Eur Arch Psychiatry Clin Neurosci (2008) 258:179–185 DOI 10.1007/s00406-007-0772-9

ORIGINAL PAPER

Müge Devrim-Üçok · H. Yasemin Keskin-Ergen · Alp Üçok

Mismatch negativity at acute and post-acute phases of first-episode schizophrenia

Received: 6 December 2006 / Accepted: 1 October 2007 / Published online: 13 November 2007

Abstract The objective of this study was to evaluate the mismatch negativity (MMN) in patients with first-episode schizophrenia at acute and post-acute phases in order to determine the contribution of trait and/or state features to MMN disturbances in schizophrenia. Subject groups comprised 30 patients with first-episode schizophrenia at the acute phase and 34 healthy controls. Ten patients were neuroleptic-naive during testing at the acute phase. Twenty-one patients were retested at the post-acute phase when their symptoms improved. All patients were taking antipsychotic medication at the post-acute retest session. MMN amplitude of the patients at acute phase did not differ from controls. However, MMN amplitude at post-acute phase was reduced compared to both controls and acute phase. Similar results were obtained when the analyses were confined to neuroleptic-naive patients. The sensory memory functions indexed by MMN seem to be unaffected at the onset of schizophrenia but deteriorated during the post-acute illness phase. MMN reduction at the post-acute phase might be emerged from antipsychotic medication.

Key words schizophrenia · first-episode · mismatch negativity · acute phase · post-acute phase · longitudinal

M. Devrim-Üçok (✉) · H.Y. Keskin-Ergen
Department of Physiology
Istanbul Medical Faculty
University of Istanbul
34093 Çapa-Istanbul, Turkey
Tel.: +90-212/635-2631
E-Mail: devrim@istanbul.edu.tr

A. Üçok
Department of Psychiatry
Istanbul Medical Faculty
University of Istanbul
34093 Çapa-Istanbul, Turkey

Introduction

Mismatch negativity (MMN) is a preattentive auditory event-related potential (ERP) elicited when a sequence of repetitive sounds is interrupted by a deviant sound [27]. Naatanen et al. [26] proposed that MMN is generated by a mismatch between the physical features of a deviant stimulus and a neuronal sensory-memory trace produced by repetitive standard stimuli. MMN has been elicited by changes in frequency [34], duration [28], intensity [27], location [32] and tone sequences [38].

Deficits in MMN generation represent a robust finding in chronic schizophrenia indicating a deficit in context-dependent information processing at the level of auditory sensory cortex [8, 13, 14, 24, 35, 39, 40, 47, 48]. MMN to duration deviants is consistently reduced in chronic schizophrenia however, some studies of frequency deviants failed to detect reductions [19, 24, 30].

The MMN abnormalities in chronic schizophrenia may be due to ongoing chronic process, antipsychotic medication and/or hospitalization. Therefore, it is of considerable interest whether the MMN reduction is a trait marker of schizophrenia and present at onset or occurs secondary to chronicity. Michie et al. [25] reported reduced MMN amplitude in unaffected first-degree relatives of patients with schizophrenia suggesting that it is an endophenotype marker of vulnerability to schizophrenia. On the other hand, Brockhaus-Dumke et al. [7] studied the prodromal subjects and showed a slight, though non-significant reduction in MMN amplitude that was intermediate between controls and schizophrenia patients. Investigating schizophrenia patients during or close to their first episode is another approach to understand whether MMN reduction is a trait feature. Only a few studies have investigated patients during those periods. Outpatients with recent-onset schizophrenia who were within 3 years of their first episode showed marginal reductions in MMN

across both frequency- and duration-deviant conditions [17]. Umbricht et al. [44] also reported reduced frequency and duration MMN in patients with recent-onset schizophrenia whose mean duration of illness was 3.5 years. However, the MMN to frequency [35, 44] and duration deviances [44] were not reduced in patients with first-episode schizophrenia (FES).

Most of the studies did not find a relation between the MMN amplitude and clinical symptomatology [48]. Only a few studies reported correlations between MMN amplitude and ratings of hallucinations [37, 50] or negative symptoms [8, 16, 37]. Studies investigating the effects of medication also could not demonstrate any effect of typical or atypical antipsychotics on MMN despite symptomatic improvement of patients [36, 45, 46].

The aim of this study was to investigate MMN and its relation with clinical features in FES. Patients were evaluated on two occasions, initially during the acute phase of the illness and secondly during the post-acute phase when their positive symptoms improved in order to determine the contribution of trait and/or state features to possible disturbances in MMN. In light of previous studies we hypothesized that MMN amplitude of FES patients at the acute phase would not be different from controls. Moreover, since no change was reported in MMN due to antipsychotics in chronic patients we assumed that at the post-acute phase it would not be also different from controls. A group of our FES patients were neuroleptic-naive during the initial evaluation which gave us the chance to eliminate the possible effects of antipsychotics on MMN. To our knowledge, MMN has not been reported before in neuroleptic-naive patients with FES.

Methods

Subjects

Subjects consisted of 30 inpatients with FES (25 paranoid, 3 catatonic, 1 undifferentiated, and 1 disorganized; 15 women) and 34 healthy controls (15 women). The groups did not differ in age, gender and education level. First-episode patients were tested on two occasions, initially during the acute phase of the illness and secondly during the post-acute phase when their positive symptoms improved (being rated 3 or below on all items of the BPRS positive subscale for at least 2 weeks). Only 21 patients could be tested during the post-acute phase. The inter-test interval ranged from 1 to 9 months (mean ± SD, 2.53 ± 2.28 months). Subject demographic characteristics are presented in Table 1. Patients were diagnosed for schizophrenia at a consensus meeting incorporating clinical, and Structured Clinical Interview for DSM-IV (SCID) data [11]. All SCID interviews were made by a trained senior interviewer (AU). Controls were screened by using the Structured Clinical Interview for DSM-III-R-Non-Patient Edition, by trained interviewers. Exclusion criteria for patients included any organic disorder known to cause psychosis or cognitive impairment and alcohol/drug abuse.

The patient was accepted in his/her first psychotic episode if all following conditions were fulfilled: no past diagnosis of nonaffective possible psychosis; no previous antipsychotic treatment and inpatient care. The date of onset of the first identifiable positive symptoms was timed by the senior psychiatrist in research team on the basis of a best-estimate approach using data gathered from multiple sources including medical records, a direct patient, and family interview. We defined duration of untreated psychosis (DUP) from the time of onset of first positive symptoms to the first hospitalization. First-episode and DUP were also defined in detail in our previous study [43]. Diagnosis of schizophrenia was confirmed, at the sixth month after discharge, with a reinterview using SCID. There were two left-handed subjects in the patient group and one in the control group.

Table 1 Demographic and clinical data

	Acute phase (n = 30)	Acute phase (n = 21)	Post-acute phase (n = 21)	Controls (n = 34)
Gender (F/M)	15/15	12/9		15/19
Age (years)	22.1 (5.7)	21.6 (5.6)		24.5 (6.4)
Education (years)	10.9 (2.9)	10.7 (2.9)		12.2 (4.0)
BPRS	66.1 (17.4)	67.4 (16.8)	36.6 (9.0)	
SANS	52.3 (24.0)	52.4 (24.6)	28.9 (21.5)	
SAPS	37.7 (18.4)	37.6 (16.2)	9.0 (8.4)	
DUP (months)	11.2 (10.4)	11.1 (10.5)		
Range	1–48	1–48		

Data are given as mean (SD)
BPRS, brief psychiatric rating scale-expanded; SANS, scale for the assessment of negative symptoms; SAPS, scale for the assessment of positive symptoms; DUP, duration of untreated psychosis

Psychopathology was evaluated with Brief Psychiatric Rating Scale-Expanded (BPRS) [23], Scale for the Assessment of Positive Symptoms (SAPS) [5], and Scale for the Assessment of Negative Symptoms (SANS) [4]. All measures were collected by two trained raters. Inter-rater reliabilities for BPRS, SANS and SAPS total scores were acceptable (κ = 0.78, κ = 0.76, and κ = 0.83, respectively). Clinical measures of the patients are presented in Table 1.

Antipsychotic medications were given to control the acute excitation to the majority of patients before the initial recording (mean ± SD duration of medication, 8.6 ± 4 days). Therefore, although all first-episode patients were neuroleptic-naive when admitted to hospital, only 10 of them were still neuroleptic-naive, whereas 5 patients were taking typical (mean haloperidol equivalent dose = 11.4 ± 2.7 mg) and 15 patients were taking atypical antipsychotics either risperidone (n = 7, mean ± SD dose, 4.1 ± 0.7 mg/day) or olanzapine (n = 6, mean ± SD dose, 16.7 ± 3.9 mg/day) or quetiapine (n = 2, mean dose = 600 mg/day) during the experiment.

During the post-acute testing five patients were taking typical (mean haloperidol equivalent dose = 6.5 ± 3 mg) and 16 patients were taking atypical antipsychotics either risperidone (n = 8, mean ± SD dose, 4.1 ± 0.8 mg/day) or olanzapine (n = 5, mean ± SD dose, 12.3 ± 1.9 mg/day) or quetiapine (n = 3, mean ± SD dose, 630 ± 306 mg/day). All subjects gave written informed consent after procedures had been fully described. The study protocol was accepted and approved by the local Ethical Committee.

ERP testing

The ERPs were obtained during an auditory oddball paradigm. Oddball paradigm consisted of standard (1,000 Hz) and deviant (1,500 Hz) tones with respective probabilities of 0.8 and 0.2. All tones were 80 dB and 50 ms in duration. Four hundred tones were binaurally presented in a random series with the restriction that at least three standard tones preceded the deviant tones. The interstimulus interval was 1.5 s. Subjects were instructed to ignore the tones they would hear. We did not use a distracter task in order to engage subjects' attention away from the auditory stimuli since patients at the acute illness phase would be less able to comply with the 'attend' instruction leading to MMN differences between groups.

ERP recording

ERPs were recorded from 9 Ag–AgCl bridge electrodes placed at F3, Fz, F4, C3, Cz, C4, P3, Pz, P4 according to the 10–20 system in reference to linked earlobes. Electrooculogram (EOG) was recorded by

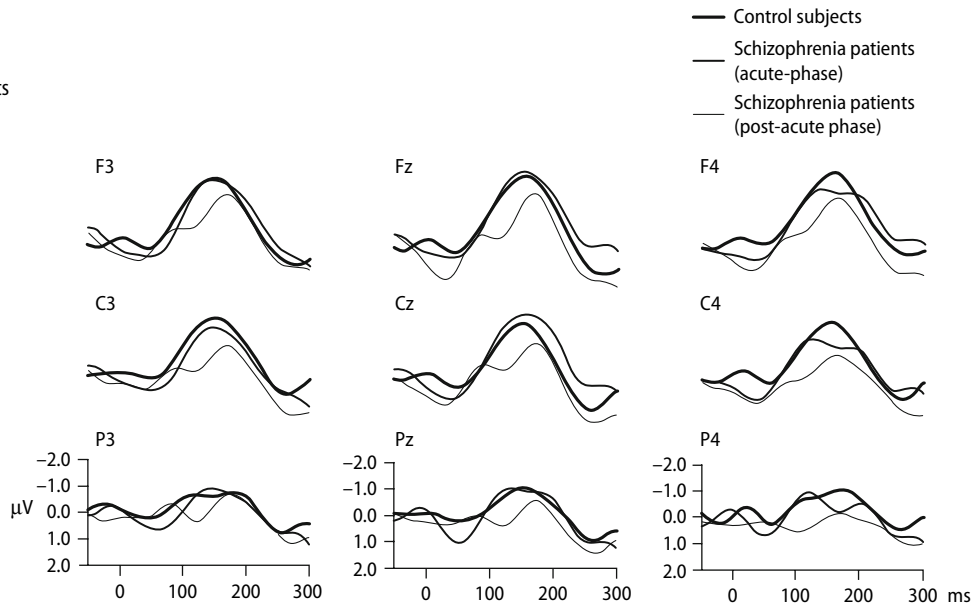

Fig. 1 Mismatch negativity difference waveforms in first-episode schizophrenia patients at the acute (n = 30) and post-acute phases (n = 21) and control subjects (n = 34)

two electrodes, placed just below the infraorbital ridge and above the eyebrow of the right eye. Electrode impedances were below 5 kΩ. The EEG was recorded with a band-pass filter of 0.5–70 Hz and digitised at 256 Hz.

Data analysis

Trials on which the EEG or EOG voltages exceeded ±75 μV were rejected automatically. Remaining trials were inspected visually for additional artifacts such as smaller EOG excursions and muscle activity. The artefact-free standard tones closest to the following deviant tones were selected with the restriction that they must be preceded by at least two standard tones. Averages were computed for the deviant and the standard tones. The minimum number of averaged trials was 40. The mean numbers of averaged deviants were 48 (SD = 8) and 51 (SD = 8) for patients during the acute and post-acute phase, respectively and 55 (SD = 9) for controls. The mean numbers of averaged standards were 55 (SD = 8) and 60 (SD = 7) for patients during the acute and post-acute phase, respectively and 62 (SD = 9) for controls. Difference waveforms were obtained by subtracting the standard waveforms from the deviant waveforms. These waveforms were digitally low-pass filtered at 15 Hz and baseline corrected to a prestimulus 250 ms. MMN was defined as the peak negativity within the 100–250 ms latency range. Peak amplitudes were measured.

Statistical analysis

MMN amplitudes were assessed with three main analyses of variance (ANOVA) repeated measures design. In the first and second analysis, group (acute patients vs. controls and post-acute patients vs. controls) was the between-subjects factor. There were two within-subjects factors which were anteroposterior regions (frontal: F3, Fz, F4, central: C3, Cz, C4 and parietal: P3, Pz, P4) and lateral regions (left: F3, C3, P3, midline: Fz, Cz, Pz and right: F4, C4, P4). In the third analysis, the change in MMN amplitude between acute and post-acute phase was assessed. Medication group (atypical vs. typical antipsychotic medication) was the between-subjects factor. There were three within-subject factors which were phase of illness (acute and post-acute phase), anteroposterior regions and lateral regions. The changes in clinical measures between acute phase and post-acute phase were also assessed by repeated measures ANOVAs with antipsychotic medication as between-subjects factor and phase of illness as within-subjects factor. Greenhouse-Geisser correction was applied when factors had more than two levels, with only the corrected probability values reported. Difference contrasts were used to analyze the significant main and/or interaction effects.

Partial-correlation analysis was used to assess the relationships between MMN amplitude and clinical measures at acute and post-acute phases. DUP was included as a covariant since it was associated with BPRS (r = 0.475, P = 0.030) and SANS scores (r = 0.497, P = 0.022) at the post-acute phase. Relationships between percent changes in MMN amplitude and percent changes in clinical measures from acute (T1) to post-acute phase (T2) (percent changes = ((T2 − T1)/|T1|)× 100) was also evaluated. Using a Bonferroni correction, only two-tailed P-values below 0.0019 were considered significant for correlation coefficients.

Results

Patients vs. controls

MMN amplitude did not differ between the patients at acute phase and controls [$F(1, 62)$ = 0.002, P = ns] (see Fig. 1 and Table 2). MMN amplitude was largest over the frontal sites and reduced posteriorly [$F(2, 124)$ = 21.68, P = 0.001]. MMN amplitude was larger along the midline compared to the lateral sites [$F(2, 124)$ = 3.92, P = 0.025]. MMN topography did not differ between groups [group × anteroposterior site: $F(2, 124)$ = 0.60, P = ns; group × lateral site [$F(2, 124)$ = 1.10, P = ns]. When the analysis was confined to the neuroleptic-naive patients, no difference in MMN amplitude was observed compared to controls as well.

MMN amplitude was reduced in patients at post-acute phase compared to controls [$F(1, 53)$ = 4.62, P = 0.036] (see Fig. 1 and Table 2). Both groups showed the largest MMN amplitude frontally and the smallest MMN amplitude parietally [$F(2, 106)$ = 22.55, P = 0.001]. MMN topography did not differ between groups [group × anteroposterior site: $F(2, 106)$ = 0.78, P = ns; group × lateral site [$F(2, 106)$ = 0.36, P = ns].

Table 2 Mismatch negativity amplitudes

	Acute phase (n = 30)	Acute phase (n = 21)	Post-acute phase (n = 21)	Control (n = 34)
Fz	−3.9 (2.4)	−4.2 (2.3)	−3.0 (1.4)	−3.9 (2.8)
F3	−3.4 (2.3)	−3.5 (2.2)	−2.6 (1.6)	−3.6 (1.9)
F4	−3.6 (2.6)	−3.7 (2.6)	−2.7 (1.6)	−4.0 (2.9)
Cz	−3.8 (2.2)	−3.9 (2.2)	−2.4 (1.5)	−3.5 (2.1)
C3	−3.1 (1.8)	−3.2 (1.7)	−2.2 (1.2)	−3.5 (2.8)
C4	−3.2 (2.0)	−3.1 (1.9)	−2.2 (1.3)	−3.3 (2.4)
Pz	−2.9 (2.6)	−2.5 (1.9)	−1.8 (1.7)	−2.5 (2.1)
P3	−2.5 (1.8)	−2.3 (1.6)	−1.9 (1.3)	−2.4 (1.6)
P4	−2.5 (2.1)	−2.2 (1.6)	−1.5 (1.4)	−2.4 (1.8)

Data are given as mean (SD) microvolts

Change in clinical measures between acute and post-acute phase

BPRS total [$F(1, 19) = 37.12$, $P = 0.001$], SANS [$F(1, 19) = 9.96$, $P = 0.005$] and SAPS scores [$F(1, 19) = 32.78$, $P = 0.001$] were significantly lower at post-acute phase than acute phase (see Table 1). Typical and atypical antipsychotics did not differ in their effects on clinical measures.

Change in MMN amplitude between acute and post-acute phase

A reduction in MMN amplitude was observed in patients with FES at post-acute phase compared to acute phase [$F(1, 19) = 6.45$, $P = 0.02$] (see Fig. 1 and Table 2). Typical and atypical antipsychotics did not differ in their effects on MMN amplitude [medication × phase of illness: $F(1, 19) = 0.51$, P = ns]. MMN amplitude was largest over the frontal sites and reduced posteriorly [$F(2, 124) = 21.68$, $P = 0.001$]. MMN topography did not differ between the acute and the post-acute phase [phase of illness × anteroposterior site: $F(2, 38) = 1.00$, P = ns; phase of illness × lateral site [$F(2, 38) = 1.14$, P = ns].When the analysis was confined to the initially neuroleptic-naive patients, again a reduction in MMN amplitude was observed at the post-acute phase compared to acute phase [$F(1, 6) = 6.19$, $P = 0.047$].

Relationship between MMN amplitude and clinical measures

There were no correlations between MMN amplitude and clinical severity measures both at acute and post-acute phases. We also did not find relations between percent changes in MMN amplitude and percent changes in clinical measures from acute to post-acute phase. There were no correlations between MMN amplitude and DUP at acute and post-acute phases. When we dichotomized the group by using the median of the DUP (9 months), no difference in MMN was found between patients having a longer and a shorter DUP.

Discussion

At the acute phase, patients with first-episode schizophrenia did not differ from the controls in MMN amplitude and topography. Our findings are consistent with previous FES studies in which normal frequency [35, 44] and duration MMN [44] responses were found. Therefore, our results support their suggestion that sensory memory functions indexed by MMN seem to be unaffected at the onset of schizophrenia.

On the other hand in contrast to our expectations during the post-acute phase when the symptoms improved, MMN was reduced compared to the acute phase and to the controls. MMN reduction at the post-acute phase might be resulted from several sources. First, retesting might have resulted in a reduction of MMN at the post-acute phase. However, several studies reported that the MMN amplitude showed significant test–retest reliability. Some studies [18, 42] found that frequency MMN was less replicable than duration MMN. However, Frodl-Bauch et al. [12] reported that the test–retest reliability of the frequency MMN was higher than the duration MMN. Most importantly, no significant differences were found in the MMN amplitudes across sessions [10, 18, 22, 37]. This means that systematic changes do not occur in MMN over short periods of time. Therefore, the reduction in MMN at the post-acute phase does not seem to be resulted from retesting. Second, MMN reduction may start to occur just after the first episode and that the MMN reduction at the post-acute phase reflects progression of schizophrenia. Umbricht et al. [44] evaluated MMNs of schizophrenia patients at their first-episode and later within a mean of 3.5 years after their first admission. A reduction in MMN was observed in recent-onset, but not in first-episode patients. Javitt et al. [17] also reported a marginal reduction in MMN in recent-onset schizophrenia patients who were within 3 years of their first episode. In the present study the mean interval between the tests at the first acute phase and the post-acute phase was 2.5 months. Considering the shortness of the inter-test interval it is hard to state that MMN reduction at the post-acute phase reflects progression of the disease. Additionally, in our sample DUP ranges widely from 1 to 48 months and was not related to MMN. This finding supports that the MMN reduction at the post-acute phase was not due to progressive pathophysiological processes. Third, the improvement in clinical state may be the reason for MMN reduction at the post-acute phase. In line with this paradoxical interpretation, Salisbury et al. [35] found that more pathological symptoms were associated with larger MMN activity in patients with FES. However, we did not find a relation between MMN amplitude and clinical severity measures in schizophrenia patients at acute and post-acute phases. Also

no association was observed between changes in MMN amplitudes and changes in clinical measures from acute to post-acute phase. Since MMNs and clinical measures were evaluated on two different occasions, their possible relations were more reliably tested than cross-sectional analysis. Therefore, it seems that MMN reduction in the post-acute phase could not be explained by the improvement in symptomatology. Fourth, antipsychotic treatment might have resulted in a reduction of MMN. Catts et al. [8] found that the reduction in MMN did not differ among chronic schizophrenia patients with or without antipsychotic medications. Furthermore, it was reported that switching from typical to atypical antipsychotics, clozapine [36, 45] and risperidone [46], did not affect the MMN amplitude in schizophrenia. In these mentioned studies chronic schizophrenia patients were evaluated. The effects of antipsychotics on MMNs of first-episode patients may be different from chronic patients. Therefore, the most probable explanation for the reduction in MMN at the post-acute phase might be the effects of antipsychotic treatment. However, our study design did not allow us to definitely conclude on this.

Shinozaki et al. [41] investigated MMN amplitudes in chronic schizophrenia patients also on two occasions, initially during acute exacerbation and later when the symptoms improved. In contrast to our findings, they reported mid-frontal MMN reduction not only in the post-acute phase but also in the acute phase of schizophrenia compared to controls. There was no difference in MMN amplitude between acute and post-acute phases. Shinozaki et al. [41] evaluated chronic schizophrenia patients who already showed a MMN reduction at the acute phase of the illness however, in the present study first-episode patients who had a normal MMN at the acute phase were evaluated. Kirino and Inoue [20] also studied MMN in schizophrenia patients before and after treatment and did not find a difference compared to controls. Only two thirds of their patients were during their first episodes and neuroleptic-naive. Hence, the study group was not a homogenous sample of FES (the mean number of episodes was 1.6 ± 0.9, the mean duration of illness was 6.3 ± 7.5 years). Therefore, the controversy between the results of the mentioned studies and our study could be explained by the differences in patient groups.

Although the duration was very short, majority of the patients at the acute phase were taking antipsychotic medication which made it difficult to eliminate their possible effects on MMN. However, when we evaluated only the patients who were neuroleptic-naive, MMN amplitudes were again normal at the acute phase and were reduced at the post-acute phase. These findings show that short-term neuroleptic usage at the acute phase does not seem to have an effect on MMN. To our knowledge the present study is the first to report on the MMN in FES patients who were neuroleptic-naive. Valkonen-Korhonen et al. [49] also reported normal MMN amplitude in acutely psychotic never-medicated first-episode patients. However, only approximately half of their patients were diagnosed as schizophreniform disorder or schizophrenia.

Several limitations about the present study should be noted. First, the control group was lack of the follow-up data which would have allowed the evaluation of retesting on MMN. Second, the mean numbers of averaged deviants and standards were approximately 50 and 60, respectively which are generally accepted as low to obtain a prominent MMN. However, we obtained prominent MMNs in patients and controls. In this study averaged waveforms for standards were computed by using the standard stimuli that were closest to the following deviants. This procedure might have increased the MMN in the difference waveform since Baldeweg et al. [6] demonstrated a slow positive shift to pre-deviant standards that increase in amplitude with the increase of the preceding standards. Excluding the standards immediately following the deviants from averaged response might also increased the MMN since these were not processed as true standards. Third, the probability of the deviant stimuli was high. It was reported that the degree of MMN reduction in schizophrenia was increased as deviant probability decreased [15, 39]. Therefore, the reason for not finding a difference between FES patients at the acute phase and controls might be our high deviant probability. However, studies using low probability deviants also reported normal MMN in FES [35, 44] and in the present study MMN elicited with the high probability deviant did not prevent observing a reduction in FES patients at the post-acute phase. Fourth, our ISI was 1.5 s which was pretty long. However, no differential effect of ISI on MMN generation was observed in schizophrenia patients compared to controls [15, 39]. Fifth, in this study MMN was elicited during passive ignore condition. Since the attention of the subjects was not controlled, we cannot be sure that they did not attend to the stimuli. Attended stimuli may elicit larger MMN amplitudes by the superimposition of N2b component. However, MMN was shown to be unaffected by task demands in many studies [2, 3 , 9, 31, 33], with some exceptions [1, 21]. Naatanen et al. [29] showed that MMN to frequency change was unaffected by task demands although MMN to intensity change was attenuated in the absence of attention. More importantly, Kathmann et al. [18] compared a condition when subjects were required to direct their attention strongly to a visual task with a passive ignore condition setting no task demands and observed that the MMN amplitudes did not differ between the two conditions. On the other hand, if we had given a distracter task (visual target detection or reading task) to the subjects during MMN recording as in most of the MMN studies, pa-

tients at the acute phase would have been less able to comply with the 'attend' instruction. This time the variation in attention directed to the task would be a potential confound in group comparisons. Sixth, during the post-acute testing 16 patients were taking atypical and only 5 patients were taking typical antipsychotics. Since the typical antipsychotic group was small our results of no difference between the typical and atypical antipsychotics on MMN and symptomatology should be accepted cautiously. Moreover, our patients were taking three different kinds of atypicals. As atypical antipsycotics are not a homogenous group their effects on MMN may vary.

In summary, the sensory memory functions indexed by frequency MMN seem to be unaffected at the onset of schizophrenia but deteriorated during the post-acute illness phase. This study addresses the timely issue of when in the illness course MMN deficits are present in schizophrenia. MMN reduction in first-episode schizophrenia patients at the post-acute phase might be emerged from antipsychotic medication. Randomized studies which include placebo and different antipsychotics are needed to delineate the effects of antipsychotics on MMN in first-episode patients.

Acknowledgements This work was supported by the Research Fund of The University of Istanbul. Project numbers: 173/15012004 and UDP-826/19072006.

References

1. Alain C, Woods DL (1997) Attention modulates auditory pattern memory as indexed by event-related brain potentials. Psychophysiology 34:534–546
2. Alho K, Woods DL, Algazi A (1994) Processing of auditory stimuli during auditory and visual attention as revealed by event-related potentials. Psychophysiology 31:469–479
3. Alho K, Woods DL, Algazi A, Naatanen R (1992) Intermodal selective attention. II. Effects of attentional load on processing of auditory and visual stimuli in central space. Electroencephalogr Clin Neurophysiol 82:356–368
4. Andreasen NC (1983) The scale for the assessment of negative symptoms (SANS). University of Iowa, Iowa City
5. Andreasen NC (1984) The scale for the assessment of positive symptoms (SAPS). University of Iowa, Iowa City
6. Baldeweg T, Klugman A, Gruzelier J, Hirsch SR (2004) Mismatch negativity potentials and cognitive impairment in schizophrenia. Schizophr Res 69:203–217
7. Brockhaus-Dumke A, Tendolkar I, Pukrop R, Schultze-Lutter F, Klosterkotter J, Ruhrmann S (2005) Impaired mismatch negativity generation in prodromal subjects and patients with schizophrenia. Schizophr Res 73:297–310
8. Catts SV, Shelley AM, Ward PB, Liebert B, McConaghy N, Andrews S, Michie PT (1995) Brain potential evidence for an auditory sensory memory deficit in schizophrenia. Am J Psychiatry 152:213–219
9. Dittmann-Balcar A, Thienel R, Schall U (1999) Attention-dependent allocation of auditory processing resources as measured by mismatch negativity. Neuroreport 10:3749–3753
10. Escera C, Yago E, Polo MD, Grau C (2000) The individual replicability of mismatch negativity at short and long interstimulus intervals. Clin Neurophysiol 111:546–551
11. First MB, Spitzer RL, Gibbon M, Williams JBW (1997) Structured clinical interview for DSM-IV axis I disorders (SCID-I), clinical version. American Psychiatric Press, Washington, DC
12. Frodl-Bauch T, Kathmann N, Moller HJ, Hegerl U (1997) Dipole localization and test-retest reliability of frequency and duration mismatch negativity generator processes. Brain Topogr 10:3–8
13. Javitt DC, Doneshka P, Grochowski S, Ritter W (1995) Impaired mismatch negativity generation reflects widespread dysfunction of working memory in schizophrenia. Arch Gen Psychiatry 52:550–558
14. Javitt DC, Doneshka P, Zylberman I, Ritter W, Vaughan HG Jr (1993) Impairment of early cortical processing in schizophrenia: an event-related potential confirmation study. Biol Psychiatry 33:513–519
15. Javitt DC, Grochowski S, Shelley AM, Ritter W (1998) Impaired mismatch negativity (MMN) generation in schizophrenia as a function of stimulus deviance, probability, and interstimulus/interdeviant interval. Electroencephalogr Clin Neurophysiol 108:143–153
16. Javitt DC, Shelley AM, Ritter W (2000) Associated deficits in mismatch negativity generation and tone matching in schizophrenia. Clin Neurophysiol 111:1733–1737
17. Javitt DC, Shelley AM, Silipo G, Lieberman JA (2000) Deficits in auditory and visual context-dependent processing in schizophrenia: defining the pattern. Arch Gen Psychiatry 57:1131–1137
18. Kathmann N, Frodl-Bauch T, Hegerl U (1999) Stability of the mismatch negativity under different stimulus and attention conditions. Clin Neurophysiol 110:317–323
19. Kathmann N, Wagner M, Rendtorff N, Engel RR (1995) Delayed peak latency of the mismatch negativity in schizophrenics and alcoholics. Biol Psychiatry 37:754–757
20. Kirino E, Inoue R (1999) The relationship of mismatch negativity to quantitative EEG and morphological findings in schizophrenia. J Psychiatr Res 33:445–456
21. Kramer AF, Trejo LJ, Humphrey D (1995) Assessment of mental workload with task-irrelevant auditory probes. Biol Psychol 40:83–100
22. Kujala T, Kallio J, Tervaniemi M, Naatanen R (2001) The mismatch negativity as an index of temporal processing in audition. Clin Neurophysiol 112:1712–1719
23. Lukoff D, Nuechterlein KH, Ventura J (1986) Manual for the expanded brief psychiatric rating scale. Schizophr Bull 12:594–602
24. Michie PT, Budd TW, Todd J, Rock D, Wichmann H, Box J, Jablensky AV (2000) Duration and frequency mismatch negativity in schizophrenia. Clin Neurophysiol 111:1054–1065
25. Michie PT, Innes-Brown H, Todd J, Jablensky AV (2002) Duration mismatch negativity in biological relatives of patients with schizophrenia spectrum disorders. Biol Psychiatry 52:749–758
26. Naatanen R (1990) The role of attention in auditory information processing as revealed by event-related potentials and other brain measures of cognitive function. Behav Brain Sci 13:201–288
27. Naatanen R, Gaillard AWK, Mantysalo S (1978) Early selective-attention effect on evoked potential reinterpreted. Acta Psychol 42:313–329
28. Naatanen R, Paavilainen P, Reinikainen K (1989) Do event-related potentials to infrequent decrements in duration of auditory stimuli demonstrate a memory trace in man? Neurosci Lett 107:347–352
29. Naatanen R, Paavilainen P, Tiitinen H, Jiang D, Alho K (1993) Attention and mismatch negativity. Psychophysiology 30:436–450
30. O'Donnell BF, Hokama H, McCarley RW, Smith RS, Salisbury DF, Mondrow E, et al. (1994) Auditory ERPs to non-target stimuli in schizophrenia: relationship to probability, task-demands, and target ERPs. Int J Psychophysiol 17:219–231
31. Otten LJ, Alain C, Picton TW (2000) Effects of visual attentional load on auditory processing. Neuroreport 11:875–880
32. Paavilainen P, Karlsson ML, Reinikainen K, Naatanen R (1989) Mismatch negativity to change in spatial location of an auditory stimulus. Electroencephalogr Clin Neurophysiol 73:129–141

33. Paavilainen P, Tiitinen H, Alho K, Naatanen R (1993) Mismatch negativity to slight pitch changes outside strong attentional focus. Biol Psychol 37:23–41
34. Ritter W, Paavilainen P, Lavikainen J, Reinikainen K, Alho K, Sams M, Naatanen R (1992) Event-related potentials to repetition and change of auditory stimuli. Electroencephalogr Clin Neurophysiol 83:306–321
35. Salisbury DF, Shenton ME, Griggs CB, Bonner-Jackson A, McCarley RW (2002) Mismatch negativity in chronic schizophrenia and first-episode schizophrenia. Arch Gen Psychiatry 59:686–694
36. Schall U, Catts SV, Chaturvedi S, Liebert B, Redenbach J, Karayanidis F, Ward PB (1998) The effect of clozapine therapy on frontal lobe dysfunction in schizophrenia: neuropsychology and event-related potential measures. Int J Neuropsychopharmacol 1:19–29
37. Schall U, Catts SV, Karayanidis F, Ward PB (1999) Auditory event-related potential indices of fronto-temporal information processing in schizophrenia syndromes: valid outcome prediction of clozapine therapy in a three-year follow-up. Int J Neuropsychopharmacol 2:83–93
38. Schroger E, Paavilainen P, Naatanen R (1994) Mismatch negativity to changes in a continuous tone with regularly varying frequencies. Electroencephalogr Clin Neurophysiol 92:140–147
39. Shelley AM, Silipo G, Javitt DC (1999) Diminished responsiveness of ERPs in schizophrenic subjects to changes in auditory stimulation parameters: implications for theories of cortical dysfunction. Schizophr Res 37:65–79
40. Shelley AM, Ward PB, Catts SV, Michie PT, Andrews S, McConaghy N (1991) Mismatch negativity: an index of a preattentive processing deficit in schizophrenia. Biol Psychiatry 30:1059–1062
41. Shinozaki N, Yabe H, Sato Y, Hiruma T, Sutoh T, Nashida T et al (2002) The difference in mismatch negativity between the acute and post-acute phase of schizophrenia. Biol Psychol 59:105–119
42. Tervaniemi M, Lehtokoski A, Sinkkonen J, Virtanen J, Ilmoniemi RJ, Naatanen R (1999) Test-retest reliability of mismatch negativity for duration, frequency and intensity changes. Clin Neurophysiol 110:1388–1393
43. Ucok A, Polat A, Cakir S, Genc A, Turan N (2004) Duration of untreated psychosis may predict acute treatment response in first-episode schizophrenia. J Psychiatr Res 38:163–168
44. Umbricht DS, Bates JA, Lieberman JA, Kane JM, Javitt DC (2006) Electrophysiological indices of automatic and controlled auditory information processing in first-episode, recent-onset and chronic schizophrenia. Biol Psychiatry 59:762–772
45. Umbricht D, Javitt D, Novak G, Bates J, Pollack S, Lieberman J, Kane J (1998) Effects of clozapine on auditory event-related potentials in schizophrenia. Biol Psychiatry 44:716–725
46. Umbricht D, Javitt D, Novak G, Bates J, Pollack S, Lieberman J, Kane J (1999) Effects of risperidone on auditory event-related potentials in schizophrenia. Int J Neuropsychopharmacol 2:299–304
47. Umbricht D, Koller R, Schmid L, Skrabo A, Grubel C, Huber T, Stassen H (2003) How specific are deficits in mismatch negativity generation to schizophrenia? Biol Psychiatry 53:1120–1131
48. Umbricht D, Krljes S (2005) Mismatch negativity in schizophrenia: a meta-analysis. Schizophr Res 76:1–23
49. Valkonen-Korhonen M, Purhonen M, Tarkka IM, Sipila P, Partanen J, Karhu J, Lehtonen J (2003) Altered auditory processing in acutely psychotic never-medicated first-episode patients. Cogn Brain Res 17:747–758
50. Youn T, Park HJ, Kim JJ, Kim MS, Kwon JS (2003) Altered hemispheric asymmetry and positive symptoms in schizophrenia: equivalent current dipole of auditory mismatch negativity. Schizophr Res 59:253–260