Impaired duration mismatch negativity in developmental dyslexia

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A mismatch negativity event-related potential protocol was administered to dyslexic children and their respective controls to test whether a specific auditory deficit concerning phonetic processing or a lower level auditory processing deficit was present in developmental dyslexia. Three different contrast conditions were explored, including nonphonological sounds, contrasted in pitch and duration, and phonemes. Mismatch negativity amplitudes differed significantly between groups in the duration condition, whereas no differences were found in the frequency and phoneme conditions. Moreover, the dyslexic children had delayed mismatch negativity latencies in the three contrast conditions. Our results suggest a deficit in low-level auditory discrimination in dyslexic children, in particular when detecting stimulus duration, and support the rapid auditory processing theory of dyslexia.

Keywords: auditory discrimination, developmental dyslexia, event-related potentials, mismatch negativity

Introduction

Developmental dyslexia is a specific disability in learning to read, write and spell, despite adequate educational resources, normal intelligence, no obvious sensory deficits and adequate socio-cultural opportunities. Its causes remain unknown, and thus several models have been proposed [1]. The phonological model postulates that dyslexics have a specific deficit in and limited to the representation, storage and/or retrieval of speech sounds, so that they suffer from a ‘phoneme awareness’ deficit, that is to say, a deficit in the ability to manipulate in an abstract form the sound constituents of oral language [2,3]. Another theory that derives from the previous one is that of the rapid-auditory processing deficit, which postulates that the phonological deficit is secondary to a more basic auditory impairment, one involving the perception of short or rapidly varying sounds [4,5]. According to this theory, deficits in rapid auditory processing impair the ability to discriminate auditory cues necessary to distinguish phonemes. This impairment compromises the development of stable phonological representations, which in turn leads to the difficulties in phonological processing observed in dyslexia [4]. A unifying proposal has attempted to integrate all the dyslexic symptoms into a ‘magnocellular theory’, which suggests that dyslexia results from a neurodevelopmental abnormality of the magnocellular system that generalizes to all manifestations of dyslexia [6,7].

In the present study, the first two models were under examination by exploring whether deficits in dyslexic children reflect impairments in linguistic processing or a more general low-level auditory impairment. For that purpose, the mismatch negativity (MMN) component of the event-related brain potentials (ERPs) is especially suited. The MMN is elicited, with no task requirements, by occasionally ‘deviant’ sounds occurring in a sequence of repetitive (‘standard’) stimuli [8]. When the brain’s response to the standard stimuli is subtracted from the deviant one, the MMN can be seen at 100–200 ms from stimulus-change onset. The MMN can be elicited by any perceptible physical change, that is, pitch or duration, or by contrasting more complex sound features such as abstract invariances [9], tone patterns [10] and phonemes [11], and reflects conscious perception of sound attributes [8,12]. The MMN has generator sources in the auditory cortex with contributions from frontal regions [13–15]. The MMN is often followed by the P3a ERP component, a fronto-centrally distributed positivity peaking at 250–350 ms, thought to reflect an involuntary attention switch towards the eliciting deviant sound [14,16].

Studies of MMN in dyslexic subjects have yielded contradictory results when aiming to study auditory/phonological dysfunction, partially owing to paradigm and sample differences. Some of these studies reported specific differences in phonological processing, supporting...
the speech-perception deficit hypothesis [17], whereas other provided data in support of deficits in lower levels of auditory stimulus discrimination [18–20]. Here, we used an MMN protocol including frequency, duration and phonetic contrasts to elucidate whether dyslexic children have specific deficits concerning phoneme processing, or affecting lower levels of auditory discrimination. A deficit in low-level auditory processing would appear as an impaired duration and/or frequency MMN with preserved phonetic MMN in dyslexic children. On the other hand, a phonological deficit would be supported by preserved MMN to simple contrasts but impaired MMN to phonetic changes.

Methods

Subjects

Seventeen dyslexic children and a control group of eighteen normal readers participated in the study. Owing to excessive artifact rejection, several blocks, however, were excluded from the participant’s averages, leaving the minimum number of participants included in a particular condition as 13 dyslexics (11.6 ± 1.8 years; four girls; two left-handed) and 11 normal readers (11.8 ± 2.1 years; five girls; two left-handed).

The two groups were matched for age, sex and educational level, as well as for a full-scale intelligence quotient (IQ: WISC-R) greater than 85 and nonsignificant differences between verbal (mean score: dyslexics = 113, controls = 109; F1,23 = 0.279, NS) executive (mean score: dyslexics = 121, controls = 131; F1,23 = 2.05, NS), and general (mean score: dyslexics = 120, controls = 131; F1,23 = 0.046, NS) IQ. All participants were native bilingual speakers of both Catalan and Spanish languages. The participants were selected by normal or corrected-to-normal vision and hearing. Gross behavioral, psychiatric illness or neurological disorders were the excluding criteria. The dyslexic children were recruited among those attending follow-up clinics, and had a diagnostic of developmental dyslexia according to Diagnostic and Statistical Manual Of Mental Disorder-IV criteria. Four of these children had symptoms of attention deficit hyperactivity disorder co-morbility, but not a confirmed attention deficit hyperactivity disorder diagnosis, and therefore were on methylphenidate medication for helping them at school. These four children, however, were withdrawn from medication at least 48 h before the experiment. Five dyslexic children reported having at least one relative with language disorders, contrasting with the lack of family history of language disorders in normal readers. Written informed consent was obtained from all children and their parents for participating in the study, which was approved by the Ethical Committee of University of Barcelona. All participants were rewarded with a self-chosen educational toy. An audiometric test was administered to each participant before the experimental session, resulting in similar hearing thresholds, all below 40 dB sound pressure level in both groups.

Stimuli and procedure

ERPs were recorded in three different sound-contrast conditions: two of them including sounds structured into harmonically rich tones, with the magnitude of one of their simple features changing (i.e. frequency and duration), and a third one involving phonemes. Three stimulus blocks, one in each condition, were presented in random order. The participants sat in a comfortable armchair, in a sound-attenuated and dimly lit room, and were instructed to watch a silent video movie and to ignore the auditory stimulation, while avoiding blinking and extra body movements.

The frequency condition consisted of 1000 harmonically rich sounds composed of four harmonic partials [21]. The standard stimuli (N = 800, P = 0.8) had a fundamental frequency of 500 Hz, whereas the deviant stimuli (N = 200, P = 0.2) had all partial frequencies incremented in 10% with regard to the standard ones, that is, a fundamental frequency of 550 Hz. All four partials were of equal intensity. Stimuli were delivered binaurally through headphones at an intensity of 85 dB with a duration of 100 ms (including a rise/fall of 10 ms), and a constant stimulus onset asynchrony (SOA) of 300 ms.

The duration condition consisted of 1000 stimuli in which the standard (N = 800, P = 0.8) and deviant stimuli (N = 200, P = 0.2) were identical with regard to their partial frequencies, but differed in duration (standard, 100 ms; deviant, 33 ms). Intensity, presentation mode and SOA were as in the frequency condition.

In the phonetic condition, the auditory stimuli were 500 semisynthetic phonemes [11,22]. These stimuli varied in their second formant (F2), whereas the F1 (450 Hz), F3 (2540 Hz) and F4 (3500 Hz), as well as the fundamental frequency (105 Hz), were the same for both the standard and the deviant phonemes. The standard phoneme was the vowel /o/ (F2 = 851 Hz; P = 0.8), and the deviant phoneme was a Spanish prototypic /e/ (F2 = 1940 Hz; P = 0.2). The standard and deviant phonemes were of 400 ms in duration (10 ms of rise/fall included). The constant SOA in this condition was 900 ms.

Electrophysiological recordings

The electroencephalogram (EEG) was continuously recorded and digitized (band pass, 0.1–100 Hz; A/D rate, 500 Hz) by SynAmps (Neuroscan, El Paso, Texas, USA) from 21 electrodes: Fp1, Fp2, Fz, F3, F4, F7, F8, Cz, C3, C4, T3, T4, T5, T6, Pz, F3, P4, O1, O2, and left and right mastoids. The voltage changes caused by eye movements and blinks were monitored with recordings at Fp1 and Fp2, and from an additional electrode attached to the outer canthus of the left eye (HEOG). The common electrooculogram and EEG reference was attached to the tip of the nose.

ERPs were averaged offline for standard and deviant stimuli separately for each participant and condition. Epochs with electrooculogram or EEG exceeding ±75 μV at any channel, as well as the first five trials of each block, were automatically excluded from averaging. The epoch was of 480 ms for the frequency and duration conditions, and of 700 ms for the phonetic condition, including in all cases a prestimulus baseline of 100 ms. Standard stimulus epochs occurring immediately after deviant stimulus epochs were also excluded from the averages. Individual ERP’s were digitally band-pass filtered between 0.1 and 30 Hz.

Data analysis

The MMN was measured as the mean amplitude in a 40-ms latency window centered at its maximum peak as identified in the difference waves obtained by subtracting the standard ERPs from those elicited to deviant stimuli. Latency windows for MMN measurement were as follows: 260–300 ms in dyslexic and 240–280 ms in controls, for the
frequency condition; 210–230 ms in dyslexics and 186–206 ms in controls, for the duration condition. In the phonetic condition, two consecutive peaks could be identified in the MMN latency range, early and late, and their amplitude was measured in a 20 ms latency window centered on them: eMMN, 192–212 ms in dyslexics and 170–190 ms in controls; lMMN, 244–264 ms in dyslexics and 204–224 ms in controls.

In the duration condition, a P3a component was also present, and therefore measured as the mean amplitude in a 100 ms latency window centered at its maximum peak as identified in the same difference waves obtained as above (240–340 ms in dyslexics and 230–330 ms in controls).

Significant elicitation of MMN was tested in each condition and group with one-tailed t-tests comparing its mean amplitude at Fz against zero. Three-way analyses of variance (ANOVAS) for repeated measures were performed in the frequency and duration conditions as well as on the eMMN and lMMN of the phonetic condition, using group (dyslexic and control) as a between-subject factor and two within-subject factors, which examined laterality (right: F4, C4 right mastoid vs. left: F3, C3, left mastoid) and frontality (frontal: F4, Fz, F3 vs. central: C4, Cz, C3) of MMN. In the duration condition, an additional ANOVA including group and electrode (F3, Fz, F4, C3, Cz, C4) as factors served to compare P3a amplitude and latencies. In all the ANOVAs, the Greenhouse-Geisser correction was applied when appropriate, and the corrected P-values are reported.

**Results**

A significant MMN with clear polarity reversal at mastoid locations was elicited in all three conditions in both groups (Fig. 1). The MMN mean amplitude at Fz frequency was as follows: dyslexics, $-1.5 \pm 1.7 \mu V, t_{12} = -3.19, P < 0.008$; controls, $-1.0 \pm 1.7 \mu V, t_{10} = -2.69, P < 0.022$; duration: dyslexics, $-0.8 \pm 2.3 \mu V, t_{12} = -2.82, P < 0.015$; controls, $-1.0 \pm 2.3 \mu V, t_{10} = -2.30, P < 0.041$; phonetic eMMN: dyslexics, $-1.1 \pm 1.14, t_{12} = -2.46, P < 0.028$; controls, $-2.0 \pm 1.9 \mu V, t_{10} = -3.28, P < 0.008$; phonetic lMMN: dyslexics, $-1.5 \pm 1.8 \mu V, t_{12} = -2.95, P < 0.011$; controls, $-2.1 \pm 2.5 \mu V, t_{10} = -2.75, P < 0.02$.

In the duration condition, differences between dyslexics and controls were found in both MMN amplitude and latency. The MMN amplitude was larger at right and central electrodes in the dyslexic group than in normal readers, as supported by significant Laterality x Group ($F_{1,22} = 4.59, P < 0.043$) and Frontality x Group ($F_{1,22} = 3.33, P < 0.046$) interactions (Fig. 1). Duration MMN latency was also delayed in dyslexic children compared with controls (Fz: dyslexics = 219 ms, controls = 193 ms; $F_{1,22} = 124.44, P < 0.001$). Moreover, the P3a component also yielded significant differences between groups in amplitude ($F_{1,22} = 9.47, P < 0.005$) and latency (Cz: dyslexics = 301 ms, controls = 283 ms; $F_{1,22} = 4.43, P < 0.047$), being smaller and delayed in dyslexic children than in normal readers.

In the frequency condition, no amplitude differences were found between groups in MMN, although its peak latency was significantly delayed in the dyslexic subjects (Fz: dyslexics = 280 ms, controls = 258 ms; $F_{1,22} = 49.83, P < 0.001$). Similar results were obtained in the phonetic condition, in which MMN amplitude of neither its two consecutive peaks (eMMN and lMMN) differed between participants, although differences in their peak latencies between groups were significant (Fz: eMMN dyslexics = 203 ms, controls = 178 ms; $F_{1,22} = 696.39, P < 0.001$; lMMN dyslexics = 249 ms, controls = 212 ms; $F_{1,22} = 15.95, P < 0.001$).
Discussion

The present study aimed to elucidate, by means of an MMN protocol, whether deficits in auditory processing in developmental dyslexic children derived from a basic auditory discrimination level or from a higher linguistic level. The MMN response was elicited to frequency, duration and phonetic contrasts in both dyslexic children and normal readers, but MMN amplitude differences appeared only for the duration condition, supporting a specific deficit in low-level auditory discrimination in developmental dyslexia. These results are in agreement with those of a behavioral study using masking noises, in which children suffering from specific language impairment were shown to have an impairment in their ability to separate a brief sound from a following sound of similar frequency [5]. In the present study, the same SOA was used for the two simple sound-contrast conditions, but MMN amplitude differences were found in the duration and not in the frequency condition. This suggests that dyslexic children have a preserved ability in discriminating auditory stimuli relying in frequency cues, but they would have an impairment in their ability to discriminate brief sounds relying on duration cues. Moreover, the reduced P3a amplitude also observed in the duration condition in dyslexics confirms a specific deficit in discriminate brief sounds in dyslexia, which results, in turn, in an abnormal orientation of attention towards these small duration changes [14–16].

The similar MMN amplitudes observed in dyslexic subjects and normal readers in the frequency condition contrasts with previous MMN studies of developmental dyslexia using pitch discrimination paradigms [17,18]. At least two methodological differences might explain this lack of agreement. In the first place, these studies [17,18] used simple sinusoidal tones, whereas in the present study the auditory stimuli were harmonically rich sounds, which stimulate a wider spectral band in the auditory cortex [21], perhaps helping the dyslexic subjects to overcome a frequency discrimination deficit. Moreover, in the Baldeweg et al. [18] study, group differences between dyslexic subjects and controls were observed for conditions contrasting frequency differences smaller than 6%, whereas the 9% frequency difference yielded similar MMN in the two groups. Notably, in the present study, the stimulus frequency difference was of 10% and therefore above that critical level. On the other hand, our duration MMN results also contrast with those of the study by Baldeweg et al. [18] with regard to their duration MMN. Here again, stimulus difference may account for the apparent contradictory findings, as these authors [20] used a much longer stimulus duration (i.e. 200 ms) than that in our study, which might have helped their dyslexic individuals to cope with a possible duration discrimination impairment.

The present data also failed to reveal MMN amplitude differences in the phonetic condition, in contrast with other studies [17,20,23]. It should be noted, however, that these studies used syllables as phonological stimuli, whereas we used semisynthetic vowels varying in their second formant (F2). Therefore, it might be possible that the deficit of dyslexic children in these studies was at discriminating the rapid transient acoustic features between consonant–vowel within the syllable, instead of processing simple basic units of speech (phonemes) as used in our study. Moreover, our phonetic stimulus duration was of 400 ms, and thus it is plausible that the stimuli were long enough to be properly discriminated by the dyslexic subjects.

As a general effect, we observed a significant delay in the MMN peak latency in the dyslexic group compared with controls in the frequency and duration conditions, as well as in both the eMMN and IMMN of the phoneme condition. This supports, again, generalized low-level auditory discrimination impairment, according to which the auditory cortex of dyslexic children would have difficulties in mobilizing the necessary processing resources to perform even simple auditory discriminations within a normal time range. The delayed MMN is in agreement with that observed in 8-week-old infants with a family history of specific language impairment [24], and also agrees with the idea that the delayed temporal auditory processing observed at the early age of 2 months of life in children with language impairment is extended, as seen in the present data, until preadolescence. Comparison of developmental dyslexia studies to those of specific language impairment must be, however, cautious, as there is still a controversy over whether these two diagnostic categories are part of a same continuum, differing only in severity, or reflect different neurobiological entities.

Conclusion

In summary, the overall results of the present study show that developmental dyslexic children have abnormal duration MMN and delayed MMNs to simple feature as well as phonetic sound-contrasts, indicating a low-level auditory discrimination deficit in developmental dyslexia, in agreement with previous studies [5,10,18]. Moreover, as the phonetic MMN was of similar amplitude in dyslexics and normal readers, the present results support the rapid auditory processing theory of dyslexia.

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