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Statistical context shapes stimulus-specific adaptation in human auditory cortex

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Herrmann B, Henry MJ, Fromboluti EK, McAuley JD, Obleser J. Statistical context shapes stimulus-specific adaptation in human auditory cortex. *J Neurophysiol* 113: 2582–2591, 2015. First published February 4, 2015; doi:10.1152/jn.00634.2014.—Stimulus-specific adaptation is the phenomenon whereby neural response magnitude decreases with repeated stimulation. Inconsistencies between recent nonhuman animal recordings and computational modeling suggest dynamic influences on stimulus-specific adaptation. The present human electroencephalography (EEG) study investigates the potential role of statistical context in dynamically modulating stimulus-specific adaptation by examining the auditory cortex-generated N1 and P2 components. As in previous studies of stimulus-specific adaptation, listeners were presented with oddball sequences in which the presentation of a repeated tone was infrequently interrupted by rare spectral changes taking on three different magnitudes. Critically, the statistical context varied with respect to the probability of small versus large spectral changes within oddball sequences (half of the time a small change was most probable; in the other half a large change was most probable). We observed larger N1 and P2 amplitudes (i.e., release from adaptation) for all spectral changes in the small-change compared with the large-change statistical context. The increase in response magnitude also held for responses to tones presented with high probability, indicating that statistical adaptation can overrule stimulus probability per se in its influence on neural responses. Computational modeling showed that the degree of coadaptation in auditory cortex changed depending on the statistical context, which in turn affected stimulus-specific adaptation. Thus the present data demonstrate that stimulus-specific adaptation in human auditory cortex critically depends on statistical context. Finally, the present results challenge the implicit assumption of stationarity of neural response magnitudes that governs the practice of isolating established deviant-detection responses such as the mismatch negativity.

stimulus-specific adaptation; stimulus statistics; event-related potentials; auditory processing

ANY BIOLOGICAL SYSTEM must flexibly adapt to the requirements imposed by the environment. With respect to the neural system, two types of adaptation that possibly reflect extremes on a continuum can be considered: stimulus-specific adaptation and adaptation to stimulus statistics. Stimulus-specific adaptation refers to a reduction in neural responsiveness caused by repeated stimulation (Jääskeläinen et al. 2007; Nelken and Ulanovsky 2007; Ringo 1996). In animals, auditory stimulus-specific adaptation is often investigated with an oddball paradigm in which a sequence of repeated tones (of the same frequency) is occasionally interrupted by a rare tone with a different frequency. Generally, neural responses to repeated tones are reduced compared with responses to rare tones (Anderson et al. 2009; Ayala and Malmierca 2013; Bäuerle et al. 2011; Ulanovsky et al. 2003; von der Behrens et al. 2009).

Adaptation to stimulus statistics refers to adjustments of neural response curves evoked by the statistical properties of the stimulation (Wark et al. 2007). For example, neuronal responses adjust to the mean, variance, and complex shape of the stimulation distribution (Benucci et al. 2013; Dahmen et al. 2010; Dean et al. 2005, 2008; Kvale and Schreiner 2004) and effectively scale in dynamic range to match the range of the stimulation input (Brenner et al. 2000; Rabinowitz et al. 2011; Wen et al. 2009). Hence, stimulus-statistical adaptation allows efficient coding of a wide range of stimuli with limited neuronal sensitivity (Fairhall et al. 2001; Wark et al. 2007).

Here we investigated the degree to which stimulus-specific adaptation is specific to the probability of particular stimuli in oddball sequences. While early reports on stimulus-specific adaptation proposed that adaptation is limited to the repeated stimulus (Ringo 1996), recent work shows that repeated stimuli also affect neural populations most responsive to rare stimuli due to coadaptation (for a review see Escera and Malmierca 2014). The observation that adaptation induced by repeated stimuli influences populations responding to rare stimuli is in line with human electroencephalography (EEG) recordings using an oddball paradigm that emphasize coadaptation (although referred to as refractoriness in those studies) across frequency-specific neural populations in auditory cortex (Jacobsen and Schröger 2001; Ruhnau et al. 2012; Schröger 2007). Importantly, inconsistencies between stimulus-specific adaptation data and computational modeling (Hershenhoren et al. 2014; Taaseh et al. 2011) as well as changes in auditory cortex coadaptation with the stimulation's spectral range (Herrmann et al. 2013a, 2014) suggest dynamic variations in stimulus-specific adaptation.

In the seminal work of Ulanovsky and colleagues (2003) investigation of stimulus-specific adaptation was partially motivated by previous research on statistical adaptation of neural responses, and subsequent work suggested an important role of local as well as global stimulus probabilities on neural response adaptation (RA) (Ulanovsky et al. 2004). Support for an interrelation of stimulus-specific adaptation and statistical context comes from studies investigating the underlying neural mechanisms of adaptation. That is, neural inhibition has been discussed as a key mechanism of statistical adaptation (Hildebrandt et al. 2011; Isaacson and Scanziani 2011; Olsen and Wilson 2008; Wilson et al. 2012) and has also been shown to modulate stimulus-specific adaptation (Duque et al. 2014; Pérez-González et al. 2012).

The present human EEG study is concerned with the extent to which adaptation is stimulus specific, and thus examines the relationship between stimulus-specific adaptation and stimulus-statistical adaptation. We hypothesize that the statistical

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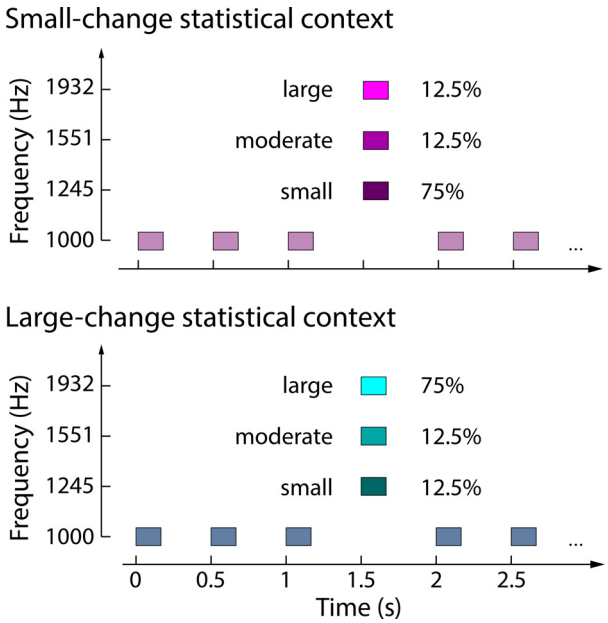

Fig. 1. Experimental design: two different statistical contexts in an oddball paradigm that vary the relative probability of rare spectral changes. In one context, a small spectral change occurred with the highest relative probability (small-change statistical context). In the other context, a large spectral change occurred with the highest relative probability (large-change statistical context). The statistical contexts were hypothesized to differently affect the degree of coadaptation in auditory cortex.

context in which repeated and rare stimuli are presented will influence the degree of stimulus-specific adaptation. We concentrated on the N1 and P2 components of the human event-related potential (ERP) for which RA to repeated stimulation and response adjustments to statistical properties have been studied previously (Briley and Krumbholz 2013; Butler 1968; Herrmann et al. 2013b, 2014; Lanting et al. 2013; Näätänen et al. 1988; Picton et al. 1978; Yvert et al. 1998). Two types of oddball sequences were presented (comparable to Kim and McAuley 2013), each comprising three types of rare spectral changes occurring with different probabilities (half of the time a small change was most probable; in the other half a large change was most probable). The data show that stimulus-specific adaptation decreases in a statistical context in which small spectral changes are most probable. Computational modeling of frequency-specific neural adaptation links these effects of statistical context to coadaptation changes in auditory cortex.

MATERIALS AND METHODS

Participants. Twenty German-speaking adults participated in the present EEG study (mean age: 24.7 yr, SD: 2.9 yr; 10 women, 10 men). Participants did not report any neurological diseases or any hearing problems. They gave written informed consent prior to the experiment and were paid €7 per hour for their participation. The study was in accordance with the Declaration of Helsinki and approved by the local ethics committee of the University of Leipzig.

Acoustic stimulation and procedure. Acoustic stimuli consisted of sequences of sine tones presented via headphones (HD 25-SP II; Sennheiser) at a comfortable listening level. Tone sequences comprised a series of repeated tones (83.33%) that were irregularly interrupted by rare tones (16.67%). The frequency of the repeated tone was 1,000 Hz, whereas rare tones had a frequency of 1,245 Hz, 1,551 Hz, or 1,932 Hz (small, moderate, large spectral change, respectively; $\log_2$ spacing; Fig. 1). Tone duration was 0.18 s (including 0.01 s rise and fall times), and tones were presented isochronously with an onset-to-onset interval of 0.5 s. Tone presentation was randomized such that at least two repeated tones were presented between two rare tones, with a maximum of eight repeated tone presentations between rare tones. The number of repeated tones preceding a rare tone was counterbalanced across the different types of rare tones.

The critical manipulation was the probability of occurrence of a particular rare tone within a block (Fig. 1). In one block type (small-change statistical context; Fig. 1), the rare tone constituting a small spectral change was presented with 75% probability (relative to all rare tones) while moderate and large spectral changes each occurred with 12.5% probability. In a second block type (large-change statistical context; Fig. 1), the rare tone constituting a large spectral change was presented with 75% probability (relative to all rare tones) while small and moderate spectral changes each occurred with 12.5% probability. Within a block, at least two high-probability spectral changes were presented between low-probability spectral changes.

Each block started with a 10-s period of silence to ensure that neural populations were fully responsive at the beginning of the acoustic stimulation. Then, each block type (small-change statistical context, large-change statistical context) was presented three times in alternating order; starting block type was counterbalanced across participants. Within each block repeated tones were presented 1,200 times, and rare tones were presented 240 times. High-probability rare tones were presented 180 times, and low-probability rare tones were presented 30 times. Ten additional 1,000-Hz tones were presented at the beginning of each block to allow for a clear representation of the repeated tone stream, and five were presented at the end to avoid the possibility of a rare tone at the very end of a block.

At the end of the experiment, an additional "no-adaptation" block was presented in which the 1,000-Hz tone occurred every 10 s (30 trials; block duration of 5 min). Responses to these tones were used to estimate neural response magnitude when neural populations are in a nonadapted state (Herrmann et al. 2014; Sams et al. 1993).

EEG recording. Participants sat in a comfortable chair in a sound-attenuated and electrically shielded booth while electroencephalograms were recorded. They watched a silent movie (no subtitles) of their choice and were instructed to ignore the acoustic stimulation. EEG signals were recorded from 26 Ag/AgCl scalp electrodes (Easycap) and additionally from left and right mastoids, nose (online reference), and ground (at the sternum). The sampling rate was 500 Hz (TMS International amplifier; 135-Hz low-pass filter; impedances <5 kΩ).

EEG preprocessing. Off-line data analysis was carried out with MATLAB software (v7.11; MathWorks). Raw data were filtered with an 80-Hz low-pass finite impulse response (FIR) filter (42 points, Hamming window) and a 0.5-Hz high-pass FIR filter (1,747 points, Hamming window). The high-pass filter was specifically designed for strong DC suppression (>100 dB) to replace baseline correction. High-pass filtering instead of baseline correction is particularly well suited for fast presentation designs as employed in the present study (Herrmann et al. 2011; Maess et al. 2007; Ruhnau et al. 2011; Tervaniemi et al. 1999; for a general discussion about the pitfalls of baseline correction see Urbach and Kutas 2006). Data were then downsampled to 250 Hz and divided into epochs ranging from -1.6 to 1.9 s time-locked to tone onsets. Subsequently, independent components analysis (ICA; runica method, Makeig et al. 1996; logistic infomax algorithm, Bell and Sejnowski 1995) was computed with FieldTrip software (v20130727; Oostenveld et al. 2011). Components containing artifacts such as blinks, heart- or muscle-related activity, or noisy channels were rejected, and the data were then projected back to the original electrodes. ICA reduces artifacts in EEG recordings and is thus advantageous for the overall data quality and the number of data points (trials) that can be submitted to further analyses. Note also that a spatial ICA as performed here does not affect the phase of EEG signals (Henry et al. 2014). After ICA, epochs still containing a signal range $>$ 120 μV in any of the electrodes were excluded ($\sim$3% of trials were rejected). Finally, similar to previous studies investigating

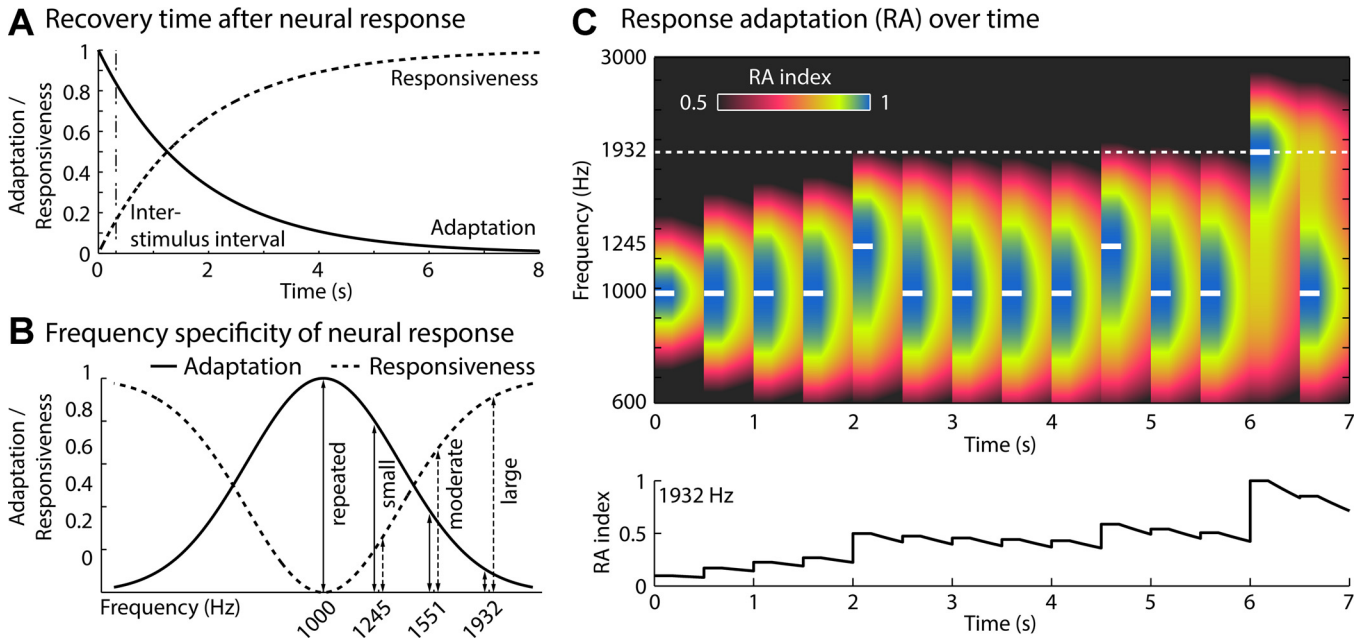

Fig. 2. Example of the response adaptation (RA) model. *A*: exponential decay function describing recovery from adaptation over time (where τ reflects the steepness of the function); dot-dashed line marks the present interstimulus interval of 0.32 s. *B*: Gaussian function describing coadaptation in frequency-specific regions of auditory cortex (where σ reflects the degree of frequency specificity); responsiveness of neural populations is defined as the inverse of adaptation. Vertical lines with arrows indicate the expected adaptation (solid) or responsiveness (dashed) for the 4 tone frequencies (repeated, small, moderate, large). *C*: example of RA indices over time for an oddball sequence ($\tau = 1.8$ s; $\sigma = 0.45$ SD). *Top*: a tone of 0.18-s duration is presented every 0.5 s (white bars; *x*-axis). Frequency-specific coadaptation occurs along the *y*-axis. RA indices (color coded; dark blue corresponds to full adaptation) increase at tone onset and decrease after tone offset (recovery). *Bottom*: time course of RA indices for the large spectral change (1,932 Hz; white dashed line, *top*). Note that lower RA indices correspond to larger expected response amplitudes (i.e., higher responsiveness of the neural population).

neural responses elicited in oddball paradigms, epochs were filtered with a 20-Hz low-pass FIR filter (129 points, Blackman window; Jacobsen and Schröger 2001; Maess et al. 2007; Pulvermüller et al. 2003) and cut to range from −0.1 to 0.4 s for data analysis.

Event-related potentials. For each of the six rare spectral changes (3 per statistical context), single-trial time courses were averaged. To investigate stimulus-specific (i.e., here frequency specific) changes in neural response magnitude, amplitudes in the N1 time window ranging from 0.09 to 0.13 s and for a fronto-central electrode cluster (Fz, F3, F4, Fc3, FC4, Cz, C3, C4) were averaged for each tone condition independently. Selection of time points and electrodes is in line with previous studies investigating N1 amplitudes (Hari et al. 1982; Herrmann et al. 2014; Jacobsen and Schröger 2001; Ruhnau et al. 2011). Furthermore, amplitude changes in the P2 time window have also been suggested to be frequency specific (Herrmann et al. 2013a; Lanting et al. 2013; Picton et al. 1978), and amplitudes were thus averaged in the 0.17–0.26 s time window and across the same fronto-central electrode cluster.

For the statistical analysis, separate two-way repeated-measures ANOVAs (rmANOVAs) with the factors Spectral Change (small, moderate, large) and Statistical Context (small change, large change) were performed with SPSS software independently for the N1 and P2 time windows. Whenever the assumption of sphericity was violated (according to a significant Mauchly test), Greenhouse-Geisser correction was applied (Greenhouse and Geisser 1959). Shapiro-Wilk tests calculated for each dependent measure (N1 amplitude, P2 amplitude) indicated normality of the data (i.e., for all $P > 0.05$), except for the small spectral change in the large-change context in the P2 time window ($P = 0.040$). We still carried out parametric statistics, which allowed us to test for the interaction between Spectral Change and Statistical Context, but additionally report the results of nonparametric Wilcoxon signed-rank tests where appropriate.

Modeling neural coadaptation in auditory cortex. To capture the effects of coadaptation with a biologically plausible approach, we used a model of frequency-specific neural RA that incorporates coadaptation across the tonotopic (frequency) gradient of auditory cortex and recovery from adaptation after stimulus presentation (Herrmann et al. 2013a, 2014; for comparable models see Mill et al. 2011; Price and Prescott 2012; Taaseh et al. 2011). We use the term "adaptation" to refer to the inverse of neural responsiveness (Fig. 2).

The model combines an exponential decay function with a Gaussian function. The decay function models the time over which neural populations recover from adaptation (Fig. 2*A*; Lü et al. 1992; Mäkelä et al. 1993; McEvoy et al. 1997; Sams et al. 1993). The Gaussian function models frequency-specific coadaptation across tonotopically organized regions of auditory cortex (Fig. 2*B*; Herrmann et al. 2013a, 2014). This is in line with previous studies using Gaussian functions to model tuning properties of auditory cortex neurons (e.g., Dahmen et al. 2008; Montgomery and Wehr 2010; Taaseh et al. 2011). Furthermore, N1 RA is symmetrical for logarithmically spaced low and high stimulation frequencies (Herrmann et al. 2013a, 2013b) and is thus appropriately represented by a Gaussian function.

RA was estimated from the model as follows. For each participant and for each block of presentation, an index of expected RA (ranging from 0 to 1, where 1 reflects full adaptation) was calculated for the onset of each presented tone based on the individual acoustic stimulation protocol, independent of EEG data:

$$\mathbf{RA}_{:,j+1} = \mathbf{RA}_{:,j} + \mathbf{a} \circ \left(1 - \mathbf{RA}_{:,j}\right) \times e^{\frac{-\Delta t}{\tau}} \quad (1)$$

RA corresponds to an $m \times n$ matrix containing expected RA indices for neural populations along the tonotopic gradient of auditory cortex ($m = 4$; i.e., the 4 tone frequencies used) at each trial's onset ($n = 1{,}455$, number of trials in a block of presentation). The variable j is the trial index ($j = 1 \ldots n$), Δt is the time over which neural populations recover before the subsequent tone onset (here set to the interstimulus interval of 0.32 s; that is, recovery starts at tone offset), and τ reflects the decay of adaptation in seconds. The operator $\circ$ refers to an entrywise multiplication (Hadamard product). The column vector **a** reflects a Gaussian function centered on the presented tone frequency $\mathbf{f}_i$ of trial j:

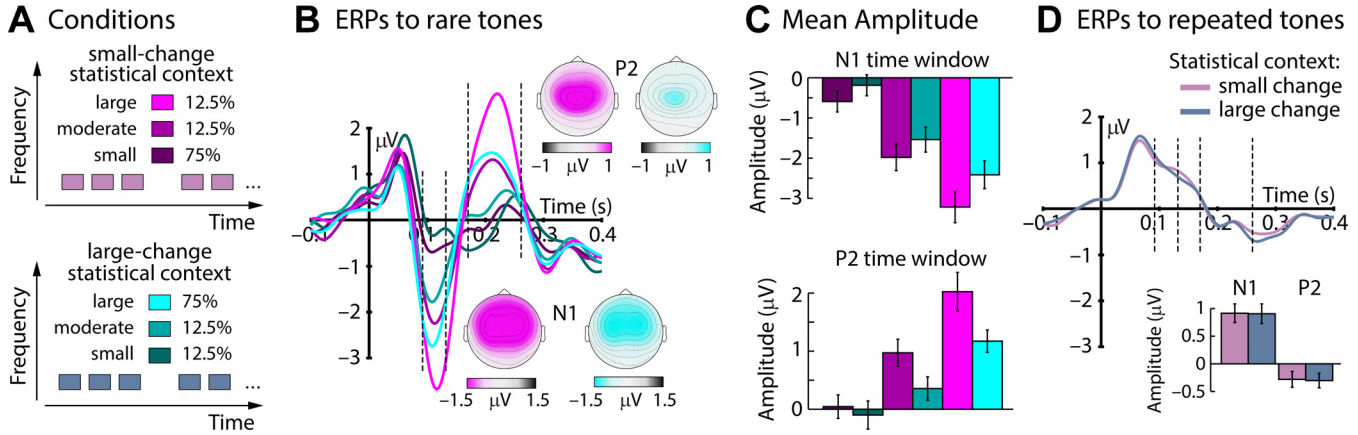

Fig. 3. Time courses and magnitudes of neural responses. *A*: small-change and large-change statistical contexts. *B*: time courses for each of the 6 spectral changes (in 2 statistical contexts). Topographical distributions are shown for the N1 (0.09–0.13 s) and P2 (0.17–0.26 s) time windows. ERP, event-related potential. *C*: mean amplitudes for the N1 and P2 time windows. *D*: time courses and mean amplitudes in response to the repeated tones directly preceding rare tones. Error bars reflect SE.

$$\mathbf{a} = e^{-0.5\times\left(\frac{\mathbf{f}-\mathbf{f}_i}{\sigma}\right)^2} \quad (2)$$

where **f** is a column vector containing the four unique tone frequencies ($\log_2$ units) and σ describes the width of the Gaussian function, that is, the degree of coadaptation along the tonotopic gradient. The index i refers to the tone frequency presented on trial j; that is, it indexes the row entry in **f** (and **RA**) on trial j. Finally, the **RA** matrix was reduced to a vector comprising only the expected RA indices for tone frequencies actually presented during the experiment (also excluding trials rejected as artifacts).

To summarize, the relevant parameters of the RA model are τ, reflecting the decay time in seconds over which neural populations recover from adaptation, and σ, reflecting the degree of frequency-specific coadaptation in auditory cortex. The other variables were predefined by the experimental setup. RA indices were calculated for each parameter combination ranging from $\tau = 0.5$ to 4.5 s (in steps of 0.1 s) and from $\sigma = 0.1$ to 2.5 SD (in steps of 0.05 SD). A large τ corresponds to slow recovery time from adaptation. A large σ corresponds to wide frequency-specific coadaptation.

Predicting single-trial amplitudes by response adaptation. To investigate the effects of the statistical context on frequency-specific coadaptation in auditory cortex, a linear function was fitted to single-trial amplitudes (separately for N1 and P2) as a function of RA indices. Linear fits were calculated for each $\tau \times \sigma$ combination separately for each block, electrode, and time point. The first five trials of each block were excluded prior to fitting to estimate adaptation-related amplitude changes within a block unbiased by the extreme values of the first few trials. For each $\tau \times \sigma$ combination separately, the resulting slopes and intercepts were averaged across blocks of the same statistical context, across samples within the N1 or P2 time window, and across electrodes within the fronto-central cluster. The slope reflects the degree of amplitude change as a function of RA, and the intercept reflects the predicted amplitude at no adaptation (RA = 0). The σ best fitting the data (for each τ separately) was selected where the difference between the predicted (intercept) and observed (from the no-adaptation block) amplitudes at no adaptation was minimum (for details see Herrmann et al. 2014). Given our constant onset-to-onset interval of 0.5 s, we did not expect changes in recovery time from adaptation. Thus statistical analyses were conducted for a fixed τ of 1.8 s, which has been estimated previously to describe recovery from adaptation for the N1 component (Sams et al. 1993; for comparable estimates see Lü et al. 1992; Mäkelä et al. 1993; McEvoy et al. 1997). Shapiro-Wilk tests calculated for each dependent measure (slope of linear fit, root mean square error of approximation, estimated σ) indicated normality of the data (i.e., for all $P > 0.05$), and parametric statistics were thus carried out.

RESULTS

In the present study, two different types of oddball sequences were presented to human participants (small-change statistical context, large-change statistical context). In each oddball sequence, the presentation of a repeated tone was randomly interrupted by a rare tone taking on one of three spectral changes of different magnitude (small, moderate, large). Critically, the spectral changes differed in relative probability of occurrence, such that either a small or a large change was relatively more likely, establishing either small- or large-change contexts. In the small-change context, the rare tone constituting a small spectral change was presented with 75% probability (relative to all rare tones) while moderate and large spectral changes each occurred with 12.5% probability. In the large-change context, the rare tone constituting a large spectral change was presented with 75% probability (relative to all rare tones) while small and moderate spectral changes each occurred with 12.5% probability (Fig. 1).

Statistical context influences response magnitude (ERP). Figure 3 shows the time courses of the neural responses (ERPs). For the N1 time window (0.09–0.13 s), the rmANOVA showed a main effect of Spectral Change ($F_{2,38} = 103.52$, $P < 0.001$). N1 amplitudes increased (i.e., were more negative) with increasing spectral difference between the repeated and rare tone frequencies (linear trend: $F_{1,19} = 146.69$, $P < 0.001$). Furthermore, a main effect of Statistical Context was observed ($F_{1,19} = 21.46$, $P < 0.001$). That is, N1 neural responses were larger for the small-change statistical context compared with the large-change statistical context (Fig. 3*C*). The Spectral Change × Statistical Context interaction was not significant ($F_{2,38} = 1.56$, $P = 0.223$). To be completely transparent (although already shown by the main effect of Statistical Context in the absence of an interaction), we confirmed that all direct comparisons of rare-stimulus responses between statistical contexts showed a significant difference (small: $t_{19} = 3.10$, $P = 0.006$; moderate: $t_{19} = 2.16$, $P = 0.044$; large: $t_{19} = 3.82$, $P = 0.001$). Most critically, the effect of Statistical Context together with the absence of the Spectral Change × Statistical Context interaction suggests statistical adaptation. That is, in the small-change statistical context, neural responses to all spectral changes were larger compared with the large-change context, indicating that statistical adap-

tation is a stronger influence on neural responses than the probability of stimulus occurrence. Under the assumption that adaptation would be driven solely by the probability of stimulus occurrence, *1*) high-probability rare spectral changes should have elicited reduced responses compared with their less probable counterparts and *2*) moderate spectral changes (physically and probabilistically identical stimuli in the 2 statistical contexts) should have elicited identical response magnitudes. Both expectations would have resulted in an interaction that we did not observe. In turn, the present N1 effects suggest a change in overall neural sensitivity. The topographical distributions of N1 responses suggest auditory cortex generators (Fig. 3*B*; Näätänen and Picton 1987).

For the P2 time window (0.17–0.26 s), the rmANOVA showed a main effect of Spectral Change ($F_{2,38} = 46.59$, $P < 0.001$) and a main effect of Statistical Context ($F_{1,19} = 14.40$, $P = 0.001$). Furthermore, the Spectral Change × Statistical Context interaction was significant ($F_{2,38} = 5.31$, $P = 0.009$). The interaction was resolved by comparing the P2 amplitudes between the two statistical contexts for each spectral change condition independently. Amplitudes were significantly larger for the small-change versus the large-change statistical context for moderate ($t_{19} = 2.74$, $P = 0.013$) and large ($t_{19} = 4.17$, $P = 0.001$) spectral changes but nonsignificant for small spectral changes ($t_{19} = 1.12$, $P = 0.276$; Wilcoxon signed-rank test: $P = 0.314$). The topographical distributions of P2 responses suggest auditory cortex generators, but they appear slightly more posterior than for the N1 (Fig. 3*B*).[1]

Responses to repeated tones that occurred just prior to rare tones were not different between different statistical contexts (N1 time window: $F_{1,19} = 0.01$, $P = 0.92$; P2 time window: $F_{1,19} = 0.33$, $P = 0.57$; Fig. 3*D*).

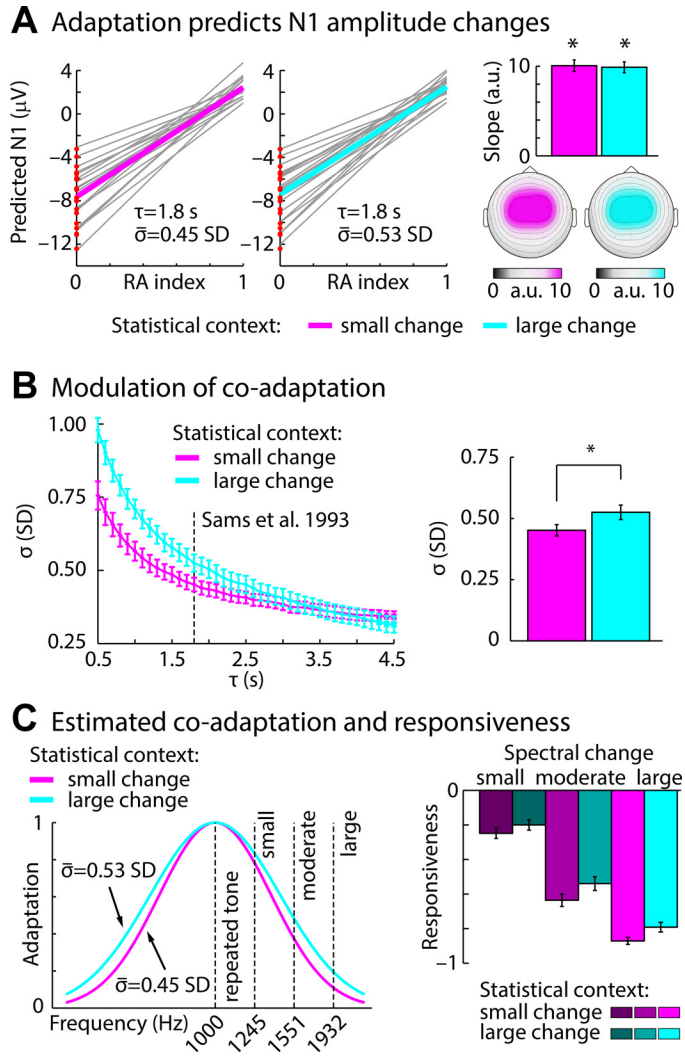

Fig. 4. Prediction of N1 amplitudes by RA and estimated coadaptation. *A*, *left*: predicted N1 amplitudes as a function of RA index. Gray lines reflect individual fits, colored lines the mean across participants. Red dots at RA = 0 reflect the observed N1 amplitude at no adaptation. *Right*: mean slopes of the linear fits and topographical distributions. a.u., Arbitrary unit. *B*: mean estimated Gaussian width (σ) describing coadaptation for each τ. Dashed line marks the recovery observed by Sams et al. (1993) ($\tau = 1.8$) for which statistics were carried out (*right*). *C*, *left*: mean estimated coadaptation function for each statistical context. *Right*: mean estimated neural responsiveness taken from the inverse of the adaptation functions (centered on the frequency of the repeated tone). The sign of the responsiveness values was flipped to match the negative amplitudes in the corresponding N1 time window. Error bars reflect SE. *$P < 0.05$.

Statistical context affects frequency-specific coadaptation. We used a model of RA to estimate the degree of frequency-specific coadaptation in auditory cortex from single-trial neural responses for the two different statistical contexts (Herrmann et al. 2013a). Figure 4*A* shows the predicted N1 amplitudes from linear fits as a function of RA index. Slopes were significantly different from zero for both statistical contexts (for both: $t_{19} > 15$, $P < 0.001$) and did not differ from each other ($t_{19} = 0.99$, $P = 0.34$). In other words, the RA index was similarly predictive of N1 amplitudes for both statistical contexts. No difference in root mean square error of approximation was

[1] As a control analysis to assess the potential influence of baseline correction, we specifically contrasted N1 amplitudes and P2 amplitudes for the moderate spectral change between statistical contexts, using an amplitude reference from a different time window. First, we calculated an overall context-specific reference. That is, for each statistical context separately, responses to all tones were averaged and the mean amplitude within the −0.05 to 0 s prestimulus time window was subtracted from the N1 and P2 responses in the respective moderate spectral change conditions. Amplitudes to moderate spectral changes were significantly larger in the small-change context than in the large-change context (N1: $t_{19} = 2.18$, $P = 0.042$; P2: $t_{19} = 2.68$, $P = 0.015$). Because of the absence of slow drift effects between statistical contexts in the data as indexed by the responses to repeated tones directly preceding rare stimuli (for which many trials were available; Fig. 3*D*) and the rigorous control of the number of repeated stimuli preceding rare stimuli, this reference analysis provides a robust baseline contrast.

Second, we calculated a reference specific to the moderate spectral changes. That is, for each statistical context separately, trials for moderate spectral changes were averaged and the mean amplitude within the −0.05 to 0 s prestimulus time window was subtracted from the respective amplitudes in the N1 and P2 time windows. Amplitudes to moderate spectral changes in the small-change context were larger than in the large-change context, although this difference was only significant for the P2 ($t_{19} = 2.25$, $P = 0.037$) and not the N1 ($t_{19} = 0.96$, $P = 0.347$) time window. Note, however, that baseline contrasts always have the potential danger to introduce amplitude changes into the time window of interest that are actually present in the baseline time window and should therefore be used with caution (for a general discussion regarding pitfalls of baseline correction see Urbach and Kutas 2006).

Third, we calculated ERP component-specific reference contrasts. That is, similar to previous studies investigating neural RA, we calculated the P1-N1 amplitude difference and the P2-N1 amplitude difference separately for each statistical context (Briley and Krumbholz 2013; Lanting et al. 2013; Näätänen et al. 1988). The P1-N1 amplitude difference as well as the P2-N1 amplitude difference for moderate changes in the small-change statistical context were significantly larger compared with the differences in the large-change statistical context (P1-N1: $t_{19} = 2.12$, $P = 0.048$; P2-N1: $t_{19} = 3.59$, $P = 0.002$).

observed between statistical contexts ($t_{19} = 0.32$, $P = 0.75$). Mean R^2 values were 0.016 (0.013 SD) and 0.028 (0.018 SD) for the small-change and large-change statistical contexts, respectively. Note, however, that *1*) small R^2 values are expected given the noisy nature of single-trial EEG recordings and *2*) that linear fits were not performed by minimizing R^2 values but instead were based on the minimum difference between observed and predicted N1 amplitudes at no adaptation.

Critically, statistical context influenced the degree of frequency-specific coadaptation in auditory cortex (Fig. 4*B*). That is, the estimated σ was smaller (i.e., the width of the Gaussian function was narrower) for the small-change statistical context compared with the large-change statistical context ($t_{19} = 3.57$, $P = 0.002$). Figure 4*C* visualizes the estimated frequency-specific adaptation functions (Gaussian) and the estimated responsiveness of neural populations (inverse of adaptation) for each condition.

For the P2 time window, the RA index predicted single-trial amplitudes in both statistical contexts. That is, the slopes of the linear fit were significantly different from zero (for both: $t_{19} > 8.5$, $P < 0.001$) and not different between statistical contexts ($t_{19} = 1.10$, $P = 0.28$; Fig. 5*A*). Root mean square errors were not different between contexts ($t_{19} = 0.97$, $P = 0.34$). Mean R^2 values were 0.007 (0.004) and 0.009 (0.006 SD) for the small-change and large-change statistical contexts, respectively. Critically, the estimated σ reflecting the degree of frequency-specific coadaptation was smaller for the small-change statistical context compared with the large-change statistical context ($t_{19} = 2.25$, $P = 0.037$; Fig. 5*B*). Figure 5*C* visualizes the estimated frequency-specific adaptation functions (Gaussian) and the estimated responsiveness of neural populations (inverse of adaptation) for each condition.[2]

Taking the ERP data and the modeling data together, it appears that observed ERP amplitudes and estimated neural responsiveness match more clearly for the N1 than the P2 time window. This could be due in part to the choice of the model's decay parameter based on N1 work ($\tau = 1.8$; Sams et al. 1993), which is well within the range of previous estimations for the N1 (Lü et al. 1992; Mäkelä et al. 1993; McEvoy et al. 1997) and which was chosen because of a lack of previous P2 decay estimations. Alternatively, it might be that an additional process underlies P2 amplitude modulations that is not captured by the adaptation model. Nevertheless, the present results show influences of statistical context on N1 and P2 stimulus-specific adaptation, which are most clear for the N1 time window.

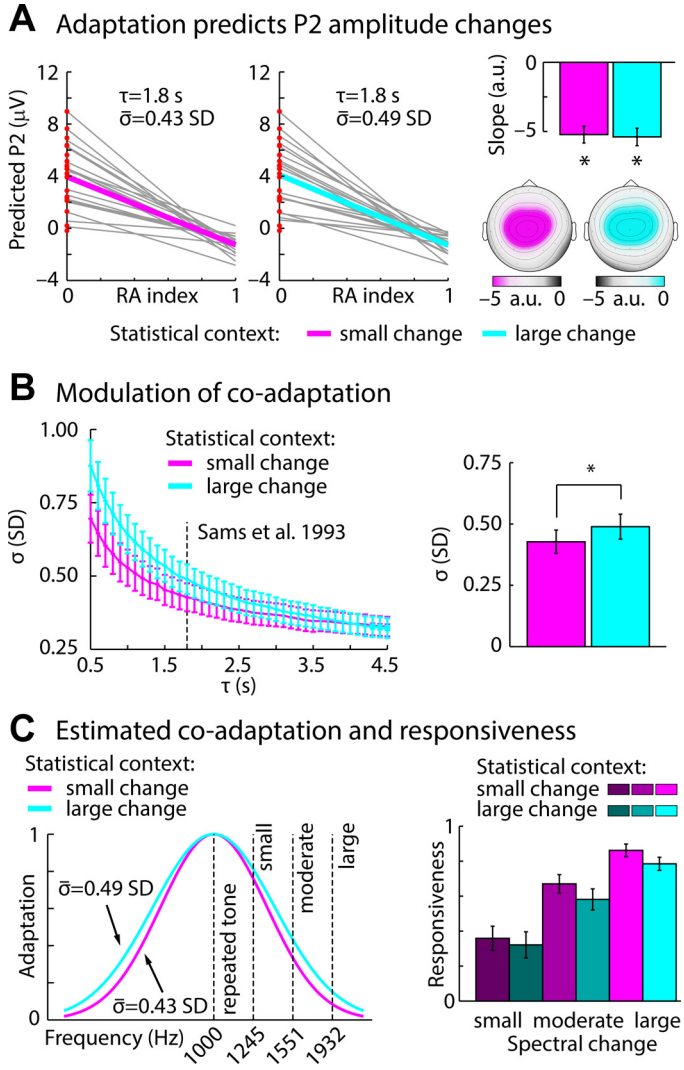

Fig. 5. Prediction of P2 amplitudes by RA and estimated coadaptation. Descriptions similar to those for Fig. 4 apply, except that no sign flip for responsiveness values in *C* was required. *$P < 0.05$.

DISCUSSION

The present human EEG study investigated the dynamics underlying stimulus-specific neural adaptation in auditory oddball sequences. Human participants listened to tones in two statistical contexts that were identical in their spectral range but differed in relative probabilities of rare spectral changes. Auditory cortex responses in those contexts in which large spectral changes occurred with high relative probability showed stronger neural adaptation than responses in contexts in which large spectral changes occurred with low relative probability. Thus the present data show that the state of stimulus-specific coadaptation in auditory cortex depends on statistical characteristics of the entire stimulation history.

Neural response magnitude depends on spectral change as well as on statistical context. In the present study we observed that neural responses (N1 and P2 components) increased with increasing spectral change between the repeated and the rare tone frequencies. This increase reflects a release from stimulus-specific neural RA and is in line with previous studies in humans (Briley and Krumbholz 2013; Butler 1968; Herrmann et al. 2013a, 2014; Lanting et al. 2013; May et al. 1999; Näätänen et al. 1988; Picton et al. 1978; Yvert et al. 1998) and studies conducting animal electrophysiology (Anderson et al. 2009; Hershenhoren et al. 2014; Malmierca et al. 2009; Taaseh et al. 2011; Ulanovsky et al. 2003; von der Behrens et al. 2009).

Critically, the present ERP and modeling data show that the degree of stimulus-specific adaptation in auditory cortex de-

[2] We also estimated coadaptation (σ) for each statistical context using $\Delta t = 0.5$ s (instead of $\Delta t = 0.32$ s), that is, assuming that recovery from adaptation starts at the onset rather than at the offset of the tone presentation. For the N1 and the P2, we again observed a significant difference between statistical contexts (N1: $t_{19} = 5.247$, $P < 0.001$; P2: $t_{19} = 2.978$, $P = 0.0077$), showing that coadaptation broadened in the large-change compared with the small-change statistical context.

pends on the statistical stimulation context. Our data are in line with early work on stimulus-specific adaptation, which was partially motivated by observations of statistical adaptation (Ulanovsky et al. 2003), and with the suggested role of local and global stimulus probabilities on adaptation of neural responses (Ulanovsky et al. 2004). Furthermore, observations of overall context effects in oddball paradigms (Yaron et al. 2012) as well as inconsistences between model fits and recent stimulus-specific adaptation data (Hershenhoren et al. 2014; Taaseh et al. 2011) have led to considerations of dynamic coadaptation involved in stimulus-specific adaptation (Hershenhoren et al. 2014). Our data suggest that the instantaneous state of coadaptation in auditory cortex is dynamically influenced by all stimuli in the acoustic oddball sequence rather than being a static property of the underlying neural population. The present data are thus in line with this recent hypothesis in that stimulus-specific adaptation depended on statistical context.

Importantly, the present results cannot be explained by assuming a general decrease (or increase) in response magnitude to rare tones that occur with higher probability (Ayala and Malmierca 2013; Ulanovsky et al. 2003) or different timescales of adaptation (Ulanovsky et al. 2004), both of which would predict a consistent effect of probability of presentation on N1 magnitudes. Counter to this prediction, we found that for a fixed tone frequency (either large or small spectral change), probability of occurrence (relatively high or low) had opposite effects. For the large spectral change, the N1 magnitude was reduced when presented with a high compared with a low probability. The reverse was true for a small spectral change: the N1 magnitude was increased when presented with a high compared with a low probability. Hence, the present results indicate that changes in neural sensitivity depend on the statistical context, and not simply on a general decrease (or increase) in response magnitude based on probability of rare stimuli to occur.

Mechanisms of stimulus-specific and statistical adaptation and proposed interactions. Stimulus-specific adaptation, that is, the decrease in response magnitude with repeated stimulation, has been linked to synaptic depression and neural inhibition (Abbott et al. 1997; Escera and Malmierca 2014; Loebel et al. 2007; Nelken 2014; Ulanovsky et al. 2004). Inhibition, however, appears to only modulate but not generate stimulus-specific adaptation (Duque et al. 2014; Pérez-González et al. 2012). Stimulus-specific adaptation of the human N1 component has been explained by refractoriness of neural populations (Budd et al. 1998; Jacobsen and Schröger 2001; Schröger 2007) and by inhibition (Loveless et al. 1989; May et al. 1999; McEvoy et al. 1997), while adaptation effects of the P2 are less well investigated (but see Herrmann et al. 2013a; Lanting et al. 2013; Picton et al. 1978) and mechanistically less well understood (Crowley and Colrain 2004).

Whether stimulus-specific adaptation observed at the single-unit or population level in nonhuman animals and modulations of human EEG responses relate to the same neural mechanism is still a matter of debate (Escera and Malmierca 2014; Fishman and Steinschneider 2012; Nelken 2014; Nelken and Ulanovsky 2007). These debates often focus on the relation between stimulus-specific adaptation and the human mismatch negativity (MMN), a component associated with change, novelty, and deviant detection that peaks after 150 ms (Näätänen et al. 1978, 2007; Ruhnau et al. 2013; Schröger 2007; Sussman et al. 2002). More recently, human midlatency neural responses (~30 ms) have also been discussed as potential candidates related to stimulus-specific adaptation observed in animals (Escera and Malmierca 2014). Human N1 and P2 responses are commonly left out of these discussions. It is thus an open question what the exact mechanisms of N1 adaptation are and whether adaptation effects observed in animals and humans have the same source.

Adaptation to statistical context is commonly associated with changes in neural sensitivity such that a limited range of neuronal responsiveness comes to match the range of the sensory stimulation (Brenner et al. 2000; Hildebrandt et al. 2011; Wark et al. 2007; Wen et al. 2009, 2012). This type of adaptation relates to changes in the input-output relation of a neuron (i.e., the stimulation-to-response mapping), such that the same stimulus (input) leads to different neural responses (output) depending on the acoustic context (Carvalho and Buonomano 2009; Hildebrandt et al. 2011; Silver 2010). On the neuronal level, statistical adaptation (i.e., change of the input-output relation) is associated with changes in neuronal firing thresholds (linear) and/or changes in neuronal response gain (nonlinear), and both have been observed in animal cell recordings (Dean et al. 2005; Hildebrandt et al. 2011; Nagel and Doupe 2006; Salinas and Thier 2000; Silver 2010).

Regarding the neural mechanisms underlying statistical context effects, some authors have reported a mechanistic distinction between linear and nonlinear changes, by which firing threshold changes (linear) are linked to synaptic depression and changes in neural gain (nonlinear) are related to neural inhibition (Hildebrandt et al. 2011). However, other authors emphasize the role of synaptic depression related to nonlinear changes (Abbott et al. 1997), while yet other authors report that both changes in neuronal firing threshold as well as changes in neuronal response gain are related to inhibitory neurons, albeit to different classes of neurons (Wilson et al. 2012).

The changes in coadaptation induced by statistical context observed in the present study are fundamentally nonlinear and thus relate to changes in neuronal response gain, yet the extent to which synaptic depression (Abbott et al. 1997) versus neural inhibition (Carvalho and Buonomano 2009; Hildebrandt et al. 2011; Olsen and Wilson 2008; Wilson et al. 2012) or even additional mechanisms (for a review on neural input-output relations see Silver 2010) contributes to the present context effects cannot be inferred from our human EEG recordings. Nonetheless, a critical role of neural inhibition in shaping frequency specificity is consistent with observations of reduced stimulus-specific adaptation under GABAergic agonists (i.e., reduction of inhibition, Ayala and Malmierca 2013; Duque et al. 2014; Pérez-González et al. 2012; although GABAergic agonists might also affect synaptic depression, Loebel et al. 2007), with the suggestion of network coding for statistical adaptation (Rabinowitz et al. 2011; see also the discussion in Willmore et al. 2014), and with the proposed neural mechanisms underlying N1 adaptation (Loveless et al. 1989; May et al. 1999; McEvoy et al. 1997).

Neural response adaptation and its relation to other ERP components. Many previous EEG studies presenting oddball sequences have investigated the MMN component of the ERP, which commonly peaks at ~150 ms after tone onset (Näätänen et al. 1978, 2010; Ruhnau et al. 2012; Sussman et al. 2002). Furthermore, an additional positive deflection at ~250–400

ms, referred to as P3a, is sometimes observed in response to rare tones in oddball sequences (Berti et al. 2004; Ruhnau et al. 2013; Winkler et al. 1998). Given the time window of the MMN and P3a in combination with the large spectral changes employed here, the present study cannot exclude potential contributions of MMN and P3a to the observed N1 and P2 responses, respectively. Regarding a potential contribution of an MMN to the observed N1, however, it should be noted that whether these two components are related to same neural mechanism has been long debated and remains an unresolved question. In fact, the MMN has repeatedly been related to neural RA and therefore regarded as an N1-type response (May et al. 1999; May and Tiitinen 2004, 2010). Furthermore, the MMN's amplitude increase with increasing magnitude of a spectral change has been shown to be mostly due to N1 neural RA effects (Horváth et al. 2008). In sum, the present effects are most likely caused by neural RA, but other response types might additionally contribute. Future experiments are needed to clearly dissociate different contributors.

Dynamics of response adaptation have implications for isolating deviant-detection responses. The present results also have implications for EEG research on deviant detection using the MMN component of the ERP (Näätänen et al. 1978; Schröger 2007; Winkler et al. 2009). To isolate deviant-detection responses, a common approach in MMN studies is to remove N1 stimulus-specific adaptation effects (referred to as refractoriness; Schröger 2007). That is, either the neural responses to repeated stimuli (Alho et al. 1998; Ermutlu et al. 2007; Näätänen et al. 1978) or the neural responses to a stimulus from a control sequence with random stimuli (Horváth et al. 2008; Jacobsen and Schröger 2001; Ruhnau et al. 2012; Schröger and Wolff 1996) are subtracted from the responses to the rare stimuli. However, this subtraction procedure implicitly assumes stationarity of stimulus-specific adaptation effects within the control as well as within the oddball sequences. In stark contrast, the present data show that the statistical context, that is, all stimuli within a sequence, affects the degree of stimulus-specific adaptation, and thus violates the assumption of stationarity of neural RA in oddball paradigms. Furthermore, recent studies have also observed dynamic changes in neural adaptation for sequences with random tone presentation that are often used as adaptation control conditions (Garrido et al. 2013; Herrmann et al. 2013a, 2013b, 2014). As a consequence, estimation of the appropriate response magnitude to be subtracted from responses to rare tones in order to isolate deviant-detection responses is not trivial: Neural responses change nonlinearly and adjust flexibly within oddball and control sequences depending on their statistical acoustic context.

Conclusions. The present human EEG study investigated the effects of statistical context on stimulus-specific adaptation in auditory oddball sequences. Results show that stimulus-specific adaptation of neural responses in human auditory cortex critically depends on the statistical context in which stimuli occur. Using a computational model of neural RA, we link the observed statistical context effects to coadaptation changes in tonotopically organized regions of auditory cortex. The present results have implications for the assumption of stationarity of neural responses when isolating deviant-detection responses using established auditory potentials such as the MMN.

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DISCLOSURES

No conflicts of interest, financial or otherwise, are declared by the author(s).

AUTHOR CONTRIBUTIONS

Author contributions: B.H., M.J.H., E.K.F., J.D.M., and J.O. conception and design of research; B.H. performed experiments; B.H. analyzed data; B.H., M.J.H., E.K.F., J.D.M., and J.O. interpreted results of experiments; B.H. prepared figures; B.H., M.J.H., E.K.F., and J.O. drafted manuscript; B.H., M.J.H., E.K.F., J.D.M., and J.O. edited and revised manuscript; B.H., M.J.H., E.K.F., J.D.M., and J.O. approved final version of manuscript.

REFERENCES

Abbott LF, Varela JA, Sen K, Nelson SB. Synaptic depression and cortical gain control. *Science* 275: 220–224, 1997.

Alho K, Winkler I, Escera C, Huotilainen M, Virtanen J, Jääskeläinen IP, Pekkonen E, Ilmoniemi RJ. Processing of novel sounds and frequency changes in the human auditory cortex: magnetoencephalographic recordings. *Psychophysiology* 35: 211–224, 1998.

Anderson LA, Christianson GB, Linden JF. Stimulus-specific adaptation occurs in the auditory thalamus. *J Neurosci* 29: 7359–7363, 2009.

Ayala YA, Malmierca MS. Stimulus-specific adaptation and deviance detection in the inferior colliculus. *Front Neural Circuits* 6: 89, 2013.

Bäuerle P, von der Behrens W, Kössl M, Gaese BH. Stimulus-specific adaptation in the gerbil primary auditory thalamus is the result of a fast frequency-specific habituation and is regulated by the corticofugal system. *J Neurosci* 31: 9708–9722, 2011.

Bell AJ, Sejnowski TJ. An information maximization approach to blind separation and blind deconvolution. *Neural Comput* 7: 1129–1159, 1995.

Benucci A, Saleem AB, Carandini M. Adaptation maintains population homeostasis in primary visual cortex. *Nat Neurosci* 6: 724–729, 2013.

Berti S, Roeber U, Schröger E. Bottom-up influences on working memory: behavioral and electrophysiological distraction varies with distractor strength. *Exp Psychol* 51: 249–257, 2004.

Brenner N, Bialek W, de Ruyter van Steveninck R. Adaptive rescaling maximizes information transmission. *Neuron* 26: 695–702, 2000.

Briley PM, Krumbholz K. The specificity of stimulus-specific adaptation in human auditory cortex increases with repeated exposure to the adapting stimulus. *J Neurophysiol* 110: 2679–2688, 2013.

Budd TW, Barry RJ, Gordon E, Rennie C, Michie PT. Decrement of the N1 auditory event-related potential with stimulus repetition: habituation vs. refractoriness. *Int J Psychophysiol* 31: 51–68, 1998.

Butler RA. Effect of changes in stimulus frequency and intensity on habituation of the human vertex potential. *J Acoust Soc Am* 44: 945–950, 1968.

Carvalho TP, Buonomano DV. Differential effects of excitatory and inhibitory plasticity on synaptically driven neuronal input-output functions. *Neuron* 61: 774–785, 2009.

Crowley KE, Colrain IM. A review of the evidence for P2 being an independent component process: age, sleep and modality. *Clin Neurophysiol* 115: 732–744, 2004.

Dahmen JC, Hartley DE, King AJ. Stimulus-timing-dependent plasticity of cortical frequency representation. *J Neurosci* 28: 13629–13639, 2008.

Dahmen JC, Keating P, Nodal FR, Schulz AL, King AJ. Adaptation to stimulus statistics in the perception and neural representation of auditory space. *Neuron* 66: 937–948, 2010.

Dean I, Harper NS, McAlpine D. Neural population coding of sound level adapts to stimulus statistics. *Nat Neurosci* 8: 1684–1689, 2005.

Dean I, Robinson BL, Harper NS, McAlpine D. Rapid neural adaptation to sound level statistics. *J Neurosci* 28: 6430–6438, 2008.

Duque D, Malmierca MS, Caspary DM. Modulation of stimulus-specific adaptation by $GABA_A$ receptor activation or blockade in the medial geniculate body of the anaesthetized rat. *J Physiol* 592: 729–743, 2014.

Ermutlu MN, Demiralp T, Karamürsel S. The effects of interstimulus interval on sensory gating and on preattentive auditory memory in the oddball paradigm: Can magnitude of the sensory gating affect preattentive auditory comparison process? *Neurosci Lett* 412: 1–5, 2007.

Escera C, Malmierca MS. The auditory novelty system: an attempt to integrate human and animal research. *Psychophysiology* 51: 111–123, 2014.

Fairhall AL, Lewen GD, Bialek W, de Ruyter van Steveninck RR. Efficiency and ambiguity in an adaptive neural code. *Nature* 412: 787–792, 2001.

Fishman YI, Steinschneider M. Searching for the mismatch negativity in primary auditory cortex of the awake monkey: deviance detection or stimulus specific adaptation? *J Neurosci* 32: 15747–15758, 2012.

Garrido MI, Sahani M, Dolan RJ. Outlier responses reflect sensitivity to statistical structure in the human brain. *PLoS Comput Biol* 9: e1002999, 2013.

Greenhouse SW, Geisser S. On methods in the analysis of profile data. *Psychometrika* 24: 95–112, 1959.

Hari R, Kaila K, Katila T, Tuomisto T, Varpula T. Interstimulus interval dependence of the auditory vertex response and its magnetic counterpart: implications for their neural generation. *Electroencephalogr Clin Neurophysiol* 54: 561–569, 1982.

Henry MJ, Herrmann B, Obleser J. Entrained neural oscillations in multiple frequency bands co-modulate behavior. *Proc Natl Acad Sci USA* 111: 14935–14940, 2014.

Herrmann B, Henry MJ, Obleser J. Frequency-specific adaptation in human auditory cortex depends on the spectral variance in the acoustic stimulation. *J Neurophysiol* 109: 2086–2096, 2013a.

Herrmann B, Henry MJ, Scharinger M, Obleser J. Auditory filter width affects response magnitude but not frequency specificity in auditory cortex. *Hear Res* 304: 128–136, 2013b.

Herrmann B, Maess B, Friederici AD. Violation of syntax and prosody: disentangling their contributions to the early left anterior negativity (ELAN). *Neurosci Lett* 490: 116–120, 2011.

Herrmann B, Schlichting N, Obleser J. Dynamic range adaptation to spectral stimulus statistics in human auditory cortex. *J Neurosci* 34: 327–331, 2014.

Hershenhoren I, Taaseh N, Antunes FM, Nelken I. Intracellular correlates of stimulus-specific adaptation. *J Neurosci* 34: 3303–3319, 2014.

Hildebrandt KJ, Benda J, Hennig RM. Multiple arithmetic operations in a single neuron: the recruitment of adaptation processes in the cricket auditory pathway depends on sensory context. *J Neurosci* 31: 14142–14150, 2011.

Horváth J, Czigler I, Jacobsen T, Maess B, Schröger E, Winkler I. MMN or no MMN: no magnitude of deviance effect on the MMN amplitude. *Psychophysiology* 45: 60–69, 2008.

Isaacson JS, Scanziani M. How inhibition shapes cortical activity. *Neuron* 72: 231–243, 2011.

Jääskeläinen IP, Ahveninen J, Belliveau JW, Raij T, Sams M. Short-term plasticity in auditory cognition. *Trends Neurosci* 30: 653–661, 2007.

Jacobsen T, Schröger E. Is there pre-attentive memory-based comparison of pitch? *Psychophysiology* 38: 723–727, 2001.

Kim E, McAuley JD. Effects of pitch distance and likelihood on the perceived duration of deviant auditory events. *Atten Percept Psychophys* 75: 1547–1558, 2013.

Kvale MN, Schreiner CE. Short-term adaptation of auditory receptive fields to dynamic stimuli. *J Neurophysiol* 91: 604–612, 2004.

Lanting CP, Briley PM, Summer CJ, Krumbholz K. Mechanisms of adaptation in human auditory cortex. *J Neurophysiol* 110: 973–983, 2013.

Loebel A, Nelken I, Tsodyks M. Processing of sounds by population spikes in a model of primary auditory cortex. *Front Neurosci* 1: 197–209, 2007.

Loveless N, Hari R, Hämäläinen MS, Tiihonen J. Evoked responses of human auditory cortex may be enhanced by preceding stimuli. *Electroencephalogr Clin Neurophysiol* 74: 217–227, 1989.

Lü ZL, Williamson SJ, Kaufman L. Human auditory primary and association cortex have differing lifetimes for activation traces. *Brain Res Rev* 572: 236–241, 1992.

Maess B, Jacobsen T, Schröger E, Friederici AD. Localizing pre-attentive auditory memory-based comparison: magnetic mismatch negativity to pitch change. *Neuroimage* 37: 561–571, 2007.

Makeig S, Bell AJ, Jung TP, Sejnowski TJ. Independent component analysis of electroencephalographic data. In: *Advances in Neural Information Processing Systems*, edited by Touretzky D, Mozer M, Hasselmo M. Cambridge, MA: MIT Press, 1996.

Mäkelä JP, Ahonen A, Hämäläinen MS, Hari R, Ilmoniemi RJ, Kajola M, Knuutila J, Lounasmaa OV, McEvoy L, Salmelin R, Salonen O, Sams M, Simola J, Tesche C, Vasama JP. Functional differences between auditory cortices of the two hemispheres revealed by whole-head neuromagnetic recordings. *Hum Brain Mapp* 1: 48–56, 1993.

Malmierca MS, Cristaudo S, Pérez-González D, Covey E. Stimulus-specific adaptation in the inferior colliculus of the anesthetized rat. *J Neurosci* 29: 5483–5493, 2009.

May PJ, Tiitinen H. The MMN is a derivative of the auditory N100 response. *Neurol Clin Neurophysiol* 20: 1–5, 2004.

May PJ, Tiitinen H. Mismatch negativity (MMN), the deviance-elicited auditory deflection, explained. *Psychophysiology* 47: 66–122, 2010.

May PJ, Tiitinen H, Ilmoniemi RJ, Nyman G, Taylor JG, Näätänen R. Frequency change detection in human auditory cortex. *J Comput Neurosci* 6: 99–120, 1999.

McEvoy L, Levänen S, Loveless N. Temporal characteristics of auditory sensory memory: neuromagnetic evidence. *Psychophysiology* 34: 308–316, 1997.

Mill R, Sheik S, Indiveri G, Denham SL. A model of stimulus-specific adaptation in neuromorphic analog VLSI. *IEEE Trans Biomed Circuits Syst* 5: 413–419, 2011.

Montgomery N, Wehr M. Auditory cortical neurons convey maximal stimulus-specific information at their best frequency. *J Neurosci* 30: 13362–13366, 2010.

Näätänen R, Astikainen P, Ruusuvirta T, Huotilainen M. Automatic auditory intelligence: an expression of the sensory-cognitive core of cognitive processes. *Brain Res Rev* 64: 123–136, 2010.

Näätänen R, Gaillard AW, Mäntysalo S. Early selective-attention effect on evoked potential reinterpreted. *Acta Psychol* 42: 313–329, 1978.

Näätänen R, Paavilainen P, Rinne T, Alho K. The mismatch negativity (MMN) in basic research of central auditory processing: a review. *Clin Neurophysiol* 118: 2544–2590, 2007.

Näätänen R, 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.

Näätänen R, Sams M, Alho K, Paavilainen P, Reinikainen K, Sokolov EN. Frequency and location specificity of the human vertex N1 wave. *Electroencephalogr Clin Neurophysiol* 69: 523–531, 1988.

Nagel KI, Doupe AJ. Temporal processing and adaptation in the songbird auditory forebrain. *Neuron* 51: 845–859, 2006.

Nelken I. Stimulus-specific adaptation and deviance detection in the auditory system: experiments and models. *Biol Cybern* 108: 655–663, 2014.

Nelken I, Ulanovsky N. Mismatch negativity and stimulus-specific adaptation in animal models. *J Psychophysiol* 21: 214–223, 2007.

Olsen SR, Wilson RI. Lateral presynaptic inhibition mediates gain control in an olfactory circuit. *Nature* 452: 956–960, 2008.

Oostenveld R, Fries P, Maris E, Schoffelen JM. FieldTrip: open source software for advanced analysis of MEG, EEG, and invasive electrophysiological data. *Comput Intell Neurosci* 2011: 156869, 2011.

Pérez-González D, Hernández O, Covey E, Malmierca MS. $GABA_A$-mediated inhibition modulates stimulus-specific adaptation in the inferior colliculus. *PLoS One* 7: e34297, 2012.

Picton TW, Woods DL, Proulx GB. Human auditory sustained potentials. II. Stimulus relationships. *Electroencephalogr Clin Neurophysiol* 45: 198–210, 1978.

Price NS, Prescott DL. Adaptation to direction statistics modulates perceptual discrimination. *J Vis* 12: 1–17, 2012.

Pulvermüller F, Shtyrov Y, Ilmoniemi RJ. Spatiotemporal dynamics of neural language processing: an MEG study using minimum-norm current estimates. *Neuroimage* 20: 1020–1025, 2003.

Rabinowitz NC, Willmore BD, Schnupp JW, King AJ. Contrast gain control in auditory cortex. *Neuron* 70: 1178–1191, 2011.

Ringo JL. Stimulus specific adaptation in inferior temporal and medial temporal cortex of the monkey. *Behav Brain Res* 76: 191–197, 1996.

Ruhnau P, Herrmann B, Maess B, Brauer J, Friederici AD, Schröger E. Processing of complex distracting sounds in school-aged children and adults: evidence from EEG and MEG data. *Front Psychol* 4: 717, 2013.

Ruhnau P, Herrmann B, Maess B, Schröger E. Maturation of obligatory auditory responses and their neural sources: evidence from EEG and MEG. *Neuroimage* 58: 630–639, 2011.

Ruhnau P, Herrmann B, Schröger E. Finding the right control: the mismatch negativity under investigation. *Clin Neurophysiol* 123: 507–512, 2012.

Salinas E, Thier P. Gain modulation: a major computational principle of the central nervous system. *Neuron* 27: 15–21, 2000.

Sams M, Hari R, Rif J, Knuutila J. The human auditory sensory memory trace persists about 10 sec: neuromagnetic evidence. *J Cogn Neurosci* 5: 363–370, 1993.

Schröger E. Mismatch negativity: a microphone into auditory memory. *J Psychophysiol* 21: 138–146, 2007.

Schröger E, Wolff C. Mismatch response of the human brain to changes in sound location. *Neuroreport* 7: 3005–3008, 1996.

Silver RA. Neuronal arithmetic. *Nat Rev Neurosci* 11: 474–489, 2010.

Sussman ES, Winkler I, Huotilainen M, Ritter W, Näätänen R. Top-down effects can modify the initially stimulus-driven auditory organization. *Cogn Brain Res* 13: 393–405, 2002.

Taaseh N, Yaron A, Nelken I. Stimulus-specific adaptation and deviance detection in the rat auditory cortex. *PLoS One* 6: e23369, 2011.

Tervaniemi M, Kujala T, Alho K, Virtanen J, Ilmoniemi RJ, Näätänen R. Functional specialization of the human auditory cortex in processing phonetic and musical sounds: a magnetoencephalographic (MEG) study. *Neuroimage* 9: 330–336, 1999.

Ulanovsky N, Las L, Farkas D, Nelken I. Multiple time scales of adaptation in auditory cortex neurons. *J Neurosci* 24: 10440–10453, 2004.

Ulanovsky N, Las L, Nelken I. Processing of low-probability sounds by cortical neurons. *Nat Neurosci* 6: 391–398, 2003.

Urbach TP, Kutas M. Interpreting event-related brain potential (ERP) distributions: implications of baseline potentials and variability with application to amplitude normalization by vector scaling. *Biol Psychol* 72: 333–343, 2006.

von der Behrens W, Bäuerle P, Kössl M, Gaese BH. Correlating stimulus-specific adaptation of cortical neurons and local field potentials in the awake rat. *J Neurosci* 29: 13837–13849, 2009.

Wark B, Lundstrom BN, Fairhall A. Sensory adaptation. *Curr Opin Neurobiol* 17: 423–429, 2007.

Wen B, Wang GI, Dean I, Delgutte B. Dynamic range adaptation to sound level statistics in the auditory nerve. *J Neurosci* 29: 13797–13808, 2009.

Wen B, Wang GI, Dean I, Delgutte B. Time course of dynamic range adaptation in the auditory nerve. *J Neurophysiol* 108: 69–82, 2012.

Willmore BD, Cooke JE, King AJ. Hearing in noisy environments: noise invariance and contrast gain control. *J Physiol* 592: 3371–3381, 2014.

Wilson NR, Runyan CA, Wang FL, Sur M. Division and subtraction by distinct cortical inhibitory networks in vivo. *Nature* 488: 343–348, 2012.

Winkler I, Denham SL, Nelken I. Modeling the auditory scene: predictive regularity representations and perceptual objects. *Trends Cogn Sci* 13: 532–540, 2009.

Winkler I, Tervaniemi M, Schröger E, Wolff C, Näätänen R. Preattentive processing of auditory spatial information in humans. *Neurosci Lett* 242: 49–52, 1998.

Yaron A, Hershenhoren I, Nelken I. Sensitivity to complex statistical regularities in rat auditory cortex. *Neuron* 76: 603–615, 2012.

Yvert B, Bertrand O, Pernier J, Ilmoniemi RJ. Human cortical responses evoked by dichotically presented tones of different frequencies. *Neuroreport* 9: 1115–1119, 1998.