

Working Memory Processing In Normal Subjects and Subjects with Dyslexia

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ABSTRACT

MEG was used to determine the neuroanatomical location of working memory processes and their underlying neuronal pathways. Differences between subjects with dyslexia and normal readers were studied during a spatial and verbal working memory tasks. Differences in regions of activation between normal subjects and subjects with dyslexia are described. This study demonstrates the possibility of identifying differences in memory processing in subjects with and without learning disorders and creates an avenue for memory-based remediation and non-invasive testing.

KEYWORDS: Memory, Dyslexia, MEG, MR-FOCUSS

INTRODUCTION

Early studies of verbal and spatial working memory processes described the organization as content specific and as occurring through distinct processing pathways or streams [Courtney, 1997; D'Esposito, 1997]. For example, verbal working memory is more lateralized to left hemispheric regions and spatial working memory is more lateralized to the right hemisphere. In addition, recent fMRI investigations have also suggested that process specific organization occurs [Crosson, 1999; D'Esposito, 1998]. That is, encoding and storage may be more strongly lateralized to left rather than right hemispheric processes, regardless of whether it is a verbal or visual task. Working memory, a critical aspect of initial learning, may reorganize in a more contralateral manner in patients with learning disorders, consistent with findings in episodic learning and facial memory in epilepsy [Golby, 2002]. MEG [Pizzagalli, 2002; Ioannides, 2000; Halgren, 2000] has been used to explore the mesial temporal aspects of memory functioning such as object and facial memory, which have greater hemispheric specialization and localization. Working memory was mapped with MEG in patients with and without dyslexia to determine if similar areas of activation suggest similar substrates for working memory or if contralateral reorganization of these processes occurs in dyslexia. The difference between results from fMRI and MEG involve the temporal resolution and the activation of source points. fMRI results display a static picture that incorporates source activity averaged over a long time interval. MEG can provide a precise picture of neuronal activation at different instants of both memory and language processing. MEG results illuminate the pathways of cortical processing involved in memory. MEG also provides information regarding the onset of encoding and retrieval processes so that we can examine the question regarding content relative to process organization, and whether this is different in individuals with dyslexia.

METHODS

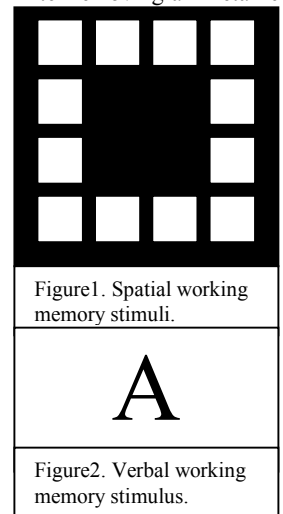
Our 148 channel whole head Neuromagnetometer (4D Neuroimaging) was used to measure magnetic fields from five individuals with dyslexia, between 9 and 50 years of age and five age, gender, and handedness, matched controls. Measurements were taken inside a magnetically shielded room located in the Neuromagnetism Laboratory at Henry Ford Hospital (HFH), utilizing a protocol approved by HFH's Internal Review Board (IRB). All subjects were administered the Edinburgh Handedness test [Oldfield, 1971] and underwent a neuropsychological evaluation to diagnose dyslexia. Individuals with dyslexia were recruited by a Ph.D. level neuropsychologist from the Division of Neuropsychology in the Department of Behavioral Health at HFH. The diagnosis of dyslexia was determined following the Diagnostic and Statistical Manual of Mental Disorders [American Psychiatric Association, 1994] diagnostic criteria that include individuals who display reading achievement (measured by individually administered standardized tests of reading accuracy or comprehension) substantially below that normally expected of persons of similar chronological age, measured intelligence, and age appropriate education. Normal (reading) individuals were used for the controls. Members of this group had normal, age appropriate, reading ability. They were also matched based on age, gender, handedness, and estimate of intellectual ability to subjects with Dyslexia. Normal reading individuals underwent the same neuropsychological evaluation as subjects with Dyslexia.

Each subject signed an informed consent form approved by the HFH Internal Review Board. In the case of children, a parent/guardian give informed consent. Each subject was prepped for the MEG study in the usual manner [Bowyer, 2003]. The subject then lay comfortably on the bed inside the magnetically shielded room. (A parent was allowed to remain with a minor child inside the shielded room. After removing all metallic objects, the parent remained seated in a corner of the room.) Standard automatic probe position routines were used to locate the subject's head with respect to the neuromagnetometer detector coils. The neuromagnetometer helmet containing the detector array was placed around the subject's head in close proximity to the skull surface. The subject was asked to avoid excessive eye blinks and body movements during data collection. Data collection runs lasted 8-12 minutes. Each subject was monitored by video camera and two-way audio speaker system during the time he/she was in the shielded room. All MEG data was band-pass filtered 0.1 to 100 Hz, and digitally sampled at 508.63 Hz.

MEG Test 1: Spatial working memory was studied by measuring the subject's MEG field responses to visual presentations of a series of white squares presented for 2 seconds every 3 seconds [D'Esposito, 1998]. A square was presented in one of 12 different locations around an imaginary circle (all 12 locations are shown in figure 1). During each presentation the subject was asked to mentally determine whether each square being presented was in the same position as the square presented two prior images ago. Subjects were instructed to respond only to displays in which this was the case by pushing a keypad with their right fore finger. This test was made up of two trials lasting ~7-minutes each.

MEG Test 2: Verbal working memory was studied by measuring the subject's MEG field responses to visual presentations of a series of upper case letters (figure 2) for 2 seconds presented every 3 seconds [D'Esposito, 1998]. During each presentation the subject was asked to mentally determine whether the letter being presented was the same as the letter presented two images ago. Subjects were instructed to respond only to correct targets by pushing a keypad with their right finger. This test was made up of two trials lasting ~7-minutes each.

Data Analysis: Data analyses were performed using a PC after the data had been filtered 1-50 Hz and exported from



the Sun acquisition computer. The averaged epoch data was analyzed with MR-FOCUSS [Moran, 2001] a non-linear current density imaging technique. For each subject the latency (in ms), location (x,y,z coordinates) and average amplitude of response (nanoAmp-meter) was extracted from the MR-FOCUSS imaging results for each memory process step. Also an image of the averaged cortical activity from 0-600 ms was created to determine the most dominant cortical areas during these tasks. To correlate MEG areas of cortical activity with specific anatomical structures, each subject's MRI was co-registered with their head digitization points collected at the beginning of the MEG study.

RESULTS

Cortical activation between 0-650 ms was analyzed by MR-FOCUSS, to determine the latency and source of neuronal activity of spatial and verbal working memory processes. All subjects showed occipital lobe activity at ~100ms after onset of visual stimulation in both memory tasks, this is consistent with visual activation. Analysis of the location of activity in the subjects without dyslexia during the spatial working memory showed cortical activity at approximately 200 ms after stimulus onset in the right superior temporal gyrus (STG) and right angular gyrus (AG). Subjects with dyslexia were similarly activated with a slight delay of approximately 20 ms. These latency and location differences were not statistically significant between the subjects with and without dyslexia ($p=0.37$, student t-test).

During the verbal working memory task, activity was seen in the **LEFT** STG and left AG, in subjects without dyslexia, at approximately 200ms after stimulus onset. Figure 1 displays the cortical localization of averaged activity from 200-230 ms in one subject. Subjects with dyslexia were not similarly activated. Activation was in the **RIGHT** STG and right AG. Figure 2 displays the cortical activation seen in a subject with dyslexia. Note the activity is in the opposite hemisphere as the normal control seen in figure 1. These differences were statistically significant between the subjects with and without dyslexia ($p=0.001$, student t-test).

DISCUSSION

This study supports the hypothesis that there are differences in how memory is processed in subjects with dyslexia compared to normal reading subjects. The current findings reveal a core deficit in verbal, but not nonverbal working memory in dyslexia as demonstrated by MEG. This suggests that the addition of intervention modalities to specifically address auditory attention and working memory in conjunction with traditional methods used to treat phonological deficits should be considered in treatment. It also demonstrates the ability of MEG, utilizing MR-FOCUSS, to detect cortical pathways involved in processing memory. Further studies of MEG data may reveal the cortical network involved in memory processing and possibly provide a key to the variants of dyslexia observed clinically. MEG may be able to discern the more accurate theoretical model of memory. The promise of this study is that biomagnetic field mapping will increase our understanding of memory, a critical aspect of initial learning.

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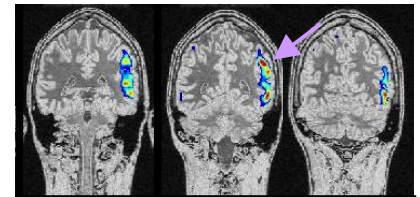


Figure 1 MR-FOCUSS analysis of the MEG recordings from a subject without dyslexia during the verbal working memory task. Averaged MEG image activation results of cortical activity, over 30 ms from 200-230ms after onset of stimuli. Note the cortical areas of activation in the left hemisphere (arrow).

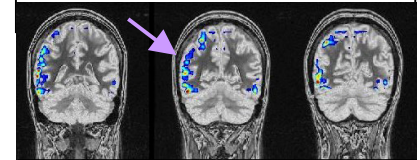


Figure 2 MR-FOCUSS analysis of the MEG recordings from a subject with dyslexia during the verbal working memory task. Averaged MEG image activation results of cortical activity, over 30 ms from 200-230ms after stimulus onset. Note the cortical areas of activation in the right hemisphere (arrow).