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INTER-TRIAL PHASE SYNCHRONISATION IN THE ERP DELTA BAND ACCOUNTS FOR DIFFERENCES IN ODDBALL P300

Thang Nam Hoang, Wael El-Deredy, Paulo J. G. Lisboa and Francis Mcglone*

School of Computing and Mathematical Sciences, Liverpool John Moores University, Liverpool L3 3AF, UK
***Centre for Cognitive Neuroscience, University of Wales, Bangor LL57 2DG, UK**

Correspondent: Thang Nam Hoang
Tel: 44-(0)-151-231-2188, Email: hoangnamthang@yahoo.co.jp

Abstract
In a visual oddball reward conditioning task, we demonstrate that changes in the distinctive late positive event related brain potential (P300) can be attributed to differences in phase synchronisation in the delta band of the electroencephalogram, detectable by single trial analysis, where responses to rewarding stimuli exhibit consistent inter-trial phase synchronisation. Consequently, the mean latency of the P300 peak, estimated from the single trials, is significantly different from the latency of the averaged signal, and the distribution of the latencies affects the amplitude of the average. Our result strengthens the suggestion that P300 results from phase oscillation of ongoing EEG and emphasize the importance single trial analysis for investigating brain dynamic.

INTRODUCTION

The basic premise in conventional analysis of scalp recorded brain potentials is that each stimulus presentation evokes a time locked response whose temporal pattern is identical across repeated presentation of this stimulus such that averaging across trials reveals a noise-free signal with distinctive event related components (Rugg and Coles, 1995). An alternative view suggests that the observed components in the EEG average emerge as a result of synchronisation between the otherwise random ongoing oscillatory activities in different frequency ranges due to stimulus presentation and processing (Basar et al., 2001; Makeig et al., 2002). In the former view, latency variations between trials are treated as jitter that requires counteracting in order to re-align the trials (Mocks et al., 1988), whilst in the latter view these variations are means to explore cortical dynamics (Delorme et al., 2002; Penny et al., 2002; Varela et al., 2001).

This study aims to characterize and distinguish the emotional response of subjects under monetary reward or penalty conditions, on the basis of modulation to the P300 of oddball single trial ERP. The P300 is the most studied ERP recorded at the surface of the scalp because of its amplitude (5-20 μV) and the ease by which it is elicited. The signal consists of a positive deflection (0-4 Hz) that is maximal over parietal/central areas with latency between 300-900 ms, and represents a widely distributed system. It is evoked by the presentation of infrequent visual events to the human subject and is seen, in part, as a context updating (or a novelty detector) while its latency is considered a marker of stimulus evaluation time(Rugg and Coles, 1995).

Here we investigate the manifestation of monetary reward processing on event related brain potentials (ERP) using conditioning to assess the extent to which reward modulates known cognitive markers. One of the most studied ERP signals is the P300: A late positive potential occurring 300-600 ms post stimulus and dominated by delta band oscillations (0.5 – 4Hz). Recorded by Sutton et al in 1965 (Sutton et al., 1965) in response to stimulus uncertainty, it was later found to contain several components which vary under different sensory, cognitive and affective conditions (Begleiter et al., 1983; Polich and Kok, 1995). The P300 is used clinically as a marker for cognitive efficiency in aging, dementia and neurological and psychiatric disorders (Polich and Herbst, 2000). We demonstrate, using a monetary reward-conditioning task, that the oddball P300 differences between conditions can be attributed to

changes in inter-trial phase synchronisation in the EEG delta band detectable by single trial analysis.

EXPERIMENTAL PROTOCOL

We evoked the P300 using standard oddball paradigm with one frequent (prob. 5/7) and two rare (prob. 1/7 each) visual stimuli of abstract nonsense shapes (**Figure 1**). Three blocks of data were recorded. In the first block subjects were instructed to count the rare stimuli (subjects less than 90% accurate were excluded from the study). In the second and third blocks (the conditioning blocks) we modulated the P300 response by instructing the subjects that they would receive a monetary reward each time one of the rare stimuli appeared and lose money if the other rare stimulus appeared. The frequent stimulus was neutral, no win or lose. No other feedback was given and no response was required. Between the second and third block subjects were given a break when a verbal feedback of their earnings was provided. All subjects had positive earnings. The local ethics committee approved the protocol and subjects were debriefed after the experiment.

Data were collected from 11 subjects. Continuous EEG was recorded (bandpass 0.1–40 Hz, sampling rate 500 Hz, Synamps amplifiers © Neuroscan, impedance below 5 kΩ.) from the 18 scalp locations (10-20 system) referenced to linked earlobes using Ag/AgCl electrodes attached to the scalp by an electrode cap. Vertical and horizontal electrooculograms were recorded and used to remove eye movement artefacts.Analysis result using conventional averaging technique

The grand averaged ERPs of all subjects in each of 3 blocks are shown in **Figure 2.** From this figure, the conclusions drawn would normally be as follows:
In the 1st block, when subjects are naïve to 'reward' or/and 'penalty' factor, the latency of P300 in both condition are around 340 ms. In the 2nd and 3rd blocks, the averaged ERPs signal increases in amplitude, with longer latency (around 450ms for 'reward' condition and 530ms for 'penalty' condition). By comparing the distribution of latency and amplitude of P300 in single trial ERPs, we will show evidence indicating that the apparent increase in the amplitude of the averaged ERP is in fact an a by product of synchronisation of ERP latencies in the reward condition.

Figure 1: Example of abstract shapes used as visual stimuli. There were sixteen variants from each stimulus, including rotations and mirror images. Subjects were shown the stimuli before recording and tested on recognising and categorising them. The frequent stimulus set was the same in all experiments. In the conditioning blocks half the subjects received a monetary reward each time Rare 1 appeared and lost a similar amount when Rare 2 appeared. For the other half, the reward and penalty stimuli were reversed. Each stimulus measured 4cm x 4cm and was displayed for 100 ms followed by a fixation point for 1000-1200ms. The actual stimuli displayed were white on a black background (i.e the negative image of what is shown here)**.**

ANALYSIS METHOD

A Meyer wavelet bandpass filter (0~4Hz) was used to filter the delta band activity from the single trials ERPs. Meyer wavelets have the advantage of being defined in the frequency domain and hence are appropriate for tuning to desired EEG bands (Goswami and Chan, 1999). The latency of this filtered ERPs by looking at timing of the maximum positive peak of the signal between 250 and 1000ms timing (**Figure 3**).

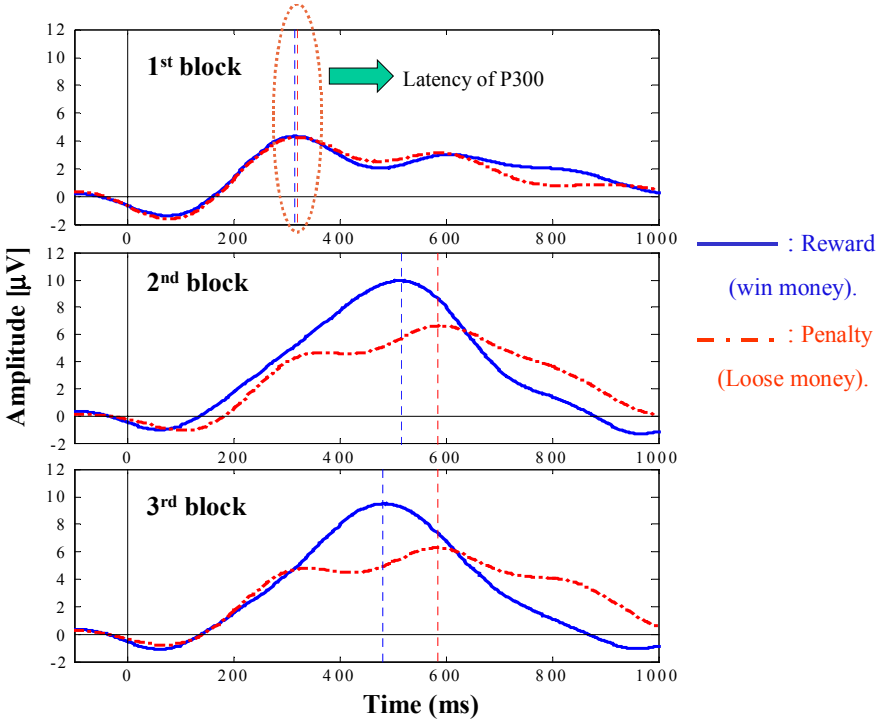

Figure 2: Grand averaged of ERPs (filtered) signal at Pz. Blue and red vertical dotted line in each graph shows the latency (timing of peak) of P300 peak of each averaged ERP signal. The graph shows that the latencies of both 'reward' and penalty condition move to the right in 2nd and 3rd blocks. However the latency of 'penalty' condition move further to the right than the latency of 'reward'. This type of conclusion is typical for traditional analysis of averaged ERPs.

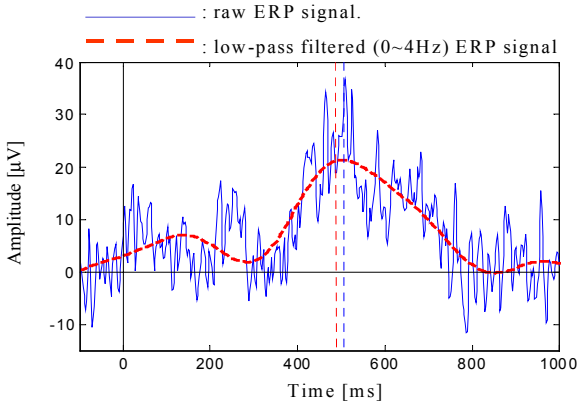

Figure 3: Calculating the latency of delta response from single trial ERPs. The latency is taken to be that of the positive peak in the interval 250-800 ms post stimulus. The vertical dotted lines show the location of the positive peak of raw ERP signal (blue) and filtered ERP signal (red).

RESULTS

The joint amplitude-latency histogram in **Figure 4** shows that the significant difference ($p < 01$) between reward and penalty is attributed to a larger number of trials in the rewarding condition being phase synchronised with peaks around 540 ms. Stimuli before conditioning and from the penalty condition remained broadly distributed across the epoch duration. Therefore, the apparent increase in the Oddball P300 amplitude in the average ERP cannot be solely attributed to an increase in amplitude of P300. Furthermore, there is a discrepancy between the latency of the ERP average and the average latency of the single trials, significant ($p < 0.02$) in the case of the reward condition. Most analysis of P300 latency misses these variations in the single trials by imposing a windowed filter to re-calibrate the trials. **Figure 2 & 4** suggest that the amplitude and latency of the averaged ERP depend on the distribution of latencies of the single trial and that phase synchronisation may be a key property of this distribution.

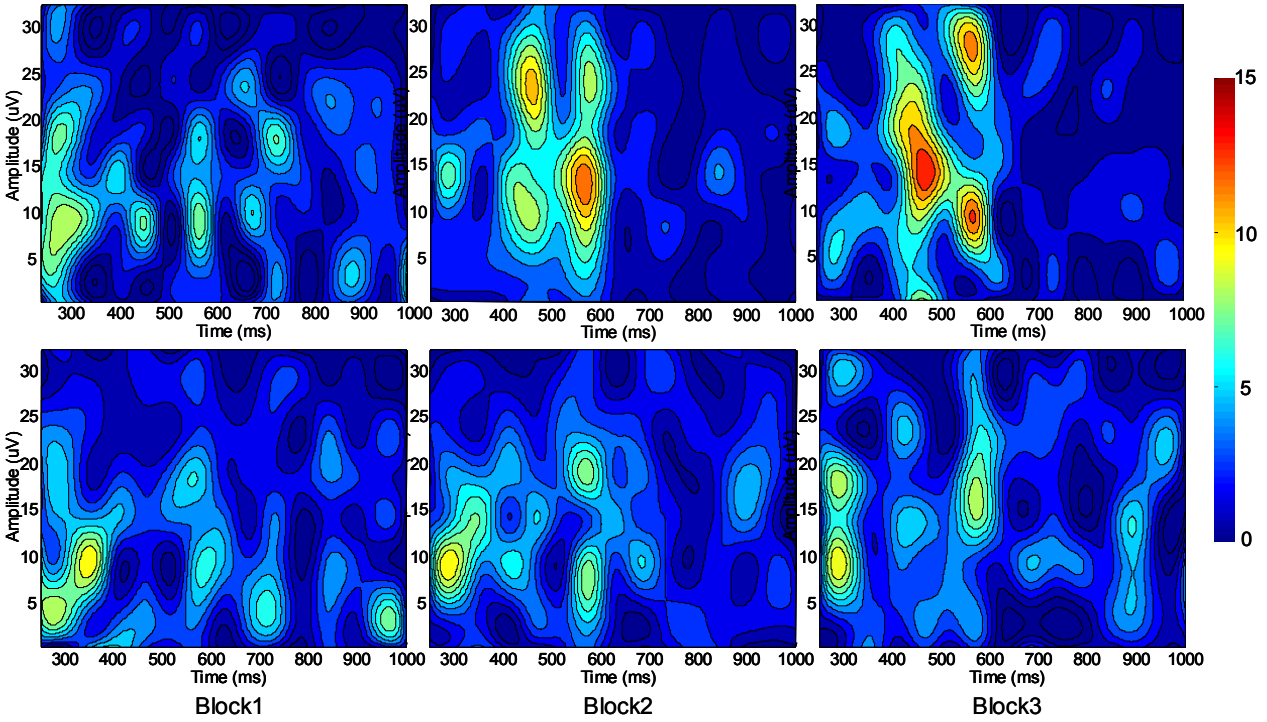

Figure 4: Amplitude-Latency histograms of peak delta oscillations in reward (top) and penalty (bottom) single trial ERPs, before conditioning (Block1) and during two conditioning blocks (Block2&3). The colour bar scale is frequency of occurrence. Latencies of the peak delta of the rewarding trials are highly synchronised (this is in addition to the significant increase in the amplitude following the motivational instructions about the reward and penalty). The synchronisation increases from blocks 2 and 3 when subjects are given a feedback about their reward value.

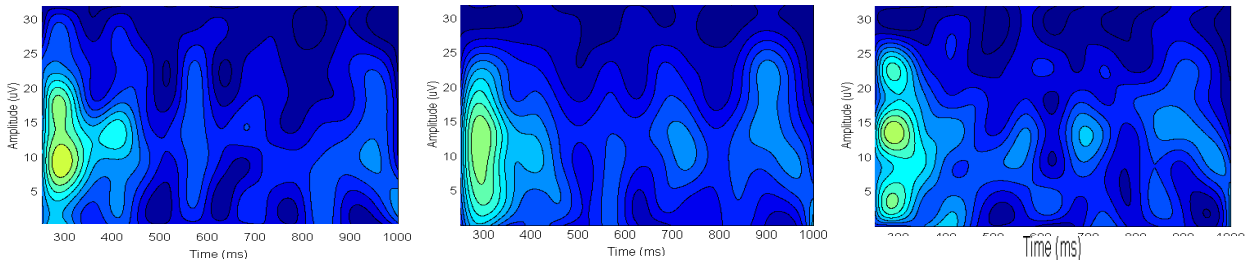

Figure 5: Amplitude-Latency histograms of peak delta oscillations of the frequent stimulus (prob. 5/7) trials at Pz, before conditioning (left) and during the two conditioning blocks (centre and right). The figure shows that the amplitude and latency of the delta band due to the frequent stimulus are not altered as a result of the introducing the monetary reward or penalty. This suggests that the changes in fig. 3 are specific to the stimuli incentive rather than to an overall change in brain state due to the change in the experimental conditions introduced by the monetary incentive and the difference is a direct result of the conditioning. Because of the difference in the number of trials between the rare and frequent stimuli, the colour bar (frequency of occurrence) has been calibrated to the same range as the rare stimuli for consistency (Figure 3).

The increase in processing ability may be argued to have resulted from a general state of arousal or awareness induced by the motivational instructions (Carrillo-de-la-Pena and Cadaveira, 2000), and consequently in the increased amplitude and phase synchronisation. In which case, heightened arousal, as global state, would be expected to have an effect on the processing of the frequent (neural) stimuli as well. However, in this experiment, neither the distributions of the amplitudes and the latencies in response to the frequent stimulus nor their joint distribution changed between the three blocks (**Figure 5**). This suggests that the observed change in response to the rare stimuli (**Figure 2 & 4**) is due to the relative affective saliency of the stimuli themselves created by reward/penalty conditioning. Interaction between attention and affect (Dolan, 2002) may explain the increased amplitude and the latency synchronisation. Attention, known to increase P300 averaged ERP, has been shown to increase synchronised activities in the alpha and gamma (Herrmann and Knight, 2001) bands of the EEG – here we show that it enhances synchronisation in delta band as well.

Figure 6 shows the sorted latency of single trial from the subject, who has the strongest synchronisation activity. The variation of the degree of synchronisation between subjects may result from the different in individual emotion response to the experiment stimuli.

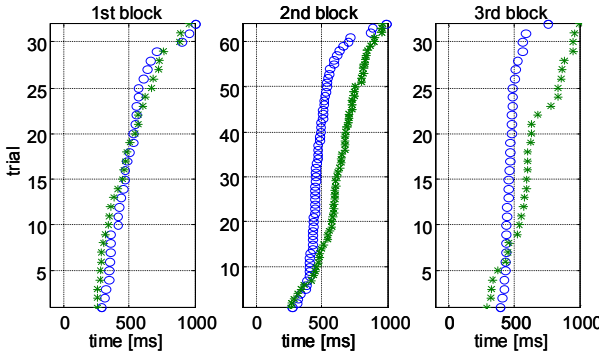

Figure 6: Example of results.. X-axis: time (ms); Y-axis: index of sorted trials. 'o': latency of single trial ERPs at Pz in 'reward' condition; '*': latency of single trial ERPs at Pz in 'penalty' condition. The latencies of 'reward' condition are more synchronised around 500 ms, compare to the latencies of 'penalty' condition.

CONCLUSION

Although oddball P300 has been associated with synchronised alpha and theta oscillations, synchronisation of the delta band, the main constituent of the P300 signal, has been hypothesised (Schurmann et al., 2001) but not previously demonstrated. If latency synchronisation of the single trials, here demonstrated by reward conditioning, proves to be a general feature of the P300, a new clinical utility, additional to the standard averaged P300 analysis, may be provided. We may then argue that reduced averaged P300 in dementia, Parkinson disease and alcoholism (Polich and Herbst, 2000), for example, may be due to reduced synchronisation and not solely due to reduced activation – all three conditions are also associated with attentional decline (Sarter and Turchi, 2002; Schulte et al., 2001).

Latency synchronisation reveals that the amplitude and latency of the averaged ERP are not independent attributes. Therefore, averaged ERP can no longer be regarded as a noise free version of a time locked ERP – but a result of systematic perturbations in the single trials. Here the amplitude of the average depended on the distribution of the latencies in the single trials. Consequently, it cannot be used directly for dipole source localisation. Other methods (Makeig et al., 2002) may be necessary to extract the activation sources from single trials prior to finding the spatial inverse solution and unravelling brain dynamics.

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