Current Status and Future Prospects of Perinatal MEG

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Abstract Neurodevelopment is a vast and critically important area of neuroscience, yet there is a paucity of functional imaging research during the perinatal and infant period when development is most rapid and significant. MEG offers compelling advantages over EEG and other neuroimaging methods for perinatal research. Over the last few decades, interest in this area has vacillated, but it is likely to reemerge in the coming years as neurodevelopmental disorders attract greater attention. This short contribution comments on the current status and future prospects of fetal and neonatal MEG, and highlights the SERF (spin exchange relaxation-free) magnetometer as an important new technology.

Neurodevelopment is a vast and critically important area of neuroscience, yet there is a paucity of functional imaging research during the perinatal and infant period when development is most rapid and significant. There are several reasons for this. First, the studies are difficult to perform due to the inability of the subjects to cooperate and the need to make serial measurements. Second, only techniques believed to be completely safe and noninvasive can be used.

MEG offers compelling advantages over EEG and other neuroimaging methods for perinatal research, and has the potential to become the preferred technique. Over the last few decades, interest in this area has vacillated, but it is likely to reemerge in the coming years as neurodevelopmental disorders attract greater attention. This short contribution comments on the current status and future prospects of fetal and neonatal MEG, and highlights the (SERF) spin exchange relaxation-free magnetometer as an important new technology.

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1 Fetal MEG

Intrauterine evaluation of human fetal brain function has been a long-standing and elusive goal, due largely to the inaccessibility of the fetal brain. The main approaches have been indirect. Researchers have studied such outputs of brain function as fetal heart rate variability, fetal body and fetal breathing movements; however, there is little evidence that any method in current use has the specificity to be employed as an effective screening tool for detection of abnormal fetal neurological functioning. The impetus to make progress in this area is the dire prognosis of babies born with cerebral palsy and severe mental retardation, which afflicts more than 10,000 babies per year in the US.

Fetal MEG is one of the few functional brain imaging technologies that can be applied to the fetus, and it is more direct than other techniques. It also provides one of the best examples of the potential advantages of magnetic, versus electric, detection. Fetal electric signals are much weaker than one would expect due to the presence of the *vernix caseosa*, which forms on the fetal skin and impedes the transmission of electrical currents to the maternal surface. Fetal magnetic signals, in contrast, are much less dependent on volume conduction and thus are relatively unaffected. A number of groups have demonstrated the feasibility of using MEG to detect evoked and spontaneous fetal brain activity. But despite the aforementioned advantages of MEG, the modest quality and success rate of fetal recordings preclude routine clinical application and limit the veracity of basic studies. Further advancement will likely require technological improvements. Research in this area, however, should not be abandoned.

2 Neonatal MEG

The neonatal period is a fascinating time to study electrical brain activity. The developmental changes are so rapid that they can be seen from week to week. Furthermore, brain activity in neonates can exhibit striking differences, compared to what is seen in adults. In neonates, the auditory evoked response is dominated by a single component that corresponds to surface positivity of the evoked potential, whereas in adults the response is biphasic and the dominant component, the N1, corresponds to surface negativity. In neonates, the auditory "off" response can be larger than the "on" response, whereas in adults the "off" response is always smaller. In early infancy, sleep spindles are strongly associated with slow wave sleep, whereas in adults spindling exhibits a negative association with slow wave sleep.

The true value of MEG for neonatal studies lies in its high sensitivity to developmental changes in brain activity, combined with its ability to serially track changes in the underlying sources with high spatiotemporal resolution. In principle, EEG is also capable of high resolution source localization in the neonate. In practice, however, the localization accuracy is confounded by the fontanels,

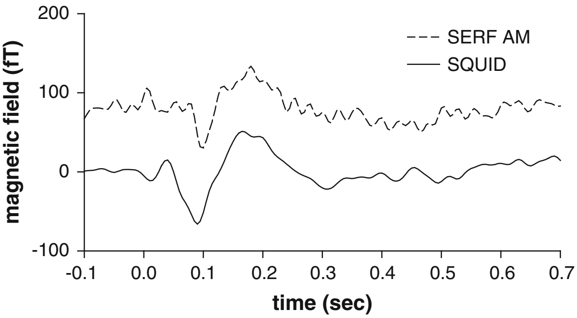

Fig. 1 Comparison of auditory evoked responses obtained from the same subject by a SQUID and a SERF magnetometer. The stimuli consisted of 50 ms, 1 kHz tones; 150 trials were averaged

which effect EEG topography much more than MEG topography. Thus, the simple transmission properties of magnetic signals again confer a significant advantage to MEG.

The neonatal brain provides an invaluable opportunity to study the development of brain rhythms. Some brain rhythms, such as sleep spindles, can be studied from their genesis. Over the last decade, connectivity has become a popular area of brain research. Neonatal studies may allow researchers to observe of the formation of brain networks and to correlate changes in connectivity with changes in evoked and spontaneous MEG activity and behavior.

3 The SERF Magnetometer: A Major Breakthrough

Since the introduction of whole-head systems, MEG has not benefitted from any major advances in sensor technology. Although the magnetic field resolution of SQUID magnetometers is sufficient for the vast majority of applications, the cost has remained stubbornly high. A recent advance that seems likely to have a major impact on MEG and other areas of biomagnetism is the so-called SERF atomic magnetometer (AM), which has achieved a breakthrough in sensitivity. The main advantage of AMs is low cost, which can make MEG much more affordable and widely available. For neonatal MEG, an additional advantage is that the positions of the channels can be adjusted to accommodate different head shapes and sizes. This is not possible with SQUID arrays because the channels are confined within a cryogenic dewar.

Several groups have used AMs to record brain evoked responses, but the results shown were obtained by averaging many more trials than is typically required using a SQUID magnetometer. Recently, we recorded adult auditory evoked responses using an AM fabricated by Vishal Shah at QuSpin, Inc. The recordings were made in a standard shielded room and were compared with recordings made during the same session with a SQUID magnetometer, using the same stimuli (50 ms, 1 kHz tones, 1–3 s ISI) and acquisition parameters. As exemplified in Fig. 1, which shows the average of 150 trials for the AM and a representative

SQUID channel, the responses were remarkably similar in quality and appearance. Although development of a commercial system may take several or more years, there are no fundamental obstacles that prevent the realization of low-cost, high-performance AM systems for MEG.