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Influence of trait-anxiety on inhibition function: Evidence from ERPs study

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ABSTRACT

Patients suffering from anxiety disorder may experience a few problems in the inhibition function. Using event-related potentials, the current study investigated the differences between subjects with high versus low trait-anxiety when they tried to inhibit disturbances in novel emotional pictures in an oddball task. The results showed that P3 amplitudes evoked by negative pictures relative to neutral pictures were decreased in subjects with high as well as low anxiety. In the high-anxious group, P3 amplitudes were also decreased in the positive condition relative to the neutral condition, whereas in the low anxious group, P3 amplitudes showed no significant differences between the positive and neutral stimuli. This implies that people with high anxiety may exhibit some degree of over-inhibition in emotional processing as compared to people with low anxiety. These people tend to indiscriminately inhibit all types of disturbing emotional information.

Anxiety disorder is one of the most common mental disorders. Many researchers have reported that anxious patients are more sensitive to emotional stimuli, particularly negative stimuli. It should be noted that both attention and inhibition are the most important executive functions [11] of our brain. The synergetic effect of attention and inhibition ensures that the psychological task is executed successfully. Mental disorders such as obsessive-compulsive disorder, attention deficit disorder, and anxiety disorder are associated with inhibition dysfunction [2,7,17]. Growing literature indicates that studies on inhibition could further our understanding of stress processes and the underlying psychopathological mechanisms. On one hand, people with anxiety disorder are sensitive to emotional stimuli. On the other, they have obvious inhibition tendency, which causes them to avoid understanding the core reasons of the distressing events. Mogg et al. [18,19] postulated the alertness–avoidance theory, which assumes that the manner in which anxious individuals process distracting stimuli is by becoming alert as a first response and subsequently, evading the stimuli. Anxious individuals focus excessively on threat-related stimuli, which induces anxiety and subsequently, exhibit avoidance behavior, which decreases the possibility of adapting to and objectively appraising the threat-related stimuli. McNaughton and Gray [17] illustrated the anxiety disorder with respect to the inhibition function. They proposed that people have a behavior activation system (BAS) and a behavior inhibition system (BIS), which interact with each other. Anxiety disorders are associated with excessive activation of BIS. Newman [22] proposed that there is another nonspecific arousal system (NAS), which is modulated by both BAS and BIS. The enhancement of NAS accelerates priming of attention and inhibition; concurrently, it shortens the appraisal of the information from BAS and BIS. He also pointed out that unusual activation of BIS is positively correlated with anxiety.

Previous studies used the emotional Stroop task and the oddball paradigm to investigate the inhibition function. In contrast to healthy subjects, anxious individuals (including patients with clinical anxiety disorder and those with non-clinical anxiety) are affected to a larger extent by threat-associated words in the emotional Stroop tasks. Even if the stimuli are presented under subliminal condition, the results are similar to those obtained under supraliminal condition, i.e., relative to normal subjects, anxious individuals have more difficulties in suppressing the disturbances in emotional information [18,19]. As another example, Morita et al. [20] used the auditory oddball paradigm with emotional faces as interference stimuli. They found that amplitudes of P300 under happy conditions are smaller than those under the sad or neutral conditions, which is regarded as the manifestation of attention inhibition by the happy faces.

There is limited research with the relationship between inhibition function and trait anxiety. In the present study, we attempted to investigate the difference in inhibition function between high and low trait-anxiety individuals. With reference to previous studies, we adopted the oddball paradigm involving novel stimuli, i.e., inserting an additional stimulus as the interference when subjects are performing the discrimination task. In order to complete cognition tasks, subjects should inhibit the sudden emotional interference stimuli. This paradigm is supposed to be able to probe

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inhibition mechanisms of emotional interferences [27] and can be widely used in studies on attention and emotion. In the current study, we were mainly concerned about the P3 component that is related to the inhibition process.

A total of 210 undergraduate students completed the State-Trait Anxiety Inventory (STAI) [25] in Chinese version [24,29] which has good validity and reliability evidenced by a large sample survey. The mean trait-anxiety score from the normal population is 41.11 ± 7.74 for the male and 41.31 ± 7.54 for the female [29]. The average trait-anxiety score from participants investigated in the current study was 40.1 ± 10.1. Participants whose trait-anxiety scores were over 45 (75 percentile) were grouped as high-anxiety individuals, whereas the low anxiety group comprised subjects whose scores were equal or less than 35 (25 percentile). It is indicated that the response bias may influence the reliability of psychological assessment and measurement, especially in the self-report measurement. In order to decrease the bias from the socially desirable responding, we asked the participants to complete the Marlowe-Crowne Social Desirability Scale (MCSD) [5,26]. The mean MCSD score from the sample of university students is 15.5 ± 4.4 [26]. In the current study the average MCSD score was 15.6 ± 4.4. Participants whose scores were over 20 were excluded from the EEG data acquisition. Finally, the study comprised 28 right-handed subjects without neurological or mental illness, ranging in age from 18 to 25 years (mean age: 22 years). Among them, 14 participants were included in the high-anxiety group (6 men and 8 women) and 14 participants in the low anxiety group (4 men and 10 women). The trait-anxiety score of the high-anxiety group was significantly higher than that of the low anxiety group (51.6 versus 27.9, $P < 0.001$). The difference in MCSD scores between the two groups was not salient (13.9 versus 12.1, $P > 0.05$). They signed the informed consent before the experiment, and received remuneration on completion of the study.

We constructed standard stimuli, target stimuli, and novel stimuli. Standard stimuli and target stimuli were geometric figures (round, square, or triangle) and had the same shape. Target stimuli were larger than standard figures in area by 5%. There were 1440 standard stimuli and 180 target stimuli. Novel stimuli were 180 color pictures selected from the Chinese Affective Picture System (CAPS) [1], including 60 positive pictures (e.g., delicious food), 60 neutral pictures (e.g., household appliances), and 60 negative pictures (e.g., scene of a car accident). The emotional valence in positive and negative pictures was significantly different from that in the case of neutral pictures (7.42 versus 5.11, $P < 0.01$; 2.40 versus 5.11, $P < 0.01$); also, positive and negative pictures caused significantly higher arousal of emotion than neutral pictures (5.89 versus 3.43, $P < 0.01$; 5.84 versus 3.43, $P < 0.01$). The valence extremity and the arousal level were matched across positive and negative pictures. The rating scores of pictures are from a body of Chinese university students who have similar backgrounds with participants of the current study. Subjects' eyes were 1 m away from the screen. The height of the pictures was 8.0 cm and length was 10.6 cm. The visual angle of the pictures was $6.07^\circ \times 4.58^\circ$.

Prior to the experiment, subjects were asked to complete the STAI again. The trait-anxiety scores of the high- and low-anxiety groups were 53.4 and 29.4, respectively. There was no significant difference in trait-anxiety level between the two tests. Subjects had some practice before attempting the formal tasks. The experimental paradigm was the oddball task with three types of stimuli, of which, 75% were standard stimuli; 12.5%, target stimuli; and 12.5% novel stimuli. The entire experiment consisted of 6 blocks including 240 standard stimuli, 30 target stimuli, and 30 novel stimuli (10 pieces of positive, neutral, and negative pictures each) in each block. The trials were presented in a random order within each block. Among them, the target stimuli and standard stimuli were geometric figures with subtle differences in size, and each novel stimulus was only presented once during the entire experiment. Standard stimuli were presented for 500 ms, the target and the novel stimuli were presented for 750 ms at the center of the screen. The interval between them randomly ranged from 900 to 1000 ms. Subjects were required to focus on the subtle size difference between the standard and target stimuli and press the space bar immediately after seeing the target stimuli. The response hands and the order of blocks were counterbalanced between subjects. There was a short break between each block. We instructed the subjects to concentrate during the discrimination task and try their best to inhibit the influence of novel stimuli.

All subjects were made to wear an elastic cap with 64 tin electrodes, with the reference electrode attached on the left mastoid. The EEG data were re-referenced offline to linked-mastoid electrodes. The vertical electrooculogram (EOG) was recorded supra- and infra-orbitally at the left eye. The horizontal EOG was recorded from the left versus the right orbital rim. The scalp impedances were kept below 5 kΩ. The signals were amplified using a 0.05–100 Hz bandpass. The sampling rate was 500 Hz/channel. A regression procedure was used in which the signal component correlating with the vertical EOG activity was removed from the EEG signal. Trials with peak-to-peak deflection exceeding ±50 μV were excluded from averaging.

Each participant's individual trials were aggregated based on the type of novel stimuli (positive, neutral, or negative). Thus, three averages were generated from each participant. The analyzing epoch was time-locked to the onset of novel stimuli, and the length of the ERP epoch was 1000 ms with a prestimulus baseline of 100 ms. We focused on the P3 component and also analyzed the other significant components (N1, P2, and N2) on the grand average pictures so as to get a complete description of the results. Since the brain areas associated with executive inhibition were mainly located in the frontal and the cingulate areas, we chose F3, Fz, F4, FC3, FCz, FC4, C3, Cz, C4, CP3, CPz, and CP4 sites for statistical analysis. We measured the baseline-peak amplitudes and the peak latencies of N1 (time window: 90–150 ms), P2 (time window: 150–200 ms), N2 (time window: 200–280 ms), and P3 component (time window: 280–430 ms). A repeated-measure ANOVA was used with anxiety level (high, low), emotion property (positive, neutral, negative), laterality (left, right, midline), and anteriority (frontal, fronto-central, central, and centro-parietal) as statistical factors. The Greenhouse–Geisser epsilon correction was applied to adjust the degrees of freedom of the F-ratios when necessary.

Dipole analyses were conducted over the 64 electrodes with BESA2000 (Grafelfing, Germany) using a four-shell elliptical head model. Since we focused on the P3 component, which is associated with executive inhibition, the dipole source was fitted within the 250–450 ms time window after the novel stimuli were presented. The solutions were determined based on free location and minimum-distance criteria.

The analysis on the reaction time was conducted on the trials with correct responses. The reaction time of the high-anxiety group and the low anxiety group was 527.37 ± 39.13 ms and 534.55 ± 42.89 ms, respectively. The difference between the groups was not significant ($t = 7.17$, $P > 0.05$). The mean response accuracies of both groups were about 70%.

We compared the ERP data induced by negative and positive pictures, with the neutral condition as the control group. As shown in Fig. 1, the three types of emotional pictures all evoked N1, P2, N2, and P3 components in the scalp. The arrangement rules of the P3 component elicited by the three types of pictures were different between the high- and low-anxiety groups. The difference between the groups largely embodied the differentiation of P3 amplitudes evoked by positive stimuli.

N1, P2, and N2: The only significant effect of the N1 amplitude was found on the anteriority factor [$F(3,78) = 58.48$, $P < 0.01$]. N1 amplitudes were relatively higher in the anterior scalp.

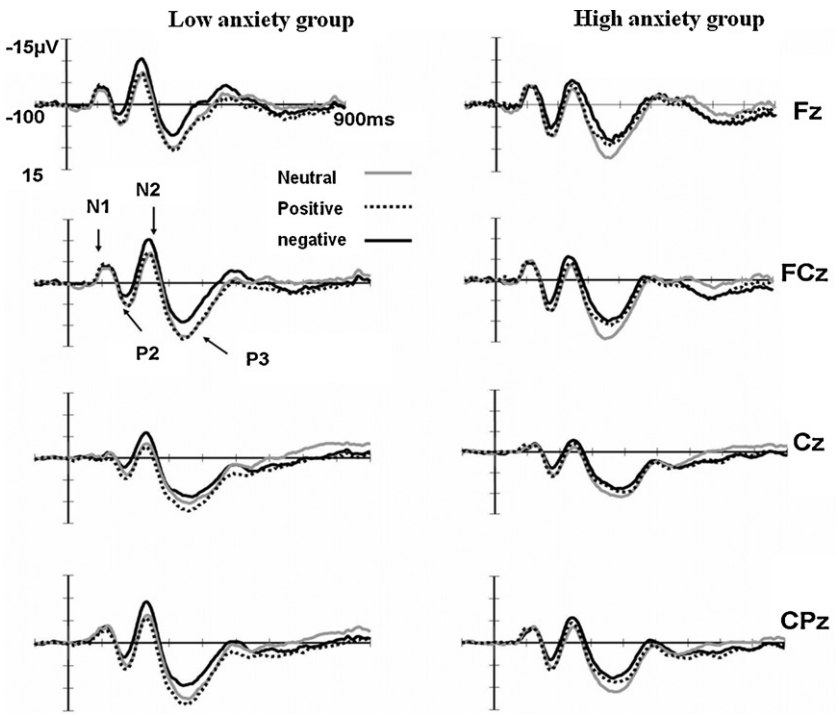

Fig. 1. Grand average ERPs corresponding to the three types of novel stimuli.

ANOVA conducted on P2 amplitudes revealed significant main effects of the emotion property factor [$F(2,52) = 16.44$, $P < 0.01$]. P2 amplitudes evoked by negative pictures were relatively lower than those evoked by other types of stimuli. P2 latencies also showed main effects for emotion property [$F(2,52) = 7.83$, $P < 0.01$]. Negative stimuli elicited relatively shorter P2 latencies.

With respect to N2 amplitudes, the main effect for emotion property was significant [$F(2,52) = 23.72$, $P < 0.01$]. N2 amplitudes were highest when induced by negative pictures, and those induced by neutral pictures were the lowest. N2 amplitudes were also found to peak over the midline of the scalp, and the amplitudes over the right hemisphere were greater than those over the left hemisphere [$F(2,52) = 14.39$, $P < 0.01$]. The anxiety level significantly affected N2 latencies [$F(1,26) = 5.07$, $P < 0.05$], which was shorter in highly anxious individuals. There was a main effect of N2 latencies for emotion property as well [$F(2,52) = 5.59$, $P < 0.01$]. N2 latencies were the shortest under the negative condition and longest under the neutral condition.

P3 component: A significant main effect of P3 amplitudes was observed on emotion property [$F(2,52) = 20.08$, $P < 0.01$]. P3 amplitudes were the largest under the neutral condition and smallest under the negative condition. Laterality of P3 amplitudes was similar to the results of the N2 component, which revealed that P3 amplitudes were largest over the midline of the scalp, and the right hemispheric amplitudes were larger than the left hemispheric amplitudes [$F(2,52) = 11.80$, $P < 0.01$]. There were significant interactions between the anxiety level and the emotion property [$F(2,52) = 10.31$, $P < 0.01$]. Further, simple effect analysis showed that there was a difference in P3 amplitudes between the high trait-anxious group and the low trait-anxious group. P3 amplitudes induced by positive stimuli in the high-anxiety group were significantly smaller than those in the low anxiety group. Another interaction effect of P3 amplitude was between the laterality and the anteriority factor [$F(6,156) = 26.70$, $P < 0.01$]. P3 amplitudes peaked at CPz site.

Dipole source localization: Principal component analysis revealed that the largest principal component could explain most of the variation; thus, we localized the source with a single dipole. It was located at the right cingulate cortex (see Fig. 2, Talairach coordinates: 9.8, −29.5, 32.6; residual error: 20.067%.)

In this study, we found that in the high trait-anxiety as well as low trait-anxiety group, P3 amplitudes induced by negative pictures were smaller than those induced by neutral pictures. This implies that subjects inhibit the influences from negative stimuli. In the low trait-anxiety group, P3 amplitudes showed no significant difference between the positive and the neutral conditions. P3 amplitudes induced by positive pictures in the high trait-anxiety group were smaller than those induced by neutral pictures. It indicates that highly anxious individuals adopt the same inhibition strategy toward positive and negative pictures and have a trend of excessive inhibition.

Some researchers suggested that inhibition studies should focus on endogenic components, such as N2-P3-P4 [12]. The P3 component is considered as the index of inhibition to task-irrelevant information. Falkenstein et al. [9] proposed that P3 marks the completion of the entire inhibition process. Moser et al. [21] found that LPP amplitudes were significantly decreased when subjects were required to actively inhibit the influence of negative pictures. Fallgatter et al. [10] also suggested that P3 may associate with high-load inhibition.

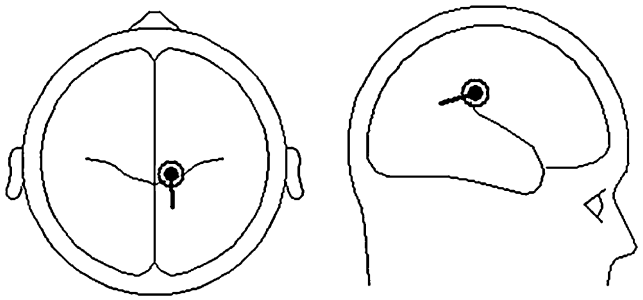

Fig. 2. The dipole identified for P3 induced by negative interference in the high-anxious trait group. Shown are the horizontal and sagittal views.

The present study used an improved oddball paradigm, in which subjects would involuntarily pay attention to novel stimuli that interfered with the discrimination of standard and target stimuli. subjects have to actively inhibit the interference in order to successfully complete the discrimination tasks. This anti-interference effort manifested as significantly decreased P3 amplitudes of both high- and low-anxious individuals under the negative condition compared with that under the neutral condition. The difference between the two groups of subjects was that they showed different degrees of inhibition to positive information. Relative to the neutral condition, P3 amplitudes elicited by positive pictures were decreased in high-anxiety individuals, while there was no such difference among the low anxiety individuals. The contrast indicates that low anxiety individuals selectively inhibit emotional stimuli and do not make much effort to inhibit the influences of positive stimuli since this kind of information is not as intrusive as the negative stimuli. Nevertheless, high-anxiety individuals appear to feel that positive stimuli are very disturbing too, which makes them treat the two types of information comparably such that they manifest an over-inhibition tendency. Behavior inhibition model postulated by McNaughton and Gray [17] suggests that BAS would be activated when one perceives some reward or beneficial information, while BIS would be activated when one meets some conflict stimuli (including non-reward stimuli, punishment stimuli, and novel stimuli irrelevant to the present tasks). The activation of BIS would increase the response inhibition and also enhance the attentional vigilance. The current study evidenced the abnormal activation of BIS in high-anxiety individuals.

Some previous studies [6,18,19] indicated that high-anxious individuals may find it harder than low-anxious individuals to inhibit the processing of emotional stimuli, especially the threatening contents. But high-anxious participants in this study did not show differences in P3 amplitudes compared to low-anxious participants when they were processing the negative pictures. One possible reason to explain this is that, because of the inhibition tendency of the high-anxious people, they might try harder to resist the interference from emotional stimuli. This kind of effort may compensate their deficiency in inhibition function to some extent. On the reaction time there was no significant difference found between the high- and low-anxious groups. It might result from the same compensation effect. We suspect that when the task is not too tough, the high-anxious people can keep some degree of balance between the stimulus-driven attentional system and the top-down, goal-driven attentional system [3,8] through voluntary efforts. These efforts may help them to resist the disruption of task-irrelevant negative stimuli. Meanwhile the high inhibition tendency might result in excessive inhibition of positive stimuli as showed in the current study. Of course this suggestion is speculative and should await future tests.

In the present study, the inhibition function localized by source analysis revealed that most of the P3 variations are attributed to the activation of the right centro-posterior cingulate cortex. As proposed by McNaughton [15,16], anxiety might result from hyperactivity of the septo-hippocampal system which includes structures such as hippocampus, entorhinal cortex and posterior cigulate cortex. The posterior cingualte cortex contributes to a dynamic remapping of the physical state of the organism in response to current behavioral and environmental contexts [4]. Its evaluative function in monitoring sensory events is important to conscious experience of emotion and emotion-related decision making [23]. In Li et al.'s study [13], abstinent cocaine users showed an inverse correlation between the change of craving rating and change of activity in the right posterior cingulate cortex during stress imagery. The posterior cingulate cortex might exert a relulatory role in inhibiting craving responses. In conclusion, the posterior cingulate gyrus may be the brain area where the behavioral inhibition system executes the conflict supervision and response inhibition function.

There is an increasing amount of literature addressing the inhibition mechanisms in emotion disorder individuals. Yee and Vaughan [28] suggest that the formation of anxiety disorder may associate with inhibition failure, and the inhibition processes in the executive function affects individuals as early as during childhood [14]. Further work is still needed to address issues such as the influence factors of the inhibition mechanisms, the relationship between inhibition and attention alertness, and the cooperative and antagonistic effects of BIS and BAS systems. Research that combine behavioural study and cognitive neuroscience would contribute to getting further understanding of anxiety mechanism and provide a theoretical support to the assessment and treatment of anxiety disorders.

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