

# Preattentive deficits in developmental disorders of scholastic skills

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Working memory deficiency has been implicated in developmental disorders of scholastic skills. The auditory P50 component of event-related potentials reflecting preattentive processing was investigated in 38 children with developmental disorders of scholastic skills and 19 sibling control children, as elicited during a working memory test. The P50 was evoked by two tones of low and high frequency (500 Hz and 3000 Hz). The group with developmental disorders of scholastic skills showed prolonged P50 latency

induced by the low tone, located at the frontal area. The amplitude of P50 induced by the low tone exhibited significantly negative associations with both age and memory performance, whereas age and memory performance were associated positively. These findings indicate that preattentive processing deficits may be implicated not only in auditory cognition but also in developmental disorders of scholastic skills. *NeuroReport* 16:1829–1832 © 2005 Lippincott Williams & Wilkins.

**Keywords:** developmental disorders of learning, dyslexia, event-related potentials, P50, working memory

## Introduction

Some children of average intelligence have difficulty learning to read, although they do not have general learning difficulties, and their reading problems are not due to extraneous factors (e.g. acuity deficits, socioeconomic disadvantage). These children manifest difficulties in acquiring basic reading sub-skills such as word identification and phonological (letter–sound) decoding [1]. Such difficulties occur in 10–15% of children of school age and are accompanied by specific deficits in cognitive abilities related to reading skills. This symptom pattern is called ‘dyslexia’, or, alternatively, ‘specific reading disorder’ [F.81.0 according to the 10th edition of the International Classification of Diseases (ICD-10)]. This is the main diagnosis of the general diagnostic category: specific developmental disorders of scholastic skills (DDSS) (F.81) [1].

The pathophysiological mechanisms underlying DDSS are still far from being identified, but some interesting suggestions have come from investigations in the field of cognitive and biological research [2]. More recently, a number of authors have suggested that the fundamental deficit in specific language impairment is a limitation in the brain’s capacity to rapidly process information of verbal working memory [3]. Contemporary neuropsychological thinking defines working memory as the capacity to keep information on line, as necessary, for an ongoing task [4]. According to this view, working memory is not for

‘memorizing’ in itself, but is used for complex cognitive activities such as language, reasoning, problem solving and decision-making.

In studying specific processes that might be impaired in DDSS, the event-related potential (ERP) technique provides information that conventional behavioural methods do not [5]. Psychophysiological research has suggested that the auditory P50 component of ERPs (generally 30–80 ms following stimulus) reflects the synchronized response of the thalamocortical system that may underlie it [6,7]. Moreover, P50 has much in common with working memory operation, because, on the one hand, P50 is part of the  $\gamma$ -band electroencephalogram (EEG) response [6] and on the other, the  $\gamma$ -band activity is thought of as a signature of synchronized cortical networks involved in working memory operation [8].

In a study by Byring and Järvillehto [9], the latency of the middle latency component (at approximately 50 ms after warning stimuli) was significantly longer in the old poor spellers’ group than in the group of normal spellers, suggesting that this prolongation could reflect disturbed early auditory input in the poor readers.

In view of the above considerations, we hypothesized that the electrophysiological brain activity, as reflected by P50, in association with working memory operations, could be of value in identifying possible pathophysiological mechanisms involved in DDSS. Thus, the present study was

designed to determine (1) whether DDSS children, as compared with healthy controls, have similar or different patterns of P50 ERP component elicited during a working memory test; (2) whether DDSS children have more difficulties than controls with regard to memory performance, and (3) whether the differences related to the P50 and memory performance, if any, would interact and whether such an effect, if any, would be similar or different in DDSS children and controls.

## Materials and methods

### Participants

Fifty-seven children participated in this experiment. Thirty-eight (26 boys and 12 girls) of them were outpatient cases who had been diagnosed as suffering from specific developmental disorders of scholastic skills (F.81) according to ICD-10. All of them were diagnosed as having specific reading disorder (dyslexia) (F.81.0). Additionally, 13 of them had a second diagnosis [eight had specific spelling disorders (F.81.1) and five had specific disorder of arithmetical skills – (F.81.2)]. The remaining 19 (7 boys and 12 girls) were their healthy siblings.

The mean age for the dyslexic children was  $11.47 \pm 2.12$  years and for that the controls was  $12.21 \pm 2.25$  years. In each case, the following assessments were performed: child psychiatric examination, psychological examination and educational evaluation. The Wechsler Intelligence Scale for Children – Third Edition (WISC-III) [10] was used to obtain the IQ of each child. The assessment of educational attainment included reading, comprehension, spelling and arithmetic ability. A standard procedure was followed using a special test for the Greek language [11]. The final diagnosis was a product of the child mental health team's consensus (D.A., K.S. and P.P. among the authors). Study participants did not enter the study if they had (1) clinically notable neurological disease (including seizure disorder), (2) a history of head injury, (3) hearing difficulties and (4) attention deficit disorder and hyperkinetic syndrome.

### Stimuli and procedure

The participants were evaluated with the digit span Wechsler auditory test [12,13]. A warning stimulus of either high (3000 Hz) or low frequency (500 Hz) was presented through earphones to the participants, who were asked to memorize the numbers that followed. The warning stimulus lasted 100 ms. A 1-s interval followed the onset of the warning stimulus and then the numbers to be memorized were presented by a male voice. At the end of the number sequence presentation, the same signal tone was repeated. If the frequency of the signal tone was low, the participants had to recall the numbers in the same order as presented. If the frequency was high, the participants had to recall the numbers in the opposite order.

Before recording any ERPs, practice trials were administered until the participants could clearly discriminate the warning stimuli (tones). After completion of the above-mentioned process, a rest period of 5 min followed, before the ERPs were recorded.

The ERPs were recorded during the 1.1-s interval between the warning stimulus and the first administered number. The electrophysiological signals were recorded with Ag/AgCl electrodes. Electrode resistance was constantly

kept below 5 k $\Omega$ . EEG activity was recorded from 15 scalp electrodes based on the International 10–20 System of EEG [14], and referred to both earlobes. An electrode placed on the participant's forehead served as ground. The bandwidth of the amplifiers was set at 0.05 Hz to 35 Hz. During the administration of stimuli, the participants had their eyes closed in order to minimize eye movements and blinks. Eye movements were recorded through an electrooculogram and recordings with EEG higher than 75 mV were rejected. Warning stimuli, as well as learning material (i.e. the numbers to recall), were presented binaurally via earphones at an intensity of 65 dB sound pressure level. The evoked biopotential signal was submitted to an analog-to-digital conversion, at a sampling rate of 1 kHz, and was averaged by a computerized system. Each recording session consisted of 52 repetitions of the trial.

As the P50 component is included in the array of early endogenous ERP components, which normally are modality specific, the ERPs induced by the two modal stimuli were averaged separately [5]. In particular, two varieties of P50 waveforms were obtained, one (low P50) evoked by the low frequency modality (26 trials) for each lead in all participants and another (high P50) evoked by the high frequency modality (26 trials) for each lead in all participants.

The following parameters were calculated:

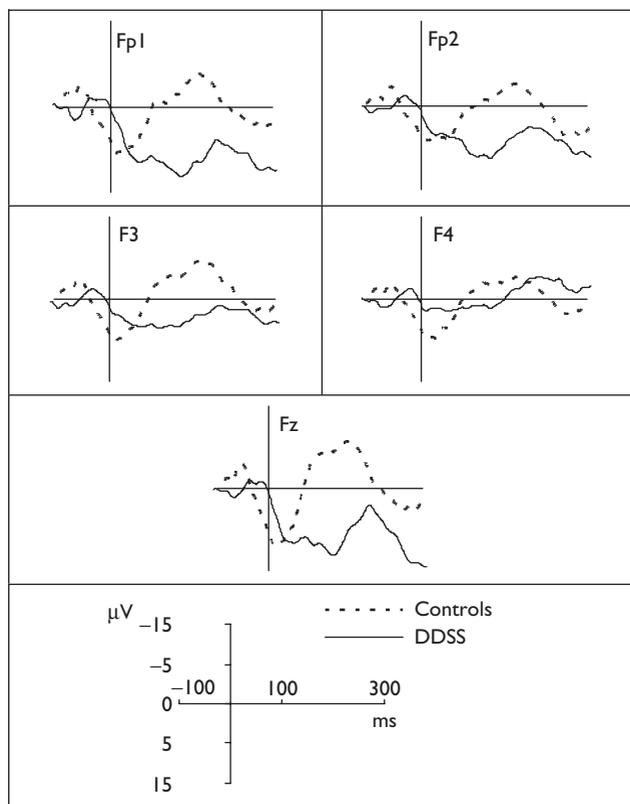
(1) ERPs were recorded for each participant at EEG leads Fp1, Fp2, F3, F4, C3, C4, C5, C6, P3, P4, O1, O2, Pz, Cz and Fz. Recordings with an acceptable EEG level were averaged for each lead by a computerized system. An algorithm was used, which identified the P50 as the most positive peak in each averaged lead curve, between 30 and 80 ms, after the warning stimulus. Peak amplitudes were measured relative to the mean amplitude of the 100-ms prestimulus baseline period and latency measurements were computed relative to stimulus onset (Fig. 1).

(2) The behavioral performance refers to the number of recalled digits. In all, 298 digits were presented in each session, 149 digits for the part of the session that engaged the low-frequency stimuli and 149 for the part that engaged the high-frequency stimuli.

### Statistical analysis

The high and low-frequency amplitudes and latencies of the P50 component, taken over the range of 30–80 ms, were separately subjected to multivariate analysis with group as the between-subjects factor. The mean values of memory performance, IQ and age for DDSS children and controls were compared using the Student's *t*-test. It should be noted that the analysis of memory performance was conducted for both low-frequency and high-frequency trials, as well as for total trials. Finally, age, memory performance and IQ were correlated among themselves and with the P50 amplitudes and latencies. Statistical significance was set at the 0.05 level.

It should also be noted that because the patients group consisted of two subgroups, as described above, we conducted an additional analysis with regard to both the psychophysiological and behavioral responses of the two subgroups. This analysis did not reveal any difference between the two subgroups. Thus, both of them formed a unique group that has been further compared with the control group.



**Fig. 1** Grand average event-related potential waveforms of the children with developmental disorders of scholastic skills (black line) and the control group (dotted line), at the frontal electrode sites, induced by the low frequency tone.

## Results

### Amplitudes and latencies of P50

With regard to high frequencies, both the amplitudes and the latencies of the P50 component did not yield any significant differences with any of the factors (group, sex and handedness), or with any of their interactions. The same applies to the low-frequency amplitudes.

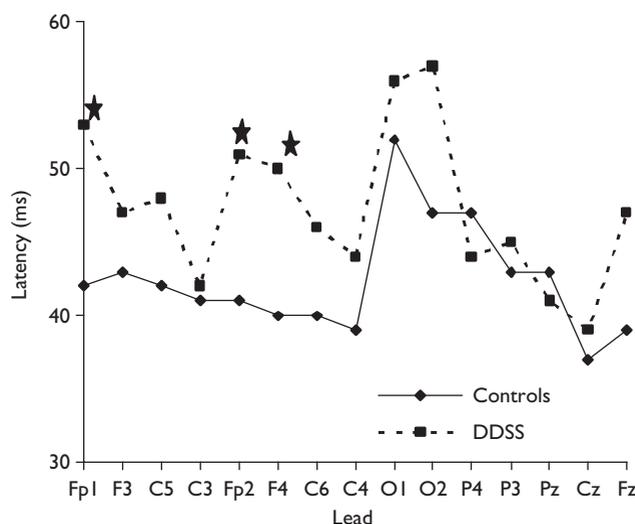
With regard to the low-frequency latencies, it was found that the group factor was important (Fig. 2). The mean latency values for the control group were significantly lower than for the DDSS group at the frontal electrodes Fp1, Fp2 and F4. Stepdown procedures revealed that group differentiation could be adequately explained by differences at only one electrode, namely Fp1. This is because of the high correlation of the latency values at the leads, especially at the frontal ones.

### Behavioral data

No differences were observed between the compared groups with regard to IQ scores (DDSS=90.74±11.86, controls=93.60±10.11,  $P=0.420$ ). Similarly, with regard to the memory performance, the main finding of the study is that DDSS children did not differ in comparison to normal controls.

### Correlations of P50 characteristics with memory and age

It is interesting that memory performance was significantly correlated with the low-frequency amplitude values, but neither with the high-frequency amplitudes, nor with the low and high-latency values. In particular, between memory



**Fig. 2** Mean values of the low-frequency latencies (ms) of the P50 component for the two groups. Asterisks denote the leads at which the mean latency value for the group with developmental disorders of scholastic skills is significantly greater than for the control group,  $*P < 0.05$ .

and the electrode sites F3, F4, P4 and Pz, the following significant associations were found:  $r=-0.276$ ,  $-0.324$ ,  $-0.279$  and  $-0.327$ , respectively.

Also, the low-frequency amplitudes of P50 were significantly correlated with age at almost all EEG leads. Specifically, between age and electrode sites Fp2, F3, F4, C3, C4, C5, C6, P4, O1, O2, Pz, Cz and Fz, the following significant correlations were found:  $r=-0.411$ ,  $-0.427$ ,  $-0.412$ ,  $-0.358$ ,  $-0.339$ ,  $-0.435$ ,  $-0.489$ ,  $-0.464$ ,  $-0.476$ ,  $-0.383$ ,  $-0.294$ ,  $-0.441$  and  $-0.370$ , respectively.

Contrary to what might be expected, IQ was not correlated either with age or with memory performance, while age and memory performance had a notable correlation in the total sample ( $r=0.366$ ), which was even higher in the case of only DDSS children ( $r=0.501$ ).

## Discussion

The main finding in the present study is that the DDSS group showed prolonged P50 latency induced by low tone, located at the frontal area. The amplitude of P50 induced by low tone exhibited significantly negative associations with both age and memory performance. Additionally, age showed a notable positive correlation with memory performance in the total sample, which is even higher in the case of DDSS children.

The obtained latency differences between the groups may be related to a common timing deficit suggested by some researchers to be one of the possible underlying pathogenetic factors in DDSS [2]. Moreover, the present findings appear to be compatible with those reported by Byring and Järvillehto [11]. With respect to the theoretical implications of the differences in P50 between groups, the present data draw attention to a possible link between thalamocortical operation and DDSS. In particular, as noted earlier, the P50 component reflects the synchronized response of the thalamocortical system [6,7]. On the other hand, data support the notion that the thalamus is involved in selective engagement of cortical mechanisms necessary to perform language tasks [15].

The significant correlations between the P50 and demographic as well as behavioral data revealed very interesting

points. First, results suggest that the amplitude of low-frequency P50 is affected during the developmental process. Age-related modulations in patterns of ERP waveforms are compatible with the hypothesis that normal development is accompanied by performance declines in tasks that access working memory, episodic memory and reasoning and may therefore contribute to cognitive aging [16]. Second, the specific attenuation of low-frequency P50 amplitude in association with increased memory performance is best understood within the information-processing theory, assuming that the P50 is part of  $\gamma$ -response synchronization of EEG, as pointed out by Clementz *et al.* [6]. As  $\gamma$ -activity is thought of as a signature of synchronized cortical networks involved in working memory operation [10], P50 has much in common with working memory operation.

In agreement with this framework, Zouridakis *et al.* [7] suggested that 'in states of hyperexcitability, there is an increase in the jitter of individual response which, in turn, results in decreased amplitude of the averaged evoked potentials'. Recognizing also that  $\gamma$ -activity has been found to be enhanced when stimuli are stored in or match with short-term memory [17], it is reasonable to expect a reduced amplitude of P50 during increased memory performance.

Interestingly, no association was observed between the high-frequency P50 waveforms and demographic and behavioral data. No differences between the compared groups were found with regard to the high-frequency P50 waveforms. Considering this fact in juxtaposition with the 'behavior' of the low-frequency P50 component, our results offer support to the observation by Talcott *et al.* [18] indicating that lower frequency tones but not higher frequency tones play an important role in children's phonological reading skill development.

As far as memory performance is concerned, the main finding of the study is that DDSS children did not differ in comparison to normal controls. This finding is in agreement with a series of other related studies [19], which concluded that the verbal memory functioning of some DDSS individuals is actually not impaired. Other studies, however, have found verbal memory deficits in DDSS [20]. Sources for divergent findings may be conceived in terms of both the heterogeneity of the study samples and differences in the measurement of the procedures. Finally, the observed positive association between age and memory performance, specifically with regard to the DDSS children, could be interpreted in terms of the notion that DDSS may also reflect a maturational lag, as demonstrated by authors observing a normal rate of progress of language development, with eventual age-appropriate outcome for a large percentage [21].

## Conclusion

The results of the present study should be interpreted with caution owing to the following limitation. Taking into account the heterogeneity of DDSS, further studies are needed to specify the effects of illness subtypes, whether they are state or trait characteristic and to determine whether there is impairment in a task-specific manner or across tasks. Nevertheless, the obtained results could support the hypothesis that DDSS children manifest abnormal aspects of preattentive processing of information

as they are reflected by P50 elicited during a working memory test.

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