



THE OLFACTORY SYSTEM AS AN EARLY INDICATOR OF NEURODEGENERATION

Mishti Sheth

KEYWORDS :

1. INTRODUCTION

Olfaction differs from the other senses in three ways, and each one matters here.

First, the receptor cells are neurons that touch the outside world. Olfactory sensory neurons sit in the epithelium of the roof of the nasal cavity, exposed to inhaled air, and send their own axons through the cribriform plate into the brain. They are the only neurons in the body contacting both the outside environment and the central nervous system (Liao et al., 2024).

Second, the route to the cortex is short. Output neurons of the olfactory bulb project straight to the primary olfactory cortex with no obligatory thalamic relay, so odour information reaches limbic structures in two synapses (Han et al., 2023). Section 5 shows this is incomplete, because a second route does relay through the mediodorsal thalamus.

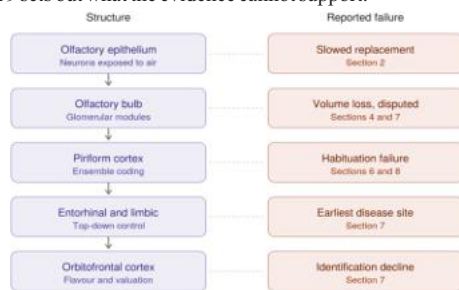
Third, the system regenerates. Olfactory sensory neurons are replaced throughout life, and the olfactory bulb is one of only two structures in the adult mammalian brain that gains new neurons (Bruehl-Jungerman, Davis & Laroche, 2007). So it needs constant upkeep, and it can fail simply by failing to keep up.

Together these features leave olfaction unusually exposed (Figure 1). The pathway is short, it begins outside the skull, and it depends on cells being replaced, so there are several ways for it to break and it may register damage before better protected pathways do.

How much this system can resolve is answered inconsistently. Han et al. (2023) say humans discriminate at least one trillion olfactory stimuli, citing Bushdid et al. (2014), then say in their own conclusion that the figure is tens of thousands, and Gu et al. (2025) give a range of ten thousand to one trillion. The estimates span eight orders of magnitude, appear within two years of each other, and none of the citing papers says how the figure was derived. This review adopts no single number.

This is a critical narrative review with a hypothesis-generating final section. No systematic search was run and no protocol registered. Twenty-five sources were appraised, twenty read in full and five from structured extraction records. For each one this review recorded the species its evidence came from, whether a claim originated there or was relayed, and how strongly its authors hedged. That procedure is the method and the main contribution.

The review asks what the evidence establishes about olfaction as an early indicator of neurodegeneration, and what it does not establish though it is widely cited as though it did. Sections 2 to 5 describe the system from nasal cavity to cortex, and each stage's anatomy explains how it fails. Section 6 sets out the evidence that odour perception depends on prior experience, section 7 takes up the disputed clinical claims, section 8 proposes a connection no source here makes, and section 9 sets out what the evidence cannot support.



Left: the pathway in order. Right: how each stage is reported to fail, with the section covering it.

Figure 1. The Olfactory Pathway and its Reported Failure Modes.

The left column gives the five stages of the pathway in order from the nasal epithelium to the orbitofrontal cortex, with the defining feature of each. The right column gives the failure reported at that stage in the literature examined, and the section of this review in which it is assessed. The pairing is the organising logic of sections 2 to 7. Original figure.

2. The Peripheral Apparatus

Odorants reach the olfactory epithelium in two ways: orthonasally on inhaled air, and retronasally from the mouth during eating, which is why flavour is not taste alone (Han et al., 2023). Neither route is efficient. The receptive surface sits high in the nasal cavity, away from the main path of inspired air, so detection depends on receptor affinity and whether a molecule reaches it.

2.1 The Olfactory Cleft

The olfactory cleft is a narrow bilateral space at the roof of the nasal cavity, bounded medially by the superior septum, laterally by the superior turbinate and above by the cribriform plate. The middle turbinate lies below it and governs how much air is pushed upward.

Exact dimensions of the cleft are widely quoted and should be treated with caution. While preparing this review, I traced those figures back to Damm et al. (2002), which does not report them. It is an MRI study of eleven intranasal volume segments in fifty healthy male volunteers. The dimensions in circulation have no traceable primary source, so we do not repeat them here.

Damm et al. (2002) reported something more useful. Two segments correlated with detection threshold: the upper meatus below the cribriform plate, and the anterior inferior meatus. So differences in threshold between healthy people depend partly on airway shape, not only on the epithelium. The volunteers were all men, the study was exploratory, and significance was reached only in the right nasal cavity.

2.2 Where the Olfactory Epithelium is

The olfactory epithelium has traditionally been placed along the cribriform plate, on the superior turbinate and on the upper septum, but the most direct human evidence suggests it is spread wider (Gomez Galarce et al., 2018).

Gomez Galarce et al. (2018) dissected seventeen cadaveric specimens, thirty-four sides, tracing olfactory fila back from the mucosa to where they cross the cribriform plate. Fila were densest at the ethmoid roof and superior turbinates, averaging 18.7 per specimen at the roof and 10.06 at the septum. They also found fila in three regions not previously counted as part of the olfactory system: the lateral nasal wall including the ethmoidal bulla, in nine specimens; between the os sphenoidale and the posterior choana, in five; and crossing the septal midline, in fifteen, with about twenty per cent of septal fila passing to the other side.

The authors state three qualifications: the sample is small, dissection is operator-dependent so fila may have been missed, and the study assumes all epithelium-carrying fila is functional. A fourth should be added: that no demographic information about the specimens is reported, in a paper citing age-dependent variability in epithelial distribution.

2.3 The Olfactory Mucosa and its Cells

The olfactory mucosa differs from the respiratory mucosa lining the rest of the nasal cavity, and it has three parts: the olfactory epithelium, the basal lamina and the lamina propria (Han et al., 2023). Five cell types live there. Bipolar olfactory sensory neurons are the receptor cells, each expressing a single receptor type. Supporting, or

sustentacular, cells hold the structure together. Horizontal basal cells act as multipotent stem cells, and globose basal cells generate replacement neurons. Microvillar cells are the fifth type, and their function is less clear; Bowman's glands sit in the lamina propria (Han et al., 2023; Gu et al., 2025). The transduction machinery is concentrated in the cilia, which is why ciliary defects, as in Bardet-Biedl syndrome, can produce anosmia.

2.4 Turnover

Olfactory sensory neurons are replaced throughout life, and globose basal cells generate the new ones. How often is reported inconsistently. Gu et al. (2025) and Han et al. (2023) both give thirty to ninety days. Liao et al. (2024) give something else: immature neurons appear within twenty four to forty eight hours, mature over about a week, and the epithelium regenerates every two to four weeks. The accounts do not fit together, none names a species, and Han and colleagues attach no citation at all, so the interval should be reported as unsettled. What is not disputed is that the process slows with age, and respiratory epithelium takes over some of the space (Marin et al., 2025).

3. Olfactory Receptors and Transduction

3.1 How Many Receptors, and What the Number Counts

Three different quantities circulate under one name, and they are not interchangeable. The first is the number of gene loci: over 800 varieties, about half functional and the rest pseudogenes. The second is the number of functional genes: roughly 400, about 2.4 per cent of the genome. The third is the number catalogued, which Gu et al. (2025) put at 391 functional human receptors with 402 characterised receptor-odorant pairs. Only about twenty per cent have been deorphanised, meaning paired with a known ligand. This review uses "about 400" for functional genes and "391" for the catalogued set, and flags ambiguity when a source gives a figure without specifying what it counts.

3.2 One Neuron, One Receptor

Each olfactory sensory neuron expresses a single receptor gene, so it responds to one class of odorant molecule, and axons of neurons expressing the same receptor converge on the same glomeruli. That combination of selective expression and axonal targeting lets discrimination begin at the periphery (Han et al., 2023).

This rule was established in mice. The two primary studies Han et al. (2023) cite are both murine, and Zhang, Lee and Igarashi (2024) refer to the pathway as the mouse olfactory pathway throughout. Gu et al. (2025) present it as applying to humans and mammals generally. Based on the evidence, it should be stated as demonstrated in mice and assumed for humans.

3.3 Transduction and Classification

Odorants dissolve in the mucus layer and bind receptors on the ciliary membrane. Binding activates the olfactory-specific G protein alpha subunit, then adenylyl cyclase III and protein kinase A, and the change in ion channel state depolarises the neuron, and there is generation of an action potential. Human olfactory sensory neurons also express six functional trace amine-associated receptors (Han et al., 2023; Gu et al., 2025).

Olfactory receptors fall into two structural classes: class I, 55 members with polar binding regions that recognise water-soluble compounds, and class II, 336 members with hydrophobic regions that recognise volatiles. Five receptors are broadly tuned, responding to between thirty and seventy-six compounds each, and thirty are classed as narrowly tuned, a classification Gu et al. (2025) call provisional.

3.4 Structure: what is Resolved and What is Predicted

Structural work on olfactory receptors arrived slowly. Two developments changed that, and they should not be conflated. The first is experimental. Cryo-electron microscopy resolved the structure of the active human receptor OR51E2 bound to propionate, showing a binding pocket of roughly 31 cubic angstroms, and consensus receptors representing whole families were later resolved the same way, extending coverage to class II (Gu et al., 2025). Those consensus proteins are engineered representatives, not naturally occurring human receptors.

The second is computational. Structures for the five broadly tuned receptors were predicted with AlphaFold 2, and no experimental confirmation of them is reported (Gu et al., 2025). A predicted structure and a resolved structure are different kinds of claims, and the difference is easily lost when they are listed together. This review keeps them apart.

4. The Olfactory Bulb

The olfactory bulbs lie beneath the frontal lobes on the cribriform plate of the ethmoid. They receive olfactory sensory neuron axons directly, making the bulb the only relay in any sensory system that sits only one synapse from the outside world. It is identifiable on prenatal MRI by about the thirtieth week (Gu et al., 2025).

4.1 Laminar Organisation

The human olfactory bulb has six radial layers: the olfactory nerve layer, the glomerular layer, the external plexiform layer, the mitral cell layer, whose axons form the secondary olfactory tract, the internal plexiform layer, and the granular layer (Gu et al., 2025). Not every source counts six, and Meyer et al. (2025) describe the mouse bulb as having five. The difference likely reflects whether the olfactory nerve layer counts as a bulb layer or as its afferent, but neither source addresses the other.

Layer identity matters functionally. Meyer and colleagues found noradrenergic input from the locus coeruleus densest in the internal plexiform layer, which was also where axon loss was most pronounced in their model.

4.2 The Glomerular Module

The functional unit of the bulb is the glomerulus (Figure 2), a spherical neuropil 100 to 200 micrometres across within which the axons of olfactory sensory neurons form excitatory synapses on the dendrites of mitral and tufted cells. With its granule and periglomerular interneurons, each glomerulus forms a module, and the mouse bulb has about 1,800 of them (Mori, Nagao & Yoshihara, 1999).

Two principles govern how axons reach these modules, both established in rodents. Under zone-to-zone projection, the epithelium divides into four zones defined by receptor expression, and neurons in a given zone project to the corresponding bulbar zone; within a zone, they are dispersed, so the map is coarse. Under glomerular convergence, neurons expressing a given receptor send their axons to a few defined glomeruli. In the mouse, each glomerulus receives input from several thousand olfactory sensory neurons and about twenty mitral cells, against an epithelium of more than two million (Mori, Nagao & Yoshihara, 1999).

The one-glomerulus-one-receptor rule should carry the caveat its authors attached. Mori and colleagues demonstrated exclusive input for one glomerulus in one knock-in mouse line, then wrote that the hypothesis needs testing for each glomerulus and that some may receive input from several receptor types. That caution has largely disappeared from the secondary literature.

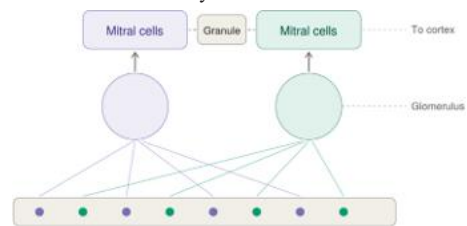


Figure 2. The Glomerular Module.

Sensory neurons expressing a given receptor are dispersed across the epithelium, shown by the alternating colours, but their axons converge on a single glomerulus. Each glomerulus is innervated by the primary dendrites of mitral cells, which are laterally inhibited through dendrodendritic reciprocal synapses with granule cells, shown dashed. In the mouse, each glomerulus receives axons from several thousand sensory neurons and is innervated by approximately twenty mitral cells. Original figure, drawn from Mori, Nagao and Yoshihara (1999).

4.3 Molecular Feature Detection and Lateral Inhibition

Each mitral or tufted cell sends one primary dendrite to one glomerulus, so its tuning reflects that glomerulus and single-unit recording is a usable proxy for glomerular specificity. Recordings from the rabbit bulb showed that individual mitral and tufted cells respond to a range of molecules sharing structural features, called the molecular receptive range. Different modules have different and partly overlapping ranges, and optical imaging in rats supported the same conclusion (Mori, Nagao & Yoshihara, 1999). Each module is therefore a molecular feature detector. Any odorant has several features, so it activates a combination of modules, and this is where the combinatorial coding of section 3 becomes a spatial pattern.

Modules do not work independently. Mitral and tufted cells form dendrodendritic reciprocal synapses with granule cells, so activating a mitral cell produces feedback inhibition of itself and lateral inhibition of its neighbours. Blocking these synapses greatly reduces the effect, which sharpens contrast between strongly and weakly activated glomeruli, so second-order cells are more sharply tuned than the sensory neurons feeding them (Mori, Nagao & Yoshihara, 1999).

4.5 The Bulb is Not a Passive Relay

Early accounts treated the bulb as a relay passing a peripherally encoded signal upward, and rodent work has made that untenable. Intrinsic optical imaging in trained mice showed an increase in activated glomeruli lasting up to five weeks. After learning, synchronised mitral activity carried information about whether an odour had been rewarded. The fraction of responsive mitral cells rose with hard discrimination and fell with easy discrimination. And bulb-to-piriform connections strengthened during rule learning (Zhang, Lee & Igarashi, 2024; Courtiol & Wilson, 2017).

The bulb also receives substantial descending input. Piriform feedback to the bulb increases during slow-wave activity, so what arrives from the nose is modified by what the cortex is doing, at least in the rat (Courtiol & Wilson, 2017). This corpus contains no equivalent human demonstration of bulbar plasticity.

4.6 Neurogenesis and Ageing

The other adult neurogenic structure is the dentate gyrus (Bruehl-Jungerman, Davis & Laroche, 2007). Progenitors in the subventricular zone give rise to neuroblasts, which migrate to the bulb and integrate as granule and periglomerular cells (Marin et al., 2025), and in mice, an enriched odour environment improves their survival (Wilson, Best & Sullivan, 2004). Adult neurogenesis is restricted to these few structures, so it cannot be a general mechanism of learning.

The bulb loses tissue with age. Glomeruli and mitral cells decline by about ten per cent per decade (Gu et al., 2025), and reduced subventricular neurogenesis cuts the supply of periglomerular cells (Marin et al., 2025). Two things follow. The bulb has maintenance requirements like the epithelium, and it depends on a supply line that starts outside the olfactory system. And absolute bulb volume falls in everyone with age, which is the background against which the disputed volumetric findings of section 7 have to be read.

5. Central Pathways and the Olfactory Cortex

Olfactory cortex is defined by connectivity: it is the set of areas receiving direct input from the olfactory bulb. Zhang, Lee, and Igarashi (2024) list nine such regions in the mouse, including the anterior olfactory nucleus, olfactory tubercle, piriform cortex, and lateral entorhinal cortex. Human accounts offer a shorter list, with the orbitofrontal cortex as a secondary olfactory cortex (Han et al., 2023). The difference is one of resolution, because the nine-region account comes from rodent tract tracing and several corresponding human structures are hard to delineate *in vivo*. For that reason, Gu et al. (2025) do not discuss human structures beyond the bulb, so most of what follows is rodent anatomy.

5.1 The Piriform Cortex

The piriform cortex is the largest olfactory cortical area and receives the densest projection from the bulb. It is a three-layered paleocortex and divides into anterior and posterior subdivisions (Courtiol & Wilson, 2017).

Odour representation differs here from that in the bulb. Bulbar representation is spatially ordered, but the piriform receives divergent projections from mitral cells and responds in distributed ensembles with no topographical pattern, shown in rodents and supported in humans by functional imaging (Courtiol & Wilson, 2017; Zhang, Lee & Igarashi, 2024).

Three functional properties follow, all established in the rat. Piriform responses habituate rapidly, which lets the cortex filter an odour from its background. Piriform ensembles perform pattern completion, so the response to a learned mixture survives removal of one component. Piriform activity also decorrelates between odours as animals learn to tell them apart, a change also reported in humans (Courtiol & Wilson, 2017). On this evidence, Courtiol and Wilson argue that the piriform is an associative cortex rather than a primary sensory cortex, an argument they endorse rather than demonstrate.

5.2 Whether Olfaction has a Thalamic Relay

Olfaction is routinely described as the only sensory modality that reaches cortex without a thalamic relay, and the point is presented as its defining structural peculiarity (Han et al., 2023; Zhang, Lee & Igarashi, 2024). The claim is half right, and the missing half matters.

The direct route is real. Mitral and tufted axons reach the primary olfactory cortex through the lateral olfactory tract with no intervening thalamic synapse, which is why odours reach limbic structures quickly.

A second route also exists (Figure 3). The mediodorsal thalamic nucleus receives direct input from primary olfactory areas including the piriform cortex, and connects reciprocally with the orbitofrontal cortex. Courtiol and Wilson (2017) call this the olfactory trans-thalamic pathway. Coupling between the two is state-dependent, and lesion work suggests the pathway is engaged selectively, because animals with mediodorsal damage perform simple odour discriminations normally but need more trials on hard ones.

Two human findings support the relayed route. Functional imaging showed that attention to odours increased coherence from the piriform cortex to the mediodorsal thalamus and from the thalamus to the orbitofrontal cortex (Courtiol & Wilson, 2017), and FDG PET showed that odour-threshold performance correlated with metabolism in the right thalamus, including the mediodorsal nucleus (Förster et al., 2010).

The literature handles this inconsistently, which is worth noting. Han et al. (2023) attribute the no-relay claim to Wilson, Xu, Sadrian, Courtiol, Cohen, and Barnes in 2014, the same research group whose later review devotes a section to the trans-thalamic pathway. Han's own schematic of the route to the orbitofrontal cortex includes the thalamus, contradicting the text beside it. Zhang, Lee and Igarashi (2024) state the absence of a relay as a defining feature of a three-layer system and never mention the alternative. The accurate formulation is that olfaction has a direct route bypassing the thalamus and a second route that does not, engaged under different conditions.

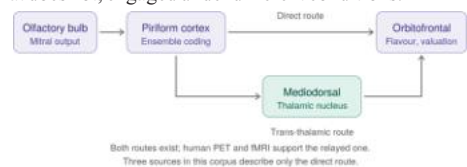


Figure 3. Two Routes from the Piriform Cortex to the Orbitofrontal Cortex.

The direct route reaches the orbitofrontal cortex without a thalamic synapse and is the one conventionally described as making olfaction unique among the senses. A second route relays through the mediodorsal thalamic nucleus. Human support for the relayed route comes from PET, where odour-threshold performance correlated with metabolism in the right thalamus, including the mediodorsal nucleus, and from fMRI, where attention to odours enhanced coherence along the piriform-thalamus-orbitofrontal pathway. Three sources in this corpus describe only the direct route. Original figure.

5.3 Limbic Connections and the Orbitofrontal Cortex

The piriform cortex has strong reciprocal connections with the basolateral amygdala and the lateral entorhinal cortex, and both shape its activity rather than merely receiving from it. The lateral entorhinal cortex matters more, because it also belongs to the memory system. Separate layer II populations serve the forward and return directions, and the neurons projecting back to the olfactory system are more broadly tuned than those projecting to the hippocampus (Zhang, Lee & Igarashi, 2024). Reversibly silencing this region in the rat increases piriform activity and impairs fine odour discrimination while leaving gross discrimination intact, so the entorhinal cortex exerts a top-down suppression that fine discrimination depends on (Courtiol & Wilson, 2017). Coupling across the network is not fixed either, because during acquisition of a hard discrimination, bulbar input to the piriform was potentiated while orbitofrontal input was depressed, both returning to baseline at criterion (Zhang, Lee & Igarashi, 2024). The orbitofrontal cortex is where olfactory input combines with gustatory, visual and mouthfeel input, and that convergence produces flavour (Han et al., 2023).

5.4 What has Been Shown in Humans

Three studies here carry direct human evidence, and their weight should be judged against the rodent material above.

Yang et al. (2021) recorded intracranial local field potentials from the piriform cortex and anterior hippocampus of eight epilepsy patients during an olfactory working memory task. Odour identity could be decoded from patterns of theta-coupled gamma in the piriform cortex but not reliably from the hippocampus, and sequence position was coded by theta phase in both. Two limits apply: the decoding margins are small, 13.9 per cent against a chance level of 10 per cent, and the sample is neurologically atypical by construction.

Förster et al. (2010), discussed in section 7.2, correlated FDG PET signal with the three Sniffin' Sticks subtests in 24 patients with early Alzheimer's disease and found the components mapping to different systems. These are the strongest human results available here, and they are thin against the rodent literature they are used to support. Section 9 returns to that imbalance.

6. Plasticity, Perceptual Learning and Olfactory Memory

Sections 2 to 5 describe a system that pulls molecular features out at the periphery, sharpens them in the bulb, and represents them as distributed ensembles in cortex. That account is incomplete, because what a person perceives depends on what they have smelled before. The behavioural evidence comes first here because it is human, and the mechanistic evidence second because it is not.

6.1 The Limits of Analytic Perception

Humans are poor at picking out the components of an odour mixture. Given mixtures of one to five odorants they had been trained to name individually, participants got every component right on 55 per cent of trials with one odorant, and that fell to 12, 6, 3 and 0 per cent as components were added. Telling them to attend selectively does not lift the ceiling, and with highly familiar odours it extends to about twelve components but no further (Wilson & Stevenson, 2003).

The ceiling is not about training. Expert perfumers and flavourists beat untrained participants on binary and ternary mixtures, but they showed no significant advantage at four or five components, where both groups did uniformly badly (Wilson & Stevenson, 2003).

Experience affects performance below that ceiling. Familiarity with the target and the background affects identification independently, from 58 per cent correct when both are unfamiliar to 87 per cent when both are familiar, and mere exposure improves later discrimination while learning a verbal label improves it further. Experience also changes what odours smell like. An odour repeatedly paired with a tastant takes on that taste quality, and odours experienced together as a mixture come to smell more alike, with triangle test performance falling from 87 per cent to 77 per cent (Wilson & Stevenson, 2003).

6.2 What Follows

Wilson and Stevenson (2003) argue that these findings do not fit an account in which peripheral feature extraction is directly available to perception. If odour perception were analytic in the way the coding of sections 3 and 4 suggests, expertise should raise the identification ceiling, and it does not. A system that merely detected features should not be shaped so strongly by which features the perceiver has met before.

Their proposal is that feature extraction is a first stage that is not itself consciously accessible, and that perception works on representations synthesised in the cortex from features that have co-occurred in experience. The odour is perceived as an object, not a set of components, and the objects available are the ones the perceiver has already formed.

6.3 Human Olfactory Memory

Reviewing the evidence on capacity, coding and neuropsychological dissociations a decade after her own earlier assessment, White (2009) concluded that the short-term and long-term distinction is still useful for thinking about olfactory memory, though perhaps not as architecturally separate stores. The hedge is the author's own and should be carried. Yang et al. (2021), described in section 5.4, give the only direct human recording during an olfactory memory task in this corpus, and odour sequences were reactivated in compressed form during maintenance, with the frequency of that reactivation predicting whether the later judgement was correct.

The neuropsychological line is older. A patient with bilateral medial temporal resection had normal olfactory sensitivity but performed at chance on whether two odours of similar intensity and different quality

were the same, while still discriminating objects by sight and touch (Wilson & Stevenson, 2003). If odour discrimination were independent of memory, that dissociation should not happen.

6.4 The Cortical Mechanism

The physiological account of how synthesis happens is rat work, almost all of it from one laboratory, and that should be said wherever the account is used.

Mitral cells and anterior piriform neurons habituate differently. Mitral cells show generalised cross-habituation across their receptive field, which fits feature detection, while anterior piriform neurons habituate selectively and maintain responses to a similar but distinct odorant, which fits a representation of the odour as a whole (Wilson & Stevenson, 2003).

This representation can be observed. After exposure to a novel binary mixture, cross-habituation to the components was weaker at fifty seconds of exposure than at ten, with responses at 35 and 31 per cent of baseline, so the cortical representation forms within tens of seconds (Wilson & Stevenson, 2003). One caveat attaches. The review cites that result as in press, and the published version should be found before it is used.

The synthesis depends on acetylcholine. Muscarinic blockade with scopolamine makes anterior piriform neurons behave like feature-detecting mitral cells and impairs perceptual learning in rats (Wilson & Stevenson, 2003; Zhang, Lee & Igarashi, 2024). Wilson, Best and Sullivan (2004) set this inside a broader account in which plasticity appears at every level of the olfactory pathway.

6.5 Synaptic and Network Levels

The synaptic mechanisms most likely to underlie cortical synthesis are those established for the hippocampus. Bruel-Jungerman, Davis and Laroche (2007) review four: long-term potentiation, long-term depression, synaptogenesis and adult neurogenesis. This is rodent hippocampal work with no olfactory content beyond naming the bulb as an adult neurogenic site, and it should be cited only for what Hebbian plasticity in piriform cortex would consist of.

At the network level, lateral entorhinal layer IIa fan cells develop responses to newly learned rewarded odour cues, which Zhang, Lee and Igarashi (2024) read as a cognitive map of odour items organised by outcome. Work in sheep and mice adds a time dimension: olfactory recognition memory first needs a distributed system, but after roughly eight hours of consolidation recall appears to depend on the bulb and piriform alone (Sánchez-Andrade, James & Kendrick, 2005). That paper states no limitations, and its model is animal social recognition, so the finding is a proposal about those species.

6.6 A Note on Independence

Three sources in this section share a senior author: Wilson and Stevenson (2003), Wilson, Best and Sullivan (2004) and Courtiol and Wilson (2017). Together, they provide most of the physiological account above. Zhang, Lee and Igarashi (2024) is independent in authorship but relays two of the same primary studies, so its agreement is no independent confirmation. The behavioural evidence in section 6.1 comes from several laboratories and does not have this problem.

7. Olfactory Dysfunction and Neurodegeneration

Olfactory dysfunction is common, mostly unnoticed by the people who have it, and linked to cognitive decline years before cognitive symptoms appear. Those three statements are well supported. What follows from them is less settled than the tone of this literature suggests.

7.1 Prevalence and Awareness

Reported prevalence runs from 1.4 to 62.4 per cent depending on measurement. A meta-analysis of 175,073 subjects gives 22.2 per cent overall, but 28.8 per cent by objective testing against 9.5 per cent by self-report (Han et al., 2023). Fewer than a quarter of people with an olfactory disorder know before testing (Marin et al., 2025).

Wang et al. (2021) measured both in the same 300 subjects. Objectively measured identification dysfunction rose from 22.9 per cent in cognitively normal controls to 53.6 per cent in subjective cognitive decline, 65.1 per cent in mild cognitive impairment and 96.2 per cent in Alzheimer's disease. Self-reported dysfunction did not differ at all, staying between 13.5 and 16.7 per cent. The gap widens as

the disease advances, and it is the strongest argument available for objective testing.

Ordinary ageing has to be set against this. Olfactory function peaks around forty and declines afterwards, affecting 62 to 80 per cent of people over eighty (Marin et al., 2025). Any disease-specific claim is made against a background in which everyone's olfactory system is deteriorating.

7.2 Which Component of Olfaction Tracks Cognition

Olfactory function is assessed as three separable components: detection threshold, discrimination and identification. Which one tracks cognitive decline is treated as settled in much of the literature, but it is not.

The prevailing account says identification is the key measure and threshold is largely uninformative. Marin et al. (2025) report that identification and discrimination track cognition while threshold shows no correlation, and Liao et al. (2024) report the same from independent primary sources. Both are reviews.

The largest primary study on that side is Wang et al. (2021), and it cannot support the claim. It used the Sniffin' Sticks Screen 16, which tests identification only, so it had nothing to show identification was better than and its conclusion was fixed by its design. Its regression models also explain only 9 to 12 per cent of the variance in cognitive performance, which its conclusions do not convey.

The one study here that measured all three components in the same subjects found the opposite. Servello et al. (2015) gave the Sniffin' Sticks Extended Test to 78 subjects and related each component to clinical dementia rating. Discrimination showed the strongest association, with an odds ratio of 0.75, followed by threshold at 0.84. Identification gave an odds ratio of exactly 1.00, with a confidence interval from 0.78 to 1.29, which means it did not predict at all.

Förster et al. (2010) address the same question from another angle. Correlating FDG PET signal with each subtest in 24 patients, they found three components mapping onto anatomically distinct systems of differing cognitive complexity, which may explain why they dissociate. It does not establish which one tracks decline, and the analysis used an uncorrected whole-brain threshold with no control imaging.

The honest position is that the components are separable, that identification has the weight of repetition behind it, and that the only direct comparison available found identification the weakest of the three. Reviews should not be counted as independent confirmations of a claim whose largest primary support could not have tested it.

7.3 Prevalence in Alzheimer's Disease

Olfactory dysfunction is reported in 85 to 90 per cent of Alzheimer's patients. The figure appears in Marin et al. (2025), Liao et al. (2024), Zhou et al. (2025), and Meyer et al. (2025), and is not original. Meyer and colleagues attribute it to Woodward and colleagues (2017) and Murphy (2019), and Wang and colleagues to Marine and Boriana (2014) and Peters and colleagues (2003). So the apparent agreement across four independent reviews reflects a small number of primary sources counted several times.

Zou et al. (2016) give a higher range, up to 100 per cent in Alzheimer's disease and 90 per cent in Parkinson's disease dementia. That paper also describes the epidemiological base most openly, noting that the surveys come mainly from developed countries, use small cross-sectional samples and lack cohort studies. Those caveats sit two paragraphs before the subtype figures and are not applied to them.

7.4 Structural Evidence: the Olfactory Bulb

If olfactory dysfunction in Alzheimer's disease reflects degeneration of olfactory structures, then bulb volume should separate patients from controls. Two independent studies tested this, and neither found that it does.

Carnemolla et al. (2022) measured olfactory bulb volume on MRI in 224 subjects at a dementia clinic: 50 with Alzheimer's disease, 119 with frontotemporal dementia variants and 55 controls. After correcting for whole-brain volume, bulb volumes did not differ, $F(5,215) = 0.432$, $p = 0.826$, with tracing by a rater blind to diagnosis.

Servello et al. (2015) measured bulb volume in 78 subjects across normal cognition, mild cognitive impairment and mild Alzheimer's

disease, with volumes computed by two independent operators. Volumes did not differ across clinical dementia rating groups ($p = 0.87$), and olfactory performance did not correlate with volume ($r = 0.04$). The group means ran slightly against the hypothesis: 33.49 cubic millimetres in controls, 34.87 in mild cognitive impairment and 35.91 in Alzheimer's disease.

Three qualifications are needed. Neither study reports a power calculation, and Servello and colleagues state openly that larger studies are needed before the correlation can be excluded. Carnemolla and colleagues did report a longitudinal reduction of 10 to 25 per cent at twelve months, but only four controls had follow-up scans, so controls were dropped, and the reduction cannot be separated from normal ageing. That study also had no objective measure of smell, using questionnaire items on appetite and food preference, informant-rated for patients and self-rated for controls.

So cross-sectional bulb volume does not separate Alzheimer's patients from controls in either independent test. The claim that bulb atrophy marks the disease should not be made without both nulls attached.

7.5 Functional Evidence and Mechanism

Where structural measures are negative, functional measures are more consistent. Odour-evoked activation of the primary olfactory cortex declines steadily from cognitively normal subjects through mild cognitive impairment to Alzheimer's disease; normal subjects habituate to prolonged odour stimulation while patients do not, and olfactory event-related potential latencies lengthen as dementia worsens (Liao et al., 2024). Section 8 covers the habituation finding.

Almost all of this is correlational. One study offers a causal mechanism, and it is a mouse study. Meyer et al. (2025) found loss of noradrenergic axons projecting from the locus coeruleus to the olfactory bulb in an amyloid knock-in model, reaching 33 per cent at six months. The loss came before plaque deposition, was specific to the bulb, and coincided with olfactory deficits at three months. We established the causal chain in two ways. Bulb microglia phagocytosed the axons, and knocking out the phagocytosis-promoting protein TSPO preserved both the axons and olfactory performance. And expressing the mutation only in locus coeruleus neurons reproduced both the axon loss and the deficit.

The human component is weaker than the framing implies. Post-mortem tissue showed reduced noradrenergic fibre density in early cases, and TSPO PET showed raised bulb signal in prodromal patients. But on odour identification, the prodromal group showed only a trend, and a significant deficit appeared only after conversion. The authors put this down to cohort size and cite eight other studies, which appeals to the wider literature rather than their own data.

7.6 Preclinical Evidence and Treatment

Whether olfactory change comes before cognitive change is best tested in people known to be developing the disease. Ramirez Gomez et al. (2022) studied 35 members of a kindred carrying the PSEN1 E280A mutation, and the primary comparison was null: carriers and non-carriers did not differ on odour identification, discrimination or episodic odour memory. A subgroup analysis found that the six carriers who had progressed to mild cognitive impairment performed worse on identification than the ten who had not ($p = 0.028$), though carriers were also older and less educated. The result should be reported as null first, from a genetically atypical cohort.

Olfactory training improves olfactory function in post-infectious, post-traumatic and idiopathic loss, and imaging studies report increased cortical thickness and bulb volume afterwards (Han et al., 2023; Marin et al., 2025). The evidence that the benefit extends to cognition is weaker than its frequency of citation suggests. Five sources report it, and all five are reviews relaying trials none of them conducted; Marin and colleagues also state in the same section that how far olfactory regions stay plastic is unknown.

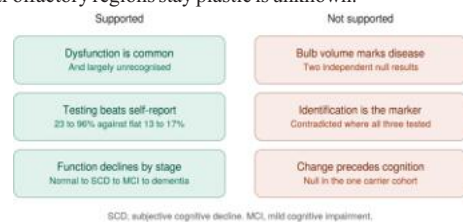


Figure 4. Which Clinical Claims the Evidence Supports.

All six claims are widely repeated in the literature examined. The three on the left are supported by the primary sources appraised for this review. The three on the right are not. SCD, subjective cognitive decline. MCI, mild cognitive impairment. Original figure.

7.7 What this Section Supports

Three claims are well supported (Figure 4): olfactory dysfunction is common and largely unrecognised, objective testing detects far more of it than self-report, and measured function declines across the clinical progression.

Three widely repeated claims are not. That bulb volume marks the disease is contradicted by two independent nulls. That identification is the component of interest rests on a study that measured nothing else, and is contradicted by the one study that measured all three. And the one preclinical cohort available here did not show that olfactory change reliably precedes cognitive change, where the primary comparison was null.

The mechanism is mouse, and the human half of the only study to address it did not reach significance at the stage that matters.

8. A Proposal: Cortical Habituation as the Link Between Mechanism and Deficit

Sections 6 and 7 described two literatures that do not cite one another: a rodent account of how the piriform cortex separates an odour from its background, and a human clinical observation that patients with mild cognitive impairment and Alzheimer's disease fail to do something healthy subjects do. This section proposes that the two concern the same process.

8.1 The Two Literatures

Anterior piriform neurons habituate to a sustained odour within tens of seconds while the mitral cells feeding them keep responding, so the adaptation is cortical and presynaptic in origin, and it is selective in a way mitral habituation is not (Wilson, Best & Sullivan, 2004; Wilson & Stevenson, 2003). Two functions are proposed. The first is figure-ground separation, since a cortex that stops responding to a continuously present odour can detect a new one against it. The second is perceptual stability, supplied by pattern completion (Courtillot & Wilson, 2017). The mechanism is cholinergically dependent, because muscarinic blockade makes anterior piriform neurons behave like feature-detecting mitral cells.

On the human side, functional imaging shows that cognitively normal subjects habituate to prolonged or repeated presentation of a high odour concentration, whereas patients with mild cognitive impairment and Alzheimer's disease do not, alongside a graded fall in activation size across those groups (Liao et al., 2024). Neither study reporting the habituation failure frames it in terms of cortical odour processing, and neither connects it to any mechanism.

8.2 The Proposal and its Predictions

The proposal is that the habituation failure seen in patients is a failure of the cortical adaptation mechanism characterised in rodents, and so a loss of figure-ground separation rather than a general fall in olfactory responsiveness.

Three predictions follow. If the deficit reflects a failure of cortical synthesis rather than peripheral detection, components that depend on cortical processing should be affected before those that do not, and Förster et al. (2010) provide the relevant anatomy. If it is cholinergically mediated, as the rodent mechanism is, it should respond to cholinergic manipulation. And if habituation failure reflects a cortical process degrading early, it should be detectable before the identification decline that clinical work currently uses as its marker.

8.3 What Supports This and What Does Not

The anatomical timing is favourable. Amyloid plaques and tangles appear in the olfactory bulb and cortex during progression, and atrophy appears in the transentorhinal and internal olfactory cortex before the hippocampus, so the structures the mechanism depends on are affected early (Liao et al., 2024).

The first prediction is only partly supported. Servello et al. (2015) found discrimination most strongly associated with dementia rating, which the proposal predicts. Threshold was also associated, which it does not predict. And identification was not associated at all, which it predicts least of all. So the account fits one of three components well,

one poorly and one not at all, in the best-controlled data available. The second and third predictions are untested.

8.4 Evidential Standing

This proposal rests on evidence not read directly for this review, and its foundations should be stated precisely. Every rodent claim in section 8.1 is relayed through Wilson and Stevenson (2003), Wilson, Best and Sullivan (2004), and Courtillot and Wilson (2017), which share a senior author. The exposure-duration finding is cited in the earliest of those as in press. No primary paper behind section 8.1 was obtained, and the human observation is relayed through a single review.

So this is a hypothesis assembled from secondary sources, inheriting whatever errors they contain. Section 7.2 criticised a claim for resting on a study that could not have tested it, and section 9 criticises treating agreement between reviews as agreement between findings. By those standards, this proposal is not evidence. It is a connection the primary literature may or may not support, offered because no source here makes it and because it can be tested.

8.5 What Would Test it

Four studies would settle the question. Obtain and verify the primary rodent work on habituation, exposure duration and pattern completion, without which the rodent half is unverified. Measure olfactory habituation directly in humans across the full progression, including the subjective cognitive decline stage that existing work leaves out. Test whether habituation failure precedes identification decline within individuals, which would separate this proposal from the current account. And test cholinergic dependence before and during cholinesterase inhibitor treatment.

9. What the Evidence Cannot Yet Support

9.1 The Literature is Largely Relayed

Of 383 claims extracted for this review, 73 per cent were relayed rather than reported as the citing paper's own work. That share is expected in a field dominated by reviews. What matters is that the relaying is often untraced, and that reviews present agreement as though it were agreement between findings. The 85 to 90 per cent prevalence figure appears in four reviews and the olfactory training claim in five sources, and none originates either. So counting citations overstates the evidence.

9.2 Species

Thirty-five per cent of the extracted claims rest on non-human evidence, and ten state no species at all. The imbalance is uneven because the peripheral and clinical literature is mostly human, while the cortical, plasticity, and mechanistic literature is mostly rodent. The account of how odour objects form in piriform cortex has no human demonstration here, and the only causal mechanism linking olfactory dysfunction to neurodegeneration is a mouse study whose human component did not reach significance at the prodromal stage.

Sources differ in how clearly they mark this. Mori, Nagao and Yoshihara (1999) combine mouse anatomy, rabbit electrophysiology and rat imaging into one account of the mammalian bulb without saying which came from which, and Gu et al. (2025) present the one-neuron-one-receptor rule as applying to humans generally, even though the primary studies are murine.

9.3 Measurement and Statistical Practice

Three measurement problems limit what the clinical literature can establish. The instruments differ: the Sniffin' Sticks screening form tests identification alone, while the extended form tests all three components separately, so pooling the literature across instruments cannot answer which component matters. Objective and subjective assessment give different answers, and self-report identifies roughly a third as many affected people. And imaging has limits, the authors state, including functional MRI temporal resolution and scalp EEG that cannot resolve bulbar activity.

Several primary findings this review relies on also carry statistical limits that their framing does not convey. Neither bulb volume study reports a power calculation, and both report nulls. Förster et al. (2010) analysed whole-brain PET correlations at an uncorrected threshold without imaging controls, Ramirez Gomez et al. (2022) report a positive subgroup of six against ten, and Wang et al. (2021) report models explaining 9 to 12 per cent of variance, a figure absent from their conclusions. None of this invalidates any study. In each case, the paper states the finding more strongly than the number supports.

9.4 Three Specific Failures of Citation

Three problems found while preparing this review are recorded here because they are traceable, not general.

The dimensions of the olfactory cleft, quoted widely in secondary sources, were traced to Damm et al. (2002), which reports MRI-derived volumes of eleven nasal segments and does not report cleft dimensions. The figures in circulation have no identifiable primary source.

Han et al. (2023) state in their introduction that humans can discriminate at least a trillion olfactory stimuli, and in their conclusion that the number is tens of thousands, both within an eight-page review. The same paper cites the Wilson group as authority for the claim that olfactory fibres reach the cortex without a thalamic relay, while its own figure of the pathway to the orbitofrontal cortex includes the thalamus.

Mori, Nagao and Yoshihara (1999) demonstrated exclusive receptor input for one glomerulus in one knock-in line and wrote that the hypothesis required testing for each. That caveat does not appear in the sources that later state the rule.

9.5 What Remains Unresolved, and Limitations of this Review

Four questions were examined and not settled. How many odours humans can discriminate, where the figures span eight orders of magnitude, and none reports how it was derived. How often olfactory sensory neurons are replaced, where two incompatible intervals circulate, and neither carries a species. How many sensory neurons converge on each glomerulus? And which component of olfactory function tracks cognitive decline.

This is a critical narrative review. No systematic search was run, no protocol was registered, and the sources were assembled iteratively. Twenty-five were appraised, twenty read in full and five from structured extraction records, and those five are all reviews carrying no claim central to the argument. The upstream primary sources behind several key claims were identified but not obtained, and where a claim rests on a source not read, the text says so directly. So this review shows that the literature relays findings without checking them.

10. CONCLUSION

This review examined what makes the olfactory system an early window into neurodegeneration, and what evidence supports that window. Three claims are well supported. Olfactory dysfunction is common and near-universal in Alzheimer's disease. The people who have it are largely unaware, and the gap between measured and self-reported dysfunction widens as the disease progresses. Measured olfactory function declines across the clinical progression.

Three further claims, each widely repeated, are not supported by the evidence here. Two independent cross-sectional null findings contradict the claim that olfactory bulb volume marks Alzheimer's disease; neither reported a power calculation, and the one longitudinal positive finding had no control group. That odour identification is the component tracking cognitive decline rests mainly on a study that measured no other component, and the only study that measured all three contradicts it. The one preclinical carrier cohort examined here did not show that olfactory change reliably precedes cognitive change, where the primary comparison was null.

The single causal mechanism available links early noradrenergic axon loss in the olfactory bulb to olfactory deficits through microglial phagocytosis. It was established in a mouse model, and its human component did not reach significance at the prodromal stage that would matter clinically.

Behind these findings sits a structural feature of the literature. Seventy-three per cent of the claims extracted were relayed rather than original; agreement between reviews is routinely presented as agreement between findings, and three specific citation failures were traced.

Section 8 proposed that the habituation failure seen in patients is a failure of the cortical adaptation mechanism characterised in rodents, and so a loss of figure-ground separation rather than a general loss of sensitivity. That proposal is assembled from secondary sources and offered as a hypothesis with four specified tests.

What the field most needs is direct measurement of olfactory habituation across the clinical progression, in humans, with the components of olfactory function measured separately.

REFERENCES

- Brüel-Jungersen, E., Davis, S., & Laroche, S. (2007). Brain plasticity mechanisms and memory: A party of four. *The Neuroscientist*, 13(5), 492–505. <https://doi.org/10.1177/1073858407302725>
- Bushdid, C., Magnasco, M. O., Vossahl, L. B., & Keller, A. (2014). Humans can discriminate more than 1 trillion olfactory stimuli. *Science*, 343(6177), 1370–1372. <https://doi.org/10.1126/science.1249168>
- Carnemolla, S. E., Kumfor, F., Liang, C. T., Foxe, D., Ahmed, R. M., & Piguet, O. (2022). Olfactory bulb integrity in frontotemporal dementia and Alzheimer's disease. *Journal of Alzheimer's Disease*, 89(1), 51–66. <https://doi.org/10.3233/JAD-220080>
- Courtioi, E., & Wilson, D. A. (2017). The olfactory mosaic: Bringing an olfactory network together for odor perception. *Perception*, 46(3–4), 320–332. <https://doi.org/10.1177/0301006616663216>
- Damm, M., et al. (2002). Consulted as an abstract only. The study reports MRI-derived volumes of eleven intranasal segments correlated with lateralised phenyl ethyl alcohol thresholds, odour discrimination and bilateral identification in fifty healthy male volunteers aged 22 to 59. Section 9.5 depends on confirming that it does not report olfactory cleft dimensions.]
- Förster, S., Vaitl, A., Teipel, S. J., Yakushev, I., Mustafa, M., la Fougère, C., Rominger, A., Cumming, P., Bartenstein, P., Hampel, H., Hummel, T., Buerger, K., Hundt, W., & Steinbach, S. (2010). Functional representation of olfactory impairment in early Alzheimer's disease. *Journal of Alzheimer's Disease*, 22(2), 581–591.
- Gomez Galarce, M., Yanez-Siller, J. C., Carrau, R. L., Montaser, A., Ramos Lima, L., Servian, D., Otto, B. A., Prevedello, D. M., & Naudy, C. A. (2018). Endonasal anatomy of the olfactory neural network: Surgical implications. *The Laryngoscope*, 128(11), 2473–2477. <https://doi.org/10.1002/lary.27194>
- Gu, Y., Zhou, X., Sun, B., Zhang, L., Yang, Y., Qi, G., Li, P., Sun, S., & Zhang, Y. (2025). A systematic review of the structure and function of human olfactory receptors and key technologies involved. *Trends in Food Science & Technology*, 159, Article 104971. <https://doi.org/10.1016/j.tifs.2025.104971>
- Han, S. A., Kim, J. K., Cho, D.-Y., Patel, Z. M., & Rhee, C.-S. (2023). The olfactory system: Basic anatomy and physiology for general otorhinolaryngologists. *Clinical and Experimental Otorhinolaryngology*, 16(4), 308–316. <https://doi.org/10.21053/ceo.2023.00185>
- Liao, W., Wang, Y., Wang, L., Li, J., Huang, D., Cheng, W., & Luan, P. (2024). The current status and challenges of olfactory dysfunction study in Alzheimer's disease. *Ageing Research Reviews*, 100, Article 102453. <https://doi.org/10.1016/j.arr.2024.102453>
- Marin, C., Alobid, I., López-Chacón, M., Rodríguez-VanStrahlen, C., Aguilera, P., & Mullol, J. (2025). Olfactory dysfunction and cognitive decline: Are they related? *Current Allergy and Asthma Reports*, 25, Article 56. <https://doi.org/10.1007/s11882-025-01236-3>
- Meyer, C., Niedermeier, T., Feyen, P. L. C., Strübing, F. L., Rauchmann, B.-S., Karali, K., Gentz, J., Tillmann, Y. E., Landgraf, N. F., Rumpf, S.-L., Ochs, K., Wind-Mark, K., Biechele, G., Wagner, J., Guersel, S., Kurz, C. I., Schweiger, M., Prtvar, D., Shi, Y., ... Paeger, L. (2025). Early locus coeruleus noradrenergic axon loss drives olfactory dysfunction in Alzheimer's disease. *Nature Communications*, 16, Article 7338. <https://doi.org/10.1038/s41467-025-62500-8>
- Mori, K., Nagao, H., & Yoshihara, Y. (1999). The olfactory bulb: Coding and processing of odor molecule information. *Science*, 286(5440), 711–715. <https://doi.org/10.1126/science.286.5440.711>
- Ramirez Gomez, L., Albers, M. W., Baena, A., Vila-Castellar, C., Fox-Fuller, J. T., Sanchez, J., Aguillon, D., Velilla, L., Lopera, F., & Quiroz, Y. T. (2022). Olfactory function and markers of brain pathology in non-demented individuals with autosomal dominant Alzheimer's disease. *Journal of Alzheimer's Disease*.
- Sánchez-Andrade, G., James, B. M., & Kendrick, K. M. (2005). Neural encoding of olfactory recognition memory. *Journal of Reproduction and Development*, 51(5), 547–558.
- Servello, A., Fioretti, A., Gualdi, G., Di Biasi, C., Pittalis, A., Sollaku, S., Pavaci, S., Tortorella, F., Fusetti, M., Valenti, M., Masedu, F., Cacciafesta, M., Marigliano, V., Ettorre, E., & Pagliarella, M. (2015). Olfactory dysfunction, olfactory bulb volume and Alzheimer's disease: Is there a correlation? A pilot study. *Journal of Alzheimer's Disease*, 48(2), 395–402. <https://doi.org/10.3233/JAD-150232>
- Wang, Q., Chen, B., Zhong, X., Zhou, H., Zhang, M., Mai, N., Wu, Z., Huang, X., Haehner, A., Chen, X., Alberi Auber, L., Peng, Q., Hummel, T., & Ning, Y. (2021). Olfactory dysfunction is already present with subjective cognitive decline and deepens with disease severity in the Alzheimer's disease spectrum. *Journal of Alzheimer's Disease*, 79(2), 585–595. <https://doi.org/10.3233/JAD-201168>
- White, T. L. (2009). A second look at the structure of human olfactory memory. *Annals of the New York Academy of Sciences*, 1170, 338–342.
- Wilson, D. A., Best, A. R., & Sullivan, R. M. (2004). Plasticity in the olfactory system: Lessons for the neurobiology of memory. *The Neuroscientist*, 10(6), 513–524.
- Wilson, D. A., & Stevenson, R. J. (2003). Olfactory perceptual learning: The critical role of memory in odor discrimination. *Neuroscience and Biobehavioral Reviews*, 27(4), 307–328. [https://doi.org/10.1016/S0149-7634\(03\)00050-2](https://doi.org/10.1016/S0149-7634(03)00050-2)
- Yang, A. I., Dikeçligil, G. N., Jiang, H., Das, S. R., Stein, J. M., Schuele, S. U., Rosenow, J. M., Davis, K. A., Lucas, T. H., & Gottfried, J. A. (2021). The what and when of olfactory working memory in humans. *Current Biology*, 31(20), 4499–4511.e8. <https://doi.org/10.1016/j.cub.2021.08.004>
- Zhang, Y. J., Lee, J. Y., & Igarashi, K. M. (2024). Circuit dynamics of the olfactory pathway during olfactory learning. *Frontiers in Neural Circuits*, 18, Article 1437575. <https://doi.org/10.3389/fncir.2024.1437575>
- Zou, Y.-m., Lu, D., Liu, L.-p., Zhang, H.-h., & Zhou, Y.-y. (2016). Olfactory dysfunction in Alzheimer's disease. *Neuropsychiatric Disease and Treatment*, 12, 869–875. <https://doi.org/10.2147/NDT.S104886>