Dyslexia, the relative deficit in decoding visual words despite otherwise normal cognitive abilities, continues to capture the scientific and popular imagination. This fascination is likely because dyslexia is such a common disorder but also, perhaps, because it offers such a broad range of possible explanations. There are a number of ways to be a poor reader, at least as many theories attempting to account for reading disorders, and (probably) as many dyslexic subtypes. While the biological basis continues to be debated, data from twin and family studies suggest that dyslexia has a substantial genetic contribution [1]. In addition, postmortem cytoarchitectural as well as imaging studies suggest that peri-Sylvian anomalies are the characteristic neural markers.

Reading is a complex cognitive process that requires the integrity and integration of many neurologic systems. Given the number of subroutines necessary for its successful execution, it is plausible that reading can break down at many different points (hence, the subtypes). While the possible categories within dyslexia are still debated in cognitive neuropsychology, neuroscience, and neurology, there exists evidence to support numerous models. Dyslexia has been associated with (1) low-level visual problems arising from a deficit at the level of the lateral geniculate nucleus of the thalamus [2]; (2) visual processing difficulties at the level of word-form recognition or letter-to-sound recoding [3]; (3) general auditory processing problems, specifically temporal processing deficits [4]; (4) speech sound processing deficits (e.g., so-called phonological awareness deficits) [5]; (5) articulatory–motor problems associated with speech sounds, as argued recently in this journal by Heilman and colleagues [6]; and (6) various combinations of the above factors. It is also worth bearing in mind that the linguistic system proper must be intact; i.e., being impaired at language processing has the consequence of being bad at reading, a behavior presupposing language function.

Models suggesting general neural mechanisms as explanations are provocative insofar as they predict that dyslexic children or adults should exhibit deficits in domains other than reading. For example, a magnocellular deficit in the lateral geniculate nucleus [2] might be associated with difficulties in motion perception, the organization of visual space, the perception of low-contrast visual stimuli, and other functions typically associated with the magnocellular ("where") visual pathway. This proposal is particularly interesting, because, intuitively, one might surmise that reading involves high-contrast, high spatial frequency stationary visual stimuli, which one would associate with the parvocellular visual pathway ("what" system). Turning to the auditory system, a general processing deficit in temporal segmentation or integration [4] also predicts effects in other domains of hearing, such as music perception, sound localization, or auditory stream segregation.

Against the backdrop of this active field, Salmelin and co-workers [3], elsewhere in this issue of *Annals*, present a thoughtful, carefully executed magnetic source imaging (MSI) experiment on the neural correlates of reading disability in adult dyslexics. Their new observations, while consistent with a number of hypotheses, strongly support the view that word-form processing is impaired in adult dyslexics. MSI, defined as the combination of high temporal resolution electrophysiological data derived from magnetoencephalographic (MEG) recordings coregistered to high spatial resolution structural magnetic resonance images (MRI), is particularly well suited to study this disorder. An understanding of dyslexia requires information on the time course of reading as well as anatomical information, and no other functional imaging method can, at present, readily provide such data. The authors show convincingly that a left inferior temporo-occipital area is differentially engaged in normal control subjects as early as 180 msec after onset of the visual word. It is important that both the electrophysiological and the anatomical data are consistent with results obtained by other methods (e.g., depth electrodes and positron emission tomographic results [7, 8]). Salmelin and colleagues [3] suggest that the primary reason for adult dyslexia is probably the left inferior temporoparietal area dysfunction implicated by their study.

The utility of MSI lies in the combination of MEG's (sub)millisecond temporal resolution necessary to describe electrophysiological events with the millimeter-precision anatomic images provided by MRI [9–11]. The basis of MEG recordings is the detection and localization of the small magnetic fields associated with intracranial electromagnetic activity, either spontaneous or event-related (much like electroencephalography [EEG]). Unlike EEG, which measures volume currents, MEG detects the magnetic fields associated with the coherent intracellular activity of thousands of neurons, by hypothesis postsynaptic current flow in the apical dendrites of pyramidal cells. Superconducting
quantum interference devices, or SQUIDS, are used to amplify these extraordinarily small magnetic field signals with low noise. The output of the detectors are real-time waveforms.

The strength of MSI lies in the combination of rapid sampling and superior source localization. Magnetic fields are not attenuated or distorted by nervous tissue, cerebrospinal fluid, meninges, skull, or scalp. Consequently, one can estimate the sources of activity quite accurately. Activity is usually characterized as generated by "equivalent current dipoles." Although such modeling schemes are acknowledged to be an idealized representation of activity, they have been shown in some cases to provide a reasonable estimate of focal events. The composite images constructed by overlaying electrophysiological measurements (eg, dipoles) with anatomic images derived from MRI or computed tomography (CT) illustrate the anatomic location of activity at a given time-sampling point. State-of-the-art whole-head MEG systems can record from more than 100 sites simultaneously, and new analysis algorithms make it possible to reconstruct the three-dimensional activity millisecond by millisecond. The article by Salmelin and colleagues [3] reports an excellent example of the whole-head MEG recording technique, including the subsequent coregistration with MR images.

The noninvasive nature of MSI makes it a useful tool for both research and clinical purposes [9]. Basic organizational features of the visual, auditory, and somatosensory cortices are regularly revealed in experimental studies, in particular through the use of large-array biomagnetometers [11]. Several centers are already using MSI clinically for presurgical mapping and for the evaluation of patients with epilepsy. In presurgical mapping, certain locations on the sensorimotor homunculi are determined relative to a tumor or AVM. MSI protocols can help determine the choice between surgical or nonsurgical management, can assist in surgical planning, and can help predict functional consequences of tissue resection. In the assessment of epilepsy, MSI can play an important role in defining the epileptogenic zone, in particular for cases in which EEG has yielded ambiguous results with regard to lateralization. In addition, first attempts at using MSI to lateralize language function are showing that this technology, combined with the appropriate behavioral protocols, will be able to reliably index hemispheric dominance.

The MEG component of MSI currently has two important limitations. First, the physics of the detection process is such that MEG is selectively sensitive to fissural cortex and relatively insensitive to activity at gyral surfaces. Second, the determination of intracerebral sources based on extracranial data is a so-called inverse problem (a computationally ill-posed problem with no unique solution in the absence of constraints). The effective derivation of source locations therefore depends critically on modeling assumptions. Nevertheless, correlations of MEG data with data obtained by other methods indicate that source modeling yields very reliable source localization information. One practical limitation is that MEG installations are expensive. The cost of MSI systems is still quite high, and only a few sites (four in the United States) are equipped with large-array devices. The continued success of this functional imaging modality in clinical and basic research, however, suggests that it will play a significant role in the future.

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References