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# Altered hemispheric asymmetry of auditory N100m in adults with developmental dyslexia

Sabine Heim,[CA] Carsten Eulitz[1] and Thomas Elbert[1]

Center for Molecular and Behavioral Neuroscience, Rutgers University, 197 University Avenue, Newark, NJ 07102, USA; [1]Department of Psychology, University of Konstanz, Konstanz, Germany

[CA]Corresponding Author: heim@axon.rutgers.edu

The current study aimed at determining whether the deviance of hemispheric asymmetry in the auditory cortex of children with dyslexia is also evident in dyslexic adults. Ten adult dyslexic subjects and 10 normally literate controls were presented with the syllable [ba:] while event-related brain activity was recorded from both hemispheres using whole-head magnetoencephalography. In control subjects, the auditory N100m source was found to be asymmetrical with a more anterior localization in the right than in the left perisylvian cortex (difference = 0.78 cm). The N100 m dipoles in dyslexic adults did not exhibit the same interhemispheric asymmetry (difference = −0.06 cm). The results indicate that reduced hemispheric laterality of perisylvian regions in dyslexia persists into adulthood. *NeuroReport* 14:501–504 © 2003 Lippincott Williams & Wilkins.

**Key words**: Auditory; Dyslexia; Hemispheric asymmetry; Magnetoencephalography; N100m

## INTRODUCTION

Structural and functional studies of the human brain have shown altered hemispheric asymmetry, particularly of temporal lobe structures, in people with developmental dyslexia [1–5]. Magnetoencephalographic (MEG) data from our own laboratory complement these findings [6]: In children and adolescents with dyslexia, the right-hemispheric sources of auditory P100m in response to the syllable [ba:] were found to be located ~1 cm posterior to those in normally literate controls. No such group difference was observed in the left perisylvian region. Thus, the dyslexic group displayed a rather symmetrical source configuration between the hemispheres, whereas the control group showed the right–left asymmetry typical for adult components of the same latency range [7–9].

The current study aimed at examining whether a deviance of hemispheric asymmetry in the organization of the auditory cortex is also evident in adults with dyslexia or reflects a maturational phenomenon. We report the findings from an MEG experiment in which the syllable [ba:] was presented to adult dyslexic subjects and normally literate controls. The latencies, amplitudes, and source parameters of the magnetic wave around 100 ms after stimulus onset were compared between the subject groups. This wave was assigned differently in the adult sample than in the group of children and adolescents participating in our earlier study [6]; here the dipole orientation of this component indexed a negative polarity and is therefore referred to as the N100m.

## MATERIALS AND METHODS

***Subjects:*** Ten developmentally dyslexic adults (mean age 38.21 ± 12.46 years, four females) and 10 normally literate control subjects (mean age 32.83 ± 13.18 years, five females), all native speakers of German, gave informed written consent to participate in this study. They received a small financial bonus for participating. Subject groups were comparable in age ($t(18) = 0.9$, $p > 0.05$, n.s.) and intellectual capacity (Table 1). All subjects had finished the minimum of formal education (9 years in Germany). Handedness was assessed with the Edinburgh Handedness Inventory [10]. Subjects with a laterality quotient (LQ) $\geq +70$ were considered right-handers. Two of the dyslexic and control subjects were ambidextrous ($-60 \geq \text{LQ} \leq +60$). Dyslexic and control subjects were free of psychiatric disorders requiring consultation (present or past) and any psychotropic medication; they had no history of neurological disease and evidenced normal hearing thresholds.

The dyslexic subjects were recruited by advertisement from among members of the German Dyslexia Association. They reported significant difficulties in school lessons including reading, spelling, writing, and learning foreign languages. As a group, the dyslexics still experienced discomfort on measures of reading, phonological decoding, and orthography (Table 1).

***Materials and procedure:*** The synthetic stop consonant-vowel syllable [ba:] was created in a cascade mode by using Speechlab software [11] based on a Klatt cascade/parallel

**Table 1.** Psychometric data for study groups (median).

| | Controls ($n = 10$) | Dyslexic subjects ($n = 10$) | U[a] | $p$ |
|---|---|---|---|---|
| Non-verbal intelligence | | | | |
| Raw scores (max = 60) | 54 | 51.5 | 41 | n.s. |
| Word reading | | | | |
| Points (max = 300) | 300 | 286 | 1 | 0.001 |
| Time (s) | 97.5 | 140 | 22.5 | 0.04 |
| Pseudoword reading | | | | |
| Points (max = 300) | 277.5 | 189.5 | 0 | 0.001 |
| Time (s) | 151.5 | 296.5 | 1 | 0.001 |
| Spelling ability | | | | |
| Raw scores (max = 40) | 39 | 31 | 3.5 | 0.001 |

[a]Mann-Whitney U-test; n.s., not significant ($p > 0.05$). Non-verbal intelligence was assessed with Raven's Standard Progressive Matrices, SPM [23]. Since the SPM provides only percentiles normalized for non-German-speaking adults from the age of 20 up, raw scores are presented. Reading and phonological decoding skills were documented using non-standardized word- and pseudoword-reading tests (points system: 0 = no response or error, 1 = self-correction, 2 = complete/partial repetition of an item, 3 = correct response). At the time of conducting this study, no standardized spelling test was available for the adult population, in which participants are asked to write down single spoken words. Therefore, the most demanding spelling-assessment tool available for children, the Westermann Rechtschreibtest, WRT 6+ [24], was administered.

formant synthesizer [12]. The total stimulus duration was 250 ms including a formant transition period of 40 ms. In a passive oddball paradigm, the syllable [ba:] was presented as a standard stimulus (probability of occurrence 80%) in a series of 650 stimuli. Syllables were delivered binaurally through ear tubes with a constant intertrial interval (defined as stimulus onset to stimulus onset) of 1 s at 60 dB sensation level. To control for level of arousal, participants watched silent movies or cartoons displayed on a special magnetic-field free screen. The subjects were instructed to attend to the video program and to ignore the auditory stimuli. In addition, subjects were asked to prevent unnecessary eye or body movements during recordings. Compliance was verified by video monitoring.

***MEG recording and data analysis:*** Magnetic responses were measured simultaneously from the left and right hemispheres using a 148-channel whole-head neuromagnetometer (BTi, MAGNES 2500, 4D Neuroimaging, San Diego CA, USA) housed in a magnetically shielded chamber. Subjects were seated with their legs extending horizontally on a height-adjustable bed, their backs leaning against a backrest, and their heads inside the helmet-like sensor.

Syllable-evoked brain responses were recorded continuously at a sampling rate of 508.63 Hz with a bandpass of 0.1–100 Hz. Eye movements and blinks were monitored by recording horizontal and vertical electro-oculograms (EOG). In an off-line mode, magnetic signals were first corrected for magnetocardiographic activity by means of a linear regression algorithm included with the 4D-Neuroimaging software package. Then, averaged waveforms for the standard syllables were calculated across epochs of 800 ms, including a 100 ms prestimulus baseline. Epochs with a MEG or EOG change $> 3.5$ pT or $> 120\,\mu$V, respectively, were omitted from further analysis. The baseline was corrected for each channel according to the mean value of the signal during the 100 ms prior to the stimulus. After that, evoked fields were digitally low-pass filtered to 20 Hz using a second-order zero-phase shift Butterworth filter (filter roll-off: 12 dB/oct).

The source of the neuronal activity was estimated by determining the equivalent current dipole (ECD) around the N100m root mean square (RMS) maximum using 34 channels separately over the left and right perisylvian regions. An ECD defined by the dipole moment, the orientation, and space coordinates was computed for each sample point by means of a least-squares fit. The location estimates of each ECD were specified with reference to a head-based Cartesian coordinate system. The origin of this coordinate system was set at the mid-point of the medial-lateral (y) axis interconnecting the center points of the entrance to the auditory meatus of the two ears (positive towards the left ear). The posterior-anterior (x) axis projecting from the origin to the nasion (positive towards the nasion) and the inferior-superior (z) axis being perpendicular to the x-y plane (positive towards the vertex). The following constraints were placed on the dipole fits a priori: (a) goodness of fit $> 90\%$, (b) confidence volume $< 2000\,mm^3$, (c) RMS $> 30$ fT(d) dipole moment $> 3$ nAm, (e) ECD oriented downwards, (f) stability of spatial source coordinates (x, y, and z) over a few milliseconds, (g) distance of ECD to midsagittal plane $> 2.5$ cm, and (h) inferior-superior value $> 3$ and $< 8$ cm. In both subject groups the ECD model explained on average 97% (s.e.m. = 1) of the measured field variance ($F(1,18) = 0.2$, $p > 0.05$, n.s.). The average ($\pm$ s.e.m.) confidence volume of the dipole fits was $152.12 \pm 46.28\,mm^3$ and $65.13 \pm 20.06\,mm^3$ for dyslexic and control groups, respectively ($F(1,18) = 3.0$, $p > 0.05$, n.s.).

***Statistics:*** Statistical analysis of group-specific hemispheric asymmetries was conducted on the latency, field amplitude, dipole moment, and the Cartesian source coordinates of the N100m using mixed-design ANOVA with hemisphere (left *vs* right) as a within-subjects factor and group (dyslexic *vs* control) as a between-subjects factor. Significant effects ($p < 0.05$) were followed by planned contrasts.

## RESULTS

***Latency, field amplitude, and dipole moment of N100m:*** There were no significant differences in the latency, field amplitude, or dipole moment of the N100m obtained over left and right temporal cortices for the two subject groups (Table 2). No significant between-group differences emerged on any of the dependent variables.

***Source locations of N100m:*** Table 2 presents the generator loci of the N100m in the head-based Cartesian coordinate system for the dyslexic and control subjects. The ANOVA performed on the x-coordinates (anterior-posterior axis) revealed a significant main effect for the factor hemisphere ($F(1,18) = 6.9$, $p < 0.02$) and a significant group $\times$ hemisphere

**Table 2.** Latencies, field amplitudes, and source parameters of N100 m across subject groups (mean ± s.e.m.).

| | Controls ($n = 10$) | | Dyslexic subjects ($n = 10$) | |
|---|---|---|---|---|
| | Left hemisphere | Right hemisphere | Left hemisphere | Right hemisphere |
| Latency (ms) | 119.29 ± 2.76 | 120.09 ± 2.14 | 118.72 ± 3.81 | 117.93 ± 3.37 |
| Amplitude, RMS (fT) | 76.95 ± 6.16 | 76.92 ± 10.13 | 64.15 ± 8.19 | 65.35 ± 7.62 |
| q (nAm) | 15.73 ± 3.50 | 12.68 ± 1.77 | 13.96 ± 2.37 | 11.30 ± 1.60 |
| x (cm) | 1.22 ± 0.39 | 2.00 ± 0.25 | 1.33 ± 0.21 | 1.27 ± 0.22 |
| y (cm) | 5.48 ± 0.39 | −5.66 ± 0.21 | 5.20 ± 0.35 | −5.53 ± 0.21 |
| z (cm) | 5.78 ± 0.24 | 5.74 ± 0.17 | 5.91 ± 0.24 | 6.15 ± 0.28 |

RMS = root mean square; q = dipole moment; x, y, z = source locations on the anterior-posterior, medial-lateral, and inferior-posterior axis, respectively (see Materials and Methods section); for statistical results see text.

interaction (F(1,18) = 9.6, $p < 0.006$). The interaction (Fig. 1) was considered in detail using planned comparisons analyses.

In the control group, the N100m source was located significantly more anterior in the right hemisphere than in the left (F(1,18) = 16.3, $p < 0.001$). By contrast, dyslexic subjects did not show hemispheric asymmetry in the location of the N100m ECD in the anterior-posterior direction. While there was no significant between-group difference in the center of activity over the left hemisphere, the dyslexic subjects' N100m source of the right hemisphere (x = 1.27 cm) was localized 0.73 cm posterior to the source in the control group (x = 2.00 cm; F(1,18) = 5.0, $p < 0.04$).

The group × hemisphere interaction cannot be explained as the consequence of a reversed asymmetry in some of the dyslexic participants. As can be seen by closer inspection of Fig. 2, hemispheric asymmetry is generally smaller in the dyslexic compared to the control subjects (F(1,18) = 4.6, $p < 0.05$ for the log-transformed absolute values of the hemispheric differences in the anterior-posterior direction).

The ANOVA run on the medial-lateral (y-) coordinates provided no significant effects. For both subject groups, the mean y-value was 5.34 cm in the left and −5.60 cm in the right hemisphere.

Analysis of the N100m source locations in the inferior-superior direction (z-axis) revealed no significant results. Across subject groups, mean z-coordinates of 5.85 and 5.95 cm were calculated for left and right hemispheres, respectively.

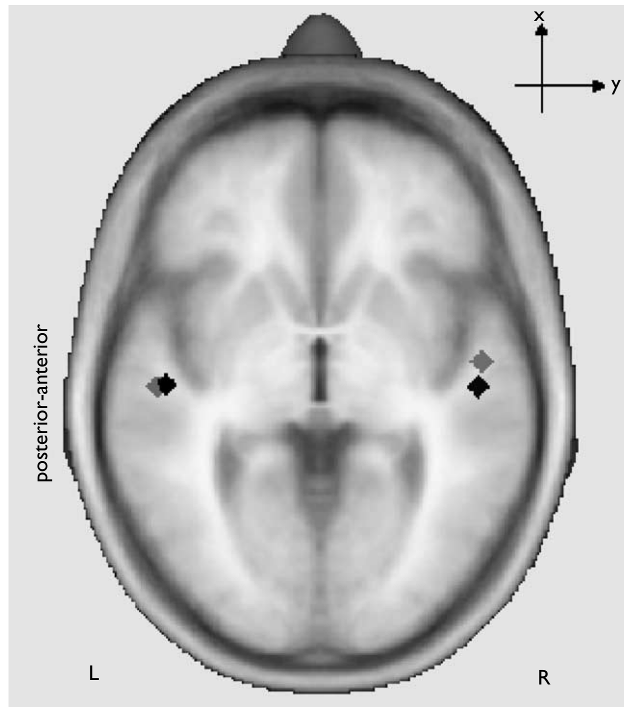


**Fig. 1.** Mean source locations of the N100m for the control (grey rhombus) and dyslexic groups (black rhombus) superimposed on the standard magnetic resonance images (MRI) included with the BESA Source Analysis Module (V.4.2, MEGIS Software GmbH, Gräfelfing, Germany). L and R denote left and right side of the brain, respectively. The combined MEG and MRI information suggests that the N100m is generated in the temporal bank of the sylvian fissure. Note, the atypical interhemispheric source configuration on the posterior-anterior (x) axis in the dyslexic group.

## DISCUSSION

The present study showed an atypical interhemispheric asymmetry in the positions of the N100m sources to the syllable [ba:] in adults with dyslexia. While in the normally literate control group the right N100m ECD was located more anterior than the corresponding ECD of the left hemisphere, the dyslexic group displayed a rather symmetrical source configuration between the hemispheres. This symmetry reflected a deviance in the right perisylvian cortex for the dyslexic subjects' N100m generated more posterior than the response in adult controls.

A number of MEG studies demonstrated interhemispheric source asymmetry for the N100m response in healthy adults [7–9]. This observation is supported by the present event-related field (ERF) recordings on normally literate adults. The planum temporale has been considered one center of activity for the adult N100m [9,13,14]. N100m source asymmetry might be concordant with anatomical data showing excesses of frontal and peri-rolandic cortex in the left hemisphere and of posterior parietal lobe in the right hemisphere [15–17]. According to Binder *et al.* [17], larger frontal and peri-rolandic mass on the left side pushes the point of upward deflection of the sylvian fissure posteriorly and tilts the planum temporale back. Conversely, larger parietal cortex on the right side might push the point of sylvian deflection anteriorly and tilt the planum forward.

The hemispheric balance in the source locations of the N100m found in our dyslexic group might agree with structural brain studies suggesting atypical asymmetry of the planum temporale in reading-disabled individuals [1,2]. However, more recent studies have challenged the view of altered planar asymmetry in dyslexia [18–20]. Less N100m lateralization might also reflect altered neuronal morphology in temporal-plane sites of dyslexic individuals [3]. It is conceivable that the different morphology interfere with efficient auditory processing, and consequently other (right

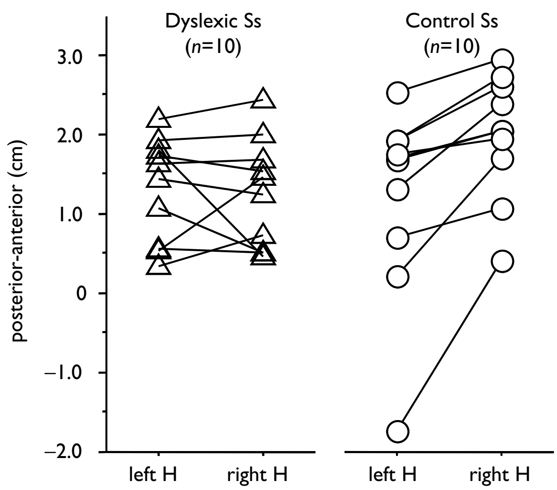


**Fig. 2.** Individual subject data from all controls and dyslexics for the N100m source localizations along the posterior-anterior (x) axis in the left and right hemispheres. H denotes hemisphere.

posterior) perisylvian regions become involved in this type of processing. These substituted regions may not perform the task as efficiently as a normally developed planum temporale would. Traditional views such as this one suggest that a structural deficit is the cause and functional deviance the consequence. In the course of neural plasticity studies of the human brain, the possibility has been acknowledged that functional alterations arising presumably from behavioral or environmental demands trigger morphological changes [21]. Thus, a different location for the processing of syllables might alter neural morphology or even brain structure. Probably maturational and environmental factors interact to yield a given result. On the basis of the presently available data it is not possible to decide which of the processes might be the major player, however.

The current results are consistent with our previous study [6] revealing (i) a more anterior-right-than-left source location of the P100m to the syllable [ba:] in normally literate children and (ii) an absence of hemispheric source asymmetry in their dyslexic peers which was related to (iii) a difference in right perisylvian sites for the P100m dipole located more posterior in dyslexic individuals than in controls. While the sources were localized in a similar latency range, their orientations indexed a positive component in the young sample and a negative component in adults. In a recent event-related potential study, Ceponiene *et al*. [22] suggested that in 9-year olds the neural generators of the auditory N1 might have different morphologies than in the mature brain. In order to find out whether the juvenile P100m and adult N100m represent the same or different components, further ERF investigation using cross-sectional and longitudinal data from childhood to adulthood would be required. Herein, the continuous observation of the dipole orientation of the componentry would be indispensable.

Nevertheless, reduced or absent lateralization in the source configuration of auditory ERFs around 100 ms after stimulus presentation appears to be a common feature observed in both children and adults with dyslexia. Moreover, less asymmetry has been associated with a deviance in the auditory cortex of the right hemisphere in both investigations. This finding might be causally related to dyslexia, but might also reflect a compensatory mechanism of a possible left hemisphere dysfunction. One promising way to clarify this issue would be the implementation of training programs tapping different aspects of literacy skills. MEG recordings before and after the training regimen would then indicate to what extent a specific intervention method might be capable of altering cerebral lateralization in dyslexic individuals.

## CONCLUSION

Reduced or absent hemispheric asymmetry in posterior perisylvian regions appears to be a stable characteristic rather than a maturational phenomenon in dyslexia. In both children and adults with dyslexia the lateral source symmetry around 100 ms after syllable presentation reflects an atypical organization in the right hemisphere.

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