Effects of brief discrimination-training on the auditory N1 wave

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We determined whether the human N1 evoked by tones with different frequencies might be affected by a brief discrimination-training at one specific frequency. During 1 h training, subjects learned to discriminate a 1062 Hz tone from another tone. Before and after training, subjects heard for 26 min tones with a frequency of 1000 Hz, replaced every sixth one by test tones with frequencies randomly and equiprobably chosen as 835, 886, 941, 1000, 1062, 1128 or 1198 Hz. The N1 to the test tone was larger when its frequency was further from the repeating frequency. After training N1s were attenuated to all tones except the trained and repeated ones, indicating a refractory frequency effect, long-term habituation, and sensitization to the repeated and trained tones. *NeuroReport* 14:2489–2492 © 2003 Lippincott Williams & Wilkins.

Key words: Auditory cortex; Cortical plasticity; N1; Refractoriness

INTRODUCTION

The N1 of the human auditory event-related potential (ERP) is a negative wave recorded maximally from the vertex peaking at about 100 ms after sound onset. The N1 reflects activation of large neuronal populations in regions of the auditory cortex on the superior surface of the temporal lobe. It is sensitive to the rate of stimulation, decreasing its size as the inter-stimulus interval (ISI) decreases from 10 to 0.5 s [1]. This refractoriness does not develop over time but occurs within one stimulus [2,3], implying that the N1 is mainly determined by the preceding inter-stimulus interval.

The prolonged refractory period is specific to the frequency of the tone eliciting the N1. The frequency specificity of the N1 refractoriness was originally studied in a paradigm wherein three intervening tones were presented in the 5 s interval between test tones [4]. Different frequencies of the intervening tones were tested in separate blocks, while the frequency of the test tone was always 1000 Hz. The N1 amplitude to the test tone increased with the increasing frequency difference (Δf) between the intervening and test tones. Greater frequency specificity (a steeper curve when N1 amplitudes are plotted against frequency) occurs when the intervening tones are presented at a more rapid rate [5]. This refractoriness specificity can be explained by the tuning curves behind N1 having different points of maximal responsiveness but overlapping skirts. The amount of overlap varies inversely with the tone Δf. Consequently, when the Δf between intervening and test tones is small, more of the N1 neurons will be refractory when the test tone occurs than when the Δf is larger. The frequency specificity of the N1 refractoriness may thus provide an indirect way to measure the width of the tuning curve of neuronal populations in the auditory cortex.

Since Hebb [6], learning and memory have been related to modifications of synaptic strength among simultaneously active neurons due to practice and experience. In animals, sound-receptive fields were altered by 20 min of aversive classical conditioning or instrumental avoidance learning by using a tone as a conditioned stimulus [7]. For instance, adult guinea pigs showed on a classical conditioning task increased neurophysiological responses in the primary auditory cortex to the conditioned frequency and reduced responses to the neurons' best frequencies after 15–40 min training [8].

In humans, the N1 can become more sensitive to a preferred spectral input. For instance, multiple 1.5 h sessions of training in frequency discrimination over a period of 3 weeks enhanced the N1 m (the magnetic N1) to the trained frequencies [9]. The aim of the present study was to determine whether the N1 and the frequency specificity of its refractory period could be affected by a brief period of discrimination training. To this end, we measured brain responses to several tones before and after subjects learned for 1 h to discriminate a particular frequency.

MATERIALS AND METHODS

Eighteen volunteers (laboratory personnel; one left-handed and one ambidextrous; six males; age 22–40 years, mean 31 years) who reported to have normal hearing consented to participate in the experiment. The experiment consisted of three sessions (two EEG recordings and one training session). During the EEG sessions, subjects watched a subtitled silent movie. The first EEG recording was divided into two blocks (13 min, each) separated by a 3 min break. A 1 h training session followed after a 15 min break. After a 5 min break, another EEG session occurred. During the sessions subjects sat comfortably in a sound isolated room, while during the longer break they could walk outside.

The training session consisted of four blocks of 100 trials, where 350 ms tones were delivered in pairs (850 ms stimulus onset asynchrony, SOA). In two blocks, subjects judged which of the two tones was higher in frequency, and in other two blocks, which was lower. Each response was followed by a visual feedback. In both blocks the tone to be identified as the lower or the higher was 1062 Hz. The order of the blocks pairs was counterbalanced across subjects. A staircase procedure (16 steps from 400 to 1 Hz) exponentially decreased or increased the tone Δf according to the response correctness [9].

To determine the training effects during the discrimination-task, the Δf steps reached by each subject at trials 20, 40, 60, 80, and 100 were compared across the four blocks of the task by a two-way ANOVA with block and trial as factors.

In both EEG sessions (5200 trials, each), subjects heard through insert-earphones binaural 100 ms tones (300 ms SOA). The intervening tone was 1000 Hz and the test tone was randomly and equiprobably chosen to have a frequency of 835, 886, 941, 1000, 1062, 1128 or 1198 Hz. Every sixth intervening tone was replaced by a test tone (1800 ms SOA). The probability of occurrence was 0.83 for the intervening 1000 Hz tones and 0.17 for the test stimuli. The tones were produced by a TDT synthesizer at 70 dB sound pressure level (SPL).

The EEG (0.05–50 Hz bandpass; 250 Hz sampling rate) was recorded from a 64-channel cap. Eye movements were monitored with electrodes at the right and left canthi, and below and above the right eye. Cz served as reference. Epochs (300 ms before and 600 ms after the onset of the test tone) were separately averaged for each test stimulus type. Eye-movement artifacts were corrected using ocular source components with BESA software [10].

In order to quantify the N1 strength and latency before and after training, we determined the N1 global field power (GFP) [11]. N1 amplitudes and latencies were calculated as the peak value of the GFP square root within the 80–150 ms window. Amplitude and latency differences between the EEG sessions before and after training were evaluated using a two-way ANOVA with training and tone as factors. A further three-way ANOVA included block as factor to study N1 long-term habituation.

RESULTS

Behavioral results: The results of the training session are illustrated in Fig. 1. The ANOVA showed a main effect of trial (F(4,56)=10.5; $p < 0.001$), resulting from the difference between the Δf step for trial 20 compared to the others ($p < 0.001$). Also a main effect of block (F(3,42)=3.2; $p < 0.05$), due to the larger Δf steps discriminated in the first block compared to all the others ($p < 0.001$), was obtained. A significant trial × block interaction was found (F(12,168)=1.9; $p < 0.05$). *Post-hoc* tests revealed that at trials 20 and 40 the Δfs discriminated by subjects in the second block were smaller than those of the first block ($p < 0.001$–0.05). In contrast, the Δfs at trials 20 and 40 of the third block were larger than those of the second block ($p < 0.05$) and then decreased again for the fourth block ($p < 0.05$). These effects decreased as the trials increased until at trial 100 only the Δfs of the third and fourth blocks were significantly smaller than those of the first block ($p < 0.05$). The mean values and standard errors of the mean (SE) of the Δfs reached by subjects were 8.7 ± 0.8 Hz after the first block, and 5 ± 0.7 Hz after the fourth.

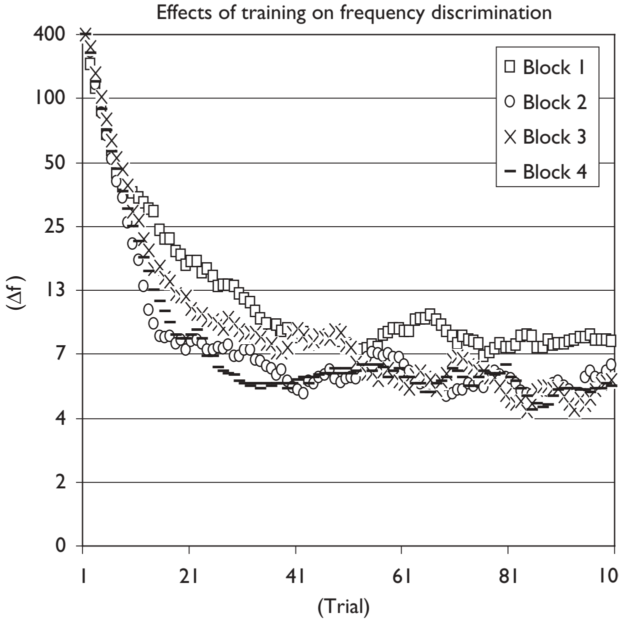

Fig. 1. Curves of discrimination training task in the behavioral session, plotting the average discriminable frequency over trials. The frequency difference (Δf) between sounds in the pair to discriminate is expressed in Hz.

ERP results: Figure 2 shows the mean GFP waveforms together with the mean N1-amplitudes. The ANOVA on N1 amplitudes yielded main effects of tone (F(6,102)=31.3; $p < 0.0001$) and training (F(1,17)=5; $p < 0.05$) with the N1 s smaller after than before training ($p < 0.05$). A significant training × tone interaction (F(6,102)=2.3; $p < 0.05$) indicated that the training effect was significantly different for different frequencies: all the intervening tones evoked reduced N1 s after training ($p < 0.005$–0.05) except for 1000 Hz and 1062 Hz.

The ANOVA on N1 amplitudes including block as a factor replicated the results obtained with N1 s averaged across the two blocks of the EEG sessions. There was also a block × tone interaction (F(1,17)=5; $p < 0.05$), indicating changes in the specificity pattern between the first and second blocks of each session.

The ANOVA on N1 latencies produced a main effect of tone (F(6,102)=9.4; $p < 0.001$): the 1000 Hz tone had a

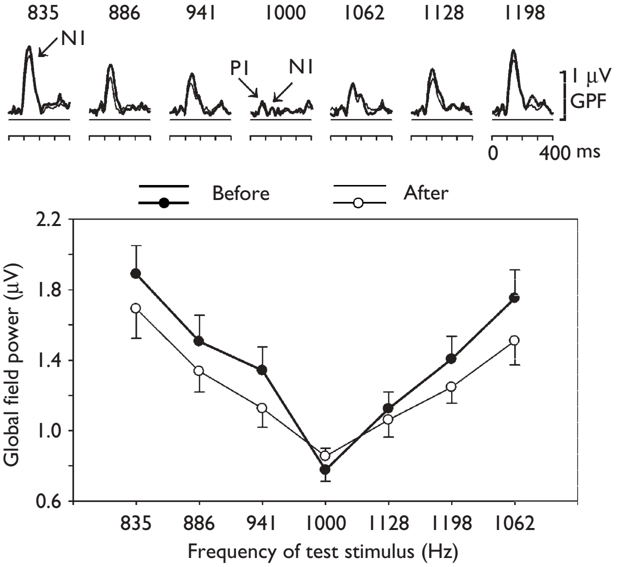

Fig. 2. The upper part of the figure shows the grand mean ERPs for each of the frequencies of the test stimuli. The bottom graph shows the mean NI amplitudes for each frequency, with the bars showing s.e.m.

shorter N1 latency (109 ± 4.2 ms) than all the other tones ($p < 0.001$ for all) which varied on average between 125 (886 Hz) and 135 (1128 Hz) ms.

DISCUSSION

Our study showed training effects on both the behavioral and physiological responses to tones. During the training session, subjects learned to discriminate the 1062 Hz frequency from the others. They more rapidly arrived at smaller Δfs in the later training blocks. The slight increase of the discriminated Δf from the second to the third block was likely due to the inversion of the task introduced with this block. The final Δf reached by subjects in this experiment (5 Hz) was larger than the value (2 Hz) reported in psychoacoustic studies of the difference limen using expert subjects [12] or after discrimination training over 15 days [9]. However, the latter study reported a limen of about 5 Hz after the first 1.5 h session.

The brain measurements confirmed previous results [4,13] concerning the N1 frequency-specificity. However, differences from the very narrow curve previously found by Näätänen *et al.* [5] were probably caused by our narrower frequency range and slower stimulus rate.

The shorter N1 latency to the 1000 Hz than to the other frequencies might be attributed to the small N1 amplitude at this frequency, being near the background noise level. This would lead to the latency being estimated with a mean near the center of the measurement range.

Most importantly, after training we observed N1 attenuation for all stimuli other than those that had been attended to in the discrimination training (the 1062 Hz tone) or that were repeated far more than the others (the 1000 Hz tone). Thus, after training the repeated and the learned tones still evoked a cortical response that was as large in amplitude as before training. In contrast, N1 s to the other tones were diminished. Consequently, the N1 refractoriness curve became smoother. These results are in contrast to what was reported in animal studies where there was a shift in the tuning curve towards the frequency of the conditioned stimulus [7]. However, it is not clear how to relate the frequency specificity of the N1, which reflects the activity of a neuronal population, to the tuning curve of single neurons.

Although different from findings with animals, our results still indicate a modification of neuronal population responses as a consequence of brief discrimination training. There was a general decrease in responsiveness over time, but responses to stimuli that occurred very frequently or that were actively attended did not attenuate. This implies the presence of a counteracting sensitization effect: these tones have begun to activate neurons that previously did not respond to them. These brief-term plastic changes might underlie the long-term modifications caused by extensive training to sounds by musicians [14], such as the increased strength of cortical sound representations [15,16], and the fine-grained discriminatory abilities of the auditory cortex [17,18].

N1 is diminished by long-term habituation [13,19]. Since habituation affects responsiveness to sounds and requires storage of information, it can be considered as a primitive form of learning decreasing the cortical reaction to stimuli [20]. Habituation as opposed to training effects would be supported by changes between the blocks within the EEG sessions. Results showed a significant attenuation of the N1 s at some but not all the frequencies. The brief breaks between blocks may have reduced habituation [21]. Furthermore, we presented seven different tones and not only one, and this, together with the distraction of the movie, might have prevented subjects from learning all the tones.

The lack of clear long-term habituation to all the tones suggests that the N1 attenuation to the infrequent stimuli was caused by a shift of the neural responsiveness towards the trained frequency. However, we could alternatively suppose that the N1 attenuation to the infrequent tones derived from a specific dishabituation effect [13,22,23] caused by discrimination training. In our experiment, we did not find any difference between N1 s to the 1000 and 1062 Hz tones before and after training in contrast to the attenuated values for N1 s to the other tones found only after training. We may, thus, hypothesize a long-term habituation after training of N1 s to the tones that were unimportant during the experimental session, and a resistance to habituation (or a dishabituation) of N1 s to the frequent stimuli and the trained ones, probably due to automatic attention towards the tone actively discriminated and to the most frequent and salient tone in the repeating sequences.

The learning of the 1062 Hz tone during discrimination-training was transferred to the subsequent EEG session, as reflected by the changes in N1 s to the trained and frequent tones. Interestingly, learning was subconscious since no subject except one noticed the previously discriminated tone in the second EEG session. Moreover, the learning effects on neuroplasticity as measured by the N1 could be observed even though subjects' attention was directed toward the movie.

CONCLUSION

A brief but intensive period of discrimination learning induces functional changes in the auditory system by specifically maintaining the neural responsiveness to the sounds relevant in the experiment while diminishing that to the other stimuli. The temporal properties of these non-invasively measured effects are consistent with animal studies demonstrating that cortical tuning to frequencies might be affected after 15–40 min of conditioned learning [8].

REFERENCES

1. Davis H, Mast T, Yoshie N and Zerlin S. The slow response of the human cortex to auditory stimuli: recovery process. *Electroencephalogr Clin Neurophysiol* **21**, 105–113 (1966).
2. Fruhstorfer H, Soveri P and Järvilehto T. Short-term habituation of the auditory evoked response in man. *Electroencephalogr Clin Neurophysiol* **28**, 153–161 (1970).
3. Ritter W, Vaughan HG and Costa LD. Orienting and habituation to auditory stimuli: a study of short term changes in average evoked responses. *Electroencephalogr Clin Neurophysiol* **25**, 550–556 (1968).
4. Butler RA. Effects of changes in stimulus frequency and intensity on habituation of the human vertex potential. *J Acoust Soc Am* **44**, 945–950 (1968).
5. Näätänen R, Sams M, Alho K, Paavilainen P, Reinikainen K and Sokolov EN. Frequency and location specificity of the human vertex N1 wave. *Electroencephalogr Clin Neurophysiol* **69**, 523–531 (1988).
6. Hebb DO. *The Organization of Behavior.* New York: Wiley; 1949.
7. Weinberger NM and Bakin JS. Learning-induced physiological memory in adult primary auditory cortex: receptive field plasticity, model, and mechanisms. *Audiol Neurootol* **3**, 145–167 (1998).
8. Bakin JS and Weinberger NM. Classical conditioning induces CS-specific receptive field plasticity in the auditory cortex of the guinea pig. *Brain Res* **536**, 271–286 (1990).
9. Menning H, Roberts LE and Pantev C. Plastic changes in the auditory cortex induced by intensive frequency discrimination training. *Neuroreport* **11**, 817–822 (2000).
10. Picton TW, van Roon P, Armilio ML, Berg P, llle N and Scherg M. The correction of ocular artifacts: a topographic perspective. *Clin Neurophysiol* **111**, 53–65 (2000).
11. Skandries W. Topographical analysis of electrical brain activity: methodological aspects. In: Zani A and Mado Proverbio A (eds). *The Cognitive Electrophysiology of Mind and Brain*. San Diego: Academic Press; 2003, pp. 401–416.
12. Moore BCJ. *An Introduction to the Psychology of Hearing*. San Diego: Academic Press; 1989.
13. Picton TW, Hillyard SA and Galambos R. Habituation and attention in the auditory system. In: Keidel WD and Neff WD (eds). *Handbook of Sensory Physiology, Vol V/3 Auditory System. Clinical and Special Topics*. Berlin: Springer Verlag; 1976, pp. 343–389.
14. Münte TF, Altenmüller E and Jäncke L. The musicians' brain as a model of neuroplasticity. *Nature Rev Neurosci* **3**, 473–478 (2002).
15. Pantev C, OoIstenveld R, Engelien A, Ross B, Roberts LE and Hoke M. Increased auditory cortical representation in musicians. *Nature* **392**, 811–814 (1998).
16. Pantev C, Roberts LE, Schultz M, Engelien A and Ross B. Timbre-specific enhancement of auditory cortical representations in musicians. *Neuroreport* **12**, 169–174 (2001).
17. Koelsch S, Schröger E and Tervaniemi M. Superior pre-attentive auditory processing in musicians. *Neuroreport* **10**, 1309–1313 (1999).
18. Tervaniemi M, Rytkönen M, Schröger E, Ilmoniemi RJ, and Näätänen R. Superior formation of cortical memory traces of melodic patterns in musicians. *Learn Mem* **8**, 295–300 (2001).
19. Callaway E. Habituation of averaged evoked potentials in man. In: Peeke HVS and Herz MJ (eds). *Habituation, vol. 2.* New York: Academic Press; 1973, pp. 153–174.
20. Sokolov EN. Brain functions: neuronal mechanisms of learning and memory. *Ann Rev Psychol* **28**, 85–112 (1977).
21. McGee T, King C, Tremblay K, Nicol TG, Cunningham J and Kraus N. Long-term habituation of the speech-elicited mismatch negativity. *Psychophysiology* **38**, 653–658 (2001).
22. Thomson RF and Spencer WA. Habituation: a model phenomenon for the study of the neuronal substrates of behavior. *Psych Rev* **173**, 16–43 (1996).
23. Näätänen R and Picton TW. The N1 wave of the human electric and magnetic response to sound: a review and an analysis of the component structure. *Psychophysiology* **24**, 375–425 (1987).

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