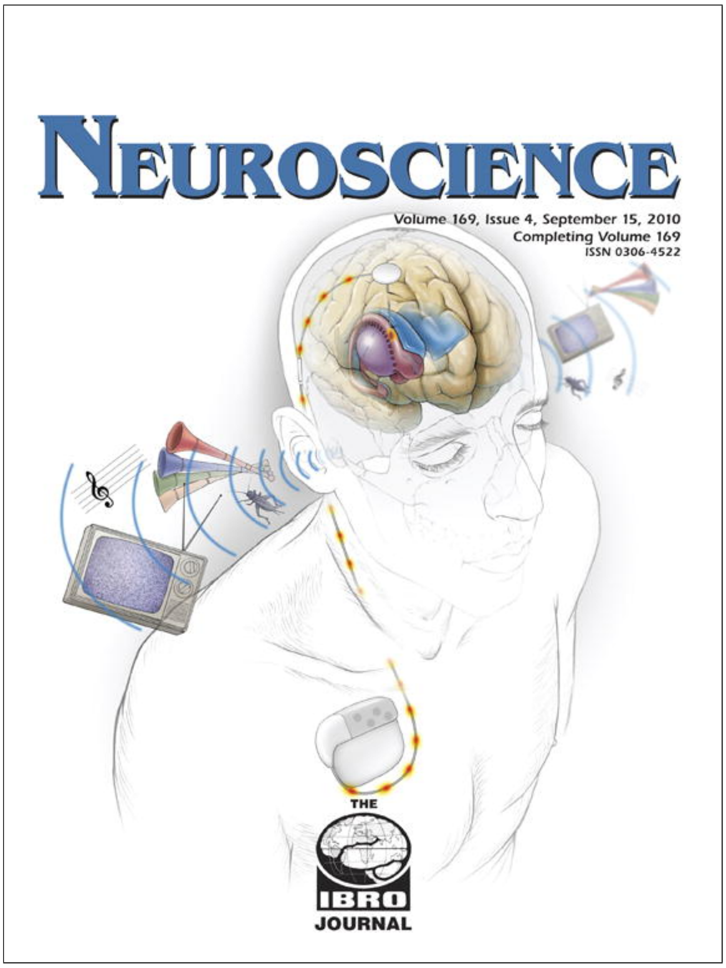

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ENHANCED SENSITIVITY TO RARE, EMOTION-IRRELEVANT STIMULI IN FEMALES: NEURAL CORRELATES

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Abstract—Numerous studies showed enhanced sensitivity of females to emotional stimuli relative to males using multiple tasks. However, in the present study, two event-related potential (ERP) experiments targeting the impact of gender on rare stimulus processing both showed enhanced sensitivity of females to rare stimulus that is neutral, irrelevant to emotion. Subjects were required to press different keys for standard and rare pictures in Experiment 1, and to do nothing but to passively view the pictures in Experiment 2. Rare pictures elicited more intense pop-out effects in females, at both neuroelectrical (multiple levels of ERP analyses) and behavioral (response latencies and pop-out assessment) levels across experiments. Thus, females are equipped with enhanced sensitivity to rare, emotion-irrelevant stimuli relative to males, probably as a result of evolutionary adaptation. This effect is ought to be considered in studies that use an oddball paradigm. © 2010 IBRO. Published by Elsevier Ltd. All rights reserved.

Key words: rare stimulus, oddball paradigm, gender, adaptation, event related potential (ERP).

The ability to detect unusual events is fundamental for adapting to a rapidly changing environment and ensuring an organism's survival (Nagy et al., 2003). Rare events often elicit orienting responses (Halgren and Marinkovic, 1995) which, as an important brain function, enables organisms to direct attention to, and consequently to cope with, accidental events rapidly (Courchesne et al., 1975; Campanella et al., 2002). Some rare events are emotionally relevant in life and lab settings (Yuan et al., 2007a,b; Coon, 2000), and gender is known to modulate emotion processing at multiple levels (Lang et al., 1993; Hofer et al., 2006). In addition to common knowledge of gender differences in processing emotionally arousing, particularly negatively-valenced stimuli (Lang et al., 1993; Montagne et al., 2005; Schirmer et al., 2002, 2004; Hofer et al., 2006), behavioral and neuroimaging studies also reported gender differences in the brain responsivity to emotion-relevant rare stimuli (Orozco and Ehlers, 1998; Campanella et al., 2004; Li et al., 2008). In early studies, using event-related potential (ERP) measures, Orozco and Ehlers (1998) discovered that rare emotional faces elicited greater amplitude and longer latency P450 component in females than in males during a facial discrimination task. More recently, Campanella et al. (2004) observed that females are faster in detecting rare happy faces relative to males. In addition, by manipulating the valence strength of emotional stimuli, our previous studies showed emotion effects for mild negative rare stimuli only in females, and females generated higher amplitude P3 than males during all rare conditions, irrespective of valence (Li et al., 2008; Yuan et al., 2009). Larger size of orbitofrontal cortex and its better collection with amygdala in females were considered as possible neural basis underlying these differences (Li et al., 2008; Gur et al., 2002).

Though the presentation of rare stimuli is associated with orienting responses and sometimes with emotion reaction such as surprise (Sokolov et al., 2002; Bradley et al., 1997), rare stimuli we come across in life settings, however, are not necessarily emotionally relevant. This is often the case when you are engaged in work at hand while detecting a sudden knock at the door: the knock elicits attention orienting rapidly while seldom evokes emotional response. Rare event, whether it is emotionally salient or neutral, is biologically important, because its happening is sudden, meaning unpredictable and unusual, to individuals (Sokolov et al., 2002; Yuan et al., 2008a). Accordingly, it is impossible for people to evaluate its meaning and treat it in advance to its occurrence (Nagy et al., 2003). Though it is established that females are more reactive to emotionally salient stimulus which is known for important adaptive values(Lang et al., 1993; Cacioppo and Bernston, 1994; Orozco and Ehlers, 1998; Campanella et al., 2004; Li et al., 2008), it remains unknown to date whether females and males are different in processing rare, emotion-irrelevant stimuli that share these values. Particularly, it is important to know whether gender differences in processing rare stimuli exist only for emotionally laden stimuli, or for rare stimuli in general.

With high temporal resolution, ERP measures are helpful to exploring spatiotemporal features of rare stimulus (RS) processing in the brain and its association with gender. Based on the above analyses, and our prior finding of larger P3 and shorter response times (RTs) for all rare stimuli in females (Li et al., 2008; Yuan et al., 2009), we hypothesized that males and females would process rare, emotion-irrelevant stimuli in different ways. Com-

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Abbreviations: EEG, electroencephalography; EOGs, electrooculograms; ERP, event-related potential; MMN, Mismatch Negativity; RS, rare stimulus; RTs, response times.

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pared to males, females are likely more sensitive to RS, just like their greater sensitivity to emotion stimuli. If this hypothesis proves true, it would be questionable to investigate gender effect in emotion processing by a direct male–female comparison in brain response to rare emotional stimuli (Orozco and Ehlers, 1998; Campanella et al., 2004), as this effect may be obscured by gender differences in processing rare stimuli. Therefore, it is highly important to investigate the impact of gender on rare stimulus processing, which would provide new knowledge of cognitive differences between men and women and an insight into methodology for studies that use an oddball paradigm.

Classic oddball task requires subjects to detect a rare target imbedded in a background of frequently occurring standard stimulus (Polich and Criado, 2006). Therefore, target-induced ERPs in this task involve not only rare stimulus processing but also target effects, response readiness and execution. As ERPs elicited by the standard stimulus did not involve rare stimulus processing as well as target and response-related effects, it is hard to obtain RS effect (i.e. pop-out effect)-related ERPs using a traditional oddball task. Moreover, three-stimulus oddball task required subjects to detect a target interspersed in a stream of the frequent stimulus and the rare task-irrelevant distracters (frequent and target stimuli had similar perceptual properties). Thus, the presentation of distracters induces RS processing (Delplanque et al., 2005; Polich, 2007). Nevertheless, brain potentials elicited by distracters were thought to be obscured by the Nogo effect induced by inhibiting motor response associated with the target (Courchesne et al., 1975; Polich, 2003; Polich and Comerchero, 2003; Falkenstein et al., 1995). Moreover, P3 has been reported larger in women than in men, irrespective of task, because of women's larger size of callosal areas (Steffensen et al., 2008; Hoffman and Polich, 1999). Thus, distracter-induced P3 in the three-stimulus oddball task, though is qualitatively different, is also likely to be larger in females versus males, irrelevant to psychological processes. For these reasons, it is inappropriate to investigate gender effects in RS processing by directly comparing distracter-induced ERPs in males with those in females using a three-stimulus oddball task.

Therefore, to investigate gender effect in RS processing and its temporal features, it is necessary to design an experiment during which standard and rare stimuli elicit similar processes except for the RS processing, consequently to obtain RS effect-related ERPs free of the above obscuring effects. For this purpose, we designed two adapted oddball experiments, both of which were target-free and equated in behavioral response to standard and rare stimuli, to obtain RS effect-related ERPs free of target (Polich and Criado, 2006), gender (Steffensen et al., 2008) and motor (Campanella et al., 2004) effect contaminations. Experiment 1 required subject to make buttonpress responses to standard and rare pictures (active task), while Experiment 2 required subjects to do nothing but to passively view the pictures (passive task). Rare stimuli in both experiments were a set of infrequent pictures that differ from one another across trials. Therefore, RS processing was triggered by unpredictable presentation of rare pictures embedded in a train of a standard stimulus, and ERPs elicited by the standard and rare stimuli in either task involve similar processes except for the RS processing. With this rationale, the current study focused on the stimulus (standard, rare) and gender (male, female) interaction effects, and then analyze the gender effect in RS processing in the rare-standard difference waves. We used both active and passive oddball tasks, instead of a single task, to investigate whether the gender effect in RS processing is stable, independent of behavioral responses.

EXPERIMENTAL PROCEDURES

Experiment 1

Subjects. As paid volunteers, 16 female (18–24 years; mean age=21.7 years) and 16 male (18–25 years; mean age=22.0 years) college students participated in the experiment. All subjects were healthy, right-handed, had normal or corrected to normal vision. Also, they reported no history of affective disorder and were free of any psychiatric medication. The study was approved by the local Review Board for Human Participant Research and each subject signed an informed consent form prior to the experiment.

Stimuli and experimental procedure. This experiment employed an adapted oddball task. The experiment had four blocks of 100 trials, with each block including 75 standard and 25 rare stimuli (75% vs. 25%). A natural scene of a cup served as the frequent standard stimulus and 100 neutral, non-emotional images[1] were used as rare stimuli (Bai et al., 2005). Thus, each rare picture was presented once in the experiment, consequently to realize the content of each picture unpredictable in advance. The onset sequence of the standard and rare pictures was randomized for each subject. In addition, standard and rare pictures used in this experiment were identical in size and resolution (15×10 cm^2, 100 pixels per inch).

Subjects were seated in an acoustically isolated room approximately 150 cm from a computer screen; thus, the horizontal and vertical visual angles were both less than 6°. 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 from 500 to 1500 ms was presented and was followed by the onset of a picture stimulus. Within each gender, half of the subjects were instructed to press the "F" key with their left index finger as accurately and then, quickly, as possible if the "cup" picture appeared, and to press the "J" key with their right index finger if other picture appeared. For the remaining subjects, the assignment of response hands was reversed (Alexander and Polich, 1995). The presentation of the stimulus picture was terminated by a key pressing which, then, was followed by 1000 ms of a blank screen. At the end of each block, accuracy rates for both standard and rare stimuli were offered as feedback for their per-

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[1] The neutral images used in this study were taken from Chinese Affective Picture System (CAPS), a system adapted from IAPS that was developed in Key Lab of Mental Health, Chinese Academy of Sciences, in order to avoid the cultural bias of emotional inducement found in Chinese participants when IAPS was used directly. All the images used in this study were normatively rated as neutral, non-emotional. The contents of the selected images include furniture, utensil, craftworks, tools, animals and so on. The valence of the selected neutral images is around the neutral midpoint of the 9-point rating scale while the arousal was low. The averaged values of these images are 5.26±0.39 (M±SD) for valence, and 3.91±0.63 (M±SD) for arousal.

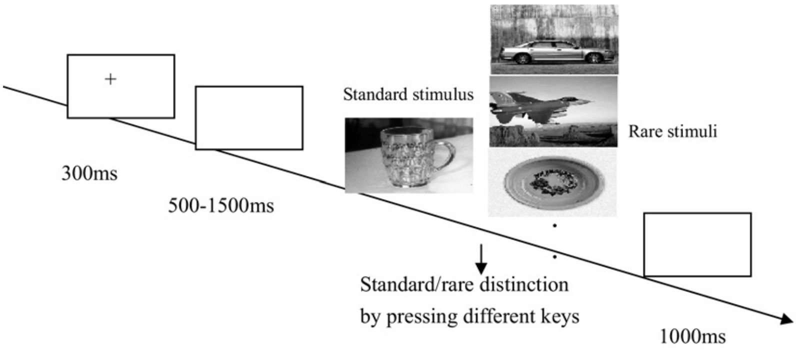


Fig. 1. Schematic illustration of the experimental procedure and the examples of stimulus pictures in Experiment 1.

formance. Twenty practice trials were used before the experiment to familiarize subjects with the procedure, and the experiment started after subjects achieved 100% accuracy in the practice session. The standard picture kept the same across practice and experiment sessions whereas rare stimuli used in practice were not chosen for the experiment (Fig. 1).

ERP recording and analysis. Electroencephalography (EEG) was recorded from 64 scalp sites using tin electrodes mounted in an elastic cap (Brain Products), with the reference electrodes 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 infraorbitally at the left eye. Horizontal EOG was recorded as the left versus right orbital rim. EEG and EOG activity was amplified with a DC $\sim$100 Hz bandpass filter and continuously sampled at 500 Hz/channel. All electrode impedances were maintained below 5 kΩ. ERP averages were computed off-line; trials with EOG artifacts (mean EOG voltage exceeding ± 80 μV), amplifier clipping artifacts, or peak-to-peak deflection exceeding ± 80 μV were excluded from averaging.

EEG activity for correct responses during either condition was averaged separately. ERP waveforms were time-locked to the onset of stimuli and the average epoch was 1000 ms, including a 200 ms pre-stimulus baseline. In order to obtain comparable trials for ERP averaging and Response Time analysis during standard and rare conditions, only standard stimuli preceding rare ones were included for data analysis. As shown by Fig. 2, amplitude differences between standard and rare conditions started at about 250 ms across genders, and these differences were manifested by a centrally peaking N2 during 250–350 ms and a parietally peaking but broadly distributed P3 at 380–560 ms intervals in the rare-standard difference waves. Based on the ERPs' topographical maps, the following 15 electrode sites were selected for statistical analysis: F3, FC3, C3, CP3, P3, Fz, FCz, Cz, CPz, Pz, F4, FC4, C4, CP4, P4. Moreover, the RS effect-related N2 and P3 components were more prominent in females than in males. Thus, the present study mainly examined stimulus (standard, rare) by gender (male, female) interaction effects for the averaged amplitudes at 250–350 and 380–560 ms intervals, by conducting a repeated measure Analysis of Variance (ANOVA) (stimuli and electrode as repeated factors while gender as a between-subjects factor). Moreover, based on the observation of significant stimulus by gender interaction effects that indicate gender effects in RS processing, we conducted an additional analysis of peak latencies and amplitudes (baseline to peak) of the N2 and P3 components at corresponding intervals, to confirm and supplement the results indicated by the raw ERP analyses. A repeated measures ANOVA was conducted on the latencies and amplitudes of these components with electrode (15 sites) as within-subject factor and gender as between-subject factor. The degrees of freedom of the F-ratio were corrected according to the Greenhouse–Geisser method in all these analyses.

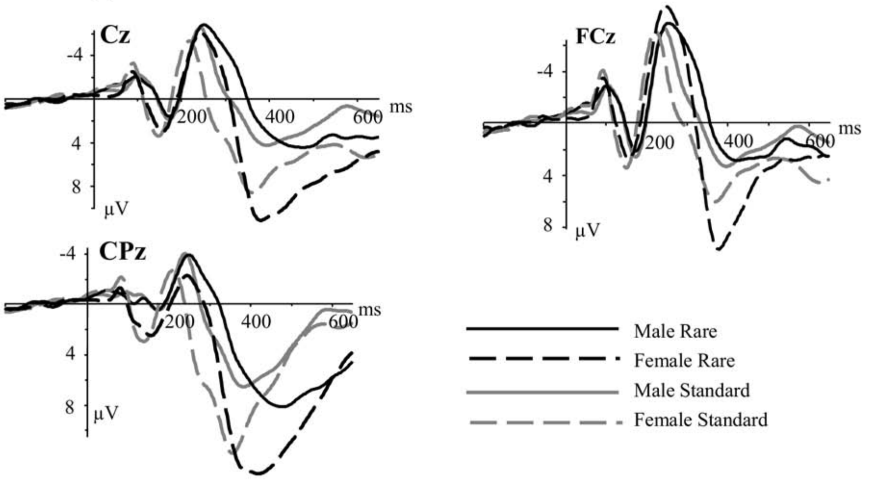
Results

Behavioral results. Erroneous responses were rare, as nearly all subjects achieved 100% accuracy for both standard and rare stimuli. The repeated measures ANOVA showed longer RTs during rare versus standard conditions ($F(1,30)=38.32$, $P<0.001$), irrespective of gender. Moreover, the stimulus and gender interaction effect was significant ($F(1,30)=7.68$, $P<0.01$). The simple effects analyses showed faster response to rare stimuli in females (M±SD: 507±61 ms) than in males (563±52 ms; $F(1,30)=5.05$, $P<0.05$) while RTs were similar across genders for the standard stimulus (males: 501±60 ms; females: 482±71 ms; $F(1,30)=0.89$, $P>0.1$).

ERP Analysis. Stimulus and gender interaction effects in raw ERPs. The repeated measures ANOVA conducted at 250–350 ms interval revealed a significant stimulus and gender interaction effect, with rare-standard amplitude difference larger in females than in males ($F(1,30)=5.82$; $P<0.05$). Additionally, rare stimuli elicited increased negativity compared to standard stimuli across genders ($F(1,30)=20.01$; $P<0.001$), and the amplitudes were larger at anterior sites than at posterior sites ($F(14,420)=44.18$; $P<0.001$). Moreover, the ANOVA demonstrated a stimulus and gender interaction at 380–560 ms interval ($F(1,30)=9.65$; $P<0.01$), with females exhibiting larger amplitude differences between rare and standard conditions than did males. Moreover, rare stimuli elicited greater positivity than standard stimuli across genders ($F(1,30)=9.29$; $P<0.01$), and consistent with prior reports (Hoffman and Polich, 1999), the amplitudes were larger in females than in males, irrespective of the stimulus condition ($F(1,30)=10.32$; $P<0.01$). The averaged amplitudes were largest at parietal sites ($F(14,420)=20.45$; $P<0.001$). Therefore, the stimulus effect and its interaction with gender were both significant at 250–350 ms and 380–560 ms intervals. This suggests that rare stimuli elicited enhanced processing, and the strength of the RS effect was different across genders at both intervals.

Gender effects in rare-standard difference ERPs. The repeated measures ANOVA of N2 amplitudes showed larger amplitudes in females than in males ($F(1,30)=9.61$; $P<0.01$; Fig. 2). In addition, the amplitudes recorded at central sites were larger than those at frontal and parietal sites across genders ($F(14,420)=18.23$; $P<0.001$). Moreover, the peak latencies of the N2 were shorter in females than in males across electrode sites ($F(1,30)=6.07$; $P<0.05$). The analysis of P3 amplitudes showed larger amplitudes in females than in males ($F(1,30)=8.28$; $P<0.01$), while P3 amplitudes were largest at parietal sites (the effect of electrode sites: $F(14,420)=9.45$; $P<0.001$). Moreover, females generated shorter peak latencies at this component than males ($F(1,30)=9.01$; $P<0.01$) and P3 latencies were longer at

(a) Raw ERPs



(b) RS effect-Related ERPs and topographical maps

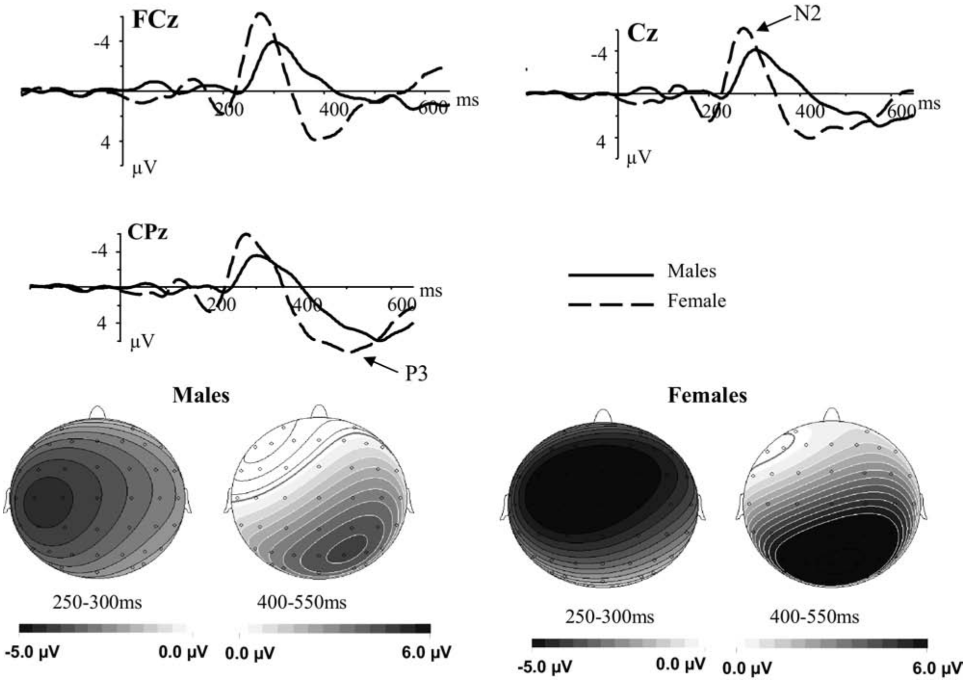


Fig. 2. Averaged ERPs in Experiment 1. Top: Raw ERPs during male standard (gray solid lines), male rare (black solid lines), female standard (gray dashed lines) and female rare (black dashed lines) conditions. Bottom: RS effect-related ERPs (rare-standard difference waves) in females (dashed lines) and males (solid lines) and topographical maps.

posterior sites than at anterior sites ($F(14,420)=3.53$; $P<0.01$). Therefore, our additional analysis of difference ERPs confirmed the results shown by the raw ERP analyses, indicating enhanced processing of rare, emotion-irrelevant stimuli in females than in males.

Discussion

Distinct from deviant stimuli in traditional oddball tasks (Campanella et al., 2002; Orozco and Ehlers, 1998), rare stimuli were not target, and their contents unpredictable in this experiment. Further, the counterbalance of response hands between subjects excluded contaminations of motor potentials and handedness on ERPs indexing RS effect (Yuan et al., 2008a,b; Alexander and Polich, 1995). In the absence of these confounds, amplitude differences between rare and standard conditions reflect RS processing. We observed a significant stimulus and gender interaction in the 250–350 ms interval where a difference N2 was observed. Many studies associated central N2 with an orienting response that directs one's attention to rare events that deviate from sensory context (Halgren and Marinkovic, 1995; Campanella et al., 2002). Therefore, our observation of a centrally peaking difference N2 suggests that both samples detected and differently processed rare stimuli by increased attention allocation. More importantly, the significant stimulus and gender interaction in this interval showed a female advantage in RS specific processing, which was confirmed by our additional analysis of difference ERPs that revealed increased amplitude and shorter latency N2 in females versus males. This may imply that females detected rare stimuli faster, and recruited greater resources for processing these stimuli than males (Barrett and Fulfs, 1998).

Moreover, we observed a stimulus and gender interaction on the amplitudes in the 380–560 ms interval where both samples displayed a pronounced RS effect-related P3 component. Parietal P3 in oddball tasks were shown to reflect cognitive evaluation of stimulus meaning and response decisional processes (Campanella et al., 2002, 2004; Yuan et al., 2007a,b). As responses were equated and counterbalanced, the difference P3 should not be attributed to motor activities (Verleger, 1997; Bentin et al., 1999). Therefore, larger P3 amplitudes for rare vs. standard stimuli here suggest that subjects recruited greater cognitive resources for RS processing (Nieuwenhuis et al., 2005) and meanwhile, to prepare a new response for rare stimuli by suppressing the habitual response to the standard stimulus (Yuan et al., 2008b). More importantly, the stimulus and gender interaction effect and our analysis of difference P3 both suggested that females probably recruited enhanced cognitive resources for rare stimulus specific processing compared to males. Consequently, females were more efficient in response decision and in preparing behavioral response for rare stimuli than males. This view was supported by the shorter P3 latencies in women, which indexes faster response decision and readiness for rare stimuli (Nieuwenhuis et al., 2005; Yu et al., 2008). Thus, females may be faster than males in using behavioral measures to cope with unusual events in life settings, which probably relates to their better ability in suppressing habitual responses (Yuan et al., 2008b). This view coincided with the shorter RTs for rare stimuli in females, and our previous finding of faster response to all rare stimuli in females, irrespective of emotion (Li et al., 2008).

Thus, behavioral and ERP data in Experiment 1 suggest that females are equipped with larger sensitivity to rare stimuli. However, as described above, the observed gender effects in RS processing, particularly the effect at P3, may be associated with gender difference in inhibiting habitual responses (Yuan et al., 2008b; Yu et al., 2008). The fast and appropriate behavioral response to environmental accidents often requires the inhibition of ongoing activity, such as people have to stop habitual walking for avoidance when detect a snake creeping in the way (Folstein and Van Petten, 2008). Despite the role of behavioral control in RS processing, whether the observed female advantage in RS processing is stable and independent of behavioral factors remains an open question. On the other hand, stimulus duration in Experiment 1 depended on the subjects' response times, which made subjects with faster response latencies (e.g. female subjects) view and process pictures at a shorter time. This may introduce a confound of picture duration on the effect of interest. To overcome this weakness and explore whether the observed gender effect is independent of behavioral factors, we conducted Experiment 2 using a passive oddball task that used fixed stimulus duration and required no behavioral responses.

Experiment 2

Subjects. As paid volunteers, 16 female (18–24 years; mean age=21.0 years) and 16 male (18–26 years; mean age=21.4 years) college students, who did not take part in Experiment 1 participated in Experiment 2. All subjects were healthy, right-handed, had normal or corrected to normal vision. They reported no history of affective disorder and were free of any psychiatric medication. The study was approved by the local Review Board for Human Participant Research and each subject signed an informed consent form prior to the experiment.

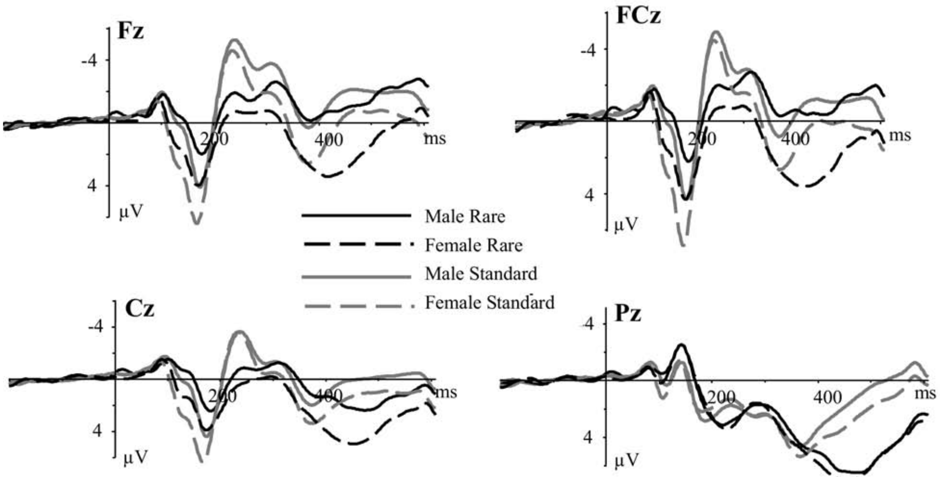
Stimuli and experimental procedure. This experiment employed a passive viewing oddball task. The stimuli and procedure in this experiment were the same as those in Experiment 1, except that subjects were told beforehand, that they were required to do nothing but to carefully view pictures in the experiment, in order to answer related questions after the experiment. The presentation of the stimulus picture lasted for 1000 ms, and was then replaced by 1000 ms of a blank screen. At the end of this experiment, subjects were debriefed about whether they experienced a "pop-out" feeling during the rare, non-cup trials. If a "yes" answer was given, they were required to rate the intensity of their "pop-out" feeling for rare stimulus presentation by a 7-point self-report scale ranging from 1 (not "pop-out" at all) to 7 (extremely "pop-out").

ERP recording and data analysis. The ERP recording and averaging was the same as that in Experiment 1. As shown by Fig. 3, the amplitude differences between standard and rare conditions started at about 100 ms across genders, and these differences were manifested by a frontocentral N1 (130–190 ms) and P2 (220–280 ms) complex, and a broadly distributed P3 (400–500 ms) component in the rare-standard difference waves. Therefore, the following 15 sites were chosen for statistical analysis: F3, Fz, F4, FC3, FC1, FCz, FC2, FC4, C3, Cz, C4 (11 central and frontal sites), CP3, CP4, CPz and Pz (four parietal sites). Moreover, the RS effect-related components, such as the N1-P2 complex and the P3, were more prominent in females than in males. Thus, the present study first examined stimulus (standard, rare) by gender (male, female) interaction effects for the averaged amplitudes during each of the 130–190 ms, 220–280 ms and 400–500 ms time intervals, by conducting a repeated measures ANOVA (stimuli and electrode were repeated factors while gender was a between-subjects factor). Similar to that in Experiment 1, we further measured and analyzed peak latencies and amplitudes (baseline to peak) of the N1, P2 and the P3 at corresponding intervals if there were significant stimulus by gender interaction effects, to confirm the results revealed by raw ERP analyses. Repeated measures ANOVA was conducted on the latencies and amplitudes of these components with electrode (15 sites) as within-subject factor and gender as between-subject factor. Further, in order to test whether rare-standard difference ERPs, as we analyzed, are valid as an index of the pop-out effect (i.e. the RS effect), we conducted a correlation analysis between difference P3 amplitudes (i.e. RS effect-related P3 amplitudes) and the subjective rating of the pop-out feelings. The degrees of freedom of the F-ratio were corrected according to the Greenhouse–Geisser method in all these analyses.

Results

ERP analysis. Stimulus and gender interaction effects in raw ERPs. The ANOVA conducted at 130–190 ms interval revealed a significant stimulus and gender interaction ($F(1,30)=7.35$; $P<0.05$), with amplitude differences between rare and standard conditions larger in females than in males. Moreover, the amplitudes were largest at central and more frontal sites ($F(14, 420)=5.58$; $P<0.01$), while rare stimuli elicited more negative deflections than the standard stimuli, irrespective of gender ($F(1,30)=38.50$; $P<0.001$). No other effects were observed at this interval. The ANOVA on the amplitudes of the 220–280 ms interval showed a stimulus and gender interaction ($F(1,30)=8.39$; $P<0.05$) and a stimulus and electrode site interaction ($F(14,420)=9.08$; $P<0.01$). In addition, the 220–280 ms amplitudes were largest at frontal sites (e.g. Fz, FCz; $F(14,420)=14.96$; $P<0.01$), and were more positive during rare versus standard conditions ($F(1,30)=34.12$; $P<0.001$).

Moreover, the ANOVA demonstrated a significant stimulus by gender by electrode sites interaction effect on the amplitudes of the 400–500 ms interval ($F(14,420)=5.13$; $P<0.01$). Further, the amplitudes were largest at parietal sites (i.e. Pz; $F(14,420)=18.92$; $P<0.001$), and rare stimuli elicited more positive deflections than the standard stimuli ($F(1,30)=5.32$; $P<0.01$). The decomposition of the three-factor interaction showed a significant stimulus and gender interaction effect across central and frontal regions ($F(1,30)=5.51$; $P<0.05$), with rare-standard amplitude differences larger in females （a）Raw ERPs



(b) RS-related ERPs and topographical maps

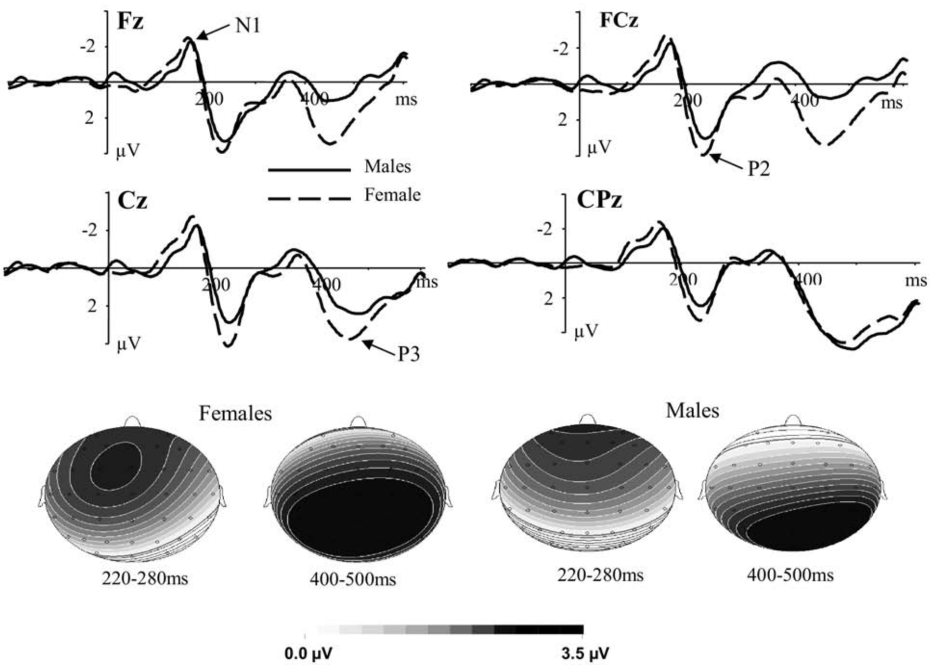


Fig. 3. Averaged ERPs in Experiment 2. Top: Raw ERPs during male standard (gray solid lines), male rare (black solid lines), female standard (gray dashed lines) and female rare (black dashed lines) conditions at Fz, FCz, Cz and Pz. Bottom: RS effect-related ERPs (rare-standard difference waves) in females (dashed lines) and males(solid lines) and topographical maps.

than in males in this region. Conversely, the stimulus by gender interaction effect was not significant at the posterior-parietal sites (i.e. CP3, CPz, CP4, Pz; $F(1,30)<1$). Therefore, there were significant gender and stimulus interaction effects on the amplitudes at each of the three intervals, suggesting that females and males are different in RS processing despite the lack of overt responses (Fig. 3).

Gender effects in rare-standard difference ERPs. The analysis of N1 showed greater amplitudes in females than in males ($F(1,30)=6.06$; $P<0.05$). The N1 amplitudes were largest at central and more frontal sites, in particular, at the sites located in the left and midline areas ($F(14,420)=3.90$; $P<0.01$; Fig. 3). Moreover, the peak latencies of N1 were shorter in females ($F(1,30)=6.88$; $P<0.02$; Fig. 3). The ANOVA of P2 showed larger amplitudes in females than in males ($F(1,30)=5.96$; $P<0.05$), and P2 amplitudes were larger at central and frontal sites than at parietal sites ($F(14,420)=13.65$; $P<0.001$; Fig. 3). Furthermore, the ANOVA of P3 amplitudes displayed a gender and electrode sites interaction ($F(14,420)=4.34$; $P<0.001$). The P3 amplitudes were largest at parietal sites ($F(14,420)=13.76$; $P<0.001$; Fig. 3). The breakdown of the interaction effect revealed larger amplitudes in females versus males at central ($F(1,30)=4.92$; $P<0.05$), centrofrontal ($F(1,30)=7.31$; $P<0.05$) and frontal ($F(1,30)=5.20$; $P<0.05$) regions. Conversely, the effect of gender was not significant at central-parietal and parietal sites ($F(1,30)<1$). Additionally, the P3 peaked earlier at frontal than at parietal sites ($F(14,420)=3.23$; $P<0.01$). Thus, the analysis of raw and RS effect related ERPs both revealed enhanced sensitivity of females to rare, emotion-irrelevant stimuli.

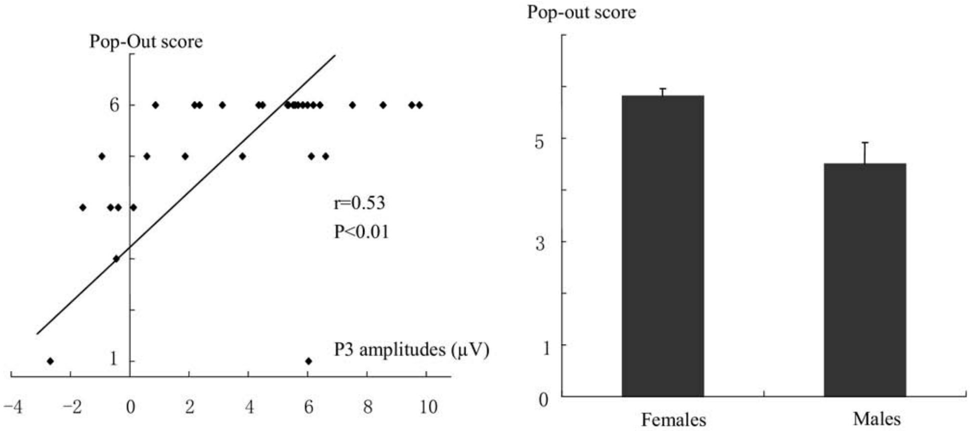


Fig. 4. (Left): The scatterplot for the correlation between RS effect related P3 amplitudes and the pop-out rating report scores. (Right) Schematic illustration of the pop-out intensity scores rated by males and females for rare picture trials (M±se).

Post-experiment debriefing and the "pop-out" assessment. In the post-experiment debriefing session, all subjects ($n=32$) reported many repetitions of a cup picture, and their experience of a sudden, attention-arousing and pop-out feeling when other pictures were presented. The correlation analysis conducted for the P3 amplitudes (collapsed across the 15 sites) and the pop-out reports showed a significant positive correlation between P3 amplitude and subjective report measures ($r=0.53$, $P<0.01$, see Fig. 4), suggesting that the P3 amplitude is a valid index for the subjective intensity of the pop-out feeling. Moreover, the pop-out rating showed higher scores in females, suggesting that females (5.81) experienced greater intensity of pop-out feeling than males (4.50) in the rare trials [$t(30)=3.05$, $P<0.01$, see Fig. 4]. Therefore, ERP data and the behavioral rating both displayed enhanced sensitivity to rare stimuli in females than in males.

Discussion

In Experiment 2, we used a passive viewing oddball task to investigate gender effect in RS processing and its neural correlates using ERP measures. The results showed that the stimulus effect and its interaction with gender were both significant at 130–190 ms, 220–280 ms and 400–500 ms intervals. Accordingly, females scored higher in the pop-out assessment, and exhibited greater N1, P2 and P3 amplitudes in the rare-standard difference waves that purely index RS processing relative to males (Nagy et al., 2003; Yuan et al., 2008a).

We observed significant amplitude differences between rare and standard conditions in the 130–190 ms and 220–280 ms intervals. These effects were manifested by obvious N1 and P2 activity in the rare-standard difference waves over central and frontal sites. It has been established that Mismatch Negativity (MMN), whose amplitudes were largest at frontal sites, appears at about 100–250 ms interval post-stimulus during oddball tasks (Wei et al., 2002; Kenemans et al., 1992). Therefore, the N1 observed in this experiment fits the archetype of visual MMN (Carretie′ et al., 2001). Because MMN is known to index preattentive processing of sensory inputs and the automatic deviance detection (Pazo-Alvarez et al., 2003), the visual MMN observed in 130–190 ms most likely reflects automatic sensory detection of rare events (Pazo-Alvarez et al., 2003; Del Cul et al., 2007). Therefore, both males and females detected the occurrence of rare events that deviate from visual background at this stage. Moreover, the stimulus and gender interaction as well as shorter latency and larger amplitude N1 in females both suggested females' enhanced sensory processing of rare stimuli. Probably, females detected rare stimuli earlier and their initial pop-out reaction was more intense than males. The enhanced sensory processing of rare stimuli may enable them to engage more attention and cognitive resources for later RS processing (Yuan et al., 2008b; Carretie′ et al., 2001). This may account for our observation of larger RS effects in females at later stages.

Frontal P2 is considered an index for attentional recruitment that provides a basis for subsequent cognitive processing (Yuan et al., 2008b; Carretie′ et al., 2001; Huang and Luo, 2006). Furthermore, P2 amplitudes were shown to increase with attention allocation (Carretie′ et al., 2001; Huang and Luo, 2006). The stimulus and gender interaction was significant and females elicited larger P2 amplitudes than males in the P2 interval. Therefore, there were gender differences in attention processing of rare, emotion-irrelevant stimuli. Specifically, females reacted more intensely to rare stimuli, and directed more attention for RS processing compared to males. Moreover, the stimulus and gender interaction remained significant in the 400–500 ms interval, while RS effect-related P3 was larger in females than in males in this passive viewing task. Therefore, our observation of a larger RS effect-related P3 in females is independent of possible gender effects in behavioral control and in motor abilities (Bjorkland and Kipp, 1996; Thomas and French, 1985; Yuan et al., 2008b). Moreover, this finding does not reflect other phenomena, such as prior reports of larger P3 in females even in a task without rare stimulus processing (Steffensen et al., 2008; Hoffman and Polich, 1999), because the measure of the P3 was based on the rare-standard difference ERPs that index pure RS processing. Instead, our observation of larger P3 in females should index enhanced cognitive resources allocated for evaluating the meanings of rare stimuli, probably with experiences referenced and more factors considered (Huang and Luo, 2006; Ito et al., 1998).

GENERAL DISCUSSION

The stability of the gender effect

Using two target-free oddball tasks, the two experiments of the present study consistently observed increased sensitivity of females to rare, emotion-irrelevant events compared to males. Females exhibited larger RS effects than males in Experiment 1 (Fig. 2). However, as stated before, the females' greater response to rare stimuli in Experiment 1 may be related to the gender effect in behavioral control (Yuan et al., 2008b; Bjorkland and Kipp, 1996). Although overt response and behavioral control may be important components for coping with rare, unusual events in life settings, whether the observed gender effect is independent of behavioral factors could not be answered with Experiment 1 alone. The results of Experiment 2 that used a response-free passive viewing task, however, confirmed the validity of the gender effect. Thus, these findings indicate that the enhanced sensitivity of females to rare stimuli is a stably existent phenomenon, irrelevant to factors of behavioral control and overt responses.

Evolutionary correlates

Greater sensitivity of females to rare stimuli might be the result of evolutionary adaptation (Espenschade and Eckert, 1980; Malina and Johnson, 1967). Evolutionary psychology has suggested that the amount and duration of investment needed to ensure the survival of offspring is greater for mothers than for fathers (Bjorkland and Kipp, 1996; Bjorklund and Shackelford, 1999). Mothers are often the primary caregivers to offspring and in that role they make substantial investments to ensure the survival of their offspring (Bjorklund and Shackelford, 1999). Accordingly, greater sensitivity and attentional bias to rare events may better equip females to respond effectively in dangerous situations (Geary, 1998; Campanella et al., 2002; Yuan et al., 2008a). Indeed the present electrophysiological (e.g. N1, P2, N2 and P3 variations) and behavioral (RT and pop-out ratings) findings are consistent with this account. On the other hand, females might have evolved an advantage for dealing with unexpected events as a compensation for physiological disadvantages relative to males (Thomas and French, 1985), such as smaller size due to earlier long bone growth termination (Roche and Malina, 1983), a lesser muscle to fat ratio and less upper body strength (Malina and Johnson, 1967; Roche and Malina, 1983). Moreover, pregnancy, lactation, and responsibility for child-rearing create further vulnerabilities for females (Teperi and Rimpela, 1989). Hence, enhanced attention sensitivity and faster responses may have evolved in females to enable them to detect accidents more quickly, and to mobilize greater psycho-physiological resources for effective management of potentially dangerous events (Yuan et al., 2007a). This would, in turn, enhance the likelihood for females and their offspring to survive in an emergency.

Implications

As is known, oddball task, which usually consists of a frequent background stimulus and infrequent deviant stimuli, is one of the most popular tasks in cognitive neuroscience studies (Orozco and Ehlers, 1998; Campanella et al., 2002, 2004). The presentation of infrequent stimulus in this task, whether the stimulus is target or not, may elicit some extent of pop-out response (Nagy et al., 2003; Campanella et al., 2002; Pazo-Alvarez et al., 2003). The functional significance of ERP components evoked during oddball tasks, such as MMN indexing deviance detection and N2b-P3a complex indicative of alerting and attentional orienting, are relevant to rare stimulus processing (Campanella et al., 2002; Yuan et al., 2008a; Wei et al., 2002). Therefore, based on the present findings, future studies using oddball paradigm should take into account the factor of gender difference in rare stimulus processing. For example, if a study using this paradigm involves only males (or mostly males), it is necessary to consider this factor when generalizing the results to females, even if gender isn't explicitly studied. Particularly, gender difference studies of other processes (e.g. linguistics, emotion) using an oddball task should take this difference into consideration.

On the other hand, numerous studies revealed that females are more sensitive to emotionally salient stimuli than men (Orozco and Ehlers, 1998; Campanella et al., 2004; Li et al., 2008; Luck, 2005). Women are faster in detecting emotional cues and greater in neural response to salient stimuli (Orozco and Ehlers, 1998; Campanella et al., 2004; Li et al., 2008). Noteworthy, females are susceptible to mild negative stimuli, which is absent in men (Li et al., 2008). As is known, emotional stimuli convey biologically important signals, such as threats, or food. The fast decoding of these signals is beneficial to individuals' adaptive living (Campanella et al., 2002; Huang and Luo, 2006; Cacioppo and Bernston, 1994). Similarly, rare stimulus is also biologically important, because any rare stimulus, whether emotional or neutral, is unusual and it happens unpredictably. Consequently, the human is sensitive to rare events so that these events are processed rapidly in the brain. This is why rare event constantly elicits orienting response, though the event is emotion-irrelevant. Because of women's physiological vulnerabilities and vital responsibility for child caring, it is evolutionarily important for females to be more sensitive to rare events relative to men, irrespective of whether the event is emotional or neutral. This mechanism would compensate for the females' physiological and other disadvantages during evolution, consequently, equipping them to better live in the changing environments. Therefore, the increased sensitivity of females to rare stimuli and to emotional stimuli is likely underlain by the same evolutionary basis.

Thus, using two adapted oddball experiments, the present study observed, for the first time, that females are equipped with enhanced sensitivity to rare, emotion-irrelevant stimuli compared to males. The greater sensitivity of females toward rare events may be an evolutionary adaptation that enhances females' abilities to cope with environmental accidents, given their physiological vulnerabilities and vital responsibility for child caring.

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