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Gender and suppression of mid-latency ERP components during stress

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Abstract

Substantial research evidence suggests that women may be more reactive to stress than men. This study examined the influence of gender and stress on suppression of the P50 and N100 components of the auditory event-related potential. During a stressor task, women ($n = 13$) showed disrupted P50 and N100 suppression whereas men ($n = 15$) exhibited only alterations in N100 suppression. Additionally, reduced skin conductance level during stress correlated with impaired P50 suppression and elevated Click 2 amplitude of the P50 response in women. These data suggest that gender differences in response to perceived stress may be an important factor to consider in studies relying upon the P50 suppression paradigm.

Descriptors: P50 suppression, N100 suppression, Electrodermal activity, Stress, Gender

Suppression of mid-latency components of the auditory event-related potential (ERP), especially the P50 component, have been proposed as experimental indices of auditory inhibition to irrelevant sensory information. Freedman and colleagues initially demonstrated that schizophrenia patients and unaffected family members of schizophrenia probands fail to exhibit typical P50 suppression to the second stimulus during a paired click paradigm (Freedman, Adler, Waldo, Pachtman, & Franks, 1983; Freedman et al., 1987). Impaired suppression of P50 also has been observed in bipolar disorder (Baker et al., 1990; Olincy & Martin, 2005), and post-traumatic stress disorder (Gillette et al., 1997; Neylan et al., 1999). In addition to observed deficits in clinical populations, arousal has been shown to disrupt P50 suppression in healthy subjects. In separate investigations, for example, we experimentally manipulated psychological stress and demonstrated that concurrent performance of a mental arithmetic task can diminish P50 suppression in nonpsychiatric subjects (White & Yee, 1997; Yee & White, 2001).

Most researchers studying inhibitory processes and ERPs have focused on P50 suppression, but several researchers have demonstrated coexisting disrupted suppression for the N100 component in clinical populations (Boutros, Belger, Campbell, D'Souza, & Krystal, 1999; Boutros, Korzyukov, Jansen, Feingold, & Bell, 2004; Clementz & Blumenfeld, 2001; Grunwald et al., 2003). N100 is hypothesized to provide an index of selective attention such that N100 in a paired click paradigm might be sensitive to attentional manipulation, whereas P50 is more likely to be largely preattentive and less affected by voluntary attention (Jerger, Biggins, & Fein, 1992; Kho et al., 2003; White & Yee, 1997). It is unclear, however, to what degree concurrent disruptions of P50 and N100 in clinical populations represent the same or distinct inhibitory processes (see Boutros & Belger, 1999; Grunwald et al., 2003).

The possibility of gender differences in P50 and N100 suppression also remains equivocal. Freedman and colleagues (1987) found that P50 amplitude to the first of paired click stimuli is larger for women than men, yet failed to observe gender differences in P50 suppression. In contrast, Judd, McAdams, Budnick, and Braff (1992) detected a complicated pattern involving age and gender among schizophrenia patients. Among younger patients, men exhibited a slightly larger P50 than women; among older patients, women produced a larger P50 than men. Hetrick et al. (1996) examined P50 gating in healthy and relatively young adults, finding that women had less suppression as reflected in higher N100 ratio scores and were less likely to exhibit P50 suppression than men, in the absence of gender differences in P50 amplitude to the first stimulus. In contrast, Clementz and Blumenfeld (2001) found no gender differences in N100 suppression. These conflicting findings could result from subtle but distinct differences between men and women in the impact of stress on inhibitory suppression that may not be revealed consistently in smaller samples and from differences in the amount of stress experienced by men and women during psychophysiological recording. Women have been shown to produce greater cardiac response to stress in studies with both healthy (Keltikangas-Järvinen & Heponiemi, 2004) and clinical populations (e.g., Grossman, Wilhelm, Kawachi, & Sparrow, 2001).

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Despite autonomic evidence of greater stress reactivity in women, research on gender differences in P50 suppression is somewhat limited and has yet to include an examination of the possible moderating influences of stress. The present study included assessment of P50 and N100 suppression during both passive baseline and stressor conditions to investigate possible differences in arousal between men and women and their relationship to inhibitory suppression. Autonomic nervous system (ANS) measures also were included to serve as indices of accompanying physiological arousal.

Method

Participants

Participants were college students (13 women and 16 men) recruited for two previously reported studies that examined the influence of psychological stress on P50 suppression (White & Yee, 1997; Yee & White, 2001). Participants ranged in age from 18 to 31 years ($M = 21.28$, $SD = 3.41$). All participants provided informed consent and received hearing tests to confirm normal hearing levels. Exclusion criteria for participants included daily tobacco use or smoking, self-reported personal or family history of neurological or psychiatric disorders, or personal history of drug or alcohol abuse.

Psychophysiological Recording Methods and Apparatus

As described in detail previously (White & Yee, 1997; Yee & White, 2001), electroencephalogram (EEG) activity was recorded from Sensormedics miniature Ag/AgCl electrodes at the three midline sites (Fz, Cz, and Pz) with a binaural reference. The electrooculogram (EOG) was recorded from electrodes placed above and below the right eye. All impedances were kept below 5000 Ω. EEG and EOG signals were collected with a Grass Model 12 Neurodata Acquisition System with analog filters set at 0.1 and 1000 Hz. After correcting for EOG artifact (Gratton, Coles, & Donchin, 1983; Miller, Gratton, & Yee, 1988), single EEG trials were digitally filtered at 10–50 Hz and 1–20 Hz for measurement of the P50 and N100, respectively. ERP averages were constructed from 80 trials in the first sample ($n = 13$; White & Yee, 1997) and 60 trials in the second sample ($n = 16$; Yee & White, 2001). The intertrial interval varied between 10 and 14 s for the first sample and 7 and 10 s for the second sample.

Heart rate was obtained with two standard Grass Ag/AgCl electrodes located bilaterally at each lower rib. The electrocardiogram signal was transferred through a Grass Model 12 amplifier to a Coulbourn Dual Comparator/Window Discriminator. The amplified signals were subjected to a digital Schmitt trigger, which detected R-waves. The intervals between R-waves were recorded in milliseconds. Average heart rate was calculated for each trial in beats per minute and averaged across trials.

Electrodermal activity was recorded with two 1.5-cm Ag/AgCl electrodes (0.5-cm recording surface) filled with sodium chloride in a Unibase conductance medium (Fowles et al., 1981), and placed on subjects' middle and index fingers on their nondominant hand following rinsing with water. Skin conductance level and nonspecific skin conductance responses were computed for each trial and then averaged across condition (for further details, see White and Yee, 1997).

Auditory stimulation. During both the passive baseline and stressor task, paired clicks were delivered at an intensity of 90 dB SPL with 40 dB SPL background white noise. All clicks were 3 ms in duration, and all paired clicks were separated by a 500-ms interval. All auditory stimuli were delivered via headphones.

Procedure

P50 suppression data were collected during baseline and an oral mental arithmetic stressor in a soundproof room. For both tasks, subjects were instructed to sit upright and avoid movement. Participants completed 7-point scales to assess anxiety and perceived task difficulty following each task.

During the baseline condition, subjects were instructed to relax and listen to clicks. During the stressor task, subjects performed serial subtractions aloud as quickly as possible while paired clicks were presented. Subtraction problems were given to subjects through headphones with a new problem presented approximately every 2 min (i.e., subtraction 1: 3605 by 3s, subtraction 2: 5428 by 7s, subtraction 3: 6507 by 13s, etc.). The experimenter corrected mistakes and at four designated times, encouraged subjects to perform more quickly. All subjects were given practice examples, with level of difficulty for experimental conditions determined by performance during practice.

Results

In the following analyses, data from one male participant were excluded from all analyses because autonomic data were not available for this subject. Data from the remaining 28 subjects were included in all analyses with the exception of skin conductance responses for one male participant that were three *SD*s above the mean. This subject was excluded only from these electrodermal analyses. ERP ratio scores were calculated as the amplitude of the ERP to Click 2 divided by the amplitude of the ERP to Click 1. After verifying that the ERP components and suppression ratios did not differ significantly between the two study cohorts, the data were combined for the present analyses.

Gender Differences in Stress Response

Self-report. Men and women showed no significant differences in self-reported levels of anxiety and perceived task difficulty during the baseline condition and stressor task (see Table 1).

Stressor task performance. Men and women did not differ in response accuracy or the number of subtractions attempted. In fact, men and women had remarkably similar performance levels during the stressor (see Table 1).

Autonomic responses. Using independent variables of gender and task in the repeated-measures ANOVA, no significant differences between men and women were found for skin conductance level or responses under baseline and stressor conditions. With regard to heart rate, a repeated-measures ANOVA revealed significant main effects for gender, $F(1,26) = 5.08$, $p < .05$, $\eta_p^2 = .16$, and task, $F(1,26) = 23.20$, $p < .001$, $\eta_p^2 = .47$). Women had a higher heart rate than men across both tasks and both men and women exhibited an elevated heart rate during the stressor relative to baseline levels (see Table 1), suggesting that the stressor was effective in producing autonomic arousal. The finding of generally elevated heart rate in women is consistent with results of a meta-analysis conducted by Stoney, Davis, and Matthews (1987).

P50 suppression ratio and amplitude. With independent factors of gender and task, a repeated-measures ANOVA on P50

Table 1. *Mean Values for ERP, Autonomic Variables, and Self-Report Measures*

	Women		Men	
Measure	*M*	*SD*	*M*	*SD*
Baseline				
Self-report measures				
Self-reported anxiety	1.85	1.21	2.27	1.33
Self-reported difficulty	2.00	1.47	1.67	0.90
Autonomic measures				
Heart rate (bpm)	71.19	12.81	63.86	9.45
Skin conductance level	3.31	2.17	3.40	2.37
Nonspecific skin conductance responses	11.84	11.94	7.29	8.46
Stressor				
Self-report measures				
Self-reported anxiety	4.46	1.71	3.73	1.26
Self-reported difficulty	6.00	1.15	5.20	1.26
Autonomic measures				
Heart rate (bpm)	81.28	12.15	71.29	10.56
Skin conductance level	3.28	1.77	3.60	1.92
Nonspecific skin conductance responses	52.23	32.50	35.43	23.40
Performance measures				
Accuracy	0.85	0.08	0.84	0.09
Number of attempts/min	10.42	4.05	10.77	3.70

ratio revealed a significant main effect of task, $F(1,26) = 10.62$, $p < .01$, $\eta_p^2 = .29$, qualified by an interaction of Gender × Task, $F(1,26) = 6.75$, $p < .05$, $\eta_p^2 = .21$, indicating that women exhibited significantly impaired P50 suppression during the stressor condition but men did not (see Figure 1).

With independent factors of gender, task, and click, P50 amplitude showed main effects of gender, $F(1,26) = 8.34$, $p < .01$, $\eta_p^2 = .24$, task, $F(1,26) = 35.27$, $p < .001$, $\eta_p^2 = .58$, and click, $F(1,26) = 84.58$, $p < .001$, $\eta_p^2 = .77$, qualified by interactions of Task × Click, $F(1,26) = 35.00$, $p < .001$, $\eta_p^2 = .57$, and Gender × Task × Click, $F(1,26) = 9.18$, $p < .01$, $\eta_p^2 = .26$. Examining the genders separately, P50 to Click 1 but not Click 2 was reduced during stress compared to baseline for women, whereas men showed significant reductions in P50 amplitude for both clicks from baseline to stress. As shown in Figure 1, women exhibited a significantly larger P50 to Click 1 than men during the baseline condition whereas men and women did not differ in response magnitude to Click 2. During the stressor condition, in contrast, men and women produced comparable responses to Click 1 but women had a significantly larger P50 to Click 2, suggesting that the impact of psychological stress on P50 suppression was greater in women then in men.

N100 suppression ratio and amplitude. Although no gender differences were revealed in N100 ratio across the two tasks, both

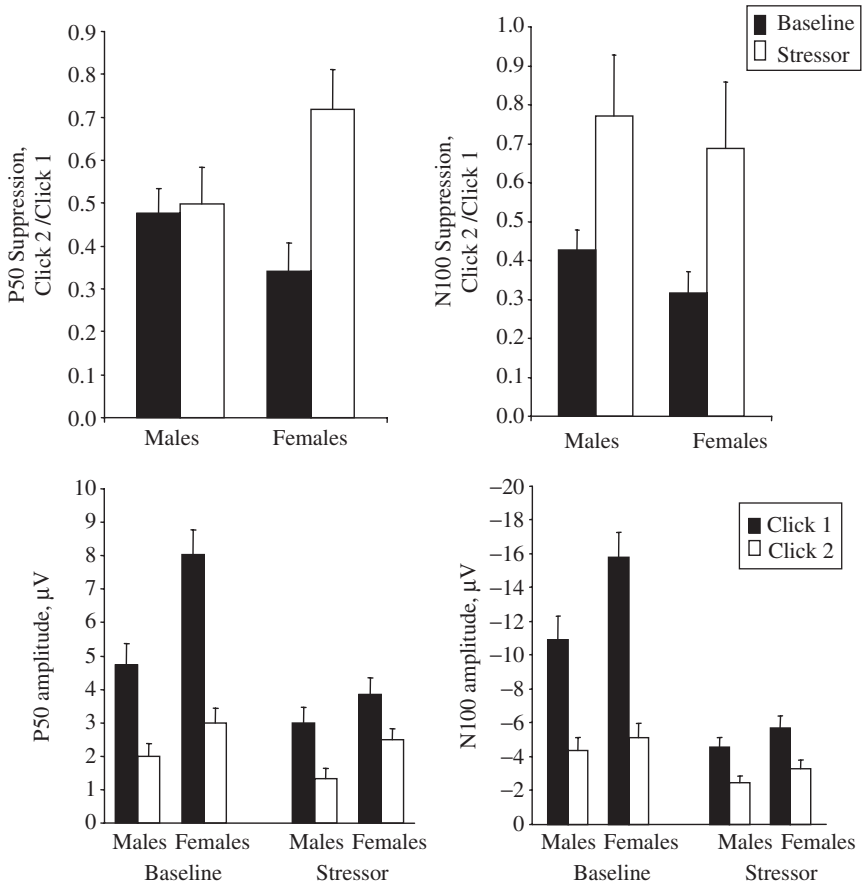

Figure 1. Gender differences in P50 suppression and N100 suppression across test conditions. Women exhibited significantly impaired P50 suppression and a significantly reduced P50 to Click 1 amplitude but not Click 2 during the stressor condition, but men did not. In contrast, both women and men exhibited significantly impaired N100 suppression and reduced N100 to Click 1 amplitude during the stressor condition.

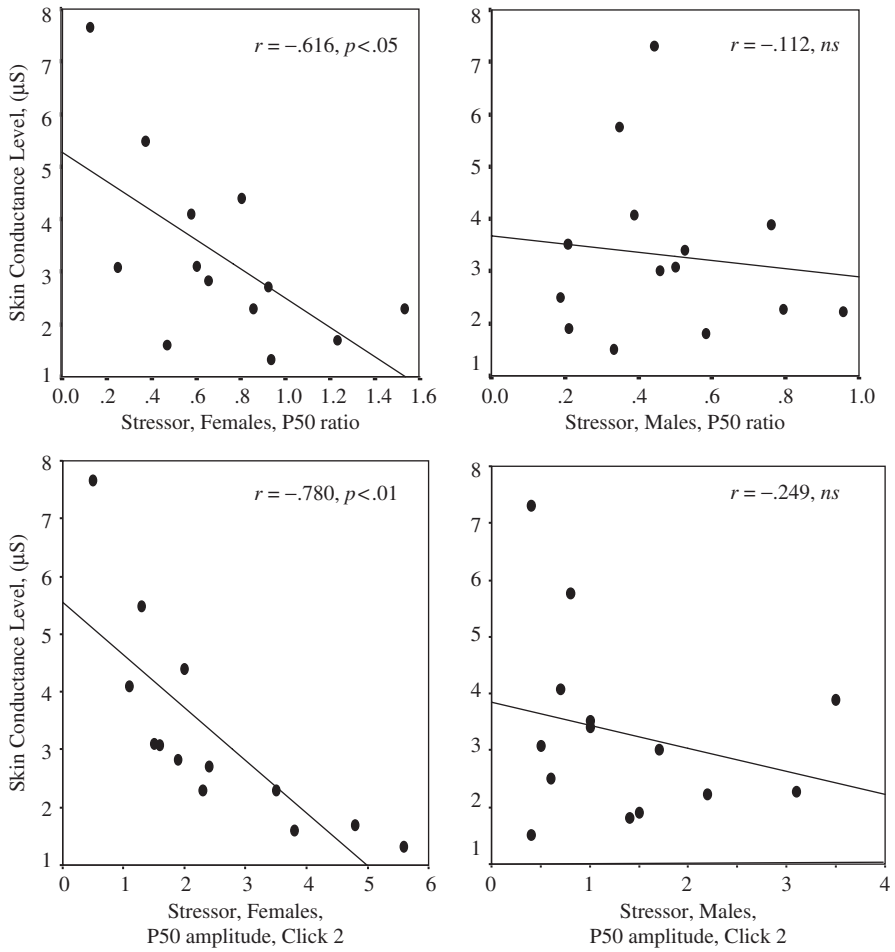

Figure 2. Gender differences in the relationship between skin conductance level and mid-latency components during the stressor task. During stress, skin conductance level showed a significant correlation with P50 suppression among women but not men. Skin conductance level was significantly related to P50 amplitude to Click 2 (not Click 1) among women but not men.

men and women had larger N100 ratios during the stressor condition than during baseline, $F(1,26) = 10.25$, $p < .01$, $\eta_p^2 = .28$, indicating that stress can disrupt N100 suppression.

A repeated-measures ANOVA on N100 amplitude revealed main effects of task, $F(1,26) = 64.80$, $p < .001$, $\eta_p^2 = .71$, and click, $F(1,26) = 83.17$, $p < .001$, $\eta_p^2 = .76$, qualified by Task × Click, $F(1,26) = 75.79$, $p < .001$, $\eta_p^2 = .75$, and Gender × Task × Click interactions, $F(1,26) = 7.09$, $p < .05$, $\eta_p^2 = .21$. Although Click 1 elicited a larger N100 in women than men during baseline, as with P50, men and women did not differ in their response to either Click 1 or Click 2 during stress, in contrast to P50 (see Figure 1). Thus, although the impact of psychological stress on P50 was greater in women then in men, the genders no longer differed in the effect of stress on N100.

Gender, autonomic measures, and inhibitory suppression. Average heart rate, skin conductance level, and nonspecific electrodermal responses were assessed for their relationship to baseline and stressor P50 and N100 suppression ratios within each gender. Among women, but not men, skin conductance level was related to P50 but not N100 suppression during stress, $r = -.62$, $p < .05$, two-tailed. This effect reflects an association between heightened skin conductance level and reductions in P50 amplitude to Click 2, $r = -.78$, $p < .01$, two-tailed, but not Click 1 (see Figure 2).

Discussion

The primary aim of this study was to assess differences between men and women in the influence of stress on inhibitory suppression of mid-latency components of the auditory ERP. Although previous presentation of these data (White & Yee, 1997; Yee & White, 2001) demonstrated stress-induced changes to the P50 suppression ratio, this investigation revealed that experimentally manipulated stress also can alter the N100 ratio in both genders. Concurrent stress-induced changes to P50 and N100 ratios are consistent with the growing body of literature finding that both P50 and N100 suppression are disrupted in clinical populations (e.g., Boutros et al., 1999; Clementz & Blumenfeld, 2001; Grunwald et al., 2003). Although women might be expected to show greater stress reactivity than men based on previous autonomic research, gender differences were observed only for P50 and not N100 suppression, with stress-induced elevation of the P50 ratio evident only in women in the present, combined sample.

Examination of the P50 amplitude data suggests that alterations in response to both clicks contributed to disruptions in P50

suppression among women during the stressor task. In contrast to men, who showed reductions in P50 to both clicks during the stressor task, women exhibited significant attenuation in P50 amplitude to Click 1 but not Click 2 during stress. In addition, although P50 amplitude to Click 2 did not differ initially between men and women during baseline, women produced a larger P50 response to Click 2 than men during the stressor task. The contribution of disrupted P50 Click 1 and Click 2 amplitude values to the P50 ratio score also have been observed in studies of P50 suppression in schizophrenia (Click 1: Clementz, Geyer, & Braff, 1997; Clementz & Blumenfeld, 2001; Click 2: Freedman et al., 1983, 1987), and underscores unresolved issues concerning the computation and interpretation of a ratio score (e.g., Smith, Boutros, & Schwarzkopf, 1994).

N100 amplitude also showed gender differences to Click 1 during baseline, but neither N100 response to Click 1 nor Click 2 showed differences between men and women during stress. In sum, women exhibited stress-induced elevation of both P50 and N100 suppression ratios whereas men showed this effect only for N100 ratios. Although the effect size was modest and warrants cautious interpretation, this finding is consistent with a body of literature that suggests that women may experience greater disruptive effects from stress than men (e.g., Davis, Matthews, & Twamley, 1999). These gender differences should be interpreted with caution, however, given that other factors could contribute to the observed group differences (e.g., neither clinical interviews nor drug screens were performed).

Women also showed an association between sympathetic arousal and P50 suppression, not seen in men. Specifically, repressed or low skin conductance levels during stressful arousal (as reflected by self-report and elevated heart rate) were associated with the greatest disruptions to P50 suppression in women. An association between repressed electrodermal activity and greater disruption to ERP inhibitory processes may initially appear counterintuitive but is consistent with observations of autonomic suppression during stress in clinical samples. For example, physiological data demonstrate that at least some generalized anxiety disorder patients may respond to psychological stress with less skin conductance and cardiac reactivity (Borkovec, Lyonfields, Wiser, & Diehl, 1993; Hoehn-Saric, McLeod, & Zimmerli, 1989). In summary, this work suggests the importance of monitoring stress and anxiety levels, particularly among women, when utilizing the P50 suppression paradigm. Additional study of gender differences also might shed light on underlying mechanisms associated with disrupted inhibitory suppression in clinical samples.

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