Feedback that confirms reward expectation triggers auditory cortex activity

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Weis T, Brechmann A, Puschmann S, Thiel CM. Feedback that confirms reward expectation triggers auditory cortex activity. J Neurophysiol 110: 1860–1868, 2013. First published July 31, 2013; doi:10.1152/jn.00128.2013.—Associative learning studies have shown that the anticipation of reward and punishment shapes the representation of sensory stimuli, which is further modulated by dopamine. Less is known about whether and how reward delivery activates sensory cortices and the role of dopamine at that time point of learning. We used an apparatus instrumental learning task in which participants had to learn that a specific class of frequency-modulated tones predicted a monetary reward following fast and correct responses in a succeeding reaction time task. These fMRI data were previously analyzed regarding the effect of reward anticipation, but here we focused on neural activity to the reward outcome relative to the reward expectation and tested whether such activation in the reward reception phase is modulated by L-DOPA. We analyzed neural responses at the time point of reward outcome under three different conditions: 1) when a reward was expected and received, 2) when a reward was expected but not received, and 3) when a reward was not expected and not received. Neural activity in auditory cortex was enhanced during feedback delivery either when an expected reward was received or when the expectation of obtaining no reward was correct. This differential neural activity in auditory cortex was only seen in subjects who learned the reward association and not under dopaminergic modulation. Our data provide evidence that auditory cortices are active at the time point of reward outcome. However, responses are not dependent on the reward itself but on whether the outcome confirmed the subject’s expectations.

PRIORITY Evidence suggests that the expectation of reward and punishment shapes the representation of stimuli in sensory cortices (David et al. 2012). Animal data indicate that reward expectation can influence neural activity in sensory cortices (Brosch et al. 2011; Pantoja et al. 2007; Shuler and Bear 2006). In primary visual cortex, Shuler and Bear (2006) discovered neurons that predicted the timing of water reward delivery. In primary somatosensory cortex, Pantoja and colleagues (2007) found stimulus-related neural responses that correlated with reward delivery in a tactile discrimination task. These stimulus-related activities were only present when the task was well learned, suggesting that neural activity in sensory cortex is strongly modulated by reward contingency in association with learning. Brosch et al. (2011) studied primates performing an auditory categorization task and found that neural activity in auditory cortex not only reflected reward expectancy but was directly related to the reward itself in a size-dependent manner. Responses in auditory cortex were also observed in trials with prediction errors, i.e., when a mismatch between expected and received rewards occurred. These findings demonstrate that the auditory cortex receives reward feedback that can be used for adaptation to specific task requirements.

Scheich et al. (2011) further underline the role of auditory cortex in deducing the task-specific meaning of sound by learning and suggest that even primary auditory cortex is influenced in a multimodal manner by other sensory stimuli, reward, and punishment. This evidence is supported by human fMRI and magnetoencephalography (MEG) studies showing an increased representation of auditory stimuli that signal a reward or punishment (Kluge et al. 2011; Puschmann et al. 2012; Thiel et al. 2002a, 2002b). Whereas Thiel et al. (2002a, 2002b) showed that the representation of auditory stimuli is modulated by classical aversive conditioning and the cholinergic neurotransmitter system, Puschmann et al. (2012) showed that the representation of auditory stimuli can also be increased by instrumental appetitive conditioning. However, this effect was only seen in subjects who learned the reward association. Using the same paradigm and a pharmacological fMRI approach in which half of the participants received 100 mg of the dopamine precursor L-DOPA, Weis et al. (2012) provide further evidence for a dopaminergic modulation of neural responses in auditory cortex during reward anticipation. Hence, there is ample evidence that cholinergic and dopaminergic neurotransmitter systems modulate the representation of auditory stimuli. Both studies concentrated on the time point of reward anticipation; however, since the paradigm consists of two different parts, in the present work we analyzed the data of the two previous studies (Puschmann et al. 2012; Weis et al. 2012) focusing on the reward delivery phase instead of reward anticipation.

While these studies compellingly demonstrate that sensory cortices develop increased responses to stimuli that gain behavioral relevance due to prediction of reward or punishment, only a few studies have addressed the question of whether reward delivery may activate sensory cortices. Previous studies by Pleger and colleagues (2008) showed that the somatosensory cortex is activated at the time of reward delivery in the absence of concurrent somatosensory input. This study showed for the first time in humans that rewards influence not only classical reward-related regions but also processing in early sensory cortices. A subsequent study demonstrated that the behavioral and neural effects were enhanced by L-DOPA and attenuated by haloperidol (Pleger et al. 2009), suggesting that the dopaminergic system may also modulate reward-related
activity in sensory cortices. Similar results for the visual cortex were provided by Weil et al. (2010), who found in a visual discrimination task that a financial reward increased neural activity in striatum and orbitofrontal cortex as well as in visual areas. Again, the activity in visual areas appeared at the time point of reward delivery, when no visual stimulus was present. In line with the results of Pleger et al. (2008), the delivery of reward at the end of the trial led to improved performance and enhanced neural activity in visual cortex in the subsequent trial, suggesting some kind of “teaching signal” propagated via feedback connections from reward-related areas to sensory cortex.

In contrast to the visual and somatosensory systems, only a few studies have focused on reward-related activity in human auditory cortex. Furthermore, there are currently no human data for neural activity in sensory cortex when an expected reward is not received. To fill this gap, we here reanalyzed the data sets of Puschmann et al. (2012) and Weis et al. (2012) with focus on the time point of reward delivery instead of the time point of reward anticipation. While our previous studies have shown increased auditory cortex activity when an auditory stimulus indicates a later reward, the present analysis was performed to investigate whether the reward, which is presented in the absence of any auditory stimulation, reactivates auditory cortex as reported for other modalities and whether such reactivation is modulated by dopaminergic stimulation.

Participants had to learn that a specific category of frequency-modulated (FM) tones predicted a monetary reward when fast and correct responses were made in a succeeding reaction time task. An event-related fMRI design allowed us to temporally distinguish BOLD responses associated with auditory discrimination and reward anticipation at the beginning of each trial from those attributed to the subsequent nonauditory rewarding feedback. We focused our analysis on neural responses during the receipt of feedback under three conditions: 1) when a reward was expected and received (CS+ trial), 2) when a reward was expected but not received because of slow and incorrect responses in potentially rewarded trials (CS+ trial), and 3) when a reward was not expected and not received (CS− trial). We hypothesized that reward delivery and reward omission would modulate neural activity in auditory cortex and reward-related dopaminergic brain regions.

Since we found effects of dopaminergic modulation within the left auditory cortex during reward anticipation in our previous study (Weis et al. 2012), we expected that dopaminergic stimulation would also influence reward-related activations in auditory cortex.

METHODS

Subjects. All 105 participants were scanned with the same paradigm and fMRI data acquisition techniques including either a standard fMRI protocol or a double-blind pharmacological fMRI protocol. All participants were right-handed as indexed by a handedness inventory (Oldfield 1971), had no history of neurological or psychiatric disease, and were not on any kind of medication (except for contraceptives).

The study was conducted in accordance with the Declaration of Helsinki (World Medical Association 2008), and the experiments were approved by the ethics committee of the University of Magdeburg.

Thirty-nine healthy, right-handed, normal-hearing volunteers (18 women, 21 men; age range: 18–31 yr, mean age: 24 yr) participated in the standard fMRI protocol. Five subjects were excluded from all further analyses because of severe head movements during fMRI scanning. Sixty-six healthy, right-handed, normal-hearing volunteers (20 women, 46 men; age range: 25–42 yr, mean age: 28 yr) participated in the pharmacological fMRI protocol receiving either 100 mg of L-DOPA (Madopar LT) or placebo (solution containing glucose dissolved in water) 30 min before starting the fMRI measurement in a double-blind between-group design (see Weis et al. 2012 for more details). A clinical evaluation was first carried out to ensure that subjects had no conditions contraindicative for L-DOPA administration. The age range was restricted to >25 yr of age according to the patient information sheet. Participants were asked to avoid excessive alcohol intake on the evening before the test session and to refrain from eating, smoking, and drinking coffee for 2 hr prior to the experiment. Four subjects were excluded from all further analyses because of noncompliance with task instructions, and five subjects were excluded because of severe head movement during fMRI scanning. A further two subjects were excluded after analysis of blood samples because of nondetectable L-DOPA levels.

Fig. 1. Paradigm. In the instrumental learning paradigm, each trial started with a frequency-modulated (FM) tone that differed in various features. In half of the trials participants had the chance to gain a monetary reward (CS+), whereas the other half of the trials always remained unrewarded (CS−). The main task for the participants was to find out by trial and error which feature of the FM tones predicted a reward. After each tone, they had to state their current reward expectancy for the upcoming trial via key press. To receive the reward, participants had to solve a simple reaction time task, in which they had to indicate whether a number shown on a screen was smaller or larger than 5. If their answer in the number comparison task was fast and correct, they were rewarded with 50 euro cents, if it was a CS+ trial. Slow and incorrect answers in CS+ trials resulted in no reward (indicated by a gray square). In the other half of the trials (CS−), participants were never rewarded, independent of the correctness and speed of their response.

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The group size remaining in the analysis was 89 subjects in total: 
\( n = 34 \) (18 men, 16 women; mean age = 24 ± 1 yr) for no drug 
(standard fMRI protocol), \( n = 28 \) (20 men, 8 women; mean age = 
28 ± 1 yr) for placebo, and \( n = 27 \) (18 men, 9 women; mean age = 
29 ± 1 yr) for L-DOPA.

**Task.** We used an instrumental learning paradigm in which partic-
ipants had to learn the association of a specific category of FM tones 
with the chance to gain a monetary reward in a subsequent reaction 
time task (Knutson et al. 2000). At the beginning of each trial, an FM 
tone was presented that indicated whether the upcoming trial was 
predicted a reward chance but had to find out the relevant feature by 
trial and error. The relevant reward-prediction feature was duration 
(400 ms vs. 800 ms). Whether the short- or long-duration FM tones 
predicted the reward was randomized across subjects. The number of 
short- and long-duration FM tones (i.e., CS+ and CS− trials) was the 
same. To assess the individual learning rate, participants had to 
indicate via button press after each tone whether they expected a 
reward in the upcoming trial or not. They had to press the left button 
with the index finger if they expected a reward and the right button 
with the middle finger if they did not expect a reward.

Note that the rewards were obtained for fast responses in a 
following number comparison task. Here, participants had to indicate 
by button press whether the number (1, 4, 6, or 9) presented on the 
screen for 100 ms was smaller or larger than 5, either with the index 
finger for “smaller” or with the middle finger for “larger.” On the basis 
of an individual reaction time threshold that was piloted before the 
experiment (see below), fast and correct responses in CS+ trials were 
financially rewarded (Knutson et al. 2000; Pappata et al. 2002; 
Wittmann et al. 2005). The reward was indicated by a 50-euro cent 
coin displayed on the screen at the end of each trial 1.5 s after onset 
of the number presentation. In CS− trials no reward was given,

independent of the subject’s answer, which was signaled by a neutral 
feedback (gray square). The same feedback was also given for slow or 
incorrect answers in CS+ trials. A temporal jitter was used between 
the FM tone and the number comparison task in steps of 1.5 s ranging 
from 4.5 to 12.0 s. The intertrial interval ranged from 3.0 to 12.0 s, 
also in steps of 1.5 s. A fixation cross was presented in the middle of 
the screen during all delays and during presentation of the FM tones.
The total experiment comprised 160 trials in 42 min. Participants 
received payment of the amount of gained reward at the end of the 
experiment.

To obtain an individual reaction time threshold for fast responses, 
participants performed the number comparison tasks prior to entering
the MRI scanner. As during scanning, they had to indicate via button 
press whether the presented number was smaller or larger than 5. The 
80% value of reaction time in 80 trials was calculated and taken as a 
starting threshold for gaining a potential reward in the following 
paradigm during fMRI measurement. This reaction time threshold 
was 405 ± 11 ms in the standard fMRI protocol and 560 ± 10 ms for 
the pharmacological fMRI study [\( F(1,84) = 9.29, P < 0.001 \)]. However, 
there was no difference between 
the L-DOPA (560 ± 94 ms) and

Fig. 3. Main effect of reward condition: brain areas showing 
differential responses as a function of reward condition 
(i.e., “reward expected and received,” “reward expected 
and not received,” and “reward not expected and not 
received”). 

A: cortical regions: 1, 2, left and right auditory cortex; 6, 7, left and 
right insula; 9, 10, left and right middle and inferior occipital 
and fusiform gyrus. 

B: subcortical regions: 3, 4, left and right striatum; 5, substantia nigra/ventral 
tegmental area; 8, anterior cingulate cortex. 
Activations are superimposed on the T1 
template image available in SPM for cortical regions 
and on the mean of the individual subject T1 images for 
subcortical regions [\( P < 0.05 \), familywise error (FWE) 
corrected, cluster size \( k > 40 \)].
placebo (559 ± 64 ms) groups \(T(1,53) = 0.08, P = 0.9\). All experimental control software was programmed in MATLAB (The MathWorks, Natick, MA) with Cogent 2000.

**Stimuli.** Each stimulus dimension (frequency range, modulation rate, loudness, direction, and duration) consisted of two principal levels. There was a low- and a high-frequency band, each containing five onset frequencies separated by half-tone steps (500 Hz, 530 Hz, 561 Hz, 595 Hz, 630 Hz; 1,630 Hz, 1,732 Hz, 1,826 Hz, 1,915 Hz, 2,000 Hz). Frequencies varied either with 0.25 octaves/s or 0.5 octaves/s. Sound level was individually adjusted under scanner noise for both louder and quieter sounds, differing approximately by 10 phon. Sound duration was either 400 ms (short) or 800 ms (long). The modulation direction was either rising or falling. In total, the combination of all possible values of the five dimensions resulted in 160 different stimuli, with 80 of them predicting a potential reward (all short or all long FM tones).

**fMRI data acquisition.** fMRI data acquisition was performed on a 3-T Siemens MAGNETOM Trio MRI scanner (Siemens, Erlangen, Germany) with an eight-channel head array. Key presses were recorded with a MR-compatible response keypad (LUMITouch, Photon Control, Burnaby, BC, Canada). Acoustic stimuli were delivered by MR-compatible headphones (MR confoPTIME1, MR confo, Magdeburg, Germany).

During functional measurements, 1,680 T2*-weighted gradient echo planar imaging (EPI) volumes [time of repetition (TR) = 1.5 ms, time of echo (TE) = 30 ms, flip angle \(\alpha = 80^\circ\), field of view (FoV) = 192 × 192 mm2, voxel size = 3.0 × 3.0 × 3.0 mm3] were obtained within one session. Volumes consisted of 24 interleaved slices (gap of 0.3 mm) ranging from the anterior cingulate cortex dorsally to the inferior colliculus in the brain stem. After the experimental task a high-resolution T1-weighted structural volume was obtained from each subject.

**Behavioral data analysis.** To assess whether participants learned the tone-reward association, we analyzed individual learning rates. The expectation of reward was indicated by the subjects after presentation of the FM tone and reflects whether the tone-reward association was learned. For each subject, we determined the individual learning curve, using the cumulative sum of correct responses as a function of experimental trial according to Gallistel et al. (2004). The final sum of the correct responses was compared across groups by means of a Kruskal-Wallis test. In a second step we grouped subjects into learners and nonlearners. Subjects who never exceeded 65% correct responses during the whole paradigm were classified as nonlearners. This resulted in 8 subjects in the L-DOPA group, 12 in the placebo group, and 19 in the no-drug study were classified as learners. Subjects who never exceeded 65% correct responses during the whole paradigm were classified as nonlearners. This resulted in 8 subjects in the L-DOPA group, 12 in the placebo group, and 19 in the no-drug study were classified as learners. We had to exclude 13 subjects in the L-DOPA group, 12 in the placebo group, and 19 in the no-drug study within the group of nonlearners. We had to exclude 13 subjects in the L-DOPA group, 12 in the placebo group, and 19 in the no-drug study were classified as nonlearners. This resulted in 8 subjects in the L-DOPA group, 12 in the placebo group, and 19 in the no-drug study were classified as learners. Subjects who never exceeded 65% correct responses during the whole paradigm were classified as nonlearners.

**fMRI data analysis.** All MRI data were processed and analyzed with SPM8 (FIL, Wellcome Trust Centre for Neuroimaging, University College London, London, UK). To correct for head motion, the functional time series were spatially realigned and unwarped. The structural T1-weighted image was registered to mean functional image and segmented in order to obtain spatial normalization parameters. With these parameters functional and structural images were normalized to the Montreal Neurological Institute (MNI) template brain. Finally, normalized functional volumes were smoothed with a three-dimensional Gaussian kernel of 4-mm full-width half-maximum.

**Effects of reward of reward.** The single-subject model contained six regressors. The first two regressors modeled the BOLD responses to CS+ and CS~ tones, respectively, whereas the last four regressors modeled the feedback phase. For CS+ trials with correct reward expectations, one regressor accounted for receipt of reward after fast and correct responses (called “reward expected and received” in further analysis) and another one for neutral feedback after slow responses (“reward expected and not received”). For CS~ trials, we used one regressor modeling neutral feedback after correct reward expectations (“reward not expected and not received”). All other event types (i.e., CS+ or CS~ trials with wrong reward expectations or trials with no button press in the reaction time task) were pooled into one additional error regressor because of the low amount of total errors. Time series in each voxel were high-pass filtered to 1/128 Hz and modeled for temporal autocorrelation across scans with an AR(1) process. Note that the data on reward anticipation have been published elsewhere (Puschmann et al. 2012; Weis et al. 2012).

Single-subject contrasts coding for neural activity increases during different reward conditions were entered into a full-factorial ANOVA design for further analysis. The following factors were included in the ANOVA model: group (L-DOPA/placebo/no drug), learning status (learner/nonlearner), and reward condition (“reward expected and received”/“reward not expected and not received”). Within this full-factorial ANOVA model, we calculated F-contrasts for all main effects and interactions. Results of this and all other analyses are reported as statistically significant at a threshold of \(P < 0.05\), corrected for whole brain with familywise errors (FWE) and a minimum cluster size \(k = 40\) or at \(P < 0.05\) corrected for auditory cortex as a region of interest as in our previous study (Weis et al. 2012). To further visualize significant effects in auditory cortex and striatum during reward delivery, we extracted average beta values as a function of reward condition, group, and learning status in a sphere of radius of 6 mm around the activation peak maxima. Additionally, we calculated the time course of the BOLD response within those regions, as a function of reward condition, relative to the two important time points within the paradigm: 1)

### Table 1. Brain regions showing differential activity as a function of reward condition (i.e., main effect of reward in full-factorial ANOVA)

<table>
<thead>
<tr>
<th>Region</th>
<th>x</th>
<th>y</th>
<th>z</th>
<th>Z</th>
</tr>
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<tbody>
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<td>52</td>
<td>-4</td>
<td>-2</td>
<td>6.75</td>
</tr>
<tr>
<td>Left auditory cortex*</td>
<td>-56</td>
<td>-6</td>
<td>0</td>
<td>6.19</td>
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<tr>
<td>Right striatum</td>
<td>10</td>
<td>6</td>
<td>-6</td>
<td>&gt;8</td>
</tr>
<tr>
<td>Left striatum</td>
<td>-10</td>
<td>8</td>
<td>-6</td>
<td>&gt;8</td>
</tr>
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<td>Right pallidum</td>
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<td>-4</td>
<td>-8</td>
<td>&gt;8</td>
</tr>
<tr>
<td>Left pallidum</td>
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<td>-4</td>
<td>-8</td>
<td>&gt;8</td>
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<tr>
<td>Right insula</td>
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<td>20</td>
<td>-14</td>
<td>&gt;8</td>
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<tr>
<td>Left insula</td>
<td>-30</td>
<td>20</td>
<td>-12</td>
<td>&gt;8</td>
</tr>
<tr>
<td>Anterior cingulate cortex</td>
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<td>Middle cingulate cortex</td>
<td>6</td>
<td>-2</td>
<td>28</td>
<td>&gt;8</td>
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<tr>
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<td>-22</td>
<td>-16</td>
<td>&gt;8</td>
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<td>30</td>
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<td>&gt;8</td>
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</table>

Values are peak Montreal Neurological Institute (MNI) coordinates, Z values, and corresponding brain regions. *Brain regions resulting from region of interest (ROI) analysis.
reward anticipation (sound presentation) and 2) reward delivery (feedback presentation).

**RESULTS**

*Behavioral data.* Overall, subjects learned the task quickly and had a high number of correct reward expectations. There were no significant differences in accuracy between the no-drug, l-DOPA, and placebo groups [$\chi^2(1,2) = 3.52, P = 0.1$, Kruskal-Wallis test]. Figure 2 illustrates the learning curves for learners and nonlearners in each group. Note that learning curves in the pharmacological study were numerically steeper for both placebo and l-DOPA compared with the no-drug condition. Similarly, there was no significant difference in the amount of reward received in the pharmacological study for the l-DOPA compared with the placebo group [l-DOPA: 31 ± 0.8 €, placebo: 31.8 ± 0.5 €; $T(1,53) = -0.84, P = 0.4$]. However, subjects in the no-drug condition received significantly less reward [no-drug study: 27.2 ± 1.2 €, pharmacological study: 31.4 ± 0.5 €; $T(1,84) = 3.59, P < 0.001$].

*Functional MRI data.* We found a significant main effect of reward condition and a reward condition $\times$ learning status interaction. All other main effects and interactions were not significant.

A main effect of reward condition was seen in reward-related dopaminergic areas such as substantia nigra/ventral tegmental area, the left and right striatum, and the pallidum (see Fig. 3B and Table 1). The mean time course plots of the BOLD response during the phase of reward delivery (i.e., feedback, Fig. 4B, right) illustrate that this main effect was due to significantly higher neural activity when a reward was expected and received in CS$^+$ trials compared with the situation when no reward was delivered. There was no difference between neural activity when a reward was expectedly (CS$^-$ trials) or unexpectedly (CS$^+$ trials) not received. This result clearly shows that the striatum was only activated when a reward was received. Note that striatal BOLD activity during the reward phase was higher than during the reward anticipation phase (i.e., sound, Fig. 4B, left). Differences in neural activity as a function of reward condition were also seen in anterior and middle cingulate cortex as well as in the ventral stream of the visual pathway including bilateral middle, inferior occipital, and fusiform gyrus. As for the striatum, this main effect of reward condition was due to enhanced BOLD activity when a reward was received.

A modulation of neural activity as a function of reward condition was also found within the left and right auditory cortex (Fig. 3A). The mean time course plots of the BOLD response (i.e., feedback, Fig. 4A, right) illustrate that the main effect in auditory cortex was due to significantly higher neural activity in the case of correct expectation of a reward in CS$^+$

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**Fig. 4.** Time course of the BOLD response for reward anticipation and reward delivery within the left auditory cortex (A) and striatum (B) as a function of reward condition: “reward expected and received,” “reward not expected and not received,” and “reward expected and not received.” This figure depicts the time course of the BOLD signal at 2 different time points within the experiment (reward anticipation phase when the sound was presented, left; reward phase when the feedback was presented, right). Note that the time courses are means over all groups; therefore, the l-DOPA effect resulting from analyzing the reward anticipation reported in Weis et al. (2012) is not seen within this figure.
trials and correct expectation of no reward in CS− trials. In other words, neural activity in auditory cortex reflects correct expectations independent from the delivery of reward. Note that neural activity in auditory cortex during the reward phase was half the size of neural activity during the reward anticipation phase when the sound was present (sound, Fig. 4A, left).

Results of the reward condition × learning status interaction suggest that the findings in auditory cortex were dependent on learning status (see Fig. 5). We extracted mean beta values as a function of reward condition, learning status, and group (Fig. 6A) to illustrate the interaction and to confirm that results are similar for all three groups (placebo, L-DOPA, no drug). The results suggest that only those participants who learned the reward association showed increased neural activity in auditory cortex in the case of a correct expectation.

Other regions showing a similar learning-dependent effect were in the right insula and the anterior cingulate cortex as well as in the left and right angular gyrus and the precuneus (Table 2, Fig. 5). Neural activity in the striatum was not found to be modulated by learning status (Fig. 6B). This effect was similar in all groups (placebo, L-DOPA, no drug).

DISCUSSION

We aimed to investigate whether reward delivery in an auditory instrumental learning task activates auditory cortex at the time point of the receipt of reward and whether reward-related activations in auditory cortex are modulated by dopamine. Our results show that neural activity in auditory cortex is enhanced either when an expected reward is obtained or when the expectation of obtaining no reward was correct compared with unexpectedly not receiving a reward. Importantly, this pattern was only seen in volunteers who learned the reward association. In contrast, neural activity in dopaminergic brain regions was only enhanced upon receipt of a reward, and independent from learning the reward association. We found no evidence for a dopaminergic modulation at the time point of the receipt of reward.

Effects of reward delivery in auditory cortex. Our data demonstrate increased neural activity in left and right auditory cortex at the time point of reward delivery, although there is no auditory stimulation at this time. This finding is in line with monkey evidence in auditory cortex and extends human evidence from somatosensory and visual cortices, which were shown to be activated in rewarded trials compared with unrewarded trials in sensory discrimination tasks (Brosch et al. 2005, 2011; Pleger et al. 2008, 2009; Weil et al. 2010). Brosch et al. (2011) recorded neuronal activity in auditory cortex of two monkeys performing an auditory discrimination task. Correct responses were rewarded, with the size of the reward depending on performance in the previous trial. Increases in firing rate were observed for large as well as small rewards, and decreases were found when no reward was obtained after an incorrect response. However, in the latter case neuronal activity increased afterwards. Note, however, that in that study monkeys were always able to receive a reward for correct performance. In contrast, participants in our study were aware that they did not receive a reward in 50% of the trials (CS−) and that the reward was dependent on fast reaction times in the number comparison task. Despite conceptual differences between our study and the study by Brosch et al. (2011), the basic common finding of both approaches is that the auditory cortex is responsive to nonauditory feedback signaling the correctness of the previous behavioral choice within the trial.

The high amount of CS− trials and unrewarded CS+ trials enabled us to further dissociate reward delivery from confirmation of an expectation. Our data provide new evidence that the increase of activity at the point of reward delivery is linked to the confirmation of an expectation rather than to the receipt of reward per se. To our best knowledge this study is thus the first in humans to indicate that sensory cortices reflect not only reward delivery but also correct expectations of reward outcome irrespective of receipt of reward. Note, however, that in our paradigm both situations provide valuable feedback to establish a successful behavioral strategy, i.e., selecting the correct acoustic feature (stimulus duration) and attributing the correct motor behavior (pressing one button for short tones and the other for long tones). Hence, the absence of a reward in CS− trials indicates correct prior classification of the stimulus and contributes to learning in a similar way as the receipt of a reward in CS+ trials. In contrast, in the above-mentioned studies (Pleger et al. 2008, 2009; Weil et al. 2010), subjects had to solve a sensory discrimination in a two-alternative forced-choice task and received a reward for correct judgments only.

The animal data of Pantoja et al. (2007) showed that neural activity in sensory cortex increased from stimulus presentation to reward outcome but only in trials in which stimulus discrimination was important for receiving a reward compared with those trials in which animals received the reward independent of performance. This finding suggests that reward-induced activation of sensory cortices is only observed when it is relevant for improving performance. In our task, reward delivery and reward omission (in the case of CS− trials) both provided important feedback for solving the FM tone categorization and hence led to increased auditory cortex activity. That auditory cortex activity at the time point of reward...
delivery may be important for learning is further strengthened by the finding that the effect was only found in subjects who learned the reward association. We thus conclude that when reward associations are learned the auditory cortex responds whenever the outcome of a trial confirms the current strategy of solving the task. Note that neural activity in auditory cortex during reward outcome was not modulated by dopaminergic stimulation, which is in contrast to the dopaminergic modulation during reward anticipation found in the same data set previously (Weis et al. 2012).

Effects of reward delivery in reward-related brain regions. Replicating many previous studies (Delgado et al. 2000; Elliott et al. 2000; Pleger et al. 2008; Schultz 2000), we found additional reward-related neural activity in dopaminergic brain regions such as the left and right striatum and the midbrain. In contrast to neural responses in auditory cortex, striatal neural activity was not significantly modulated by learning status. Overall, the highest activity was seen for those trials in which a reward was received, compared with the other trials. Ventral striatal activity during reward delivery was also found in the sensory discrimination studies by Weil et al. (2010) and Pleger et al. (2008). Nevertheless, the result seems to be in contrast to other reward studies (e.g., Montague et al. 1996), showing that neural activity to the rewarding stimulus is switched from reward delivery to reward-predicting stimuli when participants learn the task. However, since here participants had to solve an instrumental learning task where a reward could only be obtained for fast and correct responses in CS+/H11001 trials, participants could not be sure to receive a reward at the end of the trial. Hence, the reward was not entirely predictable. It has been shown previously that striatal activations to rewards are still observed after learning when behavior-outcome con-

### Table 2. Brain regions showing significant interaction between reward condition and learning status

<table>
<thead>
<tr>
<th>Region</th>
<th>x</th>
<th>y</th>
<th>z</th>
<th>Z</th>
<th>k_E</th>
</tr>
</thead>
<tbody>
<tr>
<td>Left auditory cortex*</td>
<td>−56</td>
<td>−10</td>
<td>−4</td>
<td>4.50</td>
<td>401</td>
</tr>
<tr>
<td>Right auditory cortex*</td>
<td>58</td>
<td>2</td>
<td>−12</td>
<td>4.22</td>
<td>242</td>
</tr>
<tr>
<td>Anterior cingulate cortex</td>
<td>−12</td>
<td>62</td>
<td>20</td>
<td>7.01</td>
<td>463</td>
</tr>
<tr>
<td>Right insula</td>
<td>36</td>
<td>−12</td>
<td>24</td>
<td>6.32</td>
<td>94</td>
</tr>
<tr>
<td>Right insula</td>
<td>30</td>
<td>22</td>
<td>−6</td>
<td>5.85</td>
<td>146</td>
</tr>
<tr>
<td>Left angular gyrus</td>
<td>−44</td>
<td>−72</td>
<td>32</td>
<td>6.43</td>
<td>406</td>
</tr>
<tr>
<td>Right angular gyrus</td>
<td>50</td>
<td>−72</td>
<td>30</td>
<td>5.40</td>
<td>52</td>
</tr>
<tr>
<td>Left precuneus</td>
<td>−6</td>
<td>−54</td>
<td>18</td>
<td>5.30</td>
<td>217</td>
</tr>
</tbody>
</table>

Values are peak MNI coordinates, cluster volume in voxels (2 × 2 × 2 mm, k_E), Z values, and corresponding brain regions. *Brain regions resulting from ROI analysis.
tingencies are less predictable (Delgado et al. 2005). Note that there were also numerically higher BOLD responses within the group of nonlearners when a reward was received in a CS+ trial, which would support the idea that striatal activations to reward depend on predictability.

Reward-related activity was also present in the left and right insula and the anterior cingulate cortex, which were suggested to form part of a saliency network (Menon 2011; Menon and Uddin 2010). The anterior cingulate cortex was also activated during rewarding feedback in a visual search paradigm where reward was shown to change visual saliency (Hickey et al. 2010). Neural activity in anterior cingulate cortex and left and right insula exhibited a reward condition × learning status interaction that suggests that in those regions, in contrast to the striatum, learning state plays a major role. Further reward-related increases in neural activity were present in the ventral stream of the visual pathway including the middle occipital gyrus, the inferior occipital gyrus, and the fusiform gyrus, which may be linked to processing the visually presented reward (50-euro cent symbol).

Effect of dopaminergic modulation. As mentioned above, none of the regions showing a main effect of reward condition or reward condition × learning status interactions was sensitive to dopaminergic modulation during the reward phase in our auditory appetitive instrumental learning task. This finding is in contrast to the study by Pleger et al. (2009), who compared L-DOPA to placebo and haloperidol in a rewarded somatosensory discrimination task and showed that the behavioral and neural effects were enhanced under L-DOPA and suppressed under haloperidol. However, the effects between L-DOPA and placebo were small, and most effects reported in that study were due to differences between L-DOPA and haloperidol. Note that our previous analysis of drug effects in the same data set during the reward anticipation phase yielded increased neural activity in left auditory cortex, Broca’s area, and anterior cingulate cortex, which correlated with L-DOPA plasma levels, arguing against a general lack of sensitivity to detect drug effects in the present paradigm (Weis et al. 2012). Rather, we would like to suggest that L-DOPA modulation is stronger in the reward anticipation phase than the reward outcome phase, which has also been reported previously (Guitart-Masip et al. 2012).

Conclusions. In summary, this study shows for the first time that the human auditory cortex responds to nonauditory feedback that signals the outcome of a learning trial. Strikingly, increased responses were observed whenever the outcome of a trial confirmed the subject’s expectations irrespective of reward. This differential activity was only seen in participants who learned the stimulus-reward association. Our findings thus support the view of a highly cognitive role of auditory cortex (Scheich et al. 2011). Whereas auditory cortex responses during reward anticipation have been found to be modulated by dopamine (Weis et al. 2012), this is not the case for responses during reward outcome.

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