Selective attention controls olfaction in rodents

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Abstract:

Critical animal behaviors, especially among rodents, are guided by odors in remarkably well-coordinated manners. While many extramodal sensory cues compete for cognitive resources in these ecological contexts, that rodents can engage in such odor-guided behaviors suggests that they selectively attend to odors. We developed an operant task to reveal that rats are indeed capable of selectively attending to odors in the presence of competing extramodal stimuli and found that this selective attention facilitates accurate odor-guided behavior. Further, we uncovered that attention to odors adaptively sharpens their representation among individual neurons in a brain region considered integral for odor-driven behaviors. Thus, selective attention contributes to olfaction in rodents in a manner analogous to that observed for other sensory systems in more cognitively-advanced animals.

Main Text:

From neonatal attachment and suckling responses (*1–3*), to selecting mates, finding food sources, and avoiding predators (*4–6*), rodent behavior is guided by olfactory stimuli in remarkably well-coordinated manners. The fact that these behaviors can be successfully orchestrated lends reason to believe that rodents must selectively attend to odors in these contexts at the expense of competing extramodal cues. For instance, during foraging for food and sniffing out food odors, a rat must simultaneously 'filter' out competing auditory and visual stimuli arising from irrelevant sources. While we know that rodents readily display shifting of attentional sets, including those involving odors (*7*), and even that they can display attention towards information from other modalities (*8*, *9*), whether selective attention regulates olfactory perception and odor coding remains unresolved. This question is of great importance given the prevalence of rodents as models for olfactory function and due to the fact that we know odor-directed attention shapes olfaction in humans (*10*, *11*).

Given the aforementioned importance of olfaction for survival, we reasoned that olfactory brain centers would adaptively encode odor information in manners dependent upon attentional demands. Further, while there are many locations within the olfactory system which are modulated by attention in humans (*10*, *12*) as a starting place to uncover cellular modulation by attention, we predicted that selective attention would shape the representation of odors within the ventral striatum (VS). This is reasonable given that the VS is a collection of brain regions important for evaluating sensory information in the context of motivated behaviors (*13*), a function considered integral for attention (*14*). Offering precedence for this is evidence provided by human functional imaging for increased hemodynamic responses to odors in the VS during attention (*10*, *12*), particularly in the olfactory tubercle region of the VS, which is extensively innervated by olfactory input (*15*, *16*). Notably, the olfactory system does not have a classic thalamic relay, a component widely considered to be integral to attention and sensory awareness in other systems (*17–19*). The VS does, however, receive input from a variety of frontal cortex and neuromodulatory systems (*13*), which may allow for attention to sculpt odor coding. The coding strategy VS neurons engage in, which may underlie this phenomenon, is unknown. Here we developed a powerful operant task, and used this in combination with single-unit neural recordings, to uncover fundamental principles of how rats utilize selective attention in manners advantageous for olfactory behavior. We find that selective attention to odors facilitates

engagement in accurate olfactory decisions and enhances the contrast of odor representation in the VS by amplifying odor signal-to-noise ratios.

Results

We first sought to demonstrate that rats are capable of displaying selective attention to odors in the presence of simultaneous extramodal stimuli. To address this, we developed a novel behavioral paradigm, which we term the two-alternative choice olfactory attention task (2AC-OAT) (**Fig 1A & B)**. The 2AC-OAT is a modified version of a standard 2AC task, wherein rats nose-poke into a center port and receive a stimulus that signals which of the neighboring side ports will deliver a fluid reward, if chosen correctly. In the 2AC-OAT, across pseudorandom trials, rats were shaped to discriminate between two odors and separately, to detect and report the absence or presence of a tone. Then, both tones and odors were presented simultaneously, and the rats learned to selectively attend to only one of the modalities to retrieve rewards. The 2AC-OAT has several important features. First, it provides robust and controlled stimulus presentations by requiring animals to nose poke to await stimuli. Second, it is an operant task, which means that hundreds of trials can be completed within a single session, throughout which all conditioned stimuli are assigned equal valence, with both modalities conditioned to predict reward availability at some time during the session. Both of the above features are not inherent in main-stream attentional set-shifting tasks, preventing their use to directly study olfactory selective attention (*e.g.*, (*7*)). Third, out of the four possible trial types resulting from this design, odors may be either unattended or attended (**Fig 1B,** 'tone attention' vs 'odor attention') and further, half of these trials do not include a tone (**Fig 1B**, bottom half of trials), allowing for the comparison of behavioral and cellular responses to an odor while it is attended versus unattended, without multisensory confounds (unlike the Wisconsin-Card Sorting Task (*20*) or (*9*)). Fourth, in the same session, rats perform both the single-modality 2AC odor discrimination task and the more challenging multi-modal 2AC-OAT, which allows for questions related to task demand to be addressed by comparing data from these task types. Finally, because the attentional switch from tones to odors is not cued nor overtly anticipated by the rats, this eliminates cue-generated expectation and allows for behavioral flexibility and odor coding relative to the attentional switch to both be probed.

Rats selectively attend to odors and this dictates discrimination accuracy.

We shaped 7 water-motivated rats to successfully perform the 2AC-OAT. First, over several phases, rats were shaped to criterion performance (≥85% correct responses) on the 2AC odor discrimination and tone detection tasks (**Figs S1A-E & S2**). We then introduced modality switching, shaping rats to alternate performing between the single-modality 2AC odor discrimination and tone detection tasks within a session (**Fig S1F**). Next, we started the rats on the tone detection task for the first half of the session, and once they reached criterion performance, switched them to a variant of the odor discrimination task (**Fig S1G**). Only this time, we continued to present tones simultaneously with the odors. Here, the rats were faced for the first time with selectively attending to odors in the presence of tones, the same tones that they had just been detecting, and using to guide their behavior, at the beginning of the session. During this and the following phase, the simultaneously presented tone and odor cues were either congruent (non-competing, signaling the same reward-port side) or incongruent (competing, signaling the opposing reward-port side). Once criterion was achieved, the rats advanced to the final 2AC-OAT (**Fig 1B & S1H**). Now, during the first half of the session, which consisted of auditory attention blocks ('tone attention'), rats attended to the presence or absence of a tone, while the odors were also presented simultaneously. Once rats reached criterion performance during the session (≥80% correct responses/block for ≥ 6 blocks), the task was switched to 'odor attention' blocks and rats now had to direct their attention to the conditioned odors, while ignoring the competing auditory information to which they had been previously attending. This switch was not cued to the rats; instead, they had to rely upon the feedback they received on their behavioral responses (reward receipt or not) in order to assess that the task contingencies had switched. It took the rats on average 392.6±44.6 blocks, across 24.9±1.3 sessions, to reach the first criterion switch for this final phase of the 2AC-OAT (**Tables S1-4)**. The rats were subsequently allowed numerous successive sessions of over-training in the 2AC-OAT to establish robust behavioral performance. Among the last 4 sessions of this overtraining, the rats took an average of 10.5±0.8 and 9.7±0.5 blocks to reach criterion for the tone attention and odor attention tasks, respectively.

Several significant findings emerged from the rats' performance on the 2AC-OAT. First, we found that task accuracy is dependent upon the animal's attentional strategy. Following shaping, rats performed the 'tone attention' portion of the 2AC-OAT, despite the presence of

competing conditioned odors, with an average of 85.48% correct responses per block (±1.14 SEM, inter-animal range: 82.92-91.25%, average of the six criterion blocks pre and post switch taken from the last 2 sessions/rat). We found that directly after the task was changed from 'tone attention' to 'odor attention,' there was an immediate decrease in performance to chance levels with most rats only performing ~50% correct responses ($t(6)=9.78$, $p<0.0001$, block -1 vs block 1; **Fig 1C&D**). This decrease in performance upon task change was observed across all rats in the population. For the first few blocks after the switch, the rats initially made perseverative errors, reflective that they maintained their original strategy of attending to the tone. However, as they began to receive feedback on their errors (*i.e.,* attending to the tone did not consistently result in reward delivery), the rats modified their strategy and began directing their attention to odors, which consequently led to increased task accuracy ($t(6)=-4.88$, $p=0.0028$, block 1 vs block 6; **Fig 1D,** bold line). Rats displayed an average of 89.7% correct responses for 'odor attention' (± 1.63 SEM, inter-animal range: 85.42-96.67%, average of the six criterion blocks pre and post switch taken from the last 2 sessions/rat). Second, we observed that odor-directed selective attention is subject to plasticity with experience, as across sessions, rats improved their ability to shift their attention to odors. This can be seen among individual rats (**Fig 1C**) and across the population (**Fig 1D,** comparing dashed vs. bold lines), with high levels of performance being reached sooner in late sessions as compared to early sessions ($t(6)=-2.74$, $p=0.034$, block 6 (early) vs block 6 (late); **Fig 1D**). Additionally, it took the rats fewer blocks to reach criterion in late versus early sessions ($t(6)=3.34$, $p=0.016$; **Fig 1E**), demonstrating that they switched their attention to odors more rapidly as they gained experience. We also tested a subset of rats for their abilities to direct selective attention to odors when perceptual demands were increased, given that there is interplay between attention, performance accuracy, and perceptual difficulty observed in other sensory systems (*e.g.,* (*21*)). As odor intensity was gradually reduced over several sessions, rats required more blocks to shift their attention to odors (**Fig S3**). Together, these results demonstrate that rats can selectively attend to odors and that odor-directed attention improves with experience.

Attention profoundly dictates subtle, yet critical aspects of sensory-driven behaviors (*22, 23*). To provide insights into how selective attention may modulate odor-guided behavior, we next tested whether the coordinated behavioral responses rats display in the 2AC context (*e.g.,* sampling durations, latency to reach the reward), are shaped by attention. We hypothesized that

the higher attentional load of the multiple-modality 2AC-OAT would require more time to be invested sampling odors than the single-modality 2AC odor task. We further hypothesized that attending to one cue in the presence of an incongruent competing cue would impinge on the rat's rapid decision making, and thus that rats would invest more time directed at stimulus sampling for incongruent versus congruent trials. To test these hypotheses, we analyzed two different behavioral decision epochs: sampling durations and reward latencies. Odor sampling durations were defined as the amount of time from when the odor is delivered in the center port to the time of port withdrawal. Reward retrieval latency was defined as the amount of time from center-port withdrawal to reward port entry. In the 2AC-OAT, the trial outcomes are 'correct' (correct reward port choice), 'incorrect' (incorrect reward port choice), and 'omission' (no reward port choice), and must be made within 4s of the trial start. To prevent biasing of the data (for instance, by including omission or incorrect trials), we analyzed only correct trials from blocks in which rats performed at ≥ 80%, and from sessions in which they successfully switched, reaching criterion (≥ 80% for ≥ 6 blocks) on both tasks. These measures were grouped and analyzed across the different task types ('odor only,' 'tone attention,' and 'odor attention'), according to congruency, and further were divided among trial type (odor A + tone, odor A + no tone, etc.).

Across the three task types, the sampling duration and latency to reach reward times were not significantly different (**Fig S4B**), suggesting that, in the context of the 2AC-OAT, task demand does not influence decision deliberations overall. Several specific aspects of odor-guided behavior beyond solely discrimination accuracy, were, however, influenced during task performance. First, rats committed more errors during incongruent versus congruent trials ($t(6)=-13.11$, $p<0.0001$; **S4D**). Second, as predicted, among correct decision trials, rats invested more time sampling the stimulus if that trial was incongruent (33±8ms; $t(6)=-4.20$, $p=0.0057$; **S4E**); that is, they spent more time to make their decision when conflicting cues were present. This difference was respectively subtle, however, in the context of the mean sampling duration which was approximately 500ms. Despite these differences, there was no impact of trial congruency upon the latency to retrieve the reward, suggesting that animals did not deliberate upon their decision as they approached the reward port, nor were they less motivated to retrieve a reward ($t(6)=-1.45$, $p=0.197$; **S4F**).

Given that there was an effect of congruency on odor sampling durations, we further separated the data into the four trial types to see if one was more greatly influenced by different

combinations of sensory input. As multisensory input facilitates rapid decision-making (*24*), we hypothesized that rats would need less time to sample the stimulus when both cues were present (tone on + odor) and congruent. In accordance with this, we also hypothesized that rats would take longer to sample odors when one of the cues was absent (tone off + odor) and the cues were incongruent. While sampling durations and latencies to reward were highly similar within an attentional task (*i.e.,* comparing the four trial types to one another within either tone or odor attention), and across task types (*i.e.,* comparing the 'odor A + tone' trial type between tone and odor attention), we did find two significant differences (**Fig S4 G&H**). During odor attention, affirming that multisensory cues in the 2AC-OAT are facilitating rapid decision-making, rats sampled shorter for congruent trials in which the tone was on as compared to incongruent trials in which the tone was off ($t(6)=6.05$, $p=0.0009$, Bonferonni critical $p=0.0083$; **S4G**). Additionally, when the tone was off and the trial was incongruent, rats invested more time sampling the odor when they were attending to the odor versus when they were attending to the tone (51±15ms; $t(6)=3.352$, $p=0.015$; **S4G**). Importantly, for these trials the stimuli were exactly the same (odor + tone off), but we found that attending to tone provided a sampling duration advantage, further evidence that the rats were indeed attending to the correct modality. Altogether, while odor-directed selective attention controls performance accuracy, there are additional influences of enhanced cognitive demand (*e.g.,* trial congruency, multisensory input) on these subtle, yet critical, aspects of sensory driven behaviors.

Attention controls the neural representation of odors.

We have demonstrated that rats display selective attention to odors. Does attention also dictate the neural representation of an odor? More specifically, does the brain represent an odor, of equal intensity and valence, in a different manner, dependent upon whether it is attended? To address these questions, after rats achieved robust behavioral performance on the 2AC-OAT, they were unilaterally implanted with drivable tetrodes (*25*) into the olfactory tubercle (OT) region of their VS. Not all rats that were implanted contributed physiology data due to electrode placement errors, poor signals, or their inability to perform the cognitively demanding 2AC-OAT following surgery. We successfully performed OT single-unit recordings from 4 rats (which also contributed behavior data (**Fig 1**) during 2AC-OAT performance (**Fig S5**). Over the course of

multiple sessions per rat (range: 6-10), we lowered the tetrodes, sometimes daily, and identified 232 cell-odor pairs from these recordings across all rats (116 total single-units) **(Table S5)**.

To directly test how attention modulates odor coding, and to control for possible multisensory influences, only those trials in which the tone was not delivered ('tone off' trials) were analyzed (50% of the total) (**Fig S1H**, blue box). To assess behaviorally-relevant changes in unit firing, we identified four critical time epochs relative to stimulus onset, corresponding to the rat's behavior: (1) background (-1400 to -800ms), (2) stimulus port approach (-800 to -600ms), (3) required hold (-600 to 0ms), and (4) required minimum odor stimulus duration (0 to 400ms). We identified cell-odor pairs by categorizing units as either odor-excited, odor-inhibited, or odor-unmodulated by each odor if their firing rates were significantly greater during the odor epoch as compared to the background epoch for the three task types (see Materials and Methods). We identified 55 odor-modulated cell-odor pairs out of the 232 possibilities (23.71%, 116 units x 2 odors), 27 of which were odor-excited and 28 of which were odor-inhibited, with some cells modulated by both odors. Across the entire population, during odor attention, 36 units were modulated by odor (32.03% of 116).

We found that odor-directed selective attention bi-directionally sculpts the coding of odors in the OT by increasing the firing rates of odor-excited cell-odor pairs (**Fig 2A**), while further decreasing the firing rates of odor-inhibited cell-odor pairs (**Fig 2B**) during both the preparatory hold and odor epochs. For example, the representative odor-excited unit in **Figure S6A** displays an increased firing rate during the preparatory hold and odor epochs (top), which is further enhanced when the rat is attending to odors (bottom). In contrast, the odor-inhibited unit in **Figure S6B** displays a greater suppression in firing rate, particularly during the preparatory hold period when the rat is attending to odors (bottom).

To statistically quantify odor-responsiveness across all cell-odor pairs, we classified the data using auROC analyses (*26*, *27*) (see Materials and Methods), which represents changes in firing rate within sliding windows of time relative to a shuffled background distribution. This analysis allows for a statistical representation of significant firing rate changes for odor-excited and odor-inhibited cell-odor pairs. Across the population, greater significance emerges during odor attention for both populations during the hold and odor epochs (**Fig 2C&D**). We quantified these differences and found that during odor attention for odor-excited cell-odor pairs, a large proportion of the population was significantly excited during the hold and odor epochs, and this

increase in population response occurred rapidly (**Fig 2E**). Reflecting this, the cumulative duration of this excitement was significantly longer during both the preparatory hold and odor epochs when rats attended to odors versus when they attended to tones (hold: $t(26)=-3.20$, $p=0.0036$; odor: $t(26)=-3.51$, $p=0.0016$), while 2AC odor discrimination was not significantly different (hold: $t(26)=-2.15$, $p=0.041$; odor: $t(26)=-2.37$, $p=0.026$) (Bonferonni critical $p=0.0167$; **Fig 2F**). Similarly, for odor-inhibited cell-odor pairs, a large proportion of the population was inhibited during the hold and odor epochs and this increase occurred rapidly (**Fig 2G**). We also found a significant increase in the duration that odor-inhibited cell-odor pairs were significantly suppressed relative to background during both the preparatory hold and odor epochs during odor attention as compared to tone attention (hold: $t(27)=-3.79$, $p<0.001$; odor: $t(27)=-4.09$, $p<0.001$) and odor discrimination (hold: $t(27)=-3.87$, $p<0.0001$; odor: $t(27)=-4.67$, $p<0.0001$) (Bonferonni critical $p=0.0167$; **Fig 2H**). Thus, selective attention to odors bi-directionally controls OT ensemble activity and the representation of odors, suggesting a population shift that may enhance odor signal-to-noise ratios.

We used the cell-odor pairs classified above (n = 27 odor-excited, n = 28 odor-inhibited, n = 177 unmodulated), and calculated their change in firing rate (FR) with attention ($\Delta Hz_{attention}=FR_{attended}-FR_{unattended}$). This approach yields a simple index for the direction of change in firing and thereby allows for determining the control of single-unit activity by selective attention. Units were classified, for each epoch, as shifted negatively or positively if their firing rate either increased or decreased ≥1Hz. Among those odor-excited cell-odor pairs whose firing rates shifted, we found that the majority decreased their background firing rates (70%, 7/10), while increasing their firing rates during the hold (70.6%, 12/17) and odor (60.0%, 12/20) epochs when the rats were attending to odors versus when they were not (**Fig 3A**). The proportion of odor-excited cell-odor pairs with decreased background firing rates was greater than the proportion with increased background firing rates (One sample proportion $z=2.8$, $p<0.01$), while the proportion of cell-odor pairs with increased firing rates during the preparatory hold was greater than the proportion with decreased firings rates ($z=3.7$, $p<0.001$). The proportion of cell-odor pairs with increased firing rates during odor did not reach significance ($z=1.8$, $p=0.0679$).

An opposite direction of change was observed among the population of odor-inhibited cell-odor pairs, where among those whose firing rate changed, the majority decreased their firing

during the hold (75.0%, 12/16) and odor (68.8%, 11/16) epochs while the rats were attending to odors (**Fig 3B**). A greater proportion of odor-inhibited cell-odor pairs decreased their firing rates during the preparatory hold (z=4.6, p<0.0001) and odor epochs (z=3.2, p=0.0012) with attention. Notably, we also determined that these effects were selective to odor-modulated cell-odor pairs, as the majority of firing rates for those which were unmodulated were unchanged during background (87.01%, 154/177), hold (88.70, 157/177), and odor epochs (87.57%, 155/177; **Fig S7A**). Among those unmodulated cell-odor pairs that were shifted (11.30%, 20/177), we observed that a greater proportion had decreased firing rates during the preparatory hold (z=3.9, p< 0.0001). Overall, with odor-directed attention, odor-excited cell-odor pairs display enhanced firing relative to background in preparation for the upcoming stimulus, while odor-inhibited cell-odor pairs show decreased firing relative to background in preparation for and during the odor stimulus.

We reasoned that odor-directed attention may control single unit firing rates in two possible manners. First, within a single unit, the overall firing rates (background, hold, and odor epochs) may be broadly influenced in direction and magnitude by odor attention, which would indicate a general ramping up or down of activity across trials. Alternatively, as suggested by the firing changes in **Figure 3A**, odor attention may control odor signal-to-noise ratios among the units. It is likely that within an odor-excited unit, the preparatory hold and odor epochs may be enhanced, while background activity remains either unchanged or is decreased. Further, as suggested from the firing rate changes in **Figure 3B**, within an odor-inhibited unit, it is likely that the preparatory hold and odor epochs may be further suppressed, while background activity remains either unchanged or is increased. To determine if this is the case, in a final series of analyses, we compared the change in FR of the background to either the hold or odor epochs for both odor-excited and odor-inhibited cell-odor pairs (**Fig 3C**). If points were to fall along the unity line, this would indicate changes in FR that were similar in direction and magnitude for both the background, hold, and odor epochs, which would support a general ramping up of unit activity within a trial, irrespective of epoch-specific influences. We found, however, for odor-excited cell-odor pairs, that the change in FR during both the preparatory hold and odor epochs was increased relative to the change in FR of the background, regardless of how the background was influenced (hold: t(26)=-2.32, p=0.028, odor: t(26)=-2.54, p=0.017) **Fig 3C,** top). In many cases, but not all, the background FR decreased, while the FR during the hold and odor epochs

increased. Furthermore, for odor-inhibited cell-odor pairs, the change in FR during the preparatory hold period was more greatly decreased relative to the change in background FR (hold: $t(27)=3.227$, $p=0.003$, odor: $t(27)=1.93$, $p=0.064$; **Fig 3C,** bottom), and thus we conclude that odor-directed attention enhances the signal-to-noise within these cell-odor pairs. Notably, this effect is specific to odor-modulated units, since units classified as unmodulated to odors during odor attention displayed changes in FRs that were similar in both their direction and magnitudes (hold: $t(176)=1.38$, $p=0.169$, odor: $t(176)=1.01$, $p=0.313$; **Fig S7B**). Consequently, odor-directed attention recruited more cell-odor pairs to encode the acts of the preparatory hold (odor attention: 21.12%, 49/232 vs tone attention: 13.36%, 31/232) and odor sampling (odor attention: 21.552%, 50/232 vs tone attention: 23.707%, 55/232) by increasing the FR of odor-excited cell-odor pairs specifically during the hold and stimulus delivery epochs, while further reducing the FR of odor-inhibited cell-odor pairs (**Fig 3D**). Therefore, selective attention facilitates sensory coding in the olfactory system within task-critical moments by enhancing odor signal-to-noise.

Discussion

We have demonstrated that rats are capable of selectively attending to odors in the presence of conflicting stimuli. We predict that this phenomenon affords rodents the capacity to engage in ecologically critical behaviors (*e.g.*, foraging, predator avoidance, mate selection), which in all examples are highly multisensory contexts requiring animals to focus at times upon a single modality at the expense of others. Not only does our work show that selective attention enhances odor discrimination capacity, but also that this ability improves with experience, therefore highlighting an important interplay between attention, olfactory processing, and learning.

Equally important is our finding that selective attention contributes to olfactory processing by enhancing the contrast of odor representation in the OT by amplifying odor signal-to-noise ratios. This sculpting of odor information by attention is analogous to that observed upon attentional modulation in the visual and auditory systems of more cognitively-advanced mammals (*21*, *28*). We predict that this function, together with possible attentional modulation in other olfactory structures, is likely responsible for the effect of selective attention on facilitating more accurate odor discrimination. The OT is among several other structures which together

make up the olfactory cortex. Therefore, attention may 'gate' available odor information into the entirety of down-stream structures important for emotion, motivation, and memory. Moreover, this discovery lends credence to an important question: what system is responsible for this attentional state-dependent control of olfaction given that there is no mandatory thalamic relay in the olfactory system? Indeed, the OT neurons we recorded from herein receive the bulk of their input directly from the brain's initial odor processing stage, the olfactory bulb, and also from the neighboring piriform cortex (*15*, *16*, *29*). While the olfactory bulb is hypothesized to serve functions analogous to the thalamus (*30*), we predict that selective attention increases the strength of odor coding in the VS via neuromodulatory influences upon these neurons (*13*, *31*).

Taken together, a rodent, just like a human (*10*, *11*), can employ selective attention to aid in olfactory perceptual goals and this attention sculpts the representation of odor information within part of a brain system that is integral for evaluating sensory information in the context of changing motivational demands. This coding strategy of enhancing signal-to-noise, especially if also uncovered in additional major olfactory centers, likely serves to strengthen odor perception in the face of competing sensory input.

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Figure Legends

Fig. 1. Odor-directed attention dictates discrimination accuracy. (A) 2AC-OAT experimental trial outline. Example trials show correct 2AC choices during odor-directed attention on 'tone off' trials. Note dashed line indicating mandatory preparatory hold time. **(B)** The four possible 2AC-OAT trial types during the final phase of the 2AC-OAT. Top arrows for each trial type indicate the direction of reward for the tone cue; bottom arrows for each trial type indicate the direction of reward based on odors. Faded icons (both cues and arrow directions) indicate cues that are present, but should be ignored while the rat attends to the correct modality. **(C)** Example 2D histograms displaying performance of 7 rats over the course of six sessions of switching their attention during the 2AC-OAT. Each bin is a block of 20 trials. Solid overlaid lines indicate performance (% correct responses); dashed horizontal lines indicate criterion performance (80%). Vertical dashed line with arrowheads indicates the experimenter-controlled switch from tone to odor attention, which was uncued. See Materials and Methods for additional details on the 2AC-OAT. For each rat, the top three rows were taken from early sessions, the bottom three rows from late sessions except rat 1, which has only 5 sessions. **(D)** Average performance of all 7 rats on their first two sessions (early) and last two sessions (late, bold black line) of 2AC-OAT performance, relative to attentional shift. Performance dropped to chance levels in the block immediately after the task switch and returned to criterion levels as the rat shifted its attention to odors. Note that performance improved more quickly during late sessions. (**E**) The average number of blocks for each rat to reach criterion after the attentional shift (6 blocks ≥80%) for early and late sessions. $^{\#}p<0.0001$ (block -1 vs. 1, late), $^{\dagger}p<0.01$ (block 1 vs. 6, late), $^{\ddagger}p<0.05$ (block 6 early vs. block 6 late), $^{*}p<0.05$; two-tailed, paired *t*-test.

Fig. 2. Odor-directed attention controls odor coding. 2D histograms (50ms bins) displaying normalized firing rates of odor excited **(A)** and odor-inhibited (**B)** cell-odor pairs across the three different task states: odor only, tone attention, and odor attention, aligned to stimulus onset. Each row represents a single cell-odor pair; all units were arranged from highest to lowest firing rates, averaged over the first five bins after stimulus onset during odor attention. See Materials and Methods for normalization details. As indicated by auROC significant bins, odor attention increases the firing rates for odor-excited cell-odor pairs (**C**), and further decreases the firing

rates for odor-inhibited cell-odor pairs (**D**) during the preparatory hold and odor epochs. Each row represents the corresponding neuron from the 2D histograms in **A** and **B**. Odor-directed attention increases the percentage of odor-excited cell-odor pairs that have significantly excited activity (**E**) and the percentage of odor-inhibited cell-odor pairs that have significantly inhibited activity (**G**) relative to background earlier and for a longer duration. Odor attention thus significantly increases the duration of excitement (**F**) and inhibition (**H**) during both hold and odor epochs. $^{*}p<0.05$, $^{**}p<0.01$, two-tailed, paired *t*-test. Data from four rats (same as in Fig 1), 2-6 sessions/rat.

Fig. 3. Attention yields enhanced signal to noise among odor coding units. Changes in FR with odor directed attention, $\Delta Hz_{attention}=FR_{attended}-FR_{unattended}$, for odor-excited **(A)** and odor-inhibited **(B)** cell-odor pairs for the three behavioral epochs: background (left), preparatory hold (middle), and odor delivery (right). Pie chart: The proportion of increased or decreased FRs among units that shifted either negatively or positively (≥1Hz). **(C)** Change in background firing rate plotted against the change in the firing rate for either the hold (left) or odor (right) epochs for excited (top) or inhibited (bottom) unit populations. Excited cell-odor pairs that fall above the dotted line indicate a greater change in FR relative to background. Inhibited cell-odor pairs that fall below the dotted line indicate a greater decrease in FR relative to background. **(D)** The percentage of cell-odor pairs classified as either significantly excited or inhibited relative to background during the specified epochs are increased with attention to odor, particularly during the preparatory hold. Data from rats and sessions as in **Fig 2.** *n*s above the pie charts indicate the number of cell-odor pairs shifted out of the total number of excited or inhibited cell-odor pairs. *p*-values in (C), as denoted, are two-tailed, paired *t*-test. $^{**}p<0.01$, $^{***}p<0.001$, one-proportion z-test.

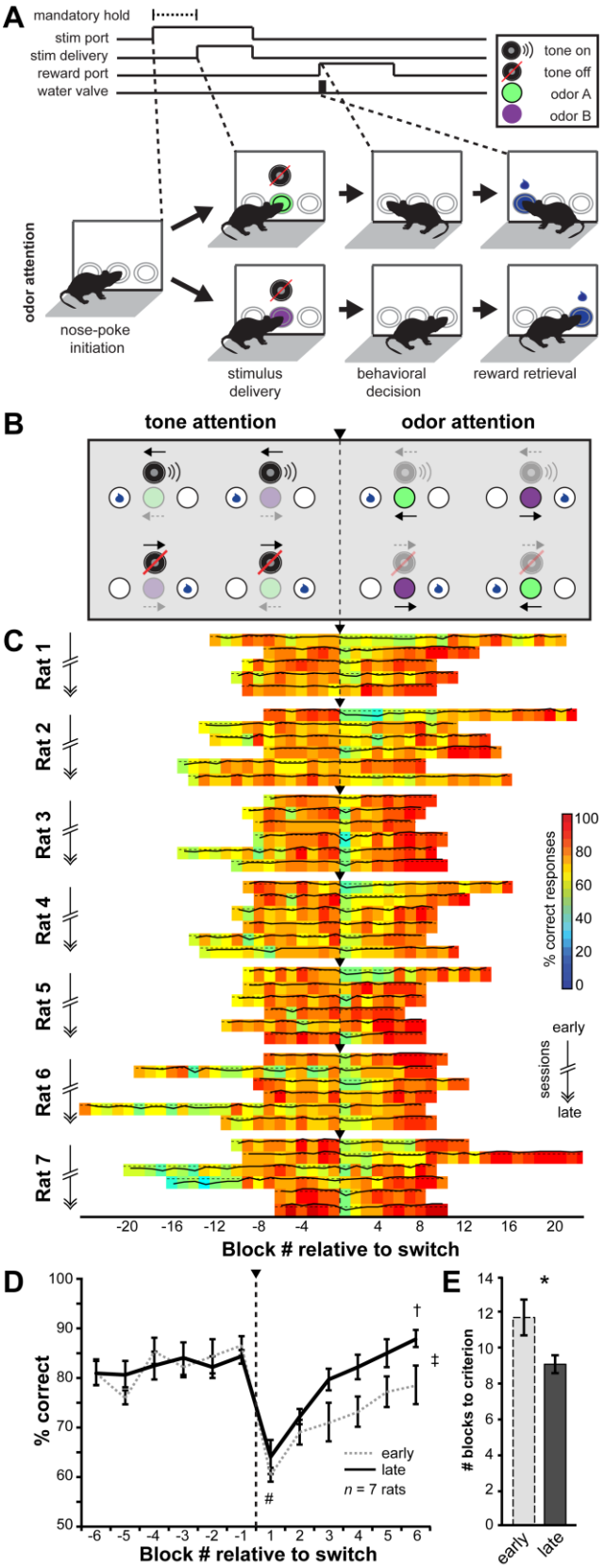
Supplementary Materials:

Materials and Methods

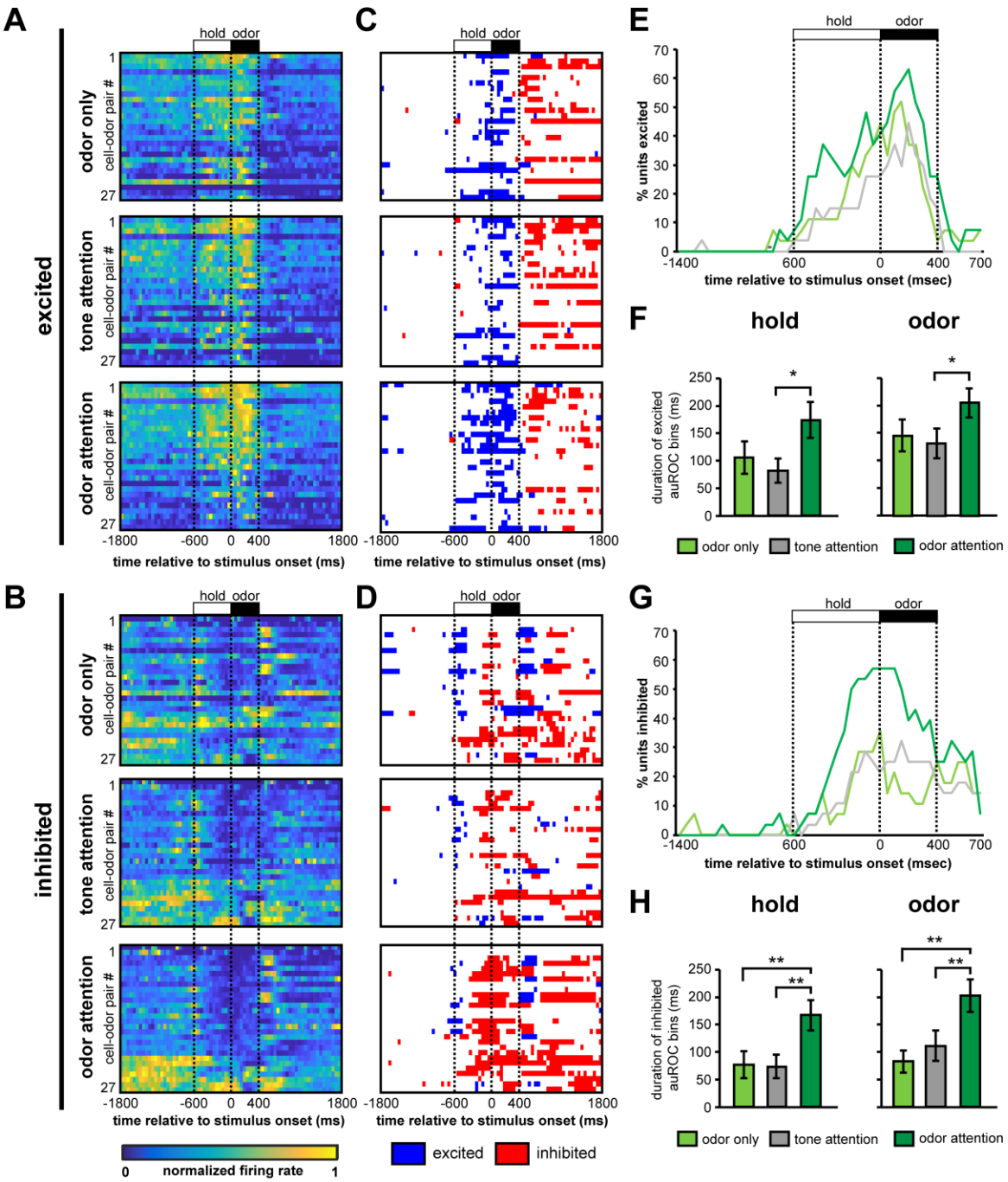
Figures S1-S7

Tables S1-S7

Carlson et al. Fig 1



Carlson et al., Fig 2



Carlson et al. Fig 3