NeuroImage 181 (2018) 513–520

Contents lists available at ScienceDirect

NeuroImage

journal homepage: www.elsevier.com/locate/neuroimage

Cognitive neuroscience using wearable magnetometer arrays: Non-invasive assessment of language function

Tim M. Tierney [a,*], Niall Holmes [b], Sofie S. Meyer [a,c], Elena Boto [b], Gillian Roberts [b], James Leggett [b], Sarah Buck [d], Leonardo Duque-Muñoz [e,f], Vladimir Litvak [a], Sven Bestmann [a], Torsten Baldeweg [d], Richard Bowtell [b], Matthew J. Brookes [b], Gareth R. Barnes [a]

[a] *Wellcome Centre for Human Neuroimaging, UCL Institute of Neurology, London, WC1N 3BG, UK*
[b] *Sir Peter Mansfield Imaging Centre, School of Physics and Astronomy, University of Nottingham, University Park, Nottingham, NG7 2RD, UK*
[c] *UCL Institute of Cognitive Neuroscience, University College London, London, WC1N 3AZ, UK*
[d] *Developmental Neurosciences Programme, UCL Great Ormond Street Institute of Child Health, London, WC1N 1EH, UK*
[e] *Departamento de Ingeniería Electrónica, Universidad de Antioquia, Medellín, Colombia*
[f] *AE&C Research Group, Insituto Tecnológico Metropolitano, Medellín, Colombia*

ARTICLE INFO

Keywords:
Optically pumped magnetometers
Language
MEG

ABSTRACT

Recent work has demonstrated that Optically Pumped Magnetometers (OPMs) can be utilised to create a wearable Magnetoencephalography (MEG) system that is motion robust. In this study, we use this system to map eloquent cortex using a clinically validated language lateralisation paradigm (covert verb generation: 120 trials, ~10 min total duration) in healthy adults ($n = 3$). We show that it is possible to lateralise and localise language function on a case by case basis using this system. Specifically, we show that at a sensor and source level we can reliably detect a lateralising beta band (15–30 Hz) desynchronization in all subjects. This is the first study of human cognition using OPMs and not only highlights this technology's utility as tool for (developmental) cognitive neuroscience but also its potential to contribute to surgical planning via mapping of eloquent cortex, especially in young children.

1. Introduction

Magnetoencephalography (MEG) measures the magnetic fields associated with the electrical activity of the brain, and thus provides a direct quantification of neural population activity. Appropriate mathematical modelling of these fields subsequently allows reconstruction of electrophysiological activity with high temporal and spatial precision (Baillet, 2017; Friston et al., 2008; Hämäläinen et al., 1993). For these reasons MEG has become a useful clinical tool for presurgical evaluation of individuals with epilepsy, particularly for localising the epileptogenic zone via assessment of inter-ictal discharges (Englot et al., 2015; Nakajima et al., 2016; Nissen et al., 2017; Nissen et al., 2016) and for mapping eloquent cortex (Doss et al., 2009; Hashimoto et al., 2017; Hirata et al., 2004, 2010; Pang et al., 2016; Papanicolaou et al., 2014; Wang et al., 2012). MEG's use in this context is highly advantageous as previous research has shown that MEG can change surgical decision making or intracranial EEG placement in up to a third of patients (Sutherling et al., 2008). The role of MEG is even more valuable when one considers that up to 30% of patients may not have an observable lesion on MRI (Duncan et al., 2016), necessitating the use of a functional (as opposed to structural) imaging technique.

As a functional imaging technology MEG has advanced to the stage where it is regularly used in a number of hospitals across Europe, the United States and Japan (Bagič, 2011; De Tiège et al., 2017; Mouthaan et al., 2016; Shiraishi et al., 2012). However in the United States and Europe it is often a few leading hospitals that perform the majority of the scanning. The limited clinical use of MEG outside of these leading centres can be explained by a number of reasons. A conventional MEG scanner is not only expensive to install and maintain but the cryogenic vessel containing the sensors is of a fixed size and generally optimised for the adult head. This means that individuals with smaller heads (i.e. children) whose brains are further from the sensors exhibit lower signal to noise ratio as the signal drops dramatically with distance from the brain (Geselowitz, 1970; Hämäläinen et al., 1993). Furthermore, successful MEG acquisition often requires the subject to keep very still (Stolk et al., 2013) which may not be possible for all subjects.

---

* Corresponding author.
E-mail address: tim.tierney.12@ucl.ac.uk (T.M. Tierney).

https://doi.org/10.1016/j.neuroimage.2018.07.035
Received 12 March 2018; Received in revised form 10 June 2018; Accepted 13 July 2018

Here we directly address these issues using a new generation of MEG sensors known as Optically Pumped Magnetometers (Boto et al., 2016). This wearable MEG system does not require cryogenic cooling (reducing cost) and can be placed directly on the scalp (Boto et al., 2016) maximizing signal to noise in paediatric populations. Moreover, recent technical developments allow MEG measurement while a subject is free to move their head (Boto et al., 2018), thus addressing the issue of subject compliance. We show this wearable, and cryogen-free OPM-MEG system can be utilised to map eloquent cortex using a clinically validated language lateralisation paradigm (Liegeois et al., 2002; Pang et al., 2011; Wang et al., 2012). Primarily this highlights how OPMs can be used to provide clinically meaningful information while the head is not constrained to be still, thus better serving non-compliant populations.

To date OPM - MEG has only been used to study primary sensory and motor systems in the human brain and has not been used to study cognitive function (Borna et al., 2017; Boto et al., 2016; Colombo et al., 2016; Kim et al., 2014; Shah and Wakai, 2013; Supek and Aine, 2014; Wyllie et al., 2011; Xia et al., 2006). Here we present a proof-of-concept study demonstrating robust language lateralisation effects at the single subject level using OPM sensors. We focused on a case plus replication study design for two reasons - firstly because within in a clinical setting it is the within subject effects that are of value and secondly because the cost of construction of individualized (MRI derived) OPM scanner-casts limits the number of subjects that can participate. These scanner-casts gave us precise knowledge of sensor orientation and position with respect to the cortex, and also served as scaffolding to support the weight of the sensors and associated wiring (see Fig. 1 and methods for further elaboration). With this demonstration of mapping eloquent cortex and language lateralisation we show that OPMs can in fact be used as a valuable tool for cognitive and clinical neuroscience. In essence this experiment represents an exciting step forward for the use of MEG as it demonstrates the utility of a new generation of wearable MEG sensors for both cognitive and clinical neuroscience with maximal sensitivity throughout the lifespan.

2. Methods

2.1. Participants

Three healthy subjects (1 female, 2 male) aged 27–50 with normal or corrected-to-normal vision and no history of psychiatric or neurological disorders were recruited to participate in this OPM-MEG study. The research protocol was approved by the University of Nottingham Medical School Research Ethics Committee and written, informed consent was obtained from all participants. The experiments took place at the University of Nottingham. All participants were assessed using the Edinburgh handedness inventory (Oldfield, 1971).

2.2. Experimental paradigm

The task presented during the MEG experiment is a variant of a previously validated verb generation task designed to assess language laterality (Liegeois et al., 2002; E. Pang et al., 2011; Wang et al., 2012). Subjects were presented visually with a noun written in the centre of the screen and instructed to think of semantically related verbs without speaking (e.g. if presented with the word “cake”, subjects might think of words such as “bake” or “eat”). They were instructed to continue doing this until the word disappeared from the screen after a 3 s period. Each verb generation period was followed by a baseline period of approximately 2 s where the subject was asked to fixate on a crosshair in the middle of the screen (and no longer think of the noun or verbs related to it). There were a total of 120 trials recorded per subject. All words presented were unique and never repeated within-subject, but noun lists were repeated across subjects after having the order of words randomized. Subjects were not required to respond or speak but reported being able to concentrate and carry out the task throughout the experiment (ca. 10 min duration per subject).

2.3. Data acquisition using a novel OPM-MEG system

The bespoke OPM-MEG system (Fig. 1) used here comprised an array of sensors attached to the scalp in a helmet arrangement (the scalp array), a second array of OPM sensors fixed relative to the room (used to characterize background field - the reference array) and a nulling coil system used to remove the effect of the background static (Earth's) magnetic field. Below, each of these components is described in more detail.

2.3.1. OPM sensors

We used an array of 26 OPM on-scalp sensors in addition to four fixed reference OPM sensors placed behind the subjects' heads. The OPMs used are commercially available (http://quspin.com). They have been described in detail elsewhere (Shah and Wakai, 2013) but, in brief, the sensors comprise 3 crucial components a laser (795 nm wavelength), a Rb^{87} vapour cell and a photodiode. The laser induces a transparent steady state in the vapour that allows light to pass through the vapour with minimal absorption of photons and therefore maximal detection of the laser light at the photodiode. As the local magnetic field changes (due to brain activity) the transparency of the gas decreases and less light is detected at the photodiode.

A sinusoidally-oscillating magnetic field, applied using electromagnetic coils which are integrated into the sensor, is used to modulate the magnetic field along two orthogonal axes perpendicular to the laser beam. This allows for the detection of both radial and tangential (to the head) components of the external (neuro-) magnetic field. In this study, only the radial field component was measured. More general overview of

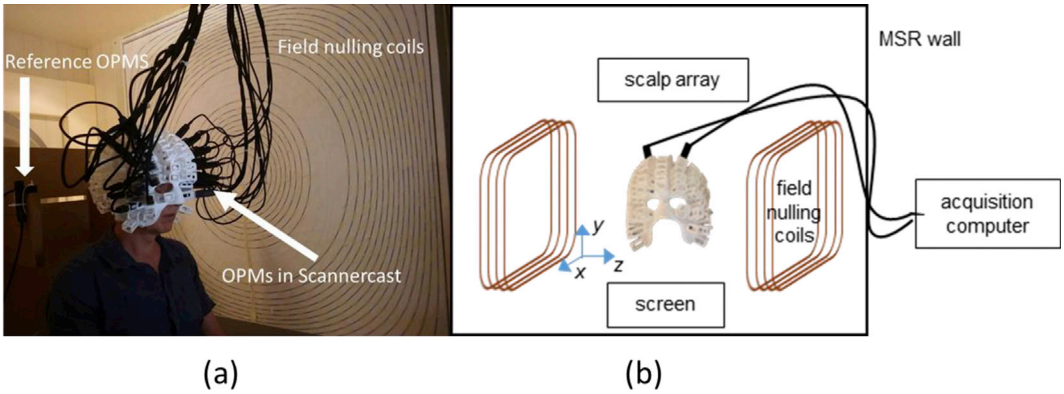

Fig. 1. ***The OPM setup for studying language lateralisation: real (a) and schematic (b)***. The subject is seated inside the magnetically shielded room wearing the scanner-cast with OPM sensors inserted into slots covering the bilateral aspects of the frontal lobes. The field nulling coils are placed either side of the subject and confer motion robustness to the system by nulling the field over a 40 × 40 × 40 cm^3 volume within which head movement is tolerated.