



# Increased event-related potential latency and amplitude variability in schizophrenia detected through wavelet-based single-trial analysis

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## Background

Intra-individual variability on reaction time tasks is increased in patients with schizophrenia (van den Bosch et al 1996). These findings can be linked to the concept of increased cortical noise, which however provides little information on the temporal dynamics of neural processing during task performance (Winterer et al 2004). A more direct link to the underlying brain dynamics can potentially be established by examining variability in single trial ERPs (Jung et al 2001). For this purpose we developed a method for analyzing single-trial event-related potentials based on a wavelet smoothing algorithm. Since the P3 component has been most consistently reported to be abnormal in schizophrenia we focussed on latency and amplitude variability of this component in an auditory Go/Nogo task (Weisbrod et al 2000).

## Methods

Since signal-to-noise ratio in single trials is often very poor and single trial peaks are often difficult to detect, we used a wavelet based denoising algorithm (see Figure 1). The wavelet transform allows a real time-frequency decomposition of the input signal, which has the advantage of studying the signal course over time independently for specific frequency bands (Samar et al 1995). We identified the frequency bands, which preserved most of the signal energy and then located the local maxima along with their latencies. This procedure corresponds to wavelet denoising with hard thresholding, i.e. wavelet coefficients other than belonging to the delta or theta band were set to zero and subsequently backtransformed to the time domain.

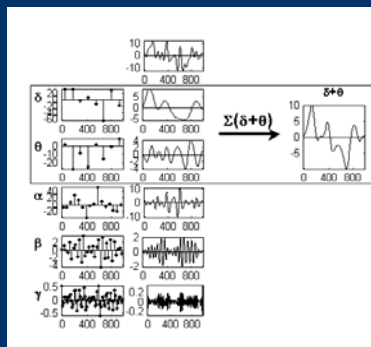


Figure 1:

Instance of a Multiresolution Analysis showing the wavelet decomposition in terms of the different frequency bands and coefficients. The original signal is shown at the uppermost panel in the second column. Left column shows the wavelet coefficients, i.e. the correlation of the chosen mother wavelet with the signal time course at the corresponding timepoint. The middle column shows the reconstructed signal reflecting the time course of the signal in the respective frequency band. Delta and theta band are marked by a box, because they were used to reconstruct the single-trial signal. This summarized signal is shown on the right hand side.

This method was applied to data from schizophrenic patients and healthy controls in an auditory Go/Nogo task. Patient and control groups were matched for age, gender and years of education. All patients received neuroleptic medication. The uncued Go/Nogo task we used was a modification of the auditory oddball paradigm. Subjects heard frequent low-pitched and rare high-pitched tones. In the Go task, a response to rare tones was required using a mouse-button. In the Nogo task, subjects responded to the frequent tones and had to withhold the response to the rare tones.

## Discussion

The application of a new wavelet denoising method to single trial ERPs revealed two distinct patterns of instable cortical processing in patients with schizophrenia. First, amplitude variability is increased at Pz, a finding which has been previously reported by Ford and colleagues, who used a Woody filter to analyse single trial ERPs (Ford et al 1994). Second, latency variability of P3a was increased at Fz. In functional terms this component most likely corresponds to the information processing stage of stimulus selection (Dien et al 2004). These findings complement previous reports on increased cortical noise in patients with schizophrenia by demonstrating instability of a precise ERP component. In addition, we find task performance to correlate with frontal latency variability, which suggests that an instability of prefrontal information processing contributes to the impaired performance in patients with schizophrenia.

## References

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## Results

Schizophrenic patients showed an increased reaction time variability as indexed by the individual standard deviation in the Go ( $F(1,30)=7.7, p<0.01$ ) as well as in the Nogo condition ( $F(1,30)=9.2, p<0.01$ ).

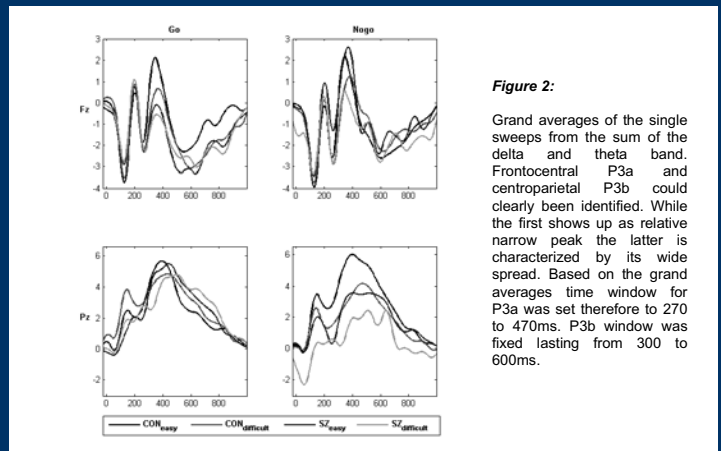


Figure 2:

Grand averages of the single sweeps from the sum of the delta and theta band. Frontocentral P3a and centroparietal P3b could clearly be identified. While the first shows up as relative narrow peak the latter is characterized by its wide spread. Based on the grand averages time window for P3a was set therefore to 270 to 470ms. P3b window was fixed lasting from 300 to 600ms.

The task reliably elicited a frontocentral P3a peak and a centroparietal P3b peak (see figure 2). Mean latencies for these components did not differ significantly between groups. In the next step we applied the wavelet denoising algorithm to single-trial ERPs and assessed single trial latency. Groups did not differ significantly in the number of single trials retained for further analysis. Group differences in single trial variability were assessed in a linear mixed model.

		Control	Schizophrenia	F	p
Fz	Go	46.5 (5.95)	50.8 (5.91)	$F(1,30) = 6.51$	<b>0.016</b>
	NoGo	46.7 (7.95)	50.6 (7.06)	$F(1,28) = 6.24$	<b>0.034</b>
Pz	Go	78.7 (8.66)	78.9 (8.68)	$F(1,30) = 0.02$	0.90
	NoGo	80.1 (11.29)	80.9 (10.66)	$F(1,30) = 0.063$	0.80

Table 1: Main effects of latency variability of maximum amplitude in ms

We found a significant increase of P3a latency variability in the schizophrenic subgroup at electrode Fz (frontal midline) in both conditions (see table 1). Latency of P3b at electrode Pz (parietal midline) did not differ significantly between groups. In contrast, P3a amplitude variability at Fz did not differ between groups, while amplitude variability at Pz was increased in patients with schizophrenia (see table 2).

		Control	Schizophrenia	F	p
Fz	Go	4.64 (2.09)	5.13 (1.84)	$F(1,28) = 3.20$	0.085
	NoGo	4.86 (1.73)	5.70 (2.00)	$F(1,29) = 2.01$	0.167
Pz	Go	4.99 (1.07)	6.94 (1.70)	$F(1,25) = 13.59$	<b>0.0011</b>
	NoGo	5.47 (1.62)	7.08 (2.52)	$F(1,28) = 7.36$	<b>0.011</b>

Table 2: Main effects of amplitude variation in V

There was a significant correlation between latency variability at Fz and error rate in the Go condition (Control  $r=0.38, p<0.05$  and Schizophrenia  $r=0.41, p<0.05$ ). There were no significant correlations between any of the variability measures and reaction time variability.