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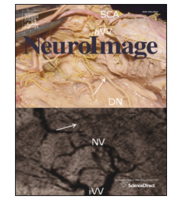

Using within-subject pattern classification to understand lifespan age differences in oscillatory mechanisms of working memory selection and maintenance

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ABSTRACT

In lifespan studies, large within-group heterogeneity with regard to behavioral and neuronal data is observed. This casts doubt on the validity of group-statistics-based approaches to understand age-related changes on cognitive and neural levels. Recent progress in brain–computer interface research demonstrates the potential of machine learning techniques to derive reliable person-specific models, representing brain behavior mappings. The present study now proposes a supervised learning approach to derive person-specific models for the identification and quantification of interindividual differences in oscillatory EEG responses related to working memory selection and maintenance mechanisms in a heterogeneous lifespan sample. EEG data were used to discriminate different levels of working memory load and the focus of visual attention. We demonstrate that our approach leads to person-specific models with better discrimination performance compared to classical person-nonspecific models. We show how these models can be interpreted both on an individual as well as on a group level. One of the key findings is that, with regard to the time dimension, the between-person variance of the obtained person-specific models is smaller in older than in younger adults. This is contrary to what we expected because of increased behavioral and neuronal heterogeneity in older adults.

Introduction

Across the lifespan, working memory (WM) performance and the underlying mechanisms of selection and maintenance undergo a tremendous change (Sander et al., 2012a). On the behavioral level, an increase in performance across childhood with a peak in young adulthood is followed by decline with advancing age. On the neural level, WM performance depends, among others, on rhythmic neural activity in the alpha band (8–12 Hz) (e.g., Freunberger et al., 2011). In particular, posterior alpha (8–12 Hz) power changes have been related to attentional shifts and WM load during retention (e.g., Obleser et al., 2012; Sander et al., 2012b; Sauseng et al., 2009). Given low WM performance in children and older adults, altered mechanisms of rhythmic neural processing are to be expected in these age groups. However, evidence on age-related changes in rhythmic neural activity related to WM maintenance and selection is scarce, and results are mixed. Some studies have found evidence for age-differential attentional effects on the modulation of alpha power (Sander et al., 2012b), whereas others did not observe any attention-related modulation in older adults (Vaden et al., 2012).

One possible explanation for the mixed results may be increased heterogeneity in children and older adults. Implicit to inferring cognitive and neural processes from group data is the strong and necessary (but not sufficient) assumption that the process under investigation is equivalent for every group member. Hence, group homogeneity is crucial for making links between cognitive and neural data. Consequently, conclusions about processes from the sample-specific level to the person-specific level are valid only under the ergodic assumption (Molenaar, 2004). Ergodicity assumptions are typically violated for developmental processes, and, in these cases, it is necessary to base analyses on intraindividual variability rather than on interindividual change. As a result, inferences on the individual level may be diluted if not meaningless (e.g., Hayes, 1953; Molenaar and Campbell, 2009; Nesselroade et al., 2007; Siegler, 1987; Voelkle et al., 2014).

Abbreviations: ANOVA, analysis of variance; BAC, balanced accuracy; BCI, brain–computer interface; CI, confidence interval; CSP, common spatial pattern; EEG, electroencephalography; ICA, independent component analysis; LDA, linear discriminant analysis; LLDA, Ledoit's linear discriminant analysis; PCA, principal component analysis; WM, working memory.

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Thus, increased interindividual variability in developmental populations may cast doubt on the validity of group statistics, and calls for the development of analyses based on intraindividual instead of interindividual models (e.g., Nesselroade et al., 2007). The high reliability and reproducibility of behavioral, as well as structural and functional brain measures in younger adults suggest reasonable homogeneity of this group. However, widespread changes in brain chemistry, anatomy, and functionality are documented, especially for child development and aging (e.g., Bäckman et al., 2006; Raz et al., 2005). These changes are typically accompanied by increased heterogeneity of functioning in behavioral tasks (e.g., Astle and Scerif, 2011; Nagel et al., 2009; Werkle-Bergner et al., 2012). Hence, especially for cross-sectional comparative studies, one may question whether meaningful between-group comparisons are feasible knowing that the within-group heterogeneity is not equal across lifespan samples.

Here, we suggest using within-subject pattern classification to better understand lifespan age differences in oscillatory mechanisms of WM selection and maintenance. More precisely, we propose a two-step approach: First, person-specific models that explore the expected relationship between brain responses and experimental conditions on the individual level are estimated. For example, in the context of multivariate time-series analyses, this can be achieved by estimating person-specific parameter estimates for a given model of interest (Nesselroade et al., 2007). In a second step, invariance of the parameter estimates can be tested within and across groups (Boker et al., 2009). Inspired by those considerations, we propose a formal approach to derive person-specific models for the identification of differential brain–behavior links in lifespan samples.

In multi-channel electroencephalographic (EEG) recordings of brain signals over time, a person-specific model that carries maximal information about the discrimination of experimental conditions can vary across several parameters: first and foremost, across time, duration, channel, and frequency. The model space spanned by these parameters is necessarily large and finding the most informative model is far from trivial. Therefore, we formalize the problem as a classification task and employ multivariate pattern classification algorithms (also know as multivariate pattern analysis (MVPA) in the (f)MRI literature Norman et al., 2006) in combination with a precisely tailored preprocessing chain to obtain a solution. Similar approaches have been dominating brain–computer interface (BCI) research. However, in many of these applications, the predictive accuracy is the primary target of the procedure rather than the inference about the underlying processes. Our framework can be regarded as a supporting tool in the recursive interplay of theory-guided and exploratory analysis of neuroimaging data that assists researchers in hypothesis generation and theory building by extracting stable patterns from data (cf. Brandmaier et al., 2013). In our work, we place a particular emphasis on interindividual differences as typically encountered in lifespan and aging research.

To test the applicability of our approach, we re-analyze data from a lifespan study that targeted brain oscillatory mechanisms for WM selection and WM maintenance in a lifespan sample including children, younger, and older adults (Sander et al., 2012b). The study used a color change-detection task (Vogel and Machizawa, 2004), in which participants were cued to attend to either the left or the right hemifield and asked to remember the colors of varying numbers of items. Hence, by design, it is possible to identify modulations of rhythmic neural responses that (a) relate to the attentional focus and (b) reflect the varying levels of WM load. We operationalized (a) attentional focus as the hemifield to which spatial attention should be shifted and (b) WM load as the amount of items to be remembered in a change-detection task. Hence, in a first step, we set out to predict the focus of visuospatial attention based on changes in (posterior) alpha power. We will refer to this as attentional focus prediction in the following. Given the robust relation of posterior alpha power modulations and attention shifts (e.g., Kelly et al., 2006; Sander et al., 2012b; Worden et al., 2000), this analysis was intended as a validation step of our classification approach (e.g., (Bahramisharif et al., 2010; van Gerven and Jensen, 2009; Kelly et al., 2005, for previous BCI approaches). This part of the study aimed to demonstrate the feasibility of deriving person-specific models with varying spatio-temporal information in groups of children, younger, and older adults. In a second step, we aimed to predict information maintained in WM based on single-trial modulations of neural activity in the alpha range. We will refer to this as WM load prediction in the following. Previous studies have successfully demonstrated load modulations of lateralized alpha power activity (Sauseng et al., 2009). However, given that studies demonstrating the possibility of WM load prediction from scalp EEG recordings are scarce (but see Roux et al., 2012, for an analysis of source activity in pre-identified regions), this part represents an extension of the applicability of our classification approach.

Material and methods

Identifying person-specific models: the classification approach

The core idea of our framework is the derivation of person-specific models that optimally discriminate between behavioral conditions and, thus, allow evaluation of the neural underpinnings of interindividual differences in behavioral responses. Here, the term *model* is used to refer to both a class of models (representing a particular functional form with unknown parameters) and a particular instance of a model with parameters estimated from data. Whenever the distinction is not clear from the context, we refer to the latter as an *estimated model*. Person-specific models are estimated models selected from a set of candidate models that vary across multiple dimensions of the observed data space. In electroencephalography (EEG), this space typically entails electrode channels, time points, and/or frequencies; but our considerations generally apply to any spatio-temporal method of brain imaging. Candidate models can be derived from a template model class and vary parametrically according to multiple dimensions, first and foremost, to the spatio-temporal segments of the original data they are exposed to. In particular, models operate on different time windows and on subsets of channels or their geometric projections. In the remainder of this subsection we will describe the proposed framework to estimate person-specific models.

In the following, the number of measured variables per sample will be denoted by M and the number of samples per individual will be denoted by T, as those typically refer to samples ordered in time. For each person, a data set $(\mathbf{x}_t, y_t) \in D$ with $t \in \{1, \ldots, T\}$ is measured, which is a set of tuples of observed brain responses $\mathbf{x}_t \in \mathbb{R}^M$ and a corresponding dichotomous target variable $y_t \in \{0, 1\}$ that typically corresponds to a given external condition, task, or state. A candidate model, mapping brain responses to the target variables, can then be conceived as a θ-parameterized function $f_\theta(\mathbf{x}) = y$, linking the observed neural responses $\mathbf{x}_t$ and behavioral states y_t. The specific parameters θ can be estimated by minimizing a loss function on data (usually called the training set). Each estimated model can then be evaluated with respect to its accuracy in predicting a behavioral condition from brain responses, whereby selection of the best model is carried out for each person separately. We propose to use the balanced accuracy (BAC), a loss function accounting for unbalanced target variables that are often encountered in EEG data sets, as the performance measure for each candidate model. The BAC is the average of the accuracies obtained for each target variable state (condition) (Brodersen et al., 2010). This metric allows us to select the best of all competing models and interpret the idiosyncratic brain-space information of that model as person-specific information.

To avoid an overoptimistic bias by confounding parameter estimation and model evaluation (Kriegeskorte et al., 2009; Stone, 1974), we estimate the BAC for a given candidate model using 10-fold stratified cross-validation (Kohavi et al., 1995). The resulting person-specific models can be interpreted as both a measure of interindividual