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Associations between the Mismatch-negativity Potential and Symptom Severity in Medication-naïve Children and Adolescents with Symptoms of Attention Deficit/hyperactivity Disorder

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Objective: The mismatch negativity (MMN) event-related potential is an index of the pre-attentive stage of neural auditory information processing and an electrophysiological signal indicative of the integrity of auditory information processing with regard to the attention deficit symptom of attention deficit hyperactivity disorder (ADHD). We investigated the association between the MMN amplitude and latency in frontal brain regions and symptom severity in children with ADHD and subclinical ADHD symptoms.
Methods: This study included 29 children: 16 (10 boys; mean age, 13.06 ± 3.67 years) with ADHD (ADHD group) and 13 (eight boys; mean age, 13.40 ± 3.31 years) with sub-clinical ADHD symptoms (subclinical ADHD group). We performed the following assessments: Korean ADHD rating scale-IV (K-ARS-IV), children depression inventory, state/trait anxiety inventory for children, and MMN (measured at Fz, FCz, Cz, and CPz).
Results: There were no sex or mean age differences between the groups (χ^2 = −0.01, p = 0.958; Z = −1.88, p = 0.060, respectively). The ADHD group had a significantly higher mean K-ARS-IV score (26.13 ± 9.56 vs. 17.15 ± 11.73, Z = −2.11, p = 0.035). Significant differences were found according to symptom severity in the MMN amplitude at FCz (Z = −2.11, p = 0.035) and MMN latency at Fz and FCz (Z = −2.48, p = 0.013; Z = −2.57, p = 0.010). The K-ARS-IV, K-ARS inattention subscale, and K-ARS hyperactivity-impulsivity subscale scores in the ADHD group correlated significantly with the MMN amplitude at Cz and CPz.
Conclusion: This study found differences in the MMN amplitude and latency according to the severity of ADHD symptoms and identified MMN as a potential adjunct to the diagnosis of ADHD.

KEY WORDS: Attention deficit disorder with hyperactivity; Evoked potentials; Child; Adolescent; Biomarkers.

INTRODUCTION

Attention deficit/hyperactivity disorder (ADHD) is a common neurodevelopmental and behavioral disorder; its worldwide prevalence among children and adolescents is approximately 5−10% [1]. Children and adolescents with ADHD are either unable to maintain attention to complete a task because they lack attention control or are overly immersed in one task when they need to shift attention to another task [1]. Event-related potentials (ERPs), which allow for the noninvasive measurement of cognitive function, have been extensively utilized to study attentional processes in children and adolescents with ADHD. The results of such studies have suggested that easily distractible individuals exhibit apparent abnormalities in attention-dependent processing [2]. Among the ERP components, the P300 has previously been studied with regard to ADHD, and the study results consistently indicate that the P300 amplitude is lower [3-6] and the latency is longer [6,7] in children with ADHD relative to controls. However, as the P300 is related to deviant auditory or visual stimulation, whether the low amplitude and long latency of P300 is a response to the stimuli

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or to the task remains ambiguous.

Mismatch negativity (MMN) involved a negative wave with a latency of 100−250 ms which is obtained when the transposition induced by a standard stimulus is substracted from the transposition induced by a deviant stimulus, after intermittently providing deviant stimuli among iterative standard auditory stimuli [8,9]. MMN is generated in the absence of behavioral responses as well as motivation and is therefore considered as indicative of pre-attentive central processing of auditory change detection [2]. With the advantage of being independent of overt behavioral requirement, MMN has been conceptualized as an optimal electrophysiological signal to elucidate the integrity of auditory information processing with regard to the attention deficit symptoms of ADHD [10,11].

Studies on MMN in children and adolescents with ADHD have also reported consistent results [10,12-14]. In a study examining the correlation between ADHD severity and MMN components in children with pervasive developmental disorder [13], the MMN amplitude was negatively correlated with the severity of ADHD symptoms. In another study on MMN in children and adolescents with ADHD [10], in line with existing research, the MMN amplitude was lower and the latency was longer in the ADHD group than in the control group. However, the fact that ADHD is associated with a comorbidity prevalence of 70% [15,16], has not been considered in these studies [10,12-14]. As research has suggested that depression, anxiety, and other psychiatric disorders—the most common comorbidities among patients with ADHD—can also lower the MMN amplitude, it is difficult to conceptualize that the MMN changes are solely attributable to the symptoms of ADHD and are independent of the effects of comorbidities [17-19].

In this study, we excluded children and adolescents who had psychological conditions that may affect the MMN, or whose major diagnosis was a disorder other than ADHD [17,18,20]. We aimed to identify differences in the MMN components in such participants according to the severity of ADHD symptoms. We hypothesized that, among children and adolescents without depression and anxiety, MMN amplitudes decrease and latencies increase with the increasing severity of ADHD symptoms.

METHODS

Participants

The participants were selected from children and adolescents aged 6−18 years who visited the psychiatry department of a university hospital in Seoul between January and December of 2018. An experienced pediatric psychiatrist conducted clinical interviews and assessments with children and adolescents and their parents, and diagnosed ADHD based on The Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5) ADHD diagnostic criteria [1]. Cases associated with brain injury, main diagnosis of a mental illness other than or in addition to ADHD, or lack of consent from the child or adolescent and his or her parents were excluded from this study. The participants in this study were children and adolescents who were either diagnosed with ADHD (ADHD group) or exhibited subclinical ADHD symptoms without a confirmed diagnosis of ADHD, because of insufficiency of conforming to the criteria of DSM-5 (subclinical ADHD group). The participants underwent evaluations with the Korean ADHD rating scale-IV (K-ARS-IV), children depression inventory (CDI), state/trait anxiety inventory for children (STAI-C), and with respect to MMN. The majority of the participants had no history of taking psychiatric medication, and those who were already taking medication (six patients) underwent a medication-washout at least 1 week prior to participating in the study. Because of the reduced MMN amplitude in children and adolescents with ADHD, such patients were normalized with methylphenidate [21]. In both the ADHD and subclinical ADHD groups, one participant was left-hand dominant, while the remaining participants were right-hand dominant. Of the 37 children and adolescents who participated in this study, eight individuals whose MMN components were difficult to analyze due to excessive movements were excluded. Thus, 29 children and adolescents (ADHD group: 16 participants, subclinical ADHD group: 13 participants) were finally selected as the study cohort. All children and adolescents and their parents provided written informed consent in accordance with the Declaration of Helsinki. All subjects and their guardians voluntarily participated in this study that had been reviewed and approved by the Institutional Review Board of the Soonchunhyang University Seoul Hospital of Korea (no. 2017-08-003).

Instruments

Korean ARS-IV

The ARS-IV was developed by Dupaul as a measure of hyperactivity and problematic behaviors in children and adolescents [22]. The scale is composed of 18 items according to the ADHD diagnostic criteria of the DSM-IV, and each item is rated on a four-point Likert scale according to the frequency of the child's problematic behavior: "never or rarely" is scored as 0; "sometimes," as 1; "often," as 2; and "very often," as 3. A score of ≥ 2 is considered abnormal relative to the developmental stage of healthy children and adolescents. It is arranged such that the total score of odd-numbered items measures inattention, and the total score of even-numbered items measures hyperactivity-impulsivity. In the K-ARS-IV, K-ARS inattention subscale (K-ARS-In), and K-ARS hyperactivity-impulsivity subscale (K-ARS-H), higher scores indicate greater severity of ADHD symptoms. In the K-ARS standardized by Jang *et al.* [23], Cronbach's alpha was 0.74−1, and the validity was 0.06−0.59, indicating a high correlation.

CDI

The CDI, developed by Kovacs [24], is a self-report test assessing the cognitive, emotional, and behavioral symptoms of childhood and adolescent depression. It consists of 27 items, each rated from 0−2 points based on mood state. A total score of 22−25 points indicates a slightly depressed condition, 26−28 points a significantly depressed condition, and ≥ 29 indicates a very severe depressed condition. In this study, depression was defined as a score of ≥ 22 points. In the Korean version of the CDI standardized by Cho and Lee [25], Cronbach's alpha was 0.88, and the correlation was high with a test-retest reliability of 0.82.

STAI-C

The STAI-C is a self-report test assessing state anxiety and trait anxiety in children and adolescents [26,27]. The test consists of 20 items, and was adapted from the STAI scale for adults developed by Spielberger [26] to be easily understood by children and adolescents. Current and typical feelings are evaluated on a three-point Likert scale. In the SAI-C, a total score of 39−42 indicates slightly high anxiety, 43−46 significantly high anxiety, and ≥ 47 indicates severely high anxiety. In the TAI-C, a total score of 41−44 indicates slightly high anxiety, 45−48 significantly high anxiety, and ≥ 49 indicates severely high anxiety. In this study, anxiety was defined as a score of ≥ 39 points on the SAI-C and ≥ 41 points on the TAI-C. The Korean version was standardized by Cho and Choi [28], and Cronbach's alpha of the SAI-C and TAI-C was 0.88 and 0.83, respectively.

Electroencephalogram Acquisition and Analysis

The participants were seated in a comfortable chair in a sound attenuated room. Stimulus presentation and data synchronization with the electroencephalogram (EEG) were conducted with E-Prime (Psychology Software Tools, Pittsburgh, PA, USA). The auditory stimuli consisted of sounds at 85 dB SPL and 1,000 Hz. Deviant tones lasting 100 ms were presented randomly, interspersed with standard tones lasting 50 ms (probabilities of 10% and 90%, respectively). In total, 400 auditory stimuli were presented; the peak duration time was 10 ms, and the inter-stimulus interval was 500 ms. These auditory stimuli were delivered via MDR-XB950N1 headphones (Sony, Tokyo, Japan). The subjects were asked to watch an Incredible animation without paying attention to the sound. The experiment required approximately 10 minutes. Breaks were permitted only when the participants stated that they wanted to rest.

EEG activity was recorded using a NeuroScan SynAmps amplifier (Compumedics USA, El Paso, TX, USA) and Ag-AgCl electrodes using a modified 10−20 placement scheme. EEG data were recorded with a 0.1−100 Hz band-pass filter at a sampling rate of 1,000 Hz. The ground electrode was placed on the forehead, and the reference electrodes were located at both mastoids. The inter-electrode impedance was maintained at < 10 kΩ. Averaging of the ERP waves and related procedures was performed using the NeuroScan version 4.3 software package (Compumedics USA).

The recorded EEG data were preprocessed using CURRY 8. Gross movement artifacts were eliminated from the recorded data by visual inspection, and eye blink artifacts were eliminated using established mathematical procedures [29]. Trials were rejected if they included significant physiological artifacts (amplitude exceeding ± 75 μV) at any cortical electrode site. After artifact removal, baseline correction was conducted by subtracting the mean voltage at 100 ms before stimulus onset from the

Table 1. Participant characteristics

Variable	Subclinical ADHD group (n = 13)	ADHD group (n = 16)	Z/χ^2	*p* value
Sex (male/female)	8/5	10/6	0.01	0.958
Age (yr)	13.40 ± 3.31	13.06 ± 3.67	−1.88	0.060
K-ARS	17.15 ± 11.73	26.13 ± 9.56	−2.11	0.035
K-ARS-In	9.23 ± 5.97	14.13 ± 5.01	−2.20	0.028
K-ARS-H	6.38 ± 4.46	11.69 ± 6.38	−2.18	0.029
TAIC	36.54 ± 8.62	36.31 ± 8.34	−0.07	0.947
SAIC	33.85 ± 8.33	35.81 ± 11.61	−0.35	0.725
CDI	17.23 ± 10.51	19.88 ± 11.37	−0.43	0.449

Values are presented as number only or mean ± standard deviation.
ADHD, attention deficit/hyperactivity disorder; K-ARS, Korean attention deficit/hyperactivity disorder rating scale-IV full version; K-ARS-In, K-ARS inattention subscale; K-ARS-H, K-ARS hyperactivity-impulsivity subscale; TAIC, trait anxiety inventory-children; SAIC, state anxiety inventory-children; CDI, children's depression inventory.

post-stimulus data for each trial. The data were band-pass filtered at 0.1−70 Hz (24 dB/octave roll-off) and then divided into 1,000 ms epochs from 100 ms pre-stimulus to 900 ms post-stimulus. The MMN wave was generated by subtracting the standard ERP wave from the deviant waves. The MMN amplitude was measured as the peak voltage and its latency between 100 and 250 ms at four electrode sites (Fz, FCz, Cz, and CPz) because the frontocentral electrodes have demonstrated larger MMN peaks [30-32]. To prevent participants from habituating to the stimuli, each trial was conducted only once.

Statistical Analyses

Statistical calculations were conducted using SPSS 23.0 for Windows (IBM Co., Armonk, NY, USA). Data are expressed as the mean ± standard deviation. The sex difference between the ADHD group and the subclinical ADHD group was confirmed with the χ^2 test, and the differences in the K-ARS-IV, STAI-C, and CDI scores and MMN between the two groups were confirmed with the Mann−Whitney *U* test. We calculated Spearman's correlation coefficient (ρ) for the relationships between the K-ARS-IV scores (including the K-ARS-In and K-ARS-H subscale scores) and electrophysiological variables. Bonferroni-corrected *p* values of < 0.05 were considered to be statistically significant.

RESULTS

Demographic Data

There were no sex or mean age differences between the ADHD group and the subclinical ADHD group ($\chi^2 = -0.01$, $p = 0.958$; $Z = -1.88$, $p = 0.060$, respectively) (Table 1). The ADHD group had a significantly higher mean K-ARS-IV score (26.13 ± 9.56) than the subclinical ADHD group (17.15 ± 11.73, $Z = -2.11$, $p = 0.035$). The ADHD group achieved significantly higher scores than the subclinical ADHD group in both the K-ARS-In and K-ARS-H ($Z = -2.20$, $p = 0.028$; $Z = -2.18$, $p = 0.029$, respectively).

In this study, the ADHD group and the subclinical ADHD group differed only in the K-ARS-IV and sub-domain scores and were confirmed to be homogeneous in general characteristics such as sex, age, anxiety, and depression (Table 1).

Comparison of MMN Amplitudes and Latencies in the ADHD Group and Subclinical ADHD Group

The MMN assessment of the ADHD group and the subclinical ADHD group indicated that the ADHD group had a significantly lower ($Z = -2.11$, $p = 0.035$) mean amplitude at FCz (−3.54 ± 1.23 μV) than did the subclinical ADHD group (−4.90 ± 2.32 μV) (Table 2). However, although there was no statistical significance between the two groups at Fz ($Z = -1.49$, $p = 0.136$), Cz ($Z = -1.14$, $p = 0.254$), and CPz ($Z = -1.40$, $p = 0.161$), the ADHD group was found to have a lower MMN amplitude than the subclinical ADHD group (Fig. 1).

MMN evaluation indicated that the latency (ms) was significantly longer at Fz and FCz ($Z = -2.48$, $p = 0.013$; $Z = -2.57$, $p = 0.010$) in the ADHD group than in the subclinical ADHD group. However, there was no significant difference in the MMN latency (ms) between the two groups at Cz ($Z = -0.86$, $p = 0.392$) and CPz ($Z = -$

Table 2. Mismatch negativity potential amplitudes and latencies

Variable	Subclinical ADHD group (n = 13)	ADHD group (n = 16)	Z	*p* value
MMN amplitude (μV)				
Fz	−4.97 ± 1.81	−4.16 ± 1.53	−1.49	0.136
FCz	−4.90 ± 2.32	−3.54 ± 1.23	−2.11	0.035
Cz	−2.90 ± 1.64	−2.23 ± 1.25	−1.14	0.254
CPz	−2.45 ± 1.15	−1.93 ± 1.38	−1.40	0.161
MMN latency (ms)				
Fz	208.84 ± 34.89	243.94 ± 23.89	−2.48	0.013
FCz	209.00 ± 31.67	239.88 ± 24.72	−2.57	0.010
Cz	205.31 ± 30.34	215.13 ± 37.51	−0.86	0.392
CPz	201.69 ± 31.07	210.31 ± 41.94	−0.79	0.430

Values are presented as mean ± standard deviation.
ADHD, attention deficit/hyperactivity disorder; MMN, mismatch negativity; Fz, frontal electrode; FCz, fronto-central electrode; Cz, central electrode; CPz, centro-parietal electrode.

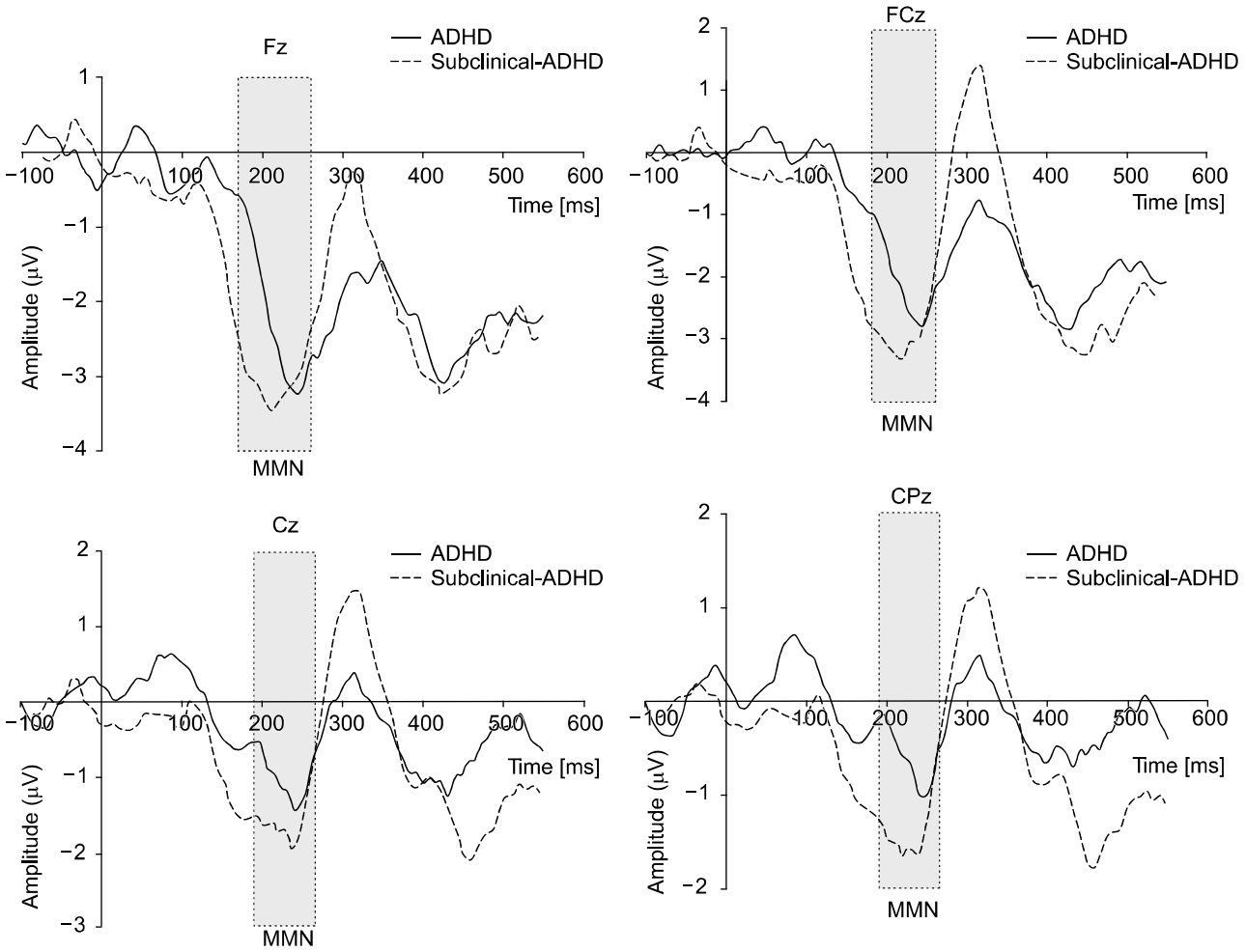

Fig. 1. Grand averages of mismatch negativity event-related potentials in children and adolescents with attention deficit/hyperactivity disorder and sub-clinical attention deficit/hyperactivity disorder.
MMN, mismatch negativity; ADHD, attention deficit/hyperactivity disorder; Fz, frontal electrode; FCz, fronto-central electrode; Cz, central electrode; CPz, centro-parietal electrode.

Table 3. Correlations between the MMN components and K-ARS-IV full version, K-ARS-In, and K-ARS-H scores in the ADHD group (n = 16)

Variable	Spearman's correlation		
	K-ARS-IV	K-ARS-In	K-ASR-H
MMN amplitude (μV)			
Fz	−0.11 (p = 0.688)	0.10 (p = 0.720)	−0.17 (p = 0.521)
FCz	−0.03 (p = 0.927)	0.12 (p = 0.647)	−0.20 (p = 0.451)
Cz	−0.64* (p < 0.001)	−0.55* (p = 0.002)	−0.61* (p < 0.001)
CPz	−0.57* (p = 0.001)	−0.55* (p = 0.002)	−0.55* (p < 0.001)
MMN latency (ms)			
Fz	0.09 (p = 0.734)	0.09 (p = 0.741)	0.22 (p = 0.403)
FCz	−0.25 (p = 0.350)	−0.27 (p = 0.308)	−0.07 (p = 0.811)
Cz	−0.00 (p = 0.987)	0.19 (p = 0.471)	−0.05 (p = 0.853)
CPz	−0.02 (p = 0.931)	0.18 (p = 0.515)	−0.06 (p = 0.819)

MMN, mismatch negativity; K-ARS-IV, Korean attention deficit/hyperactivity disorder rating scale-IV; K-ARS-In, K-ARS inattention subscale; K-ARS-H, K-ARS hyperactivity-impulsivity subscale; Fz, frontal electrode; FCz, fronto-central electrode; Cz, central electrode; CPz, centro-parietal electrode.
*Bonferroni-corrected $p < 0.05$.

0.79, p = 0.430).

Correlations among the MMN Components and the K-ARS-IV, K-ARS-In, and K-ARS-H Scores

Higher K-ARS-IV, K-ARS-In, and K-ARS-H scores in the ADHD group were negatively correlated with the MMN amplitude at Cz and CPz (Table 3 and Figs. 2−4). The K-ARS-IV, K-ARS-In, and K-ARS-H scores were not correlated with the MMN amplitude at Fz and FCz. Further, the K-ARS-IV, K-ARS-In, and K-ARS-H scores were not correlated with the MMN latency at Fz, FCz, Cz, and CPz.

DISCUSSION

In this study, we assessed the associations between the MMN amplitude and latency with ADHD symptom severity in medication-naïve children and adolescents. Our results identified several key findings. First, the more severe the ADHD symptoms, the lower the amplitude and the longer the latency of the MMN wave. Second, the MMN amplitude difference according to the severity of ADHD symptoms between the ADHD group and the subclinical ADHD group was significant at FCz, and the MMN latency difference was significant at Fz and FCz. Third, the K-ARS-IV, K-ARS-In, and K-ARS-H scores in the ADHD group were significantly and strongly negatively correlated with MMN amplitude at Cz and CPz.

Our results indicate that the MMN amplitude is lower and the latency is longer when the severity of ADHD symptoms is high. Previous studies have yielded similar results, wherein children and adolescents with ADHD exhibited a reduced MMN amplitude and prolonged MMN latency compared with those in the normal control group [7,10,21,33]. The MMN assesses the functional status of the cerebral cortex by measuring auditory processing abnormalities and sensory/perceptual abilities [34]. Cognitive/functional decline, progression of condition, level of consciousness, impaired cerebral cortex, and other structural changes are reflected in the MMN amplitude and latency [11], and our study supports the results of previous studies as we identified differences in the MMN amplitude and latency according to differences in the severity of ADHD symptoms. In contrast, some studies [14,35] have reported that, compared with the healthy control group, the ADHD group exhibited a shorter latency in the frontal MMNs, which reflects faster processing of perceptual information. It is presumed that the results of previous studies are varied due to small sample sizes and inconsistent consideration of factors that affect ERPs (intelligence, coexistence disorders, developmental age, dominant hemisphere, comorbidities etc.), which should be acknowledged in future studies.

We found that the difference in the MMN amplitude according to ADHD symptoms was significant at FCz, and the difference in the MMN latency was significant at Fz and FCz, which is consistent with our expectations. Although no statistical significance was found at Fz, Cz, and CPz, the ADHD group exhibited a reduced MMN amplitude and prolonged MMN latency at Cz and CPz compared to those observed in the subclinical ADHD

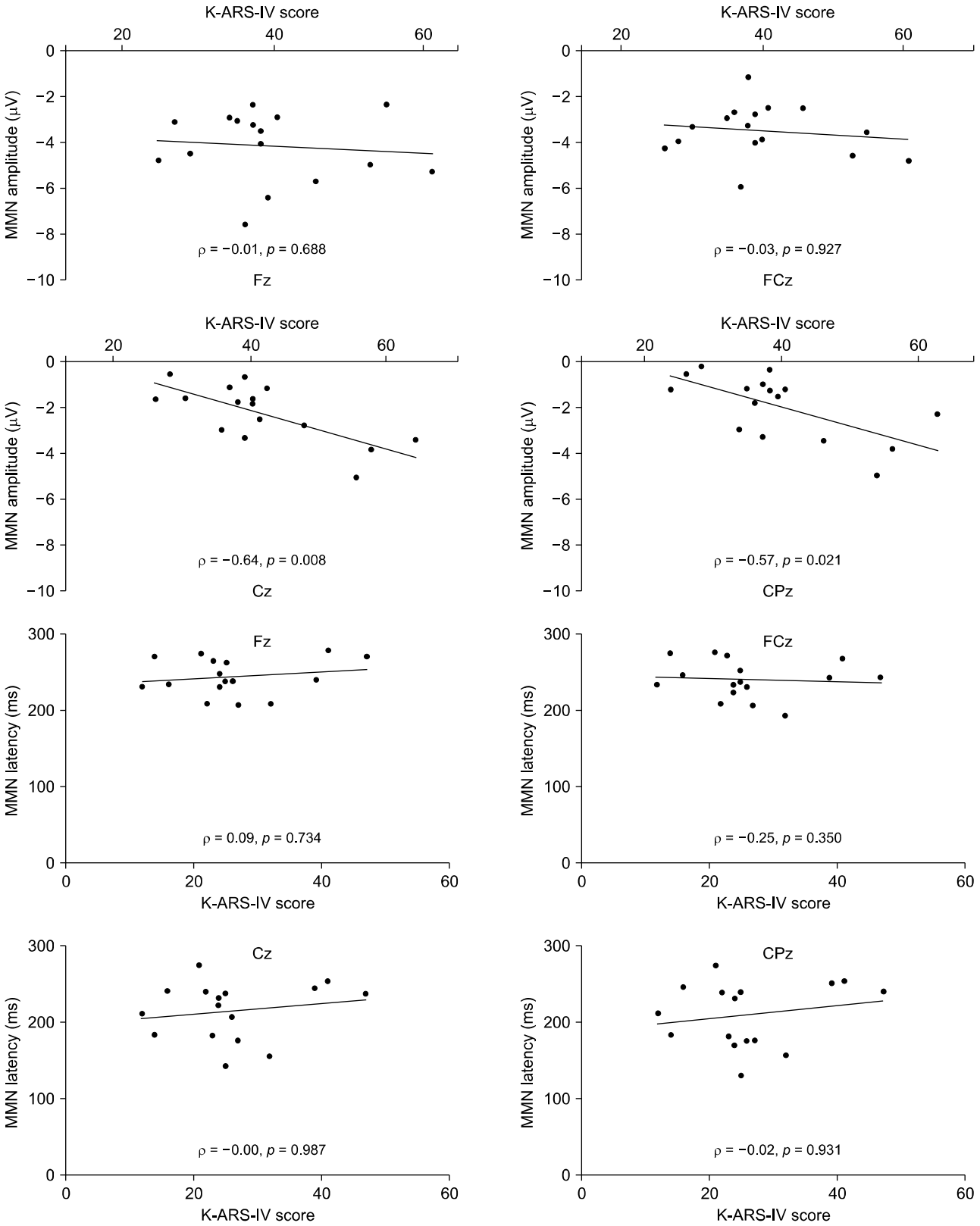

Fig. 2. Correlations between the mismatch negativity component and Korean attention deficit/hyperactivity disorder rating scale-IV scores. MMN, mismatch negativity; K-ARS-IV, Korean attention deficit/hyperactivity disorder rating scale-IV; Fz, frontal electrode; FCz, fronto-central electrode; Cz, central electrode; CPz, centro-parietal electrode.

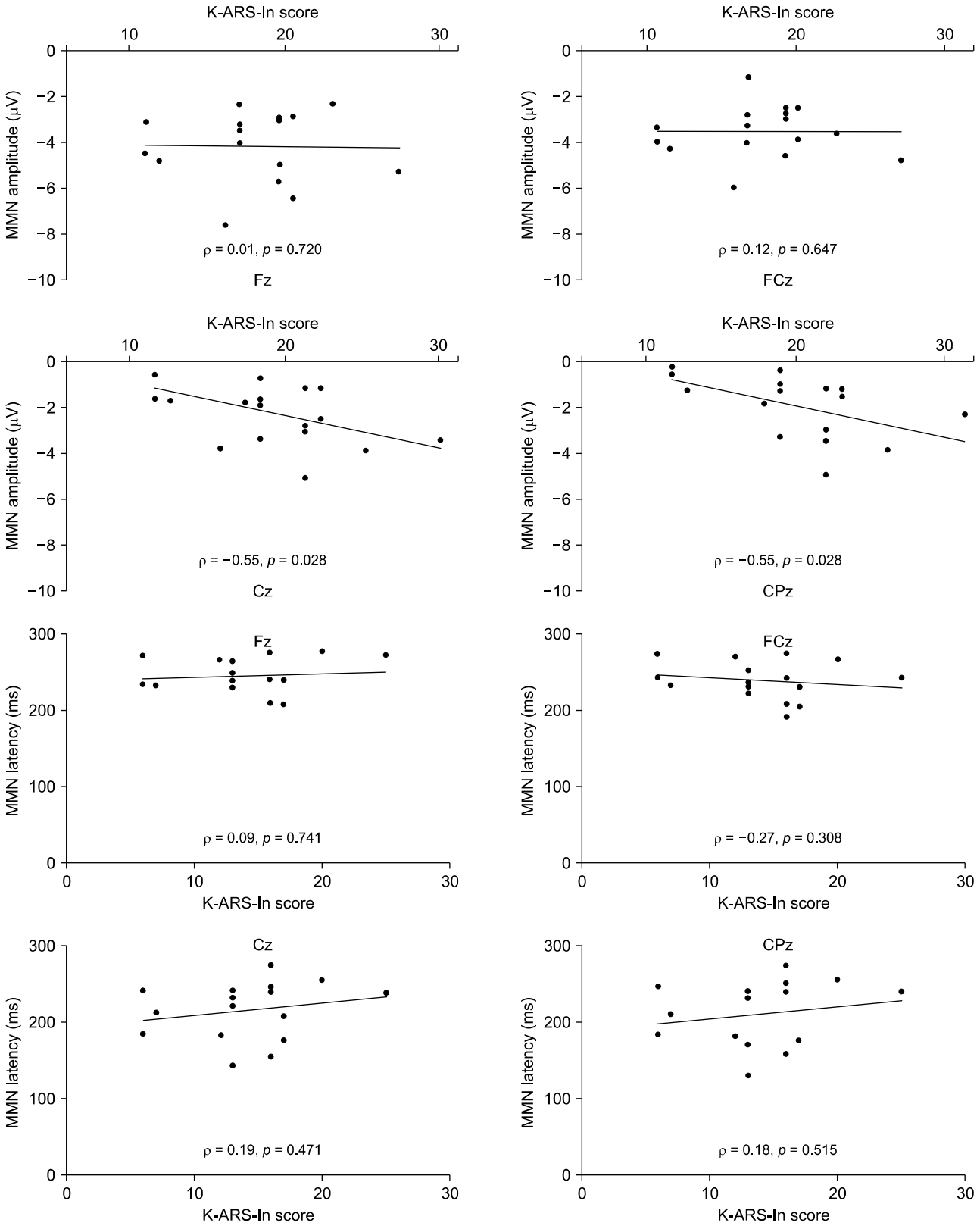

Fig. 3. Correlations between the mismatch negativity component and attention deficit/hyperactivity disorder rating scale inattention subscale scores. MMN, mismatch negativity; K-ARS-In, Korean attention deficit/hyperactivity disorder rating scale-IV inattention subscale; Fz, frontal electrode; FCz, fronto-central electrode; Cz, central electrode; CPz, centro-parietal electrode.

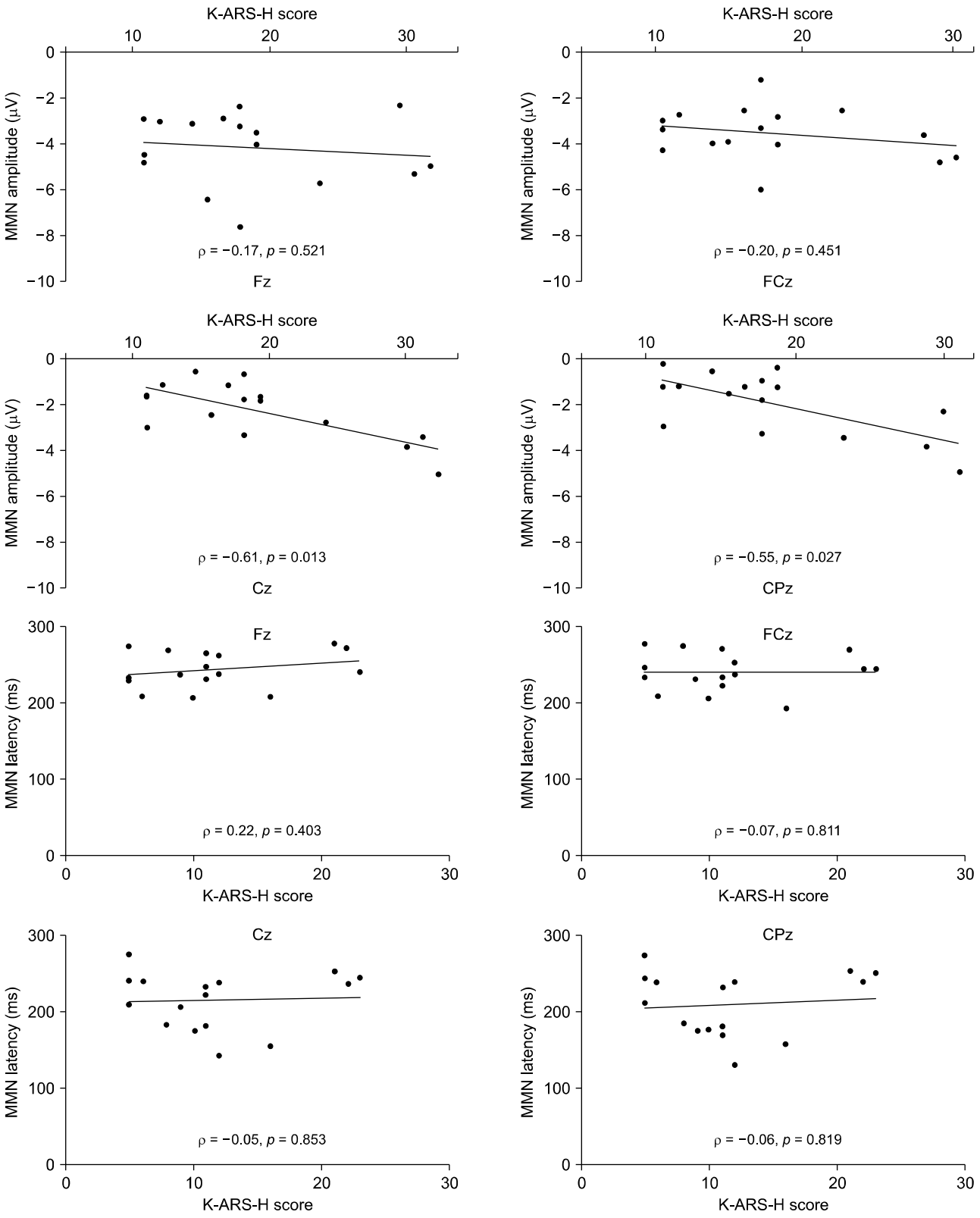

Fig. 4. Correlations between the mismatch negativity component and attention deficit/hyperactivity disorder rating scale hyperactivity-impulsivity subscale scores.

MMN, mismatch negativity; K-ARS-H, Korean attention deficit/hyperactivity disorder rating scale-IV hyperactivity-impulsivity subscale; Fz, frontal electrode; FCz, fronto-central electrode; Cz, central electrode; CPz, centro-parietal electrode.

group. Similar to our results, the ADHD group exhibited a reduced MMN amplitude and prolonged MMN latency at Fz, Cz, and Pz in a study by Yamamuro *et al.* [10] However, unlike our study, Yamamuro *et al.* [10] reported statistically significant differences between the two groups with regard to the amplitude at Cz and latency at Pz; this discrepancy is presumed to be attributable to the study's comparison of ADHD patients and healthy controls as well as their measurement of the MMN only at Fz, Cz, and Pz. However, to clearly identify the reason for such discrepancy, further studies should be conducted with larger samples; use more electrodes; and include a healthy control group, subclinical ADHD group, and ADHD group.

The MMN is thought to occur in the cortex and superior temporal lobe of the frontal lobe, and its maximum amplitude is known to be recorded in the frontal lobe (Fz, F3, F4) [36]. In neuroimaging studies, the development of ADHD symptoms was associated with impaired frontal lobe function; in particular, abnormal activity in the dorsolateral and ventrolateral prefrontal cortex [37,38]. In this study, a statistically significant difference was found at FCz near the maximum amplitude of MMN compared to other electrodes, and Fz, although not statistically significant, exhibited a reduced MMN amplitude in the ADHD group compared to the subclinical ADHD group. These results also support the findings that ADHD is associated with functional impairments in the frontal lobe.

Lastly, the K-ARS-IV, K-ARS-In, and K-ARS-H scores were significantly and strongly negatively correlated with the MMN amplitude at Cz and CPz in the ADHD group. In a study assessing the MMN potential in children with pervasive developmental disorders with attention deficit hyperactivity disorder-like symptoms [13], the ADHD-RS-IV Japanese version score and MMN amplitude were strongly negatively correlated at Cz and Pz, which was similar to our findings. In another study comparing an ADHD group to a control group [10], although not identical to our findings, there was a statistically significant negative correlation between the MMN amplitude and the full score, inattention subscale score, and hyperactivity-impulsivity subscale score with the ADHD-RS-IV Japanese version at Pz, which is near CPz. Several studies have suggested impairment of the frontal lobe as well as dysfunction of the frontal-striatal-cerebellar circuit as the neurophysiological mechanism of impaired attention and inadequate inhibitory control in ADHD [39,40]. Numerous neuroimaging studies have lent support to these hypotheses, revealing abnormalities at both subcortical (including the basal ganglia and the cerebellum) and cortical levels and indicating dysregulation of the dopaminergic neurotransmitter system in ADHD [41,42]. Our research also found that subcortical circuits of central and parietal lobes other than the frontal lobe differed with regard to the MMN amplitude according to the severity of ADHD symptoms.

There are several limitations to consider when interpreting the results of this study. First, it is difficult to generalize the results of this study as it evaluated children and adolescent patients who visited a university hospital in the past year. Therefore, long-term follow-up involving various institutions is needed in future studies. Second, the common symptoms of ADHD— depression and anxiety— did not differ between the ADHD group and the subclinical ADHD group, but not all comorbidities were fully excluded; further, no intelligence tests were performed. Future studies should supplement the overall psychological assessment, including intelligence tests. Third, only the K-ARS-IV was used to assess ADHD symptoms in this study. Future research will be able to elaborate on our findings by using the objective tools of the continuous performance test or the cognitive function test.

Implications

This study evaluated an ADHD group and a subclinical ADHD group of medication naïve children and adolescents with ADHD symptoms and found differences in the amplitude and latency of MMN according to the severity of ADHD symptoms in the absence of a difference in anxiety and depression between the groups. As a result, we identified MMN as an adjunctive test to diagnose ADHD. However, since MMN has not been standardized by age groups, there is a limit to its ability to precisely distinguish healthy children and those with ADHD symptoms. Therefore, in future studies, it is necessary to conduct a comparative study of MMN in children and adolescents with ADHD and healthy controls based on the presence of comorbidities in a large sample.

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■ Conflicts of Interest

No potential conflict of interest relevant to this article was reported.

■ Author Contributions

Conceptualization: Yeon Jung Lee. Data acquisition: Yeon Jung Lee, Mi Young Jeong. Formal analysis: Yeon Jung Lee, Jung Ho Kim. Funding: Yeon Jung Lee. Supervision: Yeon Jung Lee, Ji-Sun Kim. Writing—original draft: Yeon Jung Lee. Writing—review & editing: Yeon Jung Lee, Ji-Sun Kim.

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