学 位 論 文 の 要 旨

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学位論文名　Do Event-Related Evoked Potentials Reflect Apathy Tendency and Motivation?

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論 文 内 容 の 要 旨

INTRODUCTION

Apathy is one of the representative clinical symptoms with reduced motivation. Apathy is defined as diminished motivation that is not attributable to a disorder of consciousness, cognitive impairment, or emotional distress, and it is characterized by an absence of will, which results in decreased self-initiated behavior. Apathy is seen frequently in various neuropsychiatric disorders, but its mechanism has not been fully explored. Furthermore, it is difficult to judge clinically whether there is an absence of will or not. If apathy can be assessed by physiological measures, the exploration of neural basis of motivation may be understood more deeply.

Cognitive processing could be objectively monitored by electrophysiological indices such as the P3 event-related evoked potential (ERP), feedback-related-negativity (FRN), and stimulus preceding negativity (SPN). They have excellent temporal resolution for neural activities elicited by external and internal events. Previous studies reported that the P3 amplitude increased with the gain of large reward and decreased in people with apathy, anhedonia, or depression. This evidence suggests that the P3 may reflect cognitive processes that are sensitive to apathetic state. Second, the FRN was discovered as a negative event-related potential generated by feedback stimuli signifying false responses. The FRN is also elicited by feedback stimuli signifying monetary loss. The FRN amplitude is higher when immediately preceding feedback represents monetary gain compared to loss, thereby indicating that the FRN is affected by the motivation level in a trial base. Third, the SPN is associated with reward gain in motivation studies, including a task with feedback signals related to performance. The SPN has been studied in a time production task, and it has a larger amplitude in the case with monetary rewards. Therefore, it is plausible that the SPN also reflects motivation.

The ERP component is known to be correlated with personality traits and affective disorder. To establish a physiological index of apathy, the effect of other motivation-related factors should be considered simultaneously, such as reward dependence, novelty seeking, and depression. In this study, we developed a new simple task where the P3, FRN, and SPN components were evaluated in a single session, and motivation was modulated by changing a monetary reward. This experimental paradigm enabled us to examine the relationships among the electrophysiological measures, novelty seeking, reward dependence, depressive state, and apathy tendency.

MATERIALS AND METHOD

Fourteen neurologically healthy adult volunteers (8 males, 6 females, 25.3 +/- 4.1 years old) were recruited. The study protocol was approved by the ethics committee of Shimane University and written informed consent was given by all participants.

The participants completed the apathy scale, the temperament and character inventory (TCI), and Zung's self-rating depression scale. These questionnaires are self-entry style questionnaires.

The participants were asked to perform a number discrimination task. This task comprised three conditions (reward, non-reward, and control condition). In each trial, a number excluding five was displayed and participants judged whether the number is smaller or larger than five. The participants were asked to press the left button when the number was smaller than five and to press the right button when the number was larger than five as quickly as possible. The feedback stimulus was presented 2.5 s after the response. When the participants correctly responded faster than the criterion time, a positive feedback stimulus was presented. In contrast, when they responded correctly but slower than the criterion time, a negative feedback was presented. The feedback value was altered based on the response speed and accuracy in each trial. The probabilities of positive and negative feedback stimuli were manipulated so that they were both kept at 50%. After the feedback, the current total monetary reward was displayed for 1.0 s. Electroencephalographic (EEG) data were acquired using a BrainAmp system with 64-channel electrodes (Brain Products, Brain AMP DC, Germany). EEG signals were recorded continuously with the bandpass set at 0.01–250 Hz and a sampling frequency of 500 Hz.

RESULTS AND DISCUSSION

According to the behavioral analysis, the reaction time to targets was faster in the reward condition than in the non-reward and control conditions, thereby indicating that the participants were relatively motivated by the monetary reward. We found larger ERP components for the target and feedback stimuli in the reward condition compared with other conditions, which suggests that increased neural activities are associated with enhanced motivation.

The feedback P2 amplitude was positively correlated with reward dependence, and the feedback P3 amplitude was negatively correlated with the apathy score. These results imply that the feedback P2 and P3 reflected motivation. Other ERP components, i.e., SPN and FRN, showed no significant relationships with the motivational measures. The feedback P2 was clearly elicited in all conditions in this study. The P2 is considered to be a stimulus-dependent component related to an early stage of information processing. Our result suggests that the P2 amplitude increases through higher attention based on higher reward dependence. On the other hand, there are several studies regarding the association of reward system and reward dependence. Reward dependence was correlated with gray matter volumes in the caudate nucleus, orbitofrontal cortex, and temporal lobe, with BOLD signals of substantia nigra/ventral tegmental area, and with opioid receptor availability in striatum and nucleus accumbens. These results indicate that reward dependence is associated with the reward system based on the fronto–striatal circuit. The fronto–striatal circuit may modulate the P2 activity via attentional deployment. Next, in our study, the feedback P3 amplitude was negatively correlated with the apathy score. The P3 seen in a gambling task is related to motivational silence in feedback processing. The feedback P3 amplitude changes depending on reward expectancy and size and the feedback value. Our results support the notion that the feedback P3 is related to outcome evaluation for motivational salience. We speculate that the feedback P3 could be a physiological marker as motivational state.

CONCLUSIONS

In summary, the P2 and P3 may have distinct associations with motivation, where P2 reflects attention that is modulated by motivation and P3 reflects apathy more directly. The current stimulus paradigm may be useful for investigating the brain activity associated with apathy.