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Variability of single trial brain activation predicts fluctuations in reaction time

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ABSTRACT

Brain activation stability is crucial to understanding attention lapses. EEG methods could provide excellent markers to assess neuronal response variability with respect to temporal (intertrial coherence) and spatial variability (topographic consistency) as well as variations in activation intensity (low frequency variability of single trial global field power).

We calculated intertrial coherence, topographic consistency and low frequency amplitude variability during target P300 in a continuous performance test in 263 15-year-olds from a cohort with psychosocial and biological risk factors.

Topographic consistency and low frequency amplitude variability predicted reaction time fluctuations (RTSD) in a linear model. Higher RTSD was only associated with higher psychosocial adversity in the presence of the homozygous 6R–10R dopamine transporter haplotype.

We propose that topographic variability of single trial P300 reflects noise as well as variability in evoked cortical activation patterns. Dopaminergic neuromodulation interacted with environmental and biological risk factors to predict behavioural reaction time variability.

1. Introduction

Recently, it has been emphasized that reduced stability of task-related attention network activation may provide a crucial contribution to the pathophysiology of attention (Castellanos & Proal, 2012; Fair et al., 2010). Attentional lapses result in increased reaction time variability (Kebir & Joober, 2011; Sonuga-Barke & Castellanos, 2007), which has been suggested to be a correlate not only of vigilance instability (Tucha et al., 2006) but also of less reliable neurotransmission and reduced neuronal connectivity (Tamnes, Fjell, Westlye, Ostby, & Walhovd, 2012; Zhou et al., 2012). Note that a variety of factors influence reaction time variability; a review of different interpretations of reaction time variability is given in Karalunas, Geurts, Konrad, Bender, and Nigg (in press). However, the neurophysiological underpinnings of reaction time variability are not clear yet. Neuronal communication in the brain occurs within milliseconds. Therefore, the EEG with its high time resolution offers an excellent possibility to assess these attention-related processes (Van de Ville, Britz, & Michel, 2010) in event-related potential paradigms. The target P300

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complex reflects a stable event-related potential index of the activation of task-relevant attention networks involved in target detection and response selection with single trial target P300 latency and amplitude covarying with reaction times (Holm, Rantaaho, Sallinen, Karjalainen, & Muller, 2006; Jung et al., 2001; Saville et al., 2011; Verleger, 1997).

Consequently, the specificity of variability analyses can be increased by the use of EEG measures as they can be limited to the cognitive processes which take place in a certain time window, e.g. P300-related context-updating and response selection during 200–400 ms. Thus neuronal processing variability can be assessed regarding predetermined cognitive functions in specific time windows.

In addition, EEG allows to assess different kinds of variability in neuronal processing:

(1) The temporal 'stability' of information processing is reflected by intertrial phase coherence (Delorme, Westerfield, & Makeig, 2007). Intertrial coherence is a measure of the degree to which the phase of the evoked response aligns across trials, independently of amplitude (Delorme & Makeig, 2004; Makeig, Debener, Onton, & Delorme, 2004), thus, representing the latency variability in the evoked response of single trial P300. A perfect phase alignment of the theta and delta response corresponds to zero single trial P300 latency variability because the variability of the latency of the bandpass filtered P300 single trial peak directly relates to theta/delta phase alignment in the P300 time window (cf. Fig. 1). Intertrial coherence can presumably be used to examine neural transmission in the brain, with reduced intertrial coherence indicating increased "cortical noise" (Koychev, Deakin, Haenschel, & El-Deredy, 2011; Winterer et al., 2000).
(2) In contrast, topographic consistency (Brandeis, Naylor, Halliday, Callaway, & Yano, 1992; Koenig & Melie-Garcia, 2010) assesses the similarity between single trial potential topographies, which may give hints towards the consistency of the activated network of cortical areas as well as the amount of non stimulus-locked 'noise'. Topographic consistency indicates the degree to which similar or different *topographical* patterns of evoked potentials occur across single trials. The calculation of topographic consistency (Koenig & Melie-Garcia, 2010) is based on global field power (Lehmann & Skrandies, 1980), which represents an index of the strength of a scalp field. Topographic consistency reflects the degree to which single trial topographies differ from the average topography ('topographical standard deviation') and we propose that it can be used to measure the stability of the neural networks involved in information processing. However, it must be pointed out that to date no experimental link has been established between TC and cortical network organization. We examined here whether increased topographic singe trial potential variability correlated with increased reaction time variability.
(3) Finally, we examined low frequency variations in global field power (Lehmann & Skrandies, 1984) of the single trial event-related potential (ERP) signal, as these could represent a more precise measure of attention fluctuations than overall changes in global field power:

Low frequency variations of reaction time or errors have been found to be increased in attention deficity/hyperactivity disorder (Kuntsi & Klein, 2012; Yordanova et al., 2011), for instance, and could be related to interferences of the default mode network in controlled attention (Sonuga-Barke & Castellanos, 2007). At school, children are required to concentrate on highly variable tasks which do last several minutes, therefore attentional fluctuations in the minute range seem highly relevant. Therefore, we examined whether such slow fluctuations of reaction time and single trial ERP amplitude (low frequency amplitude variations) could be increased in the minute-range in a continuous performance test for at-risk subjects with attention deficits. While many studies have been focusing on resting state network frequencies between 0.01/0.02 and 0.05 Hz (i.e. one cycle lasts for 20–100 s; Sonuga-Barke & Castellanos, 2007), Di Martino et al. (2008), also examined slower frequency bands down to 0.004 Hz (4.2 min; 'Slow-6'). Note that due to the continuous performance test characteristics (irregular timing and rather rare occurrence of target trials), faster frequencies in the second-range as reported for intrinsic brain oscillations could not be studied because no frequencies above the sampling-rate-dependent Nyquist frequency can be examined. Instead, a different complementary low frequency parameter was assessed.

In pioneering work Helps et al. showed that the power of slow frequency EEG oscillations between 0.02 and 0.2 Hz was reduced in subjects with attention deficit hyperactivity disorder and that this reduction was associated with performance measures (Helps et al., 2010). Groom et al. (2010) examined intertrial coherence in the context of error monitoring and found that theta ITC was reduced in subjects with ADHD. This is a fact that could contribute to reduced error related negativity in ADHD. Based on a twin study, Tye et al. (2012) reported that the same genes influenced ADHD and the power in very low EEG frequencies below 0.5 Hz. However, so far it has remained unclear whether any of the EEG measures outlined above may serve as a specific endophenotype of the stability of neuronal information transmission that is related to reaction time variability. In this respect, the present study is the first to image the neurophysiological basis of fluctuations in attention level using topographic, latency-related and amplitude-related EEG indices. Moreover, we examined how these indices were modulated genetically.

Dopaminergic signalling modulates cortical activity and can focus cerebral activation (Coull, 1998; Winterer, 2006). Therefore, we examined the impact of a well-known functionally relevant dopamine transporter (DAT1) haplotype (consisting of two variable number tandem repeats in intron 8 and the 3′ untranslated region) (Laucht et al., 2007) on measures of neuronal transmission variability and reaction time variability. The analyses were undertaken according to an earlier report on effects of DAT1 haplotype and environmental factors (psychosocial adversity) on attention (Laucht et al., 2007), thus environmental factors were taken into account rather than additional genes. We assessed whether the interaction between DAT1 haplotype and psychosocial adversity with regard to inattentive symptoms which has been shown before (Laucht et al., 2007) could be explained by effects of DAT1 haplotype and psychosocial adversity on temporal, spatial or intensity variability parameters of neural information processing. This hypothesis was based on the fact that fluctuations of attention have been shown to be related to reaction time variability (Feige et al., 2013). Specifically, we tested whether variation in the DAT1 haplotype would interact with intertrial coherence, topographic consistency or low frequency amplitude variability to influence reaction time variability. Such an interaction would be expected when assuming that dopaminergic mechanisms were able to compensate for deficits in intertrial coherence/topographic consistency/low frequency amplitude variability (if these were produced by other, non-dopaminergic pathways).

We aimed to establish intertrial coherence, topographic consistency and/or low frequency amplitude variability as neurophysiological parameters for research of attention-related disorders such as attention deficit hyperactivity disorder. Note that in this paper, intertrial coherence, topographic consistency and