.73 ± 6.43	325.67 ± 40.88	5.23 ± 3.33	1.100	0.279	0.700	0.489
T7	332.52 ± 49.05	6.19 ± 3.85	325.71 ± 47.70	4.60 ± 4.29	0.414	0.682	1.186	0.243
T8	338.40 ± 57.64	6.11 ± 5.33	322.22 ± 84.54	5.83 ± 6.53	0.788	0.434	0.162	0.872
P7	334.90 ± 49.90	5.49 ± 3.25	342.22 ± 45.24	5.66 ± 4.84	-0.507	0.615	-0.150	0.881
P8	350.00 ± 64.46	5.76 ± 3.45	343.11 ± 48.77	6.54 ± 5.51	0.387	0.701	-0.590	0.559
FZ	350.67 ± 43.23	2.96 ± 1.63	319.00 ± 46.46	2.37 ± 1.71	1.248	0.232	0.568	0.579
CZ	344.00 ± 48.88	2.45 ± 1.25	345.85 ± 49.55	2.93 ± 2.78	-0.096	0.925	-0.565	0.577
PZ	351.88 ± 53.19	5.76 ± 3.34	346.09 ± 47.95	5.51 ± 4.69	0.417	0.678	0.236	0.815
OZ	356.77 ± 56.26	6.45 ± 4.16	341.64 ± 50.36	6.32 ± 6.56	1.001	0.322	0.089	0.930
FC1	339.60 ± 40.28	2.74 ± 1.52	347.33 ± 60.15	2.23 ± 1.47	-0.310	0.761	0.661	0.519
FC2	360.95 ± 52.04	2.66 ± 1.60	354.77 ± 44.13	2.26 ± 1.39	0.356	0.724	0.740	0.465
CP1	355.85 ± 49.77	4.31 ± 2.39	355.43 ± 47.42	3.49 ± 2.83	0.030	0.976	1.080	0.286
CP2	355.10 ± 54.54	4.23 ± 2.36	346.611 ± 54.55	4.45 ± 4.27	0.575	0.568	-0.241	0.811
FC5	327.00 ± 38.21	4.41 ± 2.81	341.75 ± 45.82	4.02 ± 2.49	-1.104	0.276	0.446	0.658
FC6	346.40 ± 55.88	4.61 ± 3.97	333.25 ± 50.76	4.18 ± 3.56	0.761	0.451	0.352	0.727
CP5	348.67 ± 53.09	5.17 ± 3.11	337.20 ± 45.74	4.97 ± 4.63	0.789	0.434	0.181	0.857
CP6	354.48 ± 58.81	5.35 ± 3.91	343.16 ± 49.00	6.27 ± 5.98	0.695	0.490	-0.642	0.524
TP9	344.36 ± 55.42	5.74 ± 4.13	336.67 ± 43.68	6.29 ± 5.52	0.415	0.681	-0.330	0.743
TP10	354.00 ± 68.24	6.46 ± 4.86	336.00 ± 39.25	5.76 ± 4.53	1.058	0.297	0.442	0.661

*$P < 0.05$.

Recorder (Version 1.030003) recording software and Andlyzer (Version 1.05.0004) analysis software ran automatically. Scalp impedance was ≤ 50 kΩ and band-pass filter ranged from 0.01 to 70HZ; sampling was performed continuously and the sampling rate was 1000 Hz/electrode. Analysis time (epoch) was 1000 ms with a baseline 200 ms, while the reaction time and keystroke accuracy were recorded, as well as blinking, ECG and other artifacts were automatically corrected and amplitude ± 100 μv would be automatically removed. Indicators of analysis were P3 latency and amplitude of target stimulation on 32 electrode sites and time analysis window was 250 ms-500 ms. Within analysis and measurement window, the vertex of positive peak with greatest amplitude was baseline for measuring amplitude and peak, and the actual superimposed times were 35-40.

Statistical analysis

SPSS 12.0 software package was used. Measurement data were expressed as mean ± standard deviation ($\bar{x}$ ± SD). Student t test was used for comparison between two groups. $P < 0.05$ was considered statistically significant.

Results

A total of 30 patients with a mean age of 35 ± 12 years old were included in the depression

Table 2. RAR results of SPECT cerebral perfusion in depression group and normal control group

Group	Left frontal lobe	Left temporal lobe	Right basal ganglia
Depression group	0.91 ± 0.19	0.82 ± 0.19	0.72 ± 0.15
Normal control group	0.98 ± 0.17	0.94 ± 0.17	0.95 ± 0.15
t value	3.076	3.038	3.655
P	< 0.05	< 0.01	< 0.01

group, including 12 males and 18 females, and the mean disease course was 7 ± 3 months. The normal control group consisted of 30 subjects including 12 males and 18 females whose mean age was 36 ± 12 years old.

During the Oddball Auditory identification task, there was no significant difference between the reaction time of depression patients and that in normal control group (424.28 ± 94.95 ms vs. 418.75 ± 59.35 ms, t = 0.857, P > 0.05). There was also no significant difference in P300 latencies between the two groups (P > 0.05). The P300 amplitude on F3 and F7 sites in depression patients conducting the Oddball auditory task increased significantly, as compared with normal control group (t = 2.241, 2.245, respectively; each P < 0.05) (**Table 1**). SPECT results showed that depression patients had cerebral hypoperfusion in the left frontal lobe (24 cases, 80%), the left temporal lobe (24 cases, 80%) and the right basal ganglia (25 cases, 83.3%) during execution of the Oddball auditory task (see **Table 2**).

Discussion

Current studies have shown that people's emotional state and reaction are directly linked to the subcortical limbic system and cortical advanced cognitive style, and implicit memory as well as attention network plays an important role. We know that the frontal lobe is the advanced centrum of attention processing and regulation [5], and event-related potential P300, which is related to memory system and complex cognitive process, is considered to be an objective indicator of cognitive function and can early, objectively, quantitatively reflect the level of cognition [6]. It is generally believed that: the latency of P300 reflects brain cognitive processing speed to stimulation information, while the amplitude of P300 is related to a subject's attention to target stimulation [7] and the level of amplitude represents intensity of brain information processing.

In this study, we found that, while performing the oddball task, there was no statistically significant difference in the reaction time or P300 latency between depression patients and controls (P > 0.05), but there was statistically significant difference in the amplitude increase on F3, F7 regions between depression patients and controls (P < 0.05). The result indicates that depression patients have brain stimulation cognitive processing time required similar to normal control group, but attention processing state in different brain regions vary somewhat, i.e. there is enhancement on F3 and F7 regions. The result is somewhat different from results of previous studies. Kocmur et al [6, 8] reported that in patients with early-stage depression, depression and anxiety interfere with attention to target stimulation, thereby reducing the intensity of information processing in the brain. This may be somewhat related to the fact that attention execution tasks and channels are different.

Based on a large number of results in cognitive psychology and biological science, Posner [9, 10] proposed that attention was an independent network in the brain and the network was divided into three sub-networks i.e. alertness, orientation, and execution control: a) "alertness" refers to keeping alert state in order to accept afferent information; b) "orientation" refers to selecting information from afferent information; c) "execution control" refers to the ability to resolve conflicting responses. Posner et al [11-13] found that each of three sub-networks in the brain had its own anatomical region. For example, when clues are hinted before a target appears the right frontal and parietal region was activated, therefore, it is thought that "alertness" function is related to the frontal and parietal regions of the right hemisphere. Similarly, it is thought that visual "orientation" function is related to upper parietal lobe, temporal and parietal junction subcortical region, and the superior colliculi of midbrain, pulvinars and thalamic reticular structure.

From studies on animal models and epilepsy patients, Mirsky et al [14-16] pointed out that each part of attention function had related brain region structure. For example, brain regions related to "concentration" and "execu-

tion" of attention are upper temporal lobe cortex, lower parietal cortex and striatum; brain regions functionally related to "continuousness" and "stableness" are mainly in midbrain structure, including brain midline subcortical reticular structure and hypothalamic nuclei; brain structures related to "conversion" function are the prefrontal cortex and anterior gray matter of cingulate gyri; brain structures related to "coding" function are mainly the limbic system, including hippocampi and anterior gray matter of temporal lobes. Gitelman et al [17] have reported that the frontal lobe and parietal lobe constituted neural network to mutually coordinate for finishing spatial attention function; frontal eye field (FEF) mainly controls spatial exploratory behavior; posterior parietal lobe mainly controls afference of spatial information; the attention allocation for surrounding space depends on the coordination of FEF and posterior parietal lobes. The dopamine system in anterior cingulated gyri and lateral prefrontal lobes is thought to play a leading role during the execution of control functions [18]. The dopamine transporter in the basal ganglia of depression patients showed decline of function similar to that in patients with Parkinson's disease [19], suggesting that the dopamine system plays a role in the pathophysiological mechanism of depression.

Our study has found that, during the oddball task, attention processing state in different brain regions varied in depression patients somewhat. For example, F3 and F7 region presented enhanced activity, and SPECT scanning displayed hypoperfusion on the left frontal and temporal lobe and the right basal ganglia. It is indicated that when depression patients receive non-verbal auditory cognitive stimulation, F3 and F7 brain regions are active; when no task is performed, the cortex of left frontal and temporal lobes present functional abnormality and the subcortical right basal ganglias involving dopa neurotransmitter system also presents dysfunction. It is indicated that attention execution and implicit memory processing brain regions present functional dysfunction during auditory channel information processing in depression patients.

In conclusion, our study found that, during the auditory Oddball task, the P300 amplitude on F3 and F7 sites of depression patients increased, and SPECT showed that perfusion of the right basal ganglia, left frontal and temporal lobe decreased, indicating that depression patients have functional abnormalities involving intention execution and implicit memory processing brain regions during the auditory channel information processing. Whether this phenomenon is related to repression mechanism in psychological defense model is worthy further investigation. However, the limitation of this study is that the sample was from a general hospital outpatient and is different in the severity and subtypes of the disease from a special hospital, especially from the inpatient department of a special hospital. Therefore, further research should be done to confirm the universality of the findings that when depression patients perform the Oddball auditory task, P300 amplitude on F3 and F7 sites increases but SPECT imaging shows there is hypoperfusion on the left frontal, temporal lobe and the right basal ganglia. In addition, how to combine ERP and SPECT imaging with other research techniques is worth further exploration in future studies.

Acknowledgements

This study was supported by Natural Science Foundation of Zhejiang Province (Y2091289), Medical Health Science and Technology Research Project of Zhejiang Province (2014KYB133) and Traditional Chinese Medicine Scientific Research Foundation of Zhejiang Province (2012ZB004 and 2014ZB013).

Disclosure of conflict of interest

None.

Address correspondence to: Dr. Hao Wu, Department of Psychiatry and Mental Health, Affiliated Sir Run Run Shaw Hospital, Medical School of Zhejiang University, 3 Qingchun East Rd., Hangzhou 310016, China. Tel: +86-571-86006086; Fax: +86-571-86006774; E-mail: wuhaodoc@163.com (HW); lixiaoyi_00@163.com (XYL)

References

[1] Whiteford HA, Degenhardt L, Rehm J, Baxter AJ, Ferrari AJ, Erskine HE, Charlson FJ, Norman RE, Flaxman AD, Johns N, Burstein R, Murray CJ and Vos T. Global burden of disease attributable to mental and substance use disorders: findings from the Global Burden of Disease Study 2010. Lancet 2013; 382: 1575-1586.

[2] Luo LL, Chen X, Chai Y, Li JH, Zhang M and Zhang JN. A distinct pattern of memory and attention deficiency in patients with depression. Chin Med J (Engl) 2013; 126: 1144-1149.
[3] Halari R, Simic M, Pariante CM, Papadopoulos A, Cleare A, Brammer M, Fombonne E and Rubia K. Reduced activation in lateral prefrontal cortex and anterior cingulate during attention and cognitive control functions in medication-naive adolescents with depression compared to controls. J Child Psychol Psychiatry 2009; 50: 307-316.
[4] Johnson KA, Kijewski MF, Becker JA, Garada B, Satlin A and Holman BL. Quantitative brain SPECT in Alzheimer's disease and normal aging. J Nucl Med 1993; 34: 2044-2048.
[5] Tang CM. Neuropsychology. Beijing: People's Military Medical Press, 2002.
[6] Kocmur M, Milcinski M and Budihna NV. Evaluation of brain perfusion with technetium-99m bicisate single-photon emission tomography in patients with depressive disorder before and after drug treatment. Eur J Nucl Med 1998; 25: 1412-1414.
[7] Zhang MD and Chen XS. Science of brain evoked potential. Shanghai: Shanghai Science and Technology Education Press, 1995.
[8] Tang XF. Neurology-nervous system clinical electrophysiology. Beijing: People's Military Medical Press, 2002.
[9] Posner MI and Petersen SE. The attention system of the human brain. Annu Rev Neurosci 1990; 13: 25-42.
[10] Posner MI and Gilbert CD. Attention and primary visual cortex. Proc Natl Acad Sci U S A 1999; 96: 2585-2587.
[11] Fossella J, Posner MI, Fan J, Swanson JM and Pfaff DW. Attentional phenotypes for the analysis of higher mental function. ScientificWorldJournal 2002; 2: 217-223.
[12] Corbetta M, Kincade JM, Ollinger JM, McAvoy MP and Shulman GL. Voluntary orienting is dissociated from target detection in human posterior parietal cortex. Nat Neurosci 2000; 3: 292-297.
[13] Petersen SE and Posner MI. The attention system of the human brain: 20 years after. Annu Rev Neurosci 2012; 35: 73-89.
[14] Mirsky AF and Duncan CC. A nosology of disorders of attention. Ann N Y Acad Sci 2001; 931: 17-32.
[15] Zahn TP and Mirsky AF. Reaction time indicators of attention deficits in closed head injury. J Clin Exp Neuropsychol 1999; 21: 352-367.
[16] King VL, Brooner RK, Kidorf MS, Stoller KB and Mirsky AF. Attention deficit hyperactivity disorder and treatment outcome in opioid abusers entering treatment. J Nerv Ment Dis 1999; 187: 487-495.
[17] Benes FM. Emerging principles of altered neural circuitry in schizophrenia. Brain Res Brain Res Rev 2000; 31: 251-269.
[18] Wu H, Lou C, Huang Z and Shi G. SPECT imaging of dopamine transporters with (99m)Tc-TRODAT-1 in major depression and Parkinson's disease. J Neuropsychiatry Clin Neurosci 2011; 23: 63-67.
[19] Gitelman DR, Nobre AC, Parrish TB, LaBar KS, Kim YH, Meyer JR and Mesulam M. A large-scale distributed network for covert spatial attention: further anatomical delineation based on stringent behavioural and cognitive controls. Brain 1999; 122: 1093-1106.