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Neurophysiological evidence for cortical discrimination impairment of prosody in Asperger syndrome

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Abstract

Asperger syndrome (AS), belonging to the autism spectrum of disorders, is one of the pervasive developmental disorders. Individuals with AS usually have normal development of formal speech but pronounced problems in perceiving and producing speech prosody. The present study addressed the discrimination of speech prosody in AS by recording the mismatch negativity (MMN) and behavioural responses to natural utterances with different emotional connotations. MMN responses were abnormal in the adults with AS in several ways. In these subjects, fewer significantly elicited MMNs, diminished MMN amplitudes, as well as prolonged latencies were found. In addition, the MMN generator loci differed between the subjects with AS and control subjects. These findings were predominant over the right cerebral hemisphere. These results show impaired neurobiological basis for speech-prosody processing at an early, pre-attentive auditory discrimination stage in AS.

Keywords: Asperger syndrome; Prosody; Emotion; Mismatch negativity; Auditory processing

Asperger syndrome (AS) is one of the pervasive developmental disorders characterized by abnormalities in social interaction and communication [3,16,19–21]. It belongs to the autism spectrum of disorders and shares several features with autism, but is regarded as a separate clinical entity [16]. Language development in AS is usually normal [22] and the acquired literal language skills are good. However, there are problems in understanding hidden meanings of the spoken message and in using language in a social context [8,20]. Individuals with AS have pronounced problems associated with the prosody of speech; the speech production is characterized by abnormal rhythm, intonation, and pitch, and they have difficulties in interpreting the emotional content and prosody of the speech that they hear [12,17,18]. Moreover, auditory hypersensitivity is common in AS [3,4].

There are so far only few studies on the neurophysiology of auditory perception in AS. Jansson-Verkasalo et al. [10] compared pitch (1000 Hz versus 1100 Hz) and consonant (/taa/ versus /kaa/) discrimination between children with AS and control subjects, as indexed by the mismatch negativity (MMN), which can be used for determining cortical sound-discrimination accuracy [14]. They found that for both types of sound contrasts, the children with AS had prolonged MMN latencies over the right cerebral hemisphere.

The present study aimed at determining whether individuals with AS and control subjects differ in discriminating prosodic features in naturally articulated words uttered with different emotional contents. It was hypothesized that individuals with AS are less accurate than control subjects in discriminating words uttered with different prosodies. To this end, the MMN and behavioural data were recorded from eight adult individuals with AS (four females, 22–43 years old, mean 33 years) and their age- and sex-matched control subjects (four females, 23–42 years old, mean 32 years).

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The diagnosis of the AS was based on a detailed interview conducted according to the principles outlined by Gillberg and Gillberg [7], Ehlers and Gillberg [5], and Ehlers et al. [6], and on ICD-10 [22]. Only individuals fulfilling the criteria of ICD-10 [22] and DSM-IV [2] were included in the study. In addition, a comprehensive neuropsychological assessment was carried out, including Wechsler adult intelligence scale revised (WAIS-R), Wechsler memory scale revised (WMS-R), Wisconsin card sorting test (WCST), Benton face recognition test and face recognition task of neuropsychological test battery for children (NEPSY). The subjects had no other neuropsychiatric co-morbidities or any medication for 6 months prior to the testing. The mean full-scale IQ was 114 and the range 99–140 in the subjects with AS.

The discrimination of a Finnish word (female name "Saara") uttered by a female speaker neutrally (stimulus duration 577 ms) and with different emotional connotations, commanding (538 ms), sad (775 ms), and scornful (828 ms), was compared between subjects with AS and control subjects by using the MMN and behavioural responses. The stimuli were chosen from a set of stimuli previously produced for a study on the identification of utterances with 10 different emotional connotations [11]. In that study, all these stimuli were more often identified correctly than identified as representing one of the other optional emotions. The commanding utterance was the easiest to identify, being correctly identified in 75% of the trials, whereas the corresponding numbers for the neutral (called "naming" in [11]) and scornful utterances were 48% and 52%, respectively, and for the sad one 36% of the trials.

There were two behavioural tests, a stimulus-identification and a target-discrimination task, administered after the event-related potential (ERP) recording session. In *the stimulus-identification task*, subjects were randomly presented with the stimuli used in the present study ($p = 0.25$ for each stimulus type, eight repetitions). The subject's task was to mark on a sheet whether the stimulus presented was uttered neutrally, sadly, scornfully, or in a commanding manner, or whether it had some other emotional connotation or could not be identified.

In *the target-discrimination task and in the ERP recording session*, the neutrally-uttered word served as the standard stimulus ($p = 0.79$), and the deviant stimuli were randomly presented at the p of 0.07 for each deviant type. The stimuli were presented with a 1500-ms stimulus onset asynchrony (SOA) pseudo-randomly, so that there was at least one standard stimulus between deviant stimuli. In the target-discrimination task (20 trials), the subject was instructed to press a button to target deviant stimuli with the index finger of the preferred hand. Button presses occurring 150–1500 ms from deviant-stimulus onset were regarded as hits and those occurring at any other times as false alarms.

In the ERP recording session, there were five blocks each containing 392 stimuli. Electrophysiological data were collected while the subject watched silent, subtitled movie. The EEG (bandpass 0.1–100 Hz) was recorded with a 32-channel electrode cap, with the reference attached to the nose. The horizontal (bipolar) electro-oculogram was monitored with two electrodes placed at the outer canthi of the eyes, and the vertical one with the Fpz electrode. EEG epochs with voltage exceeding ±100 μV, as well as responses to the first four stimuli were discarded from the analysis. ERPs were separately averaged for each standard and deviant stimulus type, and filtered (bandpass 1–20 Hz, slope 24 db/octave).

Table 1
The mean percentages (with standard deviations in brackets) of correctly identified emotions of the stimuli when uttered neutrally commandingly, scornfully, or sadly

Options	Control	Asperger
Neutral	75 (38)	63 (46)
Commanding	91 (19)	91 (27)
Scornful	66 (48)	59 (46)
Sad	63 (42)	25 (38)

Difference waves (ERPs elicited by the standard stimulus subtracted from those elicited by the deviant stimuli) were created for the statistical analysis. MMN amplitudes were measured from the difference waves with a 50-ms window centered at the grand-mean peak latencies identified at Fz electrode. *t*-tests were used to determine whether the MMNs significantly differed from zero at the frontal electrodes (F3, Fz, F4). The MMNs elicited by the deviant stimuli were compared between the groups over the left (Fz, F3, CT3, CP3, TP3) and right hemispheres (Fz, F4, CT4, CP4, TP4) and at fronto-central (F3, Fz, F4, Cz) scalp areas with ANOVA. Greenhouse–Geisser corrections were applied when appropriate. Fisher's LSD post hoc test was performed to calculate the sources of the significant main effects and interactions.

In the *word-identification* task, both groups identified the commanding stimulus best and the sad stimulus worst (Table 1). An ANOVA including all stimuli and both groups revealed a significant Stimulus main effect ($F(3,42) = 6.46$, $p < 0.002$). The post hoc test revealed that this was caused by a significantly higher identification rate for the commanding stimulus than for the other stimuli and for the neutral stimulus than for the sadly-uttered stimulus (p-values in all these tests <0.05).

In the behavioural *target-discrimination* session, no significant effects were found for the hit- or false-alarm rates but there was a significant reaction time (RT) main effect when all stimuli and both groups were included in the analysis ($F(2,28) = 90.62$, $p < 0.001$; Table 2). According to the post hoc test, the RT for the commanding deviant stimulus was significantly shorter than for the other deviant stimuli, and it was also shorter for the sad than for the scornful deviant stimulus (p-values in these tests <0.01).

All deviant stimuli elicited biphasic negative-going neural responses in control subjects. In subjects with AS, the scornfully and sadly uttered deviant stimuli elicited biphasic negativities, whereas for the commanding deviant stimulus, there was only one negative-going response. The first component of the responses was fronto-centrally

Table 2
The mean hit rate (HIT), false-alarm rate (FA), and reaction time (RT) (with standard deviations in the brackets) for the deviant stimuli presented randomly among the standard stimuli

Stimulus	Control		Asperger	
	HIT	RT	HIT	RT
Commanding	98 (3)	516 (173)	93 (8)	546 (138)
Scornful	98 (4)	669 (213)	93 (7)	682 (146)
Sad	95 (8)	617 (196)	93 (14)	654 (149)
FA	2 (3)		3 (8)	

distributed while the second one was prominent also in the temporal-parietal areas, particularly in control subjects (Fig. 1). All deviant stimuli elicited a significant response in at least one of the frontal channels (F3, Fz, F4) in control subjects ($t(14) = 2.3–5.3$, $p < 0.04$), whereas significant responses were found for the commanding and scornful stimuli ($t(14) = 2.3–4.0$, $p < 0.04$) but not for the sad stimulus in subjects with AS (Fig. 1; Table 3).

The MMN amplitudes tended to be larger in the control subjects than in the subjects with AS (Fig. 1). Amplitude comparisons revealed a significant group difference over the right hemisphere for the scornful deviant stimulus ($F(1,14) = 5.42$, $p < 0.04$; group main effect; peak latencies: 328 ms for the control subjects and 312 ms for the subjects with AS; Fig. 1). In addition, for the commanding deviant stimulus, there was a significant group × electrode interaction for the central electrodes ($F(3,42) = 3.63$, $p < 0.04$; peak latencies: 186 ms for the control subjects and 200 ms for subjects with AS), which resulted from a larger response in the control subjects at Cz than at the lateral frontal electrodes (Cz versus F3, $p < 0.05$; Cz versus F4, $p < 0.005$; Fig. 1). A significant group × electrode interaction was also found for these stimuli over the right hemisphere ($F(4,56) = 3.73$, $p < 0.05$), which resulted from smaller responses in the subjects with AS than in the control subjects over the temporal-parietal electrodes ($p < 0.03$).

Latency comparisons were carried out at F3, Fz, and F4 for the first response elicited by the commanding deviant stimulus, which significantly differed from zero in both groups. There was a group main effect resulting from a longer latency in subjects with AS than control subjects ($F(1,14) = 12.52$, $p < 0.01$). Furthermore, there was a group × electrode interaction ($F(2,28) = 3.89$, $p < 0.04$). According to the post hoc test, subjects with AS had a longer latency at F4 than control subjects at all electrodes (p-values <0.01) and a longer latency at Fz than control subjects at F3 ($p < 0.02$).

Our results suggest impaired prosody perception in individuals with AS, which is in agreement with previous observations [12,17,18]. These subjects tended to identify less accurately than the control subjects the emotional contents of the spoken words. Furthermore, their neural substrate was abnormal in discriminating these words since significant MMN amplitude, topography, and latency differences were found between the groups. The abnormal MMN process in individuals with AS suggests that their prosody perception is impaired at a low-level information processing stage.

Subjects, particularly the control subjects, identified the words fairly accurately (control subjects: 63–91%, subjects with AS: 25–91%). The commanding stimulus was best identified and the RTs were shortest for this deviant stimulus in the target-discrimination task. This is in agreement with the results of Leinonen et al. [11] who found that this stimulus was the easiest to identify among nine stimuli with other emotional connotations. The sadly-uttered stimulus was identified worst in our study, also having one of the lowest identification rates in Leinonen et al. [11]. Subjects with AS seemed to have the greatest difficulties with this word, having an identification rate of 25% for this stimulus, which was the lowest of all (Table 1).

The impaired neural substrate of prosody discrimination in AS was evident in several ways in the MMN responses. First, there were less significantly elicited MMNs in subjects with AS than in their controls (Table 3). Second, there was a significant MMN-amplitude difference between the groups for the scornful deviant stimulus over the right hemisphere. Furthermore, both fronto-centrally and over the right hemisphere, the MMN elicited by the commanding deviant was differently distributed in subjects with AS than in control subjects, suggesting that some MMN generator loci might be different in these two subject groups. Third, the MMN latency was prolonged in subjects with AS, particularly over

Table 3
Mean amplitudes (in μV; standard deviations in brackets) of the MMN responses at the grand-mean latencies

	Latency (ms)	Control			Latency (ms)	Asperger		
		F3	FZ	F4		F3	FZ	F4
Commanding								
1st	186	−2.2 (1.2)*	−2.2 (1.5)*	−1.9 (1.5)*	200	−1.6 (1.6)*	−2.0 (1.5)*	−1.8 (1.3)*
2nd	312	−0.2 (1.7)	−0.2 (1.9)	0.1 (2.1)		–	–	–
Scornful								
1st	142	−0.4 (1.1)	0.9 (1.4)	0.6 (1.3)	178	−0.8 (1.8)	−1.3 (1.5)*	−0.8 (1.1)
2nd	328	−2.2 (2.1)*	−2.4 (2.7)*	−2.0 (2.5)*	312	−0.7 (1.3)	−0.6 (1.3)	−0.8 (1.7)
Sad								
1st		–	–	–		–	–	–
2nd	306	−1.1 (1.7)	−1.0 (1.6)	−1.2 (1.4)*	276	−0.5 (0.9)	−0.6 (0.9)	−0.4 (1.1)

The amplitudes significantly differing from zero are marked with an asterisk ($p < 0.05$). 1st = first MMN component, 2nd = second MMN component.

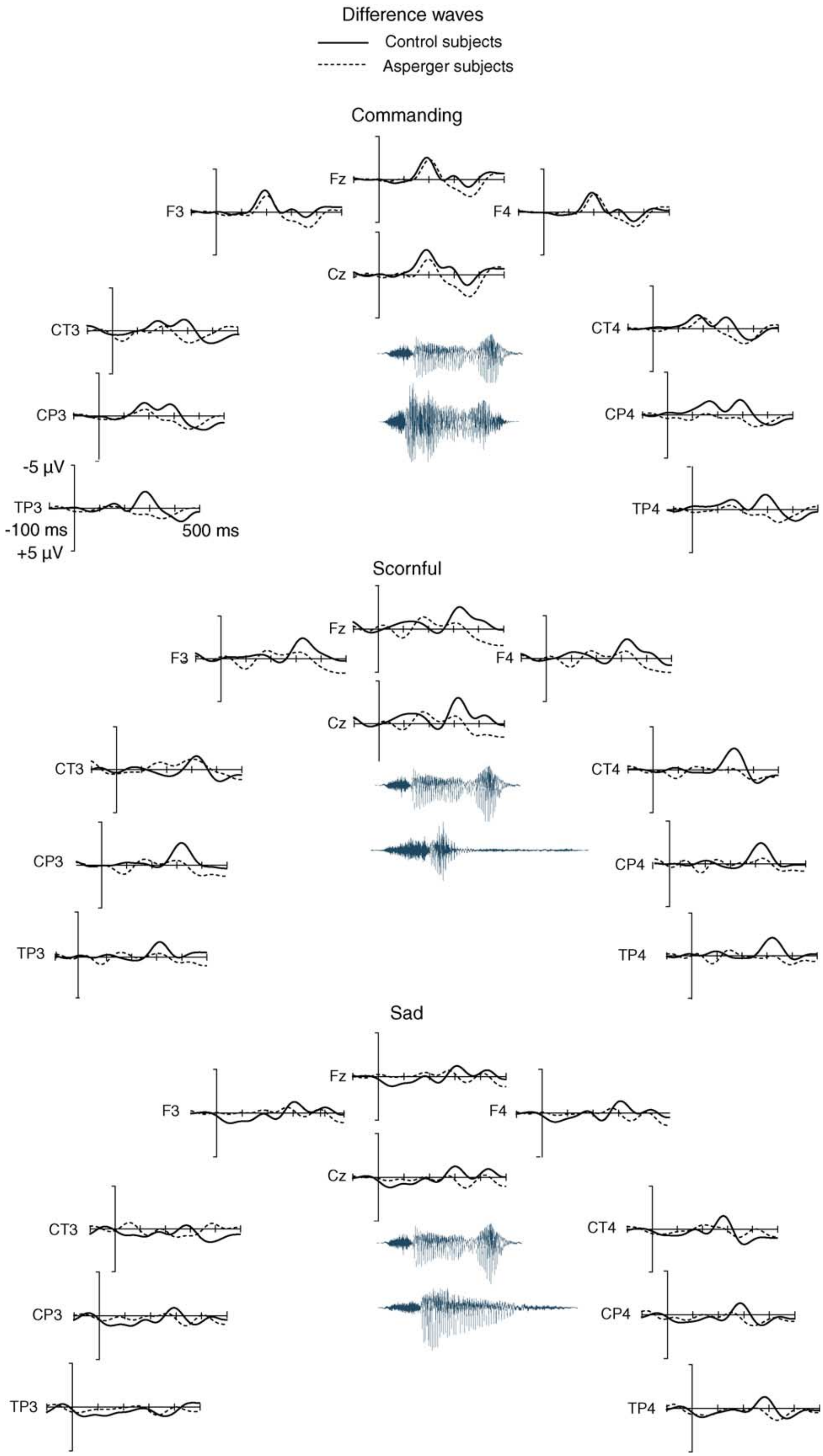

Fig. 1. Difference waves (the response elicited by the standard stimulus subtracted from that elicited by the deviant stimulus) for each deviant type in each condition at frontal-central (Fz, Cz, F3, F4) and temporal-parietal (CT3/4, CP3/4, TP3/4) scalp sites. Under the Cz electrodes, the acoustic waveforms for the deviant stimulus as well as for the neutrally-presented standard stimulus (above the deviant stimuli) are presented.

the right hemisphere, which is in agreement with previous studies [10]. The present electrophysiological results are in agreement with the suggestion, so far primarily based on clinical studies and self-reports of patients with AS [17,18], that AS is characterized by an impairment in discriminating speech prosody. This impairment originates from the early pre-attentive level of central auditory processing, since it was observed with the MMN response, suggesting a fundamental deficit.

Previous neuroimaging studies have shown abnormalities in both the right and left hemispheres in AS, but the results are somewhat inconsistent [9,10,13,15]. In the only electrophysiological study so far published on AS to our knowledge [10], evidence was found for delayed consonant- and pitch-change processing (longer-latency MMN) in the right hemisphere of children with AS. Our results are in agreement with this study, supporting the hypothesis of right-hemisphere impairment in AS [10]. This was evident both in the prolonged MMN response over the right hemisphere for the commanding stimulus and in the diminished MMN amplitude for the scornful stimulus in subjects with AS, as well as in the group × electrode interaction for the commanding stimulus over the right hemisphere. Since the group sizes were small in the present study, the results obtained await for replication. However, the present results are novel in the sense that although auditory dysfunctions are evident in and devastating for individuals with AS according to autobiographies, clinical observations, and behavioral studies [1,8], there is so far very little systematic research on the neural basis of audition in AS.

In the behavioural target-discrimination task, no statistically significant differences were found between the groups although subjects with AS tended to discriminate the stimuli worse than the control subjects. However, some of the MMNs being diminished in these subjects suggests that they failed to discriminate certain sound segments normally. This failure to discriminate some elements of physical variation in speech might compromise the perception of prosody in normal speech-listening situations in which the acoustic information comes at a rapid rate.

The advantage of using the current stimuli was that they were naturally-produced speech sounds that were ranked as good exemplars of the emotional contents that they represent [11]. Thus, they were ecologically valid for studying the question at hand. However, the disadvantage of these stimuli was that we could not specify which sound features in the prosodic signal (e.g., pitch, duration, intensity) are the most difficult to discriminate for individuals with AS. This remains to be addressed by future studies using simpler and more controlled sound differences.

In summary, we found impaired neural discrimination of prosody, using naturally spoken utterances with different emotional contents, in AS at the pre-attentive level of auditory processing. Furthermore, our results suggest that this impairment might primarily originate in the right hemisphere in these individuals.

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