

Transient brain responses predict the temporal dynamics of sound detection in humans

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The neural events leading up to the conscious experience of stimulus events have remained elusive. Here we describe stimulation conditions under which activation in human auditory cortex can be used to predict the temporal dynamics of behavioral sound detection. Subjects were presented with auditory stimuli whose energy smoothly increased from a silent to a clearly audible level over either 1, 1.5, or 2 s. Magnetoencephalographic (MEG) recordings were carried out in the passive and active recording conditions. In the active condition, the subjects were instructed to attend to the auditory stimuli and to press a response key when these became audible. In both conditions, the stimuli elicited a prominent transient response whose emergence is unexplainable by changes in stimulus intensity alone. This transient response was larger in amplitude over the right hemisphere and in the active condition. Importantly, behavioral sound detection followed this brain activation with a constant delay of 180 ms, and further the latency variations of the brain response were directly carried over to behavioral reaction times. Thus, noninvasively measured transient events in the human auditory cortex can be used to predict accurately the temporal course of sound detection and may therefore turn out to be useful in clinical settings.

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Humans can detect sounds very rapidly, with behavioral responses to the onset of an audible stimulus taking place in just a few hundred milliseconds. As manifested in their spectrotemporal receptive fields, nerve cells in the auditory system selectively respond to the spectral and temporal properties of auditory stimuli (Klein et al., 2000; Shamma, 2001). In the temporal domain, the auditory system detects long-duration sounds at lower intensities than short-duration sounds, indicating that sound detection is accomplished through a temporal integration process whereby information of the signal is gathered over time (Eddins and Green, 1995; Garner and Miller, 1947; Green et al., 1957; van den Brink and Houtgast, 1990).

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Electro (EEG)- and magnetoencephalography (MEG) methods have identified two types of mass action responses produced by auditory cortex: transient responses (such as the P50-N100-P200 complex), which are elicited immediately upon presentation of a stimulus; if the stimulus is of a long duration, the transient responses are followed by a sustained response (Picton et al., 1978a,b). The elicitation of transient responses requires abrupt changes in stimulation (typically, an intensity change from 0 to 60 dB SPL in less than 10 ms). The N100 response can be dissociated from perception because its latency and amplitude reflect poorly reaction time (Jaskowski et al., 1994) and stimulus intensity (Näätänen, 1992), respectively. The behavior of the sustained response differs in several respects from that of the transient responses, with the sustained response being, for example, more sensitive to changes in stimulus intensity (Picton et al., 1978a,b). Nevertheless, sustained responses have also been dissociated from auditory perception because the sustained response, unlike perceived loudness, attenuates towards the end of a long-duration stimulus (Picton et al., 1978b).

Utilizing active recording conditions (where the subjects attend to the stimuli), previous research has, however, indicated that sound detection is reflected in the N100 and P300 responses and stimulus recognition in the P300 (Hillyard et al., 1971; Parasuraman and Beatty, 1980; Parasuraman et al., 1982; Squires et al., 1973). These studies used a posteriori comparisons of brain responses classified and averaged according to subjective confidence ratings provided by the subject on whether an auditory stimulus had occurred. Information on the relationship between brain responses and the ability to detect sounds is therefore not available directly in the brain response itself but rather derivable only through comparisons of brain responses specified by behavioral measures. Thus, brain responses obtained in the above experimental setups result in indirect indices of perception and their value as a priori predictors of behavioral performance is limited. From passive recording conditions (where the subjects are instructed to ignore the stimuli), there is evidence that preattentive sensory memory operations reflected in the mismatch response (MMN) govern attentive stimulus detection (Näätänen, 1992; Sams et al., 1985; Tiitinen et al., 1994). The MMN, however, can also be regarded as an indirect measure of behavioral performance because it is gained in passive recording conditions and separately correlated to overt

behavior obtained in active detection conditions: The link between brain dynamics and behavioral measures can at best be inferred.

In the light of the above, no brain measure directly indexing behavioral sound detection seems to be available, and human sound detection therefore has remained a subjective phenomenon without an objective description. The establishment of an objective measurement protocol for noninvasive assessment of sound detection could be of clinical importance also. Previously advanced suggestions for the use of cortically generated electric and magnetic responses as diagnostic tools (Hyde, 1997; Näätänen, 2000; Shibasaki and Miyazaki, 1992) could be considered impractical because they entail long recording times, averaging across large subject populations, or response subtraction procedures yielding unspecific evidence on the development and degradation of cognitive functions.

To circumvent the above problems, we sought rapidly obtainable, direct physiological markers for the conscious detection of sound. We hypothesized that by using auditory stimuli whose intensity smoothly increases from a silent to a detectable level, we might be able to identify noninvasively the neural events and temporal integration process specific to the detection of an auditory stimulus at the transition point where the stimulus turns from inaudible to audible.

Methods

Stimuli, subjects, and recordings

The sound pressure envelope of the stimuli rose exponentially from 6.3 μPa to 20 mPa over 1, 1.5, or 2 s (see Fig. 1). This corresponded with a perceptually linear rise from -10 to 60 dB (SPL). The sounds (frequency 750 Hz), each delivered >150 times, were presented in a random order with random interstimulus intervals (ISIs) of 0.5–4.5 s.

The subjects ($n = 10$) were studied with their written and informed consent and with the approval of the Ethical Committee of Helsinki University Central Hospital. The measurements were conducted in both active and passive recording conditions. In the active condition, the subjects indicated when the sounds became audible by pressing a response key with their right-hand index finger. In the passive condition, the subjects read text of their own choice and were under instruction to ignore auditory stimuli. For control purposes, a sinusoidal tone (onset and offset ramp 10 ms, duration 100 ms, frequency 1000 Hz, 80 dB SPL, ISI 800 ms) was presented to the subjects to establish the source location of the N100 response.

Behavioral and MEG (306-channel device, Vectorview, NeuroMag Oy, Finland) measurements were performed in a magnetically

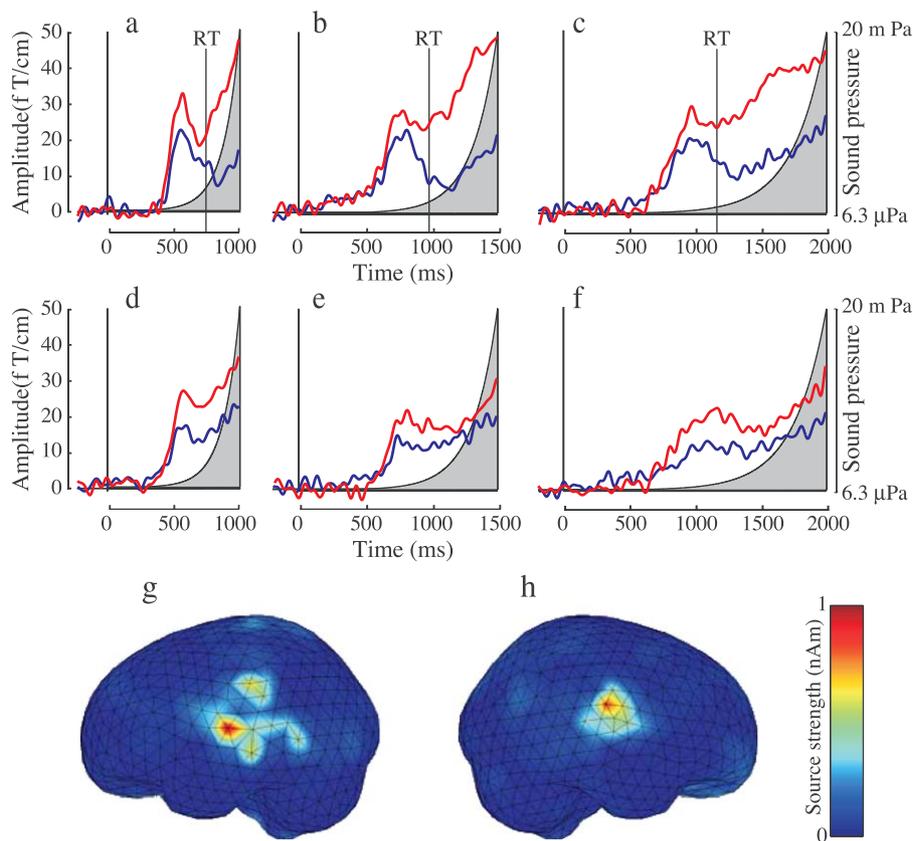


Fig. 1. Grand-averaged ($n = 10$) cortical responses elicited by the auditory stimuli. The stimuli (gray-shaded area) increased in intensity from a silent to a clearly audible level over a period of either 1, 1.5, or 2 s and gave rise to prominent brain responses in the left (blue) and right (red) hemisphere both in the active (a–c) and passive (d–f) recording conditions. Responses recorded in the active condition were more prominent than those recorded in the passive condition. Response amplitudes were larger over the right than left temporal lobes. The source of the transient response was near the auditory cortex in both the left (g) and right hemisphere (h) as revealed by minimum current estimates (MCEs; L-1 norm, no region-of-interest weighting function used). The activity in the right hemisphere was spatially more constrained.

shielded room. The noise level inside the room was 24 dB (A-weighted) and the silencing earpiece through which the auditory stimuli were delivered to the subject's ear lowered the noise level to 20 dB. The accuracy of the sound system output was ± 1.5 dB in the 8- to 60-dB range and the jitter between trigger pulse and sound output was < 1 ms.

Data analysis

MEG responses were referenced to a 200-ms prestimulus baseline and low-pass filtered at 20 Hz. Artifacts, determined as activity exceeding 150 μV or 3000 fT/cm using electrooculogram and absolute amplitude variation of the trials, respectively, were automatically rejected during the measurement. On-line signal-space projection (SSP; Tesche et al., 1995) was used for removing external noise. Response peak latencies were derived from the gradiometer channel exhibiting the maximum response amplitude. Response source locations were visualized using minimum current estimates (MCEs; Uutela et al., 1999) and quantified for the 1-s sound with unrestricted equivalent current dipoles (ECDs; filter passband 2–15 Hz) using a selection of 81 sensors over the right and left temporal areas. The ECDs were placed in a head-based coordinate system defined by the x -axis passing through the preauricular points (positive locations to the right of the center of the head and negative locations to the left), the y -axis passing in an anterior–posterior direction through the nasion (positive locations

anterior to the center of the head), and the z -axis being the vector cross product of the x and y unit vectors (positive locations vertically upward from the center of the head). Reaction time (RT) variation was calculated for each subject by ordering the RTs of each trial and subtracting the average of the slowest half from that of the fastest half. The variation of the brain response latency was obtained for each subject by separately averaging the MEG trials corresponding to the fast and slow RTs (filter passband 0.5–15 Hz) and calculating the difference between the peak latencies of the resulting responses. Statistical significances were determined with repeated measures analyses of variance (ANOVAs), t tests, and Pearson correlation coefficients.

Results

We found that sounds smoothly increasing in intensity elicited a prominent transient brain response both in the active ($t[29] = 9.47$, $P < 0.001$, $t[29] = 12.62$, $P < 0.001$ for left and right hemisphere, respectively) and passive ($t[29] = 7.33$, $P < 0.001$, $t[29] = 15.70$, $P < 0.001$) recording conditions (Fig. 1). This response was followed by sustained brain activity tracking the development of the stimulus intensity envelope. The emergence of the transient response contradicts the traditional view that abrupt changes in sound energy are required for the elicitation of cortical electromagnetic responses (Clynes, 1969; Näätänen, 1992). The diver-

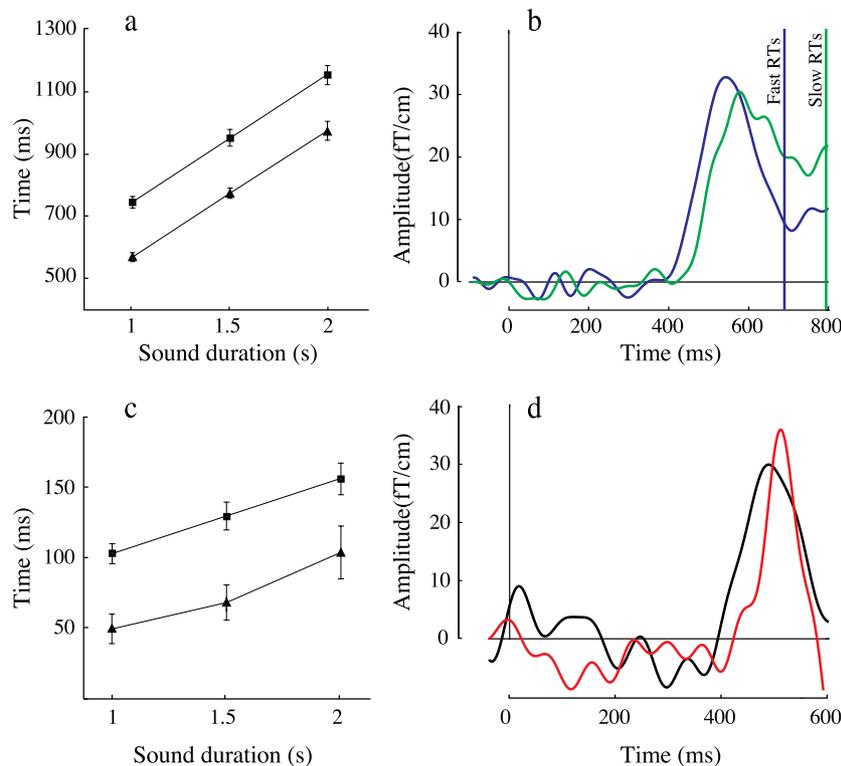


Fig. 2. The temporal relationship between brain dynamics and behavioral responses. (a) The behavioral responses averaged across subjects occurred at latencies 700–1100 ms (squares), whereas the brain responses preceded RT in the 500- to 900-ms range (triangles). The difference between RT and brain response latency remained constant at 180 ms (scale bars represent SEM). (b) Selective averaging of the data revealed that variation in brain response latency is directly carried over to RT variation. Fast and slow RTs were preceded by transient brain activity occurring rapidly (blue) and with a slight delay (green; 1-s sound, active condition), respectively. (c) Selective averaging showed that the variation in the peak latency (triangles) of the transient brain response accurately predicted the variation (squares) in RT (grand average; scale bars represent SEM). (d) Typical single-subject responses obtained in both the active (red) and passive (black) recording conditions (1-s sound, approximately 50 stimulus presentations, recording time 3 min).

gence between the expected response and the one actually measured can be estimated by assuming that the stimuli elicit only a sustained response but no transient responses and that the magnitude of the sustained response linearly reflects sound intensity (Picton et al., 1978a,b). If this sustained response is taken to commence at the point when brain activity deviates from baseline noise level and to reach its final level at stimulus offset, the transient response results in an unexpected amplitude increase of 200% and 110% in the active and passive condition, respectively (estimate gained from grand-averaged responses over subjects and stimuli).

Source localization revealed that the transient response was generated near the auditory cortex. The mean x -, y -, and z -coordinates of the ECDs in the active condition were $-44/5/65$ and $48/14/53$ mm in the left and right hemisphere, respectively. The corresponding source locations for the response in the passive condition were $-49/2/56$ and $49/13/53$ mm and, for the N100 response, $-49/5/55$ and $49/7/51$ mm, the source location differences being statistically nonsignificant.

Both the transient and the sustained brain activity were more prominent and spatially constrained in the right hemisphere where the amplitude of the transient response was diminished by 19% when measured in the passive recording condition (response amplitudes were larger in the active condition in 9 out of 10 subjects; $F[1,8] = 6.82$, $P < 0.05$). In the active condition, the transient response peaked at different latencies depending on the energy slope of the stimulus (568, 774, and 973 ms for the 1-, 1.5-, and 2-s sounds, respectively; $F[2,18] = 253.6$, $P < 0.001$). We tested also the idea that the transient response is triggered when the intensity of the stimulus exceeds a fixed threshold value. As the source locations and morphologies of the N100 and the transient response observed here were similar, we used the N100 peak latency to estimate the time lag between stimulus intensity exceeding this hypothesized threshold and the transient response reaching its peak amplitude. The intensity levels of the stimuli were significantly different 100 ms before the peak latency of the transient response (22.8, 21.5, and 20.5 dB for the 1-, 1.5-, and 2-s sounds, respectively; $F[2,18] > 3.8$, $P < 0.05$), indicating that it is unlikely that a fixed threshold underlies the triggering of the transient response.

As the stimulus envelope was devoid of sudden changes in sound energy, there was nothing in the stimulus envelope in itself that would lead one to expect a transient brain response to emerge at any particular latency. However, the timing of this brain response was clearly linked to the behavioral responses (mean RT = 744, 951, and 1154 ms for the 1-, 1.5-, and 2-s sounds, respectively; Fig. 2), which always occurred 180 ms after the transient brain response ($r = 0.97$, $P < 0.001$). Further, classifying the responses according to RT, we found that the transient response preceding fast RTs always occurred earlier than the activation preceding slow RTs. As stimulus intensity slope was decreased, RT variation increased (103, 130, and 156 ms for the 1-, 1.5-, and 2-s sounds, respectively; $F[2,18] = 57.7$, $P < 0.001$), which could be explained by increased variation in the peak latency of the transient response (49, 68, and 104 ms for the 1-, 1.5-, and 2-s sounds, respectively; $F[2,18] = 5.9$, $P = 0.01$; correlation between the two measures: $r = 0.52$, $P < 0.005$). That is, the results indicate the presence of one constant RT variation component (of around 50 ms) that does not depend on the stimulus intensity slope and of another one (of around 50, 70, and 105 ms for the 1-, 1.5-, and 2-s sounds, respectively), which is equal to the response peak latency

variation and depends on the stimulus slope. These results show that changes in the latency of activation in auditory sensory areas are directly carried over to behaviorally measured timing of sound detection.

Discussion

To summarize, the current study establishes stimulation conditions under which a transient brain response elicited by sounds smoothly increasing in intensity accurately predicts the dynamics of behavioral sound detection, with the peak latency of this response precisely correlating with the moment when humans detect auditory stimuli. Further, even the slight jitter in the timing of this brain response is directly carried over to behavioral responses. Previous research has provided evidence that the fluctuations in behavioral reaction time are produced by the motor areas of cerebral cortex (Hanes and Schall, 1996). Complementing this, our findings show that auditory sensory areas can influence response timing. When stimulation conditions of this study are used, auditory areas appear to become solely responsible for changes in RT variation while the contribution of motor areas to this variation is constant.

The intensity level required for the elicitation of the transient brain response was different for different stimuli: as sound intensity increase was made slower, the intensity level required for the emergence of the response decreased. This indicates that it is unlikely that the transient response is triggered by sound intensity exceeding some fixed threshold level. Rather, our results are consistent with the idea that temporal integration of sound energy underlies sound detection (van den Brink and Houtgast, 1990; Eddins and Green, 1995; Garner and Miller, 1947; Green et al., 1957), with the chain of cortical events leading to perception of sound being triggered when a sufficient amount of acoustic cues related to the stimulus have been gathered.

Increasing sound intensity can indicate that the sound source is approaching the organism and therefore it is likely to be an ecologically important signal (Neuhoff, 1998). In accordance with this concept, rising intensity sounds generally produce more pronounced neurophysiological (Lu et al., 2001; Seifritz et al., 2002) and behavioral (Freiberg et al., 2001; Ghazanfar et al., 2002) responses than decreasing sound envelopes. The present study sheds further light on the neural mechanisms underlying the behavioral detection of rising intensity stimuli by showing that this detection is preceded by a distinct transient mass action response in the human brain. We found that this response is more pronounced in the right hemisphere, corroborating previous observations on the right hemispheric specificity of the processing of sounds whose source appears to be approaching the organism (Seifritz et al., 2002) and of auditory space in general (Palomäki et al., 2002; Rauschecker and Tian, 2000). It remains to be determined (e.g., by using spectrally complex stimuli such as speech) whether the lateralization of the transient response observed in the current study reflects hemispheric specialization of sound detection per se or of the processing of spatial sounds more generally.

The experimental setup described here provides an index of behavioral sound detection, which differs from previous findings relying on either a posteriori behavioral decision criteria (Hillyard et al., 1971; Parasuraman and Beatty, 1980; Parasuraman et al., 1982; Squires et al., 1973), or the use of subtraction methods

(Näätänen, 1992; Sams et al., 1985; Tiitinen et al., 1994), which result in responses with a low signal-to-noise ratio and require long recording times. The present stimulation paradigm provides a new framework where MEG responses, derived in only 3 min recording time (Fig. 2d), can be used to directly assess behavioral performance. This assessment can be done by a single experimental condition and no post hoc comparisons from behavioral performance are needed. Further, as the transient response can be reliably obtained even without the active participation of the subject, our experimental setup might allow the development of a noninvasive tool for rapid, objective assessment of the functionality of the human auditory system. The transient response could turn out to be useful in the assessment of hearing development and in the diagnosis of patients with compromised responsive capabilities.

Brain response latency fluctuations with a functional significance such as those observed here (Figs. 2b and c) pose an interesting challenge for the uniformly used averaging technique in brain research. Inherently, noisy brain measurements include stimulus-induced brain responses that are assumed to be invariant and time locked to the stimulus and which can therefore be extracted through multiple presentations of the stimulus and subsequent averaging of the measured signal. Unfortunately, the current results corroborate those of previous studies (e.g., Parasuraman et al., 1982; Squires et al., 1973) showing that brain responses can be inherently time varying. This implies that averaging diminishes the amplitude of transient responses and that amplitude changes across experimental conditions could reflect the degree of temporal jitter rather than the actual strength of the neural response.

While attentional engagement increased the amplitude of the transient response (Fig. 1), the latency and source location of the response remained stable between the active and passive conditions. This implies that the attentional amplitude enhancement reflects modulated activity in the same cortical areas as those generating the transient response in the passive condition. This enhancement could be due to attention altering the effective local feedback (Douglas et al., 1995) in the responding areas by, for example, changing the tonic inhibition from prefrontal areas (Knight et al., 1999). In this case, as the response latency was not affected by attention, top-down processes may not affect the neural events (e.g., spectrotemporal integration) preceding the transient response nor the threshold required for cortical feedback to be triggered. Alternatively, the change in response amplitude could be due to averaging, with the individual responses in the passive condition having the same amplitude as in the active condition but a greater latency variation. In this case, attention would concentrate into a narrower range the threshold at which local cortical feedback is activated without affecting the strength of the actual feedback. Therefore, while attention clearly affects the sensory processes underlying sound detection, these processes may have components describable as bottom-up in either the effective strength of cortical feedback or—depending on the mechanisms of the attentional effect—the threshold range at which this feedback is activated. Previously, human sound detection has been described in terms of top-down attentional selection mechanisms (Luck and Hillyard, 2000) or bottom-up attention-independent “automatic” brain processes (Näätänen, 1992). In this particular context, our results could be interpreted to indicate that human sound detection is both an automatic process (with the transient response obtainable in the passive condition) and one modulated by attention (which

increases the response amplitude). Given this apparent contradiction, cognitive brain research might benefit from rephrasing this question in terms of, for example, auditory scene analysis (Bregman, 1990).

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References

- Bregman, A.S., 1990. Auditory Scene Analysis: The Perceptual Organization of Sound. MIT Press, Cambridge, MA.
- Clynes, M., 1969. The dynamics of R-M function. In: Donchin, E., Lindsley, D.B. (Eds.), Average Evoked Potentials: Methods, Results and Evaluations. U.S. Government Printing Office, Washington, DC, pp. 363–374. NASA SP-191.
- Douglas, R.J., Koch, C., Mahowald, M., Martin, K.A., Suarez, H.H., 1995. Recurrent excitation in neocortical circuits. *Science* 269, 981–985.
- Eddins, D.A., Green, D.M., 1995. Temporal integration and temporal resolution. In: Moore, B.C.J. (Ed.), Hearing. Handbook of Perception and Cognition, second ed. Academic Press, San Diego, pp. 207–242.
- Freiberg, K., Tually, K., Crassini, B., 2001. Use of an auditory looming task to test infants' sensitivity to sound pressure level as an auditory distance cue. *Br. J. Dev. Psychol.* 19, 1–10.
- Garner, W.R., Miller, G., 1947. The masked threshold of pure tones as a function of duration. *J. Exp. Psychol.* 37, 293–303.
- Ghazanfar, A.A., Neuhoff, J.G., Logothetis, N.K., 2002. Auditory looming perception in rhesus monkeys. *Proc. Natl. Acad. Sci. U. S. A.* 99, 15755–15757.
- Green, D.M., Birdsall, T.G., Tanner, W.P., 1957. Signal detection as a function of signal intensity and duration. *J. Acoust. Soc. Am.* 29, 523–531.
- Hanes, D., Schall, J., 1996. Neural control of voluntary movement initiation. *Science* 274, 427–430.
- Hillyard, S.A., Squires, K.C., Bauer, J.W., Lindsay, P.H., 1971. Evoked potential correlates of auditory signal detection. *Science* 172, 1357–1360.
- Hyde, M., 1997. The N1 response and its applications. *Audiol. Neurootol.* 5, 281–307.
- Jaskowski, P., Rybarczyk, K., Jaroszyk, F., 1994. The relationship between latency of auditory evoked potentials, simple reaction time, and stimulus intensity. *Psychol. Res.* 56, 59–65.
- Klein, D.J., Depireux, D.A., Simon, J.Z., Shamma, S.A., 2000. Robust spectrotemporal reverse correlation for the auditory system: optimizing stimulus design. *J. Comput. Neurosci.* 9, 85–111.
- Knight, R.T., Staines, W.R., Swick, D., Chao, L.L., 1999. Prefrontal cortex regulates inhibition and excitation in distributed neural networks. *Acta Psychol. (Amst)* 101, 159–178.
- Lu, T., Liang, L., Wang, X., 2001. Neural representations of temporally asymmetric stimuli in the auditory cortex of awake primates. *J. Neurophysiol.* 85, 2364–2380.
- Luck, S.J., Hillyard, S.A., 2000. The operation of selective attention at multiple stages of processing: evidence from human and monkey electrophysiology. In: Gazzaniga, M.S. (Ed.), *The New Cognitive Neurosciences*. Bradford Book MIT Press, Cambridge, MA, pp. 687–700.
- Näätänen, R., 1992. Attention and Brain Function. Erlbaum, New Jersey.
- Näätänen, R., 2000. Mismatch negativity (MMN): perspectives for application. *Int. J. Psychophysiol.* 37, 3–10.

- Neuhoff, J.G., 1998. Perceptual bias for rising tones. *Nature* 395, 123–124.
- Palomäki, K., Tiitinen, H., Mäkinen, V., May, P., Alku, P., 2002. Cortical processing of speech sounds and their analogues in a spatial auditory environment. *Cogn. Brain Res.* 14, 294–299.
- Parasuraman, R., Beatty, J., 1980. Brain events underlying detection and recognition of weak sensory signals. *Science* 210, 80–83.
- Parasuraman, R., Richer, F., Beatty, J., 1982. Detection and recognition: concurrent processes in perception. *Percept. Psychophys.* 31, 1–12.
- Picton, T.W., Woods, D.L., Proulx, G.B., 1978a. Human auditory sustained potentials I. The nature of the response. *Electroenceph. Clin. Neurophysiol.* 45, 186–197.
- Picton, T.W., Woods, D.L., Proulx, G.B., 1978b. Human auditory sustained potentials II. Stimulus relationships. *Electroenceph. Clin. Neurophysiol.* 45, 198–210.
- Rauschecker, J.P., Tian, B., 2000. Mechanisms and streams for processing of “what” and “where” in auditory cortex. *Proc. Natl. Acad. Sci. U. S. A.* 97, 11800–11806.
- Sams, M., Paavilainen, P., Alho, K., Näätänen, R., 1985. Auditory frequency discrimination and event-related potentials. *Electroenceph. Clin. Neurophysiol.* 62, 437–448.
- Seifritz, E., Neuhoff, J.G., Bilecen, D., Scheffler, K., Mustovic, H., Schachinger, H., Elefante, R., Di Salle, F., 2002. Neural processing of auditory looming in the human brain. *Curr. Biol.* 12, 2147–2151.
- Shamma, S., 2001. On the role of space and time in auditory processing. *Trends Cogn. Sci.* 5, 340–348.
- Shibasaki, H., Miyazaki, M., 1992. Event-related potential studies in infants and children. *J. Clin. Neurophysiol.* 9, 408–418.
- Squires, K.C., Hillyard, S.A., Lindsay, P.H., 1973. Vertex potentials evoked during auditory signal detection: relation to decision criteria. *Percept. Psychophys.* 14, 265–272.
- Tesche, C.D., Uusitalo, M.A., Ilmoniemi, R.J., Huutilainen, M., Kajola, M., Salonen, O., 1995. Signal-space projections of MEG data characterize both distributed and well-localized neuronal sources. *Electroenceph. Clin. Neurophysiol.* 95, 189–200.
- Tiitinen, H., May, P., Reinikainen, K., Näätänen, R., 1994. Attentive novelty detection in humans is governed by pre-attentive sensory memory. *Nature* 372, 90–92.
- Uutela, K., Hämäläinen, M., Somersalo, E., 1999. Visualization of magnetoencephalographic data using minimum current estimates. *NeuroImage* 10, 173–180.
- van den Brink, W.A.C., Houtgast, T., 1990. Spectro-temporal integration in signal detection. *J. Acoust. Soc. Am.* 88, 1703–1711.