Dynamics of Cortical Responses to Tone Pairs in Relation to Task Difficulty: A MEG Study

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Abstract: We investigated the effect of task difficulty on the dynamics of auditory cortical responses. Whole-scalp magnetoencephalographic (MEG) signals were recorded while subjects performed a same/different frequency discrimination task on equiprobable tone pairs applied in blocks of five, which were separated by a 10 s intertrial interval. Task difficulty was manipulated by the interpair frequency difference. The manipulation of task difficulty affected the amplitude of the N100m response to the first tone and the latency of the N100m response to the second tone in each pair. The N100m responses were smaller and peaked significantly later in the difficult than in the easy condition. The later processing field (PF) responses were longer in duration in the difficult condition. In both conditions, the duration of the PF response was negatively correlated with the subject's performance in the task, and was longer in the less successful subjects. The PF response may thus reflect the subjects' effort to resolve the task. The N100m and the PF responses did not differ between the tone pairs along the five-pair trial as a function of task difficulty, suggesting that changes in response along the five-pair trial are not easily affected by high-level manipulations. *Hum Brain Mapp* 30:1592–1604, 2009. © 2008 Wiley-Liss, Inc.

Key words: magnetoencephalography; frequency discrimination; N100m; auditory; processing field; task difficulty

INTRODUCTION

The effects of voluntary attention on auditory cortical responses have been studied extensively using different brain imaging methods. Attention has been shown to affect early cortical responses in the primary auditory cortex [Fujiwara et al., 1998; Jäncke et al., 1999a,b], although electroencephalographic (EEG) and magnetoencephalographic (MEG) studies suggest that the most prominent effects are found at later response components and brain areas [e.g. Arthur et al., 1991; Coch et al., 2005; Grady et al., 1997; Hari et al., 1989; Michie et al., 1993; Petkov et al., 2004; Pugh et al., 1996; Rif et al., 1991; Tzourio et al., 1997; Woldorff and Hillyard, 1991].

In the classical auditory selective attention paradigm [Hillyard et al., 1973], the stimuli are presented through two separate "sensory channels" (e.g. the two ears), and subjects are required to detect rare targets within the "rele-

Contract grant sponsor: EU Large-Scale Facility Neuro-BIRCH III (Human Capital and Mobility Program of the Community); Academy of Finland Centre of Excellence Program; Sigrid Jusélius Foundation in the Brain Research Unit, Low Temperature Laboratory of Helsinki University of Technology.

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Received for publication 30 August 2007; Revised 26 April 2008; Accepted 15 May 2008

DOI: 10.1002/hbm.20629

Published online 18 August 2008 in Wiley InterScience (www.interscience.wiley.com).

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vant channel," while ignoring sounds presented in the "irrelevant channel" [Alho et al., 1987b; Coch et al., 2005; Hansen and Hillyard, 1980, 1983; Michie et al., 1993; Näätänen et al., 1978; Okita, 1979; Woldorff et al., 1993]. Under these experimental conditions, the auditory electric 100-ms response (N100) to standards in the attended channel increases compared to the ignored channel [Hansen and Hillyard, 1984; Hillyard et al., 1973; Lange et al., 2003; Okita, 1979; Rif et al., 1991; Schwent and Hillyard, 1975; Woldorff et al., 1993].

Näätänen [1982, 1992] focused on the impact of attention on later responses, noting that selective attention is mainly reflected in a "processing negativity" (PN) response, which peaks around 180–200 ms after stimulus onset, and lasts for several hundreds of milliseconds [Näätänen, 1990; for a review see Näätänen and Michie, 1979; Näätänen et al., 1978, 1981]. The earlier part of this response overlaps with the N100 response, and has been argued to be the source of the N100 enlargement, whereas the later part may have a different, frontal origin [Hansen and Hillyard, 1980, 1984; Näätänen, 1982; Nager et al., 2001]. The magnetic counterpart of this response, the "processing field" [PF, Hari et al., 1989], was found to emerge at the supratemporal auditory cortex, ~1 cm anterior to the source of the magnetic 100-ms response N100m [Arthur et al., 1991]. According to Näätänen [1988, 1992], PN reflects a comparison process between the sensory input and an "attentional trace," which is a temporary neuronal representation of the relevant physical features of the stimuli in the attended channel.

In the context of selective attention tasks, where subjects need to attend to one of two streams and detect rare targets in it, task difficulty has been reported to affect both the N100 and the PN responses. In the more difficult condition, where the target is more similar to the nontargets, or the two sensory channels contain similar stimuli, the N100 responses are usually smaller [Fitzgerald and Picton, 1983; Michie et al., 1993; Parasuraman, 1980] and peak later than under the easy condition [Goodin et al., 1983; Näätänen and Michie, 1979]. Results for the later PN responses have been somewhat mixed: whereas some authors reported PN to be delayed [Näätänen and Michie, 1979; Parasuraman, 1980; Schwent and Hillyard, 1975], longer in duration [Hansen and Hillyard, 1983] or larger in amplitude under the difficult condition [Hansen and Hillyard, 1983; Maiste and Picton, 1987; Michie et al., 1993; Okita, 1989], others found no effect of task difficulty on the PN amplitude [Alain and Izenberg, 2003; Näätänen, 1992].

We now asked whether the same effects would be found when task difficulty is manipulated in the context of a different paradigm which does not include channel selection. In the present study we therefore employed a paradigm that uses only "one channel." We designed two versions of a "same/different" frequency paradigm with equiprobable tone pairs. In the easy condition, the two tones in a pair were separated by 100-Hz frequency difference, and in the difficult condition by 15 Hz. In this equiprobable paradigm, the first low tone in a pair could be either part of a

low–low pair ("same") or a low-high pair ("different") and similarly for a first high tone (high–high or high–low). This seemingly small change from the traditional detection of rare targets embedded within frequent distracters modifies the cognitive context of the task from typical template matching to an interstimulus comparison between the two tones composing a pair. This enabled us to test whether modifying the difficulty of online stimulus comparison in a single channel task has a similar impact on responses as that of comparing a stimulus and an internal template in the context of selective attention.

In our same/different paradigm, tone pairs separated by 1 s were administered in sequences of five pairs. A long interval of 10 s separated these five-pair trials. By averaging responses at the various pair positions in a trial (1st, 2nd, etc.) we could analyze the differences in responses to consecutive tone pairs along the five-pair trial (referred to here as "across-pair dynamics"). Our choice of a brief interstimulus interval within a pair (100 ms), an intermediate (1 s) interpair interval, and a long intertrial interval (10 s) was based on previous findings suggesting that several time constants underlie the dynamics of N100m responses. N100m normally decreases in amplitude as the interstimulus interval decreases from 8–10 s to about 0.5 s [Hari et al., 1982, 1987; Lammertmann et al., 2001; Lu et al., 1992a,b; Mäkelä et al., 1993; Näätänen and Picton, 1987; Sörös et al., 2001], probably due to a temporary loss of excitability or an increase in active inhibition which recovers over a silent interval [Loveless et al., 1989, 1996]. Interestingly, when pairs of tones are presented at intervals of less than 300 ms within a pair, N100m to the second tone of a pair is enhanced compared to the first one [Levänen et al., 1996b; Loveless and Hari, 1993; Loveless et al., 1989]: an enhancement which may reflect a temporal integration process [Loveless et al., 1996; McEvoy et al., 1997].

Since we administered an easy and a difficult version of the same paradigm, we could also assess the impact of task difficulty on the across-pair dynamics of responses to consecutive pairs along the trial. Only a few studies have assessed the impact of selective attention on the dynamics of responses. The enlargement of N100 as a result of selective attention persists over a silent interval of 6 s [Donald and Young, 1982], whereas the attentional effect on PN prolongation develops progressively over several seconds [Hansen and Hillyard, 1988]. Assessing the dynamics of responses across five consecutive pairs allowed us to test whether the easy and the difficult tasks show similar dynamics along the trial, or whether the attentional effects develop, for example, more slowly in the difficult task.

METHODS

Subjects

We studied 10 normal-hearing subjects from the laboratory personnel (five females, five males; 22–41 years, mean age 28 ± 5 years; nine right-handed, one ambidextrous).

Figure 1.

A sample trial composed of five tone pairs. Each vertical bar represents a 50-ms tone. Tones within a pair were separated by 100 ms, pairs by 1 s, and trials by 10 s. In this illustration, hatched bars denote tones of 1,100 Hz and filled bars denote 1,000 Hz (i.e. stimuli used in the easy condition, see text).

Informed consent was obtained from each subject before the experiment. The study received prior approval from the Ethics Committee of the Helsinki Uusimaa Hospital District.

Stimuli and Task

The subjects' task was to compare the frequency of two 50-ms tones presented with a 100-ms interstimulus interval (from offset to onset), and determine whether the tones were the same or different. Each trial was composed of five tone pairs, with 1-s interpair interval (from offset to onset). A 10-s intertrial interval (from offset to onset) separated sequential trials. The temporal structure of the trials is schematically illustrated in Figure 1.

Two task conditions, differing in difficulty, were administered in different experimental runs. In the easy condition, each tone in a pair was either 1,000 or 1,100 Hz (i.e. a 10% difference between the tones within a pair). In the difficult condition, tones were either 1,040 or 1,055 Hz (i.e. a 1.5% difference). Under both conditions, the high and the low tones had equal probability. Thus, in both conditions high-low, low-high ("different"), low-low, and high-high ("same") pairs were equally likely at each of the five tone-pair positions composing a trial. Tones were presented binaurally through plastic tubes and earpieces. The intensity level was adjusted to be comfortable, about 70 dB above the individually determined hearing threshold.

Behavioral Procedure

Subjects participated in three sessions: a behavioral "pretest" session, a MEG recording session with partial behavior (see below), and a behavioral "post-test" session that replicated the protocol of the "pretest" session.

Behavioral pre- and post-tests

The pre- and post-tests were conducted on a portable PC computer. Both of the sessions consisted of four blocks that were administered in an "easy-difficult-easy-difficult"

order. Each block consisted of 28 trials (i.e., a total of 56 trials for each task condition) and lasted 7 min. Thus, the total duration of the behavioral test, including a 1 min break between blocks, was 31 min. The sequence of tones in each block was identical for the pre- and post-tests. Subjects were instructed to listen carefully to the sounds presented over the headphones, and respond with a left mouse click whenever tones in a pair differed in frequency (a "same/different" task). After each assessment, the percent correct (i.e., the number of correct responses vs. the total number of pairs) for the easy and difficult conditions was calculated and averaged across trials for each of the five pair positions.

Behavioral procedure during MEG recordings

During the MEG recordings, subjects performed three runs each lasting ~15 min, with 2–3 min rest between blocks. Four subjects performed two easy runs and one difficult run (in an "easy-difficult-easy" order), one performed two easy runs and two difficult runs ("easy-difficult-easy-difficult") and the other five performed two difficult runs and one easy run ("difficult-easy-difficult"). The subjects' task was to decide, for each pair, whether the two tones were of the same frequency or different. However, to avoid motor contamination, subjects were asked to respond with a minor index finger lift only if the two sounds in the last (5th) pair were different. To delay the motor-related responses and separate them from the auditory ones, subjects were instructed to wait for a few seconds during the 10-s intertrial interval before responding. All subjects reported at the end of the measurements that they listened carefully to all tone pairs, even though a response was required for the 5th pair only. The behavioral procedures are summarized in Table I.

MEG Recordings

During the MEG recordings, the subject was seated in a magnetically shielded room with his or her head supported against the helmet-shaped bottom of the neuromagnetometer. The neuromagnetic signals were recorded with a whole-scalp 306-channel device (VectorView™, Elekta Neuromag Oy, Helsinki, Finland), which comprises 102 triple sensors. Each sensor element contains two orthogonal planar gradiometers and one magnetometer, thereby providing three independent measurements of the magnetic field at each sensor location. We only analyzed signals from the 204 planar gradiometers, which measure the two orthogonal tangential derivatives $\partial B_z/\partial x$ and $\partial B_z/\partial y$ of the magnetic field component B_z normal to the helmet surface at the sensor location. These sensors detect the largest signal just above the activated brain area. Four head-position indicator coils were attached to the scalp, and their positions were measured with a 3D digitizer; the two periauricular points and the nasion specified the head coordinate frame. The head position with respect to the sensor

TABLE I. The experimental protocol

	Conditions	Runs per condition	Trials per run	Duration per run (min)	Response with button press	Order of runs
Pretest	Easy	2	28	7	For each pair	Easy and difficult alternated
	Difficult	2	28	7	For each pair	
MEG	Easy	1 or 2	>40	~15	For 5th pair	Easy-difficult-easy or difficult-easy-difficult
	Difficult	2 or 1	>40	~15	For 5th pair	
Post-test	Easy	2	28	7	For each pair	Easy and difficult alternated
	Difficult	2	28	7	For each pair	

array was then determined by feeding current to the marker coils when the subject was seated under the neuro-magnetometer.

The recording passband was 0.03–200 Hz, the sampling rate 600 Hz, and the data were low-pass filtered off-line at 40 Hz. The vertical electro-oculogram was recorded simultaneously to reject data contaminated by eye blinks and movements. Signal averaging was based on the pair position within the trial. Thus, pairs appearing in the same position in a trial were always averaged together, irrespective of the tones (high-low, low-high, low-low, high-high) included in these pairs. This averaging yielded five averages for each condition, corresponding to 1st–5th pairs. In addition, we also derived “same” averages from all subjects, in which only “same” pairs were included in the average regardless of their pair position. This kind of averaging did not take into account possible differences in responses across different pair positions, but enabled us to examine global task effects (easy vs. difficult).

A minimum of 40 responses was averaged for each pair. For each subject, the two MEG runs that were behaviorally similar were averaged together off-line.

Data Analysis

MEG data analysis

We first measured the peak amplitudes and latencies of the N100m responses from the maximum-amplitude channel as a vector-sum of the gradients $\sqrt{\left(\frac{\partial B_z}{\partial x}\right)^2 + \left(\frac{\partial B_z}{\partial y}\right)^2}$. Similarly, the offset latencies and durations of the PF response were measured from the channel with the maximal response.

To identify the neural sources of the evoked responses, equivalent current dipoles (ECDs) were searched by a least-squares fit to responses of 20–30 gradiometer channels over the temporal cortices [Hämäläinen et al., 1993]. An ECD represents the location, orientation, and strength of the net current in the activated brain area. Only ECDs explaining more than 80% of the local field variance during the response peak were accepted for further analysis.

For source analysis, the head was modeled as a homogeneous sphere. The model parameters were optimized

for the intracranial space obtained from MR images that were available for all subjects except one; the average of the nine subjects’ head models was used for the analysis of the remaining subject. The ECDs were found during the main responses N100m and PF, i.e. ~100 ms and ~300–500 ms after the stimulus onset in each hemisphere. Any single dipole was used to explain the data during the corresponding response, except in two subjects, in whom a better explanation of the data was obtained by applying the source of N100m for the time window of PF as well. The sources were searched under the condition for which two runs were available and which thus had a better signal-to-noise ratio. They were then used to explain the responses in the other condition. In most cases, the sources of N100m and PF were found for the responses to the 1st and the 5th tone pair, respectively, since these pairs typically elicited the largest responses. Since the results from the sensor-level analysis were essentially the same as the results obtained with the dipole modeling, we only report the latter results.

Response amplitudes and latencies between different conditions were statistically compared using one- or two-way repeated measures analysis of variance (ANOVA), with within-subjects factors of hemisphere (left and right), task difficulty (easy and difficult), and pair position (1st–5th). When comparing the first and second responses within a pair, a within-subjects factor of tone order (first and second) was added. The Greenhouse-Geisser epsilon correction for the Sphericity assumption was applied to all data. In addition, two-tailed Student *t* tests were used for statistical comparisons of N100m and PF source locations.

Offsets of the PF responses were measured as the delay between the onset of the first tone of a pair, and the point in the descending slope of the PF response at which two standard deviations (SD) from the baseline noise level were reached. The activation strength during the PF response was evaluated as the area under the descending slope between 350 ms after the onset of the first tone in a pair, and the point 2 SDs from the baseline noise level. For one subject, the PF responses could not be identified for the right hemisphere (RH), and her data were therefore excluded from this part of the analysis.

Figure 2.

Responses of subject S3 to 1st (black), 2nd (red), and 5th (blue) tone pairs in the easy condition. The head is viewed from above. The upper and lower traces in each location correspond to the latitudinal and longitudinal gradients of the radial magnetic field

component Bz. The inserts show enlarged responses recorded over the left and right auditory cortices. The N100m responses to the first and second tones (marked here as N100m and N100m'), as well as the PF responses, are marked in the inserts.

Behavioral data analysis

Behavioral data obtained during pre- and post-tests were analyzed using three-way repeated measures ANOVA, with task difficulty, pair position and test (pre and post) as within-subject factors. Correlations between behavioral data obtained during the MEG measurement and the MEG data were tested using Spearman's correlation coefficient.

RESULTS

The cortical responses to the five tone pairs within a trial in both the easy and difficult conditions were characterized by two main components, occurring bilaterally over the au-

ditory cortices: the N100m responses, peaking on average around 86 ms after the tone onsets, and the PF responses, overlapping the N100m responses to the second¹ tone in each pair and lasting about 350–550 ms after the second tone onset. Figure 2 illustrates the responses of subject S3 to the 1st, 2nd, and 5th tone pairs in the easy condition.

Source Locations

In line with previous studies [for a review, see Hari, 1990], the N100m responses were adequately explained by

¹Tones within pairs are marked as "first" and "second"; pairs within trials are marked as 1st, 2nd, etc.

Figure 3.

Top, right: N100m source strengths as a function of time in subject S3 for the 5th pair under the easy (gray traces) and difficult (black traces) conditions. Top, left: The locations (white dots) and the orientations (bars) of the current dipoles used to model the responses superimposed on the subject's MR image. Bottom: Average ($\pm$ SEM) locations of the N100m (open squares) and PF (filled squares) sources. In the coordinate system the x-axis goes through periauricular points from left to right, the y-axis from the back of the head to the nasion, and the z-axis points to the vertex.

two ECDs, one in the left and the other in the right supratemporal auditory cortex. Figure 3 shows the equivalent current dipoles and the corresponding source waveforms of subject S3 for the responses to the 5th pair. In this subject, the same dipoles were used to explain both N100m and PF responses. The dipoles that were searched under the easy condition adequately explained the responses in the difficult condition as well. Across subjects, the sources of PF responses tended to be deeper than the sources of N100m in the left hemisphere (LH; $P = 0.06$, Bonferroni corrected), but in other directions the source locations did not significantly differ from each other (see Fig. 3).

N100m Amplitudes

Responses to the first tone in a pair

For the first tone in a pair, the N100m response amplitudes were, on average, larger in the easy than in the diffi-

cult condition for all five pairs (Figs. 4 and 5a). The average amplitude differences (across all positions) between the easy and the difficult conditions were 6 ± 1 nAm and 5 ± 1 nAm in the LH and the RH, respectively (effect of task difficulty: $F(1,9) = 7.1$, $P < 0.03$).

The N100m responses to the first tone differed as a function of the tone pair's position: The largest N100m responses were evoked by the first tone in the 1st pair in both conditions. By the 2nd pair, these responses decreased in amplitude by more than 50% and remained fairly constant from the 2nd pair on (effect of pair position: $F(4,36) = 116$, $P < 0.000001$).

Unlike absolute amplitudes, the dynamics of the first N100m responses along the five-pair trial did not significantly differ between the easy and difficult task condition, as shown by the nonsignificant interaction between task difficulty and pair position ($F(4,36) = 1.04$, $P = 0.38$; see Fig. 5a).

Responses to the second tone in a pair

For the second tone in a pair, N100m amplitudes were again larger in the easy than in the difficult condition (Figs. 4 and 5), but only in the LH: The average difference between the easy and the difficult conditions was 6 ± 2 nAm (effect of task difficulty: $F(1,9) = 6.2$, $P < 0.05$).

Although the second tone in each pair also elicited prominent N100m responses, these behaved differently along the five-pair trial compared to the responses to the first tones: the responses to the second tones increased in amplitude from the 2nd pair on (effect of pair position: $F(4,36) = 11.2$, $P < 0.005$; see Fig. 4). The different across-pair dynamics from the first tones is shown statistically by the significant interaction of tone order (first or second) and pair number ($F(4,36) = 28.2$, $P < 0.00001$).

Similar to the responses to the first tones, the across-pair dynamics of responses to the second tones did not significantly differ between easy and difficult conditions (no interaction between task difficulty and pair position: $F(4,36) = 2.7$, $P = 0.072$).

Second/first response ratio

Figure 5c depicts the second/first response ratios, which increased significantly throughout the five pairs (effect of pair position: $F(4,28) = 15.13$, $P < 0.002$). This enhancement effect was nonsignificant between the 3rd and 5th pairs, and it did not differ significantly between the easy and difficult conditions (effect of task difficulty: $F(1,7) = 0.54$, $P = 0.48$).

N100m Latencies

Responses to the first tone in a pair

Response latencies to the first tone in a pair did not significantly differ between task conditions (effect of task difficulty: $F(1,9) = 1.1$, $P = 0.3$). However, the latencies

Figure 4.

Left: N100m responses of subject S8 to all five tone pairs in the easy (gray traces) and the difficult (black traces) conditions. The black bars at the bottom refer to the stimuli. Right: Grand averages of the N100m responses over all subjects ($N = 10$).

differed as a function of pair position (see Fig. 4) in both conditions: The responses peaked, on average, at 87 ± 2 ms and 86 ± 3 ms in the LH and RH, respectively, and shortened from the 1st to 5th pair (effect of pair position: $F(4,36) = 7.7$, $P < 0.005$). For the easy condition, responses shortened in the LH from 91 ± 2 ms (1st pair) to 86 ± 2 ms (5th pair) and in the RH from 90 ± 2 ms to 84 ± 2 ms, respectively. Similarly, for the difficult condition the latencies shortened in the LH from 89 ± 2 ms (1st) to 84 ± 2 ms (5th) and in the RH from 88 ± 2 ms to 83 ± 3 ms, respectively. The across-pair dynamics did not differ between the easy and difficult conditions (no interaction for task difficulty and pair position: $F(4,36) = 0.96$, $P = 0.42$).

Responses to the second tone in a pair

In line with earlier studies [Levänen et al., 1996a; Mäkelä, 1988; Mäkelä et al., 1988; Sörös et al., 2001], the N100m responses to the second tone in a pair were significantly delayed compared to the first in both task conditions (effect of tone order: $F(1,9) = 16.5$, $P < 0.003$): The averaged second responses peaked at 131 ± 8 ms and 130 ± 9 ms in LH and RH, respectively. Unlike responses to the first tones, the latencies of the second N100m responses tended to be longer in the difficult condition (see Fig. 7): The averaged difference between the two conditions was 12 ms in the LH and 6 ms in the RH ($F(1,9) = 5.061$, $P = 0.051$). The latencies did not significantly differ as a function of pair position ($F(4,36) = 0.45$, $P = 0.66$), and there was no significant interaction between task difficulty and pair position ($F(4,36) = 1.2$, $P = 0.3$).

Processing Fields

Figure 6 (left) illustrates the grand averages of the PF source strengths over all subjects for all tone pairs in both task conditions, and the responses to the 5th pair in subjects S1 and S8 (right). Note that although this figure appears similar to Figure 4, it is based on PF, rather than N100m sources. Since the PFs for the 1st pair typically did not return to baseline during the 1-s analysis period, the following analysis was performed for the 2nd–5th pairs only.

PFs lasted significantly longer in the difficult than in the easy condition for all five pairs (see Figs. 6 and 7b). On average, the PFs (of 2nd–5th pairs) decayed 91 ± 27 ms (LH) and 62 ± 12 ms (RH) later in the difficult than in the easy condition (effect of task difficulty: $F(1,8) = 10.5$, $P < 0.02$). The difference between the easy and the difficult conditions was most prominent for the 5th pair, averaging to 162 ± 39 ms (LH; t -test: $P < 0.005$) and 96 ± 36 ms (RH; t -test: $P < 0.05$).

Similarly, the area under the PF curve was larger in the difficult than in the easy condition (effect of task difficulty: $F(1,8) = 15.7$, $P < 0.005$; see Figs. 6 and 7). The average area difference between the difficult and the easy conditions (for 2nd–5th pairs) was 2.6 ± 1.1 s * nAm (LH) and 2.4 ± 0.96 s * nAm (RH). This effect was again largest for the 5th pair, averaging to 6.2 ± 1.7 s * nAm (LH; t -test: $P < 0.006$) and 4.2 ± 1.3 s * nAm (RH; t -test: $P < 0.02$). This result is summarized in Figure 7d, which shows, for each subject, the PF area in the difficult condition as a function of the PF area in the easy condition, for the 2nd–5th tone pairs.

The PF offsets showed statistically significant changes along the trial in both the easy and difficult conditions,

Figure 5.

(a) Average ($\pm$ SEM) N100m amplitudes to the first tone in a pair. (b) Average ($\pm$ SEM) N100m amplitudes to the second tone in a pair. (c) The second/first N100m response ratios. Responses are shown as a function of pair position.

gradually increasing from the 2nd to the 5th pair (effect of pair position: $F(3,24) = 10.7$, $P < 0.003$). Similarly, the area under the PF curve increased from 2nd to 5th pair (effect of pair position: $F(3,24) = 12.05$, $P < 0.002$).

Analysis of “same” pairs

The difference between the easy and difficult conditions could have stemmed from the differences in the stimulus conditions (frequency differences of 100 vs. 15 Hz between the stimuli in the easy and difficult conditions, respectively) rather than from task difficulty. To control for this possibility, we performed a similar analysis on the responses to those tone pairs in which the frequencies of the two tones were the same (“same” pairs, see Methods) in all subjects. Figure 8 demonstrates the responses to “same” pairs in both experimental conditions in subjects S1, S3, and S8. The results were consistent with those found earlier: across subjects, PF responses decayed 112 ± 39 ms (LH) and 64 ± 19 ms (RH) later in the difficult than in the easy condition ($F(1,8) = 15.7$, $P < 0.005$). Moreover,

the area under the PF curve was significantly larger in the difficult than in the easy condition ($F(1,8) = 7.8$, $P < 0.03$).

Lateralization of the Responses

The overall responses tended to be stronger in amplitude in the LH than in the RH. Moreover, the task difficulty effects were also usually more prominent in the LH: the interaction between hemisphere and task difficulty approached significance for the second N100m response amplitudes ($F(1,9) = 4.84$, $P = 0.055$), the ratio between the second and the first response amplitudes ($F(1,7) = 4.5$, $P = 0.071$) and for the PF offset latency ($F(1,8) = 4.08$, $P = 0.078$).

Behavioral Results

The behavioral results were consistently worse in the difficult than in the easy condition (overall percentage correct: $69\% \pm 10\%$ vs. $95\% \pm 4\%$, $F(1,5) = 29.43$, $P < 0.005$). The results did not significantly differ between pre- and post-tests in either condition.

Behavioral results during MEG recordings

During the MEG recordings, we collected behavioral responses for the 5th pair in each trial. Figure 9 depicts the relative averaged area of PF (for the 5th pair of each subject) vs. the subjects’ relative performance on the task. Relative performance was calculated as the ratio of the individual subject’s and best subject’s success rate. Relative PF area was calculated in a similar manner. This calculation

Figure 6.

Grand averages of PF responses to all five tone pairs in easy (gray traces) and difficult (black traces) conditions. Inserts on the right show responses of individual subjects (S1 and S8) to the 5th tone pair in both easy and difficult conditions.

Figure 7.

(a) Average ($\pm$ SEM) N100m onset latencies to the second tones in a pair as a function of pair position. (b) Average ($\pm$ SEM) PF offset times. (c) Average ($\pm$ SEM) area under PF curves. (d) PF area under the difficult condition as a function of the PF area under the easy condition. Each point in the graph represents PF area of a single subject in a single tone pair.

was done in order to obtain a normalized scale ranging between 0 and 1 for each subject, for both measures. The PF area under the difficult task was negatively correlated with the subject's performance in this condition (Spearman's $\rho = -0.66$, $P < 0.01$; $R = -0.53$, $P < 0.05$). A similar trend was seen in the easy condition (Spearman's $\rho = -0.6$, $P < 0.01$; $R = -0.71$, $P < 0.03$) but this correlation

Figure 8.

Responses to "same" pairs in the easy (gray traces) and the difficult (black traces) conditions in subjects S1, S3, and S8.

resulted mainly from a single subject with the poorest performance and the largest relative PF area. Overall, subjects with better performance on the task had smaller PF areas.

DISCUSSION

In the present study, we tested the effect of task difficulty on auditory cortical responses by using a same/different frequency discrimination task that employed pairs of equiprobable tones, with either a small (difficult condition) or a large (easy condition) frequency difference in the "different" tone pairs. Tone pairs were administered in blocks of five with a large 10-s intertrial interval that enabled us to assess the impact of task difficulty on the dynamics of the cortical responses.

Task difficulty affected the amplitude of the N100m response to the first tone and the latency of the N100m response to the second tone in each pair. The N100m responses were smaller and peaked significantly later in the difficult than in the easy condition. The later PF responses were prolonged under the difficult condition, and their strength was inversely correlated to subjects' success on the task. However, the across-pair dynamics of

Figure 9.

Relative PF area of the responses to the 5th pair versus subject's relative performance under the easy (left) and difficult (right) conditions.

both the N100m and PF responses within a trial were unaffected by task difficulty.

Task Difficulty and Auditory Cortical Responses

In line with earlier studies [Fitzgerald and Picton, 1983; Goodin et al., 1983; Michie et al., 1993; Parasuraman, 1980], N100m amplitudes were smaller and their latencies longer in the difficult condition compared to the easy one, suggesting decreased neuronal coherence during the difficult task [Thornton et al., 2007]. These effects may be due to the smaller frequency difference between the tones in this condition [Näätänen et al., 1988]. However, since similar results have been obtained in previous studies that manipulated task difficulty, this result may imply that the neuronal activity underlying the N100m response is less coherent when the task becomes more difficult.

Moreover, our results further support the notion that task difficulty already affects auditory processing around 100 ms after the stimulus onset. This claim was also raised by other authors, but usually in relation to attentional effects (i.e. attention demanding versus no-attention conditions), rather than task difficulty per se [Coch et al., 2005; Fujiwara et al., 1998; Giard et al., 1988; Hansen and Hillyard, 1984; Hari et al., 1989; Jäncke et al., 1999b; Rif et al., 1991; Woldorff et al., 1993; Woldorff and Hillyard, 1991]. We now show that similar effects on N100m can be obtained outside the context of selective attention.

Interestingly, the effects of task difficulty on the N100m amplitude were exactly the opposite to those of selective attention: while increased selective attention increases the N100 response amplitude [Coch et al., 2005; Fujiwara et al., 1998; Hansen and Hillyard, 1984; Hari et al., 1989; Woldorff and Hillyard, 1991], a more difficult task decreased it. The opposing effects of attention and task difficulty on the N100m response may suggest a link between the N100m response and perceptual clarity. Whereas attention increases the perceptual clarity of the stimulus and sharpens the signal-to-noise-ratio [Carrasco et al., 2004], increased task difficulty, by decreasing perceptual clarity, decreases the N100m amplitude.

A more dramatic effect of task difficulty was found in the PF response, which was stronger and longer in the difficult condition. This result is consistent with the few studies which have addressed task difficulty effects, usually within a selective-attention paradigm, and reported increased PN peak latencies and larger amplitudes under a difficult condition [Hansen and Hillyard, 1980, 1983; Maiste and Picton, 1987; the “negative afterwaves” of Rohrbaugh et al., 1978]. Similarly, Hansen and Hillyard [1983] showed that “easy” processing terminates fast, as indicated by a smaller PN, whereas more difficult processing continues. However, some other studies have found almost no effect for task difficulty on PN amplitude [Alain and Izenberg, 2003; Näätänen, 1982; Parasuraman, 1980]. Furthermore, our results demonstrate that subjects who succeeded better in performing both tasks had smaller and

shorter PFs. We therefore suggest that the magnitude of the PF response may correlate with the amount of effort allocated by the subjects to solve the task.

Based on the results obtained in many selective attention studies, Näätänen [1982, 1988, 1992] suggested that PN, or PF, reflects a template matching process between the sensory input and the temporary neuronal representation (“attentional trace”) of the physical features defining the relevant (attended standard) stimuli. Thus, the more similar the sensory input is to the attentional trace, the longer the discrimination process, and the larger and longer the elicited PN [e.g. Alho, 1992; Alho et al., 1987a,b, 1989, 1990]. This account was successfully applied in many previous investigations, all employing a paradigm which required selectively attending to a prechosen channel and detecting rare targets within it [Alho, 1992; Alho et al., 1990; Hansen and Hillyard, 1983, 1984; Näätänen, 1982; Nager et al., 2001]. However, the PF effects obtained in our experiment using a “same/different” rather than selective attention paradigm, do not naturally reconcile with an “attentional trace” account. First, our experimental design did not include a predefined “channel” to which subjects needed to attend. Rather, all stimuli needed to be attended to, and subjects were required to perform an online comparison of the two stimuli presented within a pair, to decide whether these stimuli were the same or different, rather than to compare them to a memory-based attentional trace. We therefore did not expect the formation of an attentional trace under such conditions. Second, the task difficulty manipulation did not involve, as in most previous experiments, a complicated discrimination between attended and unattended channels. Rather, our task operated within pairs, and attention was required for both easy and difficult conditions. Finding PF effects under these conditions may therefore require an extension of the interpretation of the PF beyond the context of “attentional trace.”

One plausible interpretation is that PF reflects the total effort allocated to resolving the task. According to this view, PF persists until the task is resolved, and thus persists longer under more difficult conditions and among weaker performers, who need more time to resolve the task. A similar explanation was suggested by Hansen and Hillyard [1983] to account for their larger PN responses under a difficult discrimination task. This explanation is also consistent with other results obtained in the context of selective attention tasks. For example, the PN response elicited by irrelevant stimuli is larger and longer in duration the more similar the stimuli are to the relevant ones, either in pitch [Alho et al., 1987b] or in spatial parameters [Alho et al., 1987a]. Similarly, PN responses decrease in amplitude with increasing probability of the relevant stimuli [Berman et al., 1989], and responses to attended and unattended stimuli differ more from each other if their frequency separation is large [Hansen and Hillyard, 1980], due to the smaller PN evoked by the irrelevant stimuli [Näätänen, 1992]. Another possible interpretation is that

the PF reflects some monitoring of the decision that subjects need to make, which may precede the dissociation between responses into easy and difficult conditions. The dissociation between these alternatives may require further investigation, in which the data are separated based on correct and incorrect decisions.

The two conditions in our experiment differed not only in task difficulty but also in the frequency difference between tones. Therefore, the PF strength and latency difference between responses to the easy and difficult conditions could have resulted from the two stimuli being very distant under the easy condition, and quite close under the difficult one. However, this was the case only for the “different” pairs, whereas for the “same” pairs there was no frequency difference between the tones in either condition. Had the interstimulus difference between the conditions been the cause of the experimental result, the effect would not have been found in the “same” pairs. However, analysis of the “same” pairs revealed the same PF effect, suggesting that the task difficulty effects found were indeed due to the behavioral manipulation rather than the degree of stimulus similarity.

Task Difficulty and Across-Pair Dynamics

Even though the task difficulty manipulation affected both the N100m and PF responses, it did not affect their dynamics along the trial (i.e. there was no significant interaction of task and pair number). Thus, the effects of task difficulty can be dissociated from the across-pair dynamics over the five-pair trial. The effects of task difficulty on the N100m response were already apparent from the 1st pair, similar to those found by Donald and Young [1982]; however, here it persisted over an interval of 10 s, rather than their 6 s interval.

The enhancement of the second response compared to the first response was also similar for both task conditions. This enhancement has been suggested in previous studies to reflect an integrative process operating over a period of ~200–300 ms in the auditory system [Loveless et al., 1996; McEvoy et al., 1997]. Given this interpretation, our results show that this process is not affected by the difficulty of the interpair discrimination.

Similarly, the PF responses featured similar across-pair dynamics along the five pairs for both task conditions, i.e. gradually increasing from the 2nd to the 5th pair. Hansen and Hillyard [1988] characterized the temporal dynamics of the Nd response, which is the difference between the responses to attended and unattended stimuli in a selective attention paradigm. They showed that Nd develops progressively over the first few stimuli during selective attention and it reaches a plateau by the 3rd stimulus in a train. Thus, although task difficulty did not affect the dynamics of the PF response in our study, the result of Hansen and Hillyard suggests that the dynamics of the Nd may be sensitive to some other attentional manipulations (in this case, selective attention).

Rapid temporal processing and hemispheric lateralization

The responses to the paired stimuli presented in this study tended to be stronger in the LH compared to the RH. Moreover, the task difficulty effects were usually stronger, though not significantly so, in the LH. Since the tones within a pair were separated by only 100 ms, the task required processing of rapidly presented stimuli. These results are therefore in line with previous studies [e.g. Ahissar et al., 2000; Leek and Brandt, 1983; Nicholls et al., 2002; Schwartz and Tallal, 1980; Schönwiesner et al., 2005; Zatorre and Belin, 2001], showing LH dominance for processing of rapidly presented acoustic signals. Note, however, that our study did not include any condition with longer intervals within pairs, so the specificity of the LH dominance to rapidly presented stimuli was not examined.

CONCLUSION

The manipulation of task difficulty affected both the N100m and PF responses, but not their across-pair dynamics. The smaller and later N100m responses in the difficult condition suggest decreased neuronal coherence, possibly due to decreased perceptual clarity. In both conditions, the strength of the PF response was inversely correlated to the subjects' performance on the task; i.e. it was larger for the less successful compared to the more successful subjects. Thus, the PF response may reflect subjects' assessment of success on the task or the attentional effort allocated towards solving the task. Task difficulty did not affect the dynamics of these responses along a trial, suggesting that across-pair dynamics are not easily affected by top-down manipulations.

ACKNOWLEDGMENTS

The authors thank Riitta Hari, Karen Banai, and Topi Tanskanen for helpful comments at various stages of this work.

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