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Median Nerve Somatosensory Evoked Potentials in Patients with Chiari Malformation

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Abstract

Abnormal SEP reflects dysfunction of the medial lemniscus and posterior cervical cord. These structures are likely to be affected in Chiari malformation. Therefore, SEP abnormalities may provide valuable information in patients with CM. However, the consistency of SEP abnormality or normality with the damage is a matter of research. Knowing whether median nerve somatosensory evoked potential (SEP) is useful in revealing subclinical damage in patients with Chiari malformation is important in the treatment and follow-up plan of the disease. The aim of this study was to investigate the relationship between median nerve SEP values and the severity of cerebellar ectopia in patients with Chiari type 1 malformation. Median nerve SEP values were obtained from 30 healthy individuals and 146 individuals with Chiari malformation. The cerebellar ectopia degree and McRae line length were measured. SEP values were not significantly different between groups. The McRae line was found to be significantly shorter in the control group than in the Chiari malformation group ($p = 0.031$). There was no correlation between the degree of cerebellar ectopia and the length of the McRae line ($r = 0.002$, $p = 0.979$). Neither cerebellar ectopy degree nor McRae line length had a relationship with SEP values ($r = -0.153$, $p = 0.066$; $r = -0.056$, $p = 0.500$, respectively). There was no difference in cerebellar ectopy degree or SEP values between the groups with cerebellar ectopy with and without a syrinx ($p = 0.899$; $p = 0.080$, respectively). Likewise, McRae line length was not found to be related to the presence of a syrinx ($p = 0.139$). Median nerve SEP examination was not beneficial for diagnosing asymptomatic-oligosymptomatic Chiari malformation as a subclinical injury, whether accompanied by syringomyelia or not.

Keywords

Chiari Malformation, Cerebellar Ectopy, Somatosensory Evoked Potential

1. Introduction

Chiari malformation (CM) is a neurodevelopmental disease characterized by downwards displacement of the cerebellum, either alone or together with the lower medulla, into the spinal canal. With this displacement, neural elements become compressed in the foramen magnum. There are four subtypes. CM-1 is characterized by the displacement of the cerebellar tonsils below the level of the foramen magnum, with no herniation in the brainstem. In normal adults, the cerebellar tonsils can be found up to 3 mm below the foramen magnum. If this displacement exceeds 5 mm in neuroimaging, it is considered to be indicative of CM, but there is no correlation between how low the tonsils are and clinical severity [1] [2] [3] [4]. CM-1 may be accompanied by syringomyelia, and its frequency is variable [5].

When CM is symptomatic, symptoms may include head/neck pain, syringomyelia, cerebellar dysfunction, brainstem symptoms, oropharyngeal dysfunction, cranial neuropathies, and hydrocephalus. The treatment is surgery. On the other hand, CM-1 can also be asymptomatic. If asymptomatic patients are not accompanied by a syrinx, they are followed up without intervention [6]. It is claimed that subclinical effects, if any, in these asymptomatic cases can be revealed by electrophysiological studies and that this may be important for the treatment and follow-up plan for such patients.

Dysfunction of the brainstem or upper cervical cord may cause abnormalities in median nerve SEP examination. The results of studies indicating that it may be clinically useful in the evaluation of patients with CM are contradictory. In our study, we investigated the results of median nerve SEP examination in patients with CM-1 detected by magnetic resonance imaging (MRI) due to head and neck pain and dizziness and whether there was a correlation with the degree of cerebellar ectopia.

2. Material and Methods

2.1. Study Design

We retrospectively analysed the clinical data of a cohort of 146 CM-1 patients who were referred to our electroneurophysiology laboratory for median nerve SEP examination between 2019 and 2023. This research was approved by the local ethics committee (24.05.2023/E1-23-3621). Patients with CM-1 over the age of 18 were included in the study. All included patients were asymptomatic or oligosymptomatic for CM. Patients who were oligosymptomatic had symptoms that were nonspecific for CM, such as head and neck pain and dizziness. Patients with symptoms and signs of brainstem, lower cranial nerves, cerebellum and

spinal cord compression were not included in the study. Those with other central nervous system diseases such as tumors or demyelinating diseases were excluded from the study.

The amount of displacement of the cerebellar tonsils from the foramen magnum to the cervical spinal canal was measured. This evaluation was made according to the McRae line drawn between the base and opisthion, which are the most anterior and posterior midsagittal points of the foramen magnum border, respectively. Tonsil herniation was measured in millimetres on a line drawn perpendicularly from the tips of the cerebellar tonsils to the McRae line on sagittal midline T1-weighted MRI [7] [8]. The McRae line has been used to evaluate the craniovertebral junction since the 1950s [9]. It was first used in radiographs along with other measurement methods, and then when its consistency with CT was examined, the McRae line was determined to be the most consistent and was recommended more frequently than other measurement methods because it was the easiest method to understand and remember [10]. Again, in a series of studies using CT and MRI, measurements have been shown to be reliable and reproducible [11] [12] [13].

All MR images were acquired with a 3 T superconductor with a standard head coil of 8 - 16 channels. According to the traditional MRI protocol, transverse and sagittal T1-weighted (TR: 450 msec; TE: 10 msec), transverse and sagittal T2-weighted (TR: 5290 msec; TE: 110 msec), transverse FLAIR (TR: 9000 msec; TE: 125 msec) images were obtained (slice thickness: 5 mm; section width: 1 mm).

Median nerve SEP evaluates conduction from the median peripheral nerve of upper limbs through the dorsal column pathway of the spinal cord and medial leminiscus of the brainstem to the primary somatosensory cortex. The SEP recorded from the scalp represents the integrity of the nerves from periphery to cortex. The first component generated at the cortex N20 is recorded over the centroparietal region, contralateral to the stimulated nerve [14]. Median nerve SEP recordings were made with contralateral parietal cortical wave N20 (C3/C4) and cephalic (Fpz) reference. The cephalic bipolar montage, in which both the reference and the active electrode are placed on the scalp, is often preferred for routine clinical use because it has the advantage of being relatively free from noise [15]. The ground electrode was placed on the forehead. Skin impedance was less than 4000 Ω for all recordings. The analysis time was 100 milliseconds. Filters were adjusted from 10 to 2000 Hz. Five hundred potentials were averaged, and 2 repetitions were performed. Patients' medical records were reviewed, and symptoms and signs were recorded.

2.2. Statistical Analysis

The data were evaluated in the statistical package program IBM SPSS Statistics Standard Concurrent User V 26 (IBM Corp., Armonk, New York, USA). Descriptive statistics are given as the number of units (n), percentage (%), and

mean ± standard deviation values. Normal distribution of the data of numerical variables was evaluated with the Shapiro Wilk normality test. In comparing two groups, and independent samples t test was used if the data were normally distributed, and the Mann-Whitney U test was used if the data were not normally distributed. Relationships between numerical variables were evaluated with the Spearman correlation coefficient. Categorical variables were evaluated with Fisher's exact test. Subgroup analyses in chi-square tests were performed with a two-proportion z test with Bonferroni correction. A p value < 0.05 was considered statistically significant.

3. Results

A total of 146 CM patients, 110 (75.3%) women and 36 (24.7%) men, and 30 healthy volunteers, 22 (73.3%) women and 8 (26.7%) men, were included in the study. The mean age was 36.99 ± 13.14 years in the CM patients group and 35.5 ± 13.06 years in the control group. The groups were similar in terms of age and sex; there was no significant difference (p = 0.817; p = 0.559, respectively).

Of the patients with CM, 112 (76.7%) presented with head and neck pain and 34 (23.3%) with dizziness. There were no neurological signs associated with the symptoms.

In patients with CM, the SEP values were 18.66 ± 1.82 msec on the right and 18.69 ± 1.87 msec on the left. In the control group, the SEP values were 18.59 ± 1.23 msec on the right and 18.6 ± 1.3 msec on the left. The maximum SEP values were 19.05 ± 1.92 msec in the CM patients group and 18.84 ± 1.27 msec in the control group.

The SEP values were not significantly different between groups (p = 0.698; p = 0.870; p = 0.994; respectively). The McRae line lenght was found to be significantly shorter (p = 0.031) in the control group (36.03 ± 2.8 mm) than in the CM group (37.69 ± 3.97 mm).

The degree of cerebellar ectopia measured in the patients was 10.10 ± 4.74 mm. There was no correlation between the degree of cerebellar ectopia and the length of the McRae line (r = −0.002, p = 0.979). The relationship between cerebellar ectopia and McRae line length and SEP values is presented in Table 1.

Table 1. Relationships between cerebellar ectopia degree and McRae line distance and SEP latency.

n = 146		McRae line (mm)	Right SEP (msec)	Left SEP (msec)	Maximum SEP (msec)
McRae line (mm)	r		−0.046	−0.100	−0.056
	p		0.580	0.230	0.500
cerebellar ectopia degree (mm)	r	−0.002	−0.137	−0.144	−0.153
	p	0.979	0.100	0.082	0.066

mm: millimeter; msec: milliseconds; rho: Spearman correlation coefficient.

There was no difference in the degree of cerebellar ectopy or SEP values between the groups with cerebellar ectopia with and without a syrinx. Likewise, McRae line length was not found to be related to the presence of the syrinx. They are summarized in Table 2.

4. Discussion

CM-1 is often diagnosed incidentally on MRI in adolescents and young adults. Evoked potentials (EPs) are used to support the diagnosis or to detect the extent of neurological involvement in asymptomatic cases. However, the role of UPs in the diagnosis, follow-up and prognosis has not been clearly established [8]. Abnormal somatosensory conduction reflects dysfunction of the brainstem or upper cervical cord and may be clinically useful in the evaluation of patients with symptomatic CM. Likewise, somatosensory pathways pass through critical regions of the brainstem that could be affected by CM. Abnormal SEPs have high sensitivity and high specificity in indicating abnormal function of the medial lemniscus or cervical posterior columns in patients with symptomatic CM [16]. In asymptomatic patients, the results are contradictory. Dulce *et al.* found that there were changes in both brainstem auditory evoked potentials (BAEPs) and median and posterior tibial SEPs in patients with CM-1, regardless of clinical and radiological findings [8]. Barnet *et al.* did not detect SEP abnormalities in asymptomatic patients with CM in their study. They reported that they found abnormal cortical SEPs in patients with symptomatic CM but obtained false-positive results in some patients [17]. Moncho *et al.* detected abnormal evoked potentials in 23 (50%) of 46 patients with incidental findings and who were asymptomatic. They reported that they found no significant differences in the percentages of SEP abnormalities between symptomatic and asymptomatic patient groups or between groups with and without syringomyelia. They argued that a large percentage of patients with CM-1 exhibit UP changes regardless of clinical or

Table 2. Relationship between the presence of syrinx and McRae line, right SEP, left SEP, maximum SEP latency and amount of cerebellar ectopia in the patient group.

	syrinx		W statistic	p
	without syrinx n = 112	with syrinx n = 34		
McRae line (mm)	37.95 ± 4.21	36.8 ± 2.9	1.488	0.139‡
Right SEP (msec)	18.49 ± 1.48	19.23 ± 2.6	−1.371	0.170†
Left SEP (msec)	18.5 ± 1.33	19.32 ± 2.98	−1.295	0.195†
Maximum SEP (msec)	18.84 ± 1.43	19.73 ± 2.94	−1.749	0.080†
Cerebellar ectopia degree (mm)	10.16 ± 4.91	9.9 ± 4.24	−0.127	0.899†

Numerical variables are given as mean ± standard deviation. W: Shapiro Wilk normality test, ‡: Independent samples t test; †: Mann-Whitney U test; mm: millimeter; msec: milliseconds.

radiological findings, so UPs do not add any clinically meaningful information and are not helpful in determining which symptomatic CM patients should receive surgical treatment [18]. Cheng *et al.* found no difference in the degree of tonsillar displacement between patients with normal SEPs and patients with changed SEPs [19]. Isik *et al.* reported that in the series they presented, they also encountered SEP abnormalities in patients without clinical finding so they performed a surgical procedure on them and found that their SEPs improved during follow-up [20].

UPs are in vivo measurements of central signalling and provide a quantitative measure of functional impairment in relevant pathways [21]. What does UP tell us? A normal UP test tells us that a sufficient number of fast-conducting fibres are still preserved when MRI shows clear involvement of the relevant pathways [22]. Therefore, a normal UP result cannot guarantee that the functionality of the relevant pathways is preserved. What about abnormal UPs? UP abnormalities can never be ignored, regardless of the presence of visible lesions on MRI, because they imply both insufficiency of fast-conducting fibres and a severe functional disability with adaptation. Thus, UPs may be telling us more than we think. In cases where MRI and neurological examination and anamnesis provide only the minimum conditions for diagnosis, subclinical abnormalities demonstrated on one or several UPs may also be effective as additional parameters in establishing the treatment plan.

The fact that cortical SEP is delayed rather than segmental slowing down in spinal SEP is important as it shows that there are no fast-conducting fibres left and that adaptation and functional amplification mechanisms are also affected [23] [24]. However, normal SEP values do not mean that there is no problem. Because SEPs evaluate the cervical posterior cord and brainstem lemniscal pathway, if tonsillar herniation and downward pulling of the brainstem affect other descending pathways other than the lemniscal pathways, SEP values will not show this. Therefore, it is necessary to avoid overestimating the importance of evoked potential examinations, which measure the current physiological conduction of the relevant pathways, in diagnosis, follow-up and prognosis, in advanced MRI techniques.

Evoked potential tests are a nerve conduction study in which peripheral and central conduction are evaluated and are likely to be affected by many factors such as height, age, sex, ambient temperature, body temperature, and anxiety-induced sympathetic discharge during the procedure [25]. There is a difference in latency even in tests repeated twice in a row under the same conditions at the same time, and the average of the two is accepted. This even shows us the changeability of the result.

Visual evoked potential (VEP) is more sensitive than MRI in determining optic nerve involvement. The sensitivity of VEP is 100%. The rate of detecting spinal lesions with SEP monitoring is lower (64%) [22]. With SEP monitoring, only lemniscal pathways can be evaluated among the pathways leading to the

medulla spinalis. These pathways are not the only anatomical structures that may become trapped and dysfunctional in CM. Therefore, being normal or remaining normal during follow-up does not mean that CM does not cause any damage to the spinal cord and brainstem.

In our study, we did not detect any SEP abnormalities in this series of patients who presented with symptoms of head and neck pain and dizziness that were not specific to CM malformation and were detected to have CM but had no neurological signs. We also did not detect a correlation between the degree of cerebellar ectopia and SEP latency. Whether accompanied by syringomyelia or not, SEPs did not contribute to subclinical effects in the patients with asymptomatic-oligosymptomatic CM.

It can be said that SEP is not as useful as thought in revealing subclinical damage in patients with CM. Moreover, a normal SEP examination may mislead to the absence of damage. Findings should be interpreted with caution and undue emphasis should not be placed on the test when making diagnosis, follow-up and surgical decisions.

Conflicts of Interest

The authors of this work have nothing to disclose.

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