# Congenital Anosmia and Emotional Processing

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## Abstract

Congenital anosmia (ICA) is the lifelong absence of odor recognition and underdevelopment of the olfactory bulbs and sulci. It proposes an investigation into the relationship between cross-modal plasticity and emotion recognition processes in individuals with ICA. Cross-modal plasticity refers to the adaptive reorganization of neurons to integrate the function of two or more sensory modalities, often occurring after sensory deprivation. Several studies indicate an overlap between emotional and olfactory processing, specifically in regions like the orbitofrontal cortex, insula, and amygdala. Other investigations also indicate that ICA is associated with structural brain alterations, including reduced grey matter volume in the orbitofrontal cortex, but greater volumes in the left medial frontal gyrus, right superior frontal sulcus, left entorhinal cortex, left piriform cortex, bilateral medial orbital gyrus, and right posterior orbital sulcus. ICA also exhibited a higher white matter density in the left insula and the region posterior to the parietal operculum. Though the Olfactory bulb depth remains low and the olfactory sulcus shallow, it is typical of what might be observed in anosmics. These structural adaptations suggest that compensatory mechanisms exist to compensate for the absence of olfaction. This literature review looks into the relationship between congenital anosmia and neural activation in regions of the brain associated with emotion recognition. These results support the thesis that structural changes in the brains of individuals with ICA might establish a compensatory mechanism for emotion recognition. These findings contribute to a greater understanding of smell in social and emotional cognition without olfaction.

## Keywords

Olfactory processing regions; Cross-modal plasticity; Sensory deprivation; Cortical thickness; Grey matter volume; White matter density; Olfactory bulb; Congenital anosmia; Olfactory sulcus; Orbitofrontal cortex; Insula; Entorhinal Cortex; Face Morph; Olfactory imagery; Piriform cortex; Longitudinal fasciculus

# Introduction

Around 1 in 10,000 people are born without a sense of smell; this condition is called congenital anosmia. Smell has proven vital in memory, emotion, and threat assessment, which raises the question of how these individuals adapt to maintain emotional and social cognition without the help of olfactory input. The exploration of the loss of this sensory modality poses an investigation into how such sensory loss can be mitigated through structural changes in the brain, perhaps through cross-modal plasticity. Cross-modal plasticity refers to the "adaptive reorganization of neurons to integrate the function of two or more sensory systems, which occurs after sensory deprivation, where the greatest reorganization of neural networks occurs after long-term sensory deprivation such as congenital blindness or deafness" (Kral & Sharma, 2023). The relevance of cross-modal plasticity in this topic might be found in a study that suggests that cross-modal plasticity is a compensatory mechanism in place for the absence of sight and hearing. "Changes in subcortical connectivity might lead to recruitment of the primary visual cortex by auditory inputs, as in the case of the blind mole rat. Other possible mechanisms include alterations in feedback between cortico-cortical connections and the stabilization of long-range connections, such as those found between the primary visual and auditory cortices in the monkey" (Bavellier & Neville, 2002). Studies have suggested that individuals with ICA exhibit a greater sensitivity to negative emotions, specifically anger and disgust (Peter et al., 2024). Additionally, a study that compared acquired anosmia and congenital anosmia showed greater grey matter volume in the left medial frontal gyrus, right superior frontal sulcus, left entorhinal cortex, left piriform cortex, bilateral medial orbital gyrus, and right posterior orbital sulcus in individuals with congenital anosmia, which suggests that the brain may adapt and implement compensatory mechanisms such as cross-modal plasticity to maintain cognitive function (Frasnelli et al., 2013; Karunanayaka et al., 2024). Several studies have also explored the structural relationships with anosmia, though few have examined these neurostructural adaptations to compensatory mechanisms (cross-modal plasticity) as it relates to emotional processing. The aim of this literature review is to explore this gap in research. An inference may be that congenital anosmia leads to structural changes in the brain that trigger compensatory mechanisms for the absence of olfactory input during emotional recognition processes. These changes occur in areas of the brain that overlap with both olfactory and emotional processing, which suggests that the brain may reorganize itself for stronger emotional and social cognition. To explore the validity of this thesis, this literature review examines the role of olfaction in emotion processing, structural brain adaptations in congenital anosmia, and emotion recognition in congenital anosmia. The first body section reviews literature on the olfactory system and emotional processing. The second section compares structural differences between individuals with congenital, acquired anosmia, and normal olfaction using magnetic resonance imaging (MRI) and voxel-based morphometry (VBM) studies. The last body section analyzes studies from facial emotion recognition tests conducted on ICA patients. Overall, this paper explores how the absence of smell affects emotional processing and what that might mean for a broader understanding of sensory input and plasticity.

# Discussion

## The role of olfaction in emotion processing

This section explores the relationship between olfaction and emotion by reviewing studies that describe how smells trigger emotional responses and how the brain processes emotions related to olfactory input. The typical human can “discriminate” at least one trillion odors (Bushdid et al., 2014), and what's interesting about the olfactory system is that it is positioned within the brain, where it may affect emotions and processing. Unlike other senses, olfactory signals bypass the thalamus and travel directly to the olfactory cortex (Shepherd et al., 2005), where these signals then move to areas involved in emotion, such as the amygdala, hippocampus, and orbitofrontal cortex, that are involved in the limbic pathway (BiologyInsights, 2025). When “odorant molecules” are inhaled, they travel through the nasal cavity and interact with olfactory receptor neurons, where these neurons then detect and transduce these molecules into electrical impulses. These signals are then transmitted to the brain, some areas of which are related to emotion and memory (BiologyInsights, 2025), where these signals are processed and interpreted as different scents.

Olfaction and odor perception have been widely investigated areas, though the question of how it affects emotions is still prevalent; this can be investigated through the concept of olfactory imagery, which was defined as “being able to experience the sensation of smell when an appropriate stimulus is absent” (Stevenson & Case et al., 2005). Studies on olfactory imagery suggest that olfaction is related to emotion, where a mental imagery study using fMRI and PET to imagine a scent found that “olfactory imagery” can influence the “perception of an odor” (Djordjivec et al., 2005). A neuroimaging study provided further evidence, even suggesting “embodied cognition” (the physical state of the body influences cognitive processes), where reading scent-related words such as “cinnamon” is associated with increased activity in the primary olfactory cortex (Gonzalez et. al, 2006). The activation of this area implies that the brain not only responds to actual olfactory stimuli but also to imagined scents. Other brain imaging studies showed overlap in areas of the brain activated by real and imagined odors, though the activations were reduced in “imagery conditions” (Levy et al., 1999; Henkin & Levy, 2002). Lin, Cross, and Childers examined emotional responses during “olfactory imaging”, where they found that greater olfactory ability was associated with more “vivid olfactory imaging” and emotional response. Researchers found that both real and imagined scents evoke an emotional response, supporting the idea that olfaction and emotional processing are closely related. These findings from olfactory imagery lead to a broader inquiry into how the olfactory system shares “common substrates” with emotional processing.

Building on this idea of olfaction, emotion, and substrate, Soudry et al. (2011) suggests that olfaction and emotion are not just correlated but also structurally integrated. As described in this research and previous literature, “physiologically, olfactory stimuli are processed according to their emotional content,” where, much like emotions, “odors can be given positive (appetitive), negative (aversive) or neutral valence” (Soudry, Lemogne, Malinvaud, Concoli, Bon. pg. 19). The close connection between odor and emotion are related to “common cerebral substrates”, specifically, the amygdala, hippocampus, insula, anterior cingulate cortex, and the orbitofrontal cortex, which are key processing regions for odor and emotion; further, the overlap of these areas also have implications for emotion and memory as well as the possible negative affects on emotional health due to olfactory loss. The review found that emotional responses to odours often occur somewhat unconsciously and are usually quickly processed, supporting their evolutionary role in survival and social communication. An example of the integration of emotion and odor could be a disgust response to an unpleasant odor, which may use the same pathways as visual disgust cues, which indicates shared mechanisms across sensory modalities.

Furthering the support for the connection between olfaction and emotional processing, the exploration of interpreting emotional reactions to environmental odors (smellscape odor input, which personal and social lenses can influence. Xiao, Tait, and Kans) suggests that smells affect how humans interact with their environment, as described by the smellscape concept of “physical space and the context of a place” where perception is at the core of the smellscape concept (pg. 2. Xiao et al., 2020). Initially, these researchers hypothesized that the smell model was triangular between emotion, society, and place, labeling it as a “spatial-emotional intermediary that links society, emotions, and place” (pg. 2, Xiao et al., 2020). Though after compiling the results, the smell model was arranged into a circular flow chart with “smells, physical environment, context of place, and individuals' memory” on the outside and “perceptions” on the inside of the flow chart. These researchers found during a railway station study, which aimed to uncover the “perceptual process of smellscape perceptions” among walk-along interviews, that language experiences in specific places indicated people's perceptions of their environmental settings (Bradley & Lang, 2000). Classen et al. (1994, p. 3) argued that smell is shifty and “cannot be documented in Western languages”; however, olfactory experiences are conveyed through metaphors. The study documented that in an interview, a participant described chlorine as a good smell and said it makes them feel happy and clean, and reminds them of a swimming pool. Such is an example of how an emotion-related experience influences olfactory perception. The study found that overall, participants associated certain smells with “places, social categories, and memories”, suggesting that olfactory-related emotion is not only neural but also requires associated experience.

## Brain structural adaptations in congenital anosmia

This section explores structural differences in individuals with isolated congenital anosmia (ICA), with a focus on volumetric and cortical thickness differences in regions of the brain associated with emotional processing. ICA poses an investigation into how the lifelong absence of olfactory input shapes the brain.

A review using a systematic search method using PubMed/MEDLINE and Scopus electronic databases to analyze olfactory-related structural changes in the brains of congenital and acquired anosmics found 28 studies to compare. The review listed the criteria that were to be investigated as it relates to structural changes, being (1) olfactory bulb, (2) olfactory sulcus, (3) grey matter (GM), and white matter (WM) changes. Overall, the study found that individuals with acquired anosmia exhibited “reduced volumes and thickness in the gyrus rectus, medial orbitofrontal cortex, anterior cingulate cortex, and cerebellum” (Manan et al., 2023), where the implication of this reduction may be a reduced ability to regulate emotions (Schmahmann et al., 2010). These findings differ from those observed in congenital anosmia, where a “reduced olfactory ability is associated with larger volume and higher thickness in regions like the piriform cortex, orbitofrontal cortex, and insula” (Manan et al., 2023). The voxel-based morphometry analysis verified that greater GM volumes were found in the “left medial frontal gyrus (MFG), right superior frontal sulcus (SFS) (Karstensen et al., 2018), left entorhinal cortex, left piriform cortex (Frasnelli et al., 2013), bilateral medial orbital gyrus (MOG) and right posterior orbital sulcus (POS) (Peter et al., 2020)” (pg. 14, Manan et al., 2023). Greater GM volume is often associated with greater connectivity potential and higher neuronal support through glial density, though the greater volume exhibited has collective implications for enhanced cognitive control, episodic memory (a type of long-term memory), emotion-sensory integration, and decision making. This analysis also examined WM density and found that congenital anosmics exhibited “larger WM density in the areas, including the left insula and the region posterior to the parietal operculum (Frasnelli et al., 2013)” (pg. 14, Manan et al., 2023). These results directly contrast with those of the acquired anosmics, where “the reduced olfactory function is associated with reduced GM and WM volumes and thickness (Han et al., 2018; Bitter et al., 2010a, b; Peng et al., 2013). Due to the insula being responsible for interoception (sensing the body’s internal condition, eg, temperature and heart rate), emotional processing, and decision making, and being supported by a diffusion MRI study showing that the insula is structurally connected to many other regions of the brain through white matter pathways (Menon et al., 2024). Additionally, damage to the left insula was also associated with impairment in emotion perception, as determined by lesion mapping research ( Operskalski et al., 2015). Such research suggests that emotional processing is strengthened in individuals with congenital anosmia, perhaps due to the higher density of the WM in this region, allowing neural signals to travel faster and exchange information more efficiently. This review also examined data relating to OB and OS volume and depth, which showed that both “right and left OB volumes were significantly smaller in anosmic patients than healthy controls” (Schofield et al., 2014; Manan et al., 2023). This shrinkage likely occurred due to smell signals from the nose not reaching the bulb through the cribiform plate, causing the loss of olfactory neurons (Schofeils et al., 2014). The OS depth, located between the medial orbital gyrus and gyrus rectus in the frontal lobe, is also quite a significant finding when examining olfaction. Overall, patients with congenital anosmia show the smallest OB volume and shallow OS depth compared to other participating groups (Manan et al., 2023).

Another study examining cortical changes and prefrontal and limbic brain regions in ICA individuals using MRI found thicker orbitofrontal cortices, along with larger grey matter volumes in left entorhinal and priform cortices, which are key areas in both olfactory and emotional networks ( Frasnelli et al., 2013). The study found that “congenital anosmia is associated with altered structure of brain areas of olfactory processing. Individuals with congenital anosmia had a thicker bilateral medial orbitofrontal cortex. Further, the same group exhibited a denser and thicker left piriform cortex” ( pg.4; Frasnelli et al., 2013). The implications surrounding a thicker medial orbitofrontal cortex suggest that compensatory neural reorganization may have occurred, as its role is primarily in reward evaluation, emotional regulation, and multisensory integration (combining senses) due to the absence of olfactory input. The structural enlargement in ICA patients also suggests reduced “synaptic pruning” (Synaptic pruning is a natural process in brain development where the brain eliminates unnecessary synapses, connections between neurons, enhancing its efficiency and functionality) due to a lack of olfactory input during early development (Frasnelli et al., 2013). In addition, the “left entorhinal cortex had a higher density in participants with congenital anosmia"  and a thinner patch of tissue in the posterior-lateral orbitofrontal cortex. Researchers further observed increased white matter density of the "left superior longitudinal fasciculus in an area posteromedial to the left insula, as well as of an area posterior to the parietal operculum" ( pg. 5; Frasnelli et al., 2013). Overall, these findings suggest a compensatory mechanism in place for a lack of olfaction (cross-modal plasticity) and reduced synaptic pruning.

Karstensen et al. (2018) investigated how the ICA affects brain structure, particularly in the fronto-limbic system that links smell and emotion. Researchers examined whether regional variations in gray matter volume were associated with smell ability in seventeen individuals with isolated congenital olfactory impairment (COI) matched with sixteen normosmic controls. Whole-brain magnetic resonance imaging and voxel-based morphometry were used to "estimate regional variations in gray matter volume". The analyses showed that compared to the controls, "COI subjects had significantly larger gray matter volumes in the left middle frontal gyrus and right superior frontal sulcus (SFS). COI subjects with severe olfactory impairment (anosmia) had reduced gray matter volume in the left mOFC and increased volume in right piriform cortex and SFS". Additionally, within the COI group, "olfactory ability, measured with the 'Sniffin' Sticks' test, was positively associated with larger gray matter volume in right posterior cingulate and parahippocampal cortices, whereas the opposite relationship was observed in controls" (Karstensen et al., 2018). In turn, the study concluded that differences "atypical brain development and plasticity" may have been a result of adaptive reorganization in the brain.

## Emotion recognition in individuals with ICA

This section analyses the results from facial emotion recognition studies in ICA patients to determine whether enhancements in non-olfactory emotion recognition can be observed. The link between emotion and olfaction is well supported, where odors often act as cues for affective states (Licon et al., 2018). In ICA, olfaction is absent from birth, which prompts questions about whether the brain undergoes reorganization (cross-modal plasticity) to rely on other sensory modalities for emotional processing.

A case-control study suggested that "patients with congenital anosmia and long-lasting acquired anosmia may compensate their inability to detect environmental hazards through olfaction by an increased ability to detect fear or disgust as facially expressed by others" (Lemogne et al., 2015). For each patient with congenital anosmia, the absence of the olfactory bulb was confirmed through magnetic resonance imaging. Emotion recognition abilities were examined with a "dynamic paradigm in which a morphing technique allowed displaying emotional facial expressions increasing in intensity over time". Adjusting for age, education, depression, and anxiety, patients with congenital anosmia required similar levels of emotion intensity to correctly recognize fear and disgust as healthy subjects. At the same time, they displayed decreased error rates for both fear and disgust. This study suggested that from an evolutionary standpoint, compensatory mechanisms may have occurred to detect emotions crucial for human survival, such as fear and disgust, with greater accuracy (Lemogne et al., 2015).

Similarly, another facial emotion recognition study, assessing ICA participants on static and dynamic facial morphs, reported that ICA patients exhibited a heightened sensitivity to anger and disgust but an earlier identification of the emotion during the morph (emotion was identified with less of the emotion on the face). These findings also indicate that the absence of a functioning sense of smell during development leads to compensatory changes in visual and social cognition. Furthermore, a study examining how smells affect moods, specifically, the effects of smells on stress, demonstrated that "heightened emotional states" can change sensory processing in cross-modal ways, suggesting a potential area for exploration in interpreting ICA adaptations (Krusemark et al., 2013).

## Conclusion

The review examined the role of olfaction in emotional processing, structural brain changes in ICA, and compensatory mechanisms in facial emotion recognition. Evidence from neuroscientific and behavioral studies supports the idea that olfaction is related to emotional processing (Lin et al., 2014; Soudry et al., 2011).

Structural neuroimaging studies showed that ICA is associated with volumetric and cortical thickness changes in emotion-related brain regions, such as the orbitofrontal cortex, piriform cortex, and limbic structures (Manan et al., 2022; Karstensen et al., 2018; Frasnelli et al., 2013; Yao et al., 2017). These changes suggest compensatory neuroplastic adaptations in response to the absence of olfactory input. This can be compared to other neurostructural adaptations from losing other sensory modalities (loss of sight and hearing).

Evidence of facial emotion recognition in ICA also supports this idea of compensatory mechanisms. Studies have shown that individuals with ICA exhibited a greater accuracy for emotion recognition in one study and in others a heightened sensitivity to fear, anger, and disgust (Lemogne et al., 2015; Drummond et al., 2023). This suggests that an absence of smell triggers compensatory mechanisms that mitigate potential threats by recognizing negative responses with greater accuracy and less intensity.

In turn, future studies could consider conducting long-term analysis of structural and functional changes in individuals with ICA. Future studies could also consider testing multisensory recognition tasks (visual, auditory, and tactile) and investigate whether compensatory mechanisms can be enhanced through training. This work could improve the lives of individuals with ICA and deepen our understanding of the relationship between olfactory loss and certain forms of cognition.


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# Author


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**Review for “Structural and Emotional Adaptations in Congenital Anosmia”**

**Recommendation: Revise and Resubmit (major revisions needed, acceptance not guaranteed)**

**General Comments**

This manuscript explores an important and underexamined question: how individuals with isolated congenital anosmia (ICA) adapt to the lifelong absence of olfactory input, particularly in terms of emotional processing and brain structure. The author attempts to synthesize evidence from multiple literatures, olfactory neurobiology, cross-modal plasticity, structural neuroimaging, and behavioral studies of emotion recognition, in support of the idea that ICA leads to compensatory mechanisms involving both brain reorganization and enhanced non-olfactory emotion recognition.

While the manuscript demonstrates intellectual ambition and touches on several interesting findings, the overall execution falls short of academic expectations. The central argument is inconsistently framed, the source integration is often unclear or inaccurate, and the writing lacks clarity and critical depth in key sections. Substantial revision will be required to improve the logical flow, scientific precision, and structural coherence of the paper.

**Formatting and Citation Style (APA):**
Throughout the manuscript, direct quotes are used frequently in place of paraphrasing. In scientific writing, however, direct quotations should be avoided entirely unless absolutely necessary, which is rarely the case outside of qualitative research or historical analysis. Instead, the author should paraphrase all cited content in their own words while maintaining proper attribution. This approach demonstrates deeper engagement with the material and improves the manuscript’s clarity and academic tone. I recommend that all direct quotes be removed and replaced with paraphrased summaries of the cited studies.

In addition, there are several citation formatting and referencing issues that need to be addressed to meet the standards of APA 7th edition:

- Several works are cited in-text but missing from the reference list, including Kral & Sharma (2023), Karunanayaka et al. (2024), Yao et al. (2017), Krusemark (2013), Schmahmann et al. (2010), and Bradley & Lang (2000) among others. Every in-text citation must have a corresponding full reference entry.

- The overall number of references is quite limited, especially for a review paper. The author is encouraged to expand their literature search and cite a broader range of relevant sources to support and strengthen each section of the review.
- Citation formatting should be carefully revised to follow APA guidelines, including consistent use of “et al.”, accurate author name spellings, publication years, and proper reference list structure.

Improving these aspects will enhance the scholarly rigor and readability of the manuscript.

## Major Areas for Improvement

**1. Introduction: Lacks Focus and Clear Research Framing**

The introduction introduces several relevant concepts, olfactory loss, emotional processing, cross-modal plasticity, but fails to clearly state a central research question or hypothesis. The phrase “this review explores a gap in the research” is vague and should be replaced with a specific, well-defined question (e.g., “Does congenital anosmia lead to compensatory neuroplastic changes that support emotional recognition via other sensory modalities?”).

**Actionable Suggestions:**

- Clarify and explicitly state your guiding research question or hypothesis.
- Reorganize the introduction for logical flow: definition → relevance → current evidence → specific aim.

**2. Section: Olfaction and Emotion — Overly Broad and Poorly Integrated**

This section attempts to address how olfaction is linked to emotion but suffers from trying to do too much. It spans foundational neuroanatomy, olfactory imagery, embodied cognition, and sociocultural smellscapes without establishing a coherent through-line. Studies are introduced without sufficient explanation of their methods or findings, and key terms (e.g., “embodied cognition”) are not clearly defined.

Furthermore, several claims are overstated, and some citations (e.g., Bushdid et al.’s "trillion odors" claim) are presented without proper context or caution.

**Actionable Suggestions:**

- Narrow the scope and structure the section logically (e.g., neurobiology → imagery → social context).
- Use citations critically: clearly state who found what, and why it matters.
- Remove or revise speculative or vague statements that undermine scientific clarity.

**3. Section: Brain Structural Adaptations — Confusing Attribution and Lack of Critical Synthesis**

This section is the most technically detailed but also the most confusing. The author discusses a systematic review (Manan et al., 2023) but does not clearly distinguish between the review's conclusions and those of the original studies it includes. Individual studies (e.g., Frasnelli et al., Karstensen et al.) are described in multiple places without clear attribution, leading to repetition and ambiguity.

The section lacks critical evaluation of methods (e.g., sample size, imaging techniques), and key claims (e.g., that increased grey matter supports "enhanced emotional processing") are made without proper caution.

**Actionable Suggestions:**

- Clarify what is being cited from *Manan et al.* vs. from primary sources.
- Avoid repetition and long quotes—paraphrase clearly and concisely.
- Group findings thematically (e.g., grey matter changes, white matter changes) and link back to the paper's central question on emotional processing.
- Acknowledge limitations of the cited studies (e.g., small sample sizes, cross-sectional designs).

**4. Section: Emotion Recognition in ICA — Narrow and Underdeveloped**

This section is grounded primarily in one study i.e., Lemogne et al., 2015 and lacks a broader literature base. The findings are interesting, suggesting enhanced recognition of fear or disgust, but the interpretation is overextended and lacks nuance. There is no discussion of alternative explanations or methodological limitations. Drummond et al. (2024) on congenital anosmia and facial emotion recognition would be an appropriate paper to include in this section. This source is cited in the conclusion, but not elsewhere.

Generally, a discussion on why negative emotions (fear, disgust and anger) would need to be better detected by people with congenital anosmia would be appropriate here.

In addition, key terms (e.g., "heightened sensitivity," "dynamic paradigm") are used without explanation, and the final reference to Krusemark et al. (2013) is disconnected from the rest of the section and poorly justified.

**Actionable Suggestions:**

- Clarify what the key studies actually show and distinguish clearly between the study results and your own interpretation.
- Define task types and outcome measures clearly.
- Remove tangential citations unless fully integrated and relevant.
- End the section with a clear link back to the paper's central theme of emotion processing under sensory deprivation.

### 5. Conclusion — Accurate Summary but Lacking Synthesis and Caution

The conclusion accurately summarizes the topics discussed but does not meaningfully synthesize them. It overstates the evidence, makes broad claims (e.g., "olfaction is related to emotional processing") without qualifying them.

**Actionable Suggestions:**

- Soften claims and acknowledge that evidence for compensation in ICA is limited and inconsistent.
- Clarify what is known vs. speculative.
- Clearly justify any future directions you suggest.
- End on a cohesive note that ties the three themes (emotion, structure, plasticity) together.

### Final Thoughts

This review has the potential to contribute meaningfully to discussions of sensory plasticity and emotional processing in congenital anosmia. However, the manuscript in its current form is not yet ready for publication. The paper needs substantial restructuring, careful editing, more rigorous source integration, and clearer framing of its central argument.

We encourage the author to revise the manuscript by:

- Narrowing the focus and framing a clear, testable research question.
- Synthesizing evidence more critically rather than summarizing it descriptively.
- Improving clarity in writing and avoiding overstatements.
- Ensuring every paragraph contributes directly to the central aims of the review.

With significant revision, this could become a thoughtful and valuable piece of student scholarship.

# Convergence Review of Congenital Anosmia and Emotional Processing

**Overview:** In this review, the author summarizes previous literature that relate congenital anosmia, the inability to smell, and the regions of the brain associated with emotion. The review discusses evidence showing that smell and emotion are often related and changes in the brain structure resulting from the lack of smell.

Overall, I found the review to flow well (easy to read, unlike some reviews!) and to provide sufficient justification for its claims. The review did an excellent job of summarizing the topics and providing citations. Given that it was a review, it wasn't necessarily original (understandable given that it is virtually impossible to conduct original research on this topic), but did provide a pedagogical and understandable synopsis of the topic.

That said, I believe the review should be <u>accepting once the following minor revisions to improve readability and clarity are made</u>:

**Substantive Edits**

1. The most substantive suggestion would be to drop sentences that begin many of the sections like "This section explores structural differences in individuals with isolated congenital anosmia (ICA), with a focus on volumetric and cortical thickness differences in regions of the brain associated with emotional processing." There is no need to introduce a section like this since: a) the review is short and b) the section titles already introduce the sections.

2. I would similarly delete "The first body section reviews literature on the olfactory system and emotional processing. The second section compares structural differences between individuals with congenital, acquired anosmia, and normal olfaction using magnetic resonance imaging (MRI) and voxel-based morphometry (VBM) studies. The last body section analyzes studies from facial emotion recognition tests conducted on ICA patients." No need to introduce sections that are already introduced below. I also don't know what "body sections" are. You can delete body, if not the whole quote.

3. Under the keywords provided, you need not name all of the brain structures. You should name terms that relate to the point of your review. Your review ends up not talking that much about these structures anyway.

4. I believe that the paper would be improved if you included figures illustrating: a) areas where the brain changes due to anosmia (maybe a with/without anosmia figure comparing the two brain structures) and b) the brain structures most altered by anosmia. Figures help readers solidify their understanding and develop understanding in different ways.

**Minor Edits**

1. "It proposes an investigation into the relationship between cross-modal plasticity and emotion recognition processes in individuals with ICA." What is it? Proposes is not the right word. Motivates?

2. “ICA also exhibited a higher white matter density in the left insula and the region posterior to the parietal operculum.” Should be patients with ICA aslo exhibited…

3. “These results support the thesis that structural changes in the brains of individuals with ICA might establish a compensatory mechanism for emotion recognition.” I would say “these previous studies” or “this previous literature” since you are not presenting novel results.

4. “The relevance of cross-modal plasticity in this topic might be found in a study that suggests that cross-modal plasticity is a compensatory mechanism in place for the absence of sight and hearing.” Should be “the relevance of cross-modal plasticity to this topic may be found in a study…in place of sight and hearing.”

5. “Furthering the support for the connection between olfaction and emotional processing, the exploration of interpreting emotional reactions to environmental odors (smellscape odor input, which personal and social lenses can influence. Xiao, Tait, and Kans) suggests” should be “...(smellscape odor input…influence). Xiao, Tait, and Kans suggest…”

6. “ICA poses an investigation into how the lifelong absence of olfactory input shapes the brain.” This does not make sense. Poses is likely not the correct word for what you are trying to say.

# Congenital Anosmia and Emotional Processing


## Abstract

Congenital anosmia (ICA) is the lifelong absence of odor recognition and underdevelopment of the olfactory bulbs and sulci. Through this condition, an investigation into the relationship between cross-modal plasticity and emotion recognition processes in individuals with ICA is prompted. Cross-modal plasticity refers to the adaptive reorganization of neurons to integrate the function of two or more sensory modalities, often occurring after sensory deprivation. Several studies indicate an overlap between emotional and olfactory processing, specifically in regions like the orbitofrontal cortex, insula, and amygdala. Other investigations also indicate that ICA is associated with structural brain alterations, including reduced grey matter volume in the orbitofrontal cortex, but greater volumes in the left medial frontal gyrus, right superior frontal sulcus, left entorhinal cortex, left piriform cortex, bilateral medial orbital gyrus, and right posterior orbital sulcus. Patients with ICA also exhibited a higher white matter density in the left insula and the region posterior to the parietal operculum. Though the Olfactory bulb depth remains low and the olfactory sulcus shallow, it is typical of what might be observed in anosmics. These structural adaptations suggest that compensatory mechanisms exist to compensate for the absence of olfaction. This literature review looks into the relationship between congenital anosmia and neural activation in regions of the brain associated with emotion recognition. These previous studies support the thesis that structural changes in the brains of individuals with ICA might establish a compensatory mechanism for emotion recognition. These findings contribute to a greater understanding of smell in social and emotional cognition without olfaction.



## Keywords

Congenital anosmia; cross-modal plasticity; sensory deprivation; olfactory processing; emotional recognition; cortical thickness; grey matter; white matter

# Introduction

Around 1 in 10,000 people are born without a sense of smell; this condition is called congenital anosmia. Smell has proven vital in memory, emotion, and threat assessment, which raises the question of how these individuals adapt to maintain emotional and social cognition without the aid of olfactory input. The exploration of the loss of this sensory modality poses an investigation into how such sensory loss can be mitigated through structural changes in the brain, perhaps through cross-modal plasticity. Cross-modal plasticity refers to the "adaptive reorganization of neurons to integrate the function of two or more sensory systems, which occurs after sensory deprivation, where the greatest reorganization of neural networks occurs after long-term sensory deprivation such as congenital blindness or deafness" (Kral & Sharma, 2023). The relevance of cross-modal plasticity to this topic might be found in a study that suggests that cross-modal plasticity is a compensatory mechanism in place of sight and hearing. "Changes in subcortical connectivity might lead to recruitment of the primary visual cortex by auditory inputs, as in the case of the blind mole rat. Other possible mechanisms include alterations in feedback between cortico-cortical connections and the stabilization of long-range connections, such as those found between the primary visual and auditory cortices in the monkey" (Bavellier & Neville, 2002). Studies have suggested that individuals with ICA exhibit a greater sensitivity to negative emotions, specifically anger and disgust (Peter et al., 2024). Additionally, a study that compared acquired anosmia and congenital anosmia showed greater grey matter volume in the left medial frontal gyrus, right superior frontal sulcus, left entorhinal cortex, left piriform cortex, bilateral medial orbital gyrus, and right posterior orbital sulcus in individuals with congenital anosmia, which suggests that the brain may adapt and implement compensatory mechanisms such as cross-modal plasticity to maintain cognitive function (Frasnelli et al., 2013). Several studies have explored the structural relationships with anosmia; however, few have examined how these neurostructural adaptations, specifically those related to cross-modal plasticity, impact emotional processing and recognition. This research gap leads to the central question: Does congenital anosmia (ICA) lead to compensatory neuroplastic changes that support the maintenance of emotional recognition via reorganized cortical areas? Our thesis is that the structural changes observed in ICA occur in areas of the brain that overlap with both olfactory and emotional processing, suggesting that the brain reorganizes itself for stronger reliance on other sensory inputs for emotional and social cognition. To explore the validity of this thesis, this literature review examines the role of olfaction in emotion processing, structural brain adaptations in congenital anosmia, and emotion recognition in congenital anosmia. The first body section reviews literature on the olfactory system and emotional processing. The second section compares structural differences between individuals with congenital, acquired anosmia, and normal olfaction using magnetic resonance imaging (MRI) and voxel-based morphometry (VBM) studies. The last body section analyzes studies from facial emotion recognition tests conducted on ICA patients. Overall, this paper explores how the absence of smell affects emotional processing and what that might mean for a broader understanding of sensory input and plasticity.

# Discussion

## The role of olfaction in emotion processing

The olfactory system is unique in that its sensory pathways are located deep within the brain, allowing for direct influence on regions involved in emotion and memory. Unlike other senses, olfactory signals bypass the thalamus and travel directly to the olfactory cortex (Shepherd et al., 2005). These signals then move to areas involved in emotion, such as the amygdala, hippocampus, and orbitofrontal cortex, that are involved in the limbic pathway (BiologyInsights, 2025). The olfactory system's unique thalamus-bypassing pathway offers a route to interact with the limbic system, which may contribute to the “emotional salience” of odors. When “odorant molecules” are inhaled, they travel through the nasal cavity and interact with olfactory receptor neurons, where these neurons then detect and transduce these molecules into electrical impulses. These signals are then transmitted to the brain, some areas of which are related to emotion and memory (BiologyInsights, 2025), where these signals are processed and interpreted as different scents. Taken together, understanding olfaction’s role in emotion requires integrating evidence across multiple levels of analysis, from neural circuitry linking odor and emotion to cognitive processes such as olfactory imagery, and finally to the social and environmental contexts in which smells shape affective experience.

Olfaction and odor perception have been widely investigated areas, though the question of how it affects emotions is still prevalent; this can be investigated through the concept of olfactory imagery, which was defined as “being able to experience the sensation of smell when an appropriate stimulus is absent” (Stevenson & Case et al., 2005). A mental imagery study using fMRI and PET on participants who were required to imagine specific odors while their brain activity was measured found that “olfactory imagery” can influence the “perception of an odor” (Djordjivec et al., 2005). A neuroimaging study provided further evidence for the link between odor perception and olfaction, this finding is consistent with the principles of “embodied cognition” ( the idea that our thoughts, emotions, and perceptions are influenced by the physical body, meaning that cognitive processes are shaped not just by the brain, but also by bodily sensations, movements, and interactions with the environment.), where reading scent-related words such as “cinnamon” is associated with increased activity in the primary olfactory cortex (Gonzalez et. al, 2006). The activation of this area implies that the brain not only responds to actual olfactory stimuli but also to imagined scents. Other brain imaging studies showed overlap in areas of the brain activated by real and imagined odors, though the activations were reduced in “imagery conditions” (Levy et al., 1999; Henkin & Levy, 2002). Lin, Cross, and Childers examined emotional responses during “olfactory imaging”, where they found that greater olfactory ability was associated with more “vivid olfactory imaging” and emotional response. Researchers found that both real and imagined scents evoke an emotional response. These findings demonstrate a functional overlap in emotional response between real and imagined scents, providing further evidence for the established link between olfaction and emotional processing. Overall, these findings from olfactory imagery lead to a broader inquiry into how the olfactory system shares “common substrates” with emotional processing.

Building on this idea of olfaction, emotion, and substrate, the findings of Soudry et al. (2011) may suggest that olfaction and emotion are not just correlated but also structurally integrated, though this should be investigated further. As described in this research and previous literature, “physiologically, olfactory stimuli are processed according to their emotional content," where, much like emotions, "odors can be given positive (appetitive), negative (aversive) or neutral valence" (Soudry, Lemogne, Malinvaud, Concoli, Bon. pg. 19). The close connection between odor and emotion are related to "common cerebral substrates", specifically, the amygdala, hippocampus, insula, anterior cingulate cortex, and the orbitofrontal cortex, which are key processing regions for odor and emotion; further, the overlap of these areas also have implications for emotion and memory as well as the possible negative affects on emotional health due to olfactory loss. The review found that emotional responses to odours often occur somewhat unconsciously and are usually quickly processed, a characteristic hypothesized to be related to their evolutionary role in survival and social communication. An example of the integration of emotion and odor could be a disgust response to an unpleasant odor, which may use the same pathways as visual disgust cues, a finding that suggests the potential for shared neural mechanisms across sensory modalities.

Furthering the support for the connection between olfaction and emotional processing, the exploration of interpreting emotional reactions to environmental odors (smellscape odor input, which personal and social lenses can influence). Xiao, Tait, and Kans suggest that smells affect how humans interact with their environment, as described by the smellscape concept of "physical space and the context of a place" where perception is at the core of the smellscape concept (pg. 2. Xiao et al., 2020). Initially, these researchers hypothesized that the smell model was triangular between emotion, society, and place, labeling it as a "spatial-emotional intermediary that links society, emotions, and place" (pg. 2, Xiao et al., 2020). Though after compiling the results, the smell model was arranged into a circular flow chart with "smells, physical environment, context of place, and individuals' memory" on the outside and "perceptions" on the inside of the flow chart. These researchers found during a railway station study, which aimed to uncover the "perceptual process of smellscape perceptions" among walk-along interviews, that language experiences in specific places indicated people's perceptions of their environmental settings (Bradley & Lang, 2000). Classen et al. (1994, p. 3) argued that smell is shifty and "cannot be documented in Western languages"; however, olfactory experiences are conveyed through metaphors. The study documented that in an interview, a participant described chlorine as a good smell and said it makes them feel happy and clean, and reminds them of a swimming pool. Such is an example of how an emotion-related experience influences olfactory perception. The study found that overall, participants associated certain smells with "places, social categories, and memories", which may be that olfactory-related emotion is not only neural but also requires associated experience.

## Brain structural adaptations in congenital anosmia

ICA enables the exploration of how the brain reorganizes itself in response to the lifelong absence of smell. A review using a systematic search method using PubMed/MEDLINE and Scopus electronic databases to analyze olfactory-related structural changes in the brains of congenital and acquired anosmics found 28 studies to compare. The review listed the criteria that were to be investigated as it relates to structural changes, being (1) olfactory bulb, (2) olfactory sulcus, (3) grey matter (GM), and white matter (WM) changes. Overall, the study found that individuals with acquired anosmia exhibited reduced volumes and thickness in the gyrus rectus, medial orbitofrontal cortex, anterior cingulate cortex, and cerebellum (Manan et al., 2023), where the implication of this reduction may be a reduced ability to regulate emotions (Schmahmann et al., 2010). In contrast, ICA is associated with larger volume and higher thickness in several key regions, suggesting a compensatory response. Manan et al. (2023) summarized primary source findings from Voxel-Based Morphometry (VBM) analyses: Greater GM volumes were reported in the left medial frontal gyrus (MFG) and right superior frontal sulcus (SFS) (Karstensen et al., 2018), the left entorhinal cortex and left piriform cortex (Frasnelli et al., 2013), and the bilateral medial orbital gyrus (MOG) and right posterior orbital sulcus (POS) (Peter et., 2020). Larger WM density was observed in areas including the left insula and the region posterior to the parietal operculum (Frasnelli et al., 2013). Greater GM volume is often associated with greater connectivity potential and higher neuronal support through glial density, though the greater volume exhibited has collective implications for enhanced cognitive control, episodic memory (a type of long-term memory), emotion-sensory integration, and decision making. This analysis also examined WM density and found that congenital anosmics exhibited larger WM density in the areas, including the left insula and the region posterior to the parietal operculum (Frasnelli et al., 2013). These results directly contrast with those of the acquired anosmics, where reduced olfactory function is associated with reduced GM and WM volumes and thickness (Han et al., 2018; Bitter et al., 2010; Peng et al., 2013). Due to the insula being responsible for interoception (sensing the body's internal condition, eg, temperature and heart rate), emotional processing, and decision making, and being supported by a diffusion MRI study showing that the insula is structurally connected to many other regions of the brain through white matter pathways (Menon et al., 2024). Additionally, damage to the left insula was also associated with impairment in emotion perception, as determined by lesion mapping research ( Operskalski et al., 2015). Such research suggests that emotional processing is strengthened in individuals with congenital anosmia, perhaps due to the higher density of the WM in this region, allowing neural signals to travel faster and exchange information more efficiently. This review also examined data relating to OB and OS volume and depth, which showed that both right and left OB volumes were significantly smaller in anosmic patients than healthy controls (Schofield et al., 2014; Manan et al., 2023). This shrinkage likely occurred due to smell signals from the nose not reaching the bulb through the cribiform plate, causing the loss of olfactory neurons (Schofeils et al., 2014). The OS depth, located between the medial orbital gyrus and gyrus rectus in the frontal lobe, is also quite a significant finding when examining olfaction. Overall, patients with congenital anosmia show the smallest OB volume and shallow OS depth compared to other participating groups (Manan et al., 2023). The observation of greater GM volumes and increased WM density in regions for emotion and cognition, particularly the insula, suggests that these structural adaptations in individuals with ICA may result in enhanced processing and integration of non-olfactory sensory or emotional information, a key form of neural reorganization.

Another study examining cortical changes and prefrontal and limbic brain regions in ICA individuals using MRI found thicker orbitofrontal cortices, along with larger grey matter volumes in left entorhinal and priform cortices, which are key areas in both olfactory and emotional networks ( Frasnelli et al., 2013). The study found that "congenital anosmia is associated with altered structure of brain areas of olfactory processing. Individuals with congenital anosmia had a thicker bilateral medial orbitofrontal cortex. Further, the same group exhibited a denser and thicker left piriform cortex" ( pg.4; Frasnelli et al., 2013). The implications surrounding a thicker medial orbitofrontal cortex suggest that compensatory neural reorganization may have occurred, as its role is primarily in reward evaluation, emotional regulation, and multisensory integration (combining senses) due to the absence of olfactory input. The structural enlargement in ICA patients also suggests reduced "synaptic pruning” (Synaptic pruning is a natural process in brain development where the brain eliminates unnecessary synapses, connections between neurons, enhancing its efficiency and functionality) due to a lack of olfactory input during early development (Frasnelli et al., 2013). In addition, there was a higher density in the left entorhinal cortex in individuals with congenital anosmia and a thinner patch of tissue in the posterior-lateral orbitofrontal cortex. Researchers further observed increased white matter density of the left superior longitudinal fasciculus in an area posteromedial to the left insula, as well as of an area posterior to the parietal operculum (Frasnelli et al., 2013). Overall, these findings suggest a compensatory mechanism in place for a lack of olfaction (cross-modal plasticity) and reduced synaptic pruning. These combined findings of GM enlargement and increased WM density strongly suggest a pattern of structural reorganization in ICA, where the absence of olfactory input drives compensatory neuroplastic changes to enhance other sensory and emotional functions. These structural adaptations act as the foundation for the cross-modal compensation observed in the behavioral and functional characteristics of individuals with congenital anosmia.

Karstensen et al. (2018) investigated how the ICA affects brain structure, particularly in the fronto-limbic system that links smell and emotion. Researchers examined whether regional variations in gray matter volume were associated with smell ability in seventeen individuals with isolated congenital olfactory impairment (COI) matched with sixteen normosmic controls. Whole-brain magnetic resonance imaging and voxel-based morphometry were used to estimate “regional variations” in gray matter volume. The analyses showed that compared to the controls, COI subjects reported larger gray matter volumes in the left middle frontal gyrus and right superior frontal sulcus (SFS). COI subjects with “severe olfactory impairment” (anosmia) reported reduced gray matter volume in the left mOFC and increased volume in the right piriform cortex and SFS. Additionally, within the COI group, olfactory ability, measured with the 'Sniffin' Sticks' test, was positively associated with larger gray matter volume in right posterior cingulate and parahippocampal cortices, where a contrasting relationship was observed in controls (Karstensen et al., 2018). In turn, the study concluded that differences “atypical brain development” and plasticity may have been a result of adaptive reorganization in the brain.

While these structural differences support a compensatory model, research in this area requires cautious interpretation due to methodological limitations. Many of the cited studies, including Frasnelli et al. (2013) and Karstensen et al. (2018), rely on small sample sizes and cross-sectional designs. This makes it challenging to establish a causal link between the absence of olfaction in congenital anosmics and proposed neuroplastic adaptations; specifically, we cannot be certain whether the structural changes developed because of the anosmia, or if they are merely correlated with it. Furthermore, Voxel-Based Morphometry (VBM) analyses can be limited in their ability to confirm the outcomes of increased GM or WM density, requiring further functional MRI (fMRI) investigations to accurately assess the behavioral impact of cross-modal plasticity.

## Emotion recognition in individuals with ICA

The link between emotion and olfaction is well supported, where odors often act as cues for affective states (Licon et al., 2018). In ICA, olfaction is absent from birth, which prompts questions about whether the brain undergoes reorganization (cross-modal plasticity) to rely on other sensory modalities for emotional processing.

A case-control study suggested that “patients with congenital anosmia and long-lasting acquired anosmia may compensate their inability to detect environmental hazards through olfaction by an increased ability to detect fear or disgust as facially expressed by others” (Lemogne et al., 2015). For each patient with congenital anosmia, the absence of the olfactory bulb was confirmed through magnetic resonance imaging. Emotion recognition abilities were examined with a “dynamic paradigm in which a morphing technique allowed displaying emotional facial expressions increasing in intensity over time”. Adjusting for age, education, depression, and anxiety, patients with congenital anosmia required similar levels of emotion intensity to correctly recognize fear and disgust as healthy subjects. At the same time, they displayed decreased error rates for both fear and disgust. This study suggested that from an evolutionary standpoint, compensatory mechanisms may have occurred to detect emotions crucial for human survival, such as fear and disgust, with greater accuracy (Lemogne et al., 2015).

A more recent facial emotion recognition study tested ICA participants on static and dynamic facial morphs (A static face morph is a still image that has been digitally altered to transition between two different facial expressions), (A dynamic face morph is a short video or sequence of images that gradually transition one facial expression into another). The results reported enhanced emotion detection, showing that ICA patients were better and faster at recognizing disgust and anger compared to controls (Drummond et al., 2024). The ICA group showed heightened sensitivity to these emotions, correctly identifying the emotion earlier in the morphing process (i.e., with less of the emotion visible on the face) (Drummond et al., 2024). This faster and more accurate identification suggests that the absence of olfaction during development may have led to compensatory changes in visual and social cognition. ICA individuals showing enhanced recognition of negative emotions (fear, disgust, and anger) is relevant, as these emotions are strongly linked to avoidance and survival, often serving as non-verbal cues for potential danger. Since olfaction is an important sense for detecting danger (like spoiled food or smoke), the enhanced visual recognition of these negative emotions in ICA may be a result of any reorganization that has occurred.

Furthermore, a study examining how smells affect moods, specifically, the effects of smells on stress, demonstrated that “heightened emotional states” can change sensory processing in cross-modal ways, suggesting a potential area for exploration in interpreting ICA adaptations (Krusemark et al., 2013). This finding indicates that emotion and sensory input may have a two-way relationship, where an existing mood can directly re-allocate the brain's attentional and processing resources to different senses. This emotion-driven sensory re-allocation supports the thesis that the lifelong absence of olfaction in ICA may trigger an adaptive structural reorganization to utilize the visual processing of emotional cues. However, this cannot be known, as further investigation is required.

## Conclusion

The review examined the role of olfaction in emotional processing, structural brain changes in ICA, and compensatory mechanisms in facial emotion recognition. Evidence from neuroscientific and behavioral studies supports the idea that olfaction is related to emotional processing (Lin et al., 2014; Soudry et al., 2011).

Structural neuroimaging studies showed that ICA is associated with volumetric and cortical thickness changes in emotion-related brain regions, such as the orbitofrontal cortex, piriform cortex, and limbic structures (Manan et al., 2022; Karstensen et al., 2018; Frasnelli et al., 2013). These structural differences, characterized by increased gray matter volume and white matter density in ICA, are widely interpreted by the authors as neuroplastic adaptations, some suggesting it may be compensatory. These structural differences are also comparable to those observed following the congenital loss of other sensory modalities (e.g., sight or hearing. These changes suggest there may be compensatory neuroplastic adaptations in response to the absence of olfaction.

Evidence of facial emotion recognition in ICA also supports this idea of compensatory mechanisms. Studies have shown that individuals with ICA exhibited a greater accuracy for emotion recognition in one study and in others a heightened sensitivity to fear, anger, and disgust (Lemogne et al., 2015; Drummond et al., 2023). This suggests that an absence of smell triggers compensatory mechanisms that mitigate potential threats by recognizing negative responses with greater accuracy and less intensity.

While the findings are compelling, the evidence for consistent compensation in ICA remains limited and requires cautious interpretation. Many foundational studies rely on small sample sizes and cross-sectional designs, making it difficult to establish that the structural changes are a direct consequence of anosmia, rather than just a correlation. Thus, the exact functional consequences of these structural adaptations are still largely speculative and need confirmation through longitudinal and functional studies.

In turn, future studies could consider conducting long-term analysis of structural and functional changes in individuals with ICA. Future studies could also consider testing multisensory recognition tasks (visual, auditory, and tactile) and investigate whether compensatory mechanisms can be enhanced through training. This work could improve the lives of individuals with ICA and deepen our understanding of the relationship between olfactory loss and certain forms of cognition.

## Acknowledgements

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- I changed Key words: Olfactory processing regions; Cross-modal plasticity; Sensory deprivation; Cortical thickness; Grey matter volume; White matter density; Olfactory bulb; Congenital anosmia; Olfactory sulcus; Orbitofrontal cortex; Insula; Entorhinal Cortex; Face Morph; Olfactory imagery; Piriform cortex;  Longitudinal fasciculus —--> to
  Key words: Congenital anosmia; cross-modal plasticity; sensory deprivation; olfactory processing; emotional recognition; cortical thickness; grey matter; white matter.

- The bibliography was revised to include missing citations.

- As suggested, I deleted the word "body" from "body section" for clarity in the introduction.

- I deleted "This section explores the relationship between olfaction and emotion by reviewing studies that describe how smells trigger emotional responses and how the brain processes emotions related to olfactory input.", "This section explores structural differences in individuals with isolated congenital anosmia (ICA), with a focus on volumetric and cortical thickness differences in regions of the brain associated with emotional processing." and "This section analyses the results from facial emotion recognition studies in ICA patients to determine whether enhancements in non-olfactory emotion recognition can be observed." as suggested.

- I changed " It proposes an investigation into the relationship between cross-modal plasticity and emotion recognition processes in individuals with ICA" to "Through this condition, an investigation into the relationship between cross-modal plasticity and emotion recognition processes in individuals with ICA is prompted, " as suggested.

- I changed "ICA also exhibited…" to "Patients with ICA also exhibited…" as suggested.

- I changed "These results support the thesis that structural changes in the brains of individuals with ICA might establish a compensatory mechanism for emotion recognition" to "These previous studies support the thesis that structural changes in the brains of individuals with ICA might establish a compensatory mechanism for emotion recognition," as suggested.

- I changed "The relevance of cross-modal plasticity in this topic might be found in a study that suggests that cross-modal plasticity is a compensatory mechanism in place for the absence of sight and hearing." to "the relevance of cross-modal plasticity to this topic may be found in a study…in place of sight and hearing," as suggested.

- I changed "Furthering the support for the connection between olfaction and emotional processing, the exploration of interpreting emotional reactions to environmental odors (smellscape odor input, which personal and social lenses can influence. Xiao, Tait, and Kans) suggests” to “...(smellscape odor input…influence). Xiao, Tait, and Kans suggest…” as suggested.

- For clarity, as suggested, I changed “ ICA poses an investigation into how the lifelong absence of olfactory input shapes the brain” to “ICA enables the exploration of how the brain reorganizes itself in response to the lifelong absence of smell.”

- I removed the trillion odours claim “The typical human can 'discriminate' at least one trillion odors (Bushdid et al., 2014)”.

- I softened many claims and removed vague or speculative claims (to the extent that I could identify them), such as including “may”, “potentially”, and “hypothesized” to soften them. Ex: The review found that emotional responses to odours often occur somewhat unconsciously and are usually quickly processed, a characteristic hypothesized to be related to their evolutionary role in survival and social communication.
- I redefined embodied cognition as suggested: ( the idea that our thoughts, emotions, and perceptions are influenced by the physical body, meaning that cognitive processes are shaped not just by the brain, but also by bodily sensations, movements, and interactions with the environment.)

- In my introduction I added the research question and attempted to make it more focused as suggested: This research gap leads to the central question: Does congenital anosmia (ICA) lead to compensatory neuroplasticitc changes that supports the maintenance of emotional recognition via reorganized cortical areas? Our thesis is that the structural changes observed in ICA occur in areas of the brain that overlap with both olfactory and emotional processing, suggesting that the brain reorganizes itself for stronger reliance on other sensory inputs for emotional and social cognition.

- I tried to introduce studies and their methodologies: “A mental imagery study using fMRI and PET on participants that were required to imagine specific odors while their brain activity was measured, found that…”

- I removed long and unnecessary quotes and instead paraphrased: “In addition, there was a higher density observed in the left entorhinal cortex in individuals with congenital anosmia and a thinner patch of tissue in the posterior-lateral orbitofrontal cortex.”

- I added a limitations section as suggested: “While these structural differences support a compensatory model, research in this area requires cautious interpretation due to methodological limitations. Many of the cited studies, including Frasnelli et al. (2013) and Karstensen et al. (2018), rely on small sample sizes and cross-sectional designs. This makes it challenging to establish a causal link between the absence of olfaction in congenital anosmics and proposed neuroplastic adaptations; specifically, we cannot be certain the structural changes developed because of the anosmia, or if they are merely correlated with it. Furthermore, Voxel-Based Morphometry (VBM) analyses can be limited in their ability to confirm the outcomes of increased GM or

WM density, requiring further functional MRI (fMRI) investigations to accurately assess the behavioral impact of cross-modal plasticity..”

- I defined key terms (static and dynamic paradigm) and included drummond in the analysis. I also elaborated more on Krusemark, softened claims and talked about evolutionary implications in the last section. Here is an example: A more recent facial emotion recognition study tested ICA participants on static and dynamic facial morphs (A static face morph is a still image that has been digitally altered to transition between two different facial expressions), (A dynamic face morph is a short video or sequence of images that gradually transition one facial expression into another). The results reported enhanced emotion detection, showing that ICA patients were better and faster at recognizing disgust and anger compared to controls (Drummond et al., 2024). The ICA group showed heightened sensitivity to these emotions, correctly identifying the emotion earlier in the morphing process (i.e., with less of the emotion visible on the face) (Drummond et al., 2024). This faster and more accurate identification suggests that the absence of olfaction during development may have led to compensatory changes in visual and social cognition. ICA individuals showing enhanced recognition of negative emotions (fear, disgust, and anger) is relevant, as these emotions are strongly linked to avoidance and survival, often serving as non-verbal cues for potential danger. Since olfaction is an important sense for detecting danger (like spoiled food or smoke), the enhanced visual recognition of these negative emotions in ICA may be a result of any reorganization that has occurred.
- I added limitations to the conclusion and softened claims: While the findings are compelling, the evidence for consistent compensation in ICA remains limited and requires cautious interpretation. Many foundational studies rely on small sample sizes and cross-sectional designs, making it difficult to establish that the structural changes are a direct consequence of anosmia, rather than just a correlation. Thus, the exact functional consequences of these structural adaptations are still largely speculative and need confirmation through longitudinal and functional studies.

I would like to sincerely thank Reviewer 1 for their thorough and insightful feedback. Your comments regarding the manuscript's structure, clarity, and depth of analysis were invaluable in guiding this revision. The detailed suggestions on citation practices, paraphrasing, and critical synthesis helped me strengthen the scholarly rigor and coherence of the review. I have carefully addressed each of your points by clarifying the research focus, improving the integration of sources, and ensuring full adherence to APA 7th edition guidelines. I am deeply appreciative of the time and care you invested in helping to refine and improve this work.

Here are the improvements I have made at your request:

- **I have updated and corrected my bibliography**

- **Introduction:**
  **Reviewer request:** State a clear central research question/hypothesis and reorganize: definition → relevance → current evidence → aim.
  **Response / Changes made:**
  - Rewrote the Introduction to follow the suggested flow: (a) definition of ICA, (b) functional relevance of smell to emotion/memory, (c) current evidence for structural/neuroplastic changes in ICA, and (d) explicit research question and thesis.
  - **Added:** "Does congenital anosmia (ICA) lead to compensatory neuroplastic changes that support the maintenance of emotional recognition via reorganized cortical areas?"

- **Olfaction and Emotion — overly broad / poorly integrated.**
  **Reviewer requests:** Narrow scope; structure logically (neurobiology → imagery → social context); define key terms; contextualize claims (Bushdid).
  **Response / Changes made:**
  - **Added a limitations section**

  - **Defined key terms**: "olfactory imagery" and "embodied cognition" are defined succinctly in the text (with citations).
  - Softened claims and speculative statements

- **Section: Brain Structural Adaptations — confusing attribution and lack of critical synthesis.**
  **Reviewer requests:** Distinguish Manan et al. (review) vs primary studies; avoid repetition and long quotes; group findings thematically (gray matter, white matter); acknowledge limitations.
  **Response / Changes made:**
  - **Clarified attribution:** When summarizing Manan et al. (2023), I explicitly state when a finding is from the systematic review vs. a primary study (e.g., "Manan et al. (2023) reported X based on 28 studies; primary studies such as Frasnelli et al. (2013) directly observed Y").
  - **Paraphrased long quotes**

- **Acknowledge limitations**

- **Section: Emotion Recognition in ICA — narrow and under-developed.**
  **Reviewer requests:** Broaden literature base beyond Lemogne et al. 2015; include Drummond et al. (2024); discuss alternative explanations and define task types.
  **Response / Changes made:**
- **Added Drummond et al. (2024)** and integrated it into the main Emotion Recognition section (not just the conclusion)**.**

- **Defined task types and outcome measures:** Provided short definitions of “dynamic paradigm” vs “static morphs,” and explained outcome measures (accuracy, error rate, intensity threshold, reaction time)**.**
- **Ended sections with a link back to central theme**
- **Tried to make citations more relevant/elaborated on them further**

- **Conclusion — overstates evidence; lacks synthesis and caution.**
  **Reviewer requests:** Soften claims; distinguish knowns vs speculative; justify future directions; tie themes together.
  **Response / Changes made:**
- **Rewrote conclusion to synthesize rather than summarize.** Claims are now qualified (e.g., “evidence suggests” / “findings are consistent with”), and I explicitly note that evidence for compensatory neuroplasticity in ICA is limited and sometimes inconsistent.
- **Clarified what is known vs speculative**
- **Ended paragraphs with a link**

I am very grateful to Reviewer 2 for their constructive and precise editorial feedback. Your suggestions regarding conciseness, section introductions, figure inclusion, and phrasing were extremely helpful in improving the paper's readability and presentation. I have implemented all of your recommendations except for one, including stylistic revisions, simplified keywords, and improved sentence clarity. Thank you for the thoughtful and practical comments that contributed greatly to the manuscript's clarity and overall quality.

**All of the suggestions where met except for the following**: I believe that the paper would be improved if you included figures illustrating: a) areas where
the brain changes due to anosmia (maybe a with/without anosmia figure comparing the two brain structures) and b) the brain structures most altered by anosmia. Figures help readers solidify their understanding and develop understanding in different ways.

- I would like to thank you for your valuable suggestion to include figures illustrating brain changes associated with congenital anosmia. While I agree that such visuals would significantly enhance the paper, I was unable to incorporate them for two primary reasons: limitations in accessing suitable non-copyrighted illustrations and the complexity involved in accurately generating such detailed figures with my currently available resources. We appreciate you bringing this to our attention."

<u>Here is a summary of all the corrections:</u>

- I changed Key words: Olfactory processing regions; Cross-modal plasticity; Sensory deprivation; Cortical thickness; Grey matter volume; White matter density; Olfactory bulb; Congenital anosmia; Olfactory sulcus; Orbitofrontal cortex; Insula; Entorhinal Cortex; Face Morph; Olfactory imagery; Piriform cortex;  Longitudinal fasciculus —--> to
  Key words: Congenital anosmia; cross-modal plasticity; sensory deprivation; olfactory processing; emotional recognition; cortical thickness; grey matter; white matter.

- As suggested, I deleted the word "body" from "body section" for clarity in the introduction.

- I deleted "This section explores the relationship between olfaction and emotion by reviewing studies that describe how smells trigger emotional responses and how the brain processes emotions related to olfactory input.", "This section explores structural differences in individuals with isolated congenital anosmia (ICA), with a focus on volumetric and cortical thickness differences in regions of the brain associated with emotional processing." and "This section analyses the results from facial emotion recognition studies in ICA patients to determine whether enhancements in non-olfactory emotion recognition can be observed." as suggested.

- I changed " It proposes an investigation into the relationship between cross-modal plasticity and emotion recognition processes in individuals with ICA" to "Through this condition, an investigation into the relationship between cross-modal plasticity and emotion recognition processes in individuals with ICA is prompted, " as suggested.

- I changed “ICA also exhibited…” to “Patients with ICA also exhibited…” as suggested.

- I changed “These results support the thesis that structural changes in the brains of individuals with ICA might establish a compensatory mechanism for emotion recognition” to “These previous studies support the thesis that structural changes in the brains of individuals with ICA might establish a compensatory mechanism for emotion recognition,” as suggested.

- I changed “The relevance of cross-modal plasticity in this topic might be found in a study that suggests that cross-modal plasticity is a compensatory mechanism in place for the absence of sight and hearing.” to “the relevance of cross-modal plasticity to this topic may be found in a study…in place of sight and hearing,” as suggested.

- I changed “Furthering the support for the connection between olfaction and emotional processing, the exploration of interpreting emotional reactions to environmental odors (smellscape odor input, which personal and social lenses can influence. Xiao, Tait, and Kans) suggests” to “...(smellscape odor input…influence). Xiao, Tait, and Kans suggest…” as suggested.

- For clarity, as suggested, I changed “ ICA poses an investigation into how the lifelong absence of olfactory input shapes the brain” to “ICA enables the exploration of how the brain reorganizes itself in response to the lifelong absence of smell.”

**Congenital Anosmia and Emotional Processing**

**Review #2**

Authors have done a good job in addressing reviewers' comments to improve their paper. However, there are additional items that need to be addressed before the paper can be accepted for publication. These changes are very much about the structure of the paper to ensure it aligns with a traditional academic paper, and include:

1. The Abstract is slightly confusing and can be streamlined with use of subheadings such as Background, Aim, Conclusions. Currently it is not clear which parts are from already existing literature, and which are from this study.
2. The Introduction is currently one very long paragraph. To improve readability and create better flow of ideas and structure, authors should consider creating smaller paragraphs, grouping together similar ideas, to build up the rationale for this study and then end the Introduction with the aim/s of this study.
3. Authors should refrain from referring to this paper as a "thesis".
4. Authors should include a "Methods" section to describe how they completed this study. How were papers found and synthesised for this review?
5. I feel the subheading "Discussion" is misleading. It should actually be Results, or Summary of Findings.
6. The structure of the "Discussion" needs to be improved with use of subheadings eg. Under "The role of olfaction in emotion processing" authors could use subheadings such as "Olfactory signalling pathways", then "Association of olfaction and emotions", etc. This would support the reader in following along with the findings.
7. A Limitations heading should be included between "Discussion" and "Conclusions" and limitations should be moved from the Conclusions to this section, and include any further limitations raised by reviewers.
8. Authors should address the limitation in not being able to provide figures of the brain comparisons (in response to Reviewer 2) in the Limitations of the paper, acknowledging that this would strengthen their paper.
9. The Conclusion is not a traditional Conclusion in that it does not provide a concise summary of the study's findings. It needs to be written from a higher level meaning to be more broad. For example, authors could consider language such as "This review showed conflicting evidence exists in [specific finding]", rather than writing study X found Y and study A found B, as that would more so belong in the "Discussion".

## Convergence Review of Congenital Anosmia and Emotional Processing

**Overview:** I greatly appreciate the author taking the time to further refine their paper. It is very clear that the author has addressed many of our comments, including our comments regarding the writing, keywords, and phrasing in different papers. Given these edits, I would suggest that the paper be accepted pending Minor Revisions.

If future revisions are provided, I would strongly recommend that the author copies over the reviewer requests and directly responds to them one-by-one alongside the reviewer requests. Don't abbreviate or edit the reviewer requests in the response. This one-by-one approach is helpful when reviewers like myself go to review again.

**Substantive Edits**

1. Technically, ICA stands for Isolated Congential Anosmia. That should be clearly specified if you are using the acronym ICA. If you just mean Congenital Anosmia, the abbreviation should be CA. If you do use ICA, you should explain what the isolated implies.

2. The writing of the abstract could be improved. I would strongly suggest keeping the first sentence, then skipping to "This literature review looks into the relationship…olfaction." I would then much more briefly explain what the previous studies have found (which reflects what you discussed in the review) and then conclude with your final sentence. Abstracts are generally 6-10 sentences in most fields.

3. You should clearly state what original contributions you made (I don't believe you did) vs. what you are summarizing from the literature to be clear about what was original and what's not.

4. The Introduction should be broken up into separate paragraphs that follow key themes. One can potentially break up these paragraphs along the lines of one paragraph about and motivating research into CA, one paragraph about its connection to different regions of the brain, one paragraph about how this connects emotions to CA, one paragraph about cross-modal plasticity, and lastly, one paragraph about what you set out to do in this review.

5. I would still insist on you including images of the relevant brain regions in the review. You can easily find non-copyrighted images. Alternatively, is the author's responsibility to make images in Photoshop or otherwise to convey the key points. I think images are fairly important to your thesis.

6. I think it makes sense to have the section on "Emotion recognition in individuals with ICA" follow the section on "The role of olfaction in emotion processing."

7. What you wrote for the Conclusion contains quite a bit of Discussion. Discussion is where you discuss what's wrong with the current state of the field and what should be further studied. Conclusions are where you resummarize the paper (at least in my field!).

**Minor Edits**

1. “Through this condition, an investigation into the relationship between crosss-modal plasticity and emotion recognition processes in individuals with ICA is prompted.” This sentence does not make much sense in English. I think you mean that this condition might motivate a study into the relationship between cross-modal plasticity and emotion recognition processes? See major edit #2 for further discussion.

2. In the Introduction, change “body section” to just “section” in all places.

# Congenital Anosmia and Emotional Processing


## Abstract

### Background

Congenital Anosmia (CA) is the lifelong absence of odor recognition and underdevelopment of the olfactory bulbs and sulci. This review specifically focuses on Isolated Congenital Anosmia (ICA), which is the form of CA occurring without associated congenital syndromes such as Kallman Syndrome. ICA motivates an investigation into cross-modal plasticity, which refers to the adaptive reorganization of neurons to integrate the function of two or more sensory modalities, often occurring after sensory deprivation. Several studies indicate an overlap between emotional and olfactory processing in regions like the orbitofrontal cortex, insula, and amygdala. Other investigations also indicate that ICA is associated with specific structural brain alterations: these include the shallow depth of the olfactory sulcus and underdevelopment of the olfactory bulb, alongside compensatory-like changes such as greater volumes/density in the left medial frontal gyrus, right superior frontal sulcus, left entorhinal cortex, left piriform cortex, bilateral medial orbital gyrus, and a higher white matter density in the left insula. These previous studies support the premise that structural adaptations suggest compensatory mechanisms exist to compensate for the absence of olfaction. This literature review looks into the relationship between congenital anosmia and neural activation in regions of the brain associated with emotion recognition. This review specifically investigates how these existing findings support the thesis that structural changes in the brains of individuals with ICA might establish a compensatory mechanism for emotion recognition. This review suggests that the structural alterations observed in ICA are the neural foundation for compensatory mechanisms in emotional recognition. These findings contribute to a greater understanding of smell in social and emotional cognition without olfaction.



## Keywords

Congenital anosmia; cross-modal plasticity; sensory deprivation; olfactory processing; emotional recognition; cortical thickness; grey matter; white matter

# Introduction

**Congenital Anosmia (CA)** is the lifelong absence of odor recognition and underdevelopment of the olfactory bulbs and sulci. Around 1 in 10,000 people are born without a sense of smell. This review primarily focuses on **Isolated Congenital Anosmia (ICA)**, a subtype of CA where the condition occurs without any associated congenital syndrome (e.g., Kallmann Syndrome). We prioritize ICA because the majority of neuroimaging studies investigating neuroplasticity specifically screen for and include only isolated cases to control for confounding variables. Smell has proven vital in memory, emotion, and threat detection, which raises the question of how these individuals adapt to maintain emotional and social cognition without the aid of olfactory input. The exploration of the loss of this sensory modality poses an investigation into how such sensory loss can be mitigated through structural changes in the brain.

This condition motivates an investigation into the relationship between cross-modal plasticity and emotion recognition processes in individuals with ICA. Other investigations also indicate that ICA is associated with structural brain alterations, including reduced grey matter volume in the orbitofrontal cortex, but greater volumes in the left medial frontal gyrus, right superior frontal sulcus, left entorhinal cortex, left piriform cortex, bilateral medial orbital gyrus, and right posterior orbital sulcus. Patients with ICA also exhibited a higher white matter density in the left insula and the region posterior to the parietal operculum. Though the Olfactory bulb depth remains low and the olfactory sulcus shallow, it is typical of what might be observed in anosmics.

Several studies indicate an overlap between emotional and olfactory processing, specifically in regions like the orbitofrontal cortex, insula, and amygdala. These structural adaptations suggest that compensatory mechanisms exist to compensate for the absence of olfaction. Studies have suggested that individuals with ICA exhibit a greater sensitivity to negative emotions, specifically anger and disgust. These previous studies support the idea that structural changes in the brains of individuals with ICA might establish a compensatory mechanism for emotion recognition.

This compensatory mechanism is known as cross-modal plasticity, which refers to the “adaptive reorganization of neurons to integrate the function of two or more sensory systems, which occurs after sensory deprivation, where the greatest reorganization of neural networks occurs after long-term sensory deprivation such as congenital blindness or deafness.” The relevance of cross-modal plasticity to ICA stems from its established role in compensating for long-term sensory deprivation, such as congenital blindness or deafness. These findings contribute to a greater understanding of smell in social and emotional cognition without olfaction.

Overall, this literature review looks into the relationship between congenital anosmia and neural activation in regions of the brain associated with emotion recognition. It is important to note that this paper does not present new empirical data but rather contributes an original, thematic synthesis and critical interpretation of existing neuroimaging and behavioral literature to build this argument. This research gap leads to the central question: Does congenital anosmia lead to compensatory neuroplastic changes that support the maintenance of emotional recognition via reorganized cortical areas? Our main premise is that the structural changes observed in ICA occur in areas of the brain that overlap with both olfactory and emotional processing, suggesting that the brain reorganizes itself for stronger reliance on other sensory inputs for emotional and social cognition. To explore the validity of this, the literature review examines the role of olfaction in emotion processing, structural brain adaptations in congenital anosmia, and emotion recognition in congenital anosmia.

# Methods

This review is structured into three main sections with the goal of investigating the relationship between congenital anosmia (ICA) and neural activation in brain regions associated with emotion recognition, specifically focusing on evidence for cross-modal plasticity as a compensatory mechanism. The first, examining the Role of Olfaction in Emotion Processing; second, exploring Brain Structural Adaptations in Congenital Anosmia using neuroimaging studies; and finally, analyzing Emotion Recognition in Individuals with ICA through behavioral studies. The search for relevant peer-reviewed articles was conducted using the electronic database Google Scholar and MRI images taken from e-anatomy IMAIOS. The systematic search utilized combinations of keywords relating to the core condition (Congenital anosmia, isolated congenital anosmia) with the proposed mechanism and outcomes (cross-modal plasticity, sensory deprivation, neuroplasticity, emotion recognition, emotional processing, cortical thickness, grey matter, white matter, Voxel-Based Morphometry, fMRI). Inclusion criteria included peer-reviewed original research, meta-analyses, and systematic reviews published in English that specifically focused on the relationship between congenital anosmia (CA) or isolated congenital anosmia (ICA) and either brain structure/function or emotion/social cognition, utilizing neuroimaging (MRI, VBM, fMRI) or behavioral techniques (e.g., facial morph tests). Studies on acquired anosmia were selectively included for comparative context, and seminal pre-2010 studies were used for foundational knowledge. Exclusion criteria included non-peer-reviewed web sources. A critical synthesis approach was adopted to analyze the literature, incorporating findings from empirical studies to identify gaps in the literature, specifically relating to the causal link between the structural alterations and functional compensation.

# Summary of Findings

## The role of olfaction in emotion processing

### Olfactory Signaling Pathways

The olfactory system is unique in that its sensory pathways are located deep within the brain, allowing for direct influence on regions involved in emotion and memory. Unlike other senses, olfactory signals bypass the thalamus and travel directly to the olfactory cortex (Shepherd et al., 2005). These signals then move to areas involved in emotion, such as the amygdala, hippocampus, and orbitofrontal cortex, that are involved in the limbic pathway (BiologyInsights, 2025). The olfactory system's unique thalamus-bypassing pathway offers a route to interact with the limbic system, which may contribute to the “emotional salience” of odors. When “odorant molecules” are inhaled, they travel through the nasal cavity and interact with olfactory receptor neurons, where these neurons then detect and transduce these molecules into electrical impulses. These signals are then transmitted to the brain, some areas of which are related to emotion and memory (BiologyInsights, 2025), where these signals are processed and interpreted as different scents. Taken together, understanding olfaction’s role in emotion requires integrating evidence across multiple levels of analysis, from neural circuitry linking odor and emotion to cognitive processes such as olfactory imagery, and finally to the social and environmental contexts in which smells shape affective experience.

### Olfactory Imagery, Perception, and Emotional Response

Olfaction and odor perception have been widely investigated areas, though the question of how it affects emotions is still prevalent; this can be investigated through the concept of olfactory imagery, which was defined as “being able to experience the sensation of smell when an appropriate stimulus is absent” (Stevenson & Case et al., 2005). A mental imagery study using fMRI and PET on participants who were required to imagine specific odors while their brain activity was measured found that “olfactory imagery” can influence the “perception of an odor” (Djordjivec et al., 2005). A neuroimaging study provided further evidence for the link between odor perception and olfaction, this finding is consistent with the principles of “embodied cognition” ( the idea that our thoughts, emotions, and perceptions are influenced by the physical body, meaning that cognitive processes are shaped not just by the brain, but also by bodily sensations, movements, and interactions with the environment.), where reading scent-related words such as “cinnamon” is associated with increased activity in the primary olfactory cortex (Gonzalez et. al, 2006). The activation of this area implies that the brain not only responds to actual olfactory stimuli but also to imagined scents. Other brain imaging studies showed overlap in areas of the brain activated by real and imagined odors, though the activations were reduced in “imagery conditions” (Levy et al., 1999; Henkin & Levy, 2002). Lin, Cross, and Childers examined emotional responses during “olfactory imaging”, where they found that greater olfactory ability was associated with more “vivid olfactory imaging” and emotional response. Researchers found that both real and imagined scents evoke an emotional response. These findings demonstrate a functional overlap in emotional response between real and imagined scents, providing further evidence for the established link between olfaction and emotional processing.

### Structural Integration of Olfaction and Emotion (Common Substrates)

Overall, these findings from olfactory imagery lead to a broader inquiry into how the olfactory system shares "common substrates" with emotional processing. Building on this idea of olfaction, emotion, and substrate, the findings of Soudry et al. (2011) may suggest that olfaction and emotion are not just correlated but also structurally integrated, though this should be investigated further. As described in this research and previous literature, "physiologically, olfactory stimuli are processed according to their emotional content," where, much like emotions, "odors can be given positive (appetitive), negative (aversive) or neutral valence" (Soudry, Lemogne, Malinvaud, Concoli, Bon. pg. 19). The close connection between odor and emotion are related to "common cerebral substrates", specifically, the amygdala, hippocampus, insula, anterior cingulate cortex, and the orbitofrontal cortex, which are key processing regions for odor and emotion; further, the overlap of these areas also have implications for emotion and memory as well as the possible negative affects on emotional health due to olfactory loss. The review found that emotional responses to odours often occur somewhat unconsciously and are usually quickly processed, a characteristic hypothesized to be related to their evolutionary role in survival and social communication. An example of the integration of emotion and odor could be a disgust response to an unpleasant odor, which may use the same pathways as visual disgust cues, a finding that suggests the potential for shared neural mechanisms across sensory modalities.

### Social and Environmental Context of Olfactory-Emotional Experience (Smellscapes)

Furthering the support for the connection between olfaction and emotional processing, the exploration of interpreting emotional reactions to environmental odors (smellscape odor input, which personal and social lenses can influence). Xiao, Tait, and Kans suggest that smells affect how humans interact with their environment, as described by the smellscape concept of "physical space and the context of a place," where perception is at the core of the smellscape concept (pg. 2; Xiao et al., 2020). Initially, these researchers hypothesized that the smell model was triangular between emotion, society, and place, labeling it as a "spatial-emotional intermediary that links society, emotions, and place" (pg. 2, Xiao et al., 2020). Though after compiling the results, the smell model was arranged into a circular flow chart with "smells, physical environment, context of place, and individuals' memory" on the outside and "perceptions" on the inside of the flow chart. These researchers found during a railway station study, which aimed to uncover the "perceptual process of smellscape perceptions" among walk-along interviews, that language experiences in specific places indicated people's perceptions of their environmental settings (Bradley & Lang, 2000). Classen et al. (1994, p. 3) argued that smell is shifty and "cannot be documented in Western languages"; however, olfactory experiences are conveyed through metaphors. The study documented that in an interview, a participant described chlorine as a good smell and said it makes them feel happy and clean, and reminds them of a swimming pool. Such is an example of how an emotion-related experience influences olfactory perception. The study found that overall, participants associated certain smells with "places, social categories, and memories", which may be that olfactory-related emotion is not only neural but also requires associated experience.

## Emotion recognition in individuals with ICA

The link between emotion and olfaction is well supported, where odors often act as cues for affective states (Licon et al., 2018). In ICA, olfaction is absent from birth, which motivates an investigation into whether the brain undergoes reorganization (cross-modal plasticity) to rely on other sensory modalities for emotional processing.

A case-control study suggested that “patients with congenital anosmia and long-lasting acquired anosmia may compensate their inability to detect environmental hazards through olfaction by an increased ability to detect fear or disgust as facially expressed by others” (Lemogne et al., 2015). For each patient with congenital anosmia, the absence of the olfactory bulb was confirmed through magnetic resonance imaging. Emotion recognition abilities were examined with a “dynamic paradigm in which a morphing technique allowed displaying emotional facial expressions increasing in intensity over time”. Adjusting for age, education, depression, and anxiety, patients with congenital anosmia required similar levels of emotion intensity to correctly recognize fear and disgust as healthy subjects. At the same time, they displayed decreased error rates for both fear and disgust. This study suggested that from an evolutionary standpoint, compensatory mechanisms may have occurred to detect emotions crucial for human survival, such as fear and disgust, with greater accuracy (Lemogne et al., 2015).

A more recent facial emotion recognition study tested ICA participants on static and dynamic facial morphs (A static face morph is a still image that has been digitally altered to transition between two different facial expressions; A dynamic face morph is a short video or sequence of images that gradually transitions one facial expression into another). The results reported enhanced emotion detection, showing that ICA patients were better and faster at recognizing disgust and anger compared to controls (Drummond et al., 2024). The ICA group showed heightened sensitivity to these emotions, correctly identifying the emotion earlier in the morphing process (i.e., with less of the emotion visible on the face) (Drummond et al., 2024). This faster and more accurate identification suggests that the absence of olfaction during development may have led to compensatory changes in visual and social cognition. ICA individuals showing enhanced recognition of negative emotions (fear, disgust, and anger) is relevant, as these emotions are strongly linked to avoidance and survival, often serving as non-verbal cues for potential danger. Since olfaction is an important sense for detecting danger (like spoiled food or smoke), the enhanced visual recognition of these negative emotions in ICA may be a result of any reorganization that has occurred.

Furthermore, a study examining how smells affect moods, specifically, the effects of smells on stress, demonstrated that “heightened emotional states” can change sensory processing in cross-modal ways, suggesting a potential area for exploration in interpreting ICA adaptations (Krusemark et al., 2013). This finding indicates that emotion and sensory input may have a two-way relationship, where an existing mood can directly re-allocate the brain's attentional and processing resources to different senses. This emotion-driven sensory re-allocation supports the underlying proposition that the lifelong absence of olfaction in ICA may trigger an adaptive structural reorganization to utilize the visual processing of emotional cues. However, this cannot be known, as further investigation is required.

## Brain structural adaptations in congenital anosmia

ICA enables the exploration of how the brain reorganizes itself in response to the lifelong absence of smell. A review using a systematic search method using PubMed/MEDLINE and Scopus electronic databases to analyze olfactory-related structural changes in the brains of congenital and acquired anosmics found 28 studies to compare. The review listed the criteria that were to be investigated as it relates to structural changes, being (1) olfactory bulb (OB), (2) olfactory sulcus (OS), (3) grey matter (GM), and white matter (WM) changes (Manan et al., 2023).

### Olfactory Bulb (OB) and Olfactory Sulcus (OS) Depth

Turning to specific primary olfactory structures, this review examined data relating to OB and OS volume and depth, which reported that both right and left OB volumes were significantly smaller in anosmic patients than healthy controls (Schofield et al., 2014; Manan et al., 2023). This shrinkage likely occurred due to smell signals from the nose failing to reach the bulb through the cribiform plate, causing the loss of olfactory neurons (Schofield et al., 2014). The OS depth, located between the medial orbital gyrus and gyrus rectus in the frontal lobe, is also quite a significant finding when examining olfaction. Overall, patients with congenital anosmia show the smallest OB volume and shallow OS depth compared to other participating groups (Manan et al., 2023).

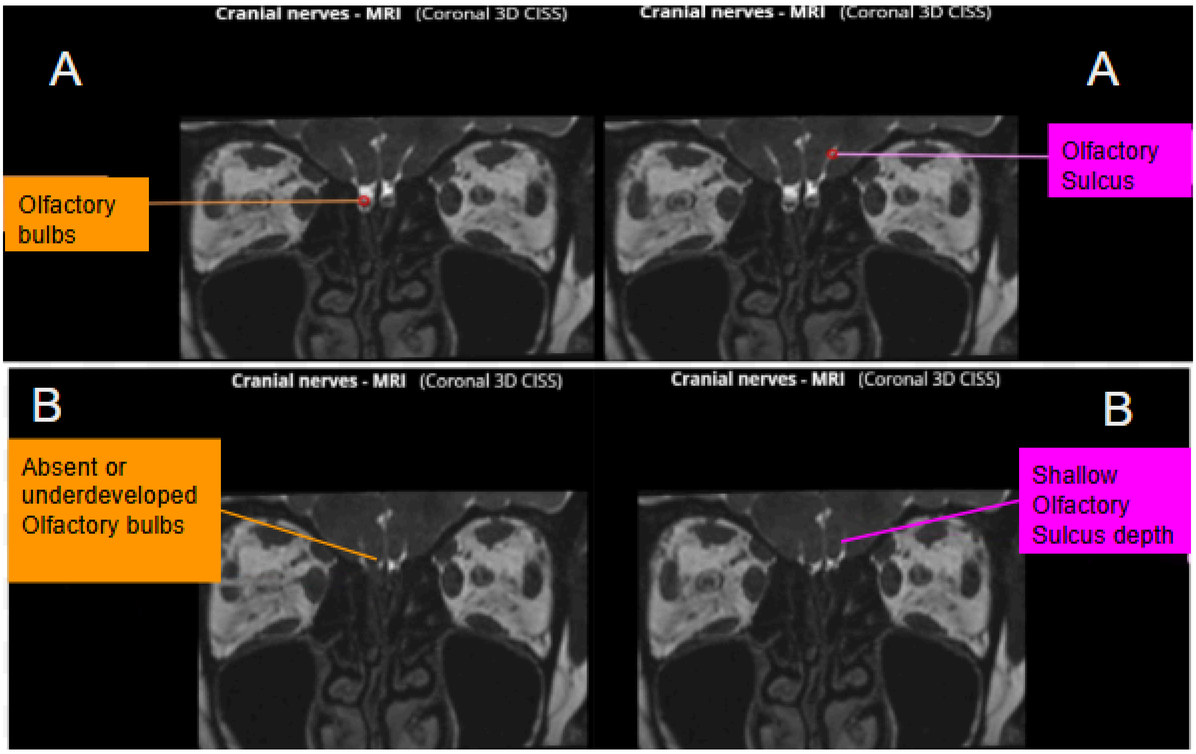


**Figure 1:** Coronal olfactory bulb and sulcus MRI image of a healthy female, where letter **"**A" represents normal olfactory ability and "B" represents Congenital Anosmia.Courtesy of IMAIOS © "Antoine MICHEAU, MD , Denis HOA, MD, e-Anatomy, published July 29th 2024, Imaging of cranial nerves and brainstem: normal 3D CISS MR of cerebral fossa, **https://doi.org/10.37019/e-anatomy/ed745028-c12f-405f-8d85-dbefa043aac3**"

### Grey Matter (GM)

In terms of GM changes, a key finding in the study was found in the contrast between acquired and congenital anosmia. Overall, the study found that individuals with acquired anosmia exhibited reduced volumes and thickness in the gyrus rectus, medial orbitofrontal cortex, anterior cingulate cortex, and cerebellum (Manan et al., 2023), where the implication of this reduction may be a reduced ability to regulate emotions (Schmahmann et al., 2010). In contrast, ICA is associated with larger volume and greater thickness in several key regions, suggesting a compensatory response. Manan et al. (2023) summarized primary source findings from Voxel-Based Morphometry (VBM) analyses: Greater GM volumes were reported in the left medial frontal gyrus (MFG) and right superior frontal sulcus (SFS) (Karstensen et al., 2018), the left entorhinal cortex and left piriform cortex (Frasnelli et al., 2013), and the bilateral medial orbital gyrus (MOG) and right posterior orbital sulcus (POS) (Peter et al., 2020). Greater GM volume is often associated with greater connectivity potential and higher neuronal support through glial density, though the greater volume exhibited has collective implications for enhanced cognitive control, episodic memory (a type of long-term memory), emotion-sensory integration, and decision making. These results directly contrast with those of the acquired anosmics, where reduced olfactory function is associated with reduced GM and WM volumes and thickness (Han et al., 2018; Bitter et al., 2010; Peng et al., 2013).

A related GM study, focusing on the fronto-limbic system, further supported compensatory changes in ICA. Karstensen et al. (2018) investigated how the ICA affects brain structure, particularly in the fronto-limbic system that links smell and emotion. Researchers examined whether regional variations in gray matter volume were associated with smell ability in seventeen individuals with isolated congenital olfactory impairment (COI) matched with sixteen normosmic controls. Whole-brain magnetic resonance imaging and voxel-based morphometry were used to estimate “regional variations” in gray matter volume. The analyses showed that compared to the controls, COI subjects reported larger gray matter volumes in the left middle frontal gyrus and right superior frontal sulcus (SFS). COI subjects with “severe olfactory impairment” (anosmia) reported reduced gray matter volume in the left mOFC and increased volume in the right piriform cortex and SFS. Additionally, within the COI group, olfactory ability, measured with the 'Sniffin' Sticks' test, was positively associated with larger gray matter volume in right posterior cingulate and parahippocampal cortices, where a contrasting relationship was observed in controls (Karstensen et al., 2018). In turn, the study concluded that differences in “atypical brain development” and plasticity may have been a result of adaptive reorganization in the brain.

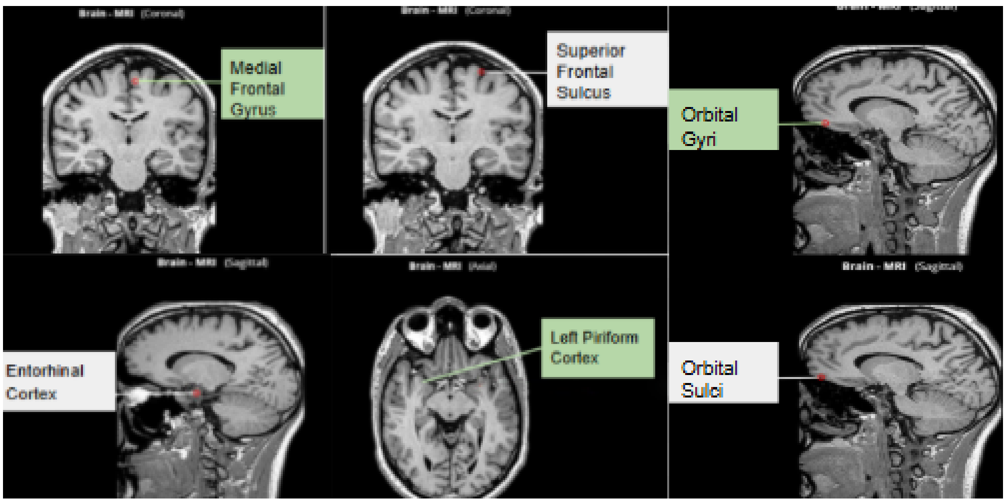

**Figure 2:** Regions of the brain associated with increased grey matter volume in congenital anosmia. Courtesy of IMAIOS © "Antoine MICHEAU, MD , Denis HOA, MD Authors' affiliations, Publication date: Aug 25, 2008, Anatomy of the brain (MRI) - cross-sectional atlas of human anatomy, **https://doi.org/10.37019/e-anatomy/163**

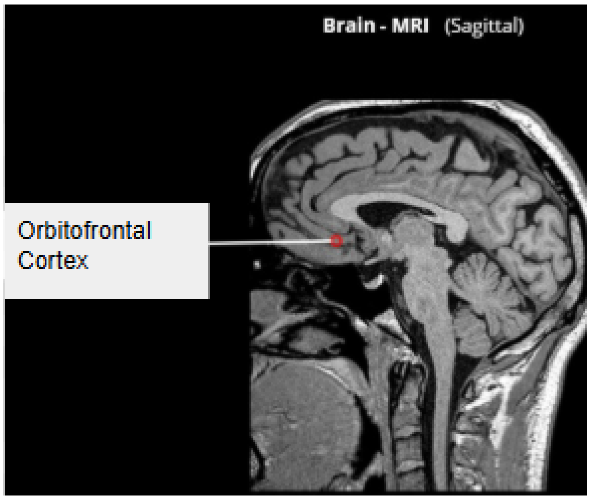


**Figure 3**: Regions of the brain associated with decreased grey matter volume in congenital anosmia. Courtesy of IMAIOS © "Antoine MICHEAU, MD , Denis HOA, MD Authors affiliations, Publication date: Aug 25, 2008, Anatomy of the brain (MRI) - cross-sectional atlas of human anatomy, **https://doi.org/10.37019/e-anatomy/163**

### White Matter (WM)

Complementing the GM findings, the analysis also revealed differences in WM density. This analysis found that congenital anosmics exhibited larger WM density in the areas, including the left insula and the region posterior to the parietal operculum (Frasnelli et al., 2013). Larger WM density was observed in areas including the left insula and the region posterior to the parietal operculum (Frasnelli et al., 2013). These results directly contrast with those of the acquired anosmics, where reduced olfactory function is associated with reduced GM and WM volumes and thickness (Han et al., 2018; Bitter et al., 2010; Peng et al., 2013). Due to the insula being responsible for interoception (sensing the body's internal condition, eg, temperature and heart rate), emotional processing, and decision making, and being supported by a diffusion MRI study showing that the insula is structurally connected to many other regions of the brain through white matter pathways (Menon et al., 2024). Additionally, damage to the left insula was also associated with impairment in emotion perception, as determined by lesion mapping research ( Operskalski et al., 2015). Such research suggests that emotional processing is strengthened in individuals with congenital anosmia, perhaps due to the higher density of the WM in this region, allowing neural signals to travel faster and exchange information more efficiently. Researchers further observed increased white matter density of the left superior longitudinal fasciculus in an area posteromedial to the left insula, as well as of an area posterior to the parietal operculum (Frasnelli et al., 2013).

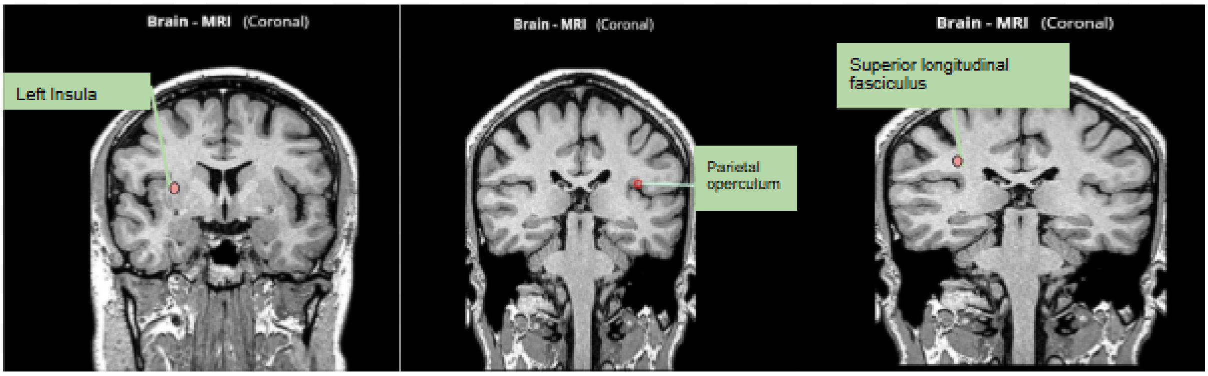


**Figure 4**: Regions of the brain resulting in increased white matter density in congenital anosmia. Courtesy of IMAIOS © "Antoine MICHEAU, MD , Denis HOA, MD Authors' affiliations, Publication date: Aug 25, 2008, Anatomy of the brain (MRI) - cross-sectional atlas of human anatomy, **https://doi.org/10.37019/e-anatomy/163**

## Cortical Thickness

Beyond volume and density, a separate study investigated cortical thickness, finding further evidence of compensatory structural changes. This study examined cortical changes and prefrontal and limbic brain regions in ICA individuals using MRI and found thicker orbitofrontal cortices, along with larger grey matter volumes in left entorhinal and priform cortices, which are key areas in both olfactory and emotional networks ( Frasnelli et al., 2013). The study found that congenital anosmia is associated with altered brain structure areas involving olfactory processing. "Individuals with congenital anosmia had a thicker bilateral medial orbitofrontal cortex. Further, the same group exhibited a denser and thicker left piriform cortex" (pg 4; Frasnelli et al., 2013). The implications surrounding a thicker medial orbitofrontal cortex suggest that compensatory neural reorganization may have occurred, as its role is primarily in reward evaluation, emotional regulation, and multisensory integration (combining senses) due to the absence of olfactory input. The structural enlargement in ICA patients also suggests reduced "synaptic pruning" (Synaptic pruning is a natural process in brain development where the brain eliminates unnecessary synapses, connections between neurons, enhancing its efficiency and functionality) due to a lack of olfactory input during early development (Frasnelli et al., 2013). In addition, a thinner patch of tissue in the posterior-lateral orbitofrontal cortex was reported.

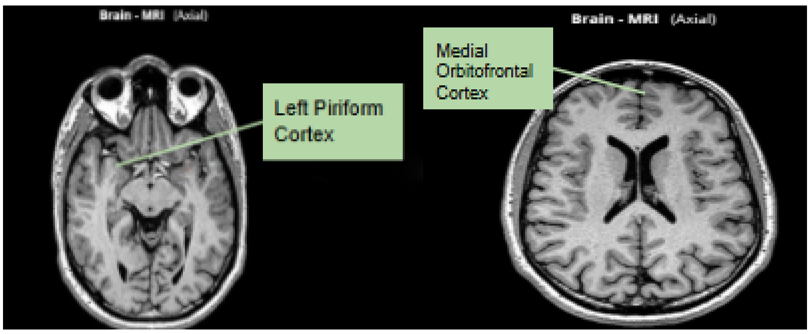


**Figure 5**: Areas of the brain associated with increased cortical thickness in congenital anosmia. Courtesy of IMAIOS © "Antoine MICHEAU, MD , Denis HOA, MD Authors' affiliations, Publication date: Aug 25, 2008, Anatomy of the brain (MRI) - cross-sectional atlas of human anatomy, **https://doi.org/10.37019/e-anatomy/163**

Taken together, the collective structural findings strongly point towards a compensatory mechanism in ICA. The observation of greater GM volumes and increased WM density in regions for emotion and cognition, particularly the insula, suggests that these structural adaptations in individuals with ICA may result in enhanced processing and integration of non-olfactory sensory or emotional information, a key form of neural reorganization. Overall, these findings suggest a compensatory mechanism in place for a lack of olfaction (cross-modal plasticity) and reduced synaptic pruning. These combined findings of GM enlargement and increased WM density strongly suggest a pattern of structural reorganization in ICA, where the absence of olfactory input drives compensatory neuroplastic changes to enhance other sensory and emotional functions. These structural adaptations act as the foundation for the cross-modal compensation observed in the behavioral and functional characteristics of individuals with congenital anosmia.

# Limitations

While these structural differences support a compensatory model, research in this area requires cautious interpretation due to methodological limitations. Many of the cited studies, including Frasnelli et al. (2013) and Karstensen et al. (2018), rely on small sample sizes and cross-sectional designs. This makes it challenging to establish a causal link between the absence of olfaction in congenital anosmics and proposed neuroplastic adaptations. We cannot be certain whether the structural changes developed because of the anosmia or if they are just correlated with it. Furthermore, Voxel-Based Morphometry (VBM) analyses can be limited to confirm the outcomes of increased GM or WM density, requiring further functional MRI (fMRI) investigations to accurately assess the behavioral impact of cross-modal plasticity. A significant limitation of the body of literature is the inconsistent use of the terms Congenital Anosmia (CA) and Isolated Congenital Anosmia (ICA). While this review prioritizes studies of ICA due to their methodological control, findings from studies using the broader CA definition may introduce heterogeneity, as some results could be influenced by underlying syndromic conditions not excluded by those authors. Lastly, it must be noted that the labelings applied to the MRI images represent an approximation, which may introduce a degree of uncertainty.

# Conclusion

The review examined the role of olfaction in emotional processing, structural brain changes in Isolated Congenital Anosmia (ICA), and the potential for compensatory mechanisms in facial emotion recognition.

Regarding ICA, the studies demonstrated a relatively consistent pattern of neuroplasticity in key emotion-related cortical and limbic regions, including the orbitofrontal cortex and piriform cortex (Frasnelli et al., 2013; Karstensen et al., 2018; Manan et al., 2022). These differences are characterized by increased gray matter volume (Karstensen et al., 2018; Peter et al., 2020) and white matter density (Frasnelli et al., 2013) in ICA individuals compared to controls. This pattern of structural change is broadly comparable to adaptations observed following the congenital loss of other sensory modalities, suggesting a neuroplastic response occurs due to the lifelong absence of a sensory modality such as olfaction.

Furthermore, the behavioral evidence indicates that the absence of smell may trigger compensatory mechanisms for evolutionary purposes. The review found that individuals with ICA show a greater accuracy or heightened sensitivity when recognizing negative emotions, specifically fear, anger, and disgust, from facial cues (Lemogne et al., 2015; Drummond et al., 2023). This finding suggests that the brain reorganizes itself to minimize potential threats by relying more on non-olfactory cues.

In turn, future studies could consider conducting long-term analysis of structural and functional changes in individuals with ICA, which would help establish causality. Future research could also be expanded to include testing multisensory recognition tasks (visual, auditory, and tactile) and investigate whether compensatory mechanisms can be enhanced through training. Addressing these gaps would not only advance our understanding of cross-modal plasticity but could also improve the lives of individuals with ICA and deepen our understanding of the relationship between olfactory loss and certain forms of cognition.

# Acknowledgements

The author wishes to thank Dr. Kimberly-Rose Clark, Consumer neuroscience professor at Dartmouth, and  Ms. Monika Rybak, Phd candidate at Harvard, psychology, for their essential contributions during this investigation.

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## Review #2

Authors have done a good job in addressing reviewers' comments to improve their paper. However, there are additional items that need to be addressed before the paper can be accepted for publication. These changes are very much about the structure of the paper to ensure it aligns with a traditional academic paper, and include:

Author Response: We would like to thank the reviewer for the **time and care** dedicated to evaluating our manuscript. Your thorough, insightful, and constructive comments have been **invaluable** in helping improve this review. We especially appreciate your guidance on structuring the Abstract and Introduction, and your suggestion to re-frame the Discussion as "Summary of Findings" truly enhances the paper's clarity and academic integrity. Every suggestion has been carefully considered and implemented.

1. The Abstract is slightly confusing and can be streamlined with use of subheadings such as Background, Aim, Conclusions. Currently it is not clear which parts are from already existing literature, and which are from this study.
    - We agree with this recommendation. We have streamlined the abstract as follows: Background, Aim, Summary of Findings, and Conclusion.

2. The Introduction is currently one very long paragraph. To improve readability and create better flow of ideas and structure, authors should consider creating smaller paragraphs, grouping together similar ideas, to build up the rationale for this study and then end the Introduction with the aim/s of this study.
    - We agree and have revised the Introduction. We broke the original text into smaller, thematic paragraphs. These paragraphs now flow logically, starting with the context of Congenital Anosmia, introducing Cross-Modal Plasticity, discussing structural alterations and behavioral findings, and stating the Aim and Structure of the review in the final two paragraphs.

3. Authors should refrain from referring to this paper as a “thesis”.
    - We agree and have carefully reviewed the manuscript to remove all references to the paper as a "thesis." It is now consistently referred to as a "literature review", "review", or “Premise”

4. Authors should include a “Methods” section to describe how they completed this study. How were papers found and synthesised for this review?
    - We agree this is essential for transparency. We have added a "Methods" section that describes the structure of the review, the systematic search strategy (databases, keywords used), the inclusion/exclusion criteria for selecting literature, and the critical synthesis approach adopted for the analysis.

5. I feel the subheading “Discussion” is misleading. It should actually be Results, or Summary of Findings.
    - We agree and have renamed the main section from "Discussion" to "Summary of Findings".

6. The structure of the “Discussion” needs to be improved with use of subheadings eg. Under “The role of olfaction in emotion processing” authors could use subheadings such as “Olfactory signalling pathways”, then

“Association of olfaction and emotions”, etc. This would support the reader in following along with the findings.

- We agree and have changed the structure within the "Summary of Findings" section (formerly "Discussion"). We have implemented multiple subheadings to create a clearer hierarchy and flow for the reader. For example, under "The role of olfaction in emotion processing," we added subheadings like "Olfactory Signaling Pathways," "Olfactory Imagery, Perception, and Emotional Response," and "Structural Integration of Olfaction and Emotion." Similar improvements were made to the other major sections ("Brain Structural Adaptations..." and "Emotion Recognition...").

7. A Limitations heading should be included between “Discussion” and “Conclusions” and limitations should be moved from the Conclusions to this section, and include any further limitations raised by reviewers.

- We agree. We have created a dedicated "Limitations" section and moved the existing discussion of methodological constraints (e.g., small sample sizes, VBM limits) from the former "Conclusion" into this new section. This new section is correctly placed between the "Summary of Findings" and "Conclusion" sections.

8. Authors should address the limitation in not being able to provide figures of the brain comparisons (in response to Reviewer 2) in the Limitations of the paper, acknowledging that this would strengthen their paper.

- Instead, we modified figures from a public database and cited them according to their guidelines.

9. The Conclusion is not a traditional Conclusion in that it does not provide a concise summary of the study’s findings. It needs to be written from a higher level meaning to be more broad. For example, authors could consider language such as “This review showed conflicting evidence exists in [specific finding]”, rather than writing study X found Y and study A found B, as that would more so belong in the “Discussion”.

- We agree and have rewritten the Conclusion. We attempted to frame it from a higher-level perspective, focusing on the broader implications of the findings. We now offer a summary of the main premise (structural adaptations support compensatory emotion recognition) and discuss how these findings contribute to the field of cross-modal plasticity and the understanding of emotional/social cognition without olfaction, rather than reiterating specific study details.

## Convergence Review of Congenital Anosmia and Emotional Processing

**Overview**: I greatly appreciate the author taking the time to further refine their paper. It is very clear that the author has addressed many of our comments, including our comments regarding the writing, keywords, and phrasing in different papers. Given these edits, I would suggest that the paper be accepted pending Minor Revisions. If future revisions are provided, I would strongly recommend that the author copies over the reviewer requests and directly responds to them one-by-one alongside the reviewer requests. Don't abbreviate or edit the reviewer requests in the response. This one-by-one approach is helpful when reviewers like myself go to review again.
Author Response: We would like to thank the reviewer for the **time and care** dedicated to evaluating our manuscript. Your thorough, insightful, and constructive comments have been **invaluable** in helping improve this review. We especially appreciate your guidance on structuring the Abstract and Introduction, which truly enhances the paper's clarity and academic integrity. Every suggestion has been carefully considered and implemented.

**Substantive Edits**

1) Technically, ICA stands for Isolated Congenital Anosmia. That should be clearly specified if you are using the acronym ICA. If you just mean Congenital Anosmia, the abbreviation should be CA. If you do use ICA, you should explain what the isolated implies.

- We agree entirely. We have ensured that ICA is defined as Isolated Congenital Anosmia upon first use. We have clarified that ICA refers to the congenital absence of smell *without* associated congenital syndromes (e.g., Kallman Syndrome). Furthermore, we use the full terms or ICA/CA consistently where appropriate, acknowledging that our review focuses primarily on the isolated form studied in neuroimaging.

2) The writing of the abstract could be improved. I would strongly suggest keeping the first sentence, then skipping to "This literature review looks into the relationship...olfaction." I would then much more briefly explain what the previous studies have found (which reflects what you discussed in the review) and then conclude with your final sentence. Abstracts are generally 6-10 sentences in most fields.

- We agree and have revised the Abstract following the structure suggested by both reviewers (now streamlined as Background, Aim, Summary of Findings, and Conclusion). The content has been significantly streamlined to focus only on the essential context, the core Aim, the key finding (that structural changes exist and support compensation), and the conclusion's broader implication.

3) You should clearly state what original contributions you made (I don't believe you did) vs. what you are summarizing from the literature, to be clear about what was original and what's not.

- We **agree**. We have clarified our **original contribution** within the Introduction. We emphasize that this paper presents a **thematic synthesis and critical interpretation** of existing literature to construct an argument that the structural changes observed in ICA serve as the neural foundation for compensatory mechanisms in emotional recognition rather than presenting new empirical data.

4) The Introduction should be broken up into separate paragraphs that follow key themes. One can potentially break up these paragraphs along the lines of one paragraph about and motivating research into CA, one paragraph about its connection to different regions of the

brain, one paragraph about how this connects emotions to CA, one paragraph about cross-modal plasticity, and lastly, one paragraph about what you set out to do in this review.

- We agree. The Introduction has been revised and broken into paragraphs (as noted in the response to the first reviewer), which closely follow the logical flow you outlined: Defining CA/ICA, Motivating the investigation (smell loss and adaptation), Structural Brain Alterations, Olfaction-Emotion Overlap, Defining Cross-Modal Plasticity, and finally, the Aim and Structure of the Review. This greatly improves readability and flow.

5) I would still insist on you including images of the relevant brain regions in the review. You can easily find non-copyrighted images. Alternatively, is the author's responsibility to make images in Photoshop or otherwise to convey the key points. I think images are fairly important to your thesis.

- We agree and have ensured that the manuscript now includes five figures (Figures 1-5) illustrating the key structural findings. These include diagrams for Olfactory Bulb/Sulcus morphology, and the specific regions of increased/decreased Grey Matter volume, increased White Matter density, and altered Cortical Thickness in ICA subjects, all of which are cited using non-copyrighted sources (e.g., e-Anatomy IMAIOS with proper attribution) or are based on schematic representations of the reviewed findings.

6) I think it makes sense to have the section on "Emotion recognition in individuals with ICA" follow the section on "The role of olfaction in emotion processing."

- We **agree**. We have re-sequenced the "Summary of Findings" section to follow a more logical progression that builds the argument.

7) What you wrote for the Conclusion contains quite a bit of Discussion. Discussion is where you discuss what's wrong with the current state of the field and what should be further studied. Conclusions are where you resummarize the paper (at least in my field!).

- We agree with this. The former Conclusion has been split into two distinct sections: Limitations (which discusses methodological issues and gaps, effectively serving the function of a field discussion) and a new, brief Conclusion.

**Minor Edits**

1) "Through this condition, an investigation into the relationship between cross-modal plasticity and emotion recognition processes in individuals with ICA is prompted." This sentence does not make much sense in English. I think you mean that this condition might motivate a study into the relationship between cross-modal plasticity and emotion recognition processes? See major edit #2 for further discussion.

- We agree the phrasing was awkward. We have rewritten this for clarity: "This condition motivates an investigation into the relationship between cross-modal plasticity and emotion recognition processes in individuals with ICA."

2) In the Introduction, change "body section" to just "section" in all places.

- We agree and have revised the text to use "section" or "main section" where appropriate.