Clinical Application and Research Progress of Common Event-Related Potentials

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Abstract This paper review focuses on the diagnostic application and clinical efficacy correlation of event-related potentials, such as P300, MMN, CNV and N400, in patients with depression, and provides a reliable theoretical basis for the diagnosis and prognosis of later depression.

Key words Depression, Cognitive function, EEG biofeedback, Research progress

1 Introduction

Depression is a mental illness with low mood and loss of pleasure as the main manifestations[1]. Approximately 4.7% of the global population has had a depressive episode in any of the past 12 months, with an average episode duration of approximately 6 months[2]. Evidence shows that as the disease progresses, the characteristics of patients' symptoms also change[3-4]. At present, the research on event-related potentials in patients with depression has become a research hotspot. Now the research progress of cognitive impairment and event-related potentials in depression at home and abroad is reviewed and summarized to provide a reference for the diagnosis and treatment of depression[5].

2 Cognitive impairment of depression and its importance

Depression is a kind of chronic mental illness with high prevalence, high disease burden, high recurrence rate, high disability rate and high suicide rate, and it is common disease in psychiatry[6]. Epidemiological survey shows that the lifelong prevalence rate of depression in China is 3.4%[7]. Up to now, major depressive disorder has become one of the main causes of disability in the world[8]. Therefore, the research on depression is of great significance. Depression is a mood disorder, and its typical clinical manifestations are low mood, delayed thinking, decreased volitional activity, impaired cognitive function, *etc.*[9]. A large number of studies at home and abroad have found that patients with depression have different degrees of cognitive impairment, and cognitive symptoms can occur earlier than other symptoms of depression. It is an important item of diagnostic criteria for depression and an important residual symptom, which seriously affects patients' life and work[10]. In recent years, with the development of magnetic resonance imaging, neurobiochemical detection, brain evoked potentials and other technologies, the research on cognitive symptoms of patients with depression has been further developed, and the research on brain evoked potentials provides electrophysiological evidence for cognitive impairment of depression[11].

3 Application of common event-related potentials in the diagnosis of depression

Event-related potentials (ERP) are brain evoked potentials, which refer to the changes of brain potentials related to human cognitive function. They are recorded on the scalp surface and separated from EEG by signal filtering and superposition. At the same time, they have high time resolution and can effectively explore the cognitive processing stage[12]. The endogenous components, such as P300, mismatch negativity (MMN), contingent negative (CNV) and N400, reflect different advanced cognitive processing processes[13]. The mismatch negativity (MMN) and P300 are common ERP components that have been studied frequently at present. MMN is an ERP component with a negative incubation period of 150 - 250 ms, which can reflect the preattentive processing. Its neurogenesis is located in the primary auditory cortex and prefrontal cortex. Decreased MMN amplitude and prolonged incubation period are helpful for the diagnosis of depression, and are correlated with the degree of depression, which can reflect the efficacy of antidepressant, and may be biomarkers for the differential diagnosis of depression and bipolar disorder[14].

3.1 Application of P300 P300 is a late forward wave with an incubation period of about 300 ms evoked by stimuli. P300 amplitude and incubation period provide information on cognitive processes such as memory, attention and mental processing speed. The reduction of P300 amplitude reflects extensive cognitive impairment in patients with depression, can improve the diagnostic accuracy of depression, and can also reflect antidepressant efficacy to some extent, which may be a potential biomarker to distinguish major depressive disorder from bipolar disorder[15].

P300 was first discovered by Sutton in 1965 and is one of the most important ERP components used to assess cognitive function[16]. P300 amplitude and incubation period provide information on cognitive processes such as memory, attention, and mental processing speed. The decrease in P300 amplitude suggests impaired

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processing of targets by individuals, reflecting widespread cognitive impairment in patients with depression[17]. A large number of studies have found that adult patients with depression undergo a decrease in P300 amplitude. Santopetro *et al.* induced P300 and reward positivity (RewP) in patients with depression through the gambler task, and found that the amplitude of P300 in patients with depression decreased, especially in patients with more severe anhedonia. They also found that individuals with high reward positivity (RewP) were more likely to be in depression if they showed lower P300, suggesting that combining P300 and RewP could improve the diagnostic accuracy of depression[18]. White *et al.* found that patients with better compliance during treatment showed higher P300 amplitude, so they believed that P300 could predict patients' treatment compliance and guide doctors' treatment plans[19]. P300 can also be used as a biological indicator to reflect the degree of depression in patients. Studies have found that P300 induced by bimodal stimulation has higher sensitivity, and its amplitude of P300 is negatively correlated with Hamilton Depression Rating Scale (HAM-D) score, suggesting that P300 induced by bimodal stimulation can better reflect the degree of depression in patients[20]. In recent years, there have been more studies on antidepressants to improve cognitive impairment in patients. For example, fluoxetine may improve the cognitive function of patients with depression by regulating P300, which shows that the incubation period of patients is significantly shortened and the amplitude is increased after treatment. For elderly patients with depression, the combination of amisulpride and citalopram showed a significant recovery of P300 incubation period and amplitude compared with citalopram alone[21]. However, in some patients with depression, the amplitude of P300 cannot be completely recovered after drug treatment, which may be related to the brain regions with cognitive impairment. Some scholars have concluded that the left superior parietal lobe and precuneus may be the targets for the treatment of depression. Therefore, it is possible to judge the efficacy of antidepressant treatment and adjust the treatment plan according to P300, which opens up a new idea for the treatment of depression[22]. With the increasing incidence of depression year by year, P300 will get more extensive research and clinical application.

3.2 Application of MNN MMN is an ERP component with a negative incubation period of 150 – 250 ms, and it is usually induced by Oddball paradigm, interspersed with "bias stimulus" in highly repetitive "standard stimulus", and the ERP induced by standard stimulus and bias stimulus is superimposed and subtracted[23]. The decrease of MMN amplitude is considered to be related to various fields of mental disorders, especially social cognitive function. Active MMN often implies that patients have higher work efficiency and better independent living ability[24]. A large number of studies have shown that the amplitude of MMN in patients with depression decreases and the incubation period is prolonged. Tseng *et al.* included 13 clinical studies for meta-analysis to explore the effects of different bias types (duration, frequency) on MMN in patients with depression, and found that the amplitude of duration-deviant MMN (dMMN) in patients with depression decreased significantly and the incubation period was significantly prolonged, but the frequency-deviant MMN (fMMN) was not significantly different from that in healthy controls, suggesting that dMMN may be an electrophysiological indicator to distinguish healthy people from patients with depression[25].

3.3 Application of CNV Contingent negative variation (CNV) is a complex wave of mental activity under a state of increased cognitive load. It is related to preparing for mental activities. It relies on the conditional connection between the two stimuli and adopts a warning—command joint sequence of stimulation, that is, a warning stimulus is presented first (S1), requiring the subject to press the button to prepare, and giving the command stimulus after a certain time interval (S2). A contingent negative variation (CNV) of potential will be generated between S1 and S2, and it is closely related to psychological activities including expectation, attention, arousal, memory, motivation, preparation and decision. Studies have found that the CNV incubation period of patients with depression is prolonged and the amplitude decreases, suggesting that they have weak expectation behavior and difficulty in attention disengagement. Domestic scholars have summarized the literature at home and abroad, and found that patients with depression show the characteristics of area reduction and poor waveform stability in addition to the reduction of CNV amplitude and the prolongation of postimperative negative variation (PINV)[26]. The reason for prolonged PINV may be that patients with depression often show negative attention bias, excessive focus on negative information of themselves and the outside world, and decrease their attention to command signals. In addition, some studies have found that CNV in patients with depression after treatment shows shortened incubation period and increased amplitude. Based on the above studies, it is speculated that the abnormal changes of CNV in patients with depression may be related to symptoms such as anhedonia, excessive attention to negative things, and difficulty in distracting attention in patients with depression. It is an objective index for early diagnosis of depression, but there are still some controversies and further exploration is needed in the future.

4 Conclusions

Event-related potentials can provide objective electrophysiological indexes for the diagnosis, treatment and prognosis of depression, especially in the cognitive impairment of depression. It has the advantages of simple operation, strong objectivity and non-invasiveness. In the future clinical and scientific research, the application prospect of event-related potentials is more and more extensive. In cognitive aspect, combining event-related potentials with high temporal resolution and magnetic resonance with high spatial resolution to study the cognitive function and structure of brain has be-

come one of the development trends in the future cognitive field, which is helpful for further understanding the cognitive function of depression. Therefore, a lot of research and analysis work needs to be carried out.

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