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The valence strength of unpleasant emotion modulates brain processing of behavioral inhibitory control: Neural correlates

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ABSTRACT

As an ability critical for adaptive social living, behavioral inhibitory control (BIC) is known to be influenced substantially by unpleasant emotion. Nevertheless, how unpleasant emotion of diverse strength influences this control, and the spatiotemporal dynamics underlying this influence, remain undetermined. For this purpose, Event-related potentials (ERPs) were recorded for standard stimulus which required no BIC, and for deviant stimuli that required controlling habitual responses, during highly unpleasant (HU), mildly unpleasant (MU) and Neutral blocks. The results showed delayed response latencies for deviant compared to standard stimuli, irrespective of emotionality. Moreover, there were significant main effects of stimulus type, and significant stimulus type and block interaction effects on the averaged amplitudes of the 230–310 ms and 330–430 ms intervals. In the deviant-standard difference waves which directly index BIC-relevant processing, these interactions were manifested by increased negative potentials as a function of the strength of unpleasant emotion across N2 and P3 components. In addition, these influences are specific to unpleasant emotion, as pleasant emotion of diverse strength produced a similar impact in the control experiment. Therefore, unpleasant emotion of diverse strength is different in impact on brain processing of behavioral inhibitory control. This impact is evident not only in early monitoring of response conflicts, but also in late processing of response inhibition.

1. Introduction

As an important aspect of executive function, the ability to withhold inappropriate behaviors is essential to the success of individuals in the modern (and presumably ancestral) society (Yuan et al., 2008a; Li et al., 2006). This ability is behavioral inhibitory control (BIC), which involves multiple processes such as monitoring of response conflicts and the subsequent response inhibition (Yuan et al., 2008a; Pfefferbaum et al., 1985). Previous event-related potential (ERP) studies consistently reported several components that characterize temporal features of BIC. In particular, frontal-central N2 (Yeung et al., 2004; Donkers & van Boxtel, 2004; Nieuwenhuis et al., 2003) and centrally peaking P3 (Sehlmeyer et al., 2010; Roberts et al., 1994; Falkenstein et al., 1999, 2000), two successive components evoked by BIC tasks such as a go/nogo task, are widely accepted as indexing response conflict monitoring and response inhibition, respectively. In addition, orbitofrontal and inferior anterior cingulate cortices (ACC) are thought to mediate the generation of N2 and P3 activity during behavioral inhibitory control tasks (Evelijne et al., 2005; Hirokazu et al., 2001).

Mood fluctuations influence individuals' ability to inhibit inappropriate responses in life settings (Yu et al., 2009). For instance, as a consequence of behavioral dyscontrol, aggression is directly associated with the experience of unpleasant emotion (Stewart et al., 2010). Moreover, the symptoms of behavioral dyscontrol in psychiatric patients (e.g. borderline or antisocial personality disorders), were reported to grow worse during unpleasant compared to neutral mood states (Posner et al., 2002). This suggests that unpleasant emotion might impair the functioning of BIC. Recently, neural mechanisms underlying the emotion impact on BIC have undergone extensive investigation using functional Magnetic Resonance Imaging (fMRI). Several cortical regions, such as ACC, medial orbitofrontal cortex, medial temporal lobe and insula, were reported to play important roles in the interaction between emotion and BIC (Goldstein et al., 2007; Stadler et al., 2007; Shafritz et al., 2006). In addition to fMRI evidence, several ERP studies investigated the temporal features of the emotion impact on BIC. For instance, Yu et al. (2009) revealed a significant modulating effect of auditory-induced emotion on response conflict monitoring, shown by the larger Nogo-N2 amplitudes during neutral compared to

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emotional conditions. In addition, Albert and colleagues observed larger Nogo-P3 amplitudes during emotional than during neural contexts, suggesting that emotional context significantly modulates neural processing of response inhibition (Albert et al., 2010).

These studies consistently indicated that emotion induction has a significant impact on brain processing of BIC. Compared with positive stimuli that are associated with satisfaction of basic needs, emotionally unpleasant stimuli, which represent threat to basic needs, are of particular biological significance (Cacioppo and Gardner, 1999). Consequently, the human brain has been indicated to be sensitive to valence intensity differences in emotionally unpleasant stimuli, such that induction of highly unpleasant emotion has a larger impact on cognitive processes than does induction of mildly unpleasant emotion, though both belong to the unpleasant valence (Yuan et al., 2007a, 2008b; Meng et al., 2009). This is often the case in life settings that highly unpleasant emotion leads to unwise decision making or violence whereas mild unpleasant emotion is treated easily by cognitive regulation. Nevertheless, whether unpleasant emotion of diverse strength, as induced by unpleasant stimuli of varying valences, influences brain processing of BIC distinctly has yet to be directly investigated.

To better explore behavioral and neural correlates of BIC specific processing and its interaction with emotion, the present research adopted a two-choice oddball task. In this task, subjects were instructed to make a standard/deviant distinction by pressing different keys as accurately and rapidly as possible, irrespective of the contents of the deviant stimuli. Because the standard stimulus was presented much more frequently than deviant stimuli, subjects had to inhibit prepotent response tendency associated with the standard stimulus, in order to respond accurately in deviant trials. Consequently, Reaction Times (RTs) should be prolonged for deviant compared to standard stimuli. Therefore, the two-choice oddball task provides RT index of BIC. This is in contrast with the go/nogo task, whose behavioral index of BIC relies solely on error rates that are relatively insensitive, often statistically non-significant between go and no-go conditions (Todd et al., 2008; Bokura et al., 2001). Moreover, by computing deviant-standard difference waves, the two-choice oddball task supplies BIC specific ERPs free of motor potential contamination, as a result of counterbalanced responses to standard and deviant stimuli (Yuan et al., 2008a). This is in contrast with the go/nogo task, during which a single response to go stimuli provides no RT index of BIC but causes motor potential contamination on ERP differences between nogo and go conditions.

Thus, deviant stimulus in this design involves BIC-relevant processing, while the standard stimulus does not. As a result, direct index of BIC-specific processing could be obtained by computing deviant-standard difference ERPs and RT costs. Accordingly, the impact of emotion on BIC processing is realized by manipulating the emotion attributes of the deviant stimuli. Specifically, this impact is quantifiable by examining how the size of deviant-standard differences in RT and ERP measures varies across emotion blocks (i.e. testing the emotion block and stimulus type interaction). As subjects are focused on the standard/deviant distinction by accurate and rapid button presses, disregarding of the contents of deviants; the differences between deviant and standard stimuli in behavioral and ERP measures should reflect the effect of BIC processing and its modulation by covert emotion induction, instead of reflecting overt processing of deviant stimuli's contents. Moreover, in order to avoid a possible trial-to-trial emotion interference that is prevalent in a random design (Chen et al., 2008), we used a block-design method for emotion induction, which included a single category of emotional deviant stimuli in each block.

Given distinct sensitivity of the human brain to emotionally unpleasant stimuli of varying valence intensities (Sprengelmeyer and Jentzsch, 2006; Leppănen et al., 2007; Yuan et al., 2007a), we hypothesized that inducing unpleasant emotion of differential strength may impact on brain processing of BIC distinctly. Specifically, using dense-array ERP measures and manipulating the valence strength of unpleasant stimuli, we predicted that BIC-relevant stimuli may elicit increased negative deflections in N2 which indexes conflict monitoring (Nieuwenhuis et al., 2003); and elicit larger positive deflections in P3 that reflects response inhibition, in comparison with BIC-irrelevant stimuli (Falkenstein et al., 1999). More importantly, it was hypothesized that BIC-related ERPs (i.e. deviant-standard difference ERPs), which are considered direct indexes of BIC specific processing in the brain, would vary depending on the valence strength of unpleasant emotion. Therefore, it would be observable that BIC-related ERPs are different between highly and mildly unpleasant blocks, and that ERPs for highly and mildly unpleasant blocks are both different from those for the neutral block.

To induce direct emotional responding, we used emotionally evocative scenes as materials, instead of other socially relevant stimuli (e.g. faces; Britton et al., 2006). As a cultural bias for the International Affective Picture System (IAPS) has been reported in Chinese subjects (Huang and Luo, 2004), the pictures used to elicit emotional responses in the current study were taken from the native Chinese Affective Picture System (CAPS; Bai et al., 2005). Moreover, according to Lang's (1995) theory of emotional dimensions, the affective significance of a stimulus is organized along the two primary dimensions: hedonic valence (i.e. pleasant-approach motivation or unpleasant-defensive motivation, ranging from unpleasant to pleasant) and arousal (i.e. degree of motivational activation, ranging from calm to excited; Bradley et al., 2001). Therefore, valence and arousal are the two primary dimensions that should be considered in emotional studies, especially in studies using emotionally salient pictures as materials (Bradley et al., 2001; Lang et al., 1997). Though it was indicated that the studies addressing valence effect need to control for arousal influences (Carretié et al., 1996; Lang, 1995; Johnson, 1993), intense emotional stimuli are usually associated with higher arousal in comparison with mild emotional stimuli, irrespective of whether the stimuli are pleasant or unpleasant (Lang et al., 1997). Thus, though it is necessary to consider balancing intense and mild unpleasant pictures in overall arousal, we predicted that our pilot study of picture assessment remains likely to show different arousal ratings for mild and intense unpleasant picture sets.

2. Materials and methods

2.1. Subjects

As paid volunteers, 16 (9 males and 7 females) undergraduate students aged 19–23 years participated in the experiment (mean age: 21.2). They are right-handed, free of any reported affective disorders, and had normal or corrected to normal vision. Each participant signed an informed consent form prior to the experiment. The experimental procedure was in accordance with the ethical principles of the 1964 Declaration of Helsinki (World Medical Organization, 1996).

2.2. Stimuli

This study used a two-choice oddball task. In addition, we used a block-design method for emotional inducement, which included a single category of emotional deviant stimuli in each block. According to the valence strength of the stimuli, the experiment was divided into three blocks: Neutral, mildly unpleasant (MU) and highly unpleasant (HU). The sequence of the three blocks was counterbalanced across participants. Each block had 200 trials, including 170 standard and 30 deviant pictures. A natural scene of a cup served as the frequent standard picture and 90 pictures grouped as HU, MU, or Neutral served as the deviant stimuli. The sequence of standard and deviant pictures was randomized in each block. All deviant pictures were taken from the Chinese Affective Picture System (CAPS).[2] Like many other

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[2] The standardized CAPS was developed in Key Laboratory of Mental Health, Chinese Academy Of Sciences in order to avoid the cultural bias of emotional

studies using IAPS (Smith et al., 2003; Schupp et al., 2003; Britton et al., 2006), the pictures used for this study covered a variety of contents, such as highly unpleasant, mildly unpleasant, or neutral animals (e.g. snakes, bugs, or eagles), natural scenes (e.g. fire distaster, flood, clouds) and human activity (e.g. homicide, violence, or sports), but did not include single faces. All the pictures were identical in size and resolution (15 cm × 10 cm, 100 pixels per inch). In addition, the luminance level of the pictures was tested prior to the experiment, and the luminance level of the pictures was matched across the three blocks. The contrast of the monitor was set to a constant value across subjects.

2.3. Valence and arousal assessment

To test the validity of the pictures selected for each emotion category (HU, MU or Neutral), we recruited another sample of subjects aged 18–28 years [$n = 71$; 36 males, 37 females; mean age: 21.57] to rate the valence and arousal of the 90 pictures using the Self-Assessment Manikin procedure (SAM; Lang et al., 1997). No subject participated in the ERP experiment. Using a self-report 9-point rating scale, subjects were required to rate the emotion valence (ranging from 1 = "very unpleasant" to 9 = "very pleasant") and arousal (ranging from 1 = "very calm" to 9 = "very excited") they felt for each image by pressing corresponding number keys in the keyboard. The sequence of the two ratings was counterbalanced across subjects. The results showed a significant main effect of emotion category in valence rating [mean: HU = 2.53 (SD = 0.65); MU = 4.09 (SD = 0.73), neutral = 5.62 (SD = 0.75); F (2, 140) = 582.36, $P < 0.001$; $\eta^2 = 0.89$]. HU pictures were rated more unpleasant than were MU pictures [F (1, 70) = 384.38, $P < 0.001$; $\eta^2 = 0.846$] which, in turn, were rated unpleasant compared with the Neutral pictures [F (1, 70) = 388.31, $P < 0.001$; $\eta^2 = 0.847$]. Also, there was a significant main effect of emotion category in arousal rating [mean: HU = 7.07 (SD = 0.80), MU = 5.61 (SD = 0.89), neutral = 4.34 (SD = 1.04); F (2, 140) = 266.47, $P < 0.001$; $\eta^2 = 0.79$], with HU pictures rated more arousing relative to MU pictures [F (1, 70) = 230.50, $P < 0.001$; $\eta^2 = 0.77$] which, again, were rated more arousing than were Neutral stimuli [F (1, 70) = 170.88, $P < 0.001$; $\eta^2 = 0.71$]. Therefore, the pictures used for each block were valid in inducing the corresponding intensity of emotion.

2.4. Behavioral procedures

Subjects were seated in a quiet room at approximately 150 cm from a computer screen with the horizontal and vertical visual angles below 6°. Prior to the experiment, all subjects were told that the purpose of the experiment was to investigate their ability to inhibit the prepotent response to the frequent standard picture when the deviant picture appears. Each trial was initiated by a 300 ms presentation of a small black cross on the white computer screen. Then, a blank screen whose duration varied randomly between 500 and 1500 ms was presented and was followed by the onset of picture stimulus. The first eight subjects were instructed to press the "F" key on the keyboard with their left index finger as accurately and then, quickly as possible if the standard picture appeared; and to press the "J" key with their right index finger as accurately and then, quickly as possible if a deviant picture appeared, disregarding of the contents of deviant pictures. For the remaining subjects, the assignment of response hands was reversed for controlling the influence of response hands on ERPs that index brain processing of BIC. The presentation of stimulus picture was terminated by a key pressing, or was terminated when the picture elapsed for 1000 ms. Therefore, subjects were informed that their responses must be made within 1000 ms. Each response was followed by 1000 ms of a blank screen. At the end of each block, accuracy rates for both standard and deviant stimuli were offered to the subjects as a feedback of their performance. Though the present study emphasized both accuracy and response speed, accuracy was emphasized more heavily over response speed, for the purpose of obtaining clear RT effects for BIC processing. Pre-training with 10 practice trials was used before formal experiment in order to familiarize subjects with the procedure. The standard picture in pre-training was the same as that in the subsequent experiment whereas the deviants for pre-training were neutral pictures that were not selected for the formal experiment. All subjects achieved 100% accuracy during practice. In an interview session conducted immediately after the experiment, each subject was debriefed with respect to their performance during the task, in particular, in regards to their feelings about responses to deviant stimuli.

2.5. ERP recording and analysis

The EEG was recorded from 64 scalp sites using tin electrodes mounted in an elastic cap (Brain Products), with the references on the left and right mastoids (average mastoid reference, Luck, 2005) and a ground electrode on the medial frontal aspect. Vertical electrooculograms (EOGs) were recorded supra- and infra-orbitally at the left eye. Horizontal EOG was recorded from the left vs. right orbital rim. EEG and EOG activity was amplified using a DC ∼ 100 Hz bandpass and continuously sampled at 500 Hz/channel. The EEG was band-pass filtered from 0.01 to 16 Hz. All electrode impedances were maintained below 5 kΩ. ERP averages were computed off-line; Trials with EOG artifacts (mean EOG voltage exceeding ±80 μV) and those contaminated with artifacts due to amplifier clipping, or peak-to-peak deflection exceeding ±80 μV were excluded from averaging.

EEG activity for correct responses in each condition was averaged separately. ERP waveforms were time-locked to the onset of stimuli and the average epoch was 800 ms, including a 200 ms pre-stimulus baseline. As shown by Fig. 1, amplitude differences between standard and deviant conditions started from about 200 ms post-stimulus, and the size of amplitude differences varied as a function of block types. For each block, these differences were manifested by an N2 component at the 230–310 ms interval, an early P3 component at the 330–430 ms interval, and a late P3 (i.e. Late Positive Component, LPC) at 450–600 ms interval in the deviant-standard difference waves [Fig. 2]. Rather than being a single component, the early P3 and the late LPC were two different components, indicated by the results of Principal Component Analysis (PCA, see supplementary material 1). In addition, the N2 was largest at frontal-central sites, the early P3 was largest at central sites, and the late LPC was largest at parietal sites (see Fig. 2 and supplementary material 1). Considerable studies indicated that frontal-central N2 (Yeung et al., 2004; Donkers and van Boxtel, 2004; Nieuwenhuis et al., 2003) and centrally-peaking P3 (Sehlmeyer et al., 2010; Roberts et al., 1994; Falkenstein et al., 1999, 2000) are associated with monitoring of response conflicts and processing of response inhibition in a BIC task, respectively. In contrast, the late parietal LPC occurring in the 450–600 ms post stimulus has been accepted as indexing late cognitive operations such as memory context updating, irrelevant to the processing of response inhibition (Delplanque et al., 2005, 2006; Polich, 2007). Again, the irrelevance of LPC amplitudes to BIC processing was confirmed by the lack of a significant correlation between LPC amplitudes and deviant-standard RT costs in our study (supplementary material 2). Therefore, the present study focused statistical analysis on the frontal-central N2 and the centrally peaking P3, two components closely associated with BIC processing. Specifically, the present study first examined the effect of stimulus and its interaction with block type by conducting a three-way repeated measures analysis of variance (ANOVA) for the averaged amplitudes of the 230–310 ms and the 330–430 ms intervals, respectively. ANOVA factors were stimulus type (standard, deviant), block (Neutral, MU, HU), and electrode sites. Considering that the frontal-central N2 and the centrally peaking P3 were observed in central and more frontal sites, the following 9 electrode sites [Fz, F1, F2 (3 frontal sites); FCz, FC1, FC2 (3 frontal-central sites); Cz, C1, C2 (3 central sites)] were selected for statistical analysis of the N2 and the P3 components.

Based on the observation of significant main effects of stimulus type and significant stimulus by block interaction effects at these intervals, the present study further measured mean amplitudes of the BIC-related N2 and P3 components at corresponding intervals of the deviant-standard difference waves. A repeated measures ANOVA was conducted on the amplitudes of the BIC-related N2 and P3, with block (Neutral, MU, HU) and electrode sites, as ANOVA factors. The degrees of freedom of the F-ratio were corrected according to the Greenhouse–Geisser method in all these analyses.

3. Results

3.1. Behavioral results

False responses were rare, as each subject achieved more than 95% accuracy rates for both standard and deviant stimuli, irrespective of block type. Nevertheless, deviant stimuli elicited more false responses than did the standard stimulus, disregarding of block types [F (1, 15) = 6.469, $P = 0.022$]. The mean accuracy rates for deviant and standard stimuli were 97.4% vs. 99.2%. The ANOVA of the RT data showed prolonged response latencies during deviant compared to standard conditions, irrespective of block types [F (1, 15) = 162.446, $P < 0.001$]. The mean RT for deviant and standard stimuli was 514 ms vs. 416 ms during HU block; 529 ms vs. 408 ms during MU block; and 529 ms vs. 406 ms during Neutral block. The delayed RTs for deviant vs. standard stimuli suggest that infrequent deviant stimuli, due to its association with BIC, required longer time for generating appropriate responses. Nevertheless, the interaction effect between stimulus type and block was not significant [F (2, 30) = 1.006, $P = 0.347$]. Thus, despite a significant BIC effect in both

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inducement found in Chinese participants when IAPS was used. The CAPS introduced a number of pictures characterized by oriental objects, humans and natural scenes. The development method of this native emotional picture system is similar to that of IAPS, using the same Self-Assessment Manikin procedure (SAM; Lang et al., 1997). For the CAPS development, originators first collected over 2000 pictures of various contents for the system development, and finally kept 852 pictures most of which are typical of Chinese cultures for the normative ratings. Chinese college students ($n = 156$, gender-matched) were recruited to rate the valence, arousal, and dominance by a self-report 9-point rating scale for the 852 pictures of the system. The pretest for this system showed that CAPS is reliable across individuals in emotional inducement (the between-subjects reliability scores were 0.982 for valence and 0.979 for arousal).

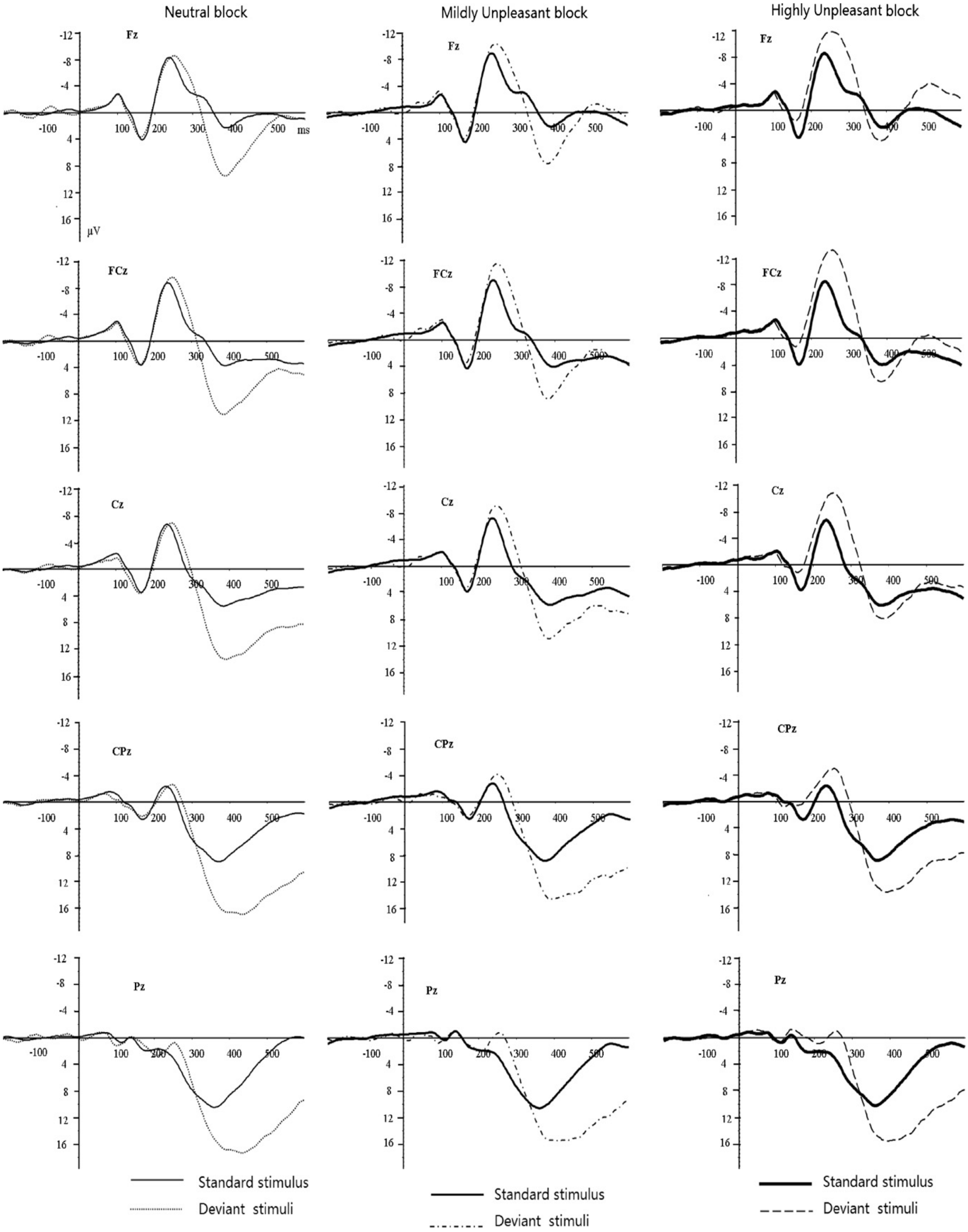

Fig. 1. Grand averaged ERPs elicited during standard and deviant stimuli in neutral (left), mildly unpleasant (middle) and highly unpleasant (right) blocks at Fz, FCz, Cz, CPz and Pz electrode sites.

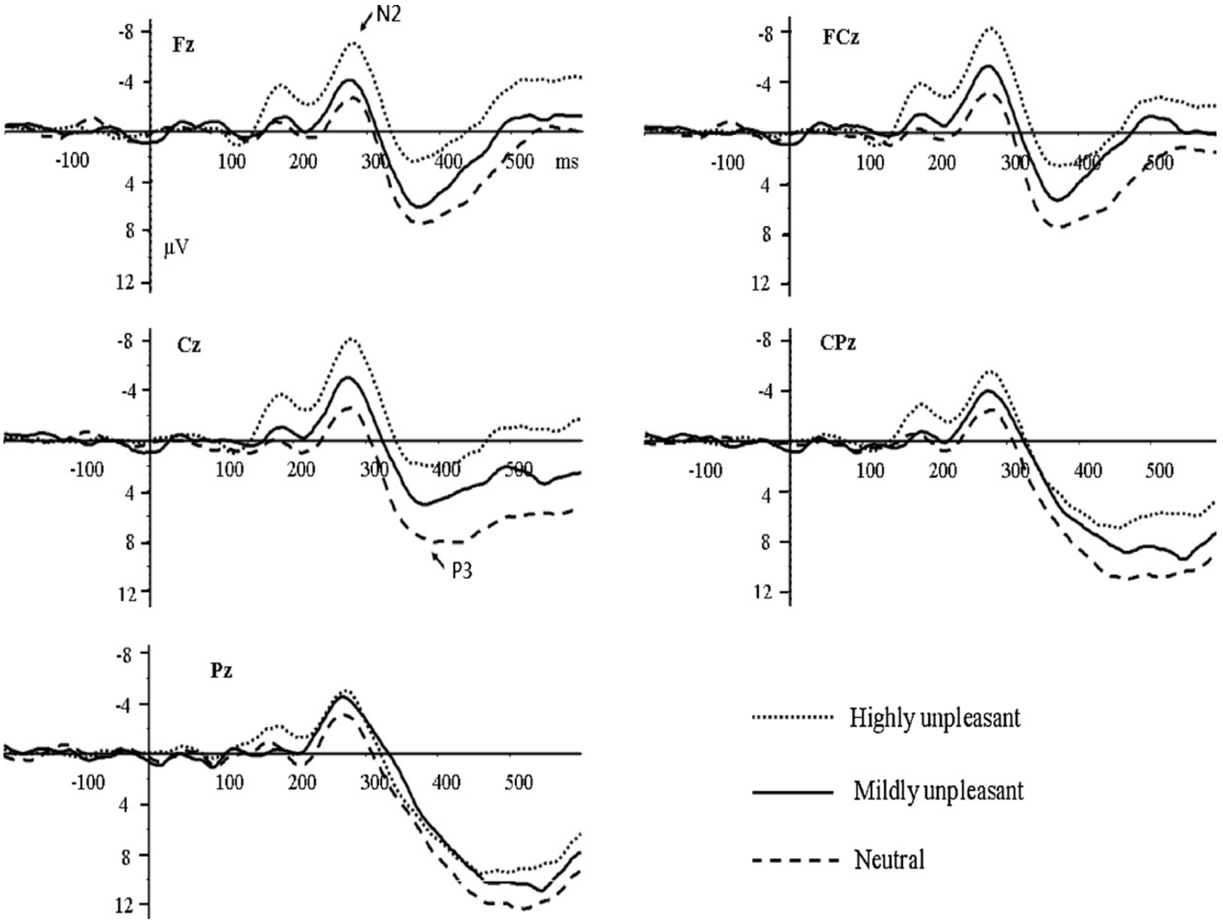

Fig. 2. The averaged deviant minus standard difference ERPs in neutral (dashed lines), mildly unpleasant (solid lines) and highly unpleasant (dotted lines) blocks at Fz, FCz, Cz, CPz and Pz electrode sites.

accuracy and RT measures, the impact of unpleasant emotion on BIC was not obvious at the behavioral level.

3.2. ERP results

3.2.1. Raw ERPs

The repeated measures ANOVA on the averaged amplitudes of the 230–310 ms interval demonstrated significant main effects of electrode sites [F (8,120) = 12.802, $P < 0.001$], stimulus type [F (1, 15) = 10.429, $P = 0.006$] and block [F (2, 30) = 5.949, $P = 0.008$], as well as a significant stimulus type and block interaction effect [F (2, 30) = 10.728, $P = 0.001$; $\eta^2 = 0.417$]. The amplitudes were more pronounced at frontal compared to central sites, while HU block displayed the largest amplitudes amongst the three blocks (Fig. 1). In addition, deviant stimuli elicited enhanced negative deflections than did the standard stimulus, regardless of block types. The stimulus and block type interaction was manifested by the largest amplitude differences between deviant and standard stimuli during the HU block.

Moreover, there were significant main effects of electrode sites [F (8, 120) = 15.744, $P < 0.001$], and stimulus type [F (1, 15) = 7.42, $P = 0.016$], as well as a significant stimulus type and block interaction [F (2, 30) = 7.206, $P = 0.003$; $\eta^2 = 0.325$] on the averaged amplitudes of the 330–430 ms interval. The amplitudes were largest at central sites. Deviant stimuli elicited greater positive amplitudes than did the standard stimulus, regardless of block types. The significant stimulus and block interaction was manifested by the largest amplitude differences between deviant and standard conditions during the neutral block. Therefore, the stimulus type and block interaction was significant at both N2 (230–310 ms) and P3 (330–430 ms) time windows. This implies that the impact of unpleasant emotion on BIC occurred not only in early monitoring of response conflicts but also in late processing of response inhibition.

3.2.2. Emotional effects in deviant-standard difference ERPs

The repeated measures ANOVA on the amplitudes of BIC-related N2 showed no other effects, except for a significant main effect of block type [F (2, 30) = 7.875, $P = 0.006$; $\eta^2 = 0.34$]. HU block [$M \pm$ SE: -5.771 ± 1.55 μV] elicited larger N2 amplitudes than MU block [-3.072 ± 1.10 μV; F (1, 15) = 5.190, $P = 0.038$; $\eta^2 = 0.26$] which, in turn, elicited larger N2 amplitudes than the neutral block [-1.732 ± 1.08 μV; F (1, 15) = 4.594, $P = 0.049$; $\eta^2 = 0.234$].

The ANOVA on the amplitudes of BIC-related P3 demonstrated a significant main effect of block [F (2, 30) = 5.718, $P = 0.008$; $\eta^2 = 0.276$]. The post hoc pairwise comparison showed that HU block [$M \pm$ SE: 1.701 ± 1.713 μV] elicited smaller P3 amplitudes than did MU [4.421 ± 1.661 μV; F (1, 15) = 6.698, $P = 0.021$; $\eta^2 = 0.309$] and neutral blocks [5.41 ± 1.667 μV; F (1, 15) = 16.45, $P = 0.005$; $\eta^2 = 0.415$]. In contrast, there were no significant differences between MU and neutral blocks [F (1, 15) = 0.663, $P = 0.428$; $\eta^2 = 0.042$].

3.3. The validity of ERP components in reflecting BIC

To test whether the above-analyzed ERP components are valid indexes of BIC, we ran a zero-order correlation analysis between the BIC-related P3 (or N2) amplitudes, and the deviant-standard RT cost

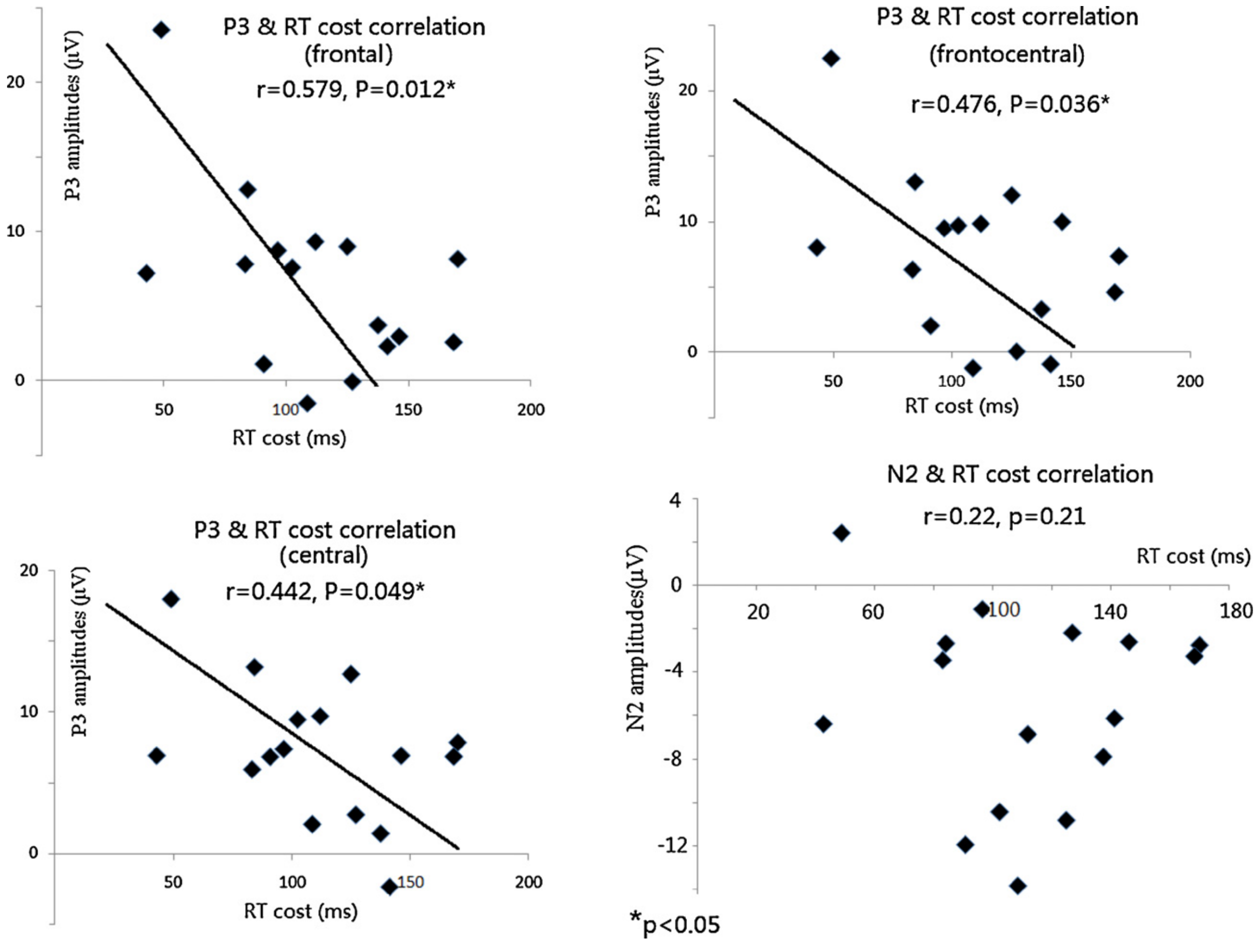

Fig. 3. The scatterplot for the correlation between RT cost and the P3 amplitudes at frontal (top left), frontocentral (top right), and central (bottom left) scalp area. Bottom right: the scatterplot for N2 amplitudes and RT cost correlation across the nine central and frontal sites.

that behaved as a behavioral index of response inhibition. Deviant-standard RT cost and the P3 (or N2) amplitudes were obtained after collapsing across the three blocks. The results demonstrated a significant negative correlation between the RT cost and the P3 amplitudes at central ($r = -0.437$; $P = 0.045$; df = 14), frontocentral ($r = -0.443$; $P = 0.043$; df = 14) and frontal scalp sites ($r = -0.519$, $P = 0.020$; df = 14). The enhancement of P3 amplitudes predicts a reduction of RT cost that implies a better performance.

To exclude the potential influence of the preceding N2 on the P3 correlation with the RT cost, we ran a partial correlation analysis between P3 amplitudes and the RT cost, with N2 amplitudes as a control variable. The negative correlation between P3 amplitudes and the RT cost, however, remained significant at both central ($r = -0.442$; $P = 0.049$; df = 13), frontocentral ($r = -0.476$; $P = 0.036$; df = 13) and frontal ($r = -0.579$; $P = 0.012$; df = 13; see Fig. 3) sites, even after excluding the potential influence of the preceding N2 component. Considering that the strength of this correlation in indexing behavioral inhibitory control might be obscured by the emotionality of unpleasant blocks, we further tested the P3 amplitude correlation with the RT cost just in the neutral block, where deviant stimuli were free of emotionality. Similarly, the results showed a significant negative correlation of P3 amplitudes with the RT cost, both before ($r = -0.463$, $P = 0.036$, df = 14) and after ($r = -0.481$, $P = 0.035$, df = 13) controlling the N2 influences.

However, the correlation between N2 amplitudes and the RT cost failed to meet statistical significance at these sites ($r = -0.059$; $P = 0.415$, df = 14). To exclude the potential influence of the subsequent P3 on the N2 correlation with the RT cost, we ran a partial correlation analysis between N2 amplitudes and the RT costs, with P3 amplitudes as a control variable. The correlation between N2 amplitudes and the RT cost, however, was still statistically non-significant even after excluding the potential influence of the subsequent P3 component ($r = -0.223$, $P = 0.212$; df = 13; see Fig. 3).

Therefore, in the present study, the BIC-related P3 amplitude is most likely a valid index of behavioral inhibitory control in the brain.

3.4. Unresolved question

Apparently, these results demonstrated that unpleasant emotions of diverse strength were distinct in impact on brain processing of BIC, not only in the early N2 stage associated with response conflict monitoring but also in the late P3 stage thought to reflect response inhibition. Nevertheless, highly unpleasant stimuli were more arousing than were mildly unpleasant stimuli which, in turn, were more arousing than the neutral stimuli. Thus, it is hard to answer whether the above results were specific to the emotion induction within unpleasant valence, or were a result of overall emotion arousal, irrespective of valence. To clarify this issue, we conducted a control experiment, during which we used the same design to investigate the impact of pleasant emotion induction on brain processing of BIC. If pleasant stimuli of diverse valence strength produce different impacts on BIC, the above results should not be attributed to the impact of unpleasant emotion, but to the impact of a general emotion arousal. Alternatively, if highly and mildly pleasant stimuli do not produce distinct impacts on BIC processing, the results detailed above should be specific to the impacts of the strength of unpleasant emotion induction.

4. The control experiment (Experiment 2)

4.1. Materials and methods

4.1.1. Subjects

As paid volunteers, 15 (7 males and 8 females) undergraduate students aged 19–25 years participated in the experiment (mean age: 22.6). No subjects had participated in Experiment 1. They are right-handed, free of any reported affective disorders, and had normal or corrected to normal vision. Each participant signed an informed consent form prior to the experiment. The experimental procedure was in accordance with the ethical principles of the 1964 Declaration of Helsinki (World Medical Organization, 1996).

4.1.2. Stimuli

According to the valence strength of emotional stimuli, the experiment was divided into three blocks: Neutral, mildly pleasant (MP) and highly pleasant (HP). The pictures used for this study covered a variety of contents, such as highly pleasant, mildly pleasant, or neutral animals (e.g. puppies, pandas or wolfs), natural scenes (e.g. landscapes, seashores, or mountains) and human activity (e.g. cheers, sports, conversation). All deviant pictures were taken from the Chinese Affective Picture System (CAPS). A natural scene of a cup served as the frequent standard picture and 90 pictures grouped as HP, MP, or Neutral served as the deviant stimuli. Other technical details (e.g. the experiment design, the method of block and trial arrangement) were the same as the main experiment.

To test the validity of the pictures selected for each emotion category (HP, MP or Neutral), another sample of 71 college students [39 males and 32 females; mean age: 22.3] who did not participate in the ERP experiment were recruited to rate the valence and arousal of the pictures, using the Self-Assessment Manikin procedure. The results showed a significant main effect of emotion category in valence rating [mean: HP = 6.862 (SD = 0.79); MP = 6.305 (SD = 0.72), neutral = 5.223 (SD = 0.63); $F(2, 140) = 282.518$, $P < 0.001$; $\eta^2 = 0.801$]. HP pictures were rated more pleasant than were MP pictures [$F(1, 70) = 132.745$, $P < 0.001$; $\eta^2 = 0.655$] which, in turn, were rated pleasant compared with the Neutral pictures [$F(1, 70) = 233.007$, $P < 0.001$; $\eta^2 = 0.769$]. Also, there was a significant main effect of emotion category in arousal rating [mean: HP = 6.617 (SD = 0.7); MP = 6.015 (SD = 0.65), neutral = 5.315 (SD = 0.58); $F(2, 140) = 206.154$, $P < 0.001$; $\eta^2 = 0.747$], with HP pictures rated more arousing relative to MP pictures [$F(1, 70) = 117.670$, $P < 0.001$; $\eta^2 = 0.717$] which, in turn, were rated more arousing than were Neutral stimuli [$F(1, 70) = 113.146$, $P < 0.001$; $\eta^2 = 0.618$]. Thus, the pictures used for MP and HP blocks were both valid in inducing corresponding intensity of pleasant emotion.

4.1.3. Behavioral procedure

The same as the main experiment.

4.1.4. ERP recording and analysis

The same as the main experiment.

4.2. Results

4.2.1. Behavioral results

The ANOVA on the accuracy data showed higher accuracy rates for standard compared to deviant stimuli, irrespective of block types [$F(1, 14) = 7.035$, $P = 0.019$], though behavioral accuracy reached a ceiling effect for both stimulus categories in each subject (>95%). The mean accuracy rates for deviant and standard stimuli was 98.7% vs. 99.6% during HP block; 97.5% vs. 99.1% during MP block; and 95.9% vs. 99.4% during Neutral block. In addition, the finding of higher response accuracy for standard vs. deviant stimuli, was more pronounced during the neutral than during the pleasant blocks [$F(2, 28) = 4.319$, $P = 0.025$]. The analysis of the RT data showed prolonged response latencies during deviant compared to standard conditions, irrespective of block types. The mean RTs for deviant and standard stimuli were 533 ms vs. 427 ms during HP block; 532 ms vs. 416 ms during MP block; and 527 ms vs. 407 ms during Neutral block. Therefore, both accuracy and RT data showed that the presentation of deviant stimuli was associated with performance of behavioral inhibitory control in our study, irrespective of block types.

4.2.2. ERP results

The repeated measures ANOVA on the averaged amplitudes of the 230–310 ms time interval demonstrated significant main effects of electrode sites [$F(8,112) = 12.992$, $P < 0.001$] and block [$F(2, 28) = 4.373$, $P = 0.022$]. The frontal sites recorded larger amplitudes than the central sites, while the amplitudes were less pronounced during HP than during Neutral and MP blocks. In addition, there was a trend of more pronounced amplitudes during deviant compared to standard conditions, regardless of block types [$F(1, 14) = 3.476$, $P = 0.083$]. Nevertheless, the block and stimulus interaction was statistically non-significant [$F(2, 30) = 2.218$, $P = 0.128$, $\eta^2 = 0.137$]. In more detail, the size of amplitude differences during deviant and standard conditions, was not statistically different between HP and MP blocks [$F(1, 14) = 0.583$; $P > 0.40$], and between MP and Neutral blocks [$F(1, 14) = 1.611$; $P > 0.20$]. Also, the size of the deviant-standard differences was not significantly different between HP and Neutral blocks [$F(1, 14) = 4.60$; $P > 0.05$].

Moreover, there were significant main effects of electrode sites [$F(8, 112) = 13.16$, $P < 0.001$] and stimulus type [$F(1, 14) = 7.703$, $P = 0.015$] on the averaged amplitudes of the 330–430 ms interval. The amplitudes were largest at central sites. Deviant stimuli elicited enhanced positive deflections compared to the standard stimulus, regardless of block types. Nevertheless, the interaction effect between stimulus type and block was not statistically significant [$F(2, 30) = 1.723$, $P = 0.203$, $\eta^2 = 0.11$]. In more detail, the size of amplitude differences during deviant and standard conditions, was not statistically different between HP and MP blocks [$F(1, 14) = 0.242$; $P = 0.63$], and between MP and Neutral blocks [$F(1, 14) = 1.968$; $P = 0.18$]. Also, the size of the deviant-standard differences was not significantly different between HP and Neutral blocks [$F(1, 14) = 2.237$; $P = 0.16$]. Thus, the impact of the valence strength of pleasant stimuli was non-significant at each stage of BIC processing (Fig. 4).

4.2.3. Is the P3 amplitude a valid index of BIC?

In the main experiment, BIC-related P3 amplitude has been verified to be a valid index for the processing of response inhibition. If the centrally peaking P3 amplitude measured in the deviant-standard difference waves is a reliable index of response inhibition in a two-choice oddball task, there should be a similar correlation between the P3 amplitudes and deviant-standard RT cost in the control experiment. Therefore, we conducted another correlation analysis between the P3 amplitudes and the RT cost in the neutral block, where the RTs and ERPs elicited by deviant stimuli are free of emotional impact. Similar to that in the main Experiment, the P3 amplitudes were significantly and negatively correlated with RT cost, with the size of RT cost reduced as a result of increasing P3 amplitudes ($r = -0.486$, $P = 0.033$; see Fig. 5). In contrast, the correlation between N2 amplitudes and the RT cost failed to meet statistical significance ($r = -0.436$, $P > 0.05$). Therefore, the correlation analyses of both experiments consistently demonstrated that the P3 amplitude measured in the deviant-standard difference waves is a valid index of response inhibition processing in the brain.

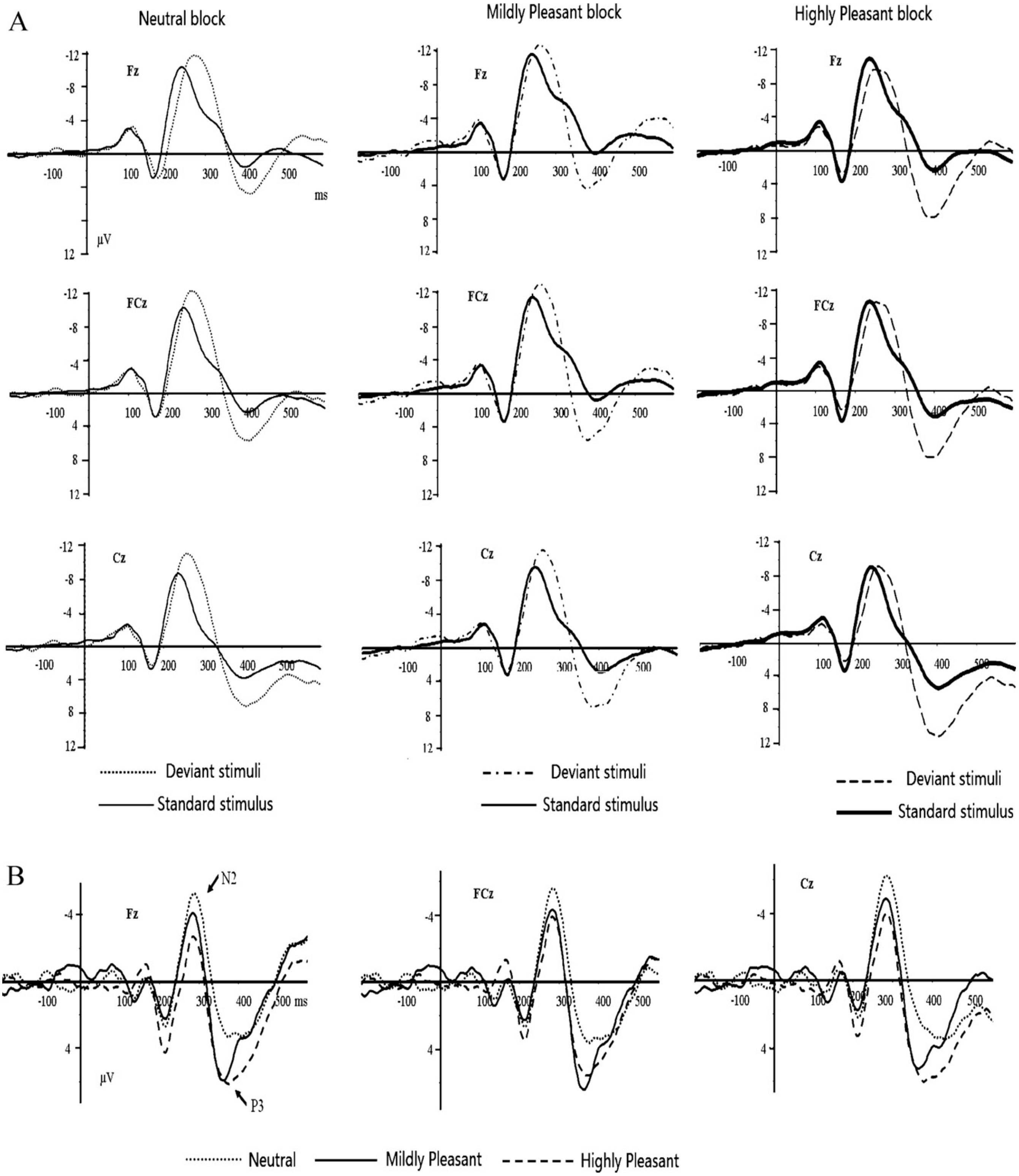

Fig. 4. Top panel: averaged ERPs elicited by the standard and deviant stimuli in neutral (left), mildly pleasant (middle) and highly pleasant (right) blocks at Fz, FCz and Cz electrode sites. Bottom panel: averaged deviant minus standard difference ERPs in the neutral (dotted lines), mildly pleasant (solid lines) and highly pleasant (dashed lines) blocks at Fz, FCz, Cz electrode sites.

5. Discussion

In the present study, subjects were required to make a standard/deviant distinction by accurately pressing different keys within 1000 ms. As indicated by previous studies, response conflicts should be large when a low-frequency response must be made in a context of producing stereotyped or habitual responses (Braver et al., 2001; Jones et al., 2002; Nieuwenhuis et al., 2003). For the low-frequency response to be executed, the brain must compete with and eventually overcome the bias toward producing the prepotent response tendency. Consistent with these observations, the present study showed prolonged RTs and more false

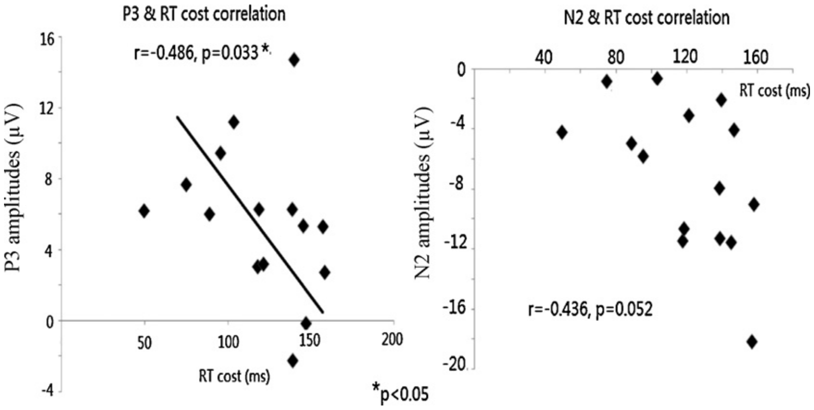

Fig. 5. The scatterplot for the correlation between P3 amplitudes (or N2 amplitudes) and deviant-standard RT costs during the neutral block of the control experiment.

responses during deviant vs. standard conditions, irrespective of block types. In addition, in the postexperiment interview session, all subjects reported more hesitant in response to deviant stimuli in case of stereotyped responding, despite many efforts they made for accurate responding to both stimulus types. In line with these behavioral results, we observed prominent BIC-related N2 and P3 components whose morphologies fit those of the classic BIC-related components. In addition, the significant correlation between the BIC-related P3 amplitudes and the deviant-standard RT cost, further confirmed that the P3 amplitude was a valid index of response inhibition processing in the brain. All these results suggest that the two-choice oddball task used in this study is valid in inducing brain processing of BIC.

The present study observed a significant main effect of Stimulus type, and a significant Stimulus type & Block interaction in the 230–310 ms interval. The main effect of stimulus was manifested by a pronounced N2 component in the deviant-standard difference waves that directly index brain processing of BIC, irrespective of block types. Consistent with prior studies, the N2 amplitudes were largest at the central-frontal sites (Yu et al., 2009; Van Veen and Carter, 2002). Frontocentral N2 in behavioral inhibitory control tasks has been accepted as an index for response conflict monitoring, and for increased attentional engagement that forms the basis for the subsequent response inhibition (Yu et al., 2009; Eimer, 1993; Yuan et al., 2008a; Van Veen and Carter, 2002). Therefore, in the N2 stage, the brain detected the occurrence of response conflicts, and prepared enhanced attention for the subsequent conflict resolution by response inhibition. More importantly, the stimulus and block type interaction was embodied by the larger N2 amplitudes during HU than during MU conditions, and then by the enhanced amplitudes during MU than during Neutral conditions in the deviant-standard difference ERPs. As established, the human brain is equipped with a capacity of automatic attention orienting to emotionally unpleasant information (Yuan et al., 2007a; Carretié et al., 2001). Therefore, the monitoring of response conflict was accompanied by attention alerting to emotion-relevant stimulus dimension during HU and MU blocks. Despite the same valence polarity, highly unpleasant deviant stimuli, due to their enhanced emotional salience, should have elicited greater intensity of attention alerting than mildly unpleasant deviant stimuli. Deviant stimuli of MU block, in turn, elicited additional attention alerting to emotionality compared to those of Neutral block, where deviant stimuli were free of emotion. This alerting probably primed subjects to conduct greater degree of cognitive control over task-irrelevant emotional information in the later stage of response inhibition during HU compared to MU blocks. Consequently, the amplitudes of BIC-related N2 were larger during HU compared to MU blocks. Similarly, the amplitudes of BIC-related N2 were larger during MU compared to Neutral blocks.

Moreover, we observed a significant main effect of stimulus and a significant Stimulus type × Block interaction effect at the 330–430 ms interval. The main effect of stimulus was manifested by a pronounced BIC-related P3 component measured in the deviant-standard difference waves. The P3 in behavioral inhibitory control tasks has been accepted as relevant to later response inhibition (Donkers and van Boxtel, 2004; Pfefferbaum et al., 1985). More noticeably, P3 elicited by no go stimuli, which indexes later response inhibition, was consistently reported to be more pronounced than that elicited by go stimuli during a go/no go task (Donkers and van Boxtel, 2004; Pfefferbaum et al., 1985). Consistent with these findings, deviant stimuli, which involved response inhibition, elicited larger positive amplitudes than the standard stimulus in the 330–430 ms interval in our study. These results were supported by our correlation analysis showing a role of the P3 amplitude in predicting behavioral performance of BIC. The P3 amplitudes were negatively correlated with the RT cost, suggesting that enhanced processing of response inhibition in the brain, reflected by the increased P3 amplitudes, is valid in predicting improved performance of BIC (indicated by reduced deviant-standard RT cost). Moreover, HU block exhibited smaller P3 amplitudes than MU and neutral blocks, possibly as a result of cognitive control over task-irrelevant, distracting emotion information (Markela-Lerenc et al., 2004; for a discussion, see Yuan et al., 2011a).

In the present study, subjects were required to respond to the frequent standard stimulus and the infrequent deviant stimuli as accurately and quickly as possible, disregarding of the contents of deviant stimuli. In order to respond correctly to the deviant stimuli, subjects had to inhibit the stereotyped response tendency associated with the standard stimulus, as well as other task-irrelevant distracting information (Yuan et al., 2008b). Whereas response inhibition that involves withholding stereotyped behavioral response is associated with enhanced P3 amplitudes (Donkers and van Boxtel, 2004; Yuan et al., 2008a), cognitive inhibition of task-irrelevant, distracting information has been established to result in smaller P3 amplitudes (Liotti et al., 2000; Markela-Lerenc et al., 2004; Yuan et al., 2011b). In this study, deviant stimuli were associated with the same motor response and were presented with equal frequency in the three blocks. Thus, the demand of response inhibition should not be different across the three blocks. Accordingly, there should not be amplitude differences in BIC-related P3 amplitudes, if there was no task-irrelevant emotion impact from the deviant stimuli of HU and MU blocks. As the task-irrelevant distracting information that involves prioritized attention, the intense unpleasant information in the HU block should impact neural processing of response inhibition to the largest extent. Consequently, cognitive control of the distracting emotion information should be strongest in HU block, which probably contributed to the smaller amplitudes during HU compared to Neutral blocks. In contrast, the P3 amplitudes were not significantly compromised during MU compared to Neutral blocks, possibly because the emotion salience of the MU deviant stimuli is not salient enough. Accordingly, fewer cognitive resources were needed, for the brain to achieve cognitive control over this mild emotion impact. Consequently, the mild unpleasant emotion did not produce a significant impact on the neural processing of response inhibition.

Therefore, in the present study, ERP data demonstrated that unpleasant emotion of varying strength has differential impact on each processing stage of BIC: this impact is not only significant in the early monitoring of conflict detection, but is also evident in the subsequent stage of response inhibition. The differential impact of highly and mild unpleasant emotion on BIC processing may be mediated by a set of neural substrates. Specifically, prefrontal and anterior cingulated cortices are not only important in brain processing of executive control (Evelijne et al., 2005; Hirokazu et al., 2001); but also play critical roles in emotion and BIC interaction (Goldstein et al., 2007). Moreover, it has been reported that there are reciprocal functional collections between amygdala and prefrontal cortices (Cremers et al., 2010; Urry et al., 2009; Gur et al., 2002): while top-down frontal regulation of amygdala activation plays critical roles in cognitive control of emotion; the bottom-up neural inputs from amygdala to ventromedial prefrontal cortices are likely to mediate the impact of emotion on executive function (Shafritz et al., 2006; Passamonti et al., 2008; Bediou et al., 2009). Consistent with this notion, it has been reported that amygdala is involved in the interaction between emotion and BIC (Goldstein et al., 2007). In addition to the role of prefrontal and anterior cingulated cortices (Goldstein et al., 2007; Shafritz et al., 2006; Hariri et al., 2003), our previous work using source localization measures observed a role of the right medial temporal lobe, particularly the right amygdala/hippocampus complex, in mediating the brain's differential sensitivity to emotionally unpleasant stimuli of diverse valence intensities (Yuan et al., 2007b). Based on these evidence, we proposed that the differential modulating effects of highly and mild unpleasant emotions on brain processing of BIC may be a result of neural interaction within a network inclusive of both prefrontal (e.g. ventromedial prefrontal and anterior cingulated cortices) and subcortical (amygdala) neural substrates. These hypotheses, evidently, require further investigation by the measures of high spatial resolution.

However, recent evidence showed that the behavioral response to infrequent (33.33%), target stimuli was slower than that to frequent (66.67%), non-target stimuli in a target detection task that is irrelevant to BIC (Ferrari et al., 2008). Thus, the delayed response to infrequent deviant stimuli in our study appears likely to reflect biased cognitive processing of the deviant stimulus contents, in addition to hypothesized processes of BIC. Nevertheless, the present study instructed subjects to respond accurately and quickly to both standard and deviant stimuli. As a result, standard and deviant stimuli were equally important for subjects to achieve a desirable behavioral performance. Therefore, deviant stimuli were free of the "target" attributes in our study. On the other hand, the present study attached primary importance to behavioral responses to the standard and deviant stimuli, by asking subjects to enhance behavioral performance through ignoring the specific contents of the deviant stimuli. Accordingly, it is unlikely that subjects focused more on the contents of deviant stimuli, regardless of their task to make a standard/deviant distinction by pressing different keys as accurately and quickly as possible. Furthermore, given that delayed responses to deviant stimuli reflect enhanced cognitive processing of deviant stimulus contents, this enhanced processing should decrease, instead of increase, false responses during deviant trials. Nevertheless, though response accuracy reached a ceiling effect for both stimulus categories, deviant stimuli were associated with greater false responses than the standard stimulus, irrespective of the block in our study. This result was observed again, in our control experiment targeting at the impact of pleasant stimuli on BIC processing. The enhanced false responses in deviant trials, however, were most likely a result of failure in behavioral inhibitory control. Therefore, the delayed responses for deviant compared to standard stimuli should reflect the effects of behavioral inhibitory control, instead of other cognitive, stimulus content-specific processing.

Another important issue is whether the observed impacts on BIC processing are specific to the induction of unpleasant emotion, or they are just a result of general emotion arousal, irrespective of emotion valence. Though we observed differential impacts of intense and mild unpleasant emotion on each stage of BIC processing, the stimuli used for emotion induction were just unpleasant stimuli whose arousal increased with unpleasant intensity in the main experiment. Without equivalent examination of the impacts of pleasant emotion of varying strength, it is hard to attribute these effects solely to the emotion induction of unpleasant valence. To clarify this issue, we conducted a control experiment using the same design, except for replacing unpleasant stimuli with pleasant stimuli of varying valence strength. However, the control experiment failed to show a significant block and stimulus interaction during both N2 and P3 time intervals. This is probably due to reduced susceptibility of the humans to pleasant events (Taylor, 1991; Yuan et al., 2007a), such that HP and MP stimuli produced similar interference with the BIC task. Furthermore, the size of BIC effects in brain potentials was not significantly different between HP, MP and neutral blocks. This is in contrast with unpleasant emotion induction that, in line with prior studies (Posner et al., 2002; Stewart et al., 2010), significantly influenced BIC processing in the present study.

However, highly and mildly emotional materials are evidently larger in the size of valence and arousal differences in the unpleasant experiment (valence dif. = 1.56; arousal dif. = 1.46) compared to the pleasant (valence dif. = 0.56; arousal dif. = 0.602) experiment. Thus, the lack of a similar impact in the control experiment is possibly a result of using materials smaller in emotion strength differences, not necessarily due to greater impact of negative emotion as indicated by the account of negative bias (Cacioppo and Gardner, 1999). Nevertheless, this possibility should be small. Specifically, HP and neutral stimuli of Experiment 2 showed larger size of valence ($6.86 - 5.22 = 1.64$) and arousal ($6.62 - 5.32 = 1.30$) differences than MU and neutral stimuli of Experiment 1 (valence dif. = 1.53; arousal dif. = 1.27). Despite a larger valence and arousal difference from the neutral stimuli, HP stimuli of Experiment 2 produced a similar size of BIC effects as the neutral stimuli at each processing stage. In contrast, MU stimuli, despite a relatively smaller valence and arousal differences from the neutral stimuli, produced a significant emotion impact on early monitoring of response conflicts in the N2 stage (230–330 ms). Therefore, in the present study, the impact of emotion strength on brain processing of BIC is a result, to some extent, specific to unpleasant emotion induction, probably as a result of closer association of unpleasant emotion with BIC in comparison with pleasant emotion (Stewart et al., 2010; Carver and Harmon-Jones, 2009). Nonetheless, it is undoubtedly necessary to replicate the present study using pleasant pictures that are more arousing (e.g. erotic pictures; Briggs and Martin, 2008), given the fact that HP pictures were rated overall less arousing than were HU pictures in the current study.

6. Conclusion

The present study observed differential impacts of highly and mildly unpleasant events on brain processing of behavioral inhibitory control. This impact was evident not only in the early stage of response conflict monitoring, but also in the late stage of responses inhibition. In addition, this effect is specific to unpleasant emotion induction, instead of a result from general emotion arousal. This develops our understanding of the interaction between emotion and BIC, by suggesting that unpleasant emotions of varying strength have differential impacts on BIC.

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Appendix A. Identification numbers of CAPS pictures presented in this study

HU: 173, 185, 191, 194, 196, 205, 206, 232, 240, 243, 244, 246, 248, 254, 255, 256, 270, 273, 280, 284, 471, 533, 541, 569, 573, 577, 580, 583, 584, 629.

MN: 585, 212, 617, 618, 150, 220, 247, 251, 252, 264, 265, 267, 272, 285, 507, 547, 553, 557, 565, 563, 228, 249, 154, 155, 157, 161, 169, 171, 621, 592.

Neutral (unpleasant): 89, 294, 306, 388, 454, 482, 538, 521, 523, 547, 614, 619, 696, 716, 722, 850, 308, 309, 321, 326, 328, 357, 377, 402, 634, 645, 719, 810, 363, 300.

HP: 1, 2, 5, 6, 8, 9, 21, 23, 24, 25, 33, 34, 36, 38, 41, 44, 46, 49, 50, 53, 56, 59, 60, 66, 79, 82, 83, 85, 87, 99.

MP: 4, 7, 10, 11, 12, 13, 14, 16, 18, 20, 28, 29, 45, 40, 52, 72, 73, 77, 78, 88, 94, 84, 39, 57, 32, 98, 27, 65, 663, 819.

Neutral (Pleasant): 840, 841, 843, 547, 89,306, 454, 482, 538, 521, 523, 614, 722, 848, 308, 321, 326, 328, 377, 402, 634, 645, 810, 363, 300, 291, 816, 818, 838, 839.

Appendix B. Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.biopsycho.2011.10.015.

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