NeuroImage 63 (2012) 1249–1256

Contents lists available at SciVerse ScienceDirect

NeuroImage

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

Sensory thresholds obtained from MEG data: Cortical psychometric functions

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ARTICLE INFO

Article history:
Accepted 5 August 2012
Available online 11 August 2012

Keywords:
Auditory
Gap-detection
MEG
Psychophysics
Threshold

ABSTRACT

Sensory sensitivity is typically measured using behavioural techniques (psychophysics), which rely on observers responding to very large numbers of stimulus presentations. Psychophysics can be problematic when working with special populations, such as children or clinical patients who may lack the compliance or cognitive skills to perform the behavioural tasks. We used an auditory gap-detection paradigm to develop an accurate measure of sensory threshold derived from passively-recorded magnetoencephalographic (MEG) data.

Auditory evoked responses were elicited by silent gaps of varying durations in an on-going noise stimulus. Source modelling was used to spatially filter the MEG data and sigmoidal 'cortical psychometric functions' relating response amplitude to gap duration were obtained for each individual participant. Fitting the functions with a curve and estimating the gap duration at which the amplitude of the evoked response exceeded one standard deviation of the prestimulus brain activity provided an excellent prediction of psychophysical threshold.

Accurate sensory thresholds can therefore be reliably extracted from MEG data recorded while participants listen passively to a stimulus. Because our paradigm required no behavioural task, the method is suitable for studies of populations where variations in cognitive skills or vigilance make traditional psychophysics unsuitable.

Introduction

Psychophysical methods to determine sensory thresholds are widely used in human neuroscience because sensory processing underlies much of our cognitive and social functioning. The aim of this study was to evaluate how a neurophysiological sensory 'threshold' (that is highly correlated with psychophysical threshold) might be obtained from passively-recorded magnetoencephalographic (MEG) data.

A method for obtaining sensory thresholds without the use of a behavioural task would be particularly useful in studies of sensory processing in young children, or in other special populations, where factors other than sensory sensitivity may affect the measured threshold. Studies in large cohorts of typically-developing children and those at risk of developmental disorder have demonstrated the subtle yet significant effects of cognitive skills on psychophysical thresholds (e.g., Hulslander et al., 2004; Talcott et al., 2002). Verbal working memory and general cognitive abilities typically predict about 15–20% of the variance in sensory sensitivity measured psychophysically in children; the same has been observed in studies of adults with and without dyslexia (Witton et al., 2002). These findings are not surprising when the cognitive demands of a typical 2-alternative forced choice auditory psychophysical task are considered: the participant is asked to listen attentively to two sounds, compare the memory-traces associated with each sound, make a judgement about which was the 'target' and provide a motor response. This process has to be repeated many times with each lapse in attention or memory having an effect on the measured threshold. McArthur and Hogben (2012) examined performance on an auditory discrimination task over multiple repeat measurements in children with dyslexia or specific language impairment, and found that over 40% of children produced widely fluctuating threshold estimates which did not improve with training. Thus, psychophysical task performance is a potentially significant confound in any developmental study aiming to measure sensory thresholds accurately.

There is an extensive literature on EEG and MEG measurements of sensory processing, describing relationships between stimulus properties and the timing, morphology, spectral characteristics, and cortical localisation of responses. Relatively few of these studies have attempted to relate the measured response characteristics to sensory threshold, but cortical responses are highly sensitive to differences in stimulus magnitude; responses in primary sensory cortex typically increase in amplitude and decrease in latency (Starr, 1978) as stimulus intensity increases. Indeed, successive recordings of the evoked response to the onset of an acoustic stimulus presented at decreasing levels are used clinically by audiologists to determine the lowest level at which a reliable evoked response is elicited, and as such are sometimes used in diagnosis of hearing loss in adults (Cone-Wesson and Wunderlich, 2003). This method provides robust physiological evidence of absolute hearing threshold, however, because it relies on a generalised response to the onset of sound, it provides little information about the *processing* of the stimulus.

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1053-8119/$ – see front matter © 2012 Elsevier Inc. All rights reserved.
http://dx.doi.org/10.1016/j.neuroimage.2012.08.013

Psychophysical measurements typically exploit sensitivity to stimulus *differences* and a more relevant neurophysiological recording paradigm uses the mismatch negativity (MMN) response (Näätänen et al., 2007). Typically, a comparatively rare target stimulus is presented in a stream of standard stimuli, and the differential response to the two stimuli indicates that the subject's brain has responded differently to the target. The MMN paradigm is considered to be 'preattentive', because the participant is instructed to ignore the stimuli during testing. MMN responses increase in amplitude and decrease in latency with increasing stimulus magnitude, and can index sensory sensitivity at the group level, but they are not a highly accurate predictor of psychophysical threshold for individual subjects (Bertoli et al., 2001; Näätänen et al., 2007). Although the primary source of the MMN response is in auditory cortex, there is a contribution from frontal sites, and impaired MMN is a biomarker for cognitive decline (Näätänen et al., 2012), limiting its application as a pure measure of sensory sensitivity.

The design of an MEG paradigm for measuring sensory thresholds without being affected by cognitive skills needs to take into account at least three important factors: First, as far as possible, an evoked response that is purely sensory in origin is required. Second, the response needs to be specific to a single stimulus property. Third, the paradigm should also yield a continuous, rather than a discrete, measure of threshold — in other words, it should be able to yield thresholds that lie between the absolute stimulus values used in testing. Ideally, the paradigm must also be quick to administer so that it can be tolerated by populations for whom psychophysical tasks are inappropriate.

To obtain a purely sensory response, we opted for passive MEG recordings that do not require the engagement of the participant in a behavioural task. Behavioural tasks engage cortical areas involved in memory and response planning, implying some reliance on cognitive processing. Specificity to a single stimulus property was achieved by obtaining responses to a change within an on-going sound. There are several examples of such MEG paradigms in the auditory domain (Martin and Boothroyd, 2000). We have focused on gap detection, where a silent gap is presented during an ongoing noise stimulus, but others include pitch-onset responses (Chait et al., 2006; Seither-Preisler et al., 2006; Witton et al., 2012) pitch-change responses (Jones et al., 1998), and responses to changes in sound laterality (McEvoy et al., 1990). Importantly, the change in parameter of interest in these paradigms is separated from the onset of the sound, so the evoked response reflects only the relevant change in the stimulus. The ideal stimulus for sensory threshold estimation in MEG is therefore an on-going stimulus where one property is repeatedly changed in order to evoke a neuronal response. To obtain continuous, rather than discrete, threshold values, we explored the shape of the function relating response amplitude to stimulus magnitude and estimated thresholds from model fitted data, as is often done in psychophysics (Green and Swets, 1966).

In the present study an MEG threshold measure is developed from auditory gap detection data. The ability to detect a silent gap in a noise burst has been proposed as a measure of the auditory system's temporal resolution (Lister et al., 2011b; Samelli and Schochat, 2008). Psychophysical thresholds for detecting gaps in noise are about 2 ms for normal adult listeners under optimal conditions, but depend on stimulus properties and task-related factors such as the temporal position of the gap within the stimulus and the listener's level of certainty about when the gap will occur (e.g. Fitzgibbons, 1983; Fitzgibbons and Wightman, 1982; Green and Forrest, 1989; Shailer and Moore, 1983, 1985). Evoked response studies (Atcherson et al., 2009; Diedler et al., 2007, 2009; Harris et al., 2012; Michalewski et al., 2005; Pratt et al., 2005, 2007) and MMN (Bertoli et al., 2001; Todd et al., 2011) studies have shown that response amplitude is related to the length of the silent gap, suggesting that cortical responses may form a kind of psychometric function, and therefore yield an estimate of sensory threshold.

Gap detection thresholds are also of particular interest as an index of temporal resolution to study neurodevelopment and ageing (e.g. Dias et al., 2012; Harris et al., 2012). Diedler et al. (2009) have reported that gap-evoked responses are different in children with language-based learning difficulties. But while all the children successfully completed the MEG recordings, only 30% were able to complete the equivalent psychophysical task, so it remains unknown whether the observed neurophysiological differences were related to differences in sensory sensitivity. The present study sought to overcome this disconnection between measures of sensory threshold and underlying neurophysiology, by estimating sensory threshold from evoked response data.

Material and methods

Participants

15 adults (8 females) took part in the study. The age range was 22–61 years (females 23–61, males 23–57), with a total of 9 people under the age of 30, 3 between 30 and 40 and 3 aged over 40 years. None reported any history of hearing loss or neurological problems.

MEG data collection and analysis

The MEG stimulus was a continuous broadband, white Gaussian noise, lasting 348 s. Silent gaps occurred on average every 700 ms (plus or minus a random jitter of up to 100 ms). To reduce spectral splatter, each gap was windowed with a 1 ms raised-cosine fall and rise time and gap duration was measured from the centre of this window (i.e. we specify the full-width half-maximum of the gap durations). Gap durations, based on pilot testing, were 3, 6, 9, 12, 18 and 30 ms, and each was presented 80 times (a total of 480 stimuli). The stimulus was saved as a 16-bit, 44.1 k-Hz PCM .wav file and played out diotically at approximately 70 dB SPL from a PC soundcard through echoless plastic tubing fitted with foam ear-tips. The participants watched a video played silently with subtitles during the recording.

MEG data were acquired using a 275-channel whole-head CTF MEG system with axial gradiometers and 3rd-order noise cancellation. Data were sampled at 600 Hz, powerline-filtered, corrected offline for baseline drift and then subdivided into eighty 600 ms epochs (including a 200 ms prestimulus period). Each epoch was visually screened for artefacts, such as those associated with eye movements, and all affected epochs were removed from subsequent analyses. Each epoch was DC-corrected again for deviations from baseline by subtracting the mean of the prestimulus data. Averages were computed for the responses to each gap duration and these were low-pass filtered at 30 Hz.

Dipole source modelling was used to spatially filter the data for further analysis. For five of the participants (33%), a structural MRI was available. For these cases, the MEG data were spatially co-registered with the participant's MRI using a modification of the procedure described by Adjamian et al. (2004). For all participants a spherical head model was fit to the left and right preauricular points and nasion. Dipole modelling was performed using the CTF DipoleFit software for the large 30 ms gap evoked-response only. A single moving dipole was fit, separately, to the data-sample at the peak of the evoked response in the channels for the left and right hemisphere. This approach minimises errors which can result from fitting bilateral sources simultaneously (Brignell et al., 2008). For seven of the participants, the dipole-fit for the left-hemisphere data was very poor (e.g. having an excessively large Monte-Carlo error-volume, exceeding 5 cm^3) or impossible to obtain due to the absence of a clear response. The majority of the variance in the field pattern in each hemisphere was accounted for by this single dipole (an average of 89.46% in the right hemisphere, and 84.52% for the left-hemisphere fits); with the unaccounted-for variance most likely reflecting physiological noise that was a consequence of the relatively small number of trials in the datasets. For the acceptable fits (i.e. for 100% of participants in the right hemisphere and 53% in the left hemisphere), the location of the dipole was then fixed, but its moment and orientation were