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Learning strategy determines auditory cortical plasticity

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Abstract

Learning modifies the primary auditory cortex (A1) to emphasize the processing and representation of behaviorally relevant sounds. However, the factors that determine cortical plasticity are poorly understood. While the type and amount of learning are assumed to be important, the actual strategies used to solve learning problems might be critical. To investigate this possibility, we trained two groups of adult male Sprague–Dawley rats to bar-press (BP) for water contingent on the presence of a 5.0 kHz tone using two different strategies: BP during tone presence or BP from tone-onset until receiving an error signal after tone cessation. Both groups achieved the same high levels of correct performance and both groups revealed equivalent learning of absolute frequency during training. Post-training terminal "mapping" of A1 showed no change in representational area of the tone signal frequency but revealed other substantial cue-specific plasticity that developed only in the tone-onset-to-error strategy group. Threshold was decreased ~10 dB and tuning bandwidth was narrowed by ~0.7 octaves. As sound onsets have greater perceptual weighting and cortical discharge efficacy than continual sound presence, the induction of specific learning-induced cortical plasticity may depend on the use of learning strategies that best exploit cortical proclivities. The present results also suggest a general principle for the induction and storage of plasticity in learning, *viz.*, that the representation of specific acquired information may be selected by neurons according to a match between behaviorally selected stimulus features and circuit/network response properties.

Keywords: Associative plasticity; Cerebral cortex; Electrophysiology; Cognitive processes; Frequency tuning; Instrumental conditioning; Memory; Plasticity

1. Introduction

The neural correlates approach to learning and memory has proven to be useful by identifying involved brain structures. The study of learning-related plasticity in sensory cortical fields has increased in recent years, in part because they provide a convenient way to further determine the particular nature of such involvement. Workers have taken advantage of the topographic functional organization and reliable receptive fields of sensory cortices to investigate the extent to which learning-related processes produce associative representational plasticity (ARP), *i.e.*, specific changes in the processing and representation of a relevant stimulus dimension. For example, receptive fields may be shifted toward behaviorally important stimuli.

Most-extensively studied in the primary auditory cortex, associative representational plasticity has been reported for cortical metabolism (Gonzalez-Lima & Scheich, 1986a), receptive field properties (Bakin & Weinberger, 1990; Blake, Strata, Churchland, & Merzenich, 2002; Edeline, Neuenschwander-el Massioui, & Dutrieux, 1990; Gao & Suga, 2000) and tonotopic maps (Rutkowski & Weinberger, 2005) in animals, as well as in studies of human brain imaging (Molchan, Sunderland, McIntosh, Herscovitch, & Schreurs, 1994; Morris, Friston, & Dolan, 1998; reviewed in Weinberger 1995, 2004a,b; Palmer, Nelson, & Lindley, 1998; Rauschecker, 2003; Buonomano & Merzenich, 1998). Learning-related plasticity in A1 develops in a wide range of tasks, including habituation (Condon & Weinberger, 1991), classical reward (Kisley & Gerstein, 2001) and aversive (Bakin & Weinberger,

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1990) conditioning, instrumental reward (Blake et al., 2002) and avoidance (Bakin, South, & Weinberger, 1996) learning, category learning (Ohl, Scheich, & Freeman, 2001), long-term training in perceptual discrimination learning (Recanzone, Schreiner, & Merzenich, 1993), working memory (Brechmann et al., 2007; Sakurai, 1994), reference memory (Sakurai, 1994) and motor planning (Villa, Tetko, Hyland, & Najem, 1999). A dominant finding has been that sounds which acquire behavioral significance receive "favored" processing, *e.g.*, as indexed by specific increased magnitude of response and CS-directed tuning shifts.

Despite the extensive and growing documentation of the involvement of A1 in learning, memory and other cognitive functions, the factors that determine whether or not plasticity develops in A1 are largely unknown. For example, auditory perceptual learning can develop in the absence of cortical plasticity (Brown, Irvine, & Park, 2004). It is widely assumed that the amount of learning (*i.e.*, asymptotic level of performance) and the type of involved learning (*i.e.*, task, subject matter of the learning) are major determinants of cortical plasticity. However, other factors may be of particular importance. Thus, the amount of expanded area of representation of the frequency band of a tone cue is directly proportional to level of motivation (Rutkowski & Weinberger, 2005). However, such effects may be subsumed under the amount of learning because learning is directly affected by motivational level.

A potentially critical factor concerns the particular learning strategy employed in solving tasks, independent of other factors. Although learning strategy appears to have been neglected in studies of learning and brain plasticity, it is known to be behaviorally important. For example, particular strategies employed to solve problems are significant factors in human cognition (Lemaire & Fabre, 2005). The goal of this study was to determine whether learning strategy affects the development of cue-specific neuronal plasticity. Our approach was to train two groups of rats to solve the same problem, achieve the same asymptotic level of performance and exhibit the same degree of learning about absolute frequency, but using different strategies. We then conducted an analysis during a terminal "mapping" experiment to study the area of representation, thresholds and frequency selectivity (bandwidth) of neurons in the primary auditory cortex.

2. Materials and methods

2.1. Subjects

Male Sprague–Dawley rats (250–275 g) from Charles River Laboratories (Wilmington, MA) were housed in individual cages in a vivarium (temperature maintained at 22 °C, 12/12 h light/dark cycle). All animals had *ad libitum* access to food but the availability of water was restricted. Water supplements were given as needed to maintain the subjects at ~90% *ad libitum* body weight for the duration of the experiment. They were housed in the vivarium except during training procedures and electrophysiological recording. All procedures were performed in accordance with the University of California Irvine Animal Research Committee and the NIH Animal Welfare guidelines.

2.2. Behavioral training: Single-tone appetitive instrumental conditioning

Motivated rats were trained to bar-press (BP) to a 5.0 kHz pure tone (10 s, 70 dB SPL) in order to receive a water reward. All training was done in an operant chamber (H10-11R, Coulbourn Instruments, Lehigh Valley, PA) contained within a sound-attenuating enclosure (H10-24A, Coulbourn Instruments). The chamber was fitted with a bar (2 cm above floor, 2 cm from right wall), a water cup attached to a lever that delivered water to an opening 9 cm to the left of the bar, a speaker 13 cm above the trough, and a cue light 13 cm above the bar. Before beginning single-tone conditioning, all animals were shaped to BP for a water reward for 4 days. Following shaping, they were trained in 45–60 min sessions 5 days a week for 4 weeks (20 sessions). The water reward was delivered through a 0.1-ml cup that was available for 5 s after any bar-press made during tone presentation. An animal could maximally receive two rewards per trial. A bar-press response made during the silent inter-trial interval (ITI, 4–25 s randomly scheduled) resulted in a time-out (*i.e.*, 3–7 s lengthening of time to the next trial) signaled by a flashing cue light. All responses made during the training session were recorded using Graphic State (Coulbourn Instruments) computer software and subsequently analyzed using Matlab©. Correct performance was calculated as the number of BPs made during the tone cue divided by the total number of BPs during a training session.

One group was trained in the standard task (STD, $n = 5$) in which responses during the signal tone were rewarded and all responses during silences were signaled as errors and resulted in time-outs. A second group was trained in the same way except that there was 2 s "grace" period immediately following the tone (immediate post-tone period, IPT) in which responses made during silence were neither punished nor rewarded (GRC, $n = 6$). Fig. 1 illustrates the two training protocols (see also Section 3).

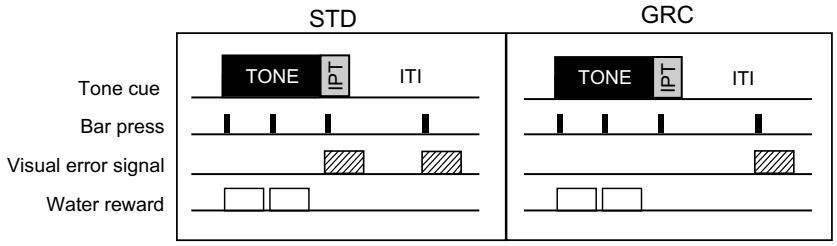

Fig. 1. Training paradigm for STD and GRC strategy groups. All animals were trained to make bar-presses (BP) to a 5.0 kHz (10 s, 70 dB) tone cue for water reward (5 s access to water dipper). BPs made during ITI silences resulted in a flashing light error signal and an additional time delay to start of the next trial. For the STD group, all BPs during the tone were rewarded and BPs during silence were signaled as errors. The GRC group had a 2 s grace-period after the termination of each tone (IPT) during which BPs were neither rewarded nor signaled as an error. The GRC protocol was designed to reveal different strategies in the pattern of behavior consisting of responding from tone-onset until receiving an error signal (tone-onset-to-error) as opposed to responding until tone offset (tone-duration).

To test for possible effects of over-training at high levels of performance (as explained later), an additional group of animals was trained in the same STD protocol for 11 instead of 20 days (ST-STD, $n = 5$).

2.3. Behavioral training data analysis

In order to study the effect of the 2 s grace period manipulation on bar-pressing behavior during training, we analyzed not only absolute performance levels ([#tone BPs/total #BPs] × 100) but also the pattern of bar-pressing behavior (a) during IPTs, (b) during ITIs, (c) the last second of tone presentations (''late-tone BP''), and (d) the latency of the first BP during a tone. The probability of IPT BPs was calculated as the number of IPT BPs divided by the total number of tone presentations in which the 5 s water reward did not extend into the 2 s after the termination of the tone. BPs during ITI were calculated as the average number of BPs made during each ITI during a session. The probability of late-tone BPs was the number of BPs occurring during the last second of tone presentations during a session, divided by the total number of tone presentations that resulted in at least one BP (*i.e.*, trials in which no BPs were made to the tone were excluded). BP latency was measured as the time the first BP occurred after tone onset.

Subjects found to have used a ''mixed'' strategy (as explained later) were not included in the initial analysis (MX-STD, $n = 3$).

2.4. Behavioral testing: Stimulus generalization

Frequency generalization gradients were obtained in a single session after training, before electrophysiological study. Six different frequencies were tested including the signal tone (2.8, 5.0, 7.5, 12.9, 15.8, and 21.7 kHz, 70 dB SPL). Ten ''warm-up'' rewarded (5.0 kHz) trials were delivered prior to testing to ensure presence of a high level of performance. Subsequent trials were unrewarded regardless of frequency in order to prevent further tone-reward associative learning (Mackintosh, 1974). Test frequencies were presented in a pseudo-random order to yield 25 trials for each frequency. Response measurements were calculated for each test frequency as a percent of total number of responses (tone and ITI BPs) within a generalization session (150 trials). Although all animals were trained with only one tone frequency, different gradients could have been observed. Animals could show a flat gradient, indicating no behavioral frequency-specificity, *i.e.*, the animals were being controlled by sound *per se*. Alternatively, frequency-specificity to the training frequency would be indicated by a generalization gradient with a peak near or at 5.0 kHz. The possibility that extinction during generalization testing could have reduced plasticity during electrophysiological recording was eliminated by pilot studies using both STD and GRC protocols, in which subjects were trained on the day following generalization. They all ($n = 4$) exhibited the same levels of performance as they had attained on the day preceding generalization, probably reflecting spontaneous recovery from any putative extinction. However, such retraining was not employed in this experiment because it might have constituted frequency discrimination between the training frequency on the retraining day and non-signal test frequencies on the generalization day, thus adding a confound to the effects of pre-generalization training.

2.5. Terminal post-training recording sessions: Electrophysiology

Electrophysiological recordings were made across all of A1. Recording sessions were conducted 24 h after generalization testing. Multiunit recordings made during random stimulus presentations were used to delineate the tuning sensitivity and specificity of A1 cells. All auditory cortical recording was performed under general anesthesia (sodium pentobarbital, 50 mg/kg, i.p.) with additional doses administered (15 mg/kg, i.p.) throughout the experiment to maintain suppression of the forepaw withdrawal reflex. Bronchial secretions were minimized by treatment with atropine (0.22 mg/kg, i.m.) and core body temperature maintained at 37 °C via a heating blanket and monitored with a rectal probe. Animals were placed in a stereotaxic frame inside a sound-attenuated chamber (Industrial Acoustics Company) and the skull fixed to a support via a pedestal made from dental acrylic, which left the ear canals unobstructed. A craniotomy over the right auditory cortex allowed multiunit extracellular recording with a four-electrode array of Parylene-coated tungsten microelectrodes (0.2–3 MΩ, FHC) in layers IV–V of auditory cortex.

Acoustic stimuli generated using Tucker Davis Technologies (TDT) hardware and software were delivered monaurally via a calibrated speaker (Aiwa) placed at the entrance to the left (contralateral) ear canal. Stimuli consisted of white noise (bandwidth = 1 Hz–50 kHz) and pure tone bursts (50 ms duration, cosine-squared gate with rise/fall time (10–90%) of 10 ms). Stimuli were presented every 700 ms. Neural activity was amplified (×1000), band-pass filtered (0.3–3.0 kHz, TDT RA16 Medusa Base Station) and monitored via an oscilloscope (Tektronix 5111) and loudspeaker system (Grass AM8). Signal-to-noise was always $\geqslant$2:1 ratio. Responses to noise bursts (0–80 dB SPL in 10 dB increments, 20 repetitions) were recorded before tone stimuli were presented. After the threshold of response to noise was determined, response to frequencies were determined by presenting pure tone bursts of 0.5–54.0 kHz, 0–80 dB SPL in 10 dB steps. Frequency/level stimuli (252 in total) were delivered pseudo-randomly 10 times.

2.6. Neuronal data analysis

Using Matlab© custom software, frequency response areas (FRA) were constructed offline using evoked spike-timing data from a 6–40 ms time window after tone onset. Evoked activity was defined as any activity greater than one standard error above mean baseline (spontaneous) activity. Baseline was recorded during a 0–50 ms time window prior to each tone presentation. The characteristic frequency (CF) of a responsive site was defined as the stimulus frequency having the lowest threshold (CF threshold) for an evoked response (*i.e.*, highest sensitivity). If more than one stimulus frequency elicited activity at the lowest threshold, then CF was calculated as the geometric mean of those frequencies. Bandwidth (BW) relative to CF threshold described the selectivity of tuning across frequency stimuli. Bandwidth at 20 dB SPL above threshold (BW20) was defined as the octave distance between the frequencies at the edges of an FRA that elicited activity 20 dB above CF threshold. Primary auditory cortex (A1) was characterized as the cortical area within a general progression from low to high CFs along the posterior to anterior axis (*i.e.*, tonotopic gradient). Anterior sites that constituted a reversal in the CF progression were considered to be a part of the anterior auditory field (AAF) and were excluded from A1 analysis (Rutkowski, Miasnikov, & Weinberger, 2003; Sally & Kelly, 1988). The remaining borders of A1 were outlined by sites that were more responsive to noise (lower threshold) than to tones which were considered to be outside A1. CF threshold and BW20 were calculated for each FRA in A1, pooled across animals within a training group and averaged within CF-octave bins (1.0–2.0, 2.1–4, 4.1–8, 8.1–16, 16.1–32, and 32.1–54.0 kHz).

CFs determined by FRA analyses were used to make CF distribution maps of A1 for each animal. Voronoi tessellations were constructed to represent the areal distribution of CFs along the A1 tonotopic gradient and the area of each polygon was calculated. Areas were averaged into octave bands according to CF (1.0–2.0, 2.1–4, 4.1–8, 8.1–16, 16.1–32, and 32.1–54.0 kHz) and the percentage of the total area of A1 that each band occupied was calculated for each animal before being averaged in a group. Comparisons in the mean percentage of total A1 area of each band were made between GRC, STD and naïve ($n = 9$) groups (ANOVA). The last band was not a complete octave because the highest frequency tested during electrophysiological recording in A1 was 54.0 kHz.

3. Results

3.1. Behavior

Because of the unique aspects of the experimental protocol, we briefly summarize our approach and its rationale here.

The apparently simple auditory-cued problem of responding contingent on the presence of a signal tone does not have a unique solution. Different strategies could be employed because a tone cue is comprised of an onset transient, its continued presence and an offset transient. In the standard instrumental conditioning task, a strategy based on responding only throughout the duration of the tone would solve the problem ("tone-duration" strategy). However, animals could start responding at tone onset and continue to respond until they received the flashing light error signal without respect to the tone's ongoing presence ("tone-onset-to-error" strategy). In standard experimental designs, subjects could use predominantly one approach or the other. But these alternatives cannot be distinguished because error signals are always given for responses made starting immediately after tone offset.

We differentiated tone-duration and tone-onset-to-error strategies by withholding the error signal during the first 2 s of inter-trial intervals (IPT) following tone offset for one set of animals. During the IPT the unrewarded bar-presses produced neither error signal nor added delay to the next trial (GRC group). This "grace period" removed the confound between tone offset and error signal, so that it became possible to distinguish between the behavioral strategies of bar-pressing until the tone ended *vs.* bar-pressing until receiving the error signal. Thus, the tone-onset-to-error strategy would be revealed as a pattern of behavior consisting of responding from tone-onset until receiving the error signal. As noted previously, the STD group was trained in the standard protocol of treating all BPs during ITIs as errors (Fig. 1).

Both groups solved the task, achieving asymptotic performances of ~75 to 80% after the 20 sessions of training (Fig. 2). The STD and GRC performance levels did not differ over the last 5 days of training (GRC = 76.8 ± 2.0%; STD = 82.2 ± 2.3%; $F_{(1,35)} = 2.05$, $p > .05$). However, the groups might have differed in learning about frequency. To resolve this issue, we obtained standard frequency generalization gradients after the completion of training, *i.e.*, testing with many frequencies after training with one frequency. Importantly, the group generalization gradients did not differ ($F_{(1,48)} = 0.003$, $p > .05$) (Fig. 2, inset). Both groups exhibited greatest responses at 7.5 kHz, near the 5.0 kHz training frequency ($F_{(5,48)} = 11.81$, $p < .001$), demonstrating they had learned that a particular frequency range, rather than merely sound, was a signal for rewarded BPs.

Although the STD and GRC groups learned to the same performance level and exhibited the same learning about frequency, these findings do not reveal any difference in learning *strategy*. To address this issue, we analyzed all BPs during inter-trial intervals, separating the analyses into the 2 s immediately after tone offset (IPT; "grace period" for the GRC group) from the rest of the ITI period. The STD group stopped responding at the start of the ITI, as indicated by the low probability (~0.05) of BPs during the IPT. In comparison, the response probability of the GRC group was substantially greater (~0.70; $F_{(1,166)} = 110.03$, $p < .0001$) (Fig. 3a). Moreover, the STD group rapidly (within the first 2 sessions) learned to reduce BPs after the tone ended ($F_{(3,89)} = 19.18$, $p < .0001$; Fisher's PLSD *post hoc*: day 1 *vs.* 2, $p < .0001$), whereas the

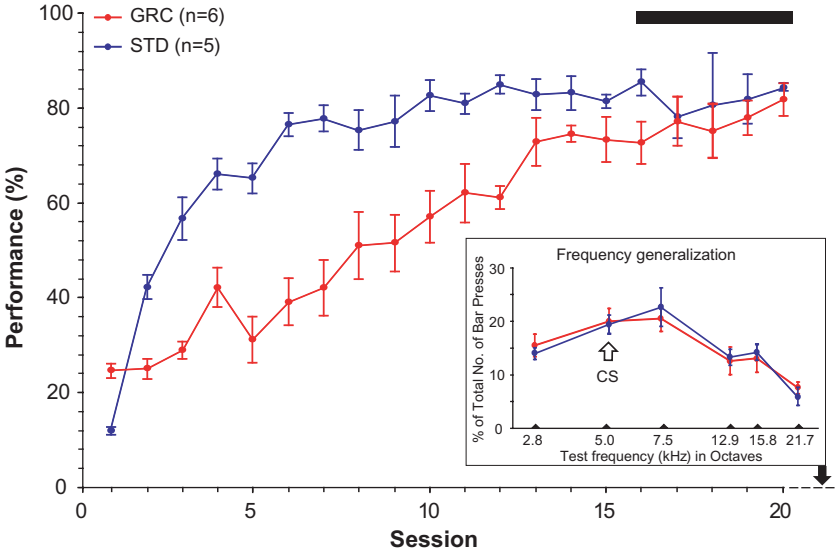

Fig. 2. Performance functions and frequency-stimulus generalization gradients (mean ± *SE*). Performance was measured as the percentage of BPs made during tone presentation relative to the total number of BPs made during a session ([#tone BPs/total #BPs] × 100). Both groups achieved high-levels of asymptotic performance. The black bar marks days during which the groups did not differ in performance level. *Inset*, Twenty-four hours after the last day of training (black arrow), frequency generalization tests were conducted. Four of the five STD animals and all of the GRC animals were tested for stimulus generalization. There was no difference in frequency generalization between groups and both groups showed frequency specificity, *i.e.*, peak responses at 5.0 and 7.5 kHz.

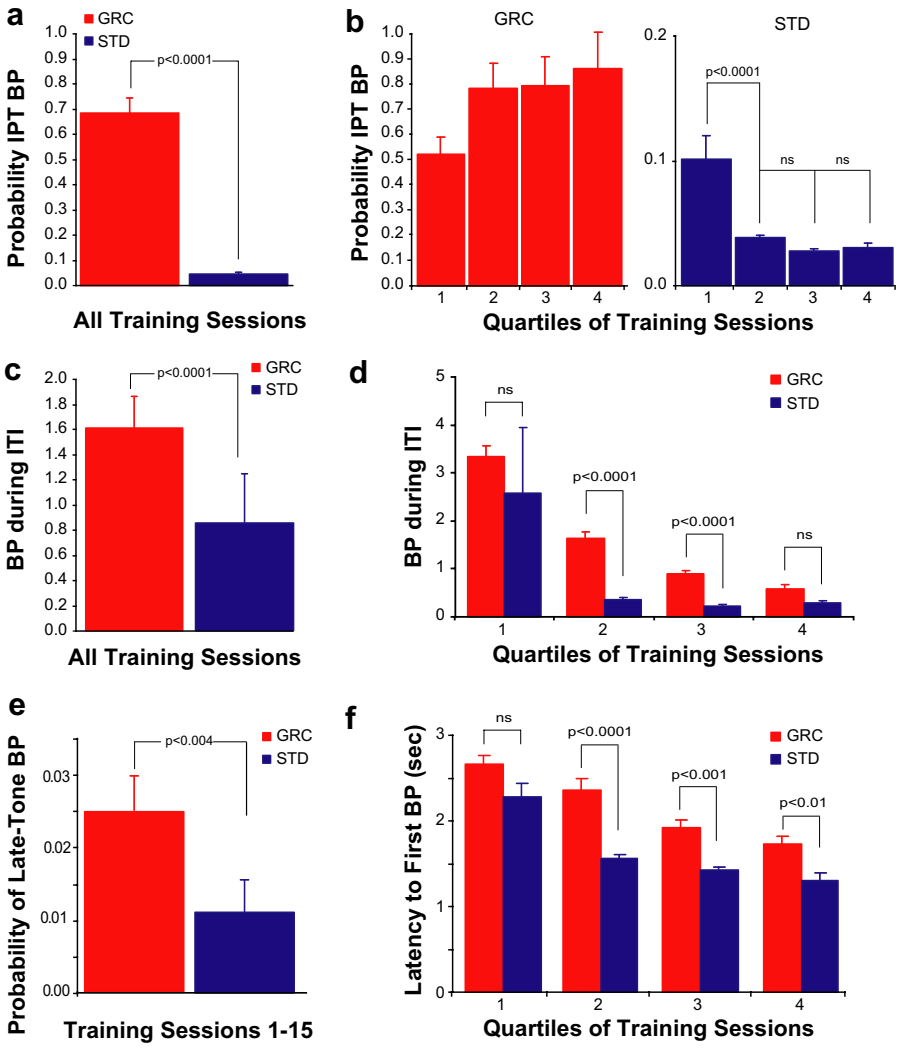

Fig. 3. Analyses of bar-presses during tones and ITIs reveal different learning strategies for the GRC and STD groups. (a) GRC animals were more likely to press during the IPT period after tone offset (*i.e.*, GRC group's grace period) than STD animals across all sessions. (b) The GRC group continued to respond during the IPT after tone offset, whereas the STD group quickly learned to reduce the number of BPs during the IPT. Note the different *y*-axis scales between the left and right panels. (c) The GRC group was more likely than the STD group to respond during ITIs. (d) Both groups learned to reduce ITI BPs. By the last quartile of training, the GRC animals were able to reduce errors to the level of the STD group. (e) The GRC group bar-pressed more during the last second of the tone. (f) The latency of the first bar-press after tone onset was longer in the GRC group. Group means ± *SE*.

GRC group never learned to stop responding during the first 2 s after tone cessation ($F_{(3,109)} = 1.80$, $p > .05$) (Fig. 3b). This pattern of behavior indicates that the GRC group used the strategy of beginning to BP after tone onset and continuing until receiving the error signal. This strategy could account for the lower performance of the GRC group compared to the STD group during the first 15 days of training (days 1–15; $F_{(1,135)} = 186.77$, $p < .0001$) (Fig. 2), because it encourages more inter-trial bar-pressing. In support of this explanation, while both groups had the same probability of responding during the tone (days 1–15; $F_{(1,164)} = 0.65$, $p > .05$), the GRC group had a greater number of ITI BPs (even after receiving the first error signal) than the STD group (days 1–15: $F_{(1,135)} = 48.64$, $p < .0001$).

While the GRC group responded more during ITIs than the STD group overall ($F_{(1,203)} = 23.33$, $p < .0001$) (Fig. 3c), the GRC group eventually learned to reduce its ITI errors across training sessions to reach the same levels as the STD group (*between groups*: quartile 1, $t_{(8)}$ $p > .05$; quartile 4, $t_{(8)}$ $p > .05$) (Fig. 3d). The large amount of variance in inter-trial bar-presses in the STD group's first quartile of training is due to the group's fast learning during the first 2 days to reduce ITI errors ($F_{(4,20)} = 63.14$, $p < .0001$; Fisher's PLSD *post hoc*: day 1 to 2, $p < .0001$). The GRC group only learned gradually to reduce ITI errors throughout training (thus its variance in the first quartile is small). The large variance of the STD group resulted in a non-significant difference between groups in the first quartile of training.

While the GRC group did employ the onset-based strategy, what strategy was used by the STD group? If it had used the same strategy as the GRC group, *i.e.*, bar-pressing until receiving the error light without regard to tone duration, then its probability of BPs toward the end of the 10 s. tone should have been as high as that of the GRC group. Therefore, we analyzed BPs during the last second of tone presentation. The STD group was less likely to bar-press during this interval than the GRC group ($F_{(1,171)} = 8.96$, $p < .004$) (Fig. 3e). These findings are incompatible with an onset-based approach but expected for a tone duration-based strategy. Furthermore, the use of an "onset-to-error strategy" does not necessitate that animals respond immediately at tone onset. In fact, the GRC group tended to respond later after the onset of the tone than the STD group throughout training (*across all sessions:* $F_{(1,201)} = 49.61$, $p < .0001$; *between group quartiles*: quartile 1, $t_{(8)}$ $p > .05$; quartile 2, $t_{(8)}$ $p < .0001$; quartile 3, $t_{(8)}$ $p < .001$; quartile 4, $t_{(8)}$ $p < .01$) (Fig. 3f) reflecting the influence of the 2-s delay of a possible error signal (*i.e.*, the grace period) by shifting responses to later during the tone. It should be noted that the terms "tone-duration" and "tone-onset-to-error" strategies are intended as convenient descriptors of different strategies and are not meant to imply that the start of a tone was important only to animals using the latter strategy. Both STD and GRC groups began to bar-press after tone onset but only the GRC group failed to be governed by continued tone presence. Although the nature of the standard design makes it impossible to be certain that the STD group used the tone-duration strategy exclusively throughout training, the behavioral data demonstrate that the groups did employ different strategies.

3.2. Neurophysiological findings

How are the onset and duration-based strategies related to plasticity? A1 was "mapped" in a terminal recording session. Frequency response areas (FRAs) were obtained across the tonotopic representation of characteristic frequencies (CF) in A1. CF, thresholds (CF threshold) and bandwidths (BW20) were determined for every recording site. There was no difference in the cortical area of frequency representation for any octave band between the GRC and STD groups, nor any difference between each group and naïve ($n = 9$) subjects (all F ratios, $p > .01$; Alpha levels were adjusted using the Bonefferoni method to correct for multiple comparisons between octave bands) (Fig. 4). The absence of plasticity of area may reflect the modest level of water restriction because subjects were maintained at ~90% of normal weight and increases in the representation of a signal frequency band are an increasing function of restriction level, *i.e.*, increased motivation in the rat (Rutkowski & Weinberger, 2005).

In contrast, both tuning sensitivity and selectivity of A1 units were significantly modified by learning strategy. The GRC group exhibited a significant decrease in threshold (*i.e.*, increased sensitivity, ~10 dB) and in bandwidth (*i.e.*, increased selectivity, ~0.7 octaves) compared to the STD group and also to naïve animals, which did not differ from each other (CF threshold in signal-tone band: $F_{(2,125)} = 8.38$, $p < .01$; *post hoc* Fisher's PLSD: STD × GRC and naïve × GRC, $p < .05$; naïve × STD, $p > .05$; BW20 in signal-tone band: $F_{(2,123)} = 7.67$, $p < .01$; *post hoc* Fisher's PLSD: STD × GRC and naïve × GRC, $p < .05$; naïve × STD, $p > .05$) (Fig. 5a). Importantly, both the decrease in threshold and the narrowing of bandwidth were specific to the

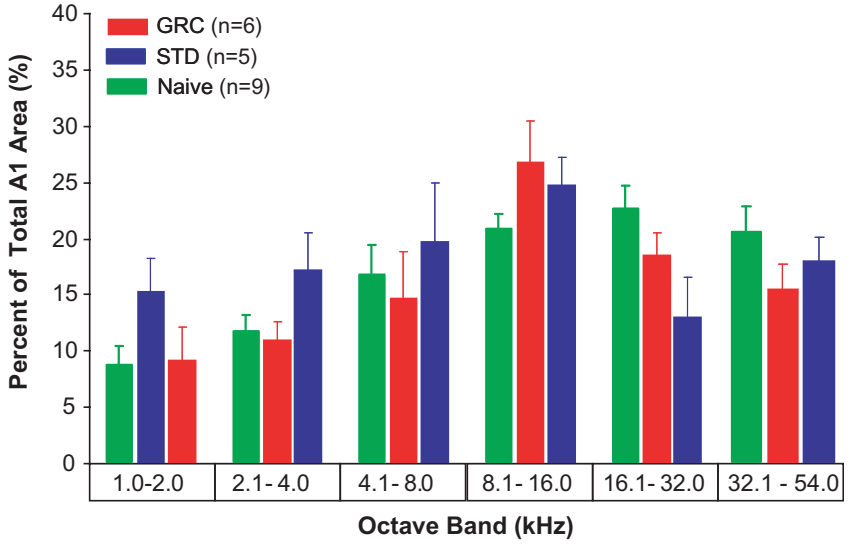

Fig. 4. Map area analyses for GRC, STD and naïve groups. A1 area CF distribution in trained animals is not significantly different from naives in any CF octave band. Each bar represents the group mean percentage (±*SE*) of total A1 area comprising CFs in the specified band. The last CF band is not a complete octave because only frequencies up to 54.0 kHz could be calibrated to determine CFs during electrophysiological recording.

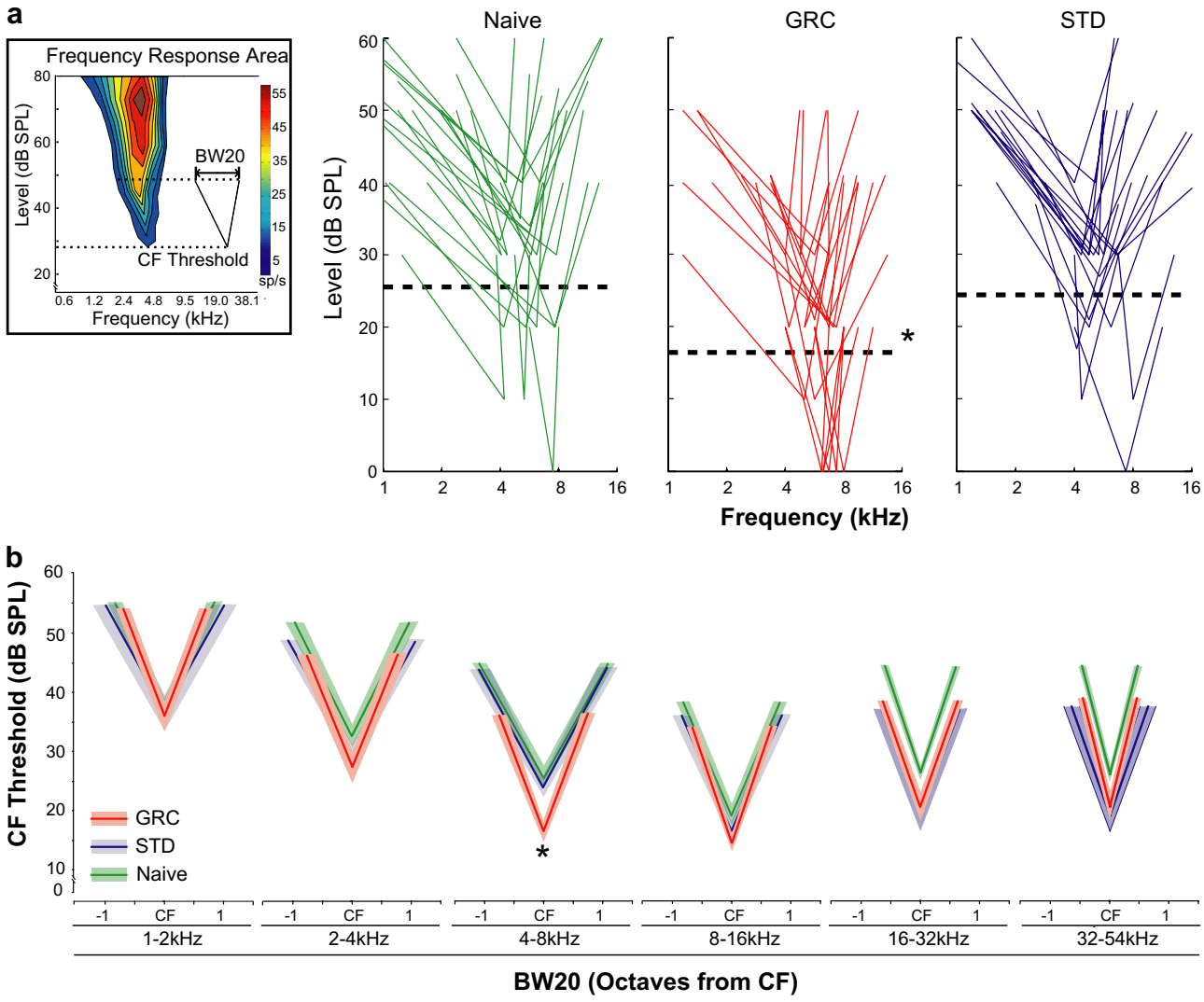

Fig. 5. Tone-onset-to-error strategy learning reduces threshold and bandwidth specifically in the signal-tone band. (a) Examples of FRA "tuning tips" in each group: GRC, STD and naïve. Each "V" shape delineates the CF threshold, and BW20 of a recorded FRA (inset) that had a CF within the signal-tone frequency band (4–8 kHz) in each respective group. For sake of clarity, subsets of the total population of FRAs are depicted starting from the lowest threshold: naïve, every third (19/55); STD, every other (18/37) and GRC, every other (18/36). Dashed lines represent the mean CF threshold for the entire population of each group. The asterisk shows that the GRC group had significantly lower CF thresholds than either naïve or STD groups which are not different from each other. (b) Plasticity in threshold and bandwidth in the GRC group is specific to the frequency band of the signal tone (asterisk). Both threshold and BW20 decreased only in the signal-tone frequency band. CF threshold and BW20 values are not significantly different from naives in any frequency band in the STD group (see Table 1). Solid lines surrounded by shaded areas represent group means ± *SE*, respectively.

frequency band of the signal tone (Fig. 5b; Table 1). Thus, frequency-specific plasticity in this study developed only for subjects that employed the tone-onset-to-error strategy.

Although the tone-onset-to-error strategy appears to determine plasticity in A1, the GRC group also showed slower learning than the STD group (Fig. 2), suggesting that rate of learning rather than learning strategy governs plasticity. Therefore, we compared to the GRC group another set of subjects that also had the same slow rate of learning but did not depend on use of the tone-onset-to-error strategy. This proved to be three animals that had used a mixture of tone-duration and tone-onset-to-error strategies (MX-STD, $n = 3$) and therefore had been excluded from the main analysis (see Section 2). An analysis of group learning rate that includes the MX-STD subjects showed a significant group effect (days 1–15: $F_{(2,207)} = 19.67$, $p < .0001$). *Post hoc* tests revealed that the MX-STD group exhibited slower learning than the STD subjects, as had the GRC group (MX-STD *vs.* STD, $p < .0001$). Furthermore, the MX-STD group had the same slow rate of learning as the GRC group (MX-STD *vs.* GRC, $p > .05$) (Fig. 6a). However, the MX-STD group apparently used both tone-duration and tone-onset-to-error strategies. They had a low probability of IPT barpresses like the STD group, but a high probability of ITI and late-tone responses like the GRC group; *IPT:* MX-STD *vs.* STD, $F_{(1,150)} = 0.63$, $p > .05$ (Fig. 6b); *ITI:*

Table 1
GRC, STD and naïve electrophysiological data

	Group	Frequency band (kHz)					
		1–2	2–4	4–8	8–16	16–32	32–54
CF threshold (dB SPL)	naïve ($n = 9$)	35.27 ± 2.30 (22)	32.97 ± 1.95 (30)	25.54 ± 1.47 (55)	18.90 ± 1.22 (67)	23.82 ± 1.45 (68)	27.74 ± 1.34 (59)
	GRC ($n = 6$)	34.33 ± 2.67 (30)	27.73 ± 2.67 (26)	16.47 ± 1.81 (36)*	14.71 ± 1.43 (62)	17.26 ± 2.53 (42)	21.79 ± 2.32 (33)
	STD ($n = 5$)	35.09 ± 3.13 (11)	29.96 ± 1.79 (23)	24.43 ± 1.73 (37)	16.73 ± 1.46 (45)	15.83 ± 2.91 (24)	20.19 ± 2.19 (26)
BW20 (octave)	naïve ($n = 9$)	1.67 ± 0.13 (22)	1.94 ± 0.16 (30)	2.18 ± 0.12 (55)	1.64 ± 0.12 (67)	1.21 ± 0.07 (68)	0.94 ± 0.07 (59)
	GRC ($n = 6$)	1.40 ± 0.11 (30)	1.58 ± 0.16 (26)	1.48 ± 0.12 (35)**	1.35 ± 0.10 (62)	1.28 ± 0.08 (42)	0.91 ± 0.08 (33)
	STD ($n = 5$)	1.99 ± 0.21 (11)	2.17 ± 0.14 (23)	2.18 ± 0.16 (36)	1.69 ± 0.16 (45)	1.32 ± 0.13 (24)	1.28 ± 0.14 (26)

Group mean CF threshold and BW20 values ±*SE* are provided for each frequency octave band. Numbers in parentheses indicate the number of values in each mean calculation for the group frequency band. Asterices mark significant one-factor ANOVAs between groups. Alpha levels were adjusted using the Bonefferoni method to correct for multiple comparisons between six frequency bands. *$F_{(2,125)} = 8.38$, $p < .0005$; Fisher's PLSD *post hoc*: GRC is different from naïve ($p < .0002$) and STD ($p < .003$). STD and naïve are not significantly different from each other ($p > .05$) . **$F_{(2,123)} = 7.67$, $p < .0008$; Fisher's PLSD *post hoc*: GRC is different from naïve ($p < .0005$) and STD ($p < .002$). STD and naïve are not significantly different from each other ($p > .05$).

MX-STD *vs.* GRC, $F_{(1,134)} = 3.64$, $p > .05$; *Late-tone*: MX-STD *vs.* GRC, $F_{(1,178)} = 0.16$, $p > .05$ (Fig. 6b). ITI errors accounted for the slower learning of the MX-STD subjects (Fig. 6c). During the last 5 days of training, all three groups performed equally well (days 16–20, $F_{(2,45)} = 0.70$, $p > .05$). Despite their slower learning, MX-STD subjects displayed no evidence of cortical plasticity (all F ratios, $p > .01$; Table 2). Therefore, we conclude that the tone-onset-to-error strategy, rather than slower learning, is responsible for the development of specific plasticity in A1.

The STD group solved the auditory task and learned the relevance of frequency to the same extent as the GRC group without developing plasticity in A1. It might be thought that plasticity actually developed rapidly in this group, but continued training at high performance levels (Fig. 2) had caused the disappearance of plasticity. To resolve this issue, we trained another group of animals in the STD task but stopped training after 11 days instead of 20 days (ST-STD group, $n = 5$). Performance level in the ST-STD group was the same as the first 11 days of performance in the STD group ($F_{(1,66)} = 1.21$, $p > .05$) (Fig. 7). However, this group also failed to develop any plasticity in A1 (all F ratios, $p > .01$; Table 3). Therefore, the absence of plasticity in the STD group was not due to lengthy training.

4. Discussion

4.1. Resume of the findings

Specific cortical plasticity developed only in the GRC group, *i.e.*, the subjects that had the "grace period" in which responses during the 2 s IPT at the start of the inter-trial interval were not "punished" by the flashing light error signal and time-out (Fig. 1). These subjects developed a significant increase in *frequency sensitivity*, *i.e.*, a ~10 dB decrease in threshold, and a significant increase in *frequency selectivity*, *i.e.*, a ~0.7 octaves narrowing of bandwidth. More importantly, increases in both sensitivity and selectivity were *specific* to the frequency band of the 5.0 kHz tone cue (Fig. 5, Table 1).

The STD group, trained in the standard protocol, failed to develop plasticity in A1. These striking differences in cortical plasticity were evident despite the fact that both groups achieved the same asymptotic level of correct performance and both groups exhibited the same frequency generalization gradients, indicating equivalent learning about absolute frequency.

It should be noted that the generalization gradients for both groups were not highly specific to the tone cue frequency of 5.0 kHz but they did exhibit significant peak responses at 5.0 and 7.5 kHz. This level of frequency specificity is concordant with prior findings that generalization gradients are not sharp in the absence of discrimination training, which produces much steeper functions (Mackintosh, 1974). In any event, the slope of the generalization

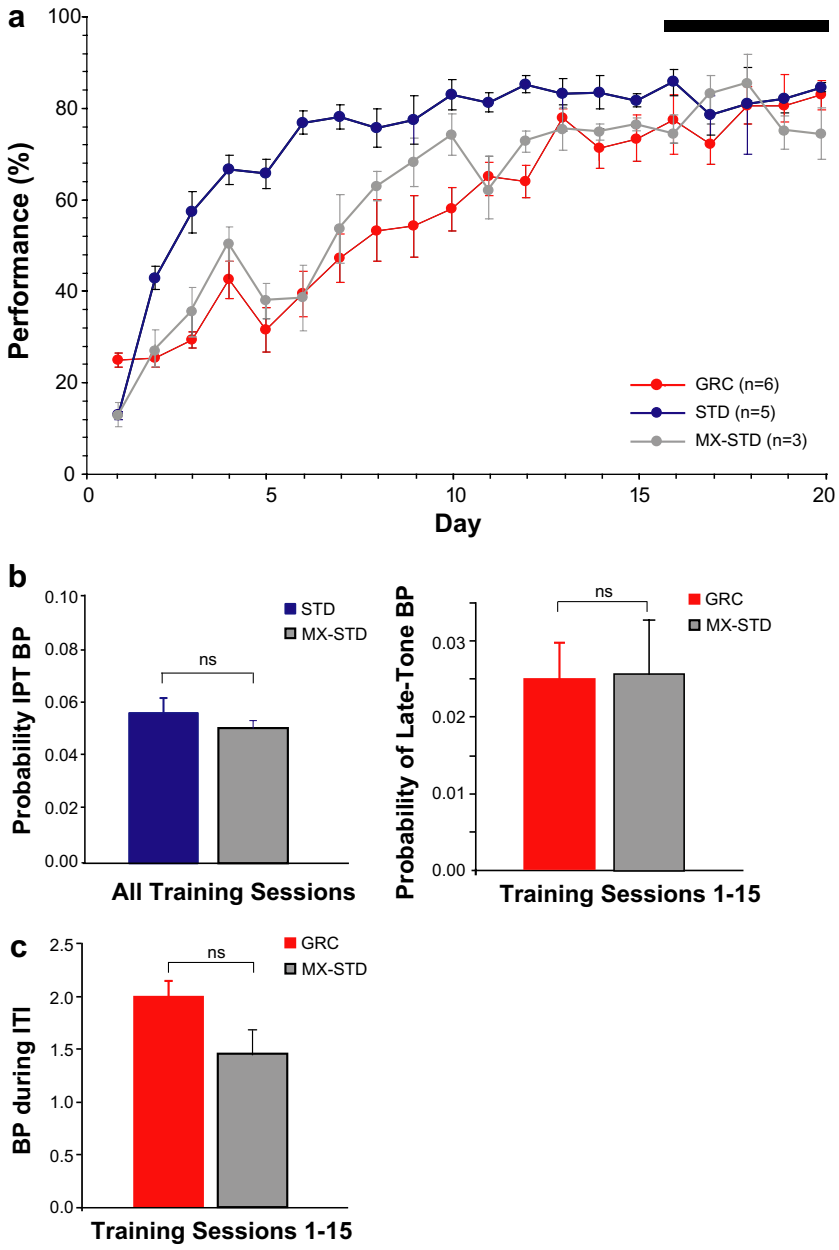

Fig. 6. Slower learning does not cause cortical plasticity. Behavioral data (mean ± *SE*) for animals that displayed a mixture of tone-duration and tone-onset-to-error strategies (MX-STD, $n = 3$). These subjects were trained in the standard (STD) protocol in which strategies employed could have varied between tone-onset-to-error and tone-duration. (a) MX-STD animals' learning was as slow as the GRC group and significantly slower than the STD group. There was no difference in performance between all 3 groups during the last 5 days of training and before A1 mapping (*black bar*). (b) MX-STD animals had the same probability of responding during the IPT periods as the STD group (left panel), but the same probability of late-tone bar-presses as the GRC group (right panel). (c) Additionally, MX-STD animals exhibited the same high number of inter-trial bar-presses as the GRC group, which similarly accounted for their slow learning. That MX-STD animals had similar behavior to the STD group during IPTs, but the same behavior as the GRC group during late-tone periods and inter-trial intervals, indicates that these animals were using a combination of tone-duration and tone-onset-to-error strategies. Despite their slower learning, these subjects failed to develop any cortical plasticity (Table 2).

gradients is not critical, only that the two groups exhibited the same generalization behavior.

4.2. Validity of the findings

The major issue addressed in this study is whether or not learning strategy affects the development of specific plasticity in the primary auditory cortex. Several findings together support an affirmative answer.

First, groups STD and GRC did employ different strategies in learning to bar-press for water. The STD group learned to respond during the presentation of the tone only. This is evident in their rapid learning to not BP during the 2 s IPT period (Fig. 3a and b), and to not BP during the continued inter-trial period (Fig. 3c and d). Therefore,

Table 2
Slow-learning MX-STD animals: electrophysiological data

	Group	Frequency band (kHz)					
		1–2	2–4	4–8	8–16	16–32	32–54
CF Threshold (dBSPL)	naïve ($n = 9$)	35.27 ± 2.30 (22)	32.97 ± 1.95 (30)	25.54 ± 1.47 (55)	18.90 ± 1.22 (67)	23.82 ± 1.45 (68)	23.82 ± 1.45 (68)
	MX-STD ($n = 3$)	34.54 ± 1.96 (13)	25.58 ± 2.93 (19)	19.0 ± 3.47 (8)	17.0 ± 1.53 (34)	21.73 ± 1.17 (33)	26.08 ± 3.80 (12)
	STD ($n = 5$)	35.09 ± 3.13 (11)	29.96 ± 1.79 (23)	24.43 ± 1.73 (37)	16.73 ± 1.46 (45)	15.83 ± 2.91 (24)	15.83 ± 2.91 (24)
BW20 (octave)	naïve ($n = 9$)	1.67 ± 0.13 (22)	1.94 ± 0.16 (30)	2.18 ± 0.12 (55)	1.64 ± 0.12 (67)	1.21 ± 0.07 (68)	1.21 ± 0.07 (68)
	MX-STD ($n = 3$)	1.90 ± 0.16 (13)	2.33 ± 0.18 (19)	2.01 ± 0.12 (8)	1.65 ± 0.11 (34)	1.17 ± 0.10 (33)	1.30 ± 0.24 (12)
	STD ($n = 5$)	1.99 ± 0.21 (11)	2.17 ± 0.14 (23)	2.18 ± 0.16 (36)	1.69 ± 0.16 (45)	1.32 ± 0.13 (24)	1.32 ± 0.13 (24)

Group mean CF threshold and BW20 values ±*SE* are provided for each frequency octave band. Numbers in parentheses indicate the number of values in each mean calculation for the group frequency band. There were no significant differences between MX-STD, naïve and STD groups in any frequency band (all *F* ratios, $p > .01$; Alpha levels were adjusted using the Bonefferoni method to correct for multiple comparisons between the six frequency bands). MX-STD animals trained using the STD protocol did not develop A1 plasticity despite their slow learning. This suggests that tone-onset-to-error strategies specifically are important in the generation of signal-tone specific tuning sensitivity and selectivity increases in A1.

the STD subjects appeared to employ a "tone duration" strategy (see also below). Group GRC's behavior was quite different. These subjects continued to bar-press after tone offset until they received the flashing light error signal. Thus, they never learned to inhibit BPs during the 2 s IPT (Fig. 3a and b). Moreover, although they did learn to reduce responding during the rest of the inter-trial intervals, their improvement was significantly slower than that of the STD group (Fig. 3c and d). Therefore, group GRC employed a "tone onset" strategy rather than a "tone duration" strategy. To be more precise, their behavior can best be explained by the stratagem "Start bar-pressing after tone onset and continue until receiving the flashing light".

As noted previously, it is impossible to conclude that the STD group *never* used the same stratagem as the GRC group, because the standard training protocol produces error-signals for responses immediately after tone offset. This confound was the rationale for the present experiment and the GRC protocol. However, if the STD group had used the same strategy as the GRC group, then their behavior *during* tone presentation should have been the same. However, an analysis of bar-pressing during the tone's final second showed that the GRC group exhibited a significantly greater probability of bar-pressing toward the end of the tone than the STD group (Fig. 3e). Also, the GRC group had a longer latency to the first bar-press after tone onset than the STD group (Fig. 3f). Moreover, if the STD group had used the same strategy as the GRC group, then it is difficult to explain why they made significantly fewer inter-trial responses and why their acquisition function was more rapid than that of the GRC subjects (Fig. 2). Therefore, at an absolute minimum, the findings show that the two groups did not use the identical stratagem of bar-pressing from tone onset until the error signal.

Two other factors might have been responsible for the differences in cortical plasticity between the STD and GRC groups. First, as noted previously and above, their acquisition functions were different. The GRC group required more training sessions to achieve asymptote. Therefore, it could be argued that slower learning, or perhaps greater task difficulty is responsible for the development of specific plasticity. To investigate this possibility we analyzed the data of three subjects that had exhibited a mixture of tone-duration and tone-onset-to-error strategies, and therefore had not been included in the original analyses (MX-STD). They exhibited the same slower rate of learning as the GRC group but like the STD group had a low probability of bar-pressing during the 2 s IPT period (Fig. 6). However, despite their slower learning, they also failed to develop any cortical plasticity (Table 2). Therefore, slower learning itself is not sufficient to explain cortical plasticity.

The other factor is the possibility that the STD group actually did develop the same A1 plasticity as the GRC group, despite their differences in learning strategy. However, such plasticity might only be evident for a few days after achieving asymptotic performance, after which it

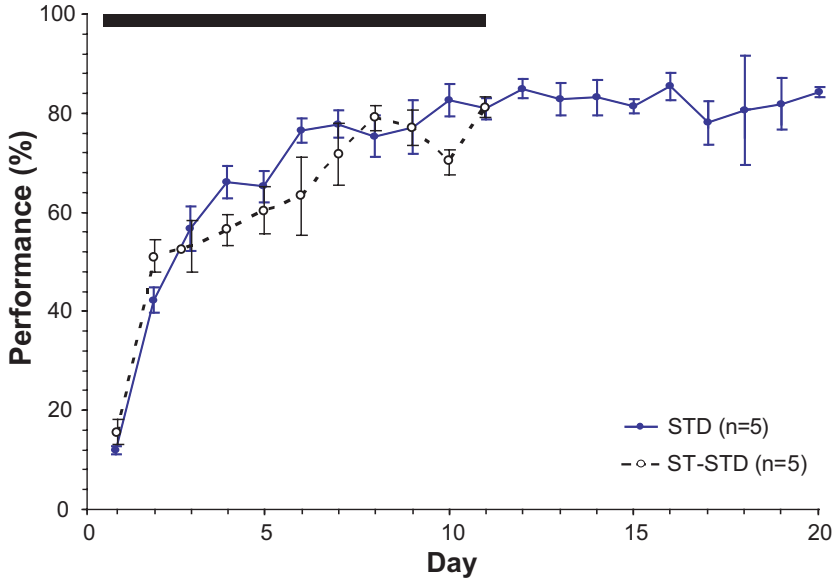

Fig. 7. Performance (mean ± *SE*) of the short term, ST-STD group throughout training (11 days) days not differ from the first 11 days of STD group performance (black bar denotes no significant difference). The ST-STD group did not develop cortical plasticity (Table 3). Hence, the lack of plasticity in the STD group was not due to loss of plasticity due to its length of training.

dissipated with continued training. Therefore, we trained another group of subjects in the same manner (ST-STD), but terminated training at 11 days instead of using 20 days of training (as was necessary for the STD group to receive the same amount of training as the GRC group). However, eliminating continued training at asymptote was without effect, *i.e.*, the ST-STD subjects also failed to develop plasticity in the auditory cortex (Fig. 7, Table 3).

In summary, the development of specific plasticity in the GRC group and the lack of such plasticity in the STD group is best explained by a difference in their learning strategies, rather than by other factors.

4.3. Auditory learning without auditory cortical plasticity

The absence of plasticity in the STD group indicates that cortical plasticity is not necessary for solving the current auditory problem. Several caveats apply to this negative finding. First, the lack of plasticity pertains only to the parameters obtained: distribution of characteristic frequencies, their thresholds and bandwidths. The possibility of specific cortical plasticity for other parameters, including temporal patterning of response, cannot be excluded by this study. Second, data were obtained from the anesthetized brain and perhaps STD plasticity that developed was vulnerable to anesthesia. While this cannot be ruled out, it should be noted that specific plasticity in A1 has been observed under general anesthesia (Recanzone, Jenkins, Hradek, & Merzenich, 1992; Weinberger, Javid, & Lepan, 1993). Third, recordings were targeted to middle cortical layers, so other cell populations might have developed undetected plasticity.

The lack of plasticity in the STD group might seem inconsistent with prior findings of specific A1 plasticity in both classical (Bakin & Weinberger, 1990; Edeline & Weinberger, 1993; Gonzalez-Lima & Scheich, 1986b; Ohl & Scheich, 1996) and instrumental avoidance (Bakin et al., 1996) fear conditioning. Fear conditioning studies have concentrated on changes in receptive field tuning and have not studied possible modifications in threshold or bandwidth. Moreover, the nature of reinforcement itself may influence the development of plasticity, such that learning about potentially injurious stimuli might engender cortical modification because of its greater survival value. Experiments on the relationships between type and level of motivation and plasticity should help resolve this issue. Even the level of motivation within the same appetitive type of task may also influence learning strategy and cortical plasticity differently. A study similar to the present experiment using a higher level of motivation produced significant tone-frequency specific cortical reorganization (Rutkowski & Weinberger, 2005) but did not include any information about strategy. The complexity of the situation is exacerbated when one considers that there may be many different learning strategies and that they may have different relationships to cortical plasticity.

In addition to its role in associative representational plasticity, learning strategy might be important for perceptual learning, *i.e.*, improved acuity due to extensive, increasingly more difficult discrimination training. For example, frequency discrimination learning in the owl monkey is accompanied by an increase in the area of representation of the frequency band relevant to the task (Recanzone et al., 1993). However, the same type of learning in the cat yielded no such plasticity in A1, which the

Table 3
Short term, ST-STD group: electrophysiological data

	Group	Frequency band (kHz)					
		1–2	2–4	4–8	8–16	16–32	32–54
CF Threshold (dBSPL)	naïve ($n = 9$)	35.27 ± 2.30 (22)	32.97 ± 1.95 (30)	25.54 ± 1.47 (55)	18.90 ± 1.22 (67)	23.82 ± 1.45 (68)	23.82 ± 1.45 (68)
	ST-STD ($n = 5$)	23.81 ± 3.77 (16)	17.5 ± 6.29 (4)	22.48 ± 2.19 (25)	14.69 ± 1.41 (45)	19.13 ± 1.35 (32)	16.48 ± 2.38 (31)
	STD ($n = 5$)	35.09 ± 3.13 (11)	29.96 ± 1.79 (23)	24.43 ± 1.73 (37)	16.73 ± 1.46 (45)	15.83 ± 2.91 (24)	15.83 ± 2.91 (24)
BW20 (octave)	naïve ($n = 9$)	1.67 ± 0.13 (22)	1.94 ± 0.16 (30)	2.18 ± 0.12 (55)	1.64 ± 0.12 (67)	1.21 ± 0.07 (68)	1.21 ± 0.07 (68)
	ST-STD ($n = 5$)	1.53 ± 0.21 (16)	1.72 ± 0.44 (4)	2.12 ± 0.18 (25)	1.66 ± 0.12 (45)	1.35 ± 0.09 (32)	1.01 ± 0.14 (31)
	STD ($n = 5$)	1.99 ± 0.21 (11)	2.17 ± 0.14 (23)	2.18 ± 0.16 (36)	1.69 ± 0.16 (45)	1.32 ± 0.13 (24)	1.32 ± 0.13 (24)

Group mean CF threshold and BW20 values ±*SE* are provided for each frequency octave band. Numbers in parentheses indicate the number of values in each mean calculation for the group frequency band. There were no significant differences between ST-STD, naïve and STD groups in any frequency band (all *F* ratios, $p > .01$; Alpha levels were adjusted using the Bonefferoni method to correct for multiple comparisons between the six frequency bands). Plasticity did not develop rapidly and then disappear with continued training in the STD group because plasticity is not evident even early in training when asymptotic levels of performance have not yet been reached in the ST-STD group.

authors attribute to "species differences" (Brown et al., 2004). Species differences in the learning strategies employed might help explain the differences in plasticity. For example, monkeys might allocate greater emphasis to the onsets of the discriminative stimuli because of the particular importance of acoustic transients in con-specific vocal communication.

4.4. Learning strategies and cortical plasticity

The present findings reveal links among learning strategies, acoustic onsets and specific cortical plasticity. The functional significance of increased sensitivity (decreased threshold) and increased selectivity (narrowed bandwidth) limited to the frequency band of the signal tone cannot be determined from the present experiment. They might enhance detection of the tonal signal for reward availability. They might reflect the storage of specific information about the tonal cue whose representation had gained particular behavioral importance. Such dual "sensory" and "learning/memory" functions are not incompatible but rather are probably mutually supporting. Thus, learning processes determine which stimuli acquire behavioral significance and thus stimuli gain salience, *i.e.*, they are more readily detected and they compete more successfully for attentional resources. Increased salience and detection are accomplished by sensory and perceptual systems, by selectively reducing threshold and narrowing receptive field bandwidth. Thus, while learning processes initially select environmental events for preferential processing, the latter depends upon the development of associative representational plasticity.

Stimulus-specific reductions in threshold and bandwidth may increase the likelihood of forming relevant neuronal ensembles or networks. For example, these modifications increase the probability of response while restricting the range of response to sounds. This combination could enable cue-responsive cells to selectively discharge in concert with other sensory or reward-related cells. Any such activity that satisfies temporal criteria for the modification of synaptic weights could thereby promote the establishment of ensembles.

The fact that the "tone-onset-to-error", rather than the "tone-duration", strategy led to the development of plasticity may reflect certain proclivities of the circuitry involved in the processing of sounds in the primary auditory cortex. Masterton (1993) has stressed the critical role of acoustic transients in behavioral adaptation, pointing out that natural sounds are generally very brief and suggesting that the auditory system is adapted to extract information from such sounds. Acoustic onsets are known to have a privileged status with respect both to perception and to auditory cortical discharge (Phillips & Heining, 2002). They are especially important in speech perception for phonetic identification (Phillips, Taylor, Hall, Carr, & Mossop, 1997) and even in music perception for identification of timbre and the type of instrument producing sound

(Saldanha & Corso, 1964). Timbre is a biologically significant feature of natural sounds. Also, sound transients appear to be of particular significance in the development of auditory cortex (Metherate & Aramakis, 1999) and A1 has a greater sensitivity to onset transients than other auditory cortical fields (Heil & Irvine, 1998).

It must be stressed that A1 plasticity is not a product of the use of transients for the GRC group *vs.* steady-state sounds for the STD group. Both groups received identical acoustic stimulation. Rather, the use of an onset strategy, which was encouraged by use of the 2 s IPT grace period, must have been based on "top-down, goal-directed" processes, rather than "bottom-up, stimulus-driven" factors. The most likely candidate is selective attention which was guided by reinforcement contingencies. Both groups were rewarded for bar-pressing after tone onset. However, the STD group was punished by the error signal and time out for its first BP after tone offset (and any responses preceding the next scheduled tone), a learning process that confined responses to the tone duration. In contrast, while GRC bar-presses during the IPT grace period were not rewarded, neither were they punished by the flashing light and time out. Thus, attention was most likely directed to the cue that was the best predictor of reward, *i.e.*, tone onset.

The current findings and these speculations indicate a need to search for particular neural substrates during training. For example, if the use of a grace period directs attention to tone onset, then one might expect tone onset to elicit a different, possibly larger, response in A1 than otherwise, when the onset strategy becomes behaviorally evident. Ideally, it would be desirable to exercise control over the type of strategy currently in use, and induce repeated alternations of strategies while tracking the processing of the acoustic tonal cue.

4.5. Implications for cortical processes in learning and memory

It might be surprising that different strategies can be used to solve the "simple" problem that water is attainable by pressing a bar when a tone is present. That either tone-duration or tone-onset approaches could be used in such an apparently straightforward task had not been adequately appreciated. In the present study, the different strategies were manifest by an apparently minor change in the training protocol, *i.e.*, inserting a 2 s "grace" period at tone offset. Therefore, seemingly negligible differences in experimental designs may have substantial effects on the development of neuronal plasticity. Thus, the details of experimental protocols require particular consideration.

There is no reason to assume that the importance of learning strategy is limited to the primary auditory cortex. Learning strategies could be critically involved in many types of learning, across sensory modalities and potentially involving the entire cerebral cortex. Moreover, it is possible that the importance of learning strategies varies with the type of involved memory. Accepting for the moment the distinction between "declarative" and "procedural" memory, the influence of strategy might be greater for the former, to the extent that it is more flexible and could involve a greater variety of "solution rules" than stimulus-response associations. Further, that learning strategies are a factor at all in determining cortical plasticity indicates the need to explicitly seek to identify them in future studies, which may also promote a comprehensive understanding of the results of past studies.

The current findings may have clinical implications for learning in the auditory system. In the cases of both auditory learning disabilities and learning to hear after receiving cochlear implants, the use of training strategies that emphasize the onsets of sounds may well be the most efficacious for the induction of specific adaptive plasticity in the auditory cortex.

At a more basic level, that learning strategy can determine specific plasticity in A1 raises the possibility that there exists a general principle underlying the formation and storage of information. Insofar as plasticity developed in primary auditory cortex only for the group that used the "tone-onset-to-error" strategy, and that acoustic onsets/transients are particularly effective in engaging A1 cells to discharge, then the neural representation of specific information may be "selected" by neurons on the basis of a match between behaviorally important stimulus features and the particular response proclivities of circuits and networks. In short, knowledge of both learning strategies and the type of stimulus characteristic best processed by a circuit/network should permit predictions about the locus of neurons that will develop specific plasticity underlying learning and memory.

Finally, the present approach underscores some close relationships between sensory neuroscience and learning neuroscience. The historically independent development of these fields is no longer tenable. As Nature apparently does not honor this divide, neither should neuroscience.

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References

Bakin, J. S., & Weinberger, N. M. (1990). Classical conditioning induces CS-specific receptive field plasticity in the auditory cortex of the guinea pig. *Brain Research, 536*(1–2), 271–286.

Bakin, J. S., South, D. A., & Weinberger, N. M. (1996). Induction of receptive field plasticity in the auditory cortex of the guinea pig during instrumental avoidance conditioning. *Behavioral Neuroscience, 110*(5), 905–913.

Blake, D. T., Strata, F., Churchland, A. K., & Merzenich, M. M. (2002). Neural correlates of instrumental learning in primary auditory cortex. *Proceedings of National Academy of Sciences of the United States of America, 99*(15), 10114–10119.

Brechmann, A., Gaschler-Markefski, B., Sohr, M., Yoneda, K., Kaulisch, T., & Scheich, H. (2007). Working memory-specific activity in auditory cortex: Potential correlates of sequential processing and maintenance. *Cerebral Cortex*.

Brown, M., Irvine, D. R., & Park, V. N. (2004). Perceptual learning on an auditory frequency discrimination task by cats: Association with changes in primary auditory cortex. *Cerebral Cortex, 14*(9), 952–965.

Buonomano, D. V., & Merzenich, M. M. (1998). Cortical plasticity: From synapses to maps. *Annual Review in Neuroscience, 21*, 149–186.

Condon, C. D., & Weinberger, N. M. (1991). Habituation produces frequency-specific plasticity of receptive fields in the auditory cortex. *Behavioral Neuroscience, 105*(3), 416–430.

Edeline, J. M., & Weinberger, N. M. (1993). Receptive field plasticity in the auditory cortex during frequency discrimination training: Selective retuning independent of task difficulty. *Behavioral Neuroscience, 107*(1), 82–103.

Edeline, J. M., Neuenschwander-el Massioui, N., & Dutrieux, G. (1990). Discriminative long-term retention of rapidly induced multiunit changes in the hippocampus, medial geniculate and auditory cortex. *Behavioral Brain Research, 39*(2), 145–155.

Gao, E., & Suga, N. (2000). Experience-dependent plasticity in the auditory cortex and the inferior colliculus of bats: Role of the corticofugal system. *Proceedings of the National Academy of Sciences in the United States of America, 97*(14), 8081–8086.

Gonzalez-Lima, F., & Scheich, H. (1986a). Classical conditioning of tone-signaled bradycardia modifies 2-deoxyglucose uptake patterns in cortex, thalamus, habenula, caudate-putamen and hippocampal formation. *Brain Research, 363*, 239–256.

Gonzalez-Lima, F., & Scheich, H. (1986b). Neural substrates for tone-conditioned bradycardia demonstration with 2 deoxyglucose, II. Auditory cortex plasticity. *Behavioral Brain Research, 20*, 281–293.

Heil, P., & Irvine, D. R. (1998). The posterior field P of cat auditory cortex: Coding of envelope transients. *Cerebral Cortex, 8*(2), 125–141.

Kisley, M. A., & Gerstein, G. L. (2001). Daily variation and appetitive conditioning-induced plasticity of auditory cortex receptive fields. *European Journal of Neuroscience, 13*(10), 1993–2003.

Lemaire, P., & Fabre, L. (2005). Strategic aspects of human cognition. In M. J. Roberts, E. J. Newton (Editors, translator and editor), *Current issues in thinking and reasoning* (pp. 11–29). New York: Psychology Press.

Mackintosh, N. J. (1974). *The psychology of animal learning*. New York, NY: Academic Press, p. 730.

Masterton, R. B. (1993). Central auditory system. *ORL; Journal for oto-rhino-laryngology and its related specialties, 55*(3), 159–163.

Metherate, R., & Aramakis, V. B. (1999). Intrinsic electrophysiology of neurons in thalamorecipient layers of developing rat auditory cortex. *Brain Research. Developmental Brain Research, 115*(2), 131–144.

Molchan, S. E., Sunderland, T., McIntosh, A. R., Herscovitch, P., & Schreurs, B. G. (1994). A functional anatomical study of associative learning in humans. *Proceedings of the National Academy of Sciences in the United States of America, 91*(17), 8122–8126.

Morris, J. S., Friston, K. J., & Dolan, R. J. (1998). Experience-dependent modulation of tonotopic neural responses in human auditory cortex. *Proceedings of the Royal Society of London. Series B, Containing papers of a Biological character. Royal Society (Great Britain), 265*(1397), 649–657.

Ohl, F. W., & Scheich, H. (1996). Differential frequency conditioning enhances spectral contrast sensitivity of units in auditory cortex (field Al) of the alert Mongolian gerbil. *European Journal of Neuroscience, 8*(5), 1001–1017.

Ohl, F. W., Scheich, H., & Freeman, W. J. (2001). Change in pattern of ongoing cortical activity with auditory category learning. *Nature, 412*(6848), 733–736.

Palmer, C. V., Nelson, C. T., & Lindley, G. A. 4th, (1998). The functionally and physiologically plastic adult auditory system. *The Journal of the Acoustical Society of America, 103*(4), 1705–1721.

Phillips, D. P., Taylor, T. L., Hall, S. E., Carr, M. M., & Mossop, J. E. (1997). Detection of silent intervals between noises activating different perceptual channels: Some properties of "central" auditory gap detection. *The Journal of the Acoustical Society of America, 101*(6), 3694–3705.

Phillips, M. L., & Heining, M. (2002). Neural correlates of emotion perception: From faces to taste. In C. Rouby, & B. Schaal (Editors, translator and editor), *Olfaction, taste, and cognition* (pp. 196–208). New York, NY: Cambridge University Press.

Rauschecker, J.P. (2003). Functional organization and plasticity of auditory cortex. *In*: I. Peretz (Editor, translator and editor), *The cognitive neuroscience of music* (pp. 357–365). London: Oxford University Press.

Recanzone, G. H., Jenkins, W. M., Hradek, G. T., & Merzenich, M. M. (1992). Progressive improvement in discriminative abilities in adult owl monkeys performing a tactile frequency discrimination task. *Journal of Neurophysiology, 67*(5), 1015–1030.

Recanzone, G. H., Schreiner, C. E., & Merzenich, M. M. (1993). Plasticity in the frequency representation of primary auditory cortex following discrimination training in adult owl monkeys. *Journal of Neuroscience, 13*(1), 87–103.

Rutkowski, R. G., & Weinberger, N. M. (2005). Encoding of learned importance of sound by magnitude of representational area in primary auditory cortex. *Proceedings of the National Academy of Sciences of the United States of America, 102*, 12664–13669.

Rutkowski, R. G., Miasnikov, A. A., & Weinberger, N. M. (2003). Characterisation of multiple physiological fields within the anatomical core of rat auditory cortex. *Hearing Research, 181*(1–2), 116–130.

Sakurai, Y. (1994). Involvement of auditory cortical and hippocampal neurons in auditory working memory and reference memory in the rat. *Journal of Neuroscience, 14*(5 Pt 1), 2606–2623.

Saldanha, E. L., & Corso, J. F. (1964). Timbre cues and the identification of musical instruments. *The Journal of the Acoustical Society of America, 36*, 2021–2026.

Sally, S. L., & Kelly, J. B. (1988). Organization of auditory cortex in the albino rat: Sound frequency. *Journal of Neurophysiology, 59*, 1627–1638.

Villa, A. E., Tetko, I. V., Hyland, B., & Najem, A. (1999). Spatiotemporal activity patterns of rat cortical neurons predict responses in a conditioned task. *Proceedings of the National Academy of Sciences of the United States of America, 96*(3), 1106–1111.

Weinberger, N. M. (1995). Dynamic regulation of receptive fields and maps in the adult sensory cortex. *Annual Review of Neuroscience, 18*, 129–158.

Weinberger, N. M. (2004a). Experience-dependent response plasticity in the auditory cortex: Issues, characteristics, mechanisms and functions. In T. N. Parks, E. Rubel, A. Popper, (Editors, translator and editor), *Plasticity of the auditory system* (pp. 173–228). Spring Handbook of Auditory Research. New York: Springer-Verlag.

Weinberger, N. M. (2004b). Specific long-term memory traces in primary auditory cortex. *Nature Reviews Neuroscience, 5*(4), 279–290.

Weinberger, N. M., Javid, R., & Lepan, B. (1993). Long-term retention of learning-induced receptive-field plasticity in the auditory cortex. *Proceedings of the National Academy of Sciences of the United States of America, 90*(6), 2394–2398.