Epilepsy & Behavior 31 (2014) 136–142

Contents lists available at ScienceDirect

Epilepsy & Behavior

journal homepage: www.elsevier.com/locate/yebeh

Changes in the duration and frequency of deviant stimuli engender different mismatch negativity patterns in temporal lobe epilepsy☆

Yuka Hirose [a,*], Keiko Hara [a,d], Miho Miyajima [b], Ayasa Matsuda [b], Taketoshi Maehara [e], Minoru Hara [d], Eisuke Matsushima [b], Katsuya Ohta [a,b,c], Masato Matsuura [a]

[a] Department of Life Sciences and Bio-informatics, Graduate School of Health Care Sciences, Tokyo Medical and Dental University, Tokyo, Japan
[b] Section of Liaison Psychiatry and Palliative Medicine, Graduate School of Medical and Dental Sciences, Tokyo Medical and Dental University, Tokyo, Japan
[c] Onda-Daini Hospital, Chiba, Japan
[d] Hara Clinic, Kanagawa, Japan
[e] Department of Neurosurgery, Tokyo Medical and Dental University, Tokyo, Japan

ARTICLE INFO

Article history:
Received 27 August 2013
Revised 18 November 2013
Accepted 27 November 2013
Available online 7 January 2014

Keywords:
Event-rerated potential (ERP)
MMN
Mismatch positivity (MMP)
Mastoid
Temporal processing
Preattentive memory function

ABSTRACT

Mismatch negativity (MMN) is an event-related potential (ERP) component that reflects preattentive sensory memory functions. Previous research revealed that MMN is generated by distinct sources in the frontal and temporal lobes. Event-related potential abnormalities have been shown in the vicinity of seizure foci in epilepsy. Additionally, no published study has investigated the MMN in response to variations in both frequency and duration deviants in patients with temporal lobe epilepsy (TLE). The aims of this study were to compare MMN changes between the frontocentral sites and the mastoid sites and to compare MMNs related to deviant stimuli with different durations and frequencies in patients with TLE. We recorded MMNs elicited by duration and frequency changes of deviant stimuli from 15 patients with TLE and 15 healthy control subjects. We found that mean MMN amplitudes related to duration deviants were lower in patients with TLE at the mastoid sites relative to controls, whereas the MMN amplitudes at the frontocentral sites did not differ between the two groups. There were no MMN differences related to frequency deviants between TLE subjects and controls at the frontocentral sites or the mastoid sites. Mismatch negativity parameters related to duration deviants did not correlate with those related to deviant frequencies in the group with TLE. The present findings suggest selective impairments among multiple mismatch generators in TLE and suggest that processing of temporal information of auditory stimuli is selectively disturbed in TLE. Changes in MMN amplitudes related to duration deviants at the mastoid sites may represent deficits in time-dependent processing in TLE.

1. Introduction

Epilepsy is a common, chronic neurological disorder characterized by abnormal neuronal activity as shown on electroencephalograms (EEGs). Temporal lobe epilepsy (TLE) is the most common type of focal epilepsy in adults. It has been repeatedly reported that cognitive functions are impaired in patients with TLE [1–3].

Mismatch negativity (MMN) is a component of auditory event-related potentials (ERPs) that is elicited when infrequent ('deviant') sounds violate the pattern of a previously detected sequence of repetitive ('standard') sounds [4]. The MMN is calculated by subtracting the ERP produced by the standard sound from the ERP produced by the deviant sound. The MMN is associated with preattentive cognitive operations [5]. This component exhibits a phase reversal (i.e., positive polarity; mismatch positivity —MMP) over mastoid and other lateral posterior sites in the same latency range when a nose reference is used [6]. Previous reports assumed that the MMN has at least two main sources, the bilateral auditory cortex and the frontal cortex [7,8]. The first source is associated with preperceptual detection of sound changes. The second is related to initiation of attention switch to sound changes [9]. Previous observations have led to the view that electrodes at the mastoid sites mainly detect mismatch sources in the superior temporal lobe, whereas electrodes on the frontal scalp reflect functions from frontal and temporal generators [10].

Recording MMNs does not require behavioral responses or attention towards the sound by the subjects [11]. Therefore, it is relatively insensitive to attention- and task-related artifacts, which depend directly on the cooperation and vigilance of the subject. Mismatch negativities can be recorded from subjects with problems in communicating or performing a discrimination task, such as newborns [12,13] and comatose individuals [14]. The MMN has been used as a tool for the clinical evaluation of auditory functions because of these characteristics. It has been reported that the MMN is affected by such common diseases as

☆ The address from which the work originated: Tokyo Medical and Dental University, 1-5-45 Yushima, Bunkyo-ku, Tokyo 113-8510, Japan.

* Corresponding author at: Department of Life Sciences and Bio-informatics, Graduate School of Health Care Sciences, Tokyo Medical and Dental University, 1-5-45 Yushima, Bunkyo-ku, Tokyo 113-8510, Japan.
E-mail address: y.hirose.16@gmail.com (Y. Hirose).
URL: http://www.tmd.ac.jp/english/ (Y. Hirose).

1525-5050/$ – see front matter © 2013 Elsevier Inc. All rights reserved.
http://dx.doi.org/10.1016/j.yebeh.2013.11.026

Alzheimer's disease [15,16], dyslexia [17,18], and schizophrenia [19–23], which indicates altered central auditory processing despite intact peripheral hearing. Additionally, it has been considered that auditory impairments may be selective to a specific type of deviation (e.g., frequency, duration, intensity, and location). For example, abnormal MMN responses to passive pitch discrimination were recorded in adult subjects with dyslexia compared with matched healthy controls, whereas their MMNs to tone duration deviants were normal [17]. It has been suggested that individuals with dyslexia have difficulties in processing acoustic differences and that this could be the cause of their problems in phonological processing. On the other hand, the effects of alcohol were greater on MMNs produced by frequency deviations than duration deviations. This result indicates that the effects of alcohol on preattentive changes in the detection of temporal information are also different from its effects on spectrum information [24]. Recently, there have been a few MMN studies using various stimuli in epilepsy [25–27]. In a magnetoencephalography (MEG) study [26], patients with epilepsy with intractable seizures were investigated using a multifeature MMN paradigm. Korostenskaja et al. found that the MMNm was diminished for all five sound feature changes (duration, frequency, intensity, location, and gap) in patients with epilepsy compared with age- and gender-matched healthy controls. There were no significant group differences in MMNm latencies. However, many studies have not focused on patients with specific types of epileptic syndromes or on specific neural foci of epileptic seizures. Event-related potential abnormalities have been described in the context of epilepsy, in particular, in the vicinity of seizure foci [27–29]. Hara et al. [27] investigated patients with TLE using Japanese vowel speech stimuli. The authors found reduced MMPs at the bilateral mastoid sites, which are considered to reflect temporal lobe activity only, whereas MMN at the frontocentral sites did not change significantly. They concluded that the MMN is generated by distinct sources in the frontal and temporal lobes and that these sources are differentially affected by TLE.

Based on these findings, we developed a hypothesis. As patients with TLE often have damage in the lateral cortices in the temporal lobe, hippocampus, and surrounding structures [2,30], we hypothesized that MMPs at the mastoid sites, which mainly reflect sources from the auditory cortex in the temporal lobe, would be attenuated in patients with TLE. In addition, we compared the characteristics of MMNs related to the deviant stimulus frequencies and durations in TLE to examine which MMN is more sensitive to impairments in TLE. In other words, the aims of this study were to compare differences in MMNs at the frontocentral and mastoid sites and between stimuli with duration and frequency deviant changes in patients with TLE.

2. Methods

2.1. Participants

Twenty-seven patients with TLE were recruited. The data in 12 out of these 27 patients with TLE were removed from further analysis because of excessive artifacts in some of the replicates in those subjects. The data from the remaining 15 patients with TLE (mean age: 33.2 ± 9.8 years, five females) were included in the analysis. Control data were collected from 15 age-matched healthy subjects (mean age: 32.4 ± 9.1 years, seven females). As is frequently the case in clinical samples, the mean length of education in the group with epilepsy (14.5 ± 1.7 years) was significantly lower than in the comparison group (17.2 ± 2.7 years) [$F(1, 28) = 10.2$, $p < 0.05$]. The handedness of the subjects was evaluated with the Edinburgh Handedness Inventory [31]. We used a laterality index of 0.8 or more as the cutoff for right-handedness.

Patients with epilepsy were recruited from the Tokyo Medical and Dental University and Hara Clinic, which were certified as training facilities by the Japan Epilepsy Society. At least two certified epileptologists diagnosed the patients as having TLE based on a combination of clinical symptoms, EEG findings, and structural/functional imaging data in each patient. All patients had partial seizures with features that were strongly suggestive of TLE, including simple partial seizures characterized by autonomic and/or psychic symptoms, phenomena such as olfactory and auditory sensations, and complex partial seizures beginning with motor arrest followed by oral automatism [32]. Exclusion criteria for both groups included psychiatric disease, substance abuse or dependence, and reports of hearing or vision problems at the time of the experiment. Control participants were excluded if they had a history of traumatic brain injury with any known cognitive consequences or loss of consciousness, a history of convulsions other than simple febrile seizures, or a history of psychiatric disease or epileptic disorder in first-degree relatives.

Tables 1 and 2 summarize the subjects' clinical characteristics. The mean age at epilepsy onset was 21.0 ± 11.6 years (range: 10 months to 43 years). Six out of 15 patients had been seizure-free for more than 12 months prior to the study. All subjects with TLE had been treated with at least one antiepileptic drug (AED) for seizure control.

The study was approved by the Ethics Committee of the Tokyo Medical and Dental University. Written informed consent was obtained from all the participants after a thorough description of the study.

2.2. Stimulus presentation

While recording EEGs, we randomly presented auditory stimuli consisting of standard and deviant items. We used oddball paradigms with duration (standard −100 millisecond (ms) and 1000 Hz; deviant −150 ms and 1000 Hz) or frequency changes (standard −100 ms and 1000 Hz; deviant −100 ms and 1050 Hz) [6], in which the standard stimuli in the two paradigms were the same. We adopted these paradigms because frequency and duration changes are the most frequent stimulus deviations used in basic and clinical MMN studies. All the stimuli had a rise/fall time of 10 ms and a stimulus onset asynchrony (SOA) of 500 ms. Trials were composed of 80% standard tones and 20% deviant tones. Stimuli were delivered binaurally via earphones at 90 dB SPL. The participants were seated comfortably in a reclining chair and instructed

Table 1
Characteristics of the subjects in the study.

Variables	Controls (n = 15)			Patients with TLE (n = 15)		
	Mean	(SD)	Range	Mean	(SD)	Range
Age (years)	32.4	9.1	22–48	33.2	9.8	20–50
Handedness (right/left/Ambidextrous)	14/0/1			13/0/2		
Education (years)	17.2	2.7	12–22	15.0[a]	1	12–16
Gender (male/female)	8/7			10/5		
Age of onset (years)	NA			21.0	11.6	0.8–43
Side of epileptic focus (left/right/bilateral or undetermined)	NA			7/3/5		
Seizures in the year prior to the study (−/+)	NA			6/9		
Number of AEDs	NA			1.9	0.9	1–4

TLE, temporal lobe epilepsy; AED, antiepileptic drug; NA, not applicable.
[a] Significant difference compared with healthy controls.