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Reconstructing ERP amplitude effects after compensating for trial-to-trial latency jitter: A solution based on a novel application of residue iteration decomposition

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ABSTRACT

Stimulus-locked averaged event-related potentials (ERPs) are among the most frequently used signals in Cognitive Neuroscience. However, the late, cognitive or endogenous ERP components are often variable in latency from trial to trial in a component-specific way, compromising the stability assumption underlying the averaging scheme. Here we show that trial-to-trial latency variability of ERP components not only blurs the average ERP waveforms, but may also attenuate existing or artificially induce condition effects in amplitude. Hitherto this problem has not been well investigated. To tackle this problem, a method to measure and compensate component-specific trial-to-trial latency variability is required. Here we first systematically analyze the problem of single trial latency variability for condition effects based on simulation. Then, we introduce a solution by applying residue iteration decomposition (RIDE) to experimental data. RIDE separates different clusters of ERP components according to their time-locking to stimulus onsets, response times, or neither, based on an algorithm of iterative subtraction. We suggest to reconstruct ERPs by re-aligning the component clusters to their most probable single trial latencies. We demonstrate that RIDE-reconstructed ERPs may recover amplitude effects that are diminished or exaggerated in conventional averages by trial-to-trial latency jitter. Hence, RIDE-corrected ERPs may be a valuable tool in conditions where ERP effects may be compromised by latency variability.

1. Introduction

Event-related brain potential (ERP) components are important and frequently employed tools in Cognitive Neuroscience, in both basic and applied settings. The components of averaged ERP waveforms can be related to specific mental sub-processes; questions usually concern amplitude or latency differences between experimental conditions (e.g., Rugg and Coles, 1995), populations (e.g., Polich and Herbst, 2000), or individuals (e.g. Kaltwasser et al., 2014). Recently, latency variability of certain ERP components has received growing attention in single trial studies (e.g. Saville et al., 2014). However, despite the prevalence of the average ERP protocol in cognitive brain research, the existence and consequences of trial-to-trial latency variability (latency jitter) is a long-standing but still under-explored problem (cf., Jung et al., 2001; Luck, 2005; Möcks et al., 1988; Picton et al., 1984; Woody, 1967). The present paper concerns the interpretation of measured amplitude effects as a mixture of amplitude variation and trial-to-trial latency jitter (denoted as 'latency jitter' in the following). Latency jitter smears or blurs averaged ERPs and – depending on the affected condition(s) – may obscure or mimic amplitude differences. For example, schizophrenic patients show consistently smaller P3 amplitudes than healthy controls (e.g., Jeon and Polich, 2003); however the effect may be partly accounted for by different extents of latency jitter as patients also show larger reaction time variability (Ford et al., 1994; Röschke et al., 1996; Roth et al., 2007). Such ambiguities may pervade any study where differences between conditions or population samples are confounded with different degrees of latency jitter, for example aging or brain damage (Fjell et al., 2011; Patterson et al., 1988; Walhovd et al., 2008). In principle, all amplitude variations in average ERP waveform across conditions are mixtures of true amplitude variations and different extents of latency jitter. As we will demonstrate, if strong enough even identical amounts of latency jitter across conditions may suppress

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true condition effects in amplitude. Therefore, it is imperative to investigate the effects of latency jitter and to find ways of correcting for it. The mixing problem and its solution are still under-explored probably because tackling this issue requires handling highly noisy single trial ERP signals.

Notably, in addition to trial-to-trial latency jitter, there are other causes of ERP waveform blurring, for examples, volume conduction, trial-to-trial variability in amplitude and morphology, inter-individual variability, etc. The present report exclusively addresses the blurring problem due to trial-to-trial latency jitter, first on a theoretical level and then by suggesting a solution based on a novel application of residue iteration decomposition (RIDE; e.g., Ouyang et al., 2015b).

1.1. The consequences of latency jitter in ERPs

ERPs are obtained by averaging many epochs – typically 30 to 60 – of EEG from single trials, assuming that the stimulus- or response-related signal embedded in the EEG is identical from trial to trial but that background noise varies independently of the signal around a mean of zero across trials. But in fact, ERP components may strongly vary in latency across trials, as recognized by ERP researchers for a long time (e.g., Jung et al., 2001; Kutas et al., 1977; Leuthold and Sommer, 1998; Pfefferbaum et al., 1980; Verleger, 1997; Woody, 1967).

The trial-to-trial latency variability of ERP components may have two major consequences on condition effects, as illustrated in Fig. 1. Firstly, (Fig. 1, Case 1) trial-to-trial latency variability blurs the waveforms, attenuating both ERP component amplitudes and amplitude differences between conditions. The reduced amplitude differences may not be large enough to outweigh the noise, diminishing the size of experimental effects and statistical test parameters.

As a second consequence different extents of latency variability across conditions may mimic amplitude effects in ERPs (Fig. 1, Case 2). If conditions with identical amplitudes differ in variability of single trial latencies, the average ERP will show amplitude differences across conditions that might become statistically significant. In this case, amplitude differences may be erroneously attributed to different strengths of activities generated by the underlying neural systems rather than to different degrees of temporal variability of the neural activities across single trials.

In reality, between-condition ERP differences might be affected by a combination of both cases. This problem could lead to the erroneous conclusions that there is an amplitude difference when there is only a difference in latency variability or that there is no amplitude difference, when latency variability obscures a true amplitude effect. Therefore it is highly desirable to solve the ambiguities caused by latency variability.

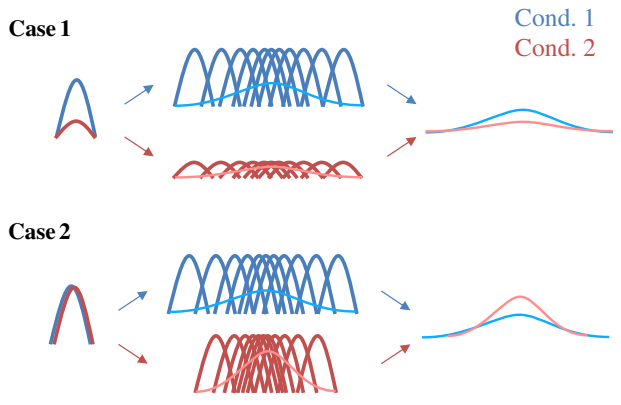

Fig. 1. Illustration of the smearing effect by trial-to-trial latency variability. The blue and red sinus half-waves represent ERP components from two conditions for different cases. Case 1: Two components show the same latency variability but differ in amplitude. The amplitude difference in the average ERPs for two conditions (red and blue) is diminished by trial-to-trial latency variability. Case 2: Two components are the same in amplitude but differ in trial-to-trial latency variability, mimicking an amplitude difference between condition averages.

1.2. Previous attempts

Although the problem of latency jitter in ERP data has been long recognized (Kutas et al., 1977; Woody, 1967), as explained next, a satisfactory solution to the problem has not yet been established. In the following we will briefly review previous suggestions to solve the latency jitter problem and their limitations.

A traditional approach to tackle trial-to-trial latency variability is response-locked averaging, with the idea that late ERP components, blurred in stimulus-locked averaging, will come out more clearly when synchronized to the response. While this assumption is true for response-related components, response-locking has several limitations: 1) It compromises the stimulus-locked components (Fig. 2). 2) There may be components that are neither locked to stimulus onsets nor to RTs, which would be smeared by both stimulus and response locking. 3) A great number of experiments do not require immediate responses or any responses, which precludes response-locked averaging. In this case, an alternative method, latency-locked averaging, is to average single trial ERP to the estimated latencies of a dominant component, for example, the P300 (Ahmadi and Quiroga, 2013; Woody, 1967; Tuan et al., 1987). This approach, however, still suffers from the above limitation since ERPs are not solely composed of a unitary dominant component or component cluster but are rather composed of multiple component clusters with varying inter-component delays (Hansen, 1983; Jung et al., 2001; Verleger, 1997).

Concisely speaking, stimulus-locked, response-locked, or abovementioned latency-locked averaging schemes share the same property of increasing the resolution of a certain component by sacrificing the resolution of other components (Fig. 2), which Poli et al. (2010) metaphorically termed magnifying-glass effect. These authors proposed a reaction-time binning method in order to partly avoid the magnifying-glass effect and suggested to average single-trial ERP from bins with similar RTs. They separated single trials into three bins, each with 30% of the trials after discarding 10% of the trials on the long tail of the RT distribution. Although this procedure is likely to improve the ERP components, the smearing effects are still present due to the spread of RTs, especially in Bin 1 and 3. The results did show that the temporal resolution of ERP in each bin was increased, especially in Bin 2 where RT jitter around the most probable RT value was relatively small. However, by discarding many trials, only part of the data was analyzed, that is, a great amount of information was lost. Since trials with long reaction times were discarded, effects that might be exclusively localized in slow responses might have been diminished. For example, the so-called worst performance rule (Larson and Alderton, 1990) shows that general intelligence is better reflected in the extreme responses (for a review, see Coyle, 2003). In addition, the RT-binning method requires large trial numbers and the analysis is limited to datasets with recorded RTs.

Jung et al. (2001) applied independent component analysis (ICA) to single trial ERP data and identified some independent components (ICs) that seem to have variable latency and correlate with RT. This approach requires to evaluate and select the ICs with variable latency. Since ICA can separate a great number of components (the same as the number of electrodes), there is a large cluster of ICs that are not easy to classify as being locked to the stimuli or RTs, or neither. Clear and applicable criteria are missing for the selection of the ICs.

Another class of methods dealing with trial-to-trial variability is the time marker-based separation of ERP components based on the assumption that ERPs exclusively consist of marker-locked components (Hansen, 1983; Knuth et al., 2006; Yin et al., 2009; Zhang, 1998; Takeda et al., 2008). The markers refer to external events such as stimulus onsets, response times or other cues. Although implemented by different algorithms, there is a common theory underlying these methods – the General Linear Model in which the markers serve as