

Effects of alcohol on auditory pre-attentive processing of four sound features: evidence from mismatch negativity

Jinbo He · Bingbing Li · Yongyu Guo · Risto Näätänen · Satu Pakarinen · Yue-jia Luo

Received: 31 March 2012 / Accepted: 18 July 2012 / Published online: 12 August 2012
© Springer-Verlag 2012

Abstracts

Rationale Studies have shown that alcohol could impair automatic pre-attentive change detection. However, several earlier studies which investigated alcohol-induced effects on single auditory feature independently were different from each other on the results. Meanwhile, only few auditory features have been investigated yet. Therefore, it is meaningful to investigate effects of alcohol on multiple auditory features in one experiment.

Objectives This study investigates the effects of alcohol on automatic pre-attentive change detection of four kinds of

auditory features (frequency, intensity, location, and duration) in one experiment.

Methods This study, using multi-feature oddball paradigm, compares and analyzes mismatch negativity (MMN) elicited by four kinds of auditory features (frequency, intensity, location, and duration), of 12 participants, under alcohol (0.65 g/kg) and non-alcohol condition.

Results Compared to non-alcohol condition, amplitudes of all the four MMN types significantly declined under alcohol condition, and their amplitude decline ratios decreased as deviant magnitude became larger. Latencies of frequency and intensity MMN were delayed while latencies of location and duration MMN were not delayed significantly.

Conclusion Alcohol impaired automatic pre-attentive change detection of all the four auditory features (frequency, intensity, location, and duration). However, the alcohol-induced impairment magnitude on automatic pre-attentive detection of the four auditory features was different from each other. According to analysis of amplitude, frequency seems to be affected most among the four auditory features. According to analysis of latency, only frequency and intensity were affected.

J. He · Y.-j. Luo (✉)
State Key Laboratory of Cognitive Neuroscience and Learning,
Beijing Normal University,
Beijing 100875, China
e-mail: luoyj@bnu.edu.cn

J. He · B. Li · Y. Guo
Key Laboratory of Adolescent Cyberpsychology and Behavior
of Ministry of Education, School of Psychology, Central China
Normal University,
Wuhan, China

R. Näätänen
Department of Psychology, University of Tartu,
Tartu, Estonia

R. Näätänen
Center of Functionally Integrative Neuroscience (CFIN),
University of Aarhus,
Aarhus, Denmark

R. Näätänen
Institute of Behavioral Sciences, University of Helsinki,
Helsinki, Finland

S. Pakarinen
Finnish Institute of Occupational Health,
Topeliuksenkatu 41 a,
00250 Helsinki, Finland

Keywords Alcohol · Event-related potential · Mismatch negativity · Multi-feature paradigm · Pre-attentive change detection

Introduction

The damage in attention function caused by alcohol may cause a variety of dangerous accidents, such as car accidents (Brewer and Sandow 1980; Näätänen and Summala 1976). Many studies have already reported the negative effects of alcohol on active attention, but there are only a few studies on pre-attentive processing in audition. Individuals not only

cope with environmental stimuli by engaging their attentive processes but also through their pre-attentive processing. These processes determine whether an object is worthy of attention (Wei and Yan 2008). Furthermore, pre-attentive processes are of great evolutionary value because of their capability to cope with large amounts of information automatically with no attentive resources.

Mismatch negativity (MMN; for review, see Näätänen et al. 2007) is a change-specific event-related potential (ERP) component elicited by any discriminable change in auditory stimulation. It is a marker for pre-attentive deviance detection (Grimm et al. 2006; Näätänen et al. 1978, 2004). Therefore, MMN provides an objective index to study the effects of alcohol on pre-attentive processing, which have already been studied by several researchers (for review, see Ahveninen et al. 2000; Jääskeläinen et al. 1996b).

Jääskeläinen et al. (1995a) used the traditional oddball paradigm and found that 0.50 g/kg (alcohol/body weight) of alcohol significantly decreases the amplitude of MMN elicited by a change in frequency and significantly delays its peak latency. Thereafter, some other researchers also studied the effects of alcohol on frequency MMN (e.g., 0.55 g/kg (Jääskeläinen et al. 1995b); 0.80 g/kg (Kähkönen et al. 2005); and 0.54 mL/kg (Kenemans et al. 2010)), using a similar paradigm, and their results were similar to those of Jääskeläinen et al. (1995a). In addition, Jääskeläinen et al. (1995b) found that frequency MMN elicited by smaller frequency changes is significantly impaired by a dose of 0.55 g/kg, but not 0.35 g/kg alcohol, whereas MMN elicited by a larger frequency change is not impaired by both doses. Aside from studies on the effects of alcohol on frequency MMN, Jääskeläinen et al. (1996a) also examined the effects of alcohol on MMN elicited by duration change. At an inter-stimulus interval (ISI) of 800 ms, they found that the amplitude and peak latency of duration MMN in subjects given a dose of 0.55 or 0.85 g/kg alcohol do not change significantly. However, at an ISI of 2,400 ms, the frontal MMN amplitude decreases significantly only under the larger dose, whereas the peak latency does not significantly change under either dose. These results suggest the following: (a) both frequency and duration MMN are impaired by alcohol, (b) the effects of alcohol on the amplitude of MMN differ from those on the peak latency, (c) the effects of alcohol on MMNs of different sound features differ from each other, and (d) alcohol impairment on MMNs is more obvious when the intake exceeds a certain dose. However, further studies should still be conducted to gain a better understanding regarding the effects of alcohol on auditory pre-attentive processing. First, earlier studies only tested the effects of alcohol on frequency and duration MMN. The effects of alcohol on MMNs elicited by other sound features should also be studied. Second, all earlier studies used the traditional single-feature oddball paradigm with pure sinusoidal

tones. As a result, the external validity of these studies is affected because different sound features always appear at the same time and elicit mixed effects in real-life situations. Therefore, we believe that using the multi-feature MMN paradigm would allow the comparison of the effects of alcohol on the pre-attentive processing of different sound features under the same dose. In addition, it would also improve external validity by examining the effects of alcohol on MMNs elicited by different sound features in one experiment.

Accordingly, the present study examined the effects of alcohol on the MMNs of four different sound features (frequency, intensity, location, and duration) by applying the multi-feature MMN paradigm promoted by Näätänen et al. (2004) and Pakarinen et al. (2007) to test whether alcohol affects the pre-attentive processing of different sound features differently. In addition, three deviant tones were used to test the effect of deviance magnitude on the effects of alcohol on MMN. In this study, we hypothesized the following: (a) alcohol impairs all MMNs elicited by the four sound features, (b) the effects of alcohol on MMN decrease as the magnitude of deviation of stimuli becomes larger, and (c) the effects of alcohol on MMNs elicited by the four sound features may differ from each other in terms of effect magnitude.

Materials and methods

Subjects

Twelve participants (right-handed, aged 19 to 26 years, one female) with normal hearing took part in this experiment. All of them were older than 18 and thus legitimate to consume alcohol in China. All participants were healthy normal social drinkers (3 to 12 standard alcohol per month during the past year) who had no chronic alcoholism or family history of alcoholism and other mental illnesses. They were asked to abstain from caffeine, alcohol, nicotine, and other psychoactive substances for 24 h prior to the experiment. They signed an informed consent form and committed to obey the above request. All participants were paid for taking part in this study. This study was approved by the institutional ethical committee of National Key Laboratory of Cognitive Neuroscience and Learning of China.

Treatment

All participants attended two experimental sessions (alcohol and placebo conditions) separated by 2 weeks. The order of alcohol and placebo sessions was counterbalanced across all participants. A single-blind procedure was employed in both sessions. Participants in the alcohol condition received a dose of 0.65 g/kg alcohol (53 % v/v white wine) and were provided with little food (e.g., peanuts). They were given

10 min to finish the drink. The breath alcohol concentration (BrAC) level was tested every 5 min after they finished drinking until the level was steady. The mean time interval between the finish of drinking and the beginning of the experiment was 18.75 min. The BrAC level was also tested immediately after the experiment was finished. The average BrAC level was 0.25 (± 0.05) mg/L before and 0.22 (± 0.06) mg/L after the experiment. Participants in the placebo condition received a dose of 0.02 g/kg alcohol (53 % v/v white wine mixed with distilled water) and were provided with little food. The same BrAC level test procedure as in the alcohol condition was performed after drink intake was finished. The time interval between drink intake and the experiment was 15 min. The BrAC level was zero both before and after the experiment in the placebo condition. The mean BrAC level in the alcohol condition was significantly higher than that in the placebo condition ($t_{(11)}=15.70$, $P<0.01$). In addition to BrAC level measurement, the participants were asked to report their intoxication on a five-point Likert-type scale right before and after the experiment in both conditions. The subjective report of intoxication was 2.67 (± 0.52) before and 2.50 (± 0.37) after the experiment in the alcohol condition, whereas it was 1.00 (± 0.00) before and 1.08 (± 0.28) after the experiment in the placebo condition. The subjective report of intoxication in the alcohol condition was significantly larger than that in the placebo condition ($t_{(11)}=6.37$, $P<0.01$).

Stimulus design and task

The stimuli and experimental procedure used were similar to Pakarinen et al. (2007). The standard tones were harmonic tones of 75 (± 5) ms composed of three sinusoidal partials (523, 1,046, and 1,569 Hz), with the second and third partials at 3 and 6 dB lower in intensity, respectively. They were binaurally presented via headphones at an intensity of 70 dB. The deviant tones, with the magnitude of the deviation varying across the three levels, differed from the standards in terms of frequency, intensity, duration, or perceived sound-source location. The frequency deviants differed from the standards by 3/8, 10/8, and 21/8 semitones in the Western musical scale (fundamental frequencies 512, 487, and 450 Hz). The intensity deviants were softer than the standards by steps of 5 dB (65, 60, and 55 dB). The location deviants were tones perceived 10°, 40°, or 90° to the left or right of the participant. The duration deviants were shorter than the standards by steps of 16 ms (59, 43, and 27 ms).

The tones were presented in 5.5 min sequences (6 sequences in total, 628 tones per sequence, each of the 12 deviants was presented 156 times, and all sequences beginning with 4 successive standards), with the presentation order of the sequences randomly varying across the subjects. The stimulus-onset asynchrony was 500 ms. During the period of

stimuli presentation (33 min), the subjects were asked to watch a silent video film and ignore the auditory stimuli.

Data acquisition

The electroencephalogram (EEG) was recorded (0 to 40 Hz, sampling rate of 500 Hz) by the NeuroScan system using a 64-channel Ag/AgCl electrode cap. An electrode was placed on the tip of the nose to serve as a reference channel. Both bipolar horizontal and vertical electrooculograms were recorded between electrodes placed at 1 cm from the canthi of the eyes. The EEG was filtered offline (pass band of 1 to 30 Hz). Eye movement artifacts were removed using the correlation method. Epochs of 600 ms (including a 100-ms pre-stimulus period served as a baseline for the amplitude measurement) were separately averaged for tones of different types and levels. Epochs of EEG elicited by the first eight tones of each sequence and exceeding ± 75 μ V were omitted from averaging.

The response to the standard tones was subtracted from the response to each type and level of deviant tones to derive MMNs. The most negative peak occurring at 100 to 250 ms after stimulus onset of the Fz channel was selected as the MMN peak amplitude and peak latency. We noticed two peaks during the MMN time window of intensity MMN. With reference to an earlier study (Jacobsen and Schröger 2001) and our observation of the wave maps of intensity deviant tones, the first peak was caused by the difference of N1 between intensity deviant tones and standard tones, which reflected the refreshing of neural cells. The second peak was the true MMN caused by the changes of intensity deviant tones compared with the standard tones, which reflected the automatic processing of stimulus change based on sensory memory. Therefore, we selected the amplitude of the second peak as the amplitude of intensity MMN.

Data analysis

The distribution of dependent measures of our experiment was not significantly different from normal distribution according to Kolmogorov–Smirnov test on the dependent measures ($P>0.05$). To examine the effects of alcohol on the MMNs of different types and levels of deviant tones, a two-way repeated measures analysis of variance (ANOVA) was conducted separately for MMNs of different types, with the factors being condition (placebo and alcohol) and magnitude of deviation (small, medium, and large magnitudes).

To compare the different effects of alcohol on MMNs among the four types, a two-way repeated ANOVA was conducted separately for the MMN amplitude decline ratio, which is calculated as $(\text{amplitude}_{\text{placebo condition}} - \text{amplitude}_{\text{alcohol condition}}) / \text{amplitude}_{\text{placebo condition}}$, and the peak latency delay ratio, calculated as $(\text{peak latency}_{\text{alcohol condition}} - \text{peak latency}_{\text{placebo condition}}) / \text{peak latency}_{\text{placebo condition}}$ for MMNs

of different types and levels. The factors used were the type (frequency, intensity, location, and duration) and magnitude (small, medium, and large magnitudes) of deviation. Greenhouse–Geisser correction was used in ANOVA when appropriate, and Bonferroni correction tests were carried out as post hoc analysis.

Results

Amplitude

The results of two-way repeated ANOVA showed no significant interaction effects between condition (placebo and alcohol) and magnitude of deviation (small, medium, and large magnitudes) for frequency, intensity, and location MMNs. The main effect of condition was significant for MMNs of all these three sound features (frequency, $F_{1, 11}=8.027$, $P<0.05$; intensity, $F_{1, 11}=9.745$, $P<0.05$; location, $F_{1, 11}=12.388$, $P<0.01$). The amplitude of MMNs for each magnitude level was larger in the placebo condition than in the alcohol condition for all the three types of MMNs. Meanwhile, the main effect of magnitude of deviation was also significant for MMNs of all these three types (frequency, $F_{1, 11}=26.066$, $P<0.01$; intensity, $F_{1, 11}=34.180$, $P<0.01$; location, $F_{1, 11}=18.704$, $P<0.01$). The amplitude of MMNs became larger as the magnitude of deviation became larger for all the three types of MMNs. However, the interaction effect between condition and magnitude of deviation was significant for duration MMN ($F_{1, 11}=3.586$, $P<0.05$). Analysis of the simple effect of condition showed that duration MMNs elicited by deviant stimuli of small and medium magnitude levels were significantly larger in the placebo condition than in the alcohol condition (small magnitude, $F_{1, 11}=14.19$, $P<0.01$; medium magnitude, $F_{1, 11}=10.11$, $P<0.01$). However, the amplitude of duration MMN elicited by large magnitude

level was not significantly changed in the alcohol condition compared with the placebo condition ($P>0.1$; see Fig. 1). The absolute value of amplitude of MMNs was illustrated in Table 1 (significant level in it was based on paired t test).

Peak latency

The results of two-way repeated ANOVA showed no significant interaction effects between condition (placebo and alcohol) and magnitude of deviation (small, medium, and large magnitudes) for all the four types of MMNs ($P>0.1$). The main effect of condition was significant for both frequency and intensity MMNs (frequency, $F_{1, 11}=20.203$, $P<0.01$; intensity, $F_{1, 11}=8.488$, $P<0.05$). The peak latency of MMNs was delayed in the alcohol condition compared with the placebo condition for both frequency and intensity MMNs. Meanwhile, the main effect of magnitude of deviation was also significant for MMNs of both sound features (frequency, $F_{1, 11}=20.437$, $P<0.01$; intensity, $F_{1, 11}=16.462$, $P<0.01$). The peak latency of MMNs of both types became shorter as the magnitude of deviation became larger. The main effect of condition was not significant for both location and duration MMNs ($P>0.1$), whereas the main effect of the magnitude of deviation was significant (location, $F_{1, 11}=15.903$, $P<0.01$; duration, $F_{1, 11}=20.396$, $P<0.01$). The peak latency of MMNs of both types also became shorter as the magnitude of deviation became larger (see Fig. 1). The absolute value of latency of MMNs was illustrated in Table 1 (significant level in it was based on paired t test).

Amplitude decline ratio

The interaction effect of type (frequency, intensity, location, and duration) and magnitude of deviation (small, medium, and large magnitudes) was significant ($F_{6, 66}=7.49$, $P<0.01$). Based on simple effect analysis, the comparison of the different types showed that the amplitude decline ratio

Fig. 1 Grand average MMN for electrode site Fz of different types and levels. From left to right are frequency, intensity, location, and duration MMNs. Rows 1, 2, and 3 show MMNs of small, medium, and large magnitudes of deviation, respectively

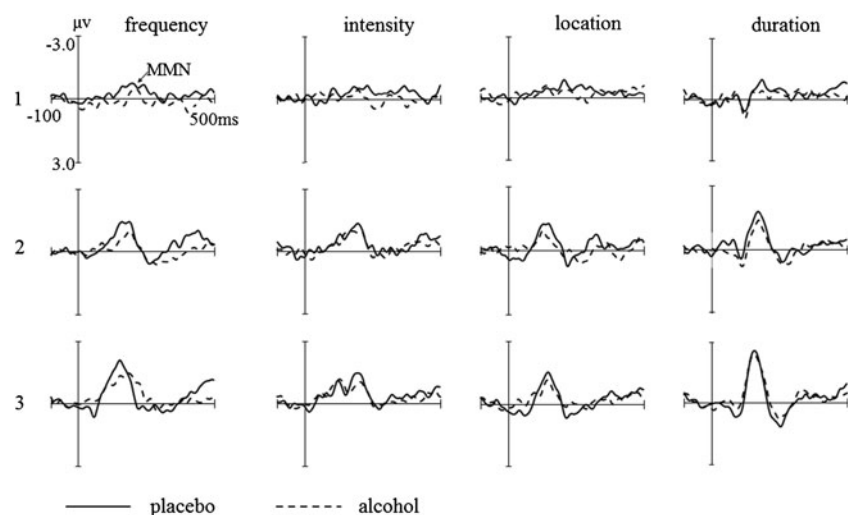


Table 1 MMN amplitudes and latencies in placebo and alcohol condition (mean±SD)

Feature	Deviant level	Amplitude (µV)		Latency (ms)	
		Placebo	Alcohol	Placebo	Alcohol
Frequency	Small	-0.96 (0.32)	-0.57 (0.39)*	183 (19)	202 (12)**
	Medium	-1.62 (0.33)	-1.28 (0.34)*	162 (15)	184 (14)*
	Large	-2.39 (0.26)	-1.87 (0.24)	149 (17)	160 (26)
Intensity	Small	-0.80 (0.29)	-0.44 (0.30)**	184 (33)	198 (35)**
	Medium	-1.35 (0.33)	-1.07 (0.34)*	178 (22)	188 (25)
	Large	-1.68 (0.28)	-1.36 (0.24)	173 (35)	186 (36)
Location	Small	-1.02 (0.54)	-0.76 (0.45)*	202 (26)	200 (37)
	Medium	-1.45 (0.30)	-1.17 (0.29)*	150 (22)	152 (15)
	Large	-1.52 (0.36)	-1.31 (0.29)	152 (19)	148 (25)
Duration	Small	-0.91 (0.33)	-0.65 (0.30)**	184 (16)	183 (21)
	Medium	-2.01 (0.35)	-1.57 (0.32)**	174 (22)	173 (25)
	Large	-2.58 (0.24)	-2.49 (0.27)	154 (17)	156 (20)

* $P < 0.05$, ** $P < 0.01$

was significantly different from one another for MMNs of the four types under medium and large magnitudes of deviation (medium, $F_{3, 33} = 4.89$, $P < 0.01$; large, $F_{3, 33} = 19.96$, $P < 0.01$). The amplitude decline ratio of frequency MMN was larger than all the other three types of MMNs under both medium and large magnitudes of deviation. No differences were observed among the amplitude decline ratios of intensity, location, and duration MMNs under medium magnitude of deviation. However, the amplitude decline ratios of intensity and location MMNs were larger than duration MMNs under large magnitude of deviation, whereas no differences were observed between the amplitude decline ratios of MMNs elicited by both sound features.

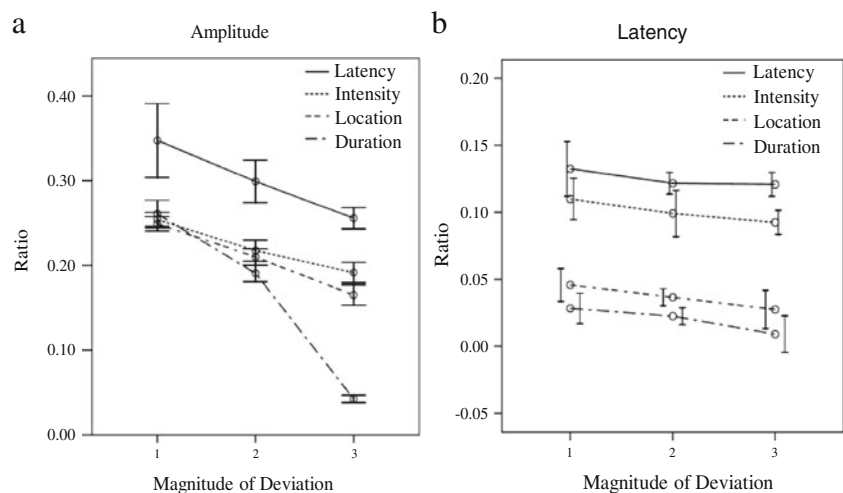
The comparison within types showed that the effects of magnitude of deviation were significant for intensity, location, and duration MMNs (intensity, $F_{2, 22} = 7.26$, $P < 0.01$; location, $F_{2, 22} = 4.79$, $P < 0.05$; duration, $F_{2, 22} = 19.07$, $P < 0.01$), whereas the effects of magnitude of deviation were approaching significance ($P = 0.068$) for the amplitude decline ratios of

frequency MMN. The amplitude decline ratio decreased as the magnitude of deviation became larger (see Fig. 2).

Peak latency delay ratio

The results of two-way repeated ANOVA showed that neither the interaction effects between type (frequency, intensity, location, and duration) and magnitude of deviation (small, medium, and large magnitudes) nor the main effects of magnitude of deviation were significant for peak latency delay ratio ($P > 0.1$). However, the main effect of type was significant ($F_{3, 33} = 4.73$, $P < 0.01$). Post hoc comparison based on Bonferroni correction showed that the peak latency decay ratios of frequency and intensity MMNs were larger than those of location and duration MMNs ($P < 0.05$). Neither the differences between the peak latency delay ratios of frequency and intensity MMNs nor the differences between the peak latency delay ratios of location and duration MMNs were significant ($P > 0.1$; see Fig. 2).

Fig. 2 **a** Amplitude decline ratios of MMNs of different types and levels. **b** Peak latency delay ratios of MMNs of different types and levels. Numbers 1, 2, and 3 in the x-axis each represent small, medium, and large magnitudes of deviation, respectively



Discussion

The results from the analysis of amplitude and peak latency of MMNs indicated that alcohol elicited different effects on the amplitude and peak latency of MMNs. The main effect of condition (alcohol and placebo) was significant for MMNs of all the four sound features. This result suggested that the amplitude of MMNs was larger in placebo condition than in the alcohol condition for MMNs of all types and levels, except for the duration MMNs elicited by tones of large magnitude of deviant levels. Moreover, the ability of pre-attentive change to detect changes in sound features (frequency, intensity, location, and duration) was significantly impaired by a dose of 0.65 g/kg alcohol. This result is consistent with our first hypothesis. In addition, the effects of alcohol on frequency and duration MMNs in this study are similar to those reported in earlier studies (Jääskeläinen et al. 1996a, 1995a, b; Kähkönen et al. 2005; Kenemans et al. 2010). This study confirmed the results of earlier studies. In addition, it also extended the results by proving that alcohol not only impairs the pre-attentive detection of frequency and duration auditory changes but also impairs that of intensity and location auditory changes.

However, the impairment of peak latency was not as steady as that of amplitude. The main effect of condition (alcohol and placebo) was significant for frequency and intensity MMNs but not for location and duration MMNs. Earlier studies also found that alcohol elicits different effects on amplitude and peak latency. Jääskeläinen et al. (1996a) found that the amplitude of duration MMN was significantly decreased after alcohol drinking, whereas the peak latency of duration MMN did not significantly change. These results indicated that the amplitude of MMN was more sensitive to alcohol than peak latency.

Amplitude decline ratio decreased as the magnitude of deviation became larger. This result suggested that alcohol impairment of pre-attentive change detection decreased as the magnitude of deviation became larger. Alcohol did not affect simple change detection but only the more complicated and subtle sensory perceptive processing of stimuli. Jääskeläinen et al. (1995b) also found that the frequency MMN of more widely deviant stimuli did not change significantly, whereas the MMN of less deviant stimuli decreased significantly after alcohol ingestion. They attributed this result to the higher threshold for the pre-attentive detection of acoustic deviations after alcohol ingestion, which meant that the pre-attentive change detection of subtle changes was impaired. Earlier studies (Jääskeläinen et al. 1996a, b) also found that N1 was not impaired by alcohol, whereas MMNs were significantly impaired. Kenemans et al. (2010) found that the amplitude of visual SFD80 (spatial frequency-dependent difference at 80 ms; Kenemans et al. 2000) did not change after alcohol ingestion, whereas visual mismatch negativity (for reviews, see Czigler 2007; Pazo-Alvarez et al. 2003) decreased

significantly. N1 and SFD80 are ERP components that reflect sensory processing, whereas MMN reflects memory-dependent processing.

The main effect of type (frequency, intensity, location, and duration) for the amplitude decline ratio was significant under medium and large magnitudes of deviation level. The decline ratios of frequency MMNs were significantly larger than all the other three MMN types under both levels. The decline ratios of intensity and location MMNs were larger than duration MMNs under both small and medium magnitudes, whereas no significant differences were found between them under both levels. This is somehow unclear. These results indicated that alcohol impaired the frequency MMN the most, intensity and location MMN less, and duration MMN the least of all the four MMN types. The amplitude decline ratio of duration MMNs elicited by tones of large magnitude of deviation level was significantly less than that of the small and medium levels and that of the other MMN types under the same deviant level. No differences were found between the amplitude of duration MMNs elicited by the large magnitude of deviation level in the placebo and alcohol conditions (Fig. 1), which indicated that alcohol elicited no effect on the pre-attentive change detection of temporal features of tones, when the magnitude of deviation was excessively large compared with the standard tones that pre-attentive processing was not deep enough.

The effects of feature and magnitude of deviation level on peak latency delay ratio were different from those on amplitude decline ratio. No significant interaction effects were found between the type (frequency, intensity, location, and duration) and magnitude (small, medium, and large magnitudes) of deviation. The main effect of magnitude of deviance level was not significant for any of the four MMN types. Different from the amplitude decline ratio, the peak latency delay ratio did not decrease as the magnitude of deviance level became larger. This result implied that peak latency was not as sensitive to the effects of alcohol as amplitude. In addition, the differences in peak latency delay ratio between the different sound features were also different from those in amplitude decline ratio. Similar peak latency delay ratios were found between frequency and intensity MMNs as well as between location and duration MMNs under the same magnitude of deviation level. However, the peak latency delay ratios of frequency and intensity MMNs were larger than those of location and duration MMNs. Further studies should be conducted to determine why the effects of alcohol on amplitude and peak latency were different. However, earlier studies reported that peak latency is not as steady as amplitude to be used as an index of the effects of alcohol on MMN. Therefore, further studies are necessary to verify the results based on peak latency.

The results showed that effects of alcohol on frequency and intensity MMNs as well as on location and duration MMNs

were similar. Moreover, the effects of alcohol on the former two MMN types were different from those of the latter two MMN types. This result indicated that the effects of alcohol on the pre-attentive change detection of spectrum auditory information (frequency and intensity) were different from those of temporal information (duration). This result may be attributed to the fact that pre-attentive change detection of spectrum information is different from that of temporal information. Whether acoustic features are processed independently or pre-attentively integrated has been under debate (e.g., Giard et al. 1995; Schairer et al. 2001; Winkler et al. 1996). Recent studies have supported the independent view. Grimm et al. (2006) found a right hemisphere preponderance for frequency MMN but not for duration MMN. Molholm et al. (2005) found that anatomically distinct networks of auditory cortices are activated by different acoustic features (frequency and duration) using functional magnetic resonance imaging technology. Changes in duration activated both the left and right frontal cortices, whereas changes in frequency only activated the right frontal cortex. Frequency and intensity features reflected spectrum information of tones, whereas location (the different initial time between two ears in this study) and duration features reflected temporal information of tones. Therefore, the results of this study not only supported the view that the pre-attentive processing of acoustic features occurred independently, but they also suggested that pre-attentive change detection of spectrum information was more sensitive to alcohol than temporal information.

This study used the multi-feature MMN paradigm to examine the effects of alcohol on MMNs of four sound features (frequency, intensity, location, and duration). In conclusion, this study showed that: (a) The MMNs of all the four sound features were impaired by alcohol, and the impairment decreased as the magnitude of deviation level became larger. In addition, the amplitude of MMN was more sensitive to alcohol than peak latency; (b) The trends of the effects of alcohol on the MMNs of different sound features differed from each other. In terms of the amplitude decline ratio, frequency MMN was impaired the most, intensity and location MMN were less impaired, and duration MMN was impaired the least. Meanwhile, the peak latency delay ratios of frequency and intensity MMNs were larger than those of location and duration MMNs, whereas no differences were observed between the latter two MMNs.

Acknowledgments The authors would like to thank Prof. Kenemans and Prof. Ahveninen for sharing their papers with us (Ahveninen et al. 2000; Kenemans et al. 2010). The experiments comply with the current laws of China where the experiments were performed. This study was supported by open fund “Effects of Alcohol on Pre-attentive Processing (200926)” of National Key Laboratory of Cognitive Neuroscience and Learning of China, 973 program (2011CB711000), and NSFC (30930031).

Conflict of interest None.

References

- Ahveninen J, Escera C, Polo MD, Grau C, Jääskeläinen IP (2000) Acute and chronic effects of alcohol on preattentive auditory processing as reflected by mismatch negativity. *Audiol Neuro Otol* 5:303–311
- Brewer N, Sandow B (1980) Alcohol effects on driver performance under conditions of divided attention. *Ergonomics* 23:185–190
- Czigler I (2007) Visual mismatch negativity: violation of nonattended environmental regularities. *J Psychophysiol* 21:224–230
- Giard M, Lavikainen J, Reinikainen K, Perrin F, Bertrand O, Pernier J, Näätänen R (1995) Separate representation of stimulus frequency, intensity, and duration in auditory sensory memory: an event-related potential and dipole-model analysis. *J Cogn Neurosci* 7:133–143
- Grimm S, Roeber U, Trujillo-Barreto NJ, Schroger E (2006) Mechanisms for detecting auditory temporal and spectral deviations operate over similar time windows but are divided differently between the two hemispheres. *NeuroImage* 32:275–282
- Jääskeläinen IP, Lehtokoski A, Alho K, Kujala T, Pekkonen E, Sinclair JD, Näätänen R, Sillanaukee P (1995a) Low dose of ethanol suppresses mismatch negativity of auditory event-related potentials. *Alcohol Clin Exp Res* 19:607–610
- Jääskeläinen IP, Pekkonen E, Alho K, Sinclair JD, Sillanaukee P, Näätänen R (1995b) Dose-related effect of alcohol on mismatch negativity and reaction time performance. *Alcohol* 12:491–495
- Jääskeläinen I, Pekkonen E, Hirvonen J, Sillanaukee P, Näätänen R (1996a) Mismatch negativity subcomponents and ethyl alcohol. *Biol Psychol* 43:13–25
- Jääskeläinen IP, Näätänen R, Sillanaukee P (1996b) Effect of acute ethanol on auditory and visual event-related potentials: a review and reinterpretation. *Biol Psychiatry* 40:284–291
- Jacobsen T, Schröger E (2001) Is there pre-attentive memory-based comparison of pitch? *Psychophysiology* 38:723–727
- Kähkönen S, Rossi EM, Yamashita H (2005) Alcohol impairs auditory processing of frequency changes and novel sounds: a combined MEG and EEG study. *Psychopharmacology* 177:366–372
- Kenemans J, Baas J, Mangun G, Lijffijt M, Verbaten M (2000) On the processing of spatial frequencies as revealed by evoked-potential source modeling. *Clin Neurophysiol* 111:1113–1123
- Kenemans JL, Hebly W, van den Heuvel EHM, Grent-T-Jong T (2010) Moderate alcohol disrupts a mechanism for detection of rare events in human visual cortex. *J Psychopharmacol* 24:839–845
- Molholm S, Martinez A, Ritter W, Javitt DC, Foxe JJ (2005) The neural circuitry of pre-attentive auditory change-detection: an fMRI study of pitch and duration mismatch negativity generators. *Cereb Cortex* 15:545–551
- Näätänen R, Summala H (1976) Road-user behavior and traffic accidents. North-Holland, Amsterdam
- Näätänen R, Gaillard AWK, Mäntysalo S (1978) Early selective-attention effect on evoked potential reinterpreted. *Acta Psychol* 42:313–329
- Näätänen R, Pakarinen S, Rinne T, Takegata R (2004) The mismatch negativity (MMN): towards the optimal paradigm. *Clin Neurophysiol* 115:140–144
- Näätänen R, Paavilainen P, Rinne T, Alho K (2007) The mismatch negativity (MMN) in basic research of central auditory processing: a review. *Clin Neurophysiol* 118:2544–2590

- Pakarinen S, Takegata R, Rinne T, Huotilainen M, Näätänen R (2007) Measurement of extensive auditory discrimination profiles using the mismatch negativity (MMN) of the auditory event-related potential (ERP). *Clin Neurophysiol* 118:177–185
- Pazo-Alvarez P, Cadaveira F, Amenedo E (2003) MMN in the visual modality: a review. *Biol Psychol* 63:199–236
- Schairer KS, Gould HJ, Pousson MA (2001) Source generators of mismatch negativity to multiple deviant stimulus types. *Brain Topogr* 14:117–130
- Wei JH, Yan KL (2008) *Fundamentals of cognitive neuroscience*. People's Education Press, Beijing
- Winkler I, Karmos G, Näätänen R (1996) Adaptive modeling of the unattended acoustic environment reflected in the mismatch negativity event-related potential. *Brain Res* 742:239–252