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Review

The functional foetal brain: A systematic preview of methodological factors in reporting foetal visual and auditory capacity

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A B S T R A C T

Due to technological advancements in functional brain imaging, foetal brain responses to visual and auditory stimuli is a growing area of research despite being relatively small with much variation between research laboratories. A number of inconsistencies between studies are, nonetheless, present in the literature. This article aims to explore the potential contribution of methodological factors to variation in reports of foetal neural responses to external stimuli. Some of the variation in reports can be explained by methodological differences in aspects of study design, such as brightness and wavelength of light source. In contrast to visual foetal processing, auditory foetal processing has been more frequently investigated and findings are more consistent between different studies. This is an early preview of an emerging field with many articles reporting small sample sizes with techniques that are yet to be replicated. We suggest areas for improvement for the field as a whole, such as the standardisation of stimulus delivery and a more detailed reporting of methods and results. This will improve our understanding of foetal functional response to light and sound. We suggest that enhanced technology will allow for a more reliable description of the developmental trajectory of foetal processing of light stimuli.

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1. Introduction

This paper explores the relationships between parameters of functional foetal brain imaging studies and how these potentially contribute to variation in published findings. Such a report could lead to important consequences for our understanding of cognitive development before birth. This review focuses on the use of foetal magnetic resonance imaging (fMRI) and foetal magnetoencephalography (fMEG) in recording foetal cortical activation in response to both visual and auditory stimuli. Many of the studies reviewed here are within the literature from a feasibility perspective, containing small sample sizes and techniques that have yet to be replicated. It is therefore

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highlighted that this is a tentative review of an emerging field.

There is much variability in the amount of description present in methods sections, with some providing detailed information (e.g., Zappasodi et al., 2001) whereas others do not include information such as attrition rate, number of trials present in final dataset or information about the stimuli (e.g., Eswaran et al., 2000). For those that do provide methodological information, there are variations in techniques, methods, and measures. It is possible that this is due to the focus of the field thus far being on the feasibility for delivering stimuli and recording a neural response in a foetal population. Consequently little has been done to address what could be causing variance in results between studies. For example, experimenters have instead focussed on different processing methods for reducing noise, which will contribute to variance (Samonas et al., 1997; Taulu et al., 2004; Vrba et al., 2004). Despite successes in processing methods, disparities in response rates and response latencies between studies remain in the literature. Many other factors can cause variance, which cannot be controlled in a typical within-subjects design, such as distance from stimuli and foetal state (Kiefer-Schmidt et al., 2013). Due to there being so much variation in factors that are difficult to control, such as foetal state, it is even more imperative that we understand the potential variance that is present due to paradigm construction and stimuli.

Despite these forms of variation, it is clear that it is feasible to both present stimuli and record foetal neural responses. Though the body of literature reporting the investigation of foetal response to external auditory and visual stimuli is small, it is now of a size where we can begin to make comparisons with the potential to answer questions on how and why researchers might, or might not, find statistically significant results. It is essential for the field to begin to provide some consistency across studies in terms of methodological factors, such as the stimulus duration, and to report such information in methods sections. Given the large number of uncontrollable variables in foetal research when compared to postnatal work, it seems particularly important to standardise and report as many of the controllable methodological variables as possible. This will enable better comparisons between results of studies as well as potentially reducing the variance in reports of foetal neural response to external stimuli. Further, establishing a consistent, effective methodology could help improve attrition rates leading to more efficient data collection. This is particularly important for a field with such an inherently difficult target sample.

2. Methods

2.1. Literature review and eligibility criteria

A literature search was performed in October 2014 using Web of Science with a topic search of "fetal" and "fMRI", "fetal" and "fMEG", Visual Evoked Response (VER) and Auditory Evoked Response (AER).

Studies were included if they were investigating the foetus utilising fMRI or MEG methodologies, reported between 1985 and 2014 in an English language journal. No limitations were used.

In selecting studies for inclusion, the PRISMA (2009) process for systematic review was followed as outlined in Fig. 1. Abstracts of articles were screened and those highlighting a response to external visual and/or auditory stimuli were reviewed in full if the results were obtained from singleton pregnancies with no complications. Additionally, potentially relevant journal articles were sought by searching citation lists of the articles that met the inclusion criteria. Papers were reviewed and assessed for exclusion under the following criteria: (a) review articles, (b) purely comparison of data analysis techniques, (c) non-foetal sample, (d) sample assessing atypical development, and (e) non-visual or auditory stimuli.

2.2. Data extraction

Dependent measures related to response statistics and these were comprised of the final number of participants and/or recordings included in the final sample, the rate of response (%), and the number of trials included in the analysis post artefact removal. Statistics were extracted manually. For studies using MEG methodology, latency data were extracted. Response rate refers to the percentage of the foetal sample that provided a response (in terms of the number of participants or number of trials included in their analysis). We have classified this in terms of poor (<30%), moderate (30–65%) and good (>65%) response rate relative to the spread of response rates across the studies. Response number refers to the number of participants or recordings entered into analysis post artefact rejection. Response latency for fMEG refers to the time it takes the foetus to respond to a stimulus and has been classified as fast (<150 ms), moderate (150–350 ms) and slow (>350 ms). This final classification is most relevant for articles that utilise an oddball paradigm.

Data was calculated where possible for missing values. Foetal response and latency statistics were compared on the basis of a number of data items including, modality of stimuli, cognitive ability addressed, methodology (fMRI or fMEG), stimuli delivery method, stimulus duration, inter-stimulus interval (ISI), ratio of stimulus duration to ISI, sample size (recruited and final), gestational age (GA), form of stimuli, number of presentations, total time of the study, frequency/wavelength, and volume/intensity.

In addition to the above measures, selection bias within the field may affect the results and conclusions of this review. Statistically significant results are more likely to be reported than non-significant results (Sterne and Egger, 2001). Further, studies with smaller samples are less likely to yield significant results unless results are strong. This is particularly relevant for this review as many of the studies report small sample sizes.

3. Results

Fig. 1 details the study selection process as recommended in the PRISMA guidelines. Characteristics of all studies discussed are presented in Tables 1–3. Characteristics of studies that are not discussed but were nevertheless analysed are presented in Tables 4–6. Tables are not provided for visual fMRI studies as just one of this kind met the eligibility criteria. In this review a number of studies meeting the general inclusion criteria had to be excluded on the following grounds. Any of the first feasibility studies investigating fMEG response to auditory stimuli (Blum et al., 1985; Wakai et al., 1996; Eswaran et al., 2000) were excluded as Lengle et al. (2001) state environmental noise may have confounded the reported results due to the methods of sound delivery. Early studies also used very few channels due to limitations of the technology. In comparison, other fMEG studies used up to 151 channels (Eswaran et al., 2005; Draganova et al., 2005). McCubbin et al. (2007) were also excluded on the basis of reporting a substantially larger variance in response latency than other studies, which could suggest a different level of acceptance of noise within the obtained fMEG data.

Not all measures are highly variable with some measures proving to be relatively stable across research reports. Problems arise when comparing studies due to missing data. A number of articles failed to report methodological details and/or specific results. For thorough analysis, we endeavoured whenever possible to calculate missing data. This was not always possible, however, and