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#### Review

# Opportunities and methodological challenges in EEG and MEG resting state functional brain network research



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#### HIGHLIGHTS

- Resting state EEG and MEG recordings are increasingly used for functional connectivity and functional brain network analysis.
- We highlight advantages and disadvantages of methodological choices throughout the recording and analysis pipeline and how this may affect construction of functional connectivity and networks.
- We give several recommendations for subject instructions and data acquisition for resting state neurophysiological research.

#### ABSTRACT

Electroencephalogram (EEG) and magnetoencephalogram (MEG) recordings during resting state are increasingly used to study functional connectivity and network topology. Moreover, the number of different analysis approaches is expanding along with the rising interest in this research area. The comparison between studies can therefore be challenging and discussion is needed to underscore methodological opportunities and pitfalls in functional connectivity and network studies. In this overview we discuss methodological considerations throughout the analysis pipeline of recording and analyzing resting state EEG and MEG data, with a focus on functional connectivity and network analysis. We summarize current common practices with their advantages and disadvantages; provide practical tips, and suggestions for future research. Finally, we discuss how methodological choices in resting state research can affect the construction of functional networks. When taking advantage of current best practices and avoid the most obvious pitfalls, functional connectivity and network studies can be improved and enable a more accurate interpretation and comparison between studies.

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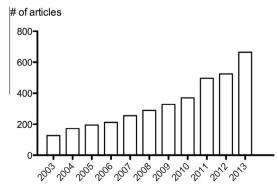
#### 1. Introduction and rationale

In recent years, there has been a growing interest in characterizing the functional network of the brain 'at rest'. This so-called 'resting state' paradigm is believed to reflect intrinsic activity of the brain, which may reveal valuable information on how different brain areas communicate (Greicius et al., 2003; Deco et al., 2011; Birn, 2012). It has linked spontaneous – task independent – fluctuations in neural activity to diseases, cognitive decline, and disturbances in consciousness (Greicius, 2008; Bassett and Bullmore, 2009; Bullmore and Sporns, 2009; Stam, 2014).

This interest in the 'resting state' is associated with several breakthroughs in functional magnetic resonance imaging (fMRI) research (Raichle, 2009). The claim, however, that valuable information on communication between brain areas can be inferred from intrinsic activity - obtained with neurophysiological techniques - is much older (for a comprehensive overview see (Pinneo, 1966; Snyder and Raichle, 2012)). The high spatial resolution might be a favourable feature of fMRI; still this technique only provides an indirect measurement of brain activity and has a limited temporal resolution. Information processing in the brain, however, acts on multiple time-scales, depending on the specific cognitive or behavioural function (Lopes da Silva, 2013). A considerable part of the information processed in the brain at rest is encoded on time scales from milliseconds to seconds (Koenig et al., 2005), a time scale that better suits techniques such as electroencephalography (EEG) and magnetoencephalography (MEG).

In the last decade, EEG and MEG connectivity and functional brain network studies have gained considerable interest resulting in a yearly growing number of published studies on this subject (Fig. 1). These studies have provided valuable information on the deviant organisation in the diseased brain, such as in Alzheimer's disease (Stam et al., 2007a; Dubovik et al., 2013), epilepsy (Bartolomei et al., 2006; Ibrahim et al., 2013), schizophrenia (Hinkley et al., 2010; Siebenhuhner et al., 2013), multiple sclerosis (Schoonheim et al., 2013; Van Schependom et al., 2014), Parkinson's disease (Fogelson et al., 2013), as well as in the healthy brain on topics as aging (Smit, 2012; Vecchio et al., 2014), gender differences (Boersma et al., 2011) and a healthy lifestyle (Douw et al., 2014). Furthermore, connectivity and functional brain network studies can be used in the clinical setting. For example, in epilepsy it has been shown to prompt early diagnosis (van Diessen et al., 2013) and to improve accuracy of epilepsy surgery by removing aberrant network nodes (Wilke et al., 2011). In Alzheimer's disease, EEG connectivity studies were used to monitor the success of novel interventions (de Waal et al., 2014). Similarly, progression of cognitive deficits in Parkinson's disease was correlated with functional brain network changes (Olde Dubbelink, 2014). Together these examples clearly underline the importance and additional value of connectivity and brain network analyses in EEG and MEG research.

When performing these analyses, one makes several assumptions and choices that may influence the eventual results. Moreover, the literature on functional connectivity and functional network studies is rapidly evolving, with an increasing number of analysis methods becoming available. Discussion is needed to obtain uniformity and comparability between different studies (Duncan and Northoff, 2013; Gross, 2014). The present paper therefore aims to highlight challenges, problems, and opportunities that are encountered when performing this type of research. As there are only few methodological studies that address these issues systematically, our review can be seen as a reflection of the current state of the field. We provide an overview of the methodological issues that should be considered when performing functional connectivity and network studies with EEG or MEG, and highlight the advantages and disadvantages of different approaches. Although we specifically focus on resting state EEG and MEG studies, most of the information provided is also applicable to task-related studies and other imaging techniques such as



**Fig. 1.** Number of articles per year from Pubmed search using keywords "(EEG OR MEG) AND (connectivity OR brain networks OR functional networks OR graph theory OR network analysis)" in the period 2003–2013.

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