Habituation and sensitization in rat auditory evoked potentials: a single-trial analysis with wavelet denoising

R. Quian Quiroga\textsuperscript{a,*}, E.L.J.M. van Luitelaar\textsuperscript{b}

\textsuperscript{a}John von Neumann Institute for Computing, Forschungszentrum Jülich, D-52425 Jülich, Germany
\textsuperscript{b}Department of Comparative and Physiological Psychology, Nijmegen Institute of Cognition and Informatics, University of Nijmegen, Nijmegen, The Netherlands

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Abstract

In this work, systematic changes of single-trial auditory evoked potentials elicited in rats were studied. Single-trial evoked potentials were obtained with the help of wavelet denoising, a very recently proposed method that has already been shown to be useful in the analysis of scalp human evoked potentials. For the evoked components in the \textsuperscript{13–24}-ms range i.e. P13, N18, P20 and N24, it was possible to identify slow exponential decreases in the peak amplitudes, most likely related to a slow habituation process, while for N18, an initial increase in amplitude was also found. On the contrary, the slower components (N38 and N52) habituated within a few trials, and we therefore propose that they are related to a different functional process. The outcomes of the present study show that wavelet denoising is a useful technique for analyzing evoked potentials in rats at the single-trial level. In fact, in the present study it was possible to obtain more information than the one described in previous related works. This allows the study of other forms of learning processes in rats with the aid of evoked potentials. Finally, the outcomes of this study may have some relevance for the comparison of human and rat evoked potentials. © 2002 Elsevier Science B.V. All rights reserved.

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1. Introduction

Sensory evoked potentials represent the activity of large groups of neurons or neural ensembles closely synchronized with stimulus events (Swick et al., 1994). They usually have a low amplitude in comparison with the background EEG, and therefore, ensemble averaging of EEG segments time-locked to the stimuli has been used to visualize the evoked responses. The averaged evoked potentials consist of a series of positive and negative waves, which are often identified by their latency from stimulus presentation. Averaging accomplishes a reduction in the number of data, as well as an increase in the signal-to-noise ratio. However, ensemble averaging assumes that each response contains a background EEG acting as an additive stationary noise, contaminating a time-

* Corresponding author.
E-mail address: r.quianquiroga@fz-juelich.de (R. Quian Quiroga).

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locked and invariant response independent of the ongoing EEG. These assumptions are, in a strict sense, not valid (see e.g. Basar, 1980). In fact, one fundamental characteristic of evoked potentials is their change from trial to trial; this information being lost in the averaged evoked potentials.

Amplitude and latency trial-to-trial variability in the components of an evoked potential can be either systematic or unsystematic. Systematic changes in response strength to repeated stimulation is a key property of all organisms with a nervous system. New stimuli first elicit an orchestrated response, named the orientation response (Sokolov, 1960). It consists of changes in a large number of autonomic variables, such as the skin conductance reaction phasic heart rate changes, and it also involves a reaction at the cerebral cortex. Habituation is, in a wide sense, defined as a response diminishment as a function of stimulus repetition and it is a constant finding in almost any behavioral response. It can be best described by an exponential decay if a single novel stimulus is repeated regularly (Sokolov, 1960). Its rate of decay will depend on physical properties of the stimulus, on the interstimulus interval and on the psychological impact of the stimulus, such as its relevance. Also, increases in the responses during the first stimuli have been described, these being related to a sensitization process (Thompson and Spencer, 1966; Groves and Thompson, 1970). Moreover, these authors proposed that response to repeated stimulation is the interaction of sensitization and habituation.

In order to study these systematic changes over time, recording sessions were subdivided into (consecutive) sets of averages of a few trials, namely sub-ensemble averages. This approach is successful only if changes within trials are much slower than the number of trials included in each sub-average. Another approach to study single-trial changes is to repeat a sequence (block) of trials, each sequence elicited after a certain recovery time. Then, single-trial changes (within a block) can be better visualized from an ‘average block’ of trials. This second method, which we will call ‘block-averaging’, assumes that changes between blocks are negligible, a requirement that is not always fulfilled. Moreover, both sub-ensemble and block-averaging require long recording sessions, and thus general arousal changes are likely to occur. Despite these drawbacks, there are quite a number of studies which demonstrate within-session changes of midlatency or late EP components in humans (Davis et al., 1966; Ritter et al., 1968; Fruhstorfer et al., 1970; Groves and Thompson, 1970; Calloway, 1973; Polich, 1989; Lew and Polich, 1993; Polich and McIsaac, 1994; Boutros and Belger, 1999; Carrillo-de-la-Pena and Garcia-Larrea, 1999) and in rats (Hall, 1968; Herr et al., 1994; Miyazato et al., 1994, 1996, 1999; Boutros et al., 1997). While investigating habituation of the vertex auditory evoked potentials, sub-ensemble averaging in rats was recently applied (de Bruin et al., 2001). With sub-ensembles of only five trials, an indication was found that habituation occurred for two components: the P17 showed a rapid (between trials 6–10 and 11–15) and significant decrease in the amplitude and the N22 also showed a slower but significant decrease. Other changes within the first 100 trials remained unnoticed. As we will show in the present study, more information will be obtained by means of single-trial analysis. Although several methods have been proposed for the analysis of single trials of the evoked responses (see a review in Lopes da Silva, 1993), up to now, none of these attempts has been successful, at least at a level that they could be applied to different type of EPs and be implemented in clinical settings (Quian Quiroga, 2000).

A method based on the wavelet transform, namely wavelet denoising, has recently been described and successfully applied to the analysis of scalp human EPs (Quian Quiroga, 2000). It allowed the visualization of single-trial responses and a further quantitative analysis of their variability, something quite difficult to achieve from the original data. The objective of this study was to apply wavelet denoising to the study of auditory single trial EPs elicited in rats in the data set from de Bruin et al. (2001). In particular we will show changes in the evoked responses during the recording session, these being related to habituation and sensitization processes.
2. Methods

2.1. Subjects and data recording

Auditory evoked potentials (AEPs) were obtained from 13 adult male albino rats of different genetic origin (four random-bred Wistar, four APO-SUS, two APO-UNSUS, and three WAG/Rij rats). Rats were 6 months old and weighed 395 (± 17) g. They were maintained on a 12-h light–dark cycle with white lights on at 07:00 h. They had ad lib access to standard food and tap water. Animals were treated in accordance with the ‘Principles of Laboratory Animal Care’ (NIH) and institutional guidelines.

Under pentobarbital anesthesia (60 mg/kg) two tripolar electrodes sets were implanted in the animals. The first two electrodes of the first set were placed at the frontoparietal cortex and the striate cortex (area 17) with coordinates A 2.0, L 3.5 and A –6.0, L 4.0 respectively, and skull surface flat and bregma zero, zero. The first electrode of the second set was aimed at the vertex (the polysensory region), placed 1 mm to the right of the central suture (L 1.0 mm), midway between bregma and lambda, skull surface flat and bregma zero, zero. The other two electrodes of the second electrode set were used as reference and ground electrodes and were placed in the cerebellum. Differential recordings were made between frontoparietal and striate cortex and between vertex and cerebellum. Coordinates are according to the atlas of Paxinos and Watson (1982). Three screws and dental acrylic cement were applied to secure the electrodes to the skull surface. The animals were allowed to recover from surgery for 2 weeks. In this study, only the vertex evoked potentials will be described.

Double-click auditory stimuli (95 dB, duration of 1 ms, inter-stimulus interval 500 ms, intertrial interval was varied between 5 and 10 s) were presented with a loudspeaker at 90 cm above the rats’ cage. Auditory evoked potentials were registered at a sample rate of 1024 Hz., the high pass filter was set at 1 Hz and the low pass filter at 500 Hz. The EEG was amplified, digitized, monitored and stored for an off-line analysis using a WINDAQ system.

During the 3 days before EEG recordings were made, rats were handled daily. The rats were connected to dummy EEG leads 12 h before starting the recordings in order to adapt to the recording conditions. The experiment was performed in freely moving animals that lived in a Plexiglas recording cage. Animals were placed with their recording cage in a Faraday cage and were exposed to background white noise (70 dB) for 2 h. The behavior of the animals during the EEG recording session was observed through a window of the Faraday cage and scored (behaviorally active or passive) on a separate EEG channel.

Since changes within a train of clicks have been reported elsewhere (de Bruin et al., 1999, 2001), we analyzed here only changes to the first stimuli of each double-click sequence. For each rat, 250 ms pre- and 250 ms post-stimulation of the first 100 trials of the vertex EEG were analyzed. Trials contaminated with artifacts, muscle activity or spike-wave discharges (van Luijtelaar and Coenen, 1986) were eliminated after a visual inspection of the recordings.

2.2. Wavelet transform

Until now, the quantitative method most used for the analysis of EEGs has been the Fourier transform. It gives a useful visualization of the periodicity of the signal in the frequency domain that, however, has two main drawbacks: (1) no time information of the frequencies is given; and (2) signals must be stationary. These problems can be partially avoided by analyzing time-evolving ‘windows’ of data tapered with an appropriate function. This method, the short-time Fourier transform, gives a convenient time–frequency representation, which however, has a critical limitation due to the uncertainty principle of signal analysis (Chui, 1992): If the data window is too short, the frequency resolution will be poor (i.e. there will be not enough oscillations to define a frequency precisely) and if the window is too large, then the time localization will be less precise. In other words, sharp time- and frequency-localizations are mutually exclusive and they have a limit called the ‘optimal’ time–frequency reso-
olution. Data involving slow frequencies will require wide windows, and for data with high frequencies, a narrow window will be more suitable. Then, due to its fixed window size (i.e. the same size for all frequencies), the short-time Fourier transform is not optimal for analyzing signals involving different ranges of frequencies.

In recent years, the wavelet transform was introduced in order to overcome this limitation (Grossmann and Morlet, 1984). The main advantage of the wavelet transform is its variable window size (being narrow for high frequencies and wide for slow ones), thus leading to an optimal time–frequency resolution adapted to each frequency range. This is especially important in the case of EPs, where interesting activity usually takes place in a fraction of a second and involves different ranges of frequencies (Quian Quiroga, 1998; Quian Quiroga and Schürmann, 1999). Moreover, since each window contains only a few oscillations, stationarity of the signal is not necessary.

The wavelet transform of a signal \( x(t) \) is defined as the inner product between the signal and the wavelet functions \( \Psi_{a,b}(t) \):

\[
W_x(\phi) = \langle x(t), \Psi_{a,b}(t) \rangle
\]

where \( \Psi_{a,b}(t) \) are dilated (contracted) and shifted versions of a unique wavelet function \( \Psi(t) \):

\[
\Psi_{a,b}(t) = |a|^{-1/2} \Psi \left( \frac{t - b}{a} \right)
\]

where \( a \) and \( b \) are the scale and translation parameters, respectively. In order to avoid redundancy and to increase the efficiency of algorithm implementations, the wavelet transform is usually defined for discrete scales \( a \) and discrete times \( b \) by choosing the dyadic set of parameters \( a^j = 2^{-j} \), \( b_{j,k} = 2^{-j}k \), for integers \( j \) and \( k \). The wavelet transform gives a decomposition of \( x(t) \) in different scales, tending to be maximum at those scales and time locations where the wavelet best resembles \( x(t) \). Contracted versions of \( \Psi_{a,b}(t) \) will match high-frequency components of \( x(t) \), whereas dilated versions will match the low-frequency ones.

2.3. Multiresolution decomposition

The information given by the wavelet transform can be organized according to a hierarchical scheme called multiresolution analysis (Mallat, 1989). This method gives a decomposition of the signal in different levels of ‘details’ (i.e. components in consecutive frequency bands) and a final approximation or ‘residual’ that is the difference between the original signal and the sum of all the details. One main advantage of the multiresolution decomposition is that it can be implemented with recursive and fast algorithms. Moreover, components corresponding to the different frequency bands can be reconstructed by applying an inverse transform.

In this study a five-level decomposition was used, thus having five scales of details \( (d_1-d_5) \) and a final approximation \( (a_5) \). Quadratic bi-orthogonal B-splines (Cohen et al., 1992) were chosen as the basic wavelet functions, due to their similarity to the evoked responses (thus having good localization of the EPs in the wavelet domain), and due to their optimal time–frequency resolution (for more details see Chui, 1992; Cohen et al., 1992; Unser et al., 1992; Quian Quiroga and Schürmann, 1999).

The gray curves in Fig. 1 show the decomposition of the averaged (over 100 trials) AEP of a typical rat. On the left side, the wavelet coefficients are plotted, and the right side shows the actual reconstruction for each scale. The sum of all the reconstructions gives the original signal again (gray curve of the uppermost right plot). The lower levels give details corresponding to the high-frequency components, and the higher levels correspond to the low frequencies.

2.4. Denoising of evoked potentials

The averaged EP shown in the left uppermost plot of Fig. 1 has fast components in the first 30 ms after stimulation and two main slow components at approximately 38 and 52 ms (see also the grand average of Fig. 3). Note that the fast components are localized in the first detail levels \( (d_1-d_3) \), between 10 and 30 ms. On the other
hand, the slower components are correlated with the coefficients of the higher scales ($d_4$, $d_5$ and $a_5$) between 40 and 60 ms. Then, as described by Quian Quiroga (2000), a straightforward way to (partially) avoid the fluctuations related with the ongoing EEG is to set equal to zero those coeffi-
ficients not correlated with the peaks of interest. However, the choice of these coefficients should not be based solely on the average EP; indeed it should also consider the time ranges in which the single-trial EPs are expected to occur (i.e. some neighboring coefficients may be included in order to allow for latency jitters). In this respect, we heuristically chose the best set of coefficients by comparing the outcomes of the denoised single-trial EPs with the raw data. We should remark that the denoising implementation described above does not completely separate between EEG and EP activities, because some ongoing EEG oscillations could appear in the same time range and with the same frequency composition as the EPs.

The black traces in the left side of Fig. 1 show the coefficients kept for the reconstruction of the denoised EPs, and the black curves on the right side show the contributions of each level obtained by eliminating all the other coefficients. According to the characteristics of the EPs previously mentioned, the first coefficients after stimulation were retained for the high-frequency scales, and for the lower frequencies, a wider time range was chosen. Note that for each scale the coefficients selected cover a reasonable time range in which the EPs are expected to occur, thus making the method sensitive to latency variations between trials.

In the final reconstruction of the averaged response (black curve in the uppermost right plot), the denoised signal does not differ much from the original averaged EP. This is because, after an average of 100 trials, background EEG oscillations are nearly cancelled (without need for denoising), but this is not the case at the single-trial level, as we will see in the next section. Once the coefficients of interest are identified from the average EP, the same procedure can be applied to each single trial, thus diminishing the contribution of background activity not related to the EPs (i.e. canceling the activity not appearing in the same time range and with the same frequency composition as the EPs).

In summary, the method consists of the following steps:

1. The averaged EP is decomposed using the wavelet multiresolution decomposition.
2. The wavelet coefficients not correlated with the EPs are identified and set to zero.
3. The inverse transform is applied, thus obtaining a denoised signal.
4. The previous procedure is applied to the single trials.

3. Results

The average EPs of a typical rat, with and without denoising, are shown in the uppermost plots of Fig. 1 and the first 10 single trials corresponding to this average are shown in Fig. 2. The gray traces are the original signals and the black traces the denoised ones. The denoised signals follow the high frequencies of the original signal in approximately the first 30 ms after stimulation. For the later times, where only slow EP components are expected, denoising acts as a low-pass filter.

We remark that the main feature of the wavelet denoising implementation is that the coefficients to be retained are selected from the average EP. Then, only activity phase-locked to the stimulus remains in the average and will therefore be considered as an EP (but we again stress that besides the coefficients correlated with the average EPs, we also keep some neighboring coefficients in order to allow for latency variations between trials). The remaining activity (e.g. in Fig. 2, the high-frequency oscillations appearing after 30 ms, related to the ongoing EEG and changing randomly from trial to trial) will be filtered. We should also remark that a ‘Fourier-based’ low-pass filtering procedure would have removed this activity, but would have also removed the evoked responses of the first 30 ms. In fact, the time–frequency localization of the wavelet denoising is its main advantage over previous methods.

Fig. 3 shows the grand average of the 13 rats. We mainly observe two positive components, at
Fig. 2. Denoising of the first 10 single trials corresponding to the average of the previous figure. Gray and black curves correspond to the original and denoised signals, respectively.

13 and 20 ms, and four negative ones at 18, 24, 38 and 52 ms. For these components, amplitude and latency variations in the first 100 trials were further studied. The amplitude and latency of each peak were automatically defined from the maximum (minimum) value in an appropriate time window. These windows were defined as: P13, 10–15 ms; P20, 17–23 ms; N18, 15–20 ms; N24, 20–25 ms; N38, 30–40 ms; and N52, 40–60 ms. In order to obtain a better visualization, the baseline level of each trial was eliminated. Then, for the first components (P13, N18, P20 and N24), the
mean between 0 and 30 ms was subtracted, and for the later components (N38, N52), the mean between 0 and 100 ms.

For the different EP components identified after denoising, the following two hypotheses were tested:

- H₀: stimulus repetition has no effect on the EP components and a straight line with zero slope best describes changes in EP amplitudes with the trial number.
- H₁: EP peak amplitudes decrease exponentially with the trial number.

Non-linear regression analysis for each rat data, as well as F tests for the goodness of fit, were carried out with the software GraphPad Prism 3.0.
Fig. 4 shows the amplitude variations of the different EP components visualized in the grand average. In the first four peaks, a clear exponential decay of the amplitude with the trial number was observed. Habituation is complete after 30–40 trials, and for the later trials no systematic changes are observed. For these components, hypothesis $H_1$ (i.e. exponential decay) best described the data with a high statistical significance, as seen in Table 1. It was also observed that these components have a similar rate of decay $\lambda$ [with $A(n) \sim e^{-\lambda n}$, where $A$ is the peak amplitude and $n$ the trial number], their differences being of the order of the mean errors. Interestingly enough, for the P13, P20, N24, and most markedly for the N18, it was observed that the response to the first trial
Table 1
Exponential decay rate $\lambda$ for each EP component and the corresponding $P$ value for the goodness of fit (see text for details)

<table>
<thead>
<tr>
<th>Peak</th>
<th>$\lambda$ (S.E.M.)</th>
<th>$P$</th>
</tr>
</thead>
<tbody>
<tr>
<td>P13</td>
<td>0.06 (0.03)</td>
<td>$&lt;0.0001$</td>
</tr>
<tr>
<td>N18</td>
<td>0.09 (0.04)</td>
<td>$0.00011$</td>
</tr>
<tr>
<td>P20</td>
<td>0.07 (0.01)</td>
<td>$&lt;0.0001$</td>
</tr>
<tr>
<td>N24</td>
<td>0.09 (0.02)</td>
<td>$&lt;0.0001$</td>
</tr>
<tr>
<td>N38</td>
<td>1.5 (1.1)</td>
<td>$0.00013$</td>
</tr>
<tr>
<td>N52</td>
<td>$^-a$</td>
<td>$^-a$</td>
</tr>
</tbody>
</table>

*These data were not best described by an exponential decay.

was smaller than the following ones (see Fig. 5). This is likely to be related to a sensitization process. Indeed, a one-way analysis of variance comparing the peak amplitude for the first three trials showed a significant increase for the N18 ($P < 0.05$). Differences in the first three trials were non-significant for the other fast components.

The two slow component (N38 and N52) require a separate analysis. The amplitude changes of the N38 are best fitted by a very fast exponential decay (i.e. within the first five trials). In fact, one-way ANOVA comparison of the amplitudes of first three trials showed a significant decrease ($P < 0.01$, see also Fig. 5). For the N52 peak, a very fast decay was also observed and this decay reached statistical significance when comparing the first three trials (one-way ANOVA, $P < 0.05$). However, the decrease in amplitude of the N52 in the first trials was of the order of baseline fluctuations observed in the later trials, and therefore the data are best fitted by a straight horizontal line rather than an exponential decay.

For all the components, no systematic changes for the latency value were found with trial repetition.

4. Discussion

4.1. Habituation of the evoked responses

Wavelet denoising led to the identification and analysis of several peaks elicited after auditory stimulation in rats, a larger number of peaks than the ones described in previous reports (Boutros et al., 1997; Miyazato et al., 1999; de Bruin et al., 2001). Next, systematic amplitude decreases of the EP components with increasing trial number were observed, these being related to habituation processes. The amplitude changes were best described by a slow exponential decay for the P13, N18, P20 and the N24, the first four peaks. In contrast, the N38 showed a fast exponential decay that turned out to reach the asymptote within a few trials. For the N52 response, the amplitude of the first trial was larger than the following ones, but in this case a horizontal line rather than an exponential decay gave a better fit to the data. Since our findings clearly differentiate the dynamics of the early and late components, we propose that these are related to different functional processes elicited after stimulation.

We also found a small amplitude increase in the first trials for the fast components P13, P20 and N24. This was most marked for the N18, were

![Fig. 5. Amplitude changes of the auditory evoked potentials in the first three trials. Bars denote S.E.M.](image-url)
the fast amplitude increase preceding slow habituation reached statistical significance. Increases of evoked responses preceding habituation have been shown in the flexion reflex in acute spinal cats (Thompson and Spencer, 1966) and in the startle response in rats (Groves and Thompson, 1970), and had been related to a sensitization process. Furthermore, these authors propose that the response to repeated stimulation is the interaction of two independent processes, namely sensitization (amplitude increases) and habituation (amplitude decreases).

With similar data to those used in the present study, de Bruin et al. (2001) already found, with sub-ensemble averages of five trials, an indication of habituation for the P20 and the N24 (in their case named P17 and N22 due to the introduction of a latency correction of +2 ms). Therefore, the present results not only confirm response decrement as a function of stimulus presentations, but they also reveal the presence of habituation for two other peaks and sensitization for one peak in the 13–24-ms domain. Next to the response diminishment of these early components, fast habituation for the N38 and the N52 took place.

A similar result for the P13 component has been reported by Miyazato et al. (1996). These authors showed decreases in the P13 responses using ‘block averages’ (i.e. averages of trains containing several stimuli) of 5–20 clicks, and they further proposed a relation between the rat P13 and the human P50, due to their similar habituation pattern, sleep-state dependency and changes under drug manipulation (Miyazato et al. 1994).

Boutros et al. (1997) described a fast habituation of the N52 (named N40 in their paper) response using block averages of trains of two clicks each. In agreement with these authors, we also observed a rapid decrease within three trials, but they were of the order of the background fluctuation of later trials, and the data were not fitted by an exponential decay. These fluctuations occur rapidly, and therefore it is thought that momentary changes in behavior and vigilance of the animals are responsible for this (Coenen, 1995). Within-session changes of evoked potentials in rats were also observed after visual stimulation. In particular, Herr et al. (1994) studied amplitude changes in the visually evoked after-discharge N160 using seven sub-ensemble averages of 50 trials each. They showed both within-session increases (sensitization) on the first testing days, and within-session decreases (habituation) on later days.

Habituation of evoked responses to repeated stimuli has been also well documented for human studies. Davis et al. (1966) describe habituation of the auditory evoked potentials using block averages of paired tone pips. Similar results were also reported by Fruhstorfer et al. (1970), and more recently by Barry et al. (1993), Carrillo-de-la-Peña and Garcia-Larrea (1999) and Boutros and Belger (1999). Moreover, habituation also seems to exist for the human P300 elicited in the auditory oddball task after a relatively large number of stimuli (Polich, 1989; Polich and Mclsaac, 1994; Lammers and Badia, 1989; Lew and Polich, 1993).

There has been a debate about the equivalence of some of the human auditory evoked or event-related potentials to evoked potentials in the rat (Picton, 1992; Miyazato et al., 1994, 1996, 1999; Molnar, 1994). Evidence from similarities or dissimilarities in their response to different sleep-stages, pharmacological treatments and changes in stimulus properties have been used in this respect. In particular, outcomes of single-trial evoked potentials with wavelet denoising, such as the presence and speed of habituation and sensitization of the different components, can play a role in the debate about equivalency of human and rat evoked potentials.

4.2. Single-trial analysis with wavelet denoising

Wavelet denoising allowed a better visualization of the single-trial EPs. We should remark that this is usually difficult to achieve with standard approaches, such as conventional filtering, due to the fact that: (1) EPs are non stationary signals involving different frequencies located at different times; and (2) EPs have components with frequency ranges overlapping those of the ongoing EEG. In this context, the main advantage of wavelet denoising over conventional filtering is that it is possible to select different time-windows for the different frequencies. These
advantages are quite important when analyzing EPs with a low signal-to-noise ratio, as shown by Quian Quiroga (2000) for scalp auditory and visual EPs in humans. In this case, single-trial EPs were hardly recognizable from the original signals, the different components being much more easily identified after denoising. This allowed a quantitative analysis of latency and amplitude variations between trials, as well as the classification of single-trial responses in order to, for example, obtain better averages.

Another standard approach for visualizing within-session changes in EPs is to use subensemble averages or block averages. In the first case, it is assumed that changes between trials are much slower than the minimum number of trials required for identifying the EPs. Indeed, the fact that sub-ensemble averages of five trials were used by de Bruin et al. (2001) explains why fast habituation for the N38 and the N52 and sensitization for the N18 had not been observed. In the case of block averages, changes between the different blocks of stimuli are neglected. Furthermore, both subensemble and block averages require long recording sessions, and general changes in arousal are then likely to occur.

Among an increasing number of studies applying wavelet analysis to EEGs (see reviews in Unser and Aldroubi, 1996; Samar et al., 1995), advantages of wavelets over Fourier-based methods were described in a didactic paper (Schiff et al., 1994) and in an analysis of alpha responses to visual EPs (Quian Quiroga and Schürmann, 1999). The first authors showed its advantages for extracting features of seizure EEGs, such as spikes. In this line of results, Bertrand et al. (1994) showed a better performance of wavelets for the simultaneously filtering of early- and middle-latitude (up to 50 ms after stimulation) averaged auditory EPs.

Finally, we would like to remark that for all the calculations carried out in this study, we kept the same set of coefficients. In other words, once the coefficients are chosen, the method is parameter-free and does not need to be re-adjuted for each case. Furthermore, the method is based on the multiresolution decomposition, the implementation of which with recursive algorithms is even faster than the fast Fourier transform. In conclusion, due to its easy and optimal implementation, wavelet denoising appears to be a very interesting tool for complementing conventional EP analysis in the time domain.

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