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Enhanced re-habituation of the orienting response of the human event-related potential

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Abstract

Previous studies found the amplitude of the orienting response (OR) of the human event-related potential to decrease with repeated stimulus presentations. This decrease has been suggested to reflect short-term habituation and/or long-term habituation, both of which are learning processes. However, this earlier research failed to provide direct evidence supporting this claim. The present study attempted to show that the OR pattern shares one important feature of habituation: an enhanced response decrement across stimulus-presentation blocks (enhanced re-habituation). Participants received four blocks of 25 auditory stimulus presentations and showed an OR decrement both within (short-term habituation) and across (long-term habituation) blocks. Importantly, the OR decreased more rapidly during later than initial trial blocks, suggesting enhanced re-habituation. The latter result supports the notion that the amplitude decrement reflects an elementary learning process.

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Habituation is a reduction in responding to a stimulus with repeated stimulus presentations and has frequently been demonstrated for peripheral, autonomic responses such as heart rate and galvanic skin response (e.g. Ref. [2]). Habituation is considered to reflect an elementary learning process if it is not caused by factors like fatigue, a refractory period, or damage to the sensory system [13]. It can be fast and only temporary (short-term habituation, STH), which is usually observed when stimuli are presented with short inter-stimulus intervals. Additionally, habituation may develop slowly, be relatively long-lived (long-term habituation, LTH) and is found at longer inter-stimulus intervals.

Evidence that this decreasing responsiveness indeed reflects an elementary learning process can be obtained using dishabituation procedures. In these procedures, the 'habituated' stimulus is either presented along with a novel stimulus, or slightly changed, or the context in which the stimulus occurs is altered. These manipulations increase responding to the habituated stimulus [13].

Spontaneous recovery and enhanced re-habituation are

two further phenomena supporting an interpretation of STH and LTH in terms of a learning process. Specifically, if multiple habituation sessions are presented, the response will first recover to some extent at the onset of a new session (spontaneous recovery), and subsequently habituate to a larger extent and more rapidly within each following session (enhanced re-habituation) [13,15].

Decrements in responding to a stimulus with repeated presentations have also been observed for a more central measure, the human event-related potential (ERP). One of the ERP components studied with repeated stimulations is the human orienting response (OR) or P3a component. This component reflects an orienting reaction in response to novel stimuli (e.g. Ref. [6]), may be found in passive listening tasks, and is most positive at frontal to central electrode sites. The more parietally elicited positivity is called the P3b and this component occurs in more complex tasks (e.g. Ref. [6]). In our experiment, we specifically focus on the OR/P3a component, most profoundly occurring at Cz.

Both short-term and long-term effects of the OR/P3a in response to repeated stimulus presentations have been studied. The OR component has shown amplitude reductions with repeated stimulus presentations within a

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passive listening task [1] and a passive oddball task [7]. Furthermore, the OR also shows long-term amplitude decrements in relatively passive paradigms [5,8].

The short-term and long-term amplitude decrements that have been found for the OR/P3a component have generally been called ‘habituation’. Although the reduction of the more autonomic responses such as heart rate indeed have been shown to reflect habituation (e.g. Ref. [15]), to our knowledge, no direct evidence has been collected until now that response reductions that may be observed in ERPs with repeated stimulus presentations reflect habituation. The purpose of the present study, therefore, was to assess whether decreased responding, as reflected in the OR of the human ERP, shows one important feature of habituation, namely enhanced re-habituation. If so, this would constitute an important piece of evidence in favor of the claim that the previously observed OR reductions as a result of repeated stimulation indeed reflect habituation.

Forty-eight healthy students (12 men and 36 women, mean age 22 years) from the University of Nijmegen, The Netherlands, participated in the experiment. They received course credits. The participants were only allowed to take part in the study if they were healthy, did not use medication, and had no psychiatric history. Students who agreed to participate signed an informed consent.

The participants were tested in a sound-attenuating cubicle. A speaker used for presenting auditory stimuli was located to the right of the participant. The auditory stimulus used consisted of a 1 s 1500 Hz, 70 dB pure tone with a 10 ms rise and fall time. Recording of the EEG and the presentation of stimuli were controlled by a standard personal computer. The present experiment was part of a larger study performed at the University of Nijmegen. For reasons unrelated to the present experiment, the cubicle was illuminated for half the participants and dark for the other. As the statistical analysis showed no main effect of illumination, the pooled data of these participants will be reported in this paper.

Silver EEG electrodes (SensorMedics) were placed at the Fz, Cz, and Pz sites (10–20 system), with the right mastoid as reference. Horizontal and vertical eye movements (EOG) were detected from the right eye. Impedance was less than 5 k Ω for all participants. EEG and EOG were filtered between 0.016 and 500 Hz and sampled at 1024 Hz.

The participant received instructions about the duration of the experiment, which was 27 min. The subject was not informed of the purpose of the experiment. Subsequently, the participant was seated in an armchair and was asked to sit as still as possible, with his/her eyes open, during the experiment. During the 27 min session, the 1 s tone was presented 100 times in four blocks of 25 presentations each. The inter-stimulus interval varied randomly between 5 and 10 s. The inter-block interval was 5 min.

In order to determine the amplitude of the single trials, we used ‘wavelet denoising’, a recently proposed method based on the wavelet transform. Wavelet denoising gives a

time-varying filter with excellent resolutions both in time and frequency. This is especially important in the case of ERPs, where interesting activity usually takes place in a fraction of a second and involves different ranges of frequencies [10]. After a wavelet decomposition, filtering is done by reconstructing the signal using only those wavelet coefficients (each one corresponding to a particular time and frequency range) that are correlated with the ERPs and setting the rest to zero. The selection of these wavelet coefficients is based on the wavelet decomposition of the average ERP (see Refs. [9–11] for details). It has been shown that the method significantly improves the visualization of single-trial ERPs in comparison to the original data and in comparison to previous approaches [10].

The amplitude of the OR/P3a component after denoising was defined as the maximum positive amplitude between 280 and 400 ms after stimulus onset.

The number of dependent variables within a block was reduced to six for reasons of statistical simplicity. Because, in the case of STH, responding to the first trials within a block decreases more than does responding to trials later in a block [13], the trials within a block were assembled, giving more weight to the first trials than to the last ones. The following trials were analyzed: Trial 1 (Test Trial 1), Trial 2 (Test Trial 2), the means of Trials 3 and 4 (Test Trial 3), Trials 5–8 (Test Trial 4), Trials 9–16 (Test Trial 5), and of Trials 17–25 (Test Trial 6). The term between parentheses refers to the term used to indicate these trials in the next sections. The authors are aware of the fact that averaged responses may be smaller in amplitude than single responses simply because of averaging. However, as can be seen in the upper panel of Fig. 2, the ORs in response to, for example, the trials containing Test Trial 6 were all smaller than was the OR to Test Trial 1. This indicates that averaging was legitimate.

A univariate analysis of variance (ANOVA) was performed using the amplitude of the OR for each of the electrode sites separately, with Test Trial (six levels) and Block (four levels) as within-subject factors. STH would be reflected in a main Test Trial effect. LTH was evaluated on the basis of a between-block comparison of the mean amplitudes within a block and was indicated by a main Block effect. Enhanced re-habituation would be reflected in a significant Test Trial \times Block interaction effect, e.g. reflecting a block effect for Test Trials 2–6, but not for Test Trial 1. The Bonferroni test was used for post-hoc analyses. The level of significance was set at 0.05 throughout. Six participants were excluded from the analysis because of excessive eye-blinking.

A main effect of Test Trial was found in the ANOVA at Fz ($F(5, 205) = 30.242$, $P < 0.001$), Cz ($F(5, 205) = 144.01$, $P < 0.001$), and Pz ($F(5, 205) = 109.58$, $P < 0.001$). Post-hoc analysis on this factor revealed that the OR/P3a of Test Trial 1 was more positive than that of Test Trials 2–6 at all leads. Because of space limitations, only the results for the Cz site are presented in the upper panel of Fig. 1. The OR in

response to Test Trial 2 was more positive than that of Test Trials 5 and 6 again at all electrode sites, Test Trial 3 was more positive than Test Trial 6 at Pz, and Test Trial 4 was larger than Test Trial 6 at Cz.

A main effect of Block was found at Cz ($F(3, 123) = 3.44, P = 0.019$) and Pz ($F(3, 123) = 4.51, P = 0.005$), but not at Fz ($F(3, 123) = 1.52$). Post-hoc analysis revealed that the amplitude in Block 1 was more positive than that in Blocks 3 and 4 at Cz and Pz, which again can be seen for Cz in the lower panel of Fig. 1.

A significant interaction between Test Trial and Block was found at Cz ($F(15, 615) = 2.07, P = 0.022$), and there was a marginally significant effect at Pz ($F(15, 615) = 1.71, P = 0.074$). No interaction was present at Fz ($F(15, 615) = 1.30$). Post-hoc analysis of the significant Test Trial \times Block interaction at Cz revealed that Test Trial 3 was more positive in Block 1 than in Blocks 3 and 4. The amplitude of the OR at Test Trial 4 was more positive in Block 1 compared to Block 3. As

Test Trial 1 did not differ between the different blocks, and as Test Trials 3 and 4 were larger in Block 1 than in Blocks 3 and 4, the amplitude in Blocks 3 and 4 decreased more compared to the amplitude in Block 1. This reflects enhanced re-habituation.

As the number of degrees of freedom in the ANOVA was large, a non-linear regression analysis of exponential decay was performed on the 25 Trials (see upper panel of Fig. 2) and the six Test Trials (see lower panel of Fig. 2) separately for each block and each electrode site, in order to verify the interaction effect. The following formula was used: $Y = (\text{Span}) \times \exp(-K \times (X - 1)) + \text{Plateau}$, where Y is the amplitude, starting at $\text{Span} + \text{Plateau}$ and decreasing to 'Plateau' with a rate constant ' K '; half span values are obtained after $\ln 2/k$ Test Trials; X is the Test Trial. The K values were determined for each of the blocks for each participant separately. Next, the non-parametric Friedman test was performed on the K values of the six Test Trials

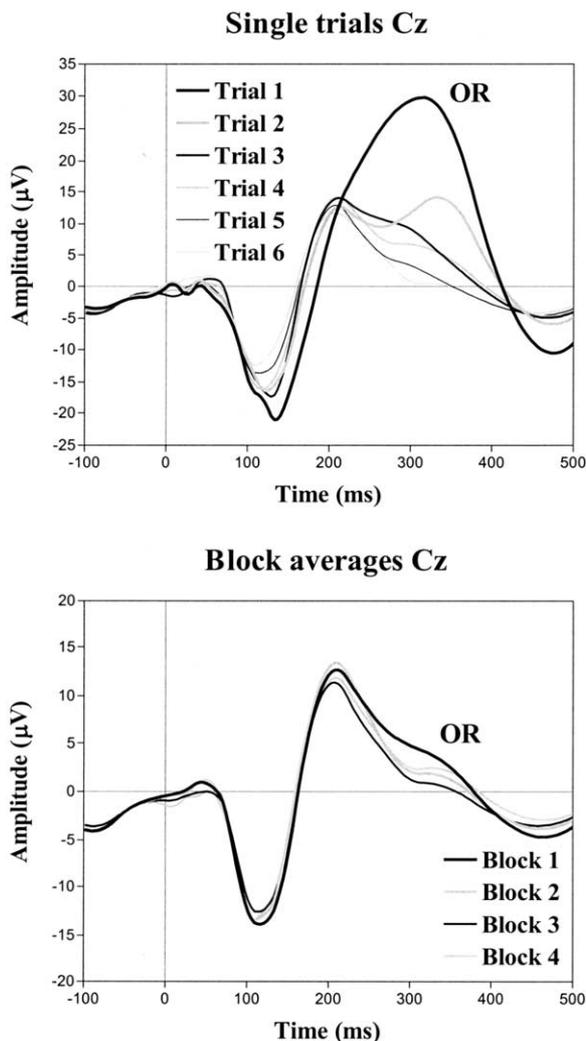


Fig. 1. (Upper) Single-trial ERPs of the six Test Trials. (Lower) Averaged ERPs of the four blocks, pooled over trials. X-axes, time in milliseconds (ms); Y-axes, amplitude in microvolts (μV).

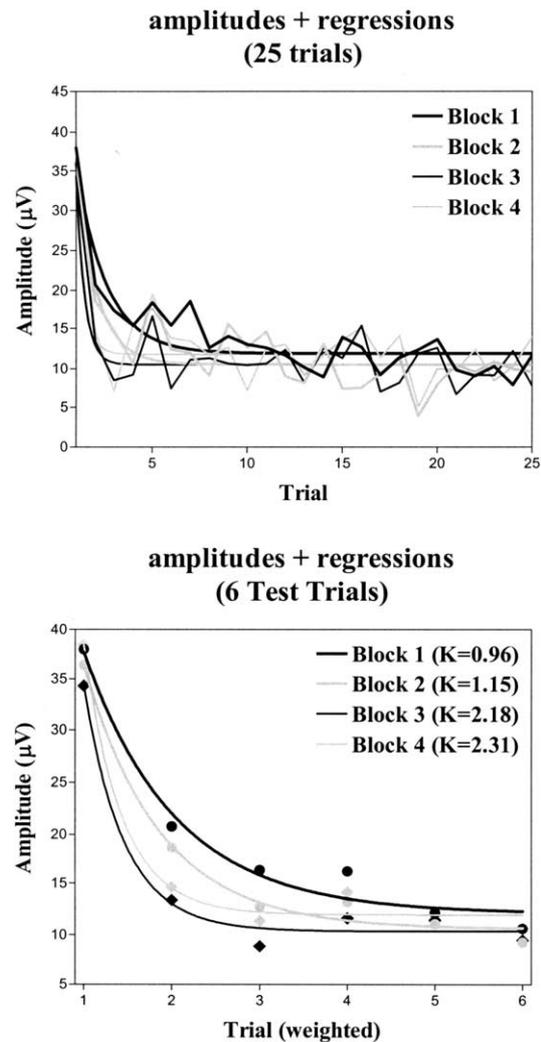


Fig. 2. (Upper) Maximum OR and regression lines of the 25 trials within each block. (Lower) Regression lines and amplitude of the six Test Trials of the OR for each block. X-axes, the six trials; Y-axes, amplitude in microvolts (μV).

only, with the four blocks as test variables. In order to verify whether the results of the ANOVA, that is, larger amplitude decrements during Blocks 3 and 4 compared to Block 1, could be replicated, additional non-parametric Wilcoxon rank order tests were performed.

The mean K values per block are shown in the lower panel of Fig. 2. The results of the non-parametric test revealed a marginally significant effect at the Fz ($\chi^2 = 6.37, P = 0.095$) and Cz sites ($\chi^2 = 7.44, P = 0.059$), but no effect at Pz ($\chi^2 = 4.76$). Post-hoc Wilcoxon ranks tests showed that the K values (the slopes) were larger for Block 4 than for Blocks 1 and 2 ($P = 0.041$ and 0.004 , respectively), and larger for Block 3 than for Block 2 ($P = 0.011$), which can be seen in the lower panel of Fig. 2 for Cz. This again indicates that the OR/P3a decreased more rapidly during the later blocks compared to the initial blocks.

The purpose of the present experiment was to assess whether the decrease in OR/P3a amplitude in humans subjected to repeated stimulus presentations is due to learning, or some non-learning process such as a refractory period or fatigue. This was studied by examining whether the OR amplitude decrease shows enhanced re-habituation. We first could replicate the short and more long-lasting decrements of the OR/P3a as was observed in other studies [1,5,7,8]. More importantly, the amplitudes of the OR decreased more rapidly during Blocks 3 and 4 than during Blocks 1 and 2 at an expected electrode position (Cz), which implies enhanced re-habituation.

Former habituation studies (e.g. Ref. [15]) used the number of trials needed to habituate as the measure of enhanced re-habituation, without showing learning curves, such as presented in Fig. 2. We presented more relevant information, all providing evidence for enhanced re-habituation.

An argument against the notion of enhanced re-habituation reflecting fatigue or a refractory period is that the inter-stimulus interval we used was rather long. A refractory period only affects the ERP components at intervals shorter than 5 s [3]. Furthermore, fatigue may develop with demanding tasks, whereas it does not develop if a task is boring [12], as was the case for the task in our study.

What does this habituation of the OR mean? According to the priming theory of Wagner [14], an organism will be surprised at the presentation of a new stimulus. After the first presentation, a representation of this stimulus is placed into short-term memory. The next stimulus is primed, which leads to a larger expectation of that stimulus. This, in turn, decreases the response. This hypothesis has been adopted to explain amplitude decrements in ERP research as well,

since the amplitudes of ERP components decreased with increasing stimulus expectancy [1,4]. Accordingly, a large expectancy of the stimuli has caused the amplitudes of the OR/P3a to decrease in our experiment.

In conclusion, the present study supports the notion that amplitude reductions of the OR of the human ERP as a result of repeated stimulus presentation do reflect an elementary learning process, that is, habituation.

References

- [1] W.T. Bourbon, K.W. Will, H.E. Gary, A.C. Papanicolaou, Habituation of auditory event-related potentials: a comparison of self-initiated and automated stimulus trains, *Electroenceph. clin. Neurophysiol.* 66 (1987) 160–166.
- [2] M.M. Bradley, P.L. Lang, B.N. Cuthbert, Emotion, novelty, and the startle reflex: habituation in humans, *Behav. Neurosci.* 107 (1993) 970–980.
- [3] N.M.W.J. De Bruin, B.A. Ellenbroek, W.J. Van Schaijk, A.R. Cools, A.M.L. Coenen, E.L.J.M. Van Luijtelaar, Sensory gating of auditory evoked potentials in rats: effects of repetitive stimulation and the interstimulus interval, *Biol. Psychol.* 55 (2001) 195–213.
- [4] H. Fruhstorfer, Habituation and dishabituation of the human vertex response, *Electroenceph. clin. Neurophysiol.* 30 (1971) 306–312.
- [5] J. Pan, T. Takeshita, K. Morimoto, P300 habituation from auditory single-stimulus and oddball paradigms, *Int. J. Psychophysiol.* 37 (2000) 149–153.
- [6] T.W. Picton, The P300 wave of the human event-related potential, *J. Clin. Neurophysiol.* 9 (1992) 456–479.
- [7] J. Polich, H.K. McIsaac, Comparison of auditory P300 habituation from active and passive conditions, *Int. J. Psychophysiol.* 17 (1994) 25–34.
- [8] J. Polich, Habituation of P300 from auditory stimuli, *Psychobiology* 17 (1989) 19–28.
- [9] R. Quian Quiroga, H. Garcia, Single-trial event-related potentials with wavelet denoising, *Clin. Neurophysiol.* 114 (2003) 376–390.
- [10] R. Quian Quiroga, Obtaining single stimulus evoked potentials with wavelet denoising, *Physica D* 145 (2000) 278–292.
- [11] R. Quian Quiroga, E.L.J.M. Van Luijtelaar, Habituation and sensitization in rat auditory evoked potentials: a single-trial analysis with wavelet denoising, *Int. J. Psychophysiol.* 43 (2002) 141–153.
- [12] A.S. Smit, P.A.T.M. Eling, A.M.L. Coenen, Mental effort causes vigilance decrease due to resource depletion, *Acta Psychol.* (2003) in press.
- [13] R.F. Thompson, W.A. Spencer, Habituation: a model phenomenon for the study of neuronal substrates of behavior, *Psychol. Rev.* 73 (1966) 16–43.
- [14] A.R. Wagner, Priming in STM: an information-processing mechanism for self-generated or retrieval-generated depression in performance, in: T.J. Tighe, R.N. Leaton (Eds.), *Habituation: Perspectives from Child Development, Animal Behavior, and Neurophysiology*, Lawrence Erlbaum Associates, Hillsdale, NJ, 1976, pp. 95–128.
- [15] W.F. Waters, D.G. McDonald, Repeated habituation and over-habituation of the orienting response, *Psychophysiology* 13 (1976) 231–235.