

Behavioral Dependence of Auditory Cortical Responses

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Abstract Neural responses in the auditory cortex have historically been measured from either anesthetized or awake but non-behaving animals. A growing body of work has begun to focus instead on recording from auditory cortex of animals actively engaged in behavior tasks. These studies have shown that auditory cortical responses are dependent upon the behavioral state of the animal. The longer ascending subcortical pathway of the auditory system and unique characteristics of auditory processing suggest that such dependencies may have a more profound influence on cortical processing in the auditory system compared to other sensory systems. It is important to understand the nature of these dependencies and their functional implications. In this article, we review the literature on this topic pertaining to cortical processing of sounds.

Keywords Auditory · Cortex · Behavior · Attention

Introduction

Much progress has been made in the last several decades in understanding the functions of the mammalian auditory cortex. However, despite our growing knowledge of the anatomical structure (e.g., Kaas et al. 1999; Romanski et al.

1999; Kaas and Hackett 2000; Lee and Winer 2005; Hackett 2011; Winer and Schreiner 2011) and physiological properties (e.g., Merzenich and Brugge 1973; Schreiner and Mendelson 1990; Shamma et al. 1993; Rauschecker et al. 1995; Schreiner et al. 2000; Liang et al. 2001; Ulanovsky et al. 2003; Wang et al. 2005; Bendor and Wang 2005; Schreiner and Winer 2007; Suga et al. 2000) of the auditory cortex, relatively little is known about how neural activity in auditory cortex is linked to auditory perception. Most of what we currently know about auditory cortical processing has come from anesthetized preparations and studies of animals under awake, but passive, conditions. Collectively, the previous work has led to the general conceptualization of the auditory cortex as being hierarchical, with information passing through a highly organized series of increasingly integrative processing stages. The primary auditory cortex (A1) is thought to encode the basic features of sounds while secondary cortical areas represent more complex features of the acoustic environment. For instance, compared to A1, secondary auditory areas in primates respond with longer latencies, higher stimulus selectivity, and can be robustly driven by band-pass noise, frequency-modulated sweeps, and species-specific vocalizations (Rauschecker et al. 1995; Rauschecker 1998; Tian et al. 2001; Wang et al. 2005; Kajikawa et al. 2008). Many of these secondary processing areas ultimately project to specific areas of prefrontal cortex (Hackett et al. 1999; Romanski et al. 1999; Romanski and Goldman-Rakic 2002; Romanski 2003) that are likely involved in even higher level processing such as stimulus categorization (Gifford et al. 2005; Cohen et al. 2006). The auditory cortex thus appears, and is often assumed to be, designed to perform increasingly complex and integrative computations as information flows from primary to secondary regions and, ultimately, to frontal areas.

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In addition to the hierarchical processing principle discussed above, a growing body of work suggests that neurons located throughout this processing hierarchy, more than passively representing a sound's acoustic structures, show adaptive response properties that can be modulated by the various behavioral and cognitive factors associated with engagement in an auditory task—including task engagement, learning effects, and decision-making factors associated with an animal's behavioral choice. Some of the earliest work demonstrating such behavioral modulation of auditory cortex was performed by Hubel et al. (1959), who showed that a small proportion of neurons (~10 %) in cat auditory cortex would respond only if the animal appeared to attend to the source location of a sound. Most of these cells were located in A1 and responded to a variety of sounds, although natural stimuli tended to evoke stronger responses (e.g., voices, tapping on a table, jingling keys, the sound of a squeak toy) than tones or noises. Although Hubel et al. (1959) termed these neurons “attention units”, attention in this study was only loosely defined as the animal simply looking toward the source of the sound. There was also little control over stimulus presentation and the methodological structure of the experiment. Indeed, the subjects were naïve animals that were not specifically trained on any behavioral task, they were allowed to simply walk around a large enclosure, and the experimenters presented acoustic stimuli manually whenever the animals were looking away.

The central question at the heart of this review, and indeed one of the most fundamental questions in neuroscience, concerns how brain activity gives rise to perception. Properly addressing this question requires, at a minimum, the ability to precisely and quantitatively control the sensory stimulus, the sensory and perceptual experience of that stimulus, and measurement of the underlying neural response to that stimulus. Since Hubel et al. (1959), a growing number of studies have described behavioral modulation of neural responses in both primary and secondary fields of auditory cortex using more precisely controlled experimental methods. Studies utilizing operant conditioning procedures allow researchers to examine neural responses in behaving preparations in which animals are trained to report on either the detection or discrimination of acoustic stimuli. Generally, the majority of these studies have described increased stimulus-driven responses when engaged in a behavior task (e.g., Gottlieb et al. 1989; Scott et al. 2007), although some studies have shown response suppression due to task engagement (e.g., Otazu et al. 2009) and a few others have described no change between the engaged and passive conditions (e.g., Hocherman et al. 1976; Gilat and Perlman 1984). These kinds of diverse observations showcase the potentially inherent variability in neural response properties that one

might expect to find as animals engage with acoustic environments comprised of different stimulus sets, task demands, and training paradigms. For example, procedures with different cognitive and attentional demands (e.g., detection vs. discrimination), different task structures (e.g., approach vs. avoidance), or different stimulus sets may each produce distinctive neural responses and, therefore, potentially conflicting descriptions of how cortical activity is modulated by task performance. In the sections below we will review studies that explore the nature of some of these behavioral dependencies.

A final note clarifying the scope of this review: We here focus almost exclusively on studies that describe single- and multi-unit neuronal representations at the level of the auditory cortex. We make note of one or two studies that touch on the relationship between cortical and thalamic activity patterns during behavioral engagement, but otherwise we do not discuss subcortical structures. It is important to keep in mind, however, that task-related changes in neural activity are likely to also exist in subcortical structures as well (see, for example Jaramillo et al. 2014 below)—and it is thus unclear where along the auditory hierarchy these kinds of behavior-related changes in neural activity originate. Furthermore, there is a growing literature examining these kinds of questions using neuroimaging (e.g., fMRI) and non-invasive neurophysiological techniques (e.g., EEG/MEG). Functional MRI studies in humans, for example, have shown attention and task-related modulation of auditory processing in both cortical (e.g., Pugh et al. 1996; Hall et al. 2000; Jäncke et al. 2003; Petkov et al. 2004; Woods et al. 2009) and subcortical structures (Rinne et al. 2008; von Kriegstein et al. 2008). The use of these non-invasive techniques, although limited in their ability to reveal neuronal suppression or enhancement, could provide a powerful means to discover new brain regions that are sensitive to auditory behavior and task-engagement and thus help point to new targets for future neurophysiological recordings.

Increased Neural Activity in Auditory Cortex by Task Engagement

Several early studies utilizing behavioral training methods were among the first to reveal that task engagement strongly affects the response properties of auditory cortical neurons (e.g., Miller et al. 1974, 1980; Pflugst et al. 1977; Pflugst and O'Connor 1981). Miller et al. (1972), for example, showed that sound evoked activity in single neurons in both primary and secondary areas of macaque monkey auditory cortex was enhanced in animals performing an auditory reaction time task compared to when they passively listened to the same stimuli. In contrast, no response

enhancement was seen in untrained, naïve animals. The task required the animals to depress a response key to initiate a variable duration trial and then release it in response to an acoustic stimulus. In a follow-up study, Beaton and Miller (1975) further showed that these auditory evoked responses in macaque monkey were dependent on the specific reinforcement conditions of the task. In one such condition, monkeys were reinforced for responses to all acoustic stimuli regardless of the particular stimulus frequency. In another condition, monkeys were only reinforced for responding to specific stimulus frequencies while other frequencies were not associated with reward. Beyond the previously reported task-related enhancement of Miller et al. (1972), Beaton and Miller (1975) observed a further response enhancement in a small population ($\sim 25\%$) of neurons when the animals were switched from a simple reaction time task to one that required a frequency discrimination. Blake et al. (2002) also described an increase in stimulus-driven activity in A1 in response to training on a frequency discrimination task. In this study, owl monkeys were trained to respond when the frequency of a target tone was higher than that of a standard. In this task, neural responses to target stimuli increased more than responses to standards.

Benson and Hienz (1978) had macaque monkeys perform an auditory selective attention task in which either the left or right ear of a monkey was designated as the ear to be attended (indicated by an illuminated report key). Acoustic stimuli were presented randomly to both ears and the animal was required to depress the illuminated report key whenever a sound stimulus was presented to the attended ear. These authors reported that 18% units showed significantly greater discharge rates for the attended ear compared to the identical, non-attended stimulus. Also, Benson et al. (1981) described increases in evoked activity when animals were required to press a key at the location of a perceived sound source of a white noise burst. These authors described increases in activity for a specific location for 22% of neurons. The study by Benson and Hienz (1978) was one of the earliest single-unit studies to report attention enhanced binaural and spatial responses in auditory cortex.

Correlation Between Neural Activity and Behavior Through Neurometric and Psychometric Analyses

In order for neural activity to be reliably and systematically correlated with auditory perception, the neural and perceptual data are often analyzed in such a way that they reflect similar metrics. This is typically accomplished by first measuring psychometric functions during task performance. The resulting cumulative probability curves

describe the trial-to-trial probabilistic variability of an animal's responses at various stimulus magnitudes. The acquired neural data are then recast as a series of trial-to-trial probabilistic responses to those same stimuli and converted into a neurometric function. The resulting curves are then subjected to the same analyses and statistics in order to compare the relationship between behavior and physiology. One example of this approach comes from the visual system and the work of Newsome and colleagues in their examinations of the relationship between perception of visual motion and neural activity in visual area MT in monkeys (Newsome et al. 1989; Britten et al. 1992). The work by Mountcastle, Romo, and colleagues in the somatosensory system provide another example of this technique, where psychophysical and physiological data from the same animal have been directly compared in order to address how perceptual experiences are represented in cortex (Mountcastle et al. 1990; Romo et al. 2002; de Lafuente and Romo 2005; Romo and de Lafuente 2013).

Scott et al. (2007) explored the effects of behavioral modulation on neural response properties in areas A1 and R of macaque monkey auditory cortex using neurometric and psychometric analyses. Monkeys were trained to actively discriminate sounds that varied in interaural phase difference, an acoustic parameter that covaries with spatial location. During task engagement, 58% of units showed increased activity while 13% of units showed decreased activity. Spontaneous rate increased during active discrimination for 71% of neurons. Overall, however, discriminability did not improve during task engagement, with 29% of units showing steeper neurometric functions and 23% showing flatter neurometric functions.

Niwa et al. (2012a, b) showed that engagement in an amplitude modulation (AM) discrimination task not only increased overall activity levels in macaque monkey auditory cortex neurons, but also improved the ability of A1 neurons to discriminate AM sounds from unmodulated sounds. In this task, two sounds were presented to the animal, the first of which was an unmodulated burst of white noise. The second sound was either identical to the first sound or contained a sinusoidally modulated carrier of varying modulation depths (6–100%). Animals were required to depress and hold a response lever throughout presentation of both stimuli and release the lever if the second sound contained AM. Neurometric analyses were used to determine how well each unit discriminated amplitude modulation from an unmodulated sound by comparing trial-by-trial responses to each stimulus type. Firing rate-based AM discrimination improved significantly in the engaged compared to the passive condition, and responses were stronger to higher modulation depths versus lower modulation depths and unmodulated sounds. In addition to these rate-based metrics, the authors described an

improvement in the overall temporal precision of phase locking to the modulated stimuli when animals were required to attend to it.

In a related study, Lemus et al. (2009) trained macaque monkeys to discriminate two sounds containing different rates of acoustic flutter. Flutter is a sensation caused by stimuli with very low repetition rates (4–40 Hz). In this task, the animals were required to report whether the acoustic flutter rate of the second stimulus was higher or lower than the first stimulus. Neurometric analyses in A1 showed that neural thresholds for firing rate, but not periodicity, were similar to the monkeys' psychophysical thresholds. The authors therefore suggested that A1 utilizes a rate code, not a temporal one, to encode low frequency repetition rates. Additionally, the neural activity recorded in A1 could not be reliably used to encode stimulus features during either the inter stimulus interval or the decision period after presentation of the second stimulus, which led the authors to further conclude that A1 does not reflect higher-level, decision-based, or cognitive processing of auditory features.

Context-Dependent Behavioral Modulation of Auditory Cortex Activity

Jaramillo et al. (2014) trained mice on a task requiring a flexible categorization of complex tone stimuli. The animals had to move to a left or right response port for a water reward when presented with a low or high frequency sound, respectively. The task was designed so that the high versus low boundary for correct categorization was moved several times during a test session, which meant that a correct response to some sounds required a different action (left vs. right) depending on the context. These authors found a subpopulation of A1 neurons (~15 %) that were modulated by context for a given stimulus. A similar proportion of neurons in auditory thalamus (16 %) was also modulated by context. A previous study by Vaadia et al. (1982) showed a comparable proportion (~17 %) of context-specific responses in a macaque monkey trained to shift a lever to the left versus right in response to either a pure tone or a noise stimulus after the stimulus–response associations were reversed. Finally, Durif et al. (2003) trained rhesus monkeys to associate two different pure tones, called the “instruction” stimuli, with either a left or right button press. A given tone was presented a second time (“confirmation stimulus”) if the animal made a correct choice. These authors reported that ~33 % of neurons recorded in auditory cortex (both A1 and lateral belt) exhibited context-specific responses to the same tone stimulus when it was an “instruction” stimulus compared to when it was a “confirmation” stimulus.

Another recent study explored the effect of performing a complex categorization task on neural responses in A1 in rats (Rodgers and DeWeese 2014). In this study, animals were trained on two tasks: One in which they had to discriminate a frequency difference between two sinusoidally modulated tones and another in which they had to localize a broadband noise burst to the left or right. A correct response on either task required the animals to move to a left or right response port for access to water. During testing, the stimuli were presented together on any given trial (e.g., high frequency tone + left noise) and the animals were trained to attend to only one stimulus category at a time in any given block of trials. The authors reported, during this task, a large proportion of units (36 %) in A1 that showed increased firing rates during one of the two behavioral contexts (frequency discrimination vs. sound localization) relative to the other context. This increase in firing rate appeared to reflect an increase in overall gain, since there was no change in neuronal response properties. A greater proportion of units in prefrontal cortex (63 %) showed the same context-based changes in firing rate, and the authors suggest that the response modulation seen in A1 could reflect a top-down influence from prefrontal cortex.

Effect of Task Engagement in Nonprimary Auditory Cortex

Single units in secondary fields of auditory cortex can also be modulated by engagement in a psychophysical task and may also reflect some degree of cognitive processing. For example, Gottlieb et al. (1989) investigated auditory cortical responses during frequency discrimination performance while recording from posterior belt regions in an olive baboon. In this task, the animal was presented with two 300 ms tones separated by a 1 s inter stimulus interval. In contrast to Lemus et al. (2009) in their investigation of A1, task engagement here resulted in enhanced spontaneous activity during the inter stimulus interval in 65 % of belt neurons compared to when the animal was not performing the task. Interestingly, 23 % of the isolated units also showed significant changes in activity levels (either enhancement or suppression) during presentation of the second stimulus only if it was identical to the first stimulus. These data appear to support the authors' contention that neurons in posterior belt regions may reflect cognitive processing associated with short-term memory.

Two additional recent studies have provided evidence of potential differences in neural responsiveness between A1 and secondary auditory cortices during task performance. Dong et al. (2013) investigated behavioral modulation of neural encoding of click trains in both A1 and secondary auditory cortices of cats. Animals were trained to

discriminate between 12.5 and 50 Hz click trains by licking a metal pipe in response to a 50 Hz stimulus and withholding responses to 12.5 Hz stimuli. Correct responses were rewarded with access to food reinforcement. Neural responses in A1 were inconsistent in the behaving condition and showed both increased and decreased evoked activity levels compared to the passive condition. Responses in secondary cortex, however, were more consistent and showed significantly increased evoked activity that resulted in an enhancement of neural discriminability of neural click trains. Similarly, a recent study by Atiani et al. (2014) described increases in evoked responses in belt compared to core regions during a conditioned avoidance task in ferrets. The animals were trained in an oddball paradigm where the animals had to discriminate tone targets from a repeating broadband reference sound. The authors described a selective increase in firing rates to targets, but not reference sounds, in belt (dPEG) compared to core (A1), which they argue likely stems from top-down selective attention mechanisms that help to extract behaviorally relevant stimuli from the environment in higher-order brain areas.

Task Engagement Can Suppress Firing Rates in Auditory Cortex

Although most of the reported changes in neural response properties due to task engagement involve increases in spontaneous and/or evoked activity levels, several studies have reported either no effect of task engagement or decreases in cortical neural activity. For example, Hocherman et al. (1976) trained monkeys on a task with both light and sound cues and required them to selectively attend to the light cue in one condition and the sound cue in the other condition. The authors then compared unit responses in auditory cortex to identical acoustic stimuli between these two selective attention conditions. Results showed that about 50 % of the unit responses changed with cueing, but that evoked activity levels were similar (~33 %) for both cues. Another study by Gilat and Perlman (1984), which utilized a similar task, also showed no significant differences between engaged and passive conditions. These authors reported roughly equal numbers of units that showed increases, decreases, or no change in their stimulus-driven firing rates.

Other authors have described a suppression of neural responses in auditory cortex when animals were engaged in an auditory task compared to when they passively listened to the same stimuli. For example, Otazu et al. (2009) trained rats in a two-alternative forced choice task in which the location of a broadband, multi-tone stimulus sound signaled which of two ports would be reinforced. Prior to

target onset, a train of clicks was presented to the animal. These authors reported suppression of neural activity to both the target and the task-irrelevant, non-target click stimuli during task performance. To explain these findings, the authors hypothesized that increases in cortical activity are dependent on selective attention, which was not required for completion of their task, and that simply engaging in a psychophysical task has the effect of suppressing neural activity. Similar results were described by Beitel et al. (2003) in owl monkeys trained to detect an increase in the envelope modulation rate of a sinusoidally modulated tone. Although the monkeys' behavioral performance improved with increasing modulation rate, the neural responses were generally suppressed in auditory cortex, although the suppression to targets was weaker than to the standards. Atiani et al. (2014), in their comparison of response changes in primary and secondary cortices in ferrets, found that the increased responsiveness to target sounds in secondary compared to primary cortex took place in the context of a global suppression of firing rates during task engagement. Finally, Buran et al. (2014) described a 26 % reduction in spontaneous activity in auditory cortex neurons during performance of a tone detection task in gerbils. The authors suggest that this response suppression may reflect a neural mechanism to enhance signal-to-noise ratio and thereby lower thresholds for signal detection.

Overall, though, the preponderance of data currently available suggests that, compared to the passive condition, engagement in a behavioral task is accompanied by an enhancement of evoked activity in auditory cortex. The degree of enhancement that is seen is likely influenced by several variables, including methodological differences between studies and differences in salience between task relevant stimuli and measured neural response characteristics, in addition to differences in task difficulty and attentional load. However, much more data is needed to fully understand the effect of task engagement on cortical response properties when detecting and discriminating changes in acoustic stimuli.

Rapid, Adaptive Changes to Receptive Fields and Cortical Representations During Task Performance

In addition to changes to stimulus-driven firing rates and the precision of temporal firing patterns, other recent studies have described adaptive changes in neural response characteristics such as alterations to receptive fields or in the cortical representation of behaviorally relevant sound features. Diamond and Weinberger (1986, 1989) and Recanzone et al. (1993) have shown striking, long-lasting, and adaptive receptive field plasticity in auditory cortex

related to learning (see “[Long-Term Effects of Learning on Neural Response Properties](#)” Section). This kind of plasticity also appears to occur rapidly and in a task-dependent manner during ongoing behavior. For example, in a pioneering series of experiments, Fritz, Shamma, and colleagues showed rapid task-specific alterations of neural response properties in A1 as a result of behavioral training (e.g., Fritz et al. 2003, 2005; Atiani et al. 2009; David et al. 2012; Yin et al. 2014). As in the Atiani et al. (2014) study, ferrets were typically trained on a conditioned avoidance task where they could lick continuously at a water spout during presentation of reference sounds but were required to withhold licking when presented with a pure tone target sound. The task was designed so that a given neuron’s spectrotemporal receptive field (STRF) could be characterized during ongoing behavior through presentation of the reference sounds, which were composed of broadband noises with time-varying, sinusoidally-modulated amplitude spectra (i.e., ripple stimuli). Fritz et al. (2003) showed that attending to a specific target frequency was associated with a rapid change in the shape of the STRF in 72 % of the neurons under study. This change was largely facilitative in nature, either through enhancement at the target frequency or suppression at nearby frequencies, and many of these adaptive changes persisted for hours following the task. When this tone detection task was performed in the presence of a concurrent noise masker, STRF gain decreased during task engagement compared to the passive condition (Atiani et al. 2009). In addition, the STRFs showed enhancements at the target tone frequency that were specific, excitatory, and strongest in cells with BFs near the target tone. These adaptations appear to serve to accentuate the representation of the target tone relative to the noise.

In another series of studies, the authors modified this avoidance task so that the reference sound included a pure tone stimulus, thus requiring the animals to perform a frequency discrimination task (Fritz et al. 2005). Using this paradigm, STRFs showed the same facilitative enhancement at the target frequency, but also showed suppression at the reference tone frequency. These kinds of effects also occurred when the targets were multi-tone complexes, where STRFs showed enhancement at each tone frequency in the complex (with the greatest change occurring at a neuron’s best frequency) and suppression at non-tone frequencies (Fritz et al. 2007). Interestingly, these STRF shape changes are highly dependent on the specific requirements of the training paradigm. In contrast to the results seen using an avoidance task, receptive field changes were reversed when an approach task was employed instead (David et al. 2012; Yin et al. 2014). That is, when ferrets were rewarded for licking at a water spout after presentation of a target sound, STRF’s showed response

suppression at the target frequency and enhancement at the reference frequency. Overall, these studies describe rapid changes in A1 neural response properties that are plastic, adaptive, and specific to the behavioral meaning of presented acoustic stimuli.

In a recent study, Massoudi et al. (2013) suggested that this adaptive plasticity in a neuron’s STRF is probably not a function of task engagement per se, but whether an animal is attending to a specific acoustic feature within a target stimulus. Massoudi et al. (2013) trained rhesus macaques to discriminate a static noise reference sound from various ripple target sounds (stimuli from which they could calculate a neuron’s STRF). These animals, therefore, were required to attend to a change in the amplitude modulation envelope of a noise stimulus rather than a change from a broadband ripple stimulus to a pure tone target frequency (as was the case in the work by Fritz et al. 2003, 2005). Massoudi et al. (2013) showed an increase in both spontaneous and evoked firing rate of neurons in areas A1 and R during task engagement compared to the passive condition, but no change in the STRFs of the recorded neurons. Because the animals in this study were likely not attending to specific acoustic features in the target stimuli (since there were many different ripple stimuli and the animals had to simply discriminate the target sound from a static noise reference), these data suggest that response plasticity in the core regions of auditory cortex may not simply be linked to behavioral relevance of a target sound but, instead, requires behavioral relevance for specific acoustic features of that target sound.

In another example of this kind of learning, gerbils were trained using a Pavlovian fear conditioning paradigm in which a conditioned tone at a neuron’s best frequency was paired with an electrodermal stimulus (Ohl and Scheich 1996). Neural tuning was assessed using unconditioned tones presented between presentations of the conditioned tones. Training on this task resulted in the creation of a notch in the receptive field (i.e., a decrease in response rate) at the conditioned frequency when that frequency was not the neuron’s best frequency.

Finally, task dependent modulation of auditory spatial receptive fields in primary auditory cortex has been reported by Lee and Middlebrooks (2011), who examined a population of units in A1 that showed significantly sharpened spatial tuning during performance of a task that required evaluation of the location of sounds compared to the passive condition. This sharpening primarily resulted from an increase in suppression to sounds occurring at non-preferred locations. Like the changes in neural response properties described by Fritz and colleagues, the changes described by Lee and Middlebrooks (2011) were adaptive and highly plastic, and often occurred within seconds.

Effects of Behavioral Choice on Auditory Cortex Activity

All of these studies have examined several of the important ways in which engaging in a behavioral task can modulate the response properties of A1 neurons in adaptive, task-specific ways. However, the influence of top-down influences, such as an animal's behavioral decision (i.e., whether or not it reports the presence or absence of a stimulus), on auditory neural activity has only recently begun to be investigated. These kinds of questions are typically addressed using a psychometric-neurometric choice-probability analysis, which quantifies the relationship between neural activity and behavioral choice on a trial-by-trial basis (Celebrini and Newsome 1994; Britten et al. 1996). Choice probability analyses are typically used in tasks measuring threshold levels of a stimulus where an animal may respond differentially even though the stimulus itself remains unchanged. Thus, a correlation can be made between an animal's perceptual report and a particular neuron's activity on a given trial.

Several studies that have examined this question report no relationship between neural activity in auditory cortex and an animal's behavioral performance. For example, Hocherman et al. (1976) reported no difference in neural activity between correct and incorrect responses in monkeys as they performed a noise versus tone discrimination task. Similarly, Scott et al. (2007) had examined whether increased neural discriminability for interaural phase differences would also lead to improved behavioral performance, but found no correlation between neural discriminability and percent correct. Lemus et al. (2009) found no significant relationship between performance and neural activity in their acoustic flutter discrimination experiments. In an experiment examining discrimination of fast and slow click train repetition rates, Dong et al. (2011) found no correlation between neural activity in A1 and an animal's behavioral report. Finally, Tsunada et al. (2011) recorded from secondary auditory cortex field AL during an experiment in which macaque monkeys discriminated between human speech sounds and these authors also found no evidence for neural activity that was modulated by behavioral choice.

A few other studies, however, have shown modest correlations between auditory cortical activity and discrimination performance. For example, Selezneva et al. (2006) examined neural activity in both primary and secondary cortices while macaque monkeys listened to sequences of tones. Each tone in the sequence could be either a repeat of the last tone or an upward or downward change in frequency. Monkeys were required to respond to a downward frequency step, regardless of the tone's absolute frequency value, by releasing a bar. The authors reported

that slow modulations of tonic firing seen during performance of this auditory categorization task were predictive of both the correct and incorrect behavioral decisions of the monkeys. These modulations were not seen in the monkeys that were not actively performing the task. Bizley et al. (2013) also showed correlations between neural activity measured in auditory cortex and behavioral choice in ferrets while performing a pitch discrimination task. They found that an activity relating to an animal's subsequent choice is increasingly reflected throughout stimulus presentation, reaching a maximum just prior to the behavioral report.

Niwa and colleagues have reported significant choice-related activity in auditory cortex of monkeys discriminating amplitude modulation (Niwa et al. 2012b, 2013). Animals were presented with two sounds and trained to release a response lever if the second sound contained AM, and to continue to hold the response lever if the second sound contained no AM. In A1, ~50 % of multi-units and ~23 % of single units showed significantly greater firing on those trials in which an animal reported the presence of AM compared to those trials in which an animal reported no AM, with the greatest increase measured for those neurons most sensitive to AM (Niwa et al. 2012a). As in Bizley et al. (2013), the influence of an animal's behavioral choice was highest just prior to lever release. Neurons in the secondary field ML showed more variable responses compared to A1, including both increases and decreases in firing rate in response to greater AM depth and a more labile relationship between neural activity and behavioral choice.

Long-Term Effects of Learning on Neural Response Properties

The studies described so far have examined the behavioral modulation of neural activity exclusively during task performance. Other work has attempted to address the time course of these changes, with a particular focus on the long-term effects of these reported changes. For example, Recanzone et al. (1993) showed that owl monkeys trained on a frequency discrimination task for several weeks showed an increase in the auditory cortical representation of behaviorally relevant frequencies after training. Compared to both naïve monkeys and control monkeys who heard the same stimuli but were trained on a tactile discrimination task, the animals trained on the auditory discrimination task showed enhanced tonotopic representation in A1, greater sharpness of tuning, and shorter response latencies for those frequencies used in the task. Similar kinds of frequency-specific receptive field changes have been described using classical conditioning procedures in

cat non-primary auditory cortex (Diamond and Weinberger 1986, 1989) and guinea pig A1 (Bakin and Weinberger 1990). Additionally, the adaptive changes in neural response properties described by Fritz et al. (2003, 2005) lasted for at least up to several hours after the end of task performance.

Bao et al. (2004) also showed long term improvements in the temporal dynamics of rat auditory cortex neurons as a result of behavioral training. Rats were trained to find a randomly and arbitrarily chosen target location in a circular “sound maze” using only the temporal repetition rate of continuously presented noise bursts as a cue. Temporal repetition rate thus varied with the animal’s distance from the target; rates increased as the animals’ distance decreased. After training, neurons in A1 showed greater stimulus-driven evoked activity to high-rate noise pulses and stronger phase locking. Control animals that listened to the same stimuli but did not engage in the task did not show such changes.

A study by Polley et al. (2006) further showed that this kind of cortical plasticity is modulated by task-specific attentional demands in both primary and secondary auditory cortex. In their task, Polley et al. (2006) trained rats to selectively attend to either the frequency or the intensity of sounds that varied across both of these stimulus dimensions. They did this by differentially reinforcing the animals for responding to either a specific frequency (independent of intensity) or a specific intensity (independent of frequency). After training, they found increases in the cortical representation of the task-relevant, but not the task-irrelevant, stimuli. For example, rats trained to attend to intensity as the relevant dimension exhibited a greater proportion of neurons with best levels in the trained intensity range while tonotopic representations were not significantly different from frequency-trained rats and controls. When frequency was the relevant dimension, there was a greater proportion of neurons with characteristic frequencies in the trained frequency range compared to intensity-trained rats and controls.

A different type of response modulation has been reported during a more complex, categorical learning paradigm. Ohl et al. (2001) examined the categorization of frequency-modulated tones (FM sweeps) in Mongolian gerbils trained using an avoidance procedure. Animals were trained to discriminate the difference between rising versus falling FM sweep pairs regardless of the sweep frequency range. When animals were trained to successfully discriminate one set of FM pairs, a novel pair was introduced. At first, each new pair required relearning of the task requirements (i.e., performance initially returned to chance levels). Over the course of several weeks, however, animals began to respond to novel sweeps correctly without needing to relearn the task. The animals had thus

formed two perceptual categories, rising FM and falling FM, into which any novel stimulus could be immediately and correctly classified regardless of its particular frequency range. Interestingly, the formation of these perceptual categories was mirrored in changes to spatiotemporal activity patterns of neurons measured in auditory cortex. That is, the activity pattern of each neuron that was measured for each within category stimulus (e.g., each rising FM stimulus) was initially very distinct before the animals had learned the relevant category dimensions. However, once category formation had occurred, the neural activity patterns for all within-category stimuli became very similar, while activity patterns for between-category stimuli had become highly dissimilar.

Selezneva et al. (2006), in their study of categorical learning of tone sequences described above, showed changes in neural activity in macaque monkeys that persisted for a period of up to 2 years during and after category formation. Neurons in both primary and secondary cortices and during both active and passive conditions, showed greater evoked activity in response to the reward-associated frequency downward steps compared to non-rewarded upward steps. These changes were not seen in naïve animals. The authors argue that this differential neural responsiveness to the “downward” versus “upward” categories may be a permanent, reward-induced change and likely represents the physiological underpinning of these animals’ learned perceptual categories.

Comparison with Visual and Somatosensory Systems

How brain activity gives rise to perception is one of the principal questions that the field of behavioral neuroscience seeks to answer. Much of the experimental work that has addressed this question has historically come from either the visual or somatosensory modalities, where precise control over the sensory stimulus, the perceptual experience of that stimulus, and measurement of the neural response to that stimulus has been achieved with the highest rates of success.

Several experimental results from the auditory system share intriguing similarities with those reported for the somatosensory system. For example, Hyvarinen et al. (1980) reported that about 16 % of S1 neurons were modulated by behavior when an animal was required to report when a tactile stimulus stopped vibrating, which is a proportion of units similar to what has been widely reported in auditory cortex. Also, in a series of somatosensory studies which parallel work done in the auditory system, monkeys were trained to discriminate between the mechanical vibration produced by two different repetition rates of tactile stimulation by responding if

the frequency of the second stimulus was higher than that of the first (Romo et al. 1998; Hernández et al. 2000; Salinas et al. 2000; Luna et al. 2005). Stimulus driven firing rates of neurons in primary somatosensory cortex (S1), like those in A1, were modulated by different stimulus repetition rates and had rate-based neurometric thresholds that were very similar to measured psychophysical thresholds. Thus, both S1 and A1 seem to use nearly functionally identical firing rate-based neural codes for discriminating stimuli that vary in repetition rate during a behavioral task. Also, neurons in secondary somatosensory cortex (S2), like those reported by Niwa et al. (2013) in nonprimary auditory fields, showed a dual code where firing rate could either increase or decrease with stimulus frequency.

Other work in the somatosensory system has described further effects of task engagement and selective attention on neuronal firing in S1 and S2. For example, in one study a rhesus monkey was trained to perform two behavioral tasks, a tactile discrimination task and a visual detection task. The discrimination task required the monkey to respond when a raised letter matched a visual image. Presentation of the tactile stimuli continued during performance of both tasks. Neural activity was recorded in response to the tactile stimuli as the animal switched its attention between the two tasks (Hsiao et al. 1993). Significant differences in evoked responses between the tactile and visual tasks were seen in ~50 % of neurons in S1 and ~80 % of neurons in S2. Further, S1 exclusively showed response enhancement while responses in S2 were more variable and showed both enhancement and suppression effects. In a follow-up study using similar methodology, Steinmetz et al. (2000) examined the effect of selective attention on neural synchrony in S2. These authors showed that most neuron pairs in S2 fired synchronously and the degree of synchrony was related to an animal's attentional state. They described 35 % of neuron pairs changing their degree of synchrony (80 % of the affected pairs increased synchrony while 20 % decreased) as the monkeys switched between the two tasks.

Compared to the auditory system, there is a richer history of studies exploring behavioral and attentional mechanisms in the visual system (for a review, see Reynolds and Chelazzi 2004 or Carrasco 2011). For example, work by Desimone and colleagues in macaque visual cortex has described attentional modulation of neural responses throughout the ventral processing stream, which encodes information for object identification and recognition (e.g., Moran and Desimone 1985; Luck et al. 1997; Reynolds et al. 1999, 2000; Fries et al. 2001). Typically, a neuron's responses are measured with one or more visual stimuli inside the neuron's receptive field while the monkey attends to a location outside the

receptive field. The animal is then cued to shift attention to the stimulus (or one of multiple stimuli) within the receptive field. These studies have shown that the neural response to visual stimuli in the ventral processing stream are determined primarily by the attended-to stimulus, even when multiple competing stimuli appear within a receptive field, and that the influence of non-attended stimuli is effectively filtered out of the neuronal signal.

Similar to experiments performed on the auditory system, a large body of this work has served to highlight rapid, adaptive, task-dependent changes that apparently function to enhance visual processing. Indeed, numerous studies have shown that directing attention to a spatial location or to a distinguishing feature of a stimulus serves to enhance both its discriminability and the evoked neural response, reduces the variability of neural spiking, and increases neural synchrony (Reynolds et al. 2000; Fries et al. 2001; Martinez-Trujillo and Treue 2002; Chen et al. 2008). In a recent study, Anton-Erxleben et al. (2009) showed that attention also results in the adaptive shifting and shrinking of a neuron's receptive field around an attended stimulus. In this study, the authors trained macaques to attend to either a preferred or a non-preferred stimulus, both of which were presented within a cell's receptive field. Neurons in area MT showed enhanced responses to the preferred stimuli when attended to and suppressed responses when non-preferred stimuli were attended to. This differential response pattern resulted in an average decrease of ~5–10 % in the spatial size of MT receptive fields as a function of attention. Like the adaptive, plastic changes seen by Fritz and colleagues in their examination of STRF changes during behavior, which are likely useful for increasing frequency resolution for attended sounds, Anton-Erxleben et al. (2009) have suggested that these adaptive changes serve to increase a neuron's visual spatial resolution, thus allowing for a more fine-grained analysis of an attended scene.

Results from A1 describing a poor correspondence between neural activity and behavioral choice are also consistent with previous neurophysiological observations in both the somatosensory and visual systems. Several studies have examined neural activity in S1 of monkeys that were trained to discriminate different frequencies of vibrotactile stimuli (Hernández et al. 2000; Salinas et al. 2000; Luna et al. 2005). In those experiments, neural activity in S1 did not correspond to an animal's perceptual performance. Instead, activity related to the comparison between the two stimuli appeared to be localized to higher processing centers such as S2 and prefrontal cortex (Romo et al. 1999, 2002; Salinas et al. 2000; Brody et al. 2003). A related experiment in the visual system showed that behavioral choice significantly influenced neural activity in V2, but not in V1 (Nienborg and Cumming 2006).

Summary

There have been a number of studies over the last 50 years investigating the effect of behavioral modulation of auditory cortical response properties. In general, these studies have shown that neurons located throughout the auditory cortical hierarchy display fast, adaptive, long-lasting changes in their neural response properties as a result of engaging in an auditory task. The most commonly reported effects tend to involve increases in stimulus-driven evoked activity in response to task-relevant sounds and decreases in evoked activity to task-irrelevant sounds, although there also appears to be differences between primary and non-primary areas in the amount of response enhancement that is reported. There is evidence that engaging in a discrimination task can also improve neural discrimination in some auditory cortex neurons (Niwa et al. 2012a, b). Neuronal response properties also change in adaptive ways to meet specific task demands, including the selective enhancement and suppression of receptive fields during task performance and more complex changes in spectrotemporal neural activation patterns in response to the acquisition of novel acoustic categories. Training on a tone discrimination task, for instance, can cause shifts in a neuron's best frequency toward the target tone frequency and an increase in the number of cells that represent that frequency (e.g., Recanzone et al. 1993). Such training can also result in an increased contrast between a neuron's responses to the different task-relevant frequencies through differential enhancement and/or suppression (e.g., Fritz et al. 2003, 2005, 2007; Witte and Kipke 2005). These data stand in contrast to the traditional view of auditory cortex as a hierarchical series of static processing stages and, instead, recast these structures as highly plastic and adaptive, where processing at all stages is continuously influenced by the changing perceptual and cognitive demands of a behaving animal.

Although there is now strong evidence that neural responses across auditory cortex are dynamically modulated during active behavior, there remains several important issues that need to be addressed in the coming years in order to more fully understand how cortical activity gives rise to auditory perception. For example, findings from different studies showing that behavior can either enhance or suppress both evoked and spontaneous firing rates is somewhat puzzling. Although most studies have seen increases in firing rates, there are several that have reported the opposite effect. The specific changes that have been observed appear to depend, at least in part, on the particulars of task structure and/or the behavioral difficulty of the task. For example, increases in spontaneous firing rates have been reported during complex categorization tasks (e.g., Rodgers and DeWeese 2014) while decreases in

spontaneous rates have been described during simpler detection and discrimination tasks (e.g., Buran et al. 2014; Atiani et al. 2014). Similarly, Beaton and Miller (1975) described an enhancement of evoked responses when an animal performed a frequency discrimination task which was greater than the enhancement measured as it performed a simpler detection task. David et al. (2012) has shown that the behavioral meaning of a stimulus (shock vs. reward) can drive neural responses in opposite directions. Thus, it is likely that procedures with different cognitive and attentional demands (i.e., detection, discrimination, categorization) or different task structures (i.e., approach vs. avoidance) will produce different neural responses and, therefore, potentially conflicting descriptions of how cortical activity is modulated by task performance.

One factor that has not been carefully examined in previous studies is the dependency of neural responses on the nature of the acoustic stimuli that drive these responses. There is often a big gap between the analyses of behaviors and those of neural responses. While an animal's behavioral response results from the working of the entire auditory system, including cortex (and other brain regions as well), typical neural analyses only probe more restricted elements of auditory cortex (i.e., individual neurons). A sound that an animal is trained to detect or discriminate may not be the stimulus that a recorded neuron responds to or responds to optimally. Wang et al. (2005) showed that an auditory cortex neuron's firing pattern is associated with the optimality of acoustic stimuli, with preferred stimuli driving a neuron to sustained firing and non-preferred stimuli evoking transient or no responses. How behavioral task engagement differentially modulates sustained and transient responses at the level of a single cortical neuron is unknown. It is possible that some variability in how behavior modulates auditory cortex neurons results from the relationship between a neuron and the sound stimulus used in the behavioral task. One may speculate that a neuron would show enhanced responses to its preferred stimuli and suppressed responses to its non-preferred stimuli.

Recent results by Niwa et al. (2012a) support the idea that the presentation of a given neuron's preferred stimulus may enhance that neuron's responsiveness during task engagement. These authors showed that, during an AM discrimination task, neurons in A1 with the greatest choice-related increase in firing rate in response to the presentation of an AM target (compared to an unmodulated reference sound) were those that were also most sensitive to AM. This result is consistent with other studies from the visual system (e.g., Moran and Desimone 1985; Celebrini and Newsome 1994; Britten et al. 1996) and suggests that choice-related activity for a particular stimulus is higher for those cells that encode a particular parameter relevant to the task. These units, as the authors argue, are thus more

likely to be involved in not only coding the relevant stimulus features, but also either driving the behavior itself or receiving top-down input from higher brain regions involved in task performance.

We have a fairly good understanding of how behavior modulates auditory cortical responses in A1, yet the role of behavior in nonprimary areas remains to be satisfactorily described. There is some evidence that belt regions show enhancement in both spontaneous (Gottlieb et al. 1989) and evoked (e.g., Dong et al. 2013; Atiani et al. 2014) firing rates and there is also good evidence that this area is the first location in the ascending auditory hierarchy to show responses governed by an animal's choice behavior (e.g., Niwa et al. 2013). However, the number of responsive neurons reported in belt are often far fewer than those in A1, probably because neurons in belt are often more selective than those in A1 (e.g., Rauschecker et al. 1995). Further, we have no data describing the response properties of parabelt neurons, which is particularly troubling since it is commonly assumed that parabelt regions are likely even more behaviorally sensitive than belt regions. Information ascending the auditory hierarchy flows from belt to parabelt before finally moving to frontal areas associated with more complex auditory perception (Gifford et al. 2005; Cohen et al. 2006), and thus we expect greater behavioral modulation of neural responses as we move further from A1. We will need to understand the response properties of these higher auditory areas, especially parabelt, if we are to generate stimuli that are better able to evoke responses from across these multiple areas.

Studies examining the processing of sound across the auditory cortical hierarchy could also benefit from examinations of population-level firing patterns such as the local field potential (LFP) and synchronization of cortical oscillations both within and between different functional regions of auditory cortex. For example, a recent study by Mesgarani and Chang (2012) using human intra-cranial recordings showed that the LFP could be modulated by attention to speech or voice content. Further, power in the gamma band of the LFP appears strongly tied to cognitive and attentional mechanisms and thus could provide a useful means of assessing task-related processing across auditory regions (Lakatos et al. 2008; Schroeder and Lakatos 2009; Schroeder et al. 2010; Bosman et al. 2012). As noted earlier, however, these kinds of non-invasive studies do not directly measure or only measure gross neural responses and are therefore inherently limited in their ability to describe underlying mechanisms of neuronal suppression or enhancement.

Overall, though there is much that we have come to understand regarding the behavioral modulation of auditory cortical responses. Fast, adaptive, long-lasting plasticity in firing rates and receptive fields are now believed to

be a common feature in the auditory cortex of an awake, behaving animal as it interacts with its acoustic environment. These changes apparently serve to highlight behaviorally relevant stimuli and increase the signal to noise ratio of attended sounds. However, there is much more that we need to understand regarding what drives the specific neural response (i.e., suppression vs. enhancement), how changing behavioral requirements (e.g., task difficulty) further modulates brain activity, and the influence of behavior on secondary auditory areas, including parabelt. Future studies addressing these kinds of questions will help better elucidate the various ways that behavior influences brain activity in auditory cortex.

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