

Adaptation of neuromagnetic N1 without shifts in dipolar orientation

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306-channel magnetoencephalography, coregistered with high-resolution volumetric magnetic resonance imaging, was used with 10 healthy participants to test if repetition adapts subsequent processing of sounds in a sequence and whether this adaptation influenced the orientation of the dipolar sources in the auditory cortex. Auditory N1m responses to 1 kHz pure tones were indexed by clusters of sensors situated bilaterally over the temporal lobes.

N1m was augmented in amplitude at an interstimulus interval of 16 s relative to 1 s. This neuromagnetic amplitude augment occurred in dipoles in the vicinity of the auditory cortex, without significant shifts in the dipolar orientation. Recent repetition thus adapts auditory cortical neurons, in a manner subject to recovery after a period of silence. *NeuroReport* 18:377–380 © 2007 Lippincott Williams & Wilkins.

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Introduction

Responsivity of the brain to auditory onsets could be critical to survival. The brain processes elicited by a sound are subject to adaptation [1,2]. That is, repetition causes a reduction in the generation of those brain processes, a reduction which is termed adaptation. This adaptation manifests as a decline in responsivity of neuronal elements to stimulation over time, in a manner that is subject to recovery after a period of silence during which time those neuronal elements remain unstimulated.

Accordingly, shortening the intervening silence between tones, the interstimulus interval (ISI), could cause a neuronal adaptation that reduces the amplitude of the N1 response of the auditory event-related potential (ERP), as is derived from conventional electroencephalograms recorded from the scalp. This N1 response, the first long-latency vertex negativity of the auditory ERP, peaks ca. 100 ms after onset and is seen to attenuate in amplitude with shorter ISIs [3]. This attenuation of N1 tenably could be mediated via an adaptation of neuronal elements that become progressively less responsive upon repeated recent stimulation. This attenuation of N1 could be related to reductions in the distracting effects of ignored sound and could also have an influence upon the audio-visual processing of phonetic material [4–10].

Although there is evidence of adaptation of neuronal populations that could generate supratemporal aspects of the auditory N1 response within the auditory cortex [1–3], at ISIs as short as 1 s, a distinct aspect of the N1 response to sounds could also be generated within another superficial region of cortex [11–13]. Scalp current density analyses indicate that this region is focal to anterior-frontal rather than temporal regions of the brain.

The possibility, however, remains that this seemingly anterior frontally generated N1 component could rather have reflected a dipolar supratemporal source, which shifted in orientation [14] with reductions in ISI. Accordingly, supratemporal dipolar sources of auditory N1 would exhibit a shift in orientation in the sagittal plane as a function of ISIs within the range 1–16 s. Such dipole models may be appropriately derived with the magnetically measured counterpart of the supratemporal N1, the N1m, as derived from magnetoencephalogram (MEG) [14]. Increasing the ISI from 1 to 16 s would thus influence the orientation of the N1m dipole. We term this the dipole orientation hypothesis.

Neuronal elements in the vicinity of the auditory cortex could be adapted by recent activation in response to a repeated sound. Those neuronal elements could thus become less responsive upon subsequent repetitions, in a manner subject to recovery when those elements are not stimulated, as occurs after a period of silence. Increasing the ISI from 1 to 16 s would thus enhance the amplitude of the N1m dipole. We term this the adaptation hypothesis.

Materials and methods

Ten healthy participants (five women, aged 24–31 years; mean 28 years, 10 months) volunteered with informed written consent in accordance with the Declaration of Helsinki with hospital ethical committee approval. All were right-handed and reported intact hearing and corrected-to-normal or normal vision. Volunteers were comfortably seated in an acoustically shielded and magnetically shielded room (ETS-Lindgren Euroshield Oy, Eura, Finland) where they watched a self-chosen subtitled film presented without the soundtrack.

Participants were instructed to ignore the auditory stimuli [1-kHz tone bursts, 85-dB(A), 50 ms duration, 10-ms rise and fall time] that were delivered by Presentation software (Neurobehavioral Systems, Albany, California, USA) binaurally via plastic tubes and small soft ear pieces. The independent variable of interest was the ISI from the beginning of the stimulus to the beginning of the next stimulus and had two levels (1 s, 16 s). Each of the 10 stimulus runs was composed of 250 or 60 stimulations delivered at constant ISI of 1 or 16 s, respectively. Runs were separated by 120 s. ISI was alternated on successive runs, and the choice of the initial ISI was counterbalanced across participants.

MEG (VectorView 306-channel system, Elektra Neuromag Oy, Finland) was acquired in the band 0.10–172.2 Hz and digitized at a rate of 600.6 Hz. Following artefact rejection (excluding responses with EOG $\pm 50 \mu\text{V}$), MEG responses for each ISI were averaged (disregarding the first sound from each block). Averaged responses were digitally filtered offline with a passband of 1–30 Hz and baseline-corrected in relation to the mean amplitude at a 100-ms prestimulus interval. In addition to temporal filtering, signal space projection was applied to suppress external magnetic noise [15,16].

Response amplitudes were then quantified from the averaged response to the stimuli using equivalent current dipoles (ECD) fitted in a least-squares sense at the individually determined peak latency of the N1m response using a subset of sensors over the temporal area of each hemisphere, each subset of which consisted of 21 sensor triplets. Each triplet was constituted by a magnetometer alongside a pair of planar gradiometers. Triplets were identical to those used in a previous N1m investigation [17].

A three-dimensional reconstruction of each brain's surface – as derived from high-resolution T1-weighted volumetric magnetic resonance images that were acquired with a 1.5-T Siemens Magnetom (Erlangen, Germany) ($n=8$) or 3-T Philips Achieva (Best, The Netherlands) ($n=2$) – was used to individually determine the optimal location of the centre of the single sphere used during this ECD fitting for each individual.

This sphere was coregistered with nasion, left-periauricular and right-periauricular points as was digitized and subsequently derived from the digitized position of head position indicator coils used to determine the relative position of the head to the sensors during the MEG measurement. This sphere was that, in sagittal, axial and coronal planes, which

best-fitted, in the least-squares sense, points that traced a smooth curve parallel to the skull upon the brain's surface, when there were roughly 20 points plotted upon one single slice oriented in each of these three planes. The single sphere for each individual, used for ECD fitting for that individual, included both hemispheres and was close to symmetrically positioned upon all slices in each plane.

Differences in the dipolar amplitudes, latencies, moments, orientations and locations were then tested with ISI (1 s, 16 s) \times hemisphere (left, right) repeated-measures analysis of variance.

Results

As illustrated for the right hemisphere of an individual participant in Fig. 1, dipoles were localized within the vicinity of the auditory cortex. As depicted in Fig. 2, in all volunteers, the amplitude of N1m responses to the tones was significantly suppressed bilaterally at the 1 s relative to the 16 s ISI, $P < 0.01$. This suppression of ECD amplitude was accompanied by a reduction in ECD latency at

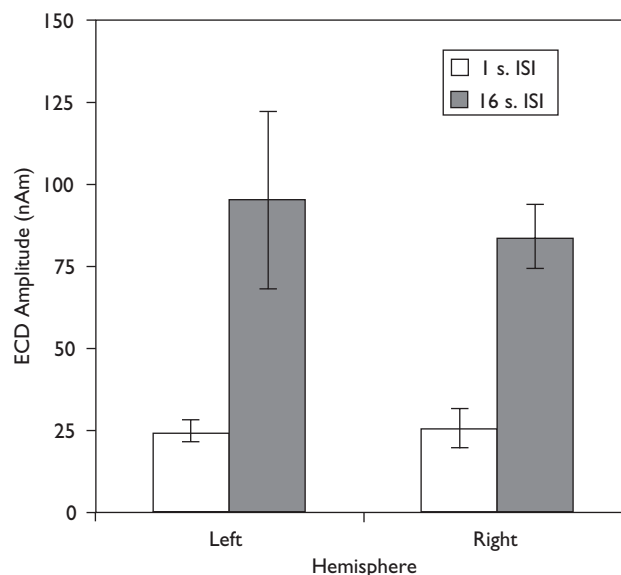


Fig. 2 Mean (\pm SEM) amplitude of N1m as a function of interstimulus interval and hemisphere.

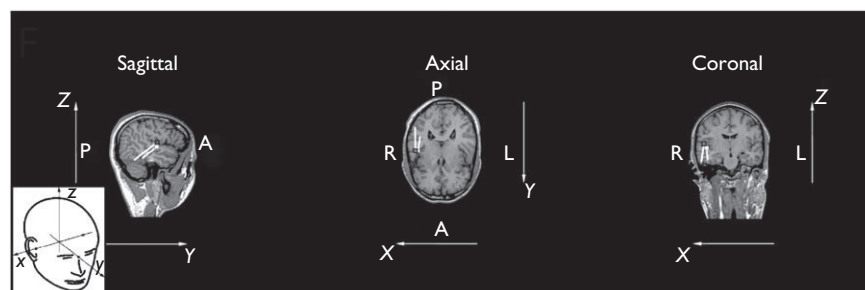


Fig. 1 Dipole locations in the right hemisphere of an individual participant as a function of interstimulus interval (white 1 s; grey 16 s) superimposed onto the participant's magnetic resonance images. Lines denote dipolar amplitudes and orientation. L, left hemisphere; R, right hemisphere; A, anterior; P, posterior. The coordinate system is depicted within the axes of each plane and the inset (inset adapted from Figure 5.2 within and reprinted with permission from [18]).

Table 1 Mean (\pm SEM) location of N1m dipoles as a function of hemisphere and ISI

ISI	Hemisphere	$ x ^a$	y	z
1 s	Left	41.6 \pm 3.1	6.0 \pm 3.9	53.4 \pm 4.8
1 s	Right	49.4 \pm 1.8	10.5 \pm 3.7	55.5 \pm 4.5
1 s	Mean	45.7 \pm 1.9	8.4 \pm 2.7	54.5 \pm 3.2
16 s	Left	40.6 \pm 3.6	9.3 \pm 5.0	52.3 \pm 3.7
16 s	Right	41.7 \pm 2.2	9.0 \pm 3.3	52.9 \pm 6.0
16 s	Mean	41.2 \pm 2.0	9.1 \pm 2.8	52.6 \pm 3.6

A right-handed Cartesian coordinate system is used relative to the centre of the sphere in which the direction of x is from left to right periauricular point, the y -axis points upward through the vertex and the z -axis points forward through nasion. The modulus of x -location was used.

ISI, interstimulus interval.

^aAxes with significant effects of ISI.

Table 2 Mean (\pm SEM) clockwise positive angle of N1m dipoles from a reference moment pointing in the positive direction of the vertical axis of Fig. 1 upon the different planes as a function of hemisphere and ISI

ISI	Hemisphere	Sagittal	Axial	Coronal
1 s	Left	223.4 \pm 13.3	202.1 \pm 8.8	212.3 \pm 18.3
1 s	Right	216.7 \pm 7.6	181.6 \pm 26.4	162.6 \pm 7.2
1 s	Mean	219.9 \pm 7.3	191.3 \pm 14.3	186.1 \pm 10.9
16 s	Left	210.4 \pm 6.2	170.7 \pm 16.1	166.7 \pm 9.6
16 s	Right	223.5 \pm 7.1	190.5 \pm 11.5	186.9 \pm 10.8
16 s	Mean	217.7 \pm 4.9	181.7 \pm 9.6	177.9 \pm 7.5

This reference moment pointed upwards (Q_y, Q_z) in the sagittal (y, z), forwards (Q_x, Q_y) in the axial (x, z) and upwards (Q_x, Q_z) in the coronal (x, z) plane.

ISI, interstimulus interval.

Table 3 Mean (\pm SEM) N1m dipolar moments as a function of hemisphere and ISI

ISI	Hemisphere	Q_x	Q_y^a	Q_z^a
1 s	Left	-5.5 \pm 2.8	-11.2 \pm 1.7	-15.6 \pm 4.1
1 s	Right	8.5 \pm 4.1	-15.1 \pm 4.7	-15.7 \pm 2.8
1 s	Mean	1.9 \pm 3.0	-13.2 \pm 2.6	-15.6 \pm 2.4
16 s	Left	25.8 \pm 26.7	-41.4 \pm 16.6	-64.2 \pm 11.1
16 s	Right	-4.7 \pm 11.1	-52 \pm 10.1	-49.8 \pm 7.9
16 s	Mean	8.9 \pm 13.4	-47.3 \pm 9.0	-56.2 \pm 6.6

ISI, interstimulus interval.

^aMoments with significant effects of ISI.

1 s relative to the 16 s (ISI 1 s: 85.9 ms \pm 1.6 < ISI 16 s: 93.3 \pm 2.7 ms), $P < 0.05$, coupled with a modest shift along the x -axis (Fig. 1, inset [18]) from a medial to lateral location, $P < 0.05$ (Table 1). The y and z locations, however, did not differ significantly with ISI, $F < 1.1$, nor did the angles denoting the orientation of dipole differ significantly with ISI, neither in the sagittal, axial nor coronal planes (Table 2). Significant influences of ISI on dipole moments, Q_y , $P < 0.05$, and Q_z (Table 3), $P < 0.0001$, were accordingly not because of shifts in dipolar orientation, but rather a bilateral increase in the amplitude of dipoles that were oriented primarily along the sagittal plane. All other main effects and interactions were nonsignificant.

Discussion

The results showed that recent repetition of a sound adapted the N1m response, which can be explained by

dipolar sources within the vicinity of the auditory cortex. That is, a reduction in ISI from 16 to 1 s attenuated the amplitude of the N1m response, as can be explained by a dipole that orients primarily sagittally in the vicinity of the auditory cortex (Fig. 1). This finding corroborates the adaptation hypothesis that, within the auditory cortices bilaterally, neuronal elements, which are responsive to sound, are adapted following recent activation such that those elements become less responsive upon subsequent repetitions, in a manner which is subject to recovery after a period of silence.

These temporal lobe dipoles did not shift in orientation with ISI, despite a significant increase in amplitude. The adaptation hypothesis thus was supported, although the dipole orientation hypothesis thus went unsupported. In turn, it remains tenable that the anterior frontal N1 [11–13] – which could be obligatorily responsive to stimuli presented at ISIs less than 8 s – is generated within the frontal lobes.

What nobody understands is why a decrease in ISI caused the temporal dipoles to shift from more medial to lateral locations. Such a finding warrants independent replication. Nor is it fully understood why the latency of N1m generation was prolonged at longer ISIs. This prolongation, however, replicated previous auditory N1 results [11].

At long ISIs, a tonal sound led to the dipolar generation of a prolonged and augmented N1m that could implicate a stronger relative contribution from the primary auditory cortex. At shorter ISIs, conversely, nonprimary auditory areas lateral to the primary auditory cortices [19,20] could exert a stronger relative contribution. Accordingly, the location of the dipole shifted laterally with a reduction in ISI.

Clues to how this shift and its consequences relate to brain function could reside within the effects of auditory distraction upon cognitive performance and the effects of the to-be-ignored background sounds upon the generation of evoked responses. A fleeting disruption of the categorization of visually presented digits (odd-versus-even) that occurs when large populations of nonadapted afferent auditory elements are activated would seem to be confined to the detection of rare auditory onsets; for example, when the ISI between auditory stimuli is long [1]. This distraction away from the primary task towards such a discontinuity in the auditory environment could have evolved to promote survival within hostile settings [1,2].

By contrast, a subtler and distinct form of auditory distraction exists that disrupts performance upon cognitive tasks with a requirement for the temporary retention of information in memory exists [4–6]. Even when the initial onset of the auditory sequence has already been detected, such cognitive performance is still disrupted by background sound. This distraction effect may be related to the preattentive perceptual processing of the sequence of to-be-ignored sounds. This effect still occurs when N1 has undergone considerable adaptation [4–5], which, in this investigation, is associated with medial-to-lateral dipole location shifts. This distraction effect increases alongside the amplitude of an anterior frontal N1 component [4–5], a component which could be generated focally within the frontal lobes [11–13].

Conclusion

Recent repetition of sound adapts auditory cortical neurons, in a manner subject to recovery after a period of silence. This

adaptation reduces the N1m amplitude without influencing the orientation of the dipolar source situated within each temporal lobe in the vicinity of the auditory cortices of the human brain.

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