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ORIGINAL PAPER

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Visual emotional stimuli modulation of auditory sensory gating studied by magnetic P50 suppression

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Abstract The auditory sensory gating system modulates its sensitivity to incoming stimuli and prevents higher brain functions from sensory overload in the primary auditory cortex. We investigated whether visually evoked emotional stimuli affect auditory sensory gating. Magnetic P50 (P50m) suppression was evaluated by magnetoencephalography in fifteen healthy subjects while they viewed slides varying in emotional valence and arousal. The ratio of strength of dipole moments of the 2^{nd} to the 1^{st} P50m and the anatomical location of their sources were calculated. Negatively valenced slides significantly attenuated P50m suppression, as compared to neutral ones, while the effects of positive slides were insignificant. No effects on latencies or the location of P50m sources were observed. Thus, negative emotional stimuli may modulate sensory gating.

Key words emotion · auditory sensory gating · magnetoencephalography (MEG) · P50 suppression

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Introduction

Sensory gating is defined as the pre-attentive ability of the brain to modulate its sensitivity to an incoming stimulus, and is hypothesized to be a protective mechanism that prevents sensory overload of higher brain functions by filtering out the irrelevant sensory input (Braff and Geyer 1990). Deficit in sensory gating could result in an overload of irrelevant stimuli, which in turn may lead to perceptual and attentional impairments associated with psychiatric disorders such as schizophrenia (McGhie and Chapman 1961).

A paired click paradigm is used to evaluate the auditory sensory gating. In this paradigm, two identical stimuli (1^{st}: conditioning stimulus and 2^{nd}: test stimulus) are presented with a short inter-stimulus interval (ISI) of 500 ms and a longer inter-pair interval. The P50 appears as a positive peak in electroencephalography (EEG), at about 50 ms after the stimulus onset. Under normal conditions the amplitude of the P50 for test stimuli is smaller than that for conditioning stimuli, and this suppression of P50 is typically quantified as a ratio (S2/S1). This phenomenon is referred to as P50 suppression (Adler et al. 1982).

Magnetoencephalography (MEG) offers a non-invasive method for functional brain studies with high temporal resolution equal to that of EEG, but it enables more accurate source localization. MEG measures selectively the activity from tangential sources and is well suited for the measurement and localization of primary auditory cortical activity (Hämäläinen et al. 1993). MEG studies indicate that the magnetic P50 (P50m) counterpart is generated in the superior aspects of temporal lobes, near the primary auditory cortex (Hari et al. 1980; Reite et al. 1988; Mäkelä et al. 1994).

Cognitive and affective processing are two basic interacting modes of information processing (LeDoux 1993). Several studies have shown that emotional visual stimuli can have an effect on visual evoked potentials (VEPs), especially late component P300 in healthy sub-

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jects (Lang et al. 1990; Laurian et al. 1991; Kayser et al. 1997; Cuthbert et al. 2000). Only a few studies have investigated the effect of visual emotional stimuli on auditory information processing and have shown that emotional stimuli may in fact affect auditory processing (Schupp et al. 1997; Surakka et al. 1998). However, the exact role of the interaction between emotion and cognition remains to be elucidated. In this study, we examined whether visually evoked emotional stimuli could affect auditory sensory gating, as measured by P50m suppression in healthy subjects.

Methods

Subjects

Fifteen healthy, right-handed volunteers (14 males and 1 female), aged 22–38 years (mean age 29.5 ± 5.1y), participated in the experiment consisting of three sessions in a randomized order. The subjects reported having no history of neurological or psychiatric disorders or of any drug use for 2 weeks before the study. Because acute nicotine ingestion within 0.5 h of testing may alter P50 suppression, subjects were not permitted to smoke at least 1 h before until the end of the measurement (Adler et al. 1992). Informed consent was obtained from each subject according to institutional guidelines, and the study was approved by an institutional ethical committee.

Task procedure

During the MEG recording, the subject sat in a comfortable chair in a magnetically shielded room. The auditory evoked magnetic fields were recorded with a 204 channel MEG (Neuromag Ltd., Finland). The paired-click paradigm with an inter-click interval of 500 ms with click pairs (0.1 ms, 60dB above the individually determined subjective hearing threshold) separated by 8 s inter-pair was used. The stimuli were delivered binaurally to subjects through a non-magnetic, echo-free plastic tube system, because all previous studies which investigated P50 suppression have used bilateral stimuli (Adler et al. 1982; Braff et al. 1990; Adler et al. 1992; Light et al. 1999; Patrick et al. 1999; Adler et al. 2001), and the ipsilateral P50 response to monoaural stimuli is so small that it is difficult to detect. Three hundred digitized pictures (one hundred per category) were chosen from the International Affective Picture System (IAPS) (Lang et al. 1997). The categories were negative, neutral, and positive (e. g., mutilations, buildings, and pleasant landscapes, respectively). The visual stimuli were presented by projection onto a screen during the interval of click pair presentation for 6 s, from 1 s after the second click to 1 s before the first click of the next pair (Fig. 1). The viewing distance was 3 m, and light was dimmed during the measurement. Three sessions were recorded for 15 minutes per session in a randomized order. The subjects rated their experiences evoked by stimuli, on two dimensions: valence and arousal (Lang et al. 1997). The ratings were made on a nine-point visual analog scale. The valence scale varied from unhappy to happy. The arousal scale varied from calm to highly arousing.

Neuroimaging data collection

The position of the subject's head relative to the recording instrument was determined by measuring the magnetic fields produced by marker coils in relation to cardinal points of the head (nasion, left and right pre-auricular points), which were determined before the experiment using an Isotrack 3D-digitizer (Polhemus, Colchester, VT, U. S. A.) (Ahlfors and Ilmoniemi 1989). The recording passband was 0.1–200 Hz for MEG and EOG, and the sampling rate was 600.025 Hz. Digital band-pass filtering was performed off-line at 5–50 Hz (Light et al. 1999). The first few responses and the entire epoch coinciding with EOG or MEG changes exceeding 150 μV or 3000 ft/cm, respec-

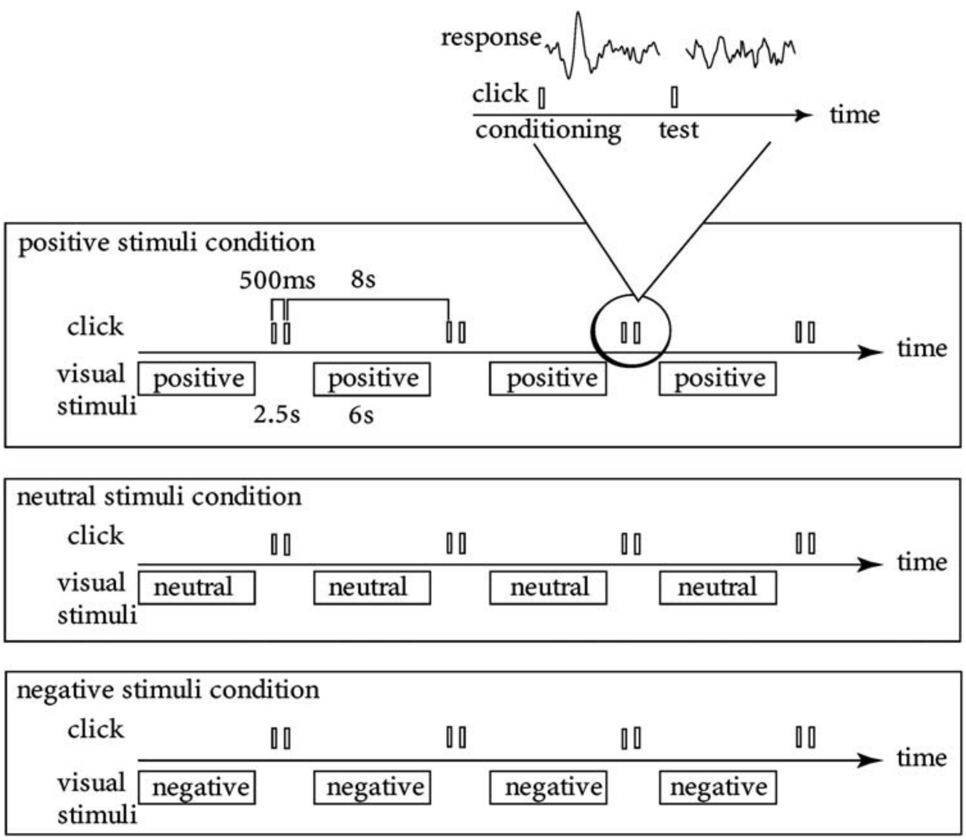

Fig. 1 Schematic diagram of the stimulus sequences in the three experimental conditions. Auditory stimuli (60dBHL, click: depicted as bars) were presented as trains of pairs in a conditioning (1st)-testing (2nd) paradigm. The inter-pair interval was 500 ms and the intra-pair interval was 8 s. The rectangles below the sounds represent visual stimuli. The visual stimuli were presented during the interval of click pairs presentation for 6 s, from 1 s after the second click to 1 s before the first click of the next pairs. Three sessions (negative, neutral, and positive slide conditions) were recorded separately

tively, were omitted from averaging. An epoch lasted 550 ms, including a 100 ms prestimulus baseline. Electrodes were attached below the right eye and above the left eye to minimize potential electrooculogram artifacts. The electrode impedances were below 5 kΩ. Subjects were monitored visually for signs of sleep. At least, 70 responses were averaged in each condition.

MEG source localization

All analyses were conducted blind to the session condition. An individual sphere model of the head was constructed from the local radius of curvature on the basis of individual MRI images. MRI was performed using a 1.5-T apparatus (General Electric Co., Milwaukee, WI, USA). The P50m peaks were obtained from the latency ranges of 35–80 ms after the stimulus presentation. The latency, location, and strength of the P50m source were analyzed with single equivalent current dipole modeling, determined by a least-squares fit using a subset of 34 channels separately over each auditory cortex (Hämäläinen et al. 1993). Dipole fits with at most 40 % residual variance and with at most 4186 mm^3 confidence volume (10 mm radius sphere) were considered successful. The latency, location and dipole moments of P50m for conditioning stimuli (Qc) and test stimuli (Qt), and the t/c ratio (Qt/Qc) in the positive and negative slide conditions were compared to those in the neutral slide condition.

Data analysis

For statistical analysis, one or two-way analyses of variance (ANOVA) for repeated measures were used. Fisher's PLSD was used for post-hoc tests. Stepwise forward multiple regression analysis was used to examine the Qc, Qt, and t/c ratio-related factors. Qc, Qt, and t/c ratio were entered into the analysis as a dependent variable. Sex, age, hemisphere, valence, and arousal during individual sessions (negative, neutral, and positive) in all subjects were entered as independent variables. In addition, the relationships between the three dependent variables and independent variables were investigated. The results are expressed as a mean ± standard deviation.

Results

The self-ratings of experiences evoked by the positive, neutral, and negative slide sessions were, respectively, 7.3 ± 0.6, 4.8 ± 0.5, and 2.2 ± 0.6 for valence; and 4.4 ± 1.1, 4.2 ± 1.0, and 7.5 ± 0.9 for arousal. A one-way ANOVA revealed a significant main effect of slide category on valence ratings ($F[2,28] = 286.4$; $p < 0.01$). Post-hoc tests showed that all the pair-wise differences were significant ($p < 0.01$). For arousal ratings ANOVA also showed a significant main effect of slide category ($F[2,28] = 67.8$; $p < 0.01$). Post-hoc test showed that the negative slides were experienced as significantly more arousing, in comparison to neutral or positive slides ($p < 0.01$).

Fig. 2 shows the typical response waveform over the left primary auditory cortex and dipole location in one

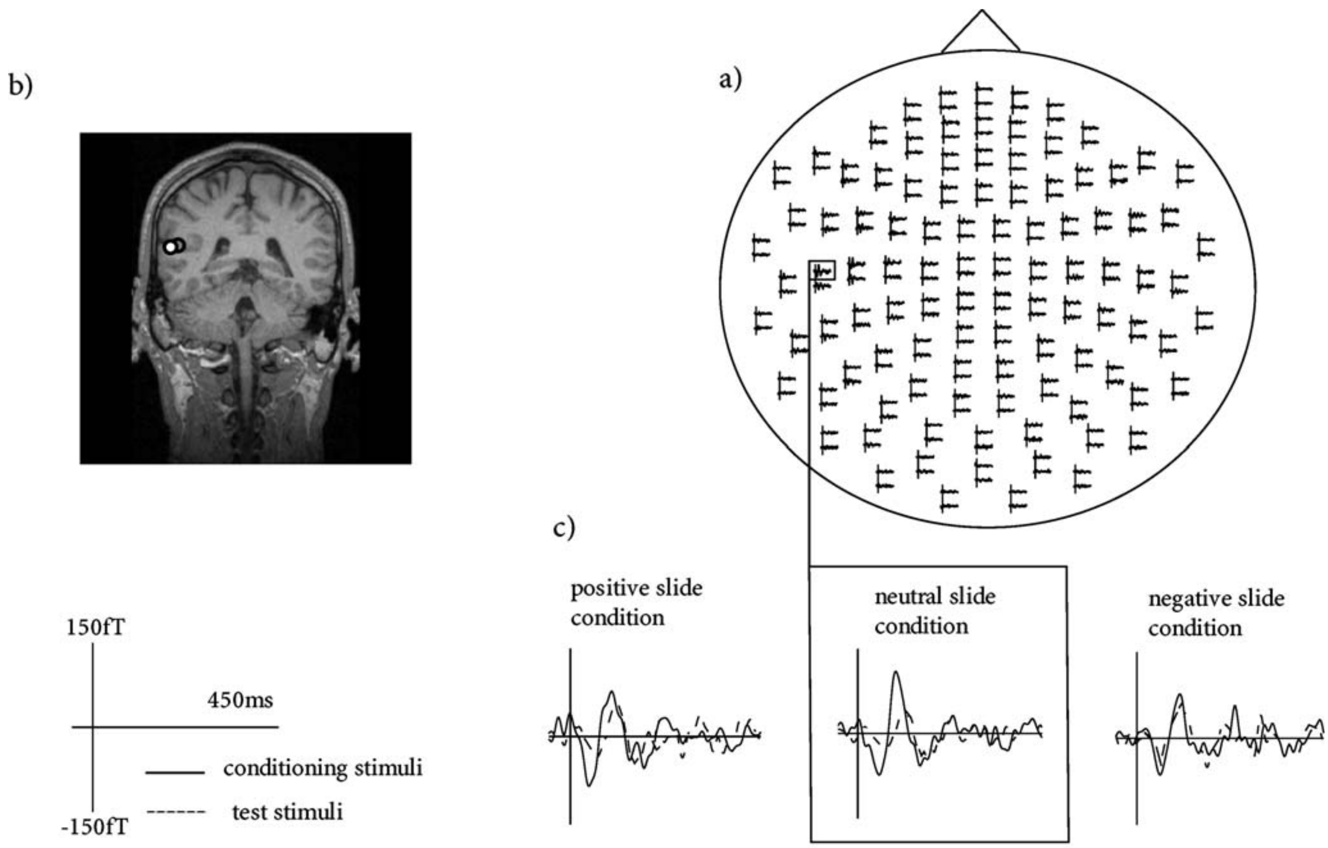

Fig. 2 **a** The average response waveform in the neutral slide condition of one representative subject. **b** Dipole locations over the left primary auditory cortex of one representative subject. The white dot represents the dipole to the conditioning click and the gray dot represents the dipole to the test click. **c** The response waveform at the channel showing maximal response in the left hemisphere in negative (left), neutral (middle), and positive slide conditions (right). The solid line represents the response to the conditioning click and the dashed line, the response to the test click. Note that the amplitude of response waveforms do not directly reflect the intensity of the underlying neural activation, which was estimated on the basis of magnetic field distribution at the sensors and the relative position of the head with respect to the sensors

subject. A significant difference between Qc and Qt in the neutral slide condition was observed in both hemispheres (left: $t = 7.85$; $p < 0.01$, right: $t = 5.19$; $p < 0.01$). The strength of Qc was not affected significantly by the slide category or hemisphere. A two-way ANOVA revealed a significant main effect of the slide category on Qt ($F[2,48] = 4.27$; $p < 0.05$), and t/c ratio ($F[2,48] = 15.97$; $p < 0.01$), and a significant main effect of hemisphere on t/c ratio ($F[1,24] = 6.29$; $p < 0.05$). Post-hoc tests showed that Qt and t/c ratio in the negative slide condition were larger than those in the positive and the neutral slide conditions, and t/c ratio in the right hemisphere was larger than that in the left hemisphere (Table 1). Slide category x hemisphere interactions were not significant in any of the analyses. P50m latencies and the source location were not significantly influenced by emotional condition (data not shown).

Table 2 shows the predictors of Qc, Qt, and the t/c ratio. There was no significant predictor of the dipole moment of the Qc response. A stepwise forward multiple regression analysis revealed that the self-rating valence of the emotional slides may have been predictive of dipole moment of Qt response, and t/c ratio and right hemisphere predicted a higher t/c ratio. The relationship between the separate independent variables and the dependent variables is shown in Table 3. The self-rating valence of the emotional slides was significantly correlated with the Qt response, and the t/c ratio. In addition, the t/c ratio was positively correlated with arousal by the emotional slides.

Table 1 Source activations in different emotional conditions

	Slide category		
	Negative	Neutral	Positive
Left hemisphere			
Qc (nAm)	15.0±3.7	18.3±7.4	18.4±6.7
Qt (nAm)	8.9±3.6*	6.0±3.4	6.5±4.2
t/c ratio	0.61±0.24**	0.33±0.17	0.33±0.17
Right hemisphere			
Qc (nAm)	14.0±7.3	16.7±7.6	16.7±7.0
Qt (nAm)	10.7±7.9*	8.0±3.6	7.2±3.9
t/c ratio	0.77±0.25**, [a]	0.48±0.21[a]	0.45±0.22[a]

* $p < 0.05$; ** $p < 0.01$, compared to Neutral and Positive slide conditions
[a] $p < 0.05$, compared to left hemisphere
Qc strength of the P50m response (dipole moment) to conditioning stimuli; *Qt* strength of the P50m response (dipole moment) to test stimuli

Table 2 Multiple regression analysis of predictors of Qc, Qt, and t/c ratio

Independent variables	Coefficient	Standardized coefficient	F	p
Qt				
Valence of stimuli	−0.508	−0.221	4.108	0.046
t/c ratio				
Valence of stimuli	−0.056	−0.454	15.338	< 0.0001
Right hemisphere	0.142	0.268		

There was no significant predictor of dipole moment of Qc response
Qt Multiple $R = 0.221$, Multiple $R^2 = 0.049$, Adjusted $R^2 = 0.037$
t/c ratio Multiple $R = 0.529$, Multiple $R^2 = 0.280$, Adjusted $R^2 = 0.261$

Discussion

The present study demonstrated that P50m suppression was attenuated by negative visual stimuli, and that this modulation effect predominated in the right, rather than the left hemisphere, and was related to emotional valence. Our study suggests that negative emotions could modulate sensory gating in the auditory cortex.

A deficit in sensory gating has been identified in a number of psychiatric disorders, most notably schizophrenia (Adler et al. 1982). Furthermore, drugs affecting emotional tone such as amphetamines (Light et al. 1999), marihuana (Patrick et al. 1999), and cocaine (Adler et al. 2001) have been reported to disrupt the P50 suppression. Although emotional stress contributes to the onset and exacerbation of illness in patients with psychiatric disorders, no study has been conducted which attempted to determine the effect of emotional stress on P50 suppression.

There have been a few studies which evaluate the effect of emotional stimuli on other components of event-related potentials (ERP). Schupp et al. (1997) reported that auditory P300 amplitudes were modulated by picture arousal, with smaller auditory P300 responses elicited when viewing highly arousing pictures regardless of their valence. They speculated that attentional resources are needed for the late information processing because they are very complicated and have more cognitive factors. On the other hand, Surakka et al. demonstrated that the mismatch negativity, an ERP component elicited by sound change that peaks about 150 ms after stimulus presentation, was attenuated by positively valenced and little arousing visual emotional stimuli (1998). Our results showed that emotional modulation of sensory processing could occur even at earlier (about

Table 3 Correlations between P50 responses and independent variables

	Qc		Qt		t/c ratio	
	r-value	p-value	r-value	p-value	r-value	p-value
age	−0.054	0.63	−0.063	0.57	−0.055	0.62
sex	0.084	0.45	0.028	0.81	−0.072	0.52
Arousal of stimuli	0.006	0.95	0.205	0.07	0.301	0.006
Valence of stimuli	0.189	0.09	−0.221	0.04	−0.456	< 0.0001

p-values were obtained with Pearson's correlation analysis

50 ms) cortical stages of auditory processing and that this modulation was related to emotional valence. Together, these results suggest that auditory processing can be affected by emotional stimuli, and in earlier stages, the emotional valence of the stimuli may predominate over the arousal effect. However, due to the small sample size, the results should be confirmed by further studies with a larger number of subjects.

The amygdala is thought to play an important role in the perception of emotionally meaningful information (Morris et al. 1996), and neurons in the amygdala of rats behave similarly to the human P50 in response to repeated auditory stimuli (Bordi and LeDoux 1992). In addition, it has been reported that fear conditioning enhances auditory evoked activity in the amygdala in response to repetitive auditory stimuli (Rogan et al. 1997). The amygdala is richly interconnected with the neocortex. Some amygdalofugal projections to auditory areas have been found, in addition to projections to visual regions (Amaral et al. 1992). Thus, we speculate that the effect of emotional visual stimuli on auditory P50m suppression, at least in part, might be mediated by the amygdala.

This P50m suppression study showed that auditory sensory gating at the primary auditory cortex was affected by emotional stimuli, and that this effect may be related more to the emotional valence than to the arousing effect of the stimuli. We suggest that a pre-attentive, automatic mechanism of the brain to gate out incoming irrelevant sensory input is affected by emotional valence.

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