Auditory sensory memory as indicated by mismatch negativity in chronic alcoholism

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Abstract

Objectives: A pre-conscious auditory sensory (echoic) memory of about 10 s duration can be studied with the event-related brain potential mismatch negativity (MMN). Previous work indicates that this memory is preserved in abstinent chronic alcoholics for a duration of up to 2 s. The authors‘ aim was to determine the integrity of auditory sensory memory as indexed by MMN in chronic alcoholism, when this memory has to be functionally active for a longer period of time.

Methods: The presence of MMN for stimuli that differ in duration was tested at memory probe intervals (MPIs) of 0.4 and 5.0 s in 17 abstinent chronic alcoholic patients and in 17 healthy age-matched control subjects.

Results: MMN was similar in alcoholics and controls when the MPI was 0.4 s, whereas MMN could not be observed in the patients when the MPI was increased to 5.0 s.

Conclusions: These results provide evidence of an impairment of auditory sensory memory in abstinent chronic alcoholics, whereas the automatic stimulus-change detector mechanism, involved in MMN generation, is preserved.

Keywords: Alcoholism; Auditory sensory memory; Echoic memory; Memory trace decay; Auditory event-related potentials; Mismatch negativity

1. Introduction

In the last two decades the exceptional temporal resolution of event-related brain potentials (ERPs) has enabled the detection of a wide range of neurophysiological alterations in chronic abstinent alcoholic patients. In the auditory modality these alterations extend from brain-stem (Begleiter et al., 1981; Díaz et al., 1990; Cadaveira et al., 1991) to middle-latency (Díaz et al., 1990) and long-latency (Porjesz and Begleiter, 1985; Cadaveira et al., 1991) auditory ERPs. Neurophysiological studies in chronic alcoholism have also been conducted recently with mismatch negativity (MMN) (Kathmann et al., 1995; Polo et al., 1999; Ahveninen et al., 1999), an ERP elicited with a maximum amplitude between 100 and 200 ms from stimulus onset. MMN can be obtained, even in the absence of behavioural responses (Näätänen, 1992), by presenting the subject with deviant stimuli that immediately follow a sequence of several repetitive (standard) stimuli (Cowan et al., 1993; Grau et al., 1998). MMN reflects the functioning of an automatic stimulus-change detector mechanism, which is activated when a deviant stimulus does not match a sensory memory trace left by the preceding standard stimuli (Näätänen, 1992). The memory trace decays over time, as reflected by the fact that MMN is no longer elicited when there is a delay (i.e. a memory probe interval or MPI) exceeding a certain limit between the last standard stimulus of the sequence and the succeeding deviant stimulus (Näätänen, 1992; Sams et al., 1993; Grau et al., 1998). This interval provides an estimation of the duration of auditory (echoic) sensory memory, which has been found to be about 10 s in young healthy adults (Sams et al., 1993) and shorter in normal ageing (Pekkonen et al., 1996). The two aforementioned processes indexed by MMN (stimulus-change detection and sensory memory) can be investigated independently by a simple experimental strategy: to test the integrity of the automatic stimulus-change detector mechanism, MMN is obtained at relatively short MPIs (of about 1 s or shorter), whereas the duration of the neural trace of the standard stimuli in auditory sensory memory can be tested by measuring MMN.
amplitude at longer MPIs (Sams et al., 1993; Pekkonen et al., 1996).

Previous work has shown the integrity of the automatic stimulus-change detector mechanism in middle-aged abstinent chronic alcoholics, as no differences in MMN amplitude between alcoholics and controls were found when the stimuli were presented with relatively short MPIs (Kathmann et al., 1995; Polo et al., 1999). The duration of auditory sensory memory seems to be also preserved in chronic alcoholics for an MPI of 2.0 s (Polo et al., 1999). However, the persistence of the memory trace in alcoholics has not been explored when it has to be active for a longer period of time.

2. Methods

2.1. Participants

Seventeen chronic alcoholics (male; mean age 41.9 ± 8.7 years), selected according to Diagnostic and Statistics Manual (DSM-IV) criteria for alcohol dependence (303.90), with no other axis-I disorders and with a history of alcoholism of at least 4 years (mean 11.0 ± 6.9 years) were studied after alcohol withdrawal lasting at least 4 weeks (mean 10.2 ± 6.0 weeks). Controls were 17 healthy age-matched volunteers (male; mean age 39.3 ± 10.9 years) who drank less than 210 g/week of alcohol. After a full description of the study to the subjects, they gave their written informed consent to participation. All subjects were free of medication (including disulfiram) during the 72 h preceding the experimental session.

2.2. Stimuli and procedure

Pure sine-wave tones of 700 Hz, with a duration of 75 ms (standard) or 25 ms (deviant), including 5 ms of rise/fall times, were delivered through headphones, binaurally, at an intensity of 85 dB SPL. An audiometric test showed similar hearing thresholds at 700 Hz pure tones for the alcoholic and control subjects (mean ± SD: 47 ± 6 and 44 ± 3 dB, respectively). According to the MMN paradigm developed by Grau et al. (1998), subjects were presented with trains of 3 tones separated by a short (300 ms) interstimulus interval, starting randomly with a deviant or a standard stimulus (50% each), the other two stimuli being standard tones. Eight hundred and 400 stimuli trains were delivered in separate blocks, with a short (0.4 s) or a long (5.0 s) intertrain MPI, respectively. Subjects performed an irrelevant visual task, while ignoring the tones and avoiding extra eye movements or blinking.

2.3. Data collection and analysis

The electroencephalogram was continuously recorded with Synamps and Neuroscan hardware and software from 8 tin electrodes inserted in a cap (Electrocap, Inc.) at a sampling rate of 500 Hz from left (F3, F7, C3, T3), from right (F4, F8, C4, T4) and from Cz, M1 and M2 locations according to the International 10–20 System, and referred to the tip of the nose. The electrooculogram was recorded from two electrodes placed at the outer canthus and below the right eye. Epochs exceeding ±100 µV were excluded automatically from averaging. ERPs to deviant and standard tones starting a 3 tone train were averaged separately for each subject and MPI (0.4 or 5.0 s), and were digitally filtered (0.1–30 Hz) and re-referenced to right mastoid (M2) electrode. The epoch was 400 ms, including 100 ms of pre-stimulus baseline.

A two-step analysis was performed on the data, without a priori assumptions about the exact MMN time range of emergence. First, to determine the presence/absence of significant MMN, ERPs to deviant and standard tones were compared at each electrode, group and MPI condition by running point to point two-tailed t tests from 125 to 300 ms. A sequence of at least 12 consecutive sampling points (24 ms) with t test values with $P < 0.05$ was required in order to consider MMN significant (Guthrie and Buchwald, 1991). The second step of the analysis was run to compare differences between groups at each MPI. The MMN difference wave was obtained by subtracting the ERPs to standard tones from those to deviant tones at each electrode. MMN mean amplitudes over 25 ms intervals from 125 to 300 ms from stimulus onset were compared with ANOVA for repeated measures, including group (alcoholics and controls) and electrode location (left and right hemisphere electrodes) as factors.

3. Results

Fig. 1 shows the grand average across subjects of ERPs to standard and deviant tones for alcoholic and control subjects in the 0.4 and 5.0 s MPI conditions. In the 0.4 s MPI, point to point t tests revealed the presence of MMN in both alcoholic (interval of significant MMN at F4: 128–220 ms) and control (interval of significant MMN at F4: 114–214 ms) subjects at all scalp locations. ANOVA showed no significant differences between groups when comparing their difference waves across 25 ms intervals in the 0.4 s MPI (mean amplitude and standard deviation in the 150–175 ms MMN interval at F4: $-2.1 \pm 1.3$ and $-1.7 \pm 1.4$ µV for alcoholics and controls, respectively).

In the 5.0 s MPI, point to point t tests showed that MMN was still present in the control group at all but the F7 electrode, though with a smaller amplitude and about 80 ms longer latency (interval of significant MMN at F4: 228–258 ms). In contrast, MMN was not significantly elicited at any electrode in the alcoholic group in the 5.0 s MPI. The absence of MMN in chronic alcoholics in the 5.0 s MPI was also confirmed by the ANOVA results, revealing significant differences ($F(1,32) = 4.38, P < 0.05$) between alcoholic and control subjects in the mean amplitude of the difference waves in the 200–225 ms interval at the right hemisphere.
electrodes (mean amplitude and standard deviation at F4: 
0.04 ± 1.4 and -0.8 ± 1.3 μV for alcoholics and controls, 
respectively).

In the ERPs to standard tones at Cz, larger peak to peak 
N1/P2 amplitudes were elicited in alcoholics than controls 
for the 0.4 s (F(1,27) = 4.04, P = 0.05) and the 5.0 s 
(F(1,32) = 5.59, P < 0.05) MPIs. The increase in the N1/ 
P2 peak to peak amplitude in alcoholics was similar in the 
two MPIs, as no significant interaction was found in 
ANOVA with group and MPI as factors (F(1,27) = 2.49, 
NS). As expected, N1/P2 amplitudes were larger in the long 
than in the short MPI (F(1,27) = 129.9, P < 0.001) (Table 
1). The N1 to deviant tones at Cz, which did not overlap 
with MMN in the longer interstimulus interval of 5.0 s, was 
of similar amplitude in alcoholics (-7.7 ± 3.2 μV) and 
controls (-6.04 ± 2.5 μV) (F(1,32) = 1.31, NS).

4. Discussion

With a short MPI of 0.4 s an MMN of similar amplitude 
was obtained in both alcoholic and control subjects. This 
finding corroborates earlier results obtained with short MPIs 
of 0.58 s (Kathmann et al., 1995) and 0.75 s (Polo et al., 
1999), and confirms the integrity of the automatic-change 
detector mechanism indexed by MMN in chronic alcohol- 
ism. With a long MPI of 5.0 s, MMN was not elicited in 
alcoholics, though it was still present in controls, albeit with

Table 1
N1 and P2 peak amplitudes and latencies in the ERPs elicited by the standard stimuli at Cz electrode

<table>
<thead>
<tr>
<th>MPI (s)</th>
<th>Amplitude (μV)</th>
<th>Latency (ms)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Alcoholics</td>
<td>Controls</td>
</tr>
<tr>
<td></td>
<td>Mean ± SD N</td>
<td>Mean ± SD N</td>
</tr>
<tr>
<td>N1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>0.4</td>
<td>-1.3 ± 0.9 17</td>
<td>-0.9 ± 1.2 15</td>
</tr>
<tr>
<td>5.0</td>
<td>-9.0 ± 3.6 17</td>
<td>-7.2 ± 2.3 17</td>
</tr>
<tr>
<td>P2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>0.4</td>
<td>1.4 ± 1.2 14</td>
<td>0.8 ± 0.6 15</td>
</tr>
<tr>
<td>5.0</td>
<td>2.8 ± 1.9 17</td>
<td>1.6 ± 1.4 17</td>
</tr>
</tbody>
</table>

* Number of subjects with a measurable wave.
a smaller amplitude. The absence of MMN with the long MPI suggests for the first time a deficit in the system of storage of auditory sensory memory in chronic alcoholism.

The peak to peak N1/P2 amplitude to standard stimuli was larger in alcoholics than controls, which confirms previous results showing larger obligatory ERPs in alcoholic patients (Cadaveira et al., 1991). There was a similar rate of increase in the N1/P2 amplitude for both the 5.0 and 0.4 s MPIs in alcoholics relative to controls. However, for the longer MPI of 5.0 s, MMN was only present in controls. Consequently, a selective modification in sensory processing with the long MPI is unlikely to account for results in MMN/auditory sensory memory found in chronic alcoholics.

MMN sources are mainly located in the supratemporal auditory cortex (Alho, 1995); if we assume that the neural trace of standard stimuli is stored in the vicinity of the MMN locus of generation, an impairment of auditory sensory memory in chronic alcoholism may functionally reflect grey matter volume loss in the auditory cortex found with magnetic resonance imaging in alcoholic patients (Pfefferbaum et al., 1998).

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