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# Engaging in an auditory task suppresses responses in auditory cortex

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**Although systems that are involved in attentional selection have been studied extensively, much less is known about nonselective systems. To study these preparatory mechanisms, we compared activity in auditory cortex that was elicited by sounds while rats performed an auditory task ('engaged') with activity that was elicited by identical stimuli while subjects were awake but not performing a task ('passive'). We found that engagement suppressed responses, an effect that was opposite in sign to that elicited by selective attention. In the auditory thalamus, however, engagement enhanced spontaneous firing rates but did not affect evoked responses. These results indicate that neural activity in auditory cortex cannot be viewed simply as a limited resource that is allocated in greater measure as the state of the animal passes from somnolent to passively listening to engaged and attentive. Instead, the engaged condition possesses a characteristic and distinct neural signature in which sound-evoked responses are paradoxically suppressed.**



Using sensory cues to drive purposeful activity requires sufficient levels of arousal and attention. The neural mechanisms of arousal have been studied by comparing neural activity in an awake state with activity recorded during sleep or anesthesia[1–4]. These studies have revealed that the neural signatures of unaroused brain states, including slow wave and REM sleep, are different from those of the awake condition.

Attention is itself complex, consisting of a well-defined selective component and a much less well-defined component encompassing arousal, vigilance and sustained attention. The neural mechanisms of selective attention have been studied in procedures in which a subject must base its behavior on one out of several sensory stimuli. These studies reveal that selective attention has a characteristic neural signature that typically consists of an increase in responsiveness to the attended stimulus[5–10].

In contrast with the extensive body of literature on sleep and selective attention, little is known about the neural correlates of the nonselective components of attention[11]. To study the neural correlates of one of these nonselective components in auditory cortex, we compared cortical activity that was elicited by auditory stimuli in rats engaged in an auditory task with activity that was elicited by identical stimuli when a rat was passive but wakeful; we use the term 'engaged' to refer to this nonselective component. We found that engaging in an auditory task suppressed stimulus-evoked responses in the auditory cortex, in contrast with selective attention, which, consistent with previous reports, enhanced responses. We propose that suppression represents the wakeful baseline condition on which other forms of attentional and nonattentional modulation are superimposed.

## RESULTS

First, we compared responses that were elicited by acoustic stimuli in the auditory cortex when the rat was passive with those that were elicited when it was engaged. Second, we examined the responses in the auditory cortex that were elicited by auditory stimuli during an intermodal (auditory olfactory) selective-attention task. Third, we compared responses during sleep and under anesthesia. Fourth, we compared cortical responses in the passive versus the engaged condition in a modified version of the task in which the subject did not initiate trials. Finally, we compared passive and engaged responses in the auditory thalamus.

### Responses are suppressed in the engaged condition

We trained adult male Long Evans rats to perform a two-alternative choice auditory-discrimination task[12,13]. The rat initiated a trial by inserting its nose into the center port of a three-port operant chamber (**Fig. 1a** and Methods). After a waiting period ($\sim$2 s), a target sound was presented from either the right or the left side of the box, indicating which goal port (right or left) would be rewarded with water. The target stimulus consisted of a 300-ms broadband stimulus that was presented monoaurally from either the right or the left speaker. Later in the training phase, we introduced nontarget stimuli during the waiting period, which allowed us to probe the response to the nontarget stimulus without retraining the rat on a new target. The nontarget stimulus consisted of a train of clicks (5-ms white noise bursts, repetition rate from 2–35 Hz, a range over which cortical responses show strong modulation[14,15]) that were presented diotically for 1.8 s, beginning after a variable (400–600 ms) period following trial initiation. The onset of the nontarget stimulus was randomized with respect

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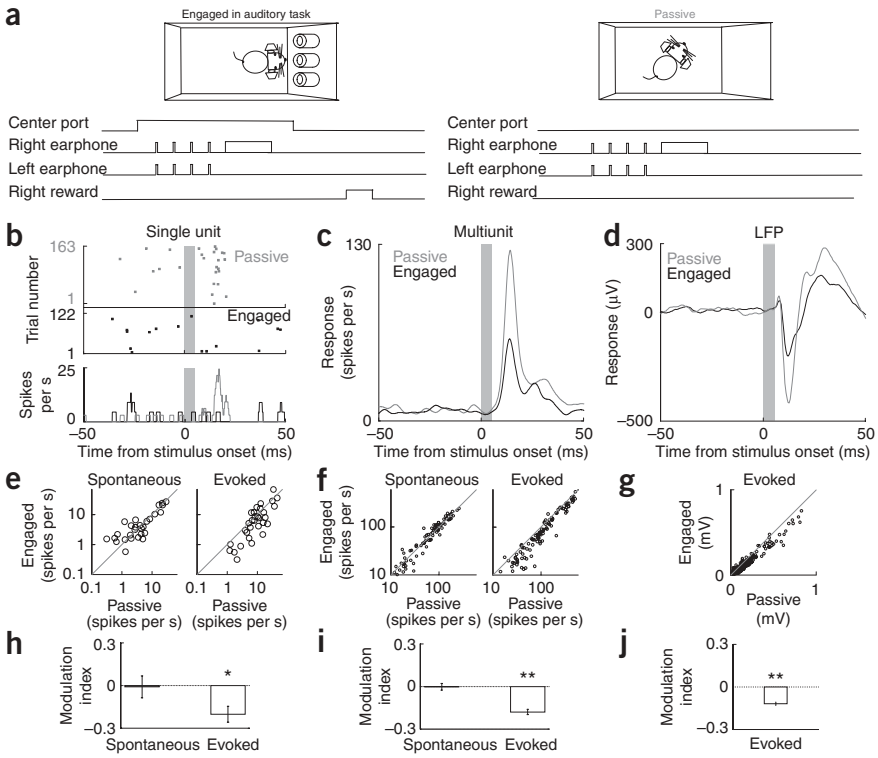


**Figure 1** Cortical evoked responses are suppressed in the engaged condition, but spontaneous activity is unchanged. (**a**) Rats implanted with earphones performed a two-alternative choice auditory task (Task 1) for ~30 min (engaged period). The rat initiated a trial by poking its nose into the center port. Before and after the engaged period, the ports were blocked and the same stimuli were presented (passive period). (**b**–**d**) Examples of single unit, multi-unit and LFP responses elicited by the first stimulus (gray bar) showing suppression in the engaged condition relative to the passive condition. (**e**–**j**) Population responses of single units, multi-units and LFPs, respectively. The data are presented as scatter plots comparing passive and engaged activity across the population (**e**–**g**) and modulation index (**h**–**j**; $(\text{Activity}_{\text{engaged}} - \text{Activity}_{\text{passive}})/(\text{Activity}_{\text{engaged}} + \text{Activity}_{\text{passive}})$) for spontaneous and evoked activity. Because LFP changes were assessed by changes in the stimulus-evoked peak, LFP spontaneous activity was not analyzed in **g** and **j**. (* $P < 0.05$ different from 0, ** $P < 0.001$ different from 0). Error bars represent s.e.m. in this and the following figures. For a more detailed legend, see **Supplementary Table 1** and **Supplementary Methods**.

to the nose poke so the rat could not predict the stimulus onset precisely. After that rats reached criterion performance (>95% correct, ~1 week), we implanted movable tetrodes in the left primary auditory cortex (area A1) to record neural activity, including single-unit responses, multi-unit responses and local field potentials (LFPs). We also implanted earphones to ensure delivery of a controlled auditory stimulus to the unrestrained rat, regardless of its position in the box.

We first compared sound-evoked neural activity when the rat was engaged in the task with activity that was elicited by the same stimulus when the rat was passive but not asleep (see **Supplementary Methods** and **Supplementary Fig. 1** online). Because the sounds were delivered through headphones, differences in neural activity in this procedure must be the results of differences in the rat's behavior or state rather than of differences in the stimulus itself arising from uncontrolled changes in the sound path from speaker to the ear. We expected that engagement in an auditory task would, as with selective attention, lead to an enhancement of stimulus-evoked responses in the auditory cortex[8,16–19]. However, we found just the opposite; in the engaged condition, neural responses to all components of the stimulus, both target and nontarget, were consistently suppressed.

We analyzed the responses that were elicited by the first nontarget stimulus (**Fig. 1b–d**). Suppression of the sound-evoked response was observed for most of the responsive (**Supplementary Methods**) single units ($P < 0.01$; **Fig. 1e**). Suppression was also observed for measures of neural population activity, including multi-unit activity ($P < 1 \times 10^{-16}$; **Fig. 1f**) and evoked LFP ($P < 1 \times 10^{-16}$; **Fig. 1g**). We quantified these effects across the population with a modulation index, defined as $(\text{Activity}_{\text{engaged}} - \text{Activity}_{\text{passive}})/(\text{Activity}_{\text{engaged}} + \text{Activity}_{\text{passive}})$. The modulation index ranges from −1 (complete suppression in the engaged condition) to +1 (complete suppression in the passive condition). The modulation index was substantially negative for all three physiological measures of the evoked response (**Fig. 1h–j**), indicating that engaging in an auditory task reduced the number of spikes used for stimulus representation. This suppression of evoked responses was not accompanied by any change in the spontaneous activity preceding stimulus presentation (**Fig. 1b,c,e,f,h,i**), in contrast with other studies reporting an increase in spontaneous activity with task engagement[19]. There was no change ($P > 0.2$) in neural activity between the first and second passive block of trials (that is, between the passive block before and after the engaged block), indicating that suppression was not a result of nonstationarities in the recording, satiety, reward expectation, arousal, etc. (see **Supplementary Analysis** online).

Although most single units showed a suppression of evoked activity in the engaged condition, a minority showed an increase (8 out of 32 units). This had the effect of concentrating the stimulus-evoked spikes into a smaller population of neurons, each with a relatively higher firing rate. We quantified this concentration of activity in terms of the kurtosis, which is a measure of the sparseness of a neural representation. The kurtosis of the firing rate distribution in the engaged condition was greater than in the passive condition ($\text{kurtosis}_{\text{engaged}} = 8.4 \pm 2.4$ versus $\text{kurtosis}_{\text{passive}} = 4.1 \pm 0.7$, $P < 0.05$; see **Supplementary Analysis**), indicating that the stimulus representation in the engaged condition was sparser.

We next analyzed the responses to the remaining stimuli (**Fig. 2**). As has been previously reported[14,15], responses to the click train diminished (**Fig. 2a**) as a function of repetition rate. At all but the highest repetition rates, however, the responses in the engaged condition were suppressed relative to the passive condition (**Fig. 2b**). Thus, suppression interacted with repetition rate but was not limited to the initial stimulus.

Finally, we analyzed the response to the target stimulus. The train of nontarget (diotic) stimuli preceding the target provided no information about the location of the reward and was therefore irrelevant to the performance of the task; only the final (monaural) target stimulus was relevant and required the rat to attend to it. This raised the possibility that a model in which the rat selectively withdraws its attention before the onset of the target stimulus could explain the

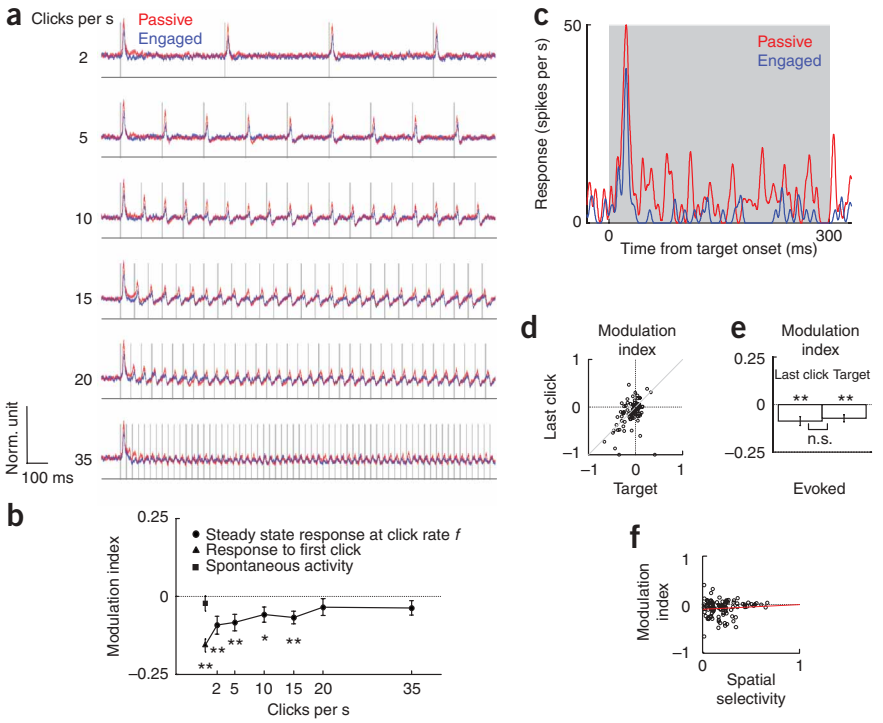


**Figure 2** Decision-relevant target is suppressed in engaged condition. (**a**) Responses evoked by clicks (that is, task-irrelevant distractors) were attenuated at higher repetition rates in both the engaged (blue) and passive (red) conditions (Task 1). The traces show the average normalized peristimulus time histogram (PSTH) of cortical multi-unit responses ($n = 60$ sites) to six different repetition rates. Line thickness is proportional to s.e.m. (**b**) Task-dependent suppression (modulation index) of the click-evoked responses decreased at higher stimulation rates. The square and triangle symbols indicate the modulation index for spontaneous firing and the first stimulus, respectively. (**c**) Example of a multi-unit cortical response to contralateral task-relevant stimulus. Responses to ipsilateral stimuli were generally weak and were not analyzed. (**d**,**e**) The modulation of the target stimulus was correlated with the modulation of the preceding (task irrelevant) stimulus (**d**) and had a comparable magnitude (**e**). (**f**) Spatial selectivity and task-engaged suppression were statistically uncorrelated (regression line in red), indicating that selective responses were not preferentially enhanced during the task. Spatial selectivity was calculated between the left and right target stimulus during the passive condition. We quantified the spatial selectivity using the absolute selectivity, defined as $2 \times |\text{area under the response operating curve} - 0.5|$ (ref. 50). This quantity is zero if the response was not selective between the left and the right target stimulus and 1 if the response was perfectly selective (see also **Supplementary Fig. 2**). Error bars represent s.e.m. * $P < 0.05$ different from 0, ** $P < 0.001$ different from 0.





previous results. According to this hypothesis, suppression would be limited to the nontarget stimuli and the response to the relevant target stimulus would be enhanced. However, the response to the target stimulus was not enhanced (**Fig. 2c**; see also **Supplementary Fig. 2** online). Instead, the suppression of the responses to the target stimulus was indistinguishable (**Fig. 2d**,**e** and **Supplementary Fig. 2**) from that of the last nontarget stimulus in the stimulus train (paired $t$ test, $P > 0.1$). The absence of response enhancement to the target stimulus is consistent with the modest attentional load in this task; had the attentional load been greater, the suppression might have been attenuated or even converted into enhancement (assuming that attentional mechanisms are distinct and additive). The equal suppression associated with target and nontarget stimuli and the lack of correlation between suppression and target selectivity suggests that engagement induces a widespread suppression of evoked activity on which any selective attentional effect is superimposed.

### Intermodal attention does not suppress responses in cortex

Comparing the passive and engaged conditions revealed that sound-evoked responses were suppressed when the rat was engaged in an auditory task relative to those that were evoked when it was not performing the task. However, this comparison did not clarify the key difference between the two behavioral conditions. One possibility was that, as suggested above, the key difference was whether the rat was engaged or passive; according to this hypothesis, suppression resulted simply from engaging in the task, regardless of the modality of the task. Alternatively, the suppression might result specifically from the engagement of the auditory cortex in this auditory task. Although this hypothesis would seem to contradict the intuitive expectation that engaging should increase rather than decrease neural activity, it is compatible with our data and makes the clear prediction that suppression in auditory cortex should not be observed if the rat were engaged but attending to a stimulus from a different sensory modality.

To distinguish these possibilities, we trained an additional group of five rats on an intermodal attention task[20] in which we could compare sound-evoked responses elicited in auditory cortex when the rats were engaged in an auditory task with responses that were elicited by the same sounds when the rats were engaged in a nonauditory (olfactory) task (see Methods). An auditory stimulus and an olfactory stimulus were presented simultaneously on every trial. To increase the difficulty of the task, and thereby increase the likelihood of detecting an effect of selective attention[21], we used a tone-discrimination task that was substantially more challenging (~3 weeks of training, performance ~80%) than the spatial-discrimination task (~1 week of training, performance >95%) presented above. Trials were grouped into olfactory and auditory blocks (~50–70 trials each) in which the rat was rewarded for basing its decision on either the olfactory or the auditory stimulus, respectively. We reasoned that if the suppression that we observed in the engaged condition were specific to engaging in an auditory task, then responses in the auditory block would be suppressed relative to those in the olfactory block, whereas if suppression were not specific to the auditory nature of the task, then no difference would be observed between the two conditions. In these experiments, we defined the modulation index as $(\text{Activity}_{\text{auditory block}} - \text{Activity}_{\text{olfactory block}})/(\text{Activity}_{\text{auditory block}} + \text{Activity}_{\text{olfactory block}})$.

There was no net suppression of sound-evoked responses elicited during the auditory block compared with those elicited during the olfactory block (**Fig. 3a**,**b**). Spontaneous activity was also not affected. Indeed, there was a slight, albeit nonsignificant ($P = 0.34$) trend toward enhancement in the auditory block, as expected from recordings in an auditory area during an auditory task. A subset of single neurons showed strong modulation (either positive or negative) between the auditory and olfactory blocks, so that the very small net change

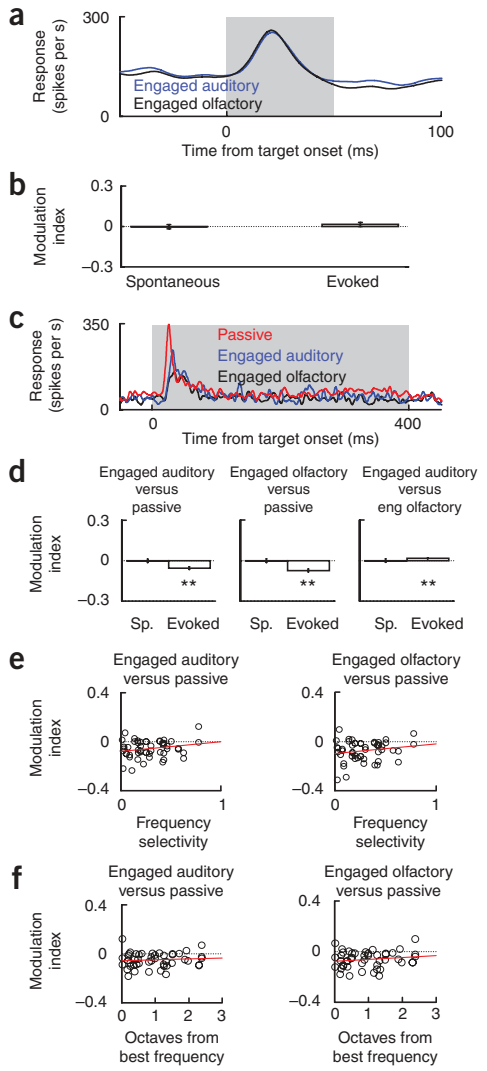


**Figure 3** Evoked auditory responses are not suppressed during an auditory task relative to an olfactory task. (**a**,**b**) Rats performed interleaved blocks (~50–70 trials) of an auditory task (engaged auditory) and an olfactory task (engaged olfactory). In some experiments (Task 3), a passive block was also tested. Auditory stimuli (a high and a low tone) were identical in the two (or three) blocks. An example tone-evoked multi-unit response in auditory cortex shows no difference between the auditory and olfactory blocks (Task 2; **a**). The modulation index $((Activity_{auditory\ block} - Activity_{olfactory\ block}) / (Activity_{auditory\ block} + Activity_{olfactory\ block}))$ showed no difference between the engaged-auditory and engaged-olfactory conditions (**b**, compare engaged versus passive; **Fig. 1**, see also **Supplementary Data** and **Supplementary Methods**). (**c**,**d**) Example PSTH and population data showing that engaged-auditory and engaged-olfactory responses were suppressed relative to the passive condition. (**e**) There was no substantial correlation between frequency selectivity and the (engaged versus passive) modulation index. Frequency selectivity was calculated during the passive condition between the two pure tone stimuli used as targets. We quantified the frequency selectivity using the absolute selectivity, defined as $2 \times |$ area under the response operating curve $-0.5|$) (ref. 50). This quantity is zero if the response was not selective between the high and the low tone and 1 if the response was perfectly selective. (**f**) We measured frequency tuning curves at each site (see **Supplementary Fig. 3**) and found no correlation between the modulation during the task for a particular tone and the distance to the best frequency in octaves. * $P < 0.05$ different from 0, ** $P < 0.001$ different from 0.



between the blocks reflected a balance between the changes in the two conditions (data not shown, see ref. 22). These results are inconsistent with the hypothesis that engaging in an auditory task *per se* suppresses responses in auditory cortex and support the interpretation advanced above that suppression results from engaging in a task, regardless of sensory modality.

As a further test, we compared responses in all three conditions (passive, engaged auditory and engaged olfactory) in a single rat performing another intermodal attention task (see Methods). As expected, sound-evoked responses were suppressed in both the auditory and the olfactory blocks compared with the passive block and responses during the auditory block were not suppressed relative to the responses during the olfactory block (**Fig. 3c**,**d**). Thus, engaging in an auditory task did not elicit a reduction in acoustically evoked responses relative to engaging in an olfactory task, in marked contrast to the robust suppression of acoustically evoked responses relative to the passive condition. We therefore conclude that the general suppression that we observed in the purely auditory task did not depend on the auditory nature of the task.

## Suppression is independent of receptive field properties

In the visual cortex, attention can suppress responses in neurons that are not tuned to the attended feature[23]. As we recorded from several neurons simultaneously in our experiments, we could not optimize the stimulus properties to match the receptive field properties of the recorded neurons. This raised the possibility that the suppression

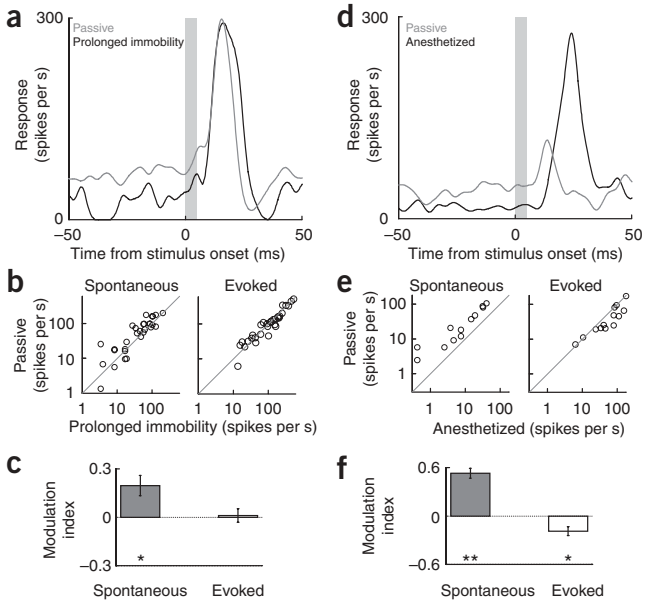


**Figure 4** Changes in arousal and anesthesia have distinct neural signatures. (**a**–**c**) Spontaneous, but not evoked, multi-unit responses were suppressed relative to the passive condition during prolonged immobility, possibly associated with sleep. The modulation index was defined as $(Activity_{passive} - Activity_{prolonged\ immobility}) / (Activity_{passive} + Activity_{prolonged\ immobility})$. (**d**–**f**) Under light anesthesia (ketamine-medetomidine), spontaneous firing rates were also suppressed and evoked responses were enhanced relative to the passive condition. The modulation index was defined as $(Activity_{passive} - Activity_{anesthetized}) / (Activity_{passive} + Activity_{anesthetized})$. * $P < 0.05$ different from 0, ** $P < 0.001$ different from 0.

**Table 1 Summary**

| | Evoked activity | Spontaneous activity |
|---|---|---|
| Auditory cortex | | |
| Passive versus engaged auditory | ↑ | = |
| Passive versus engaged olfactory | ↑ | = |
| Passive versus immobile | = | ↑ |
| Passive versus anesthetized | ↓ | ↑ |
| Engaged auditory versus engaged olfactory | ↑ | = |
| Auditory thalamus | | |
| Passive versus engaged | = | ↓ |

that we observed in the engaged condition was a result of attentional suppression in the majority of neurons that were stimulated suboptimally.

To test this hypothesis, we recorded tuning curves and assessed the relationship between the receptive field and the modulation index of the evoked responses. We expected that if suppression arose from the presentation of suboptimal stimuli, then the modulation index should increase with stimulus selectivity or with the degree to which the best frequency matched the attended frequency. However, there was no correlation between the modulation index and spatial selectivity (**Fig. 2f** and **Supplementary Fig. 2**), frequency selectivity (**Fig. 3e**), or the distance in octaves between the best frequency and the attended frequency (**Fig. 3f** and **Supplementary Fig. 3** online). Notably, suppression was correlated with spontaneous activity, a property of the cells that does not depend on the stimulus used during the task (see **Supplementary Fig. 4** online). In summary, task-engaged suppression cannot be readily predicted from receptive field properties.

### Changes in arousal have a distinct neural signature

Gross changes in arousal, such as those arising from sleep or anesthesia, can cause major changes in neural responsiveness[2,24]. Although we were careful to exclude from the passive condition periods when the rat was immobile for an extended period and therefore possibly drowsy or asleep, the passive condition might nevertheless have been associated with a general decrease in arousal. However, this did not seem likely to explain the suppression that we observed, as the increase in arousal in the engaged condition would have been expected to increase cortical excitability and thereby increase evoked or spontaneous firing rates[2,3,19], effects that are opposite in sign from those we that observed.

To further characterize the differences between the passive condition and previously described changes associated with arousal, we compared neural activity in some sessions in the passive condition to activity recorded either during prolonged periods of immobility that may have included sleep episodes (**Fig. 4a–c**) or during ketamine anesthesia (**Fig. 4d–f**). Spontaneous and evoked cortical activity showed a characteristic neural signature under each condition (**Table 1**): spontaneous cortical activity was reduced in the less-aroused states (sleep and anesthetized) compared with the awake, but passive, condition. The distinct neural signatures associated with sleep and anesthesia indicated that these states were different from the passive, but wakeful, condition.

Previous studies in auditory cortex have shown that self-triggering of auditory stimulus (for example, during vocalizations)[25,26] produces a reduction in the evoked responses compared with when the subject hears the same stimulus without triggering it[27]. In all of the behavioral procedures that we have tested, the rat triggered the stimulus during the engaged condition by inserting its nose in the center port, as opposed to the passive condition, in which the rat did not trigger the stimulus. To test whether self-triggering produced the suppression that we observed in the engaged condition, we trained four rats (**Fig. 5a** and Methods) to perform a Go/No Go task in the head-fixed configuration; in this version of the task, the rat did not trigger the stimulus in the engaged condition, but the stimulus instead started randomly. During the passive condition, the water delivery system was withdrawn and the rat heard the same stimulus as in the engaged condition. We found that evoked responses, both multi-unit (**Fig. 5b–d**) and LFP (**Supplementary Fig. 5** online), were suppressed during the task, without changes in the spontaneous activity. The modulation index of the evoked responses for multi-unit activity was $-0.20 \pm 0.03$ (very similar to the values obtained in the task in **Fig. 1**, $-0.19 \pm 0.02$). We therefore conclude that the suppression observed in the engaged condition does not depend on the rat triggering the stimulus.

### Engagement enhances spontaneous activity in thalamus

What circuit-level mechanisms might be responsible for the suppression seen during engagement? The auditory cortex is modulated by a rich system of neuromodulators and receives input from both lemniscal and non-lemniscal thalamic pathways[28]. To test whether task-engaged suppression was inherited from earlier levels in the auditory hierarchy, we recorded responses in the auditory thalamus (medial geniculate body; see **Supplementary Fig. 6** online) of two additional rats performing the task described above (**Fig. 1**). In contrast with cortex, there was no difference ($P = 0.80$) in the thalamic-evoked response (**Fig. 6a**) between the engaged and passive conditions. However, the thalamic spontaneous activity showed a robust and consistent elevation in the engaged condition ($P < 0.001$; **Fig. 6b,c**). No changes were observed in the burstiness of the thalamic cells (**Supplementary Data** online), in contrast with elevated burstiness that is associated with sleep or reduced arousal[29–32]. This increase in spontaneous activity is consistent with the increase in the cortical LFP power (**Supplementary Fig. 7** online), as the LFP is often assumed to reflect synaptic activity in an area[33,34].

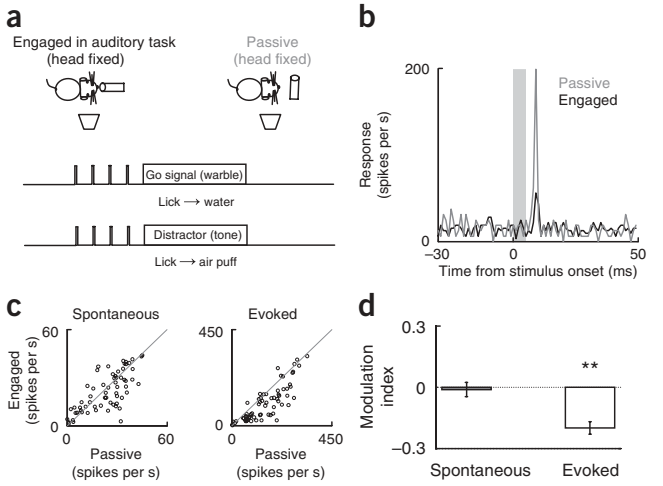


**Figure 5** Suppression of evoked responses is not caused by self-triggering of stimulus. (**a**) Head-fixed rats performed a Go/No Go auditory-discrimination task (Task 4). The stimuli started randomly and were not triggered by the subject. Multi-unit responses in the engaged-auditory condition were compared with those to the same stimuli presented when the water delivery system was withdrawn (passive). (**b–d**) Task-engaged suppression of the evoked response was observed and was comparable to that seen in **Figure 1** (data are presented as in **Fig. 1**; see also **Supplementary Fig. 5** for LFP analysis). * $P < 0.05$ different from 0, ** $P < 0.001$ different from 0.

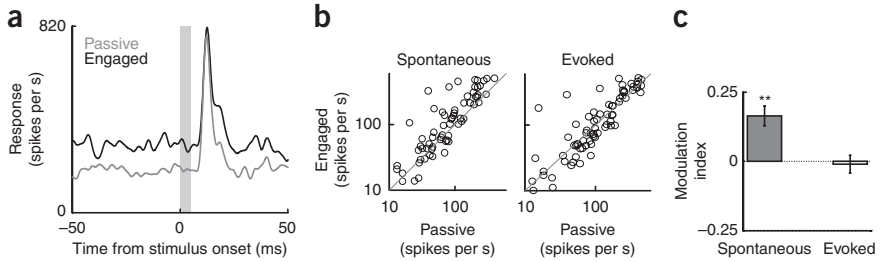


**Figure 6** Neural correlate of engagement differs in auditory thalamus. (**a**) Thalamic spontaneous responses were elevated in the engaged condition (Task 1), but evoked responses were unchanged. Top, example multi-unit thalamic PSTH. Bottom, population analysis (data are presented as in **Fig. 1**). * $P < 0.05$ different from 0, ** $P < 0.001$ different from 0.

Synaptic depression of the thalamocortical inputs[15,35] could explain how the relative enhancement of the thalamic spontaneous rate in the engaged condition might lead to suppression of the cortical evoked response without changing the cortical spontaneous activity. Synaptic depression has previously been implicated in a range of functions in sensory processing, including gain control[36]. Thalamocortical synapses show synaptic depression at high firing rates[15,35]. At sufficiently high firing rates, synaptic release probability is inversely proportional to the presynaptic firing rate[36] ($P_{release} \propto 1/F_{thalamic}$). Under these conditions, the increase in the steady-state thalamic spontaneous firing rate in the engaged condition would not lead to a corresponding increase in the cortical spontaneous rate[24], as the increased thalamic firing rate would be compensated for by a decreased synaptic release probability. Furthermore, evoked responses of identical magnitude in thalamus would lead to relatively depressed responses in the cortex in the engaged condition, as the thalamocortical synapses would be in a more depleted state as a result of the preceding spontaneous activity (for details, see **Supplementary Model** online). Synaptic depression can also account for the reduction in the steady-state modulation index at high stimulation rates (**Fig. 2a**,**b**). Synaptic depression has also been implicated in the barrel cortex, where suppression has been observed during whisking (engaged) compared with quiet wakefulness (passive)[37–39], consistent with our findings; this effect can be mimicked in anesthetized rats by stimulation of the reticular formation or by application of acetylcholine in cortex[40,41] and thalamus[42] (see also **Fig. 4d–f**). Thus, synaptic depression may account for the steady-state changes in the response to repetitive stimuli, but other mechanisms, such as feedforward inhibition or axon excitability[43], may be involved during the first few stimuli at high repetition rates[15].

## DISCUSSION

We have compared sound-evoked responses that were elicited during an auditory task with those that were elicited when the rat was wakeful but passive. We found that the neural signature of task engagement in the auditory cortex was a widespread and robust suppression of the evoked responses for both target and nontarget stimuli, without any concomitant change in spontaneous activity. Experiments using an intermodal auditory-olfactory task, and in sleeping and anesthetized rats, showed that this suppression was specific to engaging in a task and could not simply be explained by different levels of arousal. Finally, we found that spontaneous activity in the auditory thalamus was enhanced during engagement, but evoked responses were unchanged. The thalamic recordings suggest that the mechanism for cortical suppression may involve depression at thalamocortical synapses.

Our central finding that engaging in an auditory task suppressed rather than enhanced activity in the auditory cortex was initially surprising to us for two reasons. First, we expected that if the transition from the wakeful and passive condition to the engaged condition were associated with an increase in arousal, then cortical firing rates would be higher in the engaged condition[1,2]. However, evoked firing rates were lower in the engaged condition and spontaneous rates were unchanged. Indeed, diminished cortical activity consistent with decreased arousal was observed only after prolonged periods of immobility (**Fig. 4**). Furthermore, there was no increase in thalamic bursting in the passive condition, as has been reported with reduced arousal[29–32]. Second, we expected that the difference between the engaged and passive conditions might recruit attentional mechanisms and thereby increase evoked responses (see **Fig. 4** and refs. 5–9). Our results indicate that the passive, but wakeful, condition cannot be viewed simply as a point in a continuum of arousal states from sleep to active to attentive, along which neural excitability increases monotonically; the passive condition instead possesses a characteristic and distinct neural signature. Characterizing this signature represents a first step toward understanding the nonspecific components of attention[11].

Could the suppression that is associated with engagement be explained by previously described selective-attention mechanisms acting on the engaged condition? Selective attention is usually reported to enhance neural responses[5–10] but can also lead to suppression of non-optimal stimuli[23,44]. Because we recorded simultaneously with several tetrodes, we did not explicitly optimize the stimulus for any particular neuron, so most of the neurons from which we recorded were driven suboptimally. However, selectively attending to suboptimal stimuli is not likely to account for the widespread suppression that we found. First, in the intermodal selective-attention task (**Fig. 3**), in which target stimuli were similarly suboptimal, no widespread suppression was observed when the auditory stimulus was selectively attended. Intermodal attention enhanced responses in some auditory cortical neurons and suppressed it in others[20,22], but it did not generate the large population effects that we observed in task-engaged suppression. Second, suppression resulting from engagement was general for both target and nontarget stimulus and appeared to be independent of neural selectivity; responses selective for the location of the sound were not preferentially enhanced during the sound-localization task (**Fig. 2f** and **Supplementary Fig. 2**), nor were responses selective for the sound frequency enhanced during the frequency-discrimination task (see **Fig. 3e**,**f**). Third, the effects of selective attention are often limited to the later components of the response[45], whereas the suppression associated with engagement was evident even in the early onset response (see **Fig. 1** and **Supplementary Fig. 8** online). Task-dependent suppression thus appears to be distinct from, but compatible with, the enhancement resulting from selective attention[6,8], reward[46] or other stimulus-specific processes.

Suppression in the rat barrel cortex is observed during whisking (engaged) compared with quiet wakefulness (passive)[37–39], consistent with our findings. Notably, suppression of visual cortical responses during comparable passive viewing has not been widely reported, perhaps because the requisite visual fixation may represent a form of engagement. This suppression results from the transition from a synchronized to a desynchronized cortical state and can be mimicked by stimulation of the reticular formation or by cortical[24,41] or thalamic[42] application of acetylcholine. However, differences

between the behavioral procedures that we used in this study (sensory discrimination tasks modeled after primate studies) and those used in the barrel system studies (based on active exploration and passive stimulation) preclude a more detailed comparison between these results.

What might be the function of task-engaged suppression? When an animal is engaged in an auditory task, a sensory signal originating in the cochlea must ultimately be routed to motor centers to trigger the appropriate action, whereas the identical signal does not trigger the behavior in the passive condition. Neurons in the rat primary auditory cortex project to a wide range of targets, including the visual cortex, the posterior parietal cortex and the amygdala. Task-engaged suppression may represent an initial stage of this routing, in which activity in neurons that are irrelevant to the task is reduced. In the passive condition, in which no task has been defined, there is no well-defined population of neurons needed for the task, so it may be that the auditory signal is propagated to a wider range of target brain regions. This task-engaged modulation thus appears to be distinct from that observed in selective-attention tasks, in which activity in a subset of neurons representing one stimulus is often boosted relative to that in neurons representing a competing stimulus; in our task the sensory component is far from threshold, so little boosting is needed and suppression emerges as the dominant mechanism. Our results represent a first step toward understanding the synaptic and circuit mechanisms by which this suppression occurs.

## METHODS

**Animals.** All experiments were conducted in a single-walled sound booth (Industrial Acoustics Company). Rats were water deprived under a protocol approved by the Cold Spring Harbor Laboratory Animal Committee (**Supplementary Table 1** online). Subjects in all experiments were adult male Long Evans rats (Taconic Farms), with the exception of Task 4, in which 30–35-d-old rats were used.

**Task 1 (Passive versus engaged auditory).** In the engaged (task) condition, the subject was trained to poke its nose into the center port, thereby triggering the onset of the nontarget stimulus, which consisted of a train of diotic clicks (white-noise bursts, 5-ms duration), followed by the target stimulus. The onset of the train was preceded by a random delay of 400–600 ms. The nontarget stimulus lasted for 1.8 s, after which the target stimulus was presented. The target stimulus consisted of a monoaural, 0.3-s broadband sound, formed by 16 tones between 1 and 16 kHz, that were uniformly distributed in the logarithmic space according to the formula $f_n = 1{,}000 \times (1.203\ldots)^n$ Hz for $n = 0{,}1.15$. The subject remained in the center port until the end of target delivery. The target stimulus indicated the location of the reward port on that trial. Subjects performed a trial every 9.03 ± 0.16 s (mean ± s.e.m.) for ~200 trials per recording session. In the passive condition, the three ports were blocked and the same sequence of stimuli was delivered (every 9.37 ± 0.28 s, mean ± s.e.m., ~100 stimulus repetitions before and ~100 stimulus repetitions after the rat performed the task).

**Task 2 (Engaged auditory versus engaged olfactory).** We first trained the rats to perform an auditory task. The task consisted of the discrimination between two pure tones, delivered free-field at 60–65 dB SPL (sound pressure level) for at least 50 ms. The low tone was chosen in the range of 5–7 kHz and the high tone was chosen in the range of 13–20 kHz. After a subject reached a performance of >90% correct, it was trained to carry out an olfactory-discrimination task that consisted of either the discrimination between caproic acid/hexanol (2 rats), R(−)-2-octanol/S(+)-2-octanol (1 rat) or R(−)-2-octanol/S(+)-2-octanol mixture (ratio of 70/30 versus 30/70, 2 rats). Training of auditory (A) and olfactory (O) discrimination tasks followed steps similar to those described previously[12]. We first trained subjects to perform both auditory and olfactory tasks in alternating blocks (AAA…/OOO…). We then trained rats to perform in alternating auditory-only blocks and olfactory blocks with sound distracters (AA…/OaOa…/AA…), which we refer to as the half-symmetrical task. We then introduced a null odor (caproic acid) in the auditory block and the rats performed a full-symmetrical task (AoAo…/OaOa…/AoAo…). Two rats performed the full-symmetrical task and three rats performed the half-symmetrical task. The results were similar and were pooled together. The blocks lasted for ~50–70 trials. Performance was 81% during the auditory blocks and 91% during the olfactory blocks, indicating that the subjects understood the block structures of the task.

**Task 3 (Engaged auditory versus engaged olfactory versus passive).** We trained subjects to perform a modified version of the intermodal attention task (Task 2). This task used a five-port operant chamber that consisted of upper and lower reward ports on both the right and left sides in addition to the center port. The subject initiated the trial by inserting its nose in the center port, which triggered the stimulus after a variable (150–200 ms) delay. In the auditory block, the auditory stimulus consisted of two components that were presented sequentially. The first component (a diotic 65 dB SPL, 400-ms pure tone, either 5,612 Hz or 15,874 Hz) signaled whether the reward would be available at one of the upper or one of the lower ports. The second component (a monaural broadband sound from either the left or the right earphone presented 560–610 ms after the first) signaled whether the reward would be available from the left or right port. In the olfactory block, the olfactory stimulus also consisted of two components that were presented sequentially, with (+)-fenchone and (−)-fenchone signaling the upper or lower ports, respectively, and R(−)-2-octanol and S(+)-2-octanol signaling the left or right ports, respectively. In the auditory block, only the auditory stimuli were presented, but in the olfactory block, the first component of the auditory stimulus (that is, the 400-ms pure tone) was also presented as a distractor. This design allowed us to compare neural responses to the first auditory component under conditions in which attention was directed toward (auditory block) or away from (olfactory block) the auditory stimulus. In the passive condition, the same auditory stimuli were presented before the rat started the task (~100 stimulus repetitions). During this period, we also measured the frequency tuning (see **Supplementary Fig. 3**).

**Task 4 (Passive versus engaged auditory).** In the engaged-auditory condition, head-fixed subjects performed an auditory Go/No Go task in which they were required to lick a water spout after presentation of a target sound and to refrain from licking after presentation of a distractor sound. Correct licks were rewarded with water and incorrect licks were discouraged with a mild air puff and a short (1–3 s) time out (see ref. 47 for details on training and other task details). The stimulus consisted of a train of ten clicks (20 Hz, 5-ms duration, 58 dB SPL RMS (root mean square), 73 dB SPL peak value) followed either by a nontarget (pure tone, 100 ms, 24,000 Hz) or a target (amplitude-modulated warble, 6,000 Hz carrier, 78 dB SPL RMS, 86 dB SPL peak) stimulus. The intertrial interval was formed by adding 1 s to a time that was chosen randomly from an exponential distribution (1-s decay). In the passive condition, the same stimuli with the same intertrial interval were presented, but the water spout was removed so subjects could not perform the task. The rats performed two blocks of trials that were each ~20 min (engaged periods) with an intermediate period, in which the water delivery system was withdrawn, but the same sounds were played (passive period).

**Surgery.** All procedures were approved by the Cold Spring Harbor Laboratory Animal Committee. Rats were anesthetized with an intraperitoneal injection of a mixture of ketamine (60 mg per kg of body weight) and medetomidine (0.51 mg per kg). Wounds were infiltrated with lidocaine. For tetrode implants in left auditory cortex (12 rats total; **Fig. 1–4**), the temporal muscle was recessed and a craniotomy and a durotomy were performed. Electrodes were implanted between 4.5 and 5.0 mm posterior to bregma and 6.4 mm left of the midline. For implants in left auditory thalamus (2 rats; **Fig. 6**), the coordinates were between 5.5 and 6.0 mm posterior from bregma and 3.2 to 4 mm left of the midline. The electrodes were advanced to a depth of 4 mm from the brain surface. We also attached a plastic ring next to, but not touching, each pinna, which we could use to screw the earphones into place. After surgery, rats were left to recover for several days before resuming water deprivation. The surgery for the head-fixed behavior has been described previously[48]. Briefly, four young

rats (~60 g) were implanted with a well over the left auditory cortex and a post for head fixation.

**Electrophysiology.** For the freely moving rats, we implanted polyimide-coated nichrome wires (H.P. Reid, wire diameter of 12.5 μm) that were twisted in groups of four as tetrodes (each wire was gold plated to <0.5-MΩ impedance at 1 kHz). We implanted six independently movable tetrodes using a custom-built drive. We recorded spiking activity and LFPs with a Cheetah32 32 Channel System (Neuralynx). For the head-fixed rats, we used a single tungsten electrode (Model TM33C10, World Precision Instruments) with an impedance of 1 MΩ, amplified using a CyberAmp 380 (Molecular Devices) and recorded using Matlab custom software.

To detect spiking activity, we filtered the signal between 900 Hz and 6 kHz. When a threshold crossing event in any of the four leads was detected, a 1-ms waveform was acquired at 32 kHz. The sampled waveforms were automatically clustered using KlustaKwik (http://klustakwik.sourceforge.net/), with Peak6-to11 (minimum of the value in samples 6 to samples 11), Valley (maximum of the voltage deflection) and Energy (L-2 norm of the acquired waveform) as clustering features. The clusters were later checked and adjusted manually using MClust (http://mclust.sourceforge.net/). Clusters were included in the analysis only if the following criteria were met: <1% refractory period violations, an isolation distance[49] of more than 15, calculated on the basis of the MClust features Peak, Energy, waveFFT (centroid of the Fourier decomposition) and wavePC1 (Principal Component 1), and clusters were stable for at least 100 trials during the engaged condition and at least 100 trials of passive conditions. The isolation distance is defined as the Mahalanobis distance from the center of an identified cluster in which as many spikes belong to the specified cluster as to other clusters.

For the multi-unit analysis, events were included if they exceeded a threshold of 50 μV on any of the four channels of the tetrode. Re-analysis of our data by changing these thresholds between 35 μV and 75 μV did not change the results. Multi-unit sites were included in the analysis only if there were at least five total spikes in the spontaneous period (20 ms before stimulus onset) and in the evoked period (20 ms after stimulus onset).

To obtain LFPs, we filtered the signal from one of the leads of each tetrode or the tungsten electrode used for the head-fixed behavior between 1 Hz and 475 Hz. After acquisition at 3,225 Hz, we applied a high-pass four-pole Butterworth filter (10 Hz).

Each day, each tetrode or tungsten electrode was independently advanced until we could observe stable spiking activity. We did not specifically sample for sites that were responsive to our stimulus ensemble. We advanced the tetrodes at least 40 μm every day to avoid having multiple recording sessions with the same subset of cells. We used a skull screw as a ground. We used a nearby nichrome wire as a reference for the tetrode recordings and another skull screw for the head-fixed recordings.

**Stimulus delivery.** For the stimulus delivery through earphones (**Figs. 1**, **2**, **3c–f**, **4** and **6**) on each recording day, an earphone (ER-6i Isolator, Etymotic Research) was screwed into the earphone holder without anesthetizing the rat. The earphone had a soft silicone cover, which allowed us to adjust it in place without causing discomfort to the rat. Sound intensity was determined with a Brüel & Kjær type 4939 free-field microphone, Type 2670 1/4-inch Microphone Preamplifier and Type 2690A0S2 2-Channel Microphone Conditioning Amplifier (Brüel & Kjær Sound & Vibration Measurement A/S) positioned 5 mm in front of the earphone. At this position, the intensity of the chord was 69dB RMS SPL (74 dB SPL peak value) and the click was 76dB RMS SPL (82 dB SPL peak value).

For rats recorded during free-field stimulation (**Fig. 3a,b**), the stimulus was played through a calibrated PC speaker located 6 cm in front of the rat's head. For the head-fixed behavior (**Fig. 5**), we used an electrostatic speaker (ES1, Tucker-Davis Technologies) placed on the right side, 10 cm from the ear.

*Note: Supplementary information is available on the Nature Neuroscience website.*

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**AUTHOR CONTRIBUTIONS**

G.H.O. and A.M.Z. designed the overall experiments and wrote the manuscript. G.H.O. designed and performed the experiments in **Figures 1**, **2**, **4** and **6**. L.-H.T. designed and performed the experiments in **Figure 3** (intermodal attention). Y.Y. designed and performed the experiments in **Figure 4** (head-fixed behavior).

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