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Functional and effective connectivity of stopping

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ABSTRACT

Behavioral inhibition often is studied by comparing the electroencephalographic responses to stop and to go signals. Most studies simply assess amplitude differences of the N200 and P300 event-related potentials, which seem to best correspond to increased activity in the theta and delta frequency bands, respectively. However, neither have reliable indicators for successful behavioral inhibition been identified nor have the causal dependencies of stop-related neurocognitive processes been addressed yet. By studying functional and effective connectivity underlying stopping behavior, this study opens new directions for the investigation of behavioral inhibition. Group independent component analysis was used to infer functionally coherent networks from electroencephalographic data, which were recorded from healthy human participants during processing of a stop signal task. Then, the temporal dynamics of causal dependencies between independent components were identified by means of Bayesian network estimations. The mean clustering coefficient and the characteristic path length measure indicated time windows between 130 and 180 ms and between 420 and 500 ms to express significantly different connectivity profiles between conditions. Three components showed significant correlations between 120 and 260 ms with stop signal reaction times and the number of failed stops. Two of these components acted as sources of causal flow, one capturing P300/delta characteristics while the other was characterized by alpha power depletion putatively representing the evaluation or processing of stimulus features. Although results suggest that the P300 and associated delta activity seem to be statistically dependent on earlier processes associated with behavioral inhibition, the time window critical for inhibition coincides with early changes in causal patterns and largely precedes peak amplitude differences between go and stop trials. Altogether, utilizing the analysis of stopping-related connectivity, previously undetected patterns emerged that warrant further investigation.

Introduction

The ability to stop or suppress inappropriate thoughts or actions is a prerequisite for adaptive behavior. The neural mechanisms instantiating these capabilities are often studied with response inhibition paradigms of which the go/no-go and the stop signal tasks are common representatives. Animal in-vivo, human lesion, and neuroimaging studies suggest a network of regions including the frontal cortex and the basal ganglia to implement behavioral inhibition (Aron, 2007). The exact dynamics of interregional communication, e.g. by which means and in which order relevant cortical structures interact, are largely unexplored though.

Due to its high temporal resolution, electroencephalography (EEG) seems to be best suited to study dynamical changes and the connectivity of brain networks underlying response inhibition. Previous work that utilized EEG clearly focused on event-related potentials (ERP), especially the occurrence of the N200 and P300 as seen in response to stop or no-go but not go signals. Both ERPs have previously been considered indicators of a genuine motor inhibition process. A synopsis of relevant findings (see Huster et al., 2013), however, suggests the N200 to reflect other pre-motor cognitive processes such as conflict monitoring or response program updating. The P300, on the other hand, might well be associated with response- or inhibition-related processing stages, since experimental manipulations often lead to outcomes that are in accordance with our understanding of behavioral inhibition. Whereas N200 amplitudes in seldom go-trials become enlarged relative to frequent stop-trials, for example, the P300 does not show similar amplitude inversions across conditions but seems to be most pronounced whenever inhibition supposedly is engaged (e.g., Enriquez-Geppert et al., 2010). However, because of the comparatively late onset time of

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the P300, this potential has been suggested to reflect evaluative processing stages rather than the actual inhibition of a motor response (Huster et al., 2013).

Time-frequency decompositions reveal that theta and delta band activities correspond best to the N200 and P300 responses, respectively (Huster et al., 2013). Even more, manipulations of no-go probability (Yamanaka and Yamamoto, 2010) or comparisons of different age groups (Schmiedt-Fehr et al., 2011) indicate that the N200 might specifically be associated with a higher theta-component (around 7 Hz), whereas a lower and somewhat later peaking theta component (around 5 Hz) might best be associated with the N200–P300 transition. Yet again, although a valid electrophysiological marker for inhibition would be of great value, neither of the previously mentioned EEG phenomena can unambiguously be tied to this neurocognitive process (Huster et al., 2013).

Using transcranial magnetic stimulation (TMS), van den Wildenberg et al. (2010) showed that cortical inhibition within the motor cortex changes already at around 150 ms after stop stimulus presentation. This finding suggests that inhibition is instantiated and controlled some time before the activity of major ERPs or time-frequency components culminates. Thus, it is unclear whether the coordinated interplay of networks corresponding to these neurocognitive events simply does not coincide with pronounced amplitude increases in the EEG, or whether it is only loosely time-locked to the onset of a stop stimulus and therefore might not even be reflected in averaged EEG time courses. Except for some seminal studies addressing band-specific coherency patterns estimated from electrode pairings in stop-signal and go/no-go tasks (e.g., Shibata et al., 1997, 1998; Swann et al., 2012; Tallet et al., 2009; Zhang et al., 2008), research on the connectivity underlying behavioral inhibition is sparse. Nevertheless, these earlier studies reported changes in between-electrode synchronization of frontal alpha or differential desynchronization in the beta band when comparing inhibition- and go-related EEG activity. Unfortunately though, analyses were always confined to a small selection of electrodes and frequency bands, thus necessarily leaving the temporo-spatial dynamics of inhibition-related connectivity patterns largely unexplored. As a consequence, it is not known how to best characterize the neural signature of networks that may be associated with a specific EEG phenomenon (such as frontal theta or central beta activity, the N200 or P300), because such networks could as well be expected to express interactions across different frequency bands in a temporally specific manner. Similar observations have already been made in other cognitive domains, as for example regarding working memory. Here, increased theta amplitudes under conditions of high working memory load have been long known, but recent work furthermore lends support to the notion that theta-gamma cross-frequency coupling is of crucial importance for working memory performance (e.g., Sauseng et al., 2010).

This study sets out to address both functional and effective connectivity patterns underlying behavioral inhibition by consecutively utilizing group independent component analysis (ICA) and Bayesian network estimation. Staying within the Cocktail Party analogy, our approach first separates the contributions of single speakers to the various, partly overlapping conversations as recorded via multiple microphones (EEG electrodes in our case) utilizing ICA, and then reconstructs the time-varying interactions these speakers have via Bayesian network analysis. In its application to EEG data, this combination translates to the identification of functionally coherent brain networks and the concurrent investigation of changes of network-interactions across time, thus providing a multiscale characterization of functional brain networks (for an in-depth discussion on the definition of networks see, Erhardt et al., 2011; Sporns, 2010). Additionally adopting a data-driven approach to the study of stopping-related connectivity, we pursue a more complete delineation of stopping-related networks than has been achieved before. Nevertheless, we also aim for the integration of previous findings with the outcome of this study and thus dared to formulate some expectations. In light of earlier work we expected N200 amplitudes to be explained by two components reflecting activity in the high and low theta bands, whereas the actual P300 would largely be represented by a single component associated with delta band activity. Furthermore, we hypothesized that stopping-related activity in the N200 time frame, when compared to go-related activity, would represent a window of high information flow, due to an increased need for inter-regional coordination at pre- and peri-inhibitory processing stages as suggested by the temporal dynamics of intra-cortical inhibition in motor regions.

Methods

Participants

A total of 13 healthy participants took part in the study (7 female; mean age = 24.83 ± 2.83 years). The study was approved by the ethics committee of the University of Oldenburg.

Stimuli, task and behavioral data analysis

Participants performed a modified stop signal task while comfortably seated within an electrically shielded and sound attenuated cabin. Stimuli were presented on a 24″ TFT screen placed behind an electrically shielded window. Viewing distance to the screen was 100 cm such that the visual angle of stimuli was about 1.7°. Task presentation and performance was controlled using the Presentation software (version 14.08, Neurobehavioral Systems). Responses were given via a dedicated response device.

Stimuli consisted of centrally presented arrows pointing to the left or the right. On a go trial, the target arrow was displayed in purple and subjects had to indicate the direction the arrow was pointing to via a button press. On stop trials, the color of a given target would change from purple to orange, instructing the participants to withdraw from responding. Stimulus-color assignments were counterbalanced across subjects. The delay between the onset of target presentation and color change (stop signal delay, SSD) was tracked and adapted by an algorithm according to a staircase procedure. SSD values were adapted as increments or decrements in steps of 50 ms depending on whether a subjects' response on the last stop trial was correct (successful inhibition) or not (failed inhibition), respectively (Band et al., 2003). SSD adaptations were tracked separately for left- and right-hand responses. The presentation time for stimuli was the same for go and stop trials (with respect to the relevant hand). In stop trials, go stimuli were presented for the length of the SSD. Stop stimuli immediately followed the go stimuli and were presented for 216 ms. Total presentation time of go stimuli in go trials was determined by the SSD plus 216 ms. Whenever none of the previously described stimuli was presented, a fixation cross was shown in the middle of the screen instead.

Trials were grouped in blocks of 30 with an average interstimulus interval of 1360 ms. Each block contained 20 go and 10 stop trials and feedback on the participant's performance was given after each block, instructing subjects to respond faster or more accurately when detecting average response times larger than 550 ms or a rate of failed stops of more than 50% with stop signal trials, respectively. Participants completed a total of 30 blocks with self-paced breaks after every fifth block.

To assess the behavioral performance of the participants, mean reaction time (RT) to go stimuli, the percentage of erroneous go trials (response with wrong hand or omission), and the percentage of failed stop trials (unsuccessful inhibition) were calculated. In addition, the stop signal reaction time (SSRT) was assessed as the difference between mean go RT and the average stimulus onset asynchrony of the go and the stop stimuli in stop trials ($SSRT_{mean}$ according to Band et al., 2003). Statistical assessments separated for response hands did not reveal significant differences; hence, behavioral data averaged across response hands will be reported.