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COMMENTARY

Why Sniff?

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The act of sniffing is so commonplace that most people rarely give a thought about what it is doing or why it is necessary. And yet, sniffing has long been recognized as a vital component of olfactory processing and perception. The first detailed studies on sniffing were published over 40 years ago (Welker 1964), and a considerable amount of research since then has been devoted to characterizing sniffing behavior in a variety of species, in particular, in rats and humans (Kepecs et al. 2006; Mainland and Sobel 2006; Schoenfeld and Cleland 2006). However, there have been few studies on sniffing in mice, which is perhaps surprising considering the important role played by genetically manipulated mice in the elucidation of the molecular and neurophysiological mechanisms of olfaction. It is all the more surprising that this basic aspect of mouse behavior has not received more attention, given the increasing use of behavioral analysis in mouse models of human conditions. The report by Wesson et al. (2008b) makes a start at filling this gap by providing the first detailed characterization of sniffing behavior in mice, across a variety of common olfactory tasks including habituation–dishabituation, odor digging, and go/no-go odor discrimination tests.

So why do mice sniff? Sniffing plays a vital role in controlling sensory access to the olfactory system in much the same way that motor control is vital for stimulus delivery to other sensory systems, such as eye movements for vision and whisking movements for vibrissal sensation. The periodic sampling of the airborne odor environment by sniffing imposes a temporal patterning of odor input, which seems to be a common feature of olfactory systems across a wide range of species (Kepecs et al. 2006). This temporal patterning of odor input has been proposed to play a number of roles in olfactory processing including: matching odorant delivery to receptor zone on the olfactory epithelium, temporal coding of odor identity and intensity, spatial localization of odor sources, and the segregation of odors from odor background (Kepecs et al. 2006; Schoenfeld and Cleland 2006).

By monitoring changes in intranasal air pressure (reflecting nasal airflow), Wesson et al. have found that mice show qualitatively similar sniffing behavior to that reported for rats, although shifted to higher frequencies in the range of 3–13 Hz (Wesson et al. 2008a). This matches the endogenous theta rhythm of neural activity characteristic of the hippocampus and many other brain regions and which may play an important role in linking olfactory processing with cognition (Macrides et al. 1982). This is interesting in light of the consistent individual differences in sniffing frequencies in the mice reported in this study. This could imply differences in individual neural dynamics or that individuals might be adopting different odor sampling strategies but using common neural mechanisms to process the information. Further work will be needed to answer this question.

Of the behavioral tasks used in this study, the habituation–dishabituation task revealed a robust relationship between high sniffing frequency and the novelty of an odor, with decreases in sniff frequency during habituation to repeatedly presented odors. Notably, Wesson et al. report that similar responses were observed to meaningful odors, such as food or social odors, as to those elicited by monomolecular odorants. This contrasts with versions of the habituation–dishabituation task that have reported more directed investigation to social odors than nonsocial odors when an odor source is placed in or on the animal's cage. This difference probably arises due to the mice being motivated to try and make direct contact with a social odor source to investigate its nonvolatile components, whereas delivery of airborne odorants, as in the present study, measures more general sniffing behavior generated in the absence of a physical odor source.

Despite the wide range of evidence that sniffing plays an important role in odor identification, discrimination, and perception, Wesson et al. found that high frequency sniffing was not closely linked to periods of odor discrimination during the sand digging and go/no-go operant tasks. In the sand digging odor discrimination, mice were trained to dig in sand that had been laced with the conditioned odor to obtain a food reward. In this task, the frequency of sniffing increased during the approach to the sand cup but did not change during digging, and that the highest frequency sniffing occurred after digging in anticipation of reward delivery. Similarly, in the go/no-go task, mice were trained to nose poke to sample an odor and then lick to receive food reward, at a separate food spout, in response to the conditioned odor, but to withhold responding to the nonconditioned odor. Sniffing frequency increased during the period of nose poke in which the odor was delivered. But again, there was a significant increase in frequency of sniffing just before licking in anticipation of reward delivery, as has been reported in previous studies in rats (Kepecs et al. 2007). Moreover, a separate group of naive mice were trained to simply nose poke for reward in the absence of any odor delivery. This group showed increases in sniffing frequency during nose poke and just before reward delivery that were statistically similar to the increases in the group that had to make an odor discrimination to receive the reward.

Studies on rats during operant tasks and free investigation have shown that even difficult odor discriminations can be made within a single sniff cycle, with only a small improvement of performance gained by making a second sniff (Uchida and Mainen 2003; Wesson et al. 2008a). So, why should a mouse use valuable energy in maintaining high frequencies of sniffing after odor discrimination has occurred or increasing sniffing rate when an odor driven response is not required? The increased sniffing frequency prior to reward delivery suggests that sniffing may form part of a general arousal response, which is coordinated with other sensory systems such as vibrissal whisking, and used for exploration of the environment (Welker 1964). A high frequency of sniffing increases the rate at which sensory information can be gathered and allows rapid detection of changes in the odor landscape (Verhagen et al. 2007). Therefore, in trained animals performing learned tasks, sniffing may not relate so much to the difficulty of the task being performed but function as a monitor of unexpected sensory input. It would be interesting to see whether the pattern of sniffing frequency differs in mice while they are learning an operant task compared with their expert performance when fully trained.

The sand digging and nose poke tasks are somewhat artificial in that the presentation of odors and rewards are spatially predictable. Natural discrimination and recognition tasks include a spatial component to odor source, and one of the functions proposed for sniffing is in the ability to locate odor sources against a complex odor background. It is therefore notable that the sniffing behavior during the operant tasks was considerably more variable when the mice were allowed to freely explore novel objects introduced into their cage. Sniffing in this more natural context was found to be highly dynamic, varying in frequency, amplitude, waveform, and duration. This probably reflects findings in rats that sniffing behavior can be rapidly altered depending on context and odor being investigated. Indeed, changes in sniffing behavior have been proposed to play a role in olfactory discrimination by targeting deposition of odorants with different physiochemical characteristics to specific zones of the olfactory epithelium (Schoenfeld and Cleland 2006). According to this hypothesis, a mouse might use multiple sniffs with different parameters to optimize individual sniffs for the analysis of different odorant constituents that make up a complex odor. However, imaging of the olfactory bulb during high- and low-frequency sniffing has so far failed to find the predicted differences in the evoked pattern of glomerular activation (Verhagen et al. 2007).

Increased sniffing rates during free exploration by the mice in this study not only occurred in response to novel objects but also in response to unexpected external cues, such as a sudden noise, and to internal cues, such as the initiation of locomotion. Changes in sniff frequency have been proposed to act as an adaptive filter in rats, with high sniffing rates reducing the response to background odors, while providing frequent updates for the rapid detection of novel odors (Verhagen et al. 2007). This all makes good sense from a survival point of view. Arousal from any external or internal source should activate general mechanisms for providing rapid acquisition of information about an odor that could signal a potential threat or opportunity. But despite the large number of hypotheses surrounding it, the function of sniffing remains mysterious. Wesson et al.'s study is valuable not only because it provides the first detailed account of sniffing in mice but also in providing guidelines for natural patterns of stimulus delivery for future electrophysiological and imaging experiments that use the advantages of genetic manipulation in mice to probe the neural mechanisms of olfactory function.

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