Brain, Behavior, & Immunity - Health 45 (2025) 100983

Contents lists available at ScienceDirect

Brain, Behavior, & Immunity - Health

journal homepage: www.editorialmanager.com/bbih/default.aspx

SARS-CoV-2-induced sensory perturbations: A narrative review of clinical phenotypes, molecular pathologies, and possible interventions

Randal A. Serafini [a,*], Justin J. Frere [b], Ilinca M. Giosan [c], Chinwe A. Nwaneshiudu [d]

[a] Department of Neuroscience, Icahn School of Medicine at Mount Sinai, New York, USA
[b] Department of Microbiology, Icahn School of Medicine at Mount Sinai, New York, USA
[c] Department of Biology, University of Bucharest, Bucharest, USA
[d] Department of Anesthesia, Perioperative and Pain Medicine, Center for Neurogenomics, Icahn School of Medicine at Mount Sinai, New York, USA

ARTICLE INFO

Keywords:
SARS-CoV-2
COVID-19
Long-COVID
Olfaction
Gustation
Somatosensation
Vision
Auditory/vestibular function

ABSTRACT

Background: The acute and post-acute sequelae of SARS-CoV-2 infection have been of great clinical interest since the inception of the COVID-19 pandemic. Despite a high prevalence of individuals with persistent symptoms, a wholistic view of the effects of SARS-CoV-2 on special sensory systems is lacking. Considering the significant impact of normal sensory function on quality of life, the goal of this review is to highlight unresolved issues related to SARS-CoV-2-associated insults to the sensory nervous system.

Major findings: In this narrative review, we discuss the epidemiology of SARS-CoV-2-induced sensory perturbations, underlying pathological mechanisms, and possible therapeutic strategies across the olfactory, gustatory, somatosensory, visual, and auditory systems. Examined literature included studies with human biospecimens, human-derived cell lines, and naturally susceptible animal models, which highlighted evidence of persistent functional disruption in all sensory systems. SARS-CoV-2 infection was associated with persistent inflammation in the olfactory epithelium/bulb, somatosensory ganglia, and gustatory systems, long-term transcriptional perturbations in the sensory central nervous system and peripheral nervous system, and detectable degeneration/apoptosis in the gustatory and visual systems. Few studies have proposed evidence-based therapeutic strategies for attenuating specific sensory abnormalities after SARS-CoV-2 infection.

Conclusion: While the olfactory system, and to some extent the visual and somatosensory systems, have been more thoroughly investigated from symptomatology, behavioral and molecular perspectives, there is still an unmet need for the development of therapeutics to treat COVID-induced impairment of these systems. Further, additional attention must be placed on COVID-associated impairment of the gustatory, visual, and auditory systems, which lack detailed mechanistic investigations into their pathogenesis.

1. Introduction

As of October 2024, the World Health Organization estimates that over 700 million people have been infected by SARS-CoV-2 (WHO COVID-19 Dashboard). While acute SARS-CoV-2 infection is most often observed to induce flu-like respiratory symptoms, many individuals suffering from COVID-19 also appear to experience a wide-ranging array of sensory abnormalities during their acute disease course. These abnormalities notably include common features of COVID-19 such as anosmia (loss of smell), ageusia (loss of taste), myalgias, and headaches as well as rarer, but significant, sensory disturbances such as peripheral neuropathy-like sensations (i.e. tingling, numbness, shooting pain), visual alterations, and hearing disruption. While most individuals recover from COVID-19 without long-term deficits, approximately 45 % of patients have at least one unresolved symptom 28 days after infection onset (O'Mahoney et al., 2023), with several early studies suggesting symptom persistence in over 30 % of patients beyond six months (Davis et al., 2021; Nehme et al., 2021; Peghin et al., 2021; Taquet et al., 2021). However, more recent studies have lowered these estimates to between 5 % and 15 % of patients reporting persistent COVID-19 associated symptoms by at least three months after resolution of the acute infection (Adjaye-Gbewonyo et al., 2023; Hastie et al., 2023; Vahratian et al.,

Abbreviations: DRG, dorsal root ganglion; hACE2, human angiotensin-converting enzyme 2; OB, olfactory bulb; OE, olfactory epithelium; sgRNA, sub-genomic RNA; TG, trigeminal ganglion; TRC, taste receptor cells; VEGF-A, vascular endothelial growth factor A.

* Corresponding author.
E-mail address: alex.serafini@icahn.mssm.edu (R.A. Serafini).

https://doi.org/10.1016/j.bbih.2025.100983
Received 2 November 2024; Received in revised form 19 February 2025; Accepted 23 March 2025
Available online 24 March 2025

2024). This discrepancy in the prevalence of persistent symptoms may be due to changes in long-COVID criteria, such as the introduction of factors including the impact of symptoms on daily life (as in the Patient-Reported Outcomes Measurement Information System), as well as the increased adoption of vaccines. While the intensity and distribution of symptoms in post-acute infection periods has also been found to vary by viral strain, persistent cognitive, autonomic, and sensory abnormalities are prevalent in a large portion of long-COVID cases (Davis et al., 2021; Du et al., 2022; Gottlieb et al., 2023).

Lasting special sensory perturbations include the continuation of many symptoms associated with acute infection, such as hyposmia/anosmia, hypogeusia/ageusia, visual symptoms, and hearing loss/tinnitus/vertigo (Trott et al., 2022). Painful manifestations of long-COVID include musculoskeletal pain (Fernández-De-las-Peñas et al., 2022), headache (Tana et al., 2022), and paresthesia (Pinzon et al., 2022). Considering the impaired quality of life associated with sensory impairments/hypersensitivity (Assi et al., 2020; Costa-lópez et al., 2021; Elliott et al., 2003) and the global socioeconomic burden of COVID-19 and long-COVID (Cutler, 2022), we sought to review current literature on the epidemiology, proposed biological mechanisms, and possible treatments related to olfaction, gustation, touch, vision, and audition. From this scope, investigators can identify promising areas for future research efforts.

2. Epidemiology of COVID-19-related sensory perturbations

This section is intended to broadly discuss existing literature on the prevalence of sensory symptoms due to COVID-19 infection. It is by no means exhaustive, and other resources, such as those cited here, focus exclusively on this topic and discuss nuances between individual studies (Agyeman et al., 2020; Alkodaymi et al., 2022; Fernández-De-Las-Peñas et al., 2022; Jafari et al., 2022; Malik et al., 2022; Nasiri et al., 2021). As an additional caveat, several studies discussed here rely on self-reporting outside of a healthcare environment, which poses the risk of overreporting symptoms.

Acute olfactory dysfunction after SARS-CoV-2 infection has been reported at high levels - generally over 60 % - with resolution achieved in most reported cases, although at variable rates (Hopkins et al., 2020; Paderno et al., 2020; Rass et al., 2023). This loss of smell persists in a large portion of the long-COVID population, with estimates ranging between 5 % and 30 % (Davis et al., 2021; Hopkins et al., 2021; Lechien et al., 2021; Okrzeja et al., 2024; Petrocelli et al., 2021; Tan et al., 2022). However, these rates are highly variable due to measurement at different times post-infection, olfactory assessment method, and likely infection by differing viral strains. Taste dysfunction has a high rate of comorbidity with olfactory deficits in COVID-19 patients during the acute/subacute post-infection phase (Dell'Era et al., 2020; Nguyen et al., 2022). As with olfactory dysfunction, estimates of loss of taste vary substantially depending on number of months post-infection, definition of taste impairment, and method of assessment – from 1 % to over 30 % (Boesveldt et al., 2024; Davis et al., 2021; Petrocelli et al., 2021; Tan et al., 2022). Commonly identified risk factors for olfactory and taste dysfunction are female sex and milder disease presentation (Makaronidis et al., 2021; Mendes Paranhos et al., 2022; Nguyen et al., 2022; Torrell et al., 2024). Studies into genetic risk factors for COVID-associated smell loss have also implicated polymorphisms in the *UGT2A1* and *UGT2A2* genes as predisposing to anosmia; however, the mechanism by which these genes contribute to the pathology is currently unclear (Shelton et al., 2022).

As with other viral respiratory infections, a variable percentage of COVID-19 patients presented with myalgias (up to ~61 %) and headaches (up to ~34 %) (Weng et al., 2021), although many patients have described no painful symptoms (Kim et al., 2020) and others have described a reduction in chronic pain burden during the initial phase of infection (Hentsch et al., 2022). In one study, by seven months of infection, paresthesias (tingling, pins and needles, numbness) were the most prevalent sensory symptoms, appearing in almost 50 % of patients, yet over 30 % of patients reported painful neuralgias (Davis et al., 2021). However, a separate time course analysis suggests that a vast majority of myalgia, joint pain, and chest pain symptoms subside by six months, with 5–8 % of patients reporting continued pain (Fernández-De-Las-Peñas et al., 2022). The predominant form of long-COVID pain is distributed and musculoskeletal in nature, presenting as onset of a new pain conditioning or worsening of pre-existing chronic pain conditions (Fernández-De-las-Peñas et al., 2022; Khoja et al., 2022). Primary risk factors for persistent post-COVID pain include female sex, presence of painful symptoms during the acute infection phase, and worse severity of the initial infection (Fernández-De-las-Peñas et al., 2022).

Evidence of COVID-19-induced vision loss in the acute phase of infection is limited, with the conjunctivitis being the most commonly reported ocular finding (Ripa et al., 2022; Sen et al., 2021). Other prevalent symptoms included dry eye, tearing, itching, ocular pain, and discharge (Nasiri et al., 2021). In one study, approximately 30 % of long-COVID patients report blurred vision, photosensitivity, or increased eye pressure/pain (Davis et al., 2021), although this value is much lower in other studies that look at earlier timepoints (Almas et al., 2022). It is possible that visual dysfunction measurements are confounded by cognitive impairments, such as fatigue during demanding tasks (Johansson et al., 2024). A smaller number of patients also have reported conjunctivitis, peripheral visual field abnormalities, double vision, and tunnel vision (Davis et al., 2021). Complete loss of vision directly associated with infection is rarely reported. Of note, few studies provide detailed analyses of eye-related abnormalities in long COVID patients.

Acute COVID-19 infection has been associated with a relatively low, but significant, prevalence of auditory and vestibular symptoms, such as hearing loss, tinnitus, and dizziness (Jafari et al., 2022). As reflected with taste and smell, otologic symptoms have been frequently observed in female populations and tend to resolve quickly (Elibol, 2021; Ong and Cruz, 2022). While less prevalent than other persistent symptoms, audio-vestibular issues such as hearing loss and dizziness have been reported in approximately 10 % of long-COVID patients (Blomberg et al., 2021; Davis et al., 2021).

While risk factors for specific COVID-associated sensory symptoms vary, all appear to be at least partially associated with age. The effect of age on symptom presentation is most visible in children and adolescents, who appear to experience milder symptomology from SARS-CoV-2 infection generally and display markedly higher rates of asymptomatic infection compared to adults (Ma et al., 2021; Nikolopoulou and Maltezou, 2022). As a result, while children are still seen to suffer from COVID-associated anosmia—and in fact, this can oftentimes be the only symptom that is experienced by children during SARS-CoV-2 infection—incidence appears lower than what is seen in adult populations, which is estimated to occur in 15–20 % of infected children (Púa Torrejón et al., 2022; Yan et al., 2021). While other sensory disturbances such as myalgias and headaches also appear less commonly in children, smaller cohort studies have suggested that these symptoms are more likely to present in children suffering from other symptomologies, such as fever or smell loss (Púa Torrejón et al., 2022). Further, rarer sensory disturbances such as visual and otologic impairment appear to present even more uncommonly in children and are often only described in case studies (Chrysouli et al., 2024). While data on persistent sensory abnormalities in children is limited, preliminary cohort studies of children have demonstrated that some somatosensory abnormalities with both clinical and subclinical presentations can last for 2–4 months beyond initial infection. However, prevalence of persistent sensory symptomology appears rarer in pediatric populations compared to adult populations (Eitner et al., 2022).

Studies into the effects of age beyond childhood on sensory abnormalities have shown mixed results and are complicated by the fact that elderly individuals already show enhanced sensory impairment

compared to younger adult populations at baseline. For instance, increased age has long been known to be associated with reduced smell and taste sensation in otherwise healthy individuals (Chen et al., 2022; Doty et al., 1984). When age has been taken into account as a covariate of SARS-CoV-2 infection, some studies found that it did not appear to associate with COVID-19-related taste or smell alteration (Liu et al., 2022; Sharetts et al., 2024); however, others found that older patients may be less likely to lose smell/taste compared to younger adults (Coelho et al., 2022).

Throughout the pandemic, SARS-CoV-2 has also undergone mutagenesis to form new viral variant strains that have been found to exhibit differential pathogenicity. Of note, it has also been reported that distinct variant strains may have varied capacity to induce sensory abnormalities. For instance, there is evidence that later omicron variant strains may have a reduced capacity to induce anosmia compared to the delta and alpha variant strains that were predominant in the early pandemic. Curiously, different variant strains all appear to induce similar levels of somatosensory symptoms such as myalgias (Vihta et al., 2023). Despite this evidence, the impact of viral variants is difficult to interpret in large population studies, as variants that emerged later in the pandemic were also likely to infect a more immune-experienced population—either due to vaccination or prior SARS-CoV-2 exposure. These studies are also difficult to interpret given that evidence remains mixed as to whether prior infection leads to reduction in risk of anosmia or other sensory symptoms. Indeed, animal models of anosmia show that hamsters can still experience smell loss after vaccination (Reyna et al., 2023) – a finding which has also been verified in studies of vaccinated human patients (Vaira et al., 2022). However, the severity and temporality of anosmia was not assessed in these studies. Thus, it remains unclear how protective existing SARS-CoV-2 immunity is against the development of sensory abnormalities.

3. Molecular mechanisms associated with sensory perturbations

When considering pre-clinical disease models for this review, we chose to focus on models that did not require host genetic modification to enable infection, such as the golden hamster model, as the distribution of key SARS-CoV-2 infection-associated molecules in models such as hACE2-expressing mice are not necessarily reflective of naturally occurring expression levels and/or location of expression (Casel et al., 2021). While these models are a valuable resource for increasing access to SARS-CoV-2 research and studying the effects of viral binding at the human ACE2 receptor, humanized animal models can lead to increased lethality and susceptibility to infection in resistant cellular populations, such as CNS neurons. While this adds several confounding factors when attempting to draw nervous system-level and behavioral conclusions, these models can transcriptionally present similarly to humans in tissues such as the lung (Chen et al., 2024). Additionally, while several studies use sub-genomic RNA (sgRNA) as a putative biomarker of active infection, we acknowledge that recent reports suggest this is not necessarily

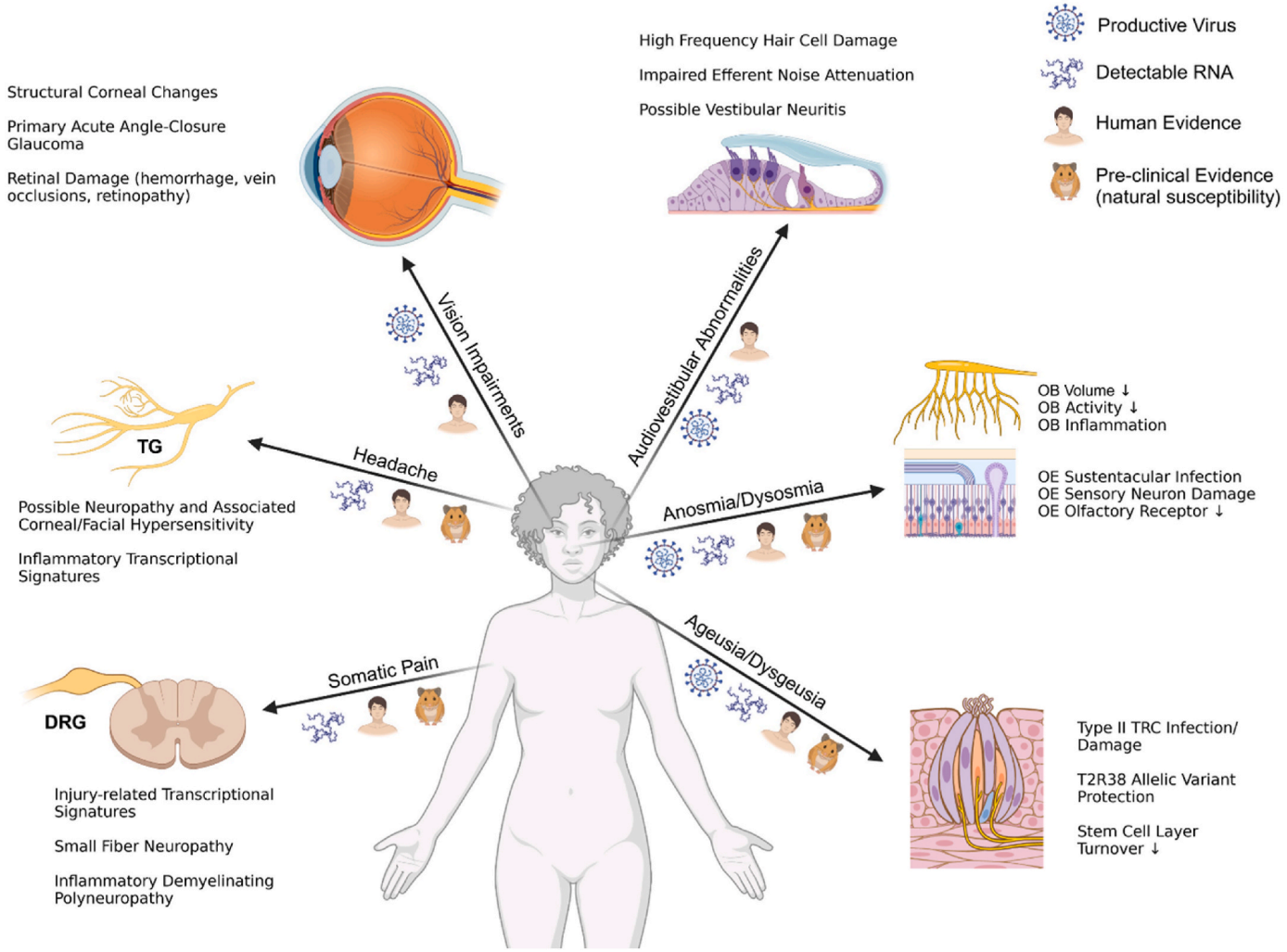

Fig. 1. Illustration of major mechanistic underpinnings of acute and persistent COVID-19-associated sensory symptoms. Abbreviations: OB = olfactory bulb, OE = olfactory epithelium, TRC = taste receptor cells, DRG = dorsal root ganglion, TG = trigeminal ganglion.

the case, and sgRNA presence may be a result of abortive infection, systemic dissemination and deposition of viral RNA (RNAemia), or evidence of debris from prior infection that is maintained due to host nuclease resistance (Alexandersen et al., 2020; Arkin et al., 2024; Carrau et al., 2023). A visual summary of our findings is available for reference in Fig. 1.

3.1. Olfactory system

Several SARS-CoV-2-associated mechanisms have been proposed for clinical presentation of acute and persistent anosmia, which have been reviewed at length (Butowt et al., 2023; Najafloo et al., 2021; Tsukahara et al., 2023). These hypotheses revolve around changes in either structure and/or function of the olfactory epithelium, olfactory bulb, and networks connected with the bulb and olfactory cortex, as well as persistently dysregulated immune responses in the same tissues.

Pathogenesis of anosmia is largely thought to initiate in the olfactory epithelium. The olfactory epithelial layer can be found in the superior-posterior aspect of the nasal cavity and is comprised of a mixed population of cells that notably includes olfactory sensory neurons (OSNs) and sustentacular cells as well as their stem-cell progenitors. Primary olfactory sensation is initiated in the OSNs, which express olfactory receptors on ciliary processes that extend into the nasal cavity and bind odorant molecules present in inspired air. OSNs are assisted in this activity by sustentacular cells, which provide metabolic and structural support to the OSNs and wider olfactory epithelium. The olfactory epithelium undergoes infection during SARS-CoV-2 infection in both humans and animal models such as the golden hamster (Frere et al., 2022; Khani et al., 2021; Reyna et al., 2022). Importantly, across species, OSNs themselves have been observed to be largely resistant to SARS-CoV-2 infection due to their minimal expression of ACE2; however, sustentacular cells express large amounts of ACE2 and are thus highly susceptible to infection (Zazhytska et al., 2022). Various studies have found that infected sustentacular cells express significant amounts of antiviral and proinflammatory cytokines—such as type I, II, and III interferons (M. A.M. Khan et al., 2022; Zazhytska et al., 2022). This immune signaling, in turn, drives enhanced recruitment of immune cells such as monocytes and neutrophils into the olfactory epithelium during acute SARS-CoV-2 infection. OSNs, while resistant to direct SARS-CoV-2 infection, are heavily stimulated by surrounding virus-induced immune signaling. This signaling can induce epigenetic changes in OSNs which can further induce the silencing of olfactory receptor loci. This, in turn, results in lower expression of olfactory receptor proteins and impairs the ability of OSNs to detect odorant molecules and initiate neural smell sensation signaling cascades—leading to anosmia (Zazhytska et al., 2022). Additional studies of OSNs during SARS-CoV-2 infection have shown that while not infected, this cell population appears histologically damaged during acute infection; while the mechanism behind this damage remains unclear, recent studies have suggested that it may be a result of stress from loss of sustentacular cell support (Verma et al., 2022) or immune-mediated toxicity (Frere et al., 2022; Zazhytska et al., 2022).

While studies in animal models (de Melo et al., 2021; Frere et al., 2022; Reyna et al., 2022) and humans (A. M. M. Khan et al., 2022) have shown that smell sensation usually recovers following the clearance of infection, a significant population of COVID-19 patients have reported suffering from chronic anosmia that can last anywhere from days to years following infection clearance. The drivers of this persistence are currently unclear; however, initial studies have suggested that infection-induced structural abnormalities, persistent inflammatory processes, and prolonged viral infection may contribute to dysfunction of both peripheral and central processing of olfactory stimuli.

Regarding structural abnormalities, studies have found that post-COVID patients that experienced anosmia had measurable damage signatures in their olfactory bulbs as well as a significant reduction in olfactory bulb volume compared to control subjects (Kandemirli et al., 2021). Other studies have identified post-COVID damage in brain regions connected to the olfactory processing structures, such as the primary olfactory cortex (Douaud et al., 2022). Along these lines, some studies have suggested that post-COVID patients may experience altered functional connectivity within olfactory networks (de Bispo et al., 2023). Together, these described changes suggest prolonged alterations of signaling along central nervous system olfactory networks following anosmia associated with acute SARS-CoV-2 infection; however, at this time, it remains unclear how these structural changes affect smell sensation and how they may contribute to prolonged anosmia.

Studies have demonstrated that SARS-CoV-2 infection leads to inflammation of olfaction-related neural structures during acute infection. While this inflammation has been noted to be most severe in the olfactory epithelium (where infection is most prominent) (Carrau et al., 2023; de Melo et al., 2021; Frere et al., 2022; Zazhytska et al., 2022), olfactory bulb tissues also show robust inflammation during COVID-19—even if viral presence is minimal in these tissues (de Melo et al., 2021; Frere et al., 2022; Radke et al., 2024). These inflammatory processes in the olfactory bulbs have, in turn, been associated with reduced neural activity in the olfactory bulbs during acute infection periods (Verma et al., 2022). Notably, these inflammatory processes appear to persist in the olfactory bulbs beyond the time of infection clearance, and studies utilizing both human post-mortem tissues and hamster animal models have demonstrated persistent inflammation of the olfactory bulb after SARS-CoV-2 infection (Käufer et al., 2022; Kishimoto-Urata et al., 2022). This inflammation has been associated with prolonged glial activation (Käufer et al., 2022; Kishimoto-Urata et al., 2022), as well as infiltration of circulating immune cells such as myeloid and T cells (Frere et al., 2022; Schwabenland et al., 2021). Furthermore, studies characterizing the olfactory epithelial tissues of post-COVID patients have shown that a subset of patients suffering from chronic anosmia appear to show heightened and prolonged immune responses compared to post-COVID patients not suffering from chronic anosmia (Finlay et al., 2022). These prolonged olfactory epithelial immune responses were notably found to include heightened infiltration of T cells—a finding also seen in studies characterizing olfactory epithelium of post-COVID animal models (Finlay et al., 2022; Frere et al., 2022). In all, these studies suggest that chronic inflammatory processes may be seen throughout the olfactory system following SARS-CoV-2 infection. While the direct mechanism by which prolonged inflammation may contribute to chronic anosmia or other post-COVID symptomology is unclear, existing studies suggest that persistent post-COVID anosmia could be driven by processes spanning across both the central and peripheral nervous systems.

Investigations into the source of chronic inflammation in post-COVID patients have generated mixed results. While some sources identify residual viral reservoirs as the culprit for ongoing immune responses (de Melo et al., 2021), others have implicated aberrant activation of complement and thrombotic machinery (Cervia-Hasler et al., 2024), microvascular ischemic injury (Rutkai et al., 2022), reactivation of latent herpes viruses (Davis et al., 2023), autoimmunity (Ehrenfeld et al., 2020), residual viral or cellular debris (Carrau et al., 2023; Frere et al., 2022; Hoagland et al., 2021), and additional mechanisms (Davis et al., 2023) as potential drivers. Investigations specifically into drivers of continued olfactory inflammation have shown evidence for continued viral reservoirs in the olfactory epithelium of patients with chronic anosmia (de Melo et al., 2021).

Further, other studies have found that while the olfactory bulbs themselves appear to be rarely infected during acute SARS-CoV-2 infection, viral RNA is able to permeate this tissue (Frere et al., 2022; Meinhardt et al., 2021; Shimizu et al., 2024; Stein et al., 2022). It remains to be elucidated whether this phenomenon is a product of mild or abortive infection or is otherwise a result of the well-described phenomenon of SARS-CoV-2 RNAemia, which results in systemic deposition of viral RNA during acute infection. Although preliminary, some investigations have demonstrated that viral RNA alone may be sufficient

to induce robust and potentially prolonged pathological effects (Arkin et al., 2024; Ram-Mohan et al., 2022; Rombauts et al., 2023). Other studies looking to assess the implications of structural anomalies induced by SARS-CoV-2 infection have suggested that the increased presence of peripheral immune cells in regions such as the olfactory bulb both during and following infection may be due to blood-brain (Erickson et al., 2021) or blood-cerebral spinal fluid barrier disruption (Pellegrini et al., 2020), although most of the research on this topic has relied on in vitro chip models or organoids.

Potential evidence-based therapeutic interventions for altered sense of smell have been directed towards attenuation of inflammatory responses in the olfactory system. These approaches include inhaled corticosteroids, phosphodiesterase inhibitors, statins, palmitoylethanolamide (PEA) and luteolin (LUT), and various neuroprotective agents including cerebrolysin (Khani et al., 2021). While many of these strategies have not been tested in well-designed, rigorous clinical studies for the treatment of COVID-19, several blinded, randomized trials are currently underway on the utility of vitamin A, omega-3 fatty acid, gabapentin, theophylline, hesperidin, ophtamesone, and PEA-LUT for the treatment of olfactory dysfunction after COVID-19 (Riccardi et al., 2023). Of note, one randomized double-blind placebo-controlled study found that longitudinal administration of nasal betamethasone had no effect on recovery from anosmia (Rashid et al., 2021). Similarly, another randomized trial found that longitudinal treatment with nasal mometasone furoate yielded no benefits compared to a control group (Abdelalim et al., 2021). However, in a triple-blinded randomized trial, Gupta et al. found improved self-reported olfactory function after nasal irrigation with the methylxanthine, theophylline (Gupta et al., 2022). Furthermore, treatment with ultra-micronized PEA-LUT and olfactory training markedly improved odor identification scores compared to PEA-LUT or olfactory training alone, suggesting a need for more complex therapy regimens that involves neuro-plastic pathways (Di Stadio et al., 2023). Accordingly, Hamed et al. found that cerebrolysin, a neurotrophic peptide, with olfactory and gustatory training improved deficits more effectively than training alone (Hamed and Ahmed, 2023). These data suggest that prolonged anosmia after SARS-CoV-2 infection is underpinned by a complex pathology that may involve processes occurring in both central and peripheral nervous tissue. The roles of distinct pro-inflammatory molecules and cellular subtypes must be elucidated further to develop targeted immunomodulatory strategies.

3.2. Gustatory system

Clinical studies have demonstrated infection of cells in the fungiform papillae of the tongue, and abnormal gustation has been associated with SARS-CoV-2-mediated inflammation and perturbation of taste bud and innervating sensory fiber architecture (Yao et al., 2023). Specifically, ACE2 is enriched in type II taste receptor cells, which have shown susceptibility to SARS-CoV-2 infection in humans with associated taste changes after onset of COVID-19 (Doyle et al., 2021). SARS-CoV-2 infection was also associated with disrupted stem cell layer function (Doyle et al., 2021). This aligns with a recent report suggesting that loss of “bitter” taste was the most prevalent form of longitudinal ageusia in COVID-19 patients (Rogn et al., 2024). One single-cell RNA sequencing study found evidence of SARS-CoV-2 infection of human salivary oral glands and mucosae and found that salivary viral burden correlated with taste loss (Huang et al., 2021). Pre-clinical evidence also suggests that SARS-CoV-2 spike proteins can induce degeneration/apoptosis of rodent taste bud cells (Yamamoto et al., 2023). Interestingly, humans with the bitter taste receptor T2R38 allelic variant have been shown to mount a stronger innate immune response to SARS-CoV-2 (Barham et al., 2021), likely because of its presence on cilia of various cells in the upper respiratory system and role in nitric oxide-dependent immune activation (Cohen, 2017).

While many studies have demonstrated high expression of SARS-CoV-2 entry molecules in the oral cavity (Sakaguchi et al., 2020; Sawa et al., 2021), few studies have outlined tangible molecular mechanisms affecting taste as a consequence of this vulnerability. Additionally, most studies appear to link anosmia with ageusia/dysgeusia. While this strategy has merit based on the interconnectedness of the two senses and reports of overlapping symptoms during and after COVID-19 (Rogn et al., 2024; Vaira et al., 2020), it may distract from distinct pathological mechanisms based on the data discussed above.

Proposed therapeutic interventions for taste abnormalities such as dysgeusia are similar to those suggested for olfactory dysfunction, such as anti-inflammatory agents (Khani et al., 2021). Other strategies evaluated in randomized clinical trials include vitamin D supplementation, which was found to reduce time to recovery from gustatory sensory loss (Sabico et al., 2021), and the cerebrolysin study mentioned above (Hamed and Ahmed, 2023). A notable limitation of clinical efforts to treat taste dysfunction is the relatively rapid recovery in a majority of patients without intervention, emphasizing the need for symptom onset standardization. Unfortunately, most studies on this topic were either case studies or control-free studies.

3.3. Somatosensory system

Altered somatosensation is a common component of various viral infections, often acutely presenting as painful symptoms such as myalgia. Recent reports have demonstrated that persistent pain is one of the most prevalent presentations of long-COVID (Aiyegbusi et al., 2021; Kerzhner et al., 2024), yet relatively few studies have been performed on the peripheral nervous system or regions of the CNS that are crucial for pain processing.

Neurons from the somatosensory ganglia are largely responsible for initiating pain signaling to the spinal cord and higher brain centers, with the dorsal root ganglia (DRG) and the trigeminal ganglia (TG) serving as the major hubs for peripheral nociceptors involved in pain transduction. Pre-clinical studies in golden hamsters have shown that SARS-CoV-2 infection causes time-dependent gene expression changes in the DRG (Serafini et al., 2023b). Behaviorally, these changes resulted in attenuated mechanical hypersensitivity during active infection compared to other viruses, such as Influenza A, but persistent hypersensitivity well after viral clearance. Pre-clinical evidence suggests that the SARS-CoV-2 spike protein may be capable of interrupting virus-induced vascular endothelial growth factor A (VEGF-A) interaction with the neuropilin-1 receptor, which is pro-nociceptive, thus attenuating acute hypersensitivity after infection (Moutal et al., 2021). Combined, these mechanisms might provide insights as to why several studies have observed a relatively high incidence of asymptomatic COVID-19 (Gao et al., 2021). However, several clinical studies have also found robust pain profiles during the acute phase of COVID-19 (Cascella et al., 2021), suggesting some yet-to-be-defined mechanisms of symptom heterogeneity exist. Aside from persistently altered DRG transcriptomics, additional proposed mechanisms for new onset or increased pain include small fiber neuropathy, peripheral demyelination, and systemic inflammation (Abrams et al., 2021; Uncini et al., 2021). The combination of these pathologies is generally observed in Guillain-Barré syndrome, which had a high incidence during the COVID-19 pandemic and was believed to be primarily sensorimotor demyelinating in nature (Uncini et al., 2020). In addition, levels of circulating interleukin 10, an immunomodulatory interleukin, were also negatively associated with the presence of painful symptoms during the course of COVID-19 (Bussmann et al., 2022), emphasizing the role of systemic inflammation in pain persistence.

The TG is a major regulator of painful symptoms involving the head and face. Headaches are prevalent in COVID-19 patients (Caronna et al., 2023; López et al., 2020) and may be a predictor of long-term symptoms including fatigue (Fernández-de-las-Peñas et al., 2021). Trigeminal neuropathy and corneal pain are facial pain conditions that have been reported in COVID-19 patients (O’Neill et al., 2023; Woltsche et al., 2023). The effects of SARS-CoV-2 on the TG are still largely unknown.

Preclinical studies in golden hamsters have demonstrated time-dependent changes in TG transcriptional profiles (Frere et al., 2022). In alignment with a more robust acute transcriptional signature, others have found additional potential mechanisms of TG neuron sensitization, including viral proteases (Mali et al., 2024).

Overall, few pre-clinical and clinical studies have attempted to measure the presence of SARS-CoV-2 in the DRG (Joyce et al., 2023; Serafini et al., 2023b) and TG (Frere et al., 2022; Meinhardt et al., 2021), with most focusing on RNA expression. This lack of data, which is most likely due to difficulty accessing these tissues, contributes to the ongoing debate as to whether the systemic effects of SARS-CoV-2 infection are due to neuro-invasion and nerve-mediated viral transmission or uncontrolled systemic inflammation. Direct viral infection of these regions is conceivable, given evidence of ACE2 expression in several cell subtypes in the DRG and TG (McFarland et al., 2021). A clinical autopsy study also found subgenomic RNA in sciatic nerve, suggesting potential infection in the somatosensory PNS (Stein et al., 2022), and one pre-clinical study found spike protein in hamster DRG and TG neurons (Joyce et al., 2023).

Other regions of the pain transduction pathway that have been perturbed after SARS-CoV-2 infection in pre-clinical and clinical studies include the spinal cord (Garg et al., 2021; Serafini et al., 2023a; Stein et al., 2022), periaqueductal grey (Jin et al., 2024), thalamus (Frere et al., 2022; Stein et al., 2022), prefrontal cortex (Frere et al., 2022; Voruz et al., 2023), striatum (Frere et al., 2022; Guarnieri et al., 2023), anterior cingulate cortex (Douaud et al., 2022), and amygdala (Serrano et al., 2022). Furthermore, a large body of research has highlighted sex specificity in pain predisposition and underlying mechanisms, particularly inflammation-mediated onset and maintenance of pain (Gregus et al., 2021; Mogil, 2020). Accordingly, certain studies have found an increased incidence of acute and persistent COVID-19-associated thoracic musculoskeletal pain (Pelà et al., 2022) and increased post-COVID pain intensity (Fernández-de-las-Peñas et al., 2022) in female patients. Given the heterogeneity of chronic pain mechanisms in general, it would be beneficial to perform further clinical and pre-clinical studies delineating peripheral and central nervous system contributions to long-COVID pain symptoms. Accordingly, the variability in presentation of persistent COVID-19-induced pain has made it difficult to pursue a standardized treatment methodology, suggesting the need for a multimodal and personalized approach that uses both existing pharmacological and non-pharmacological methods (Fernández-de-las-Peñas et al., 2023).

3.4. Visual system

Pre-clinical and clinical reports have identified several ocular pathologies after SARS-CoV-2 infection. These include ultrastructural changes in regions such as the cornea (Kolkedi et al., 2022) and potentially vision-threatening pathologies such as retinal hemorrhages, cotton wool spots, retinal vein occlusions (Sen et al., 2022), and maculopathies/neuroretinopathies (Invernizzi et al., 2020; Premi et al., 2023). Newer evidence may directly link SARS-CoV-2 infection to primary acute angle-closure glaucoma, due to abundant pro-inflammatory proteins in the aqueous humor (Gong et al., 2024). Sore eyes were also a relatively prevalent symptom in COVID-19 patients (Pardhan et al., 2020).

Interestingly, the eye has been proposed as a route of infection, as several groups have noted a robust vulnerability of the cornea to SARS-CoV-2 (Casagrande et al., 2021; Eriksen et al., 2021). Viral particles have also been detected in the retina (Araujo-Silva et al., 2021; Casagrande et al., 2020), and organoid models using human cells have suggested viral replication potential in various retinal cell subtypes (Menuchin-Lasowski et al., 2022). sgRNA has also been found in the optic nerves of patients, but in the absence of replication-competent virus/viral proteins (Casagrande et al., 2022). Interestingly, one study also found a high rate of PCR positivity by conjunctival swab, even in some patients that were negative by nasopharyngeal swab – although it was unclear whether this RNA was accompanied by infectious virus (Azzolini et al., 2021).

Treatment for ocular pathologies after COVID-19 infection has focused primarily on administering broad anti-inflammatory agents, such as corticosteroids, and topical/systemic antivirals (Yener, 2021). However, for certain pathologies in the posterior segment of the eye, such as vascular occlusions, early treatment with anticoagulants has been suggested (Sen et al., 2021). The heterogeneity of vision loss mechanisms and rare reporting of lasting visual symptoms directly attributable to COVID-19 have precluded standardized and well-controlled therapeutic investigations.

3.5. Auditory & vestibular system

As with other sensory systems, SARS-CoV-2 has also been associated with hearing abnormalities, such as hearing loss and tinnitus (Jafari et al., 2022; Maharaj et al., 2020). A detailed analysis of the efferent auditory system found that patients with COVID-19 had lower distortion product otoacoustic emission and contralateral suppression results, suggesting viral effects on the medial olivary complex and damage to higher frequency outer hair cells (Emekci et al., 2022). Of note, this group suggested that the absence of a major auditory system deficit does not preclude some level of SARS-CoV-2 induced damage – a note with particular relevance to patients that undergo a delayed onset of long-COVID or a phasic disease course. A separate study found similar otoacoustic emission results, as well as higher audiometry pure tone averages and video head impulse test vestibular deficits in COVID-19 patients (Bozdemir et al., 2024). Early evidence suggests that SARS-CoV-2 may induce vestibular neuritis, possibly contributing to these symptoms (Mat et al., 2023). Work with human-derived cell lines has demonstrated susceptibility of inner ear cell subtypes to SARS-CoV-2 infection (Jeong et al., 2021) and clinical evidence suggests that SARS-CoV-2 can infect components of the middle ear apparatus (Jeican et al., 2021; Kurabi et al., 2022).

Few studies exist for the treatment of sudden hearing loss due to COVID-19. Interestingly, one study compared intravenous steroid administration to intra-tympanic steroid administration and found no different in recovery rates when comparing patients with mild and severe hearing loss (Tsuda et al., 2023). However, no control group was included in this study. A notable confound regarding COVID-19-related hearing loss was the high rate of off-label ototoxic drug use, including hydroxychloroquine, which may have artificially elevated the perceived ototoxicity of SARS-CoV-2 (Prayuenyong et al., 2020).

4. Conclusion

In summary, this review synthesized recent literature on the epidemiology, molecular underpinnings, and early-stage therapeutic investigations of sensory perturbations both during and after COVID-19 infection. While direct infection of cells involved in the maintenance and function of sensory systems is either unclear or highly cell subtype-specific, substantial evidence exists for persistent, damaging immune responses across most of these systems. These responses often result in damage or apoptosis of sensory neurons, as well as transcriptional dysregulation. One limitation of this review is the omission of cortical/subcortical brain regions that process sensory inputs, which can further explain distorted sensory perception and could elucidate alternative therapeutic strategies. Of note, no therapeutic intervention has received regulatory approval for the treatment of a COVID-19 induced sensory abnormality. Investigations of therapeutic strategies have focused primarily on treatment with local or systemic anti-inflammatory agents. This review therefore emphasizes the need for a more mechanistic understanding of sensory defects, particularly in the gustatory, visual, and auditory systems, as well as increased efforts towards discovering targeted therapeutic strategies across all sensory modalities.

CRediT authorship contribution statement

Randal A. Serafini: Writing – review & editing, Writing – original draft, Visualization, Project administration, Data curation, Conceptualization. **Justin J. Frere:** Writing – review & editing, Data curation. **Ilinca M. Giosan:** Writing – review & editing, Data curation. **Chinwe A. Nwaneshiudu:** Writing – review & editing, Data curation.

Funding source

No funding sources were used for this review.

Declaration of competing interest

There are no conflicts of interest to declare for all authors.

Acknowledgements

We thank Jill K. Gregory, MFA/CMI for her artistic contributions to this work.

Data availability

No data was used for the research described in the article.

References

Abdelalim, A.A., Mohamady, A.A., Elsayed, R.A., Elawady, M.A., Ghallab, A.F., 2021. Corticosteroid nasal spray for recovery of smell sensation in COVID-19 patients: a randomized controlled trial. American J. Otolaryngol. Head and Neck Med. Surgery 42. https://doi.org/10.1016/j.amjoto.2020.102884.

Abrams, R.M.C., Simpson, D.M., Navis, A., Jette, N., Zhou, L., Shin, S.C., 2021. Small fiber neuropathy associated with SARS-CoV-2 infection. Muscle Nerve. https://doi.org/10.1002/mus.27458.

Adjaye-Gbewonyo, D., Vahratian, A., Perrine, C.G., Bertolli, J., 2023. Long COVID in Adults: United States, 2022. NCHS Data Brief.

Agyeman, A.A., Chin, K.L., Landersdorfer, C.B., Liew, D., Ofori-Asenso, R., 2020. Smell and taste dysfunction in patients with COVID-19: a systematic review and meta-analysis. Mayo Clin. Proc. 95. https://doi.org/10.1016/j.mayocp.2020.05.030.

Aiyegbusi, O.L., Hughes, S.E., Turner, G., Rivera, S.C., McMullan, C., Chandan, J.S., Haroon, S., Price, G., Davies, E.H., Nirantharakumar, K., Sapey, E., Calvert, M.J., 2021. Symptoms, complications and management of long COVID: a review. J. R. Soc. Med. https://doi.org/10.1177/01410768211032850.

Alexandersen, S., Chamings, A., Bhatta, T.R., 2020. SARS-CoV-2 genomic and subgenomic RNAs in diagnostic samples are not an indicator of active replication. Nat. Commun. 11. https://doi.org/10.1038/s41467-020-19883-7.

Alkodaymi, M.S., Omrani, O.A., Fawzy, N.A., Shaar, B.A., Almamlouk, R., Riaz, M., Obeidat, M., Obeidat, Y., Gerberi, D., Taha, R.M., Kashour, Z., Kashour, T., Berbari, E.F., Alkattan, K., Tleyjeh, I.M., 2022. Prevalence of post-acute COVID-19 syndrome symptoms at different follow-up periods: a systematic review and meta-analysis. Clin. Microbiol. Infection. https://doi.org/10.1016/j.cmi.2022.01.014.

Almas, T., Malik, J., Alsubai, A.K., Jawad Zaidi, S.M., Iqbal, R., Khan, K., Ali, M., Ishaq, U., Alsufyani, M., Hadeed, S., Alsufyani, R., Ahmed, R., Thakur, T., Huang, H., Antony, M., Antony, I., Bhullar, A., Kotait, F., Al-Ani, L., 2022. Post-acute COVID-19 syndrome and its prolonged effects: an updated systematic review. Annals of Med. Surgery 80. https://doi.org/10.1016/j.amsu.2022.103995.

Araujo-Silva, C.A., Marcos, A.A.A., Marinho, P.M., Branco, A.M.C., Roque, A., Romano, A.C., Matuoka, M.L., Farah, M., Burnier, M., Moraes, N.F., Tierno, P.F.G.M. M., Schor, P., Sakamoto, V., Nascimento, H., De Sousa, W., Belfort, R., 2021. Presumed SARS-CoV-2 viral particles in the human retina of patients with COVID-19. JAMA Ophthalmol 139. https://doi.org/10.1001/jamaophthalmol.2021.2795.

Arkin, L.M., Costa-da-Silva, A.C., Frere, J., Ng, A., Sharma, R., Moon, J.J., Bussan, H.E., Kim, C.H., Javaid, A., Steidl, O.R., Yatim, A., Saidoune, F., Gilliet, M., Nguyen, J.T., Nihal, A., Luong, G., Kenfield, M., Carrau, L., Tran, J.M., Hinshaw, M.A., Brooks, E. G., Ayuso, J.M., O'Connor, D.H., Casanova, J.-L., Cowen, E.W., Drolet, B.A., Singh, A.M., tenOever, B., Mays, J.W., 2024. Pandemic-associated pernio harbors footprints of an abortive SARS-CoV-2 infection. iScience 27, 110525. https://doi.org/10.1016/j.isci.2024.110525.

Assi, L., Shakarchi, A.F., Sheehan, O.C., Deal, J.A., Swenor, B.K., Reed, N.S., 2020. Assessment of sensory impairment and health care satisfaction among medicare beneficiaries. JAMA Netw. Open 3. https://doi.org/10.1001/jamanetworkopen.2020.25522.

Azzolini, C., Donati, S., Premi, E., Baj, A., Siracusa, C., Genoni, A., Grossi, P.A., Azzi, L., Sessa, F., Dentali, F., Severgnini, P., Minoja, G., Cabrini, L., Chiaravalli, M., Veronesi, G., Carcano, G., Maffioli, L.S., Tagliabue, A., 2021. SARS-CoV-2 on ocular surfaces in a cohort of patients with COVID-19 from the lombardy region, Italy. JAMA Ophthalmol 139. https://doi.org/10.1001/jamaophthalmol.2020.5464.

Barham, H.P., Taha, M.A., Broyles, S.T., Stevenson, M.M., Zito, B.A., Hall, C.A., 2021. Association between bitter taste receptor phenotype and clinical outcomes among patients with COVID-19. JAMA Netw. Open. https://doi.org/10.1001/jamanetworkopen.2021.11410.

de Bispo, D.D.C., de Brandão, P.R.P., Pereira, D.A., Maluf, F.B., Dias, B.A., Paranhos, H. R., von Glehn, F., de Oliveira, A.C.P., de Soares, A.A.S.M., Descoteaux, M., Regattieri, N.A.T., 2023. Altered structural connectivity in olfactory disfunction after mild COVID-19 using probabilistic tractography. Sci. Rep. 13. https://doi.org/10.1038/s41598-023-40115-7.

Blomberg, B., Mohn, K.G.I., Brokstad, K.A., Zhou, F., Linchausen, D.W., Hansen, B.A., Lartey, S., Onyango, T.B., Kuwelker, K., Sævik, M., Bartsch, H., Tøndel, C., Kittang, B.R., Madsen, A., Bredholt, G., Vahokoski, J., Fjelltveit, E.B., Bansal, A., Trieu, M.C., Ljostveit, S., Olofsson, J.S., Ertesvåg, N., Sandnes, H.H., Corydon, A., Søyland, H., Eidsheim, M., Jakobsen, K., Guldseth, N., Hauge, S., Cox, R.J., Langeland, N., 2021. Long COVID in a prospective cohort of home-isolated patients. Nat. Med. 27. https://doi.org/10.1038/s41591-021-01433-3.

Boesveldt, S., Postma, E.M., Boek, W., Kamalski, D.M.A., van Dijk, B., 2024. Longitudinal follow-up of taste function and trigeminal perception in COVID-19 patients with olfactory dysfunction – the COVORTS study. Clin. Nutrition Open Sci. 55, 249–262. https://doi.org/10.1016/j.nutos.2024.05.003.

Bozdemir, K., Çallıoğlu, E.E., İslamoğlu, Y., Ercan, M.K., Eser, F., Özdem, B., Kıraç, A., Bayazıt, D., Güner, R., Babademez, M. ali, 2024. Evaluation of the effects of Covid-19 on cochleovestibular system with audiovestibular tests. Ear Nose Throat J. 103. https://doi.org/10.1177/01455613211069916.

Bussmann, A.J.C., Ferraz, C.R., Lima, A.V.A., Castro, J.G.S., Ritter, P.D., Zaninelli, T.H., Saraiva-Santos, T., Verri, W.A., Borghi, S.M., 2022. Association between IL-10 systemic low level and highest pain score in patients during symptomatic SARS-CoV-2 infection. Pain Pract. 22. https://doi.org/10.1111/papr.13101.

Butowt, R., Bilinska, K., von Bartheld, C.S., 2023. Olfactory dysfunction in COVID-19: new insights into the underlying mechanisms. Trends Neurosci. https://doi.org/10.1016/j.tins.2022.11.003.

Caronna, E., van den Hoek, T.C., Bolay, H., Garcia-Azorin, D., Gago-Veiga, A.B., Valeriani, M., Takizawa, T., Messlinger, K., Shapiro, R.E., Goadsby, P.J., Ashina, M., Tassorelli, C., Diener, H.C., Terwindt, G.M., Pozo-Rosich, P., 2023. Headache attributed to SARS-CoV-2 infection, vaccination and the impact on primary headache disorders of the COVID-19 pandemic: a comprehensive review. Cephalalgia. https://doi.org/10.1177/03331024221131337.

Carrau, L., Frere, J.J., Golynker, I., Fajardo, A., Rivera, C.F., Horiuchi, S., Roonprapunt, T., Minkoff, J.M., Blanco-Melo, D., TenOever, B., 2023. Delayed engagement of host defenses enables SARS-CoV-2 viremia and productive infection of distal organs in the hamster model of COVID-19. Sci. Signal. 16. https://doi.org/10.1126/scisignal.adg5470.

Casagrande, M., Fitzek, A., Püschel, K., Aleshcheva, G., Schultheiss, H.P., Berneking, L., Spitzer, M.S., Schultheiss, M., 2020. Detection of SARS-CoV-2 in human retinal biopsies of deceased COVID-19 patients. Ocul. Immunol. Inflamm. 28. https://doi.org/10.1080/09273948.2020.1770301.

Casagrande, M., Fitzek, A., Spitzer, M., Püschel, K., Glatzel, M., Krasemann, S., Aepfelbacher, M., Nörz, D., Lütgehetmann, M., Pfefferle, S., Schultheiss, M., 2022. Detection of SARS-CoV-2 genomic and subgenomic RNA in retina and optic nerve of patients with COVID-19. Br. J. Ophthalmol. 106. https://doi.org/10.1136/bjophthalmol-2020-318618.

Casagrande, M., Fitzek, A., Spitzer, M.S., Püschel, K., Glatzel, M., Krasemann, S., Nörz, D., Lütgehetmann, M., Pfefferle, S., Schultheiss, M., 2021. Presence of SARS-CoV-2 RNA in the cornea of viremic patients with COVID-19. JAMA Ophthalmol 139. https://doi.org/10.1001/jamaophthalmol.2020.6339.

Cascella, M., Del Gaudio, A., Vittori, A., Bimonte, S., Del Prete, P., Forte, C.A., Cuomo, A., De Blasio, E., 2021. Covid-pain: acute and late-onset painful clinical manifestations in covid-19 – molecular mechanisms and research perspectives. J. Pain Res. 14. https://doi.org/10.2147/JPR.S313978.

Casel, M.A.B., Rollon, R.G., Choi, Y.K., 2021. Experimental animal models of coronavirus infections: strengths and limitations. Immune Netw 21. https://doi.org/10.4110/in.2021.21.e12.

Cervia-Hasler, C., Brüningk, S.C., Hoch, T., Fan, B., Muzio, G., Thompson, R.C., Ceglarek, L., Meledin, R., Westermann, P., Emmenegger, M., Taeschler, P., Zurbuchen, Y., Pons, M., Menges, D., Ballouz, T., Cervia-Hasler, S., Adamo, S., Merad, M., Charney, A.W., Puhan, M., Brodin, P., Nilsson, J., Aguzzi, A., Raeber, M. E., Messner, C.B., Beckmann, N.D., Borgwardt, K., Boyman, O., 2024. Persistent complement dysregulation with signs of thromboinflammation in active Long Covid. Science 383. https://doi.org/10.1126/science.adg7942, 1979.

Chen, Jingguo, Ren, X., Yan, H., Zhao, B., Chen, Jingyan, Zhu, K., Lyu, H., Li, Z., Doty, R. L., 2022. Comparison of Chinese and American subjects on the self-administered waterless empirical taste test. J. Sensory Stud. 37. https://doi.org/10.1111/joss.12745.

Chen, Z., Yuan, Y., Hu, Q., Zhu, A., Chen, F., Li, S., Guan, X., Lv, C., Tang, T., He, Y., Cheng, J., Zheng, J., Hu, X., Zhao, Jingxian, Zhao, Jincun, Sun, J., 2024. SARS-CoV-2 immunity in animal models. Cell. Mol. Immunol. https://doi.org/10.1038/s41423-023-01122-w.

Chrysouli, K., Savva, I.P., Karamagkiolas, S., 2024. The first cases of sudden sensorineural hearing loss post coronavirus disease in children. J Audiol Otol 28. https://doi.org/10.7874/JAO.2023.00227.

Coelho, D.H., Reiter, E.R., Budd, S.G., Shin, Y., Kons, Z.A., Costanzo, R.M., 2022. Predictors of smell recovery in a nationwide prospective cohort of patients with COVID-19. American J. Otolaryngol. Head and Neck Med. Surgery 43. https://doi.org/10.1016/j.amjoto.2021.103239.

Cohen, N.A., 2017. The genetics of the bitter taste receptor T2R38 in upper airway innate immunity and implications for chronic rhinosinusitis. Laryngoscope 127. https://doi.org/10.1002/lary.26198.
Costa-lópez, B., Ferrer-cascales, R., Ruiz-robledillo, N., Albaladejo-blázquez, N., Baryła-matejczuk, M., 2021. Relationship between sensory processing and quality of life: a systematic review. J. Clin. Med. https://doi.org/10.3390/jcm10173961.
Cutler, D.M., 2022. The costs of long COVID. JAMA Health Forum. https://doi.org/10.1001/jamahealthforum.2022.1809.
Davis, H.E., Assaf, G.S., McCorkell, L., Wei, H., Low, R.J., Re'em, Y., Redfield, S., Austin, J.P., Akrami, A., 2021. Characterizing long COVID in an international cohort: 7 months of symptoms and their impact. EClinicalMedicine 38. https://doi.org/10.1016/j.eclinm.2021.101019.
Davis, H.E., McCorkell, L., Vogel, J.M., Topol, E.J., 2023. Long COVID: major findings, mechanisms and recommendations. Nat. Rev. Microbiol. https://doi.org/10.1038/s41579-022-00846-2.
de Melo, G.D., Lazarini, F., Levallois, S., Hautefort, C., Michel, V., Larrous, F., Verillaud, B., Aparicio, C., Wagner, S., Gheusi, G., Kergoat, L., Kornobis, E., Donati, F., Cokelaer, T., Hervochon, R., Madec, Y., Roze, E., Salmon, D., Bourhy, H., Lecuit, M., Lledo, P.-M., 2021. COVID-19–related anosmia is associated with viral persistence and inflammation in human olfactory epithelium and brain infection in hamsters. Sci. Transl. Med. https://doi.org/10.1126/scitranslmed.abf8396.
Dell'Era, V., Farri, F., Garzaro, G., Gatto, M., Aluffi Valletti, P., Garzaro, M., 2020. Smell and taste disorders during COVID-19 outbreak: cross-sectional study on 355 patients. In: Head and Neck. https://doi.org/10.1002/hed.26288.
Di Stadio, A., Gallina, S., Cocuzza, S., De Luca, P., Ingrassia, A., Oliva, S., Sireci, F., Camaioni, A., Ferreli, F., Mercante, G., Gaino, F., Pace, G.M., La Mantia, I., Brenner, M.J., 2023. Treatment of COVID-19 olfactory dysfunction with olfactory training, palmitoylethanolamide with luteolin, or combined therapy: a blinded controlled multicenter randomized trial. Eur. Arch. Otorhinolaryngol. 280. https://doi.org/10.1007/s00405-023-08085-8.
Doty, R.L., Shaman, P., Applebaum, S.L., Giberson, R., Siksorski, L., Rosenberg, L., 1984. Smell identification ability: changes with age. Science 226. https://doi.org/10.1126/science.6505700, 1979.
Douaud, G., Lee, S., Alfaro-Almagro, F., Arthofer, C., Wang, C., McCarthy, P., Lange, F., Andersson, J.L.R., Griffanti, L., Duff, E., Jbabdi, S., Taschler, B., Keating, P., Winkler, A.M., Collins, R., Matthews, P.M., Allen, N., Miller, K.L., Nichols, T.E., Smith, S.M., 2022. SARS-CoV-2 is associated with changes in brain structure in UK Biobank. Nature 604. https://doi.org/10.1038/s41586-022-04569-5.
Doyle, M.E., Appleton, A., Liu, Q.R., Yao, Q., Mazucanti, C.H., Egan, J.M., 2021. Human type II taste cells express angiotensin-converting enzyme 2 and are infected by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Am. J. Pathol. 191. https://doi.org/10.1016/j.ajpath.2021.05.010.
Du, M., Ma, Y., Deng, J., Liu, M., Liu, J., 2022. Comparison of long COVID-19 caused by different SARS-CoV-2 strains: a systematic review and meta-analysis. Int. J. Environ. Res. Publ. Health. https://doi.org/10.3390/ijerph192316010.
Ehrenfeld, M., Tincani, A., Andreoli, L., Cattalini, M., Greenbaum, A., Kanduc, D., Alijotas-Reig, J., Zinserling, V., Semenova, N., Amital, H., Shoenfeld, Y., 2020. Covid-19 and autoimmunity. Autoimmun. Rev. https://doi.org/10.1016/j.autrev.2020.102597.
Eitner, L., Maier, C., Brinkmann, F., Schlegtendal, A., Knoke, L., Enax-Krumova, E., Lücke, T., 2022. Somatosensory abnormalities after infection with SARS-CoV-2 – a prospective case-control study in children and adolescents. Front Pediatr 10. https://doi.org/10.3389/fped.2022.977827.
Elibol, E., 2021. Otolaryngological symptoms in COVID-19. Eur. Arch. Otorhinolaryngol. 278. https://doi.org/10.1007/s00405-020-06319-7.
Elliott, T.E., Renier, C.M., Palcher, J.A., 2003. Chronic pain, depression, and quality of life: correlations and predictive value of the SF-36. Pain Med. 4. https://doi.org/10.1111/j.1526-4637.2003.03040.x.
Emekci, T., Dündar, M.A., Kirazlı, G., Men Kılınç, F., Cengiz, D.U., Karababa, E., İnceoğlu, F., Arbağ, H., 2022. Evaluation of the efferent auditory system in COVID-19 adult patients. Acta Otolaryngol. 142. https://doi.org/10.1080/00016489.2022.2093967.
Erickson, M.A., Rhea, E.M., Knopp, R.C., Banks, W.A., 2021. Interactions of sars-cov-2 with the blood–brain barrier. Int. J. Mol. Sci. https://doi.org/10.3390/ijms22052681.
Eriksen, A.Z., Møller, R., Makovoz, B., Uhl, S.A., tenOever, B.R., Blenkinsop, T.A., 2021. SARS-CoV-2 infects human adult donor eyes and hESC-derived ocular epithelium. Cell Stem Cell 28. https://doi.org/10.1016/j.stem.2021.04.028.
Fernández-De-las-Peñas, C., de-La-Llave-Rincón, A.I., Ortega-Santiago, R., Ambite-Quesada, S., Gómez-Mayordomo, V., Cuadrado, M.L., Arias-Navalón, J.A., Hernández-Barrera, V., Martín-Guerrero, J.D., Pellicer-Valero, O.J., Arendt-Nielsen, L., 2022. Prevalence and risk factors of musculoskeletal pain symptoms as long-term post-COVID sequelae in hospitalized COVID-19 survivors: a multicenter study. Pain 163. https://doi.org/10.1097/j.pain.0000000000002564.
Fernández-de-las-Peñas, C., Fuensalida-Novo, S., Ortega-Santiago, R., Valera-Calero, J. A., Cescon, C., Derboni, M., Giuffrida, V., Barbero, M., 2022. Pain extent is not associated with sensory-associated symptoms, cognitive or psychological variables in COVID-19 survivors suffering from post-COVID pain. J. Clin. Med. 11. https://doi.org/10.3390/jcm11154633.
Fernández-de-las-Peñas, C., Gómez-Mayordomo, V., Cuadrado, M.L., Palacios-Ceña, D., Florencio, L.L., Guerrero, A.L., García-Azorín, D., Hernández-Barrera, V., Arendt-Nielsen, L., 2021. The presence of headache at onset in SARS-CoV-2 infection is associated with long-term post-COVID headache and fatigue: a case-control study. Cephalalgia 41. https://doi.org/10.1177/03331024211020404.
Fernández-De-Las-Peñas, C., Navarro-Santana, M., Plaza-Manzano, G., Palacios-Ceña, D., Arendt-Nielsen, L., 2022. Time course prevalence of post-COVID pain symptoms of musculoskeletal origin in patients who had survived severe acute respiratory syndrome coronavirus 2 infection: a systematic review and meta-analysis. Pain 163. https://doi.org/10.1097/j.pain.0000000000002496.
Fernández-de-las-Peñas, C., Nijs, J., Giordano, R., Arendt-Nielsen, L., 2023. Precision management of post-COVID pain: an evidence and clinical-based approach. Eur. J. Pain 27. https://doi.org/10.1002/ejp.2095.
Finlay, J.B., Brann, D.H., Hachem, R.A., Jang, D.W., Oliva, A.D., Ko, T., Gupta, R., Wellford, S.A., Moseman, E.A., Jang, S.S., Yan, C.H., Matsunami, H., Tsukahara, T., Datta, S.R., Goldstein, B.J., 2022. Persistent post-COVID-19 smell loss is associated with immune cell infiltration and altered gene expression in olfactory epithelium. Sci. Transl. Med. 14. https://doi.org/10.1126/scitranslmed.add0484.
Frere, J.J., Serafini, R.A., Pryce, K.D., Zazhytska, M., Oishi, K., Golynker, I., Panis, M., Zimering, J., Horiuchi, S., Hoagland, D.A., Møller, R., Ruiz, A., Kodra, A., Overdevest, J.B., Canoll, P.D., Borczuk, A.C., Chandar, V., Bram, Y., Schwartz, R., Lomvardas, S., Zachariou, V., TenOever, B.R., 2022. SARS-CoV-2 infection in hamsters and humans results in lasting and unique systemic perturbations post recovery. Sci. Transl. 14, eabq3059. https://doi.org/10.1126/scitranslmed.abq3059.
Gao, Z., Xu, Y., Sun, C., Wang, X., Guo, Y., Qiu, S., Ma, K., 2021. A systematic review of asymptomatic infections with COVID-19. J. Microbiol. Immunol. Infect. https://doi.org/10.1016/j.jmii.2020.05.001.
Garg, R.K., Paliwal, V.K., Gupta, A., 2021. Spinal cord involvement in COVID-19: a review. J. Spinal Cord Med. https://doi.org/10.1080/10790268.2021.1888022.
Gong, Q., Fu, M., Wang, J., Zhao, S., Wang, H., 2024. Potential immune-inflammatory proteome biomarkers for guiding the treatment of patients with primary acute angle-closure glaucoma caused by COVID-19. J. Proteome Res. 23, 2587–2597. https://doi.org/10.1021/acs.jproteome.4c00325.
Gottlieb, M., Wang, R.C., Yu, H., Spatz, E.S., Montoy, J.C.C., Rodriguez, R.M., Chang, A. M., Elmore, J.G., Hannikainen, P.A., Hill, M., Huebinger, R.M., Idris, A.H., Lin, Z., Koo, K., McDonald, S., O'Laughlin, K.N., Plumb, I.D., Santangelo, M., Saydah, S., Willis, M., Wisk, L.E., Venkatesh, A., Stephens, K.A., Weinstein, R.A., 2023. Severe fatigue and persistent symptoms at 3 Months following severe acute respiratory syndrome coronavirus 2 infections during the pre-delta, delta, and omicron time periods: a multicenter prospective cohort study. Clin. Infect. Dis. 76. https://doi.org/10.1093/cid/ciad045.
Gregus, A.M., Levine, I.S., Eddinger, K.A., Yaksh, T.L., Buczynski, M.W., 2021. Sex differences in neuroimmune and glial mechanisms of pain. Pain. https://doi.org/10.1097/j.pain.0000000000002215.
Guarnieri, J.W., Dybas, J.M., Fazelinia, H., Kim, M.S., Frere, J., Zhang, Y., Albrecht, Y.S., Murdock, D.G., Angelin, A., Singh, L.N., Weiss, S.L., Best, S.M., Lott, M.T., Zhang, S., Cope, H., Zaksas, V., Saravia-Butler, A., Meydan, C., Foox, J., Mozsary, C., Bram, Y., Kidane, Y., Priebe, W., Emmett, M.R., Meller, R., Demharter, S., Stentoft-Hansen, V., Salvatore, M., Galeano, D., Enguita, F.J., Grabham, P., Trovao, N.S., Singh, U., Haltom, J., Heise, M.T., Moorman, N.J., Baxter, V.K., Madden, E.A., Taft-Benz, S.A., Anderson, E.J., Sanders, W.A., Dickmander, R.J., Baylin, S.B., Wurtele, E.S., Moraes-Vieira, P.M., Taylor, D., Mason, C.E., Schisler, J.C., Schwartz, R.E., Beheshti, A., Wallace, D.C., 2023. Core mitochondrial genes are down-regulated during SARS-CoV-2 infection of rodent and human hosts. Sci. Transl. Med. 15. https://doi.org/10.1126/scitranslmed.abq1533.
Gupta, S., Lee, J.J., Perrin, A., Khan, A., Smith, H.J., Farrell, N., Kallogjeri, D., Piccirillo, J.F., 2022. Efficacy and safety of saline nasal irrigation plus theophylline for treatment of COVID-19-related olfactory dysfunction: the SCENT2 phase 2 randomized clinical trial. JAMA Otolaryngol. Head Neck Surg. 148. https://doi.org/10.1001/jamaoto.2022.1573.
Hamed, S.A., Ahmed, M.A.A.R., 2023. The effectiveness of cerebrolysin, a multi-modal neurotrophic factor, for treatment of post-covid-19 persistent olfactory, gustatory and trigeminal chemosensory dysfunctions: a randomized clinical trial. Expet Rev. Clin. Pharmacol. 16. https://doi.org/10.1080/17512433.2023.2282715.
Hastie, C.E., Lowe, D.J., McAuley, A., Mills, N.L., Winter, A.J., Black, C., Scott, J.T., O'Donnell, C.A., Blane, D.N., Browne, S., Ibbotson, T.R., Pell, J.P., 2023. True prevalence of long-COVID in a nationwide, population cohort study. Nat. Commun. 14. https://doi.org/10.1038/s41467-023-43661-w.
Hentsch, L., Stancu, P., Allali, G., Lövblad, K.O., Lobrinus, J.A., Cocetta, S., Pautex, S., Uginet, M., Serratrice, J., Coen, M., 2022. Decrease in pain perception during acute SARS-CoV-2 infection: a case series. Pain 163, 1019–1022. https://doi.org/10.1097/j.pain.0000000000002512.
Hoagland, D.A., Møller, R., Uhl, S.A., Oishi, K., Frere, J., Golynker, I., Horiuchi, S., Panis, M., Blanco-Melo, D., Sachs, D., Arkun, K., Lim, J.K., tenOever, B.R., 2021. Leveraging the antiviral type I interferon system as a first line of defense against SARS-CoV-2 pathogenicity. Immunity 54. https://doi.org/10.1016/j.immuni.2021.01.017.
Hopkins, C., Surda, P., Vaira, L.A., Lechien, J.R., Safarian, M., Saussez, S., Kumar, N., 2021. Six month follow-up of self-reported loss of smell during the covid-19 pandemic. Rhinology 59. https://doi.org/10.4193/Rhin20.544.
Hopkins, C., Surda, P., Whitehead, E., Kumar, B.N., 2020. Early recovery following new onset anosmia during the COVID-19 pandemic - an observational cohort study. J. Otolaryngol. Head and Neck Surgery 49. https://doi.org/10.1186/s40463-020-00423-8.
Huang, N., Pérez, P., Kato, T., Mikami, Y., Okuda, K., Gilmore, R.C., Conde, C.D., Gasmi, B., Stein, S., Beach, M., Pelayo, E., Maldonado, J.O., Lafont, B.A., Jang, S.I., Nasir, N., Padilla, R.J., Murrah, V.A., Maile, R., Lovell, W., Wallet, S.M., Bowman, N. M., Meinig, S.L., Wolfgang, M.C., Choudhury, S.N., Novotny, M., Aevermann, B.D., Scheuermann, R.H., Cannon, G., Anderson, C.W., Lee, R.E., Marchesan, J.T., Bush, M., Freire, M., Kimple, A.J., Herr, D.L., Rabin, J., Grazioli, A., Das, S., French, B.N., Pranzatelli, T., Chiorini, J.A., Kleiner, D.E., Pittaluga, S., Hewitt, S.M., Burbelo, P.D., Chertow, D., De Melo, M.S., Dikoglu, E., Desar, S., Ylaya, K., Chung, J. Y., Smith, G., Chertow, D.S., Vannella, K.M., Ramos-Benitez, M., Ramelli, S.C.,

Samet, S.J., Babyak, A.L., Valenica, L.P., Richert, M.E., Hays, N., Purcell, M., Singireddy, S., Wu, J., Chung, J., Borth, A., Bowers, K., Weichold, A., Tran, D., Madathil, R.J., Krause, E.M., Herr, D.L., Rabin, J., Herrold, J.A., Tabatabai, A., Hochberg, E., Cornachione, C., Levine, A.R., McCurdy, M.T., Saharia, K.K., Chancer, Z., Mazzeffi, M.A., Richards, J.E., Eagan, J.W., Sangwan, Y., Sequeira, I., A. Teichmann, S., Frank, K., Lee, J., Boucher, R.C., Teichmann, S.A., Warner, B.M., Byrd, K.M., 2021. SARS-CoV-2 infection of the oral cavity and saliva. Nat. Med. 27. https://doi.org/10.1038/s41591-021-01296-8.

Invernizzi, A., Torre, A., Parrulli, S., Zicarelli, F., Schiuma, M., Colombo, V., Giacomelli, A., Cigada, M., Milazzo, L., Ridolfo, A., Faggion, I., Cordier, L., Oldani, M., Marini, S., Villa, P., Rizzardini, G., Galli, M., Antinori, S., Staurenghi, G., Meroni, L., 2020. Retinal findings in patients with COVID-19: results from the SERPICO-19 study. EClinicalMedicine 27. https://doi.org/10.1016/j.eclinm.2020.100550.

Jafari, Z., Kolb, B.E., Mohajerani, M.H., 2022. Hearing loss, tinnitus, and dizziness in COVID-19: a systematic review and meta-analysis. Can. J. Neurol. Sci. 49. https://doi.org/10.1017/cjn.2021.63.

Jeican, I.I., Aluaș, M., Lazăr, M., Barbu-Tudoran, L., Gheban, D., Inișca, P., Albu, C., Tripon, S., Albu, S., Siserman, C., Vica, M.L., Muntean, M., Opincariu, I., Junie, L.M., 2021. Evidence of sars-cov-2 virus in the middle ear of deceased covid-19 patients. Diagnostics 11. https://doi.org/10.3390/diagnostics11091535.

Jeong, M., Ocwieja, K.E., Han, D., Wackym, P.A., Zhang, Y., Brown, A., Moncada, C., Vambutas, A., Kanne, T., Crain, R., Siegel, N., Leger, V., Santos, F., Welling, D.B., Gehrke, L., Stankovic, K.M., 2021. Direct SARS-CoV-2 infection of the human inner ear may underlie COVID-19-associated audiovestibular dysfunction. Commun. Med. 1. https://doi.org/10.1038/s43856-021-00044-w.

Jin, P., Cui, F., Zhang, L., 2024. Altered metabolites in the periaqueductal gray of COVID-19 patients experiencing headaches: a longitudinal MRS study. Front. Neurol. 14. https://doi.org/10.3389/fneur.2023.1323290.

Johansson, J., Möller, M., Markovic, G., Borg, K., 2024. Vision impairment is common in non-hospitalised patients with post-COVID-19 syndrome. Clin. Exp. Optom. 107, 324–331. https://doi.org/10.1080/08164622.2023.2213826.

Joyce, J.D., Moore, G.A., Goswami, P., Harrell, T.L., Taylor, T.M., Hawks, S.A., Green, J. C., Jia, M., Yallayi, N., Leslie, E.H., Duggal, N.K., Thompson, C.K., Bertke, A.S., 2023. SARS-CoV-2 infects peripheral and central neurons before viremia. Facilitated by Neuropilin-I. bioRxiv.

Kandemirli, S.G., Altundag, A., Yildirim, D., Tekcan Sanli, D.E., Saatci, O., 2021. Olfactory bulb MRI and paranasal sinus CT findings in persistent COVID-19 anosmia. Acad. Radiol. 28. https://doi.org/10.1016/j.acra.2020.10.006.

Käufer, C., Schreiber, C.S., Hartke, A.S., Denden, I., Stanelle-Bertram, S., Beck, S., Kouassi, N.M., Beythien, G., Becker, K., Schreiner, T., Schaumburg, B., Beineke, A., Baumgärtner, W., Gabriel, G., Richter, F., 2022. Microgliosis and neuronal proteinopathy in brain persist beyond viral clearance in SARS-CoV-2 hamster model. EBioMedicine 79. https://doi.org/10.1016/j.ebiom.2022.103999.

Kerzhner, O., Berla, E., Har-Even, M., Ratmansky, M., Goor-Aryeh, I., 2024. Consistency of inconsistency in long-COVID-19 pain symptoms persistency: a systematic review and meta-analysis. Pain Pract. https://doi.org/10.1111/papr.13277.

Khan, A.M., Lee, J., Rammaha, T., Gupta, S., Smith, H., Kannampallil, T., Farrell, N., Kallogjeri, D., Piccirillo, J.F., 2022. Natural trajectory of recovery of COVID-19 associated olfactory loss. American J. Otolaryngol. Head and Neck Med. Surgery 43. https://doi.org/10.1016/j.amjoto.2022.103572.

Khan, M., Clijsters, M., Choi, S., Backaert, W., Claerhout, M., Couvreur, F., Van Breda, L., Bourgeois, F., Speleman, K., Klein, S., Van Laethem, J., Verstappen, G., Dereli, A.S., Yoo, S.J., Zhou, H., Dan Do, T.N., Jochmans, D., Laenen, L., Debaveye, Y., De Munter, P., Gunst, J., Jorissen, M., Lagrou, K., Meersseman, P., Neyts, J., Thal, D.R., Topsakal, V., Vandenbriele, C., Wauters, J., Mombaerts, P., Van Gerven, L., 2022. Anatomical barriers against SARS-CoV-2 neuroinvasion at vulnerable interfaces visualized in deceased COVID-19 patients. Neuron 110. https://doi.org/10.1016/j.neuron.2022.11.007.

Khani, E., Khiali, S., Beheshtirouy, S., Entezari-Maleki, T., 2021. Potential pharmacologic treatments for COVID-19 smell and taste loss: a comprehensive review. Eur. J. Pharmacol. https://doi.org/10.1016/j.ejphar.2021.174582.

Khoja, O., Passadouro, B.S., Mulvey, M., Delis, I., Astill, S., Tan, A.L., Sivan, M., 2022. Clinical characteristics and mechanisms of musculoskeletal pain in long COVID. J. Pain Res. https://doi.org/10.2147/JPR.S365026.

Kim, G.U., Kim, M.J., Ra, S.H., Lee, J., Bae, S., Jung, J., Kim, S.H., 2020. Clinical characteristics of asymptomatic and symptomatic patients with mild COVID-19. Clin. Microbiol. Infection 26. https://doi.org/10.1016/j.cmi.2020.04.040.

Kishimoto-Urata, M., Urata, S., Kagoya, R., Imamura, F., Nagayama, S., Reyna, R.A., Maruyama, J., Yamasoba, T., Kondo, K., Hasegawa-Ishii, S., Paessler, S., 2022. Prolonged and extended impacts of SARS-CoV-2 on the olfactory neurocircuit. Sci. Rep. 12. https://doi.org/10.1038/s41598-022-09731-7.

Kolkedi, Z., Csutak, A., Szalai, E., 2022. Corneal cellular and neuroinflammatory changes after SARS-CoV-2 infection. Cornea 41. https://doi.org/10.1097/ICO.0000000000003018.

Kurabi, A., Pak, K., DeConde, A.S., Ryan, A.F., Yan, C.H., 2022. Immunohistochemical and qPCR detection of SARS-CoV-2 in the human middle ear versus the nasal cavity: case series. Head Neck Pathol 16. https://doi.org/10.1007/s12105-021-01378-6.

Lechien, J.R., Chiesa-Estomba, C.M., Beckers, E., Mustin, V., Ducarme, M., Journe, F., Marchant, A., Jouffe, L., Barillari, M.R., Cammaroto, G., Circiu, M.P., Hans, S., Saussez, S., 2021. Prevalence and 6-month recovery of olfactory dysfunction: a multicentre study of 1363 COVID-19 patients. J. Intern. Med. 290. https://doi.org/10.1111/joim.13209.

Liu, N., Yang, D., Zhang, T., Sun, J., Fu, J., Li, H., 2022. Systematic review and meta-analysis of olfactory and gustatory dysfunction in COVID-19. Int. J. Infect. Dis. https://doi.org/10.1016/j.ijid.2022.02.004.

López, J.T., García-Azorín, D., Planchuelo-Gómez, Á., García-Iglesias, C., Dueñas-Gutiérrez, C., Guerrero, Á.L., 2020. Phenotypic characterization of acute headache attributed to SARS-CoV-2: an ICHD-3 validation study on 106 hospitalized patients. Cephalalgia 40. https://doi.org/10.1177/0333102420965146.

Ma, Q., Liu, J., Liu, Q., Kang, L., Liu, R., Jing, W., Wu, Y., Liu, M., 2021. Global percentage of asymptomatic SARS-CoV-2 infections among the tested population and individuals with confirmed COVID-19 diagnosis A systematic review and meta-analysis. JAMA Netw. Open 4. https://doi.org/10.1001/jamanetworkopen.2021.37257.

Maharaj, S., Bello Alvarez, M., Mungul, S., Hari, K., 2020. Otologic dysfunction in patients with COVID-19: a systematic review. Laryngoscope Investig. Otolaryngol. https://doi.org/10.1002/lio2.498.

Makaronidis, J., Firman, C., Magee, C.G., Mok, J., Balogun, N., Lechner, M., Carnemolla, A., Batterham, R.L., 2021. Distorted chemosensory perception and female sex associate with persistent smell and/or taste loss in people with SARS-CoV-2 antibodies: a community based cohort study investigating clinical course and resolution of acute smell and/or taste loss in people with and without SARS-CoV-2 antibodies in London, UK. BMC Infect. Dis. 21. https://doi.org/10.1186/s12879-021-05927-w.

Mali, S.S., Silva, R., Gong, Z., Cronce, M., Vo, U., Vuong, C., Moayedi, Y., Cox, J.S., Bautista, D.M., 2024. SARS-CoV-2 Papain-like Protease Activates Nociceptors to Drive Sneeze and Pain. bioRxiv.

Malik, P., Patel, K., Pinto, C., Jaiswal, R., Tirupathi, R., Pillai, S., Patel, U., 2022. Post-acute COVID-19 syndrome (PCS) and health-related quality of life (HRQoL)—a systematic review and meta-analysis. J. Med. Virol. 94. https://doi.org/10.1002/jmv.27309.

Mat, Q., Noël, A., Loiselet, L., Tainmont, S., Chiesa-Estomba, C.M., Lechien, J.R., Duterme, J.P., 2023. Vestibular neuritis as clinical presentation of COVID-19. Ear Nose Throat J. 102. https://doi.org/10.1177/0145561321995021.

McFarland, A.J., Yousuf, M.S., Shiers, S., Price, T.J., 2021. Neurobiology of SARS-CoV-2 interactions with the peripheral nervous system: implications for COVID-19 and pain. Pain Rep. https://doi.org/10.1097/PR9.0000000000000885.

Meinhardt, J., Radke, J., Dittmayer, C., Franz, J., Thomas, C., Mothes, R., Laue, M., Schneider, J., Brünink, S., Greuel, S., Lehmann, M., Hassan, O., Aschman, T., Schumann, E., Chua, R.L., Conrad, C., Eils, R., Stenzel, W., Windgassen, M., Rößler, L., Goebel, H.H., Gelderblom, H.R., Martin, H., Nitsche, A., Schulz-Schaeffer, W.J., Hakroush, S., Winkler, M.S., Tampe, B., Scheibe, F., Körtvélyessy, P., Reinhold, D., Siegmund, B., Kühl, A.A., Elezkurtaj, S., Horst, D., Oesterhelweg, L., Tsokos, M., Ingold-Heppner, B., Stadelmann, C., Drosten, C., Corman, V.M., Radbruch, H., Heppner, F.L., 2021. Olfactory transmucosal SARS-CoV-2 invasion as a port of central nervous system entry in individuals with COVID-19. Nat. Neurosci. 24. https://doi.org/10.1038/s41593-020-00758-5.

Mendes Paranhos, A.C., Nazareth Dias, Á.R., Machado Da Silva, L.C., Vieira Hennemann Koury, G., De Jesus Sousa, E., Cerasi, A.J., Souza, G.S., Simões Quaresma, J.A., Magno Falcão, L.F., 2022. Sociodemographic characteristics and comorbidities of patients with long COVID and persistent olfactory dysfunction. JAMA Netw. Open 5. https://doi.org/10.1001/jamanetworkopen.2022.30637.

Menuchin-Lasowski, Y., Schreiber, A., Lecanda, A., Mecate-Zambrano, A., Brunotte, L., Psathaki, O.E., Ludwig, S., Rauen, T., Schöler, H.R., 2022. SARS-CoV-2 infects and replicates in photoreceptor and retinal ganglion cells of human retinal organoids. Stem Cell Rep. 17. https://doi.org/10.1016/j.stemcr.2022.02.015.

Mogil, J.S., 2020. Qualitative sex differences in pain processing: emerging evidence of a biased literature. Nat. Rev. Neurosci. https://doi.org/10.1038/s41583-020-0310-6.

Moutal, A., Martin, L.F., Boinon, L., Gomez, K., Ran, D., Zhou, Y., Stratton, H.J., Cai, S., Luo, S., Gonzalez, K.B., Perez-Miller, S., Patwardhan, A., Ibrahim, M.M., Khanna, R., 2021. SARS-CoV-2 spike protein co-opts VEGF-A/neuropilin-1 receptor signaling to induce analgesia. Pain. https://doi.org/10.1097/j.pain.0000000000002097.

Najafloo, R., Majidi, J., Asghari, A., Aleemardani, M., Kamrava, S.K., Simorgh, S., Seifalian, A., Bagher, Z., Seifalian, A.M., 2021. Mechanism of anosmia caused by symptoms of COVID-19 and emerging treatments. ACS Chem. Neurosci. https://doi.org/10.1021/acschemneuro.1c00477.

Nasiri, N., Sharifi, H., Bazrafshan, A., Noori, A., Karamouzian, M., Sharifi, A., 2021. Ocular manifestations of COVID-19: a systematic review and meta-analysis. J. Ophthalmic Vis. Res. https://doi.org/10.18502/jovr.v16i1.8256.

Nehme, M., Braillard, O., Chappuis, F., Courvoisier, D.S., Guessous, I., 2021. Prevalence of symptoms more than seven months after diagnosis of symptomatic covid-19 in an outpatient setting. Ann. Intern. Med. 174. https://doi.org/10.7326/M21-0878.

Nguyen, N.N., Hoang, V.T., Dao, T.L., Meddeb, L., Cortaredona, S., Lagier, J.C., Million, M., Raoult, D., Gautret, P., 2022. Long-term persistence of olfactory and gustatory disorders in COVID-19 patients. Front. Med. 9. https://doi.org/10.3389/fmed.2022.794550.

Nikolopoulou, G.B., Maltezou, H.C., 2022. COVID-19 in Children: where do we Stand? Arch. Med. Res. https://doi.org/10.1016/j.arcmed.2021.07.002.

Okrzeja, J., Sołomacha, S., Alimowski, M., Sowa, P., Dubatówka, M., Łapińska, M., Kiszkiel, Ł., Szczerbiński, Ł., Laskowski, P.P., Czupryna, P., Kubas, B., Garkowski, A., Kamiński, K.A., Moniuszko-Malinowska, A., 2024. Assessment of smell disturbances 6 months after COVID-19 in Polish population. Sci. Rep. 14, 11251. https://doi.org/10.1038/s41598-024-62114-y.

O'Mahoney, L.L., Routen, A., Gillies, C., Ekezie, W., Welford, A., Zhang, A., Karamchandani, U., Simms-Williams, N., Cassambai, S., Ardavani, A., Wilkinson, T. J., Hawthorne, G., Curtis, F., Kingsnorth, A.P., Almaqhawi, A., Ward, T., Ayoubkhani, D., Banerjee, A., Calvert, M., Shafran, R., Stephenson, T., Sterne, J., Ward, H., Evans, R.A., Zaccardi, F., Wright, S., Khunti, K., 2023. The prevalence and long-term health effects of Long Covid among hospitalised and non-hospitalised populations: a systematic review and meta-analysis. EClinicalMedicine 55. https://doi.org/10.1016/j.eclinm.2022.101762.

O'Neill, F., De Stefano, G., Pridgeon, M., Bhargava, D., Marshall, Anne, Marshall, Andrew, Frank, B., 2023. Trigeminal neuropathy presenting secondary to SARS-CoV-2 infection. Pain Rep 8. https://doi.org/10.1097/PR9.0000000000001103.

Ong, K.M.C., Cruz, T.L.G., 2022. Otologic and vestibular symptoms in COVID-19: a scoping review. World J. Otorhinolaryngol. Head Neck Surg. https://doi.org/10.1002/wjo2.57.

Paderno, A., Schreiber, A., Grammatica, A., Raffetti, E., Tomasoni, M., Gualtieri, T., Taboni, S., Zorzi, S., Lombardi, D., Deganello, A., Redaelli De Zinis, L.O., Maroldi, R., Mattavelli, D., 2020. Smell and taste alterations in COVID-19: a cross-sectional analysis of different cohorts. Int Forum Allergy Rhinol. 10. https://doi.org/10.1002/alr.22610.

Pardhan, S., Vaughan, M., Zhang, J., Smith, L., Chichger, H., 2020. Sore eyes as the most significant ocular symptom experienced by people with COVID-19: a comparison between pre-COVID-19 and during COVID-19 states. BMJ Open Ophthalmol. 5. https://doi.org/10.1136/bmjophth-2020-000632.

Peghin, M., Palese, A., Venturini, M., De Martino, M., Gerussi, V., Graziano, E., Bontempo, G., Marrella, F., Tommasini, A., Fabris, M., Curcio, F., Isola, M., Tascini, C., 2021. Post-COVID-19 symptoms 6 months after acute infection among hospitalized and non-hospitalized patients. Clin. Microbiol. Infection 27. https://doi.org/10.1016/j.cmi.2021.05.033.

Pelà, G., Goldoni, M., Solinas, E., Cavalli, C., Tagliaferri, S., Ranzieri, S., Frizzelli, A., Marchi, L., Mori, P.A., Majori, M., Aiello, M., Corradi, M., Chetta, A., 2022. Sex-related differences in long-COVID-19 syndrome. J. Womens Health 31. https://doi.org/10.1089/jwh.2021.0411.

Pellegrini, L., Albecka, A., Mallery, D.L., Kellner, M.J., Paul, D., Carter, A.P., James, L.C., Lancaster, M.A., 2020. SARS-CoV-2 infects the brain choroid plexus and disrupts the blood-CSF barrier in human brain organoids. Cell Stem Cell 27. https://doi.org/10.1016/j.stem.2020.10.001.

Petrocelli, M., Cutrupi, S., Salzano, G., Maglitto, F., Salzano, F.A., Lechien, J.R., Saussez, S., Boscolo-Rizzo, P., De Riu, G., Vaira, L.A., 2021. Six-month smell and taste recovery rates in coronavirus disease 2019 patients: a prospective psychophysical study. J. Laryngol. Otol. 135. https://doi.org/10.1017/S002221512100116X.

Pinzon, R.T., Wijaya, V.O., Jody, A. Al, Nunsio, P.N., Buana, R.B., 2022. Persistent neurological manifestations in long COVID-19 syndrome: a systematic review and meta-analysis. J. Infect Public Health. https://doi.org/10.1016/j.jiph.2022.06.013.

Prayuenyong, P., Kasbekar, A.V., Baguley, D.M., 2020. Clinical implications of chloroquine and hydroxychloroquine ototoxicity for COVID-19 treatment: a mini-review. Front. Public Health. https://doi.org/10.3389/fpubh.2020.00252.

Premi, E., Acampora, R., Salmi, D., Ilie, I.A., Pagnoncelli, N., Germano, F., Gandolfi, G., Sanicas, M., Seed, A., Michael, B.D., Donati, S., Azzolini, C., Lanfranchi, F., 2023. Clinical and diagnostic findings of acute macular neuroretinopathy and paracentral acute middle maculopathy in the COVID-19 era. Ophthalmologica. https://doi.org/10.1159/000533530.

Púa Torrejón, R.C., Ordoño Saiz, M.V., González Alguacil, E., Furones García, M., Cantarín Extremera, V., Ruiz Falcó, M.L., Soto Insuga, V., 2022. Smell and taste dysfunction in pediatric patients with SARS-CoV-2 infection. Pediatr. Neurol. 136. https://doi.org/10.1016/j.pediatrneurol.2022.07.006.

Radke, J., Meinhardt, J., Aschman, T., Chua, R.L., Farztdinov, V., Lukassen, S., Ten, F.W., Friebel, E., Ishaque, N., Franz, J., Huhle, V.H., Mothes, R., Peters, K., Thomas, C., Schneeberger, S., Schumann, E., Kawelke, L., Jünger, J., Horst, V., Streit, S., von Manitius, R., Körtvélyessy, P., Vielhaber, S., Reinhold, D., Hauser, A.E., Osterloh, A., Enghard, P., Ihlow, J., Elezkurtaj, S., Horst, D., Kurth, F., Müller, M.A., Gassen, N.C., Melchert, J., Jechow, K., Timmermann, B., Fernandez-Zapata, C., Böttcher, C., Stenzel, W., Krüger, E., Landthaler, M., Wyler, E., Corman, V., Stadelmann, C., Ralser, M., Eils, R., Heppner, F.L., Mülleder, M., Conrad, C., Radbruch, H., 2024. Proteomic and transcriptomic profiling of brainstem, cerebellum and olfactory tissues in early- and late-phase COVID-19. Nat. Neurosci. 27. https://doi.org/10.1038/s41593-024-01573-y.

Ram-Mohan, N., Kim, D., Rogers, A.J., Blish, C.A., Nadeau, K.C., Blomkalns, A.L., Yang, S., 2022. Association between SARS-CoV-2 RNAemia and postacute sequelae of COVID-19. Open Forum Infect. Dis. 9. https://doi.org/10.1093/ofid/ofab646.

Rashid, R.A., Zgair, A., Al-Ani, R.M., 2021. Effect of nasal corticosteroid in the treatment of anosmia due to COVID-19: a randomised double-blind placebo-controlled study. American J. Otolaryngol. Head and Neck Med. Surgery 42. https://doi.org/10.1016/j.amjoto.2021.103033.

Rass, V., Tymoszuk, P., Sahanic, S., Heim, B., Ausserhofer, D., Lindner, A., Kofler, M., Mahlknecht, P., Boehm, A., Hüfner, K., Pizzini, A., Sonnweber, T., Kurz, K., Pfeifer, B., Kiechl, S., Peball, M., Kindl, P., Putnina, L., Fava, E., Djamshidian, A., Huber, A., Wiedermann, C.J., Sperner-Unterweger, B., Wöll, E., Beer, R., Schiefecker, A.J., Bellmann-Weiler, R., Bachler, H., Tancevski, I., Pfausler, B., Piccoliori, G., Seppi, K., Weiss, G., Löffler-Ragg, J., Helbok, R., 2023. Distinct smell and taste disorder phenotype of post-acute COVID-19 sequelae. Eur. Arch. Otorhinolaryngol. 280. https://doi.org/10.1007/s00405-023-08163-x.

Reyna, R.A., Kishimoto-Urata, M., Urata, S., Makishima, T., Paessler, S., Maruyama, J., 2022. Recovery of anosmia in hamsters infected with SARS-CoV-2 is correlated with repair of the olfactory epithelium. Sci. Rep. 12. https://doi.org/10.1038/s41598-021-04622-9.

Reyna, R.A., Walker, J., Mitchell, B., Shinde, D.P., Plante, J.A., Weaver, S.C., Plante, K.S., 2023. Vaccination against SARS-CoV-2 does not protect against the development of anosmia in a hamster model. Vaccines (Basel) 11. https://doi.org/10.3390/vaccines11101564.

Riccardi, G., Niccolini, G.F., Bellizzi, M.G., Fiore, M., Minni, A., Barbato, C., 2023. Post-COVID-19 anosmia and therapies: stay tuned for new drugs to sniff out. Diseases. https://doi.org/10.3390/diseases11020079.

Ripa, M., Motta, L., Schipa, C., Rizzo, S., Sollazzi, L., Aceto, P., 2022. "Vision loss" and COVID-19 infection: a systematic review and meta-analysis. Vision (Switzerland). https://doi.org/10.3390/vision6040060.

Rogn, Å., Jensen, J.L., Iversen, P.O., Singh, P.B., 2024. Post-COVID-19 patients suffer from chemosensory, trigeminal, and salivary dysfunctions. Sci. Rep. 14. https://doi.org/10.1038/s41598-024-53919-y.

Rombauts, A., Infante, C., de Lagos, M., del, Á.M., Alba, J., Valiente, A., Donado-Mazarrón, C., Carretero-Ledesma, M., Rodríguez-Álvarez, R., Omatos, S., Palacios-Baena, Z.R., Abelenda-Alonso, G., Silva-Sánchez, M. del M., Goikoetxea-Agirre, A.J., Oteo, J.A., Rodríguez-Baño, J., Cordero, E., Gudiol, C., Sánchez-Céspedes, J., Carratalà, J., 2023. Impact of SARS-CoV-2 RNAemia and other risk factors on long-COVID: a prospective observational multicentre cohort study. J. Infect. https://doi.org/10.1016/j.jinf.2022.11.009.

Rutkai, I., Mayer, M.G., Hellmers, L.M., Ning, B., Huang, Z., Monjure, C.J., Coyne, C., Silvestri, R., Golden, N., Hensley, K., Chandler, K., Lehmicke, G., Bix, G.J., Maness, N.J., Russell-Lodrigue, K., Hu, T.Y., Roy, C.J., Blair, R.V., Bohm, R., Doyle-Meyers, L.A., Rappaport, J., Fischer, T., 2022. Neuropathology and virus in brain of SARS-CoV-2 infected non-human primates. Nat. Commun. 13. https://doi.org/10.1038/s41467-022-29440-z.

Sabico, S., Enani, M.A., Sheshah, E., Aljohani, N.J., Aldisi, D.A., Alotaibi, N.H., Alshingetti, N., Alomar, S.Y., Alnaami, A.M., Amer, O.E., Hussain, S.D., Al-Daghri, N. M., 2021. Effects of a 2-week 5000 iu versus 1000 iu vitamin d3 supplementation on recovery of symptoms in patients with mild to moderate covid-19: a randomized clinical trial. Nutrients 13. https://doi.org/10.3390/nu13072170.

Sakaguchi, W., Kubota, N., Shimizu, T., Saruta, J., Fuchida, S., Kawata, A., Yamamoto, Y., Sugimoto, M., Yakeishi, M., Tsukinoki, K., 2020. Existence of SARS-CoV-2 entry molecules in the oral cavity. Int. J. Mol. Sci. 21. https://doi.org/10.3390/ijms21176000.

Sawa, Y., Ibaragi, S., Okui, T., Yamashita, J., Ikebe, T., Harada, H., 2021. Expression of SARS-CoV-2 entry factors in human oral tissue. J. Anat. 238. https://doi.org/10.1111/joa.13391.

Schwabenland, M., Salié, H., Tanevski, J., Killmer, S., Lago, M.S., Schlaak, A.E., Mayer, L., Matschke, J., Püschel, K., Fitzek, A., Ondruschka, B., Mei, H.E., Boettler, T., Neumann-Haefelin, C., Hofmann, M., Breithaupt, A., Genc, N., Stadelmann, C., Saez-Rodriguez, J., Bronsert, P., Knobeloch, K.P., Blank, T., Thimme, R., Glatzel, M., Prinz, M., Bengsch, B., 2021. Deep spatial profiling of human COVID-19 brains reveals neuroinflammation with distinct microanatomical microglia-T-cell interactions. Immunity 54. https://doi.org/10.1016/j.immuni.2021.06.002.

Sen, M., Honavar, S.G., Sharma, N., Sachdev, M.S., 2021. COVID-19 and eye: a review of ophthalmic manifestations of COVID-19. Indian J. Ophthalmol. https://doi.org/10.4103/ijo.IJO_297_21.

Sen, S., Kannan, N.B., Kumar, J., Rajan, R.P., Kumar, K., Baliga, G., Reddy, H., Upadhyay, A., Ramasamy, K., 2022. Retinal manifestations in patients with SARS-CoV-2 infection and pathogenetic implications: a systematic review. Int. Ophthalmol. https://doi.org/10.1007/s10792-021-01996-7.

Serafini, R.A., Frere, J.J., tenOever, B., Zachariou, V., 2023a. SARS-CoV-2 and Influenza A virus induce longitudinal transcriptomic changes in hamster spinal cord tissue. Spine. https://doi.org/10.1097/BRS.0000000000004765.

Serafini, R.A., Frere, J.J., Zimering, J., Giosan, I.M., Pryce, K.D., Golynker, I., Panis, M., Ruiz, A., tenOever, B.R., Zachariou, V., 2023b. SARS-CoV-2 airway infection results in the development of somatosensory abnormalities in a hamster model. Sci. Signal. 16. https://doi.org/10.1126/scisignal.ade4984.

Serrano, G.E., Walker, J.E., Tremblay, C., Piras, I.S., Huentelman, M.J., Belden, C.M., Goldfarb, D., Shprecher, D., Atri, A., Adler, C.H., Shill, H.A., Driver-Dunckley, E., Mehta, S.H., Caselli, R.J., Woodruff, B.K., Haarer, C.F., Ruhlen, T., Torres, M., Nguyen, S., Schmitt, D., Rapscak, S.Z., Bime, C., Peters, J.L., Alevritis, E., Arce, R.A., Glass, M.J., Vargas, D., Sue, L.I., Intorcia, A.J., Nelson, C.M., Oliver, J., Russell, A., Suszczewicz, K.E., Borja, C.I., Cline, M.P., Hemmingsen, S.J., Qiji, S., Hobgood, H. M., Mizgerd, J.P., Sahoo, M.K., Zhang, H., Solis, D., Montine, T.J., Berry, G.J., Reiman, E.M., Röltgen, K., Boyd, S.D., Pinsky, B.A., Zehnder, J.L., Talbot, P., Desforges, M., Deture, M., Dickson, D.W., Beach, T.G., 2022. SARS-CoV-2 brain regional detection, histopathology, gene expression, and immunomodulatory changes in decedents with COVID-19. J. Neuropathol. Exp. Neurol. 81. https://doi.org/10.1093/jnen/nlac056.

Sharetts, R., Moein, S.T., Khan, R., Doty, R.L., 2024. Long-term taste and smell outcomes after COVID-19. JAMA Netw. Open 7, e247818. https://doi.org/10.1001/jamanetworkopen.2024.7818.

Shelton, J.F., Shastri, A.J., Fletez-Brant, K., Auton, A., Chubb, A., Fitch, A., Kung, A., Altman, A., Kill, A., Shastri, A.J., Symons, A., Weldon, C., Coker, D., Shelton, J.F., Tan, J., Pollard, J., McCreight, J., Bielenberg, J., Matthews, J., Lee, J., Tran, L., Lowe, M., Royce, M., Tang, N., Gandhi, P., d'Amore, R., Tennen, R., Dvorak, S., Hadly, S., Aslibekyan, S., Park, S., Morrow, T., Sonmez, T.F., Le, T., Zheng, Y., Aslibekyan, S., Auton, A., 2022. The UGT2A1/UGT2A2 locus is associated with COVID-19-related loss of smell or taste. Nat. Genet. 54. https://doi.org/10.1038/s41588-021-00986-w.

Shimizu, S., Nakayama, M., Nguyen, C.T., Ishigaki, H., Kitagawa, Y., Yasui, F., Yagi, Y., Kusayanagi, T., Kohara, M., Itoh, Y., Tojima, I., Kouzaki, H., Shimizu, T., 2024. SARS-CoV-2 induces inflammation and intracranial infection through the olfactory epithelium-olfactory bulb pathway in non-human primates. J. Neuroimmunol. 387, 578288. https://doi.org/10.1016/j.jneuroim.2024.578288.

Stein, S.R., Ramelli, S.C., Grazioli, A., Chung, J.Y., Singh, M., Yinda, C.K., Winkler, C.W., Sun, J., Dickey, J.M., Ylaya, K., Ko, S.H., Platt, A.P., Burbelo, P.D., Quezado, M., Pittaluga, S., Purcell, M., Munster, V.J., Belinky, F., Ramos-Benitez, M.J., Boritz, E. A., Lach, I.A., Herr, D.L., Rabin, J., Saharia, K.K., Madathil, R.J., Tabatabai, A., Soherwardi, S., McCurdy, M.T., Babyak, A.L., Perez Valencia, L.J., Curran, S.J.,

Richert, M.E., Young, W.J., Young, S.P., Gasmi, B., Sampaio De Melo, M., Desar, S., Tadros, S., Nasir, N., Jin, X., Rajan, S., Dikoglu, E., Ozkaya, N., Smith, G., Emanuel, E.R., Kelsall, B.L., Olivera, J.A., Blawas, M., Star, R.A., Hays, N., Singireddy, S., Wu, J., Raja, K., Curto, R., Chung, J.E., Borth, A.J., Bowers, K.A., Weichold, A.M., Minor, P.A., Moshref, M.A.N., Kelly, E.E., Sajadi, M.M., Scalea, T. M., Tran, D., Dahi, S., Deatrick, K.B., Krause, E.M., Herrold, J.A., Hochberg, E.S., Cornachione, C.R., Levine, A.R., Richards, J.E., Elder, J., Burke, A.P., Mazzeffi, M.A., Christenson, R.H., Chancer, Z.A., Abdulmahdi, M., Sopha, S., Goldberg, T., Sangwan, Y., Sudano, K., Blume, D., Radin, B., Arnouk, M., Eagan, J.W., Palermo, R., Harris, A.D., Pohida, T., Garmendia-Cedillos, M., Dold, G., Saglio, E., Pham, P., Peterson, K.E., Cohen, J.I., de Wit, E., Vannella, K.M., Hewitt, S.M., Kleiner, D.E., Chertow, D.S., 2022. SARS-CoV-2 infection and persistence in the human body and brain at autopsy. Nature 612. https://doi.org/10.1038/s41586-022-05542-y.

Tan, B.K.J., Han, R., Zhao, J.J., Tan, N.K.W., Quah, E.S.H., Tan, C.J.W., Chan, Y.H., Teo, N.W.Y., Charn, T.C., See, A., Xu, S., Chapurin, N., Chandra, R.K., Chowdhury, N., Butowt, R., Von Bartheld, C.S., Kumar, B.N., Hopkins, C., Toh, S.T., 2022. Prognosis and persistence of smell and taste dysfunction in patients with covid-19: meta-analysis with parametric cure modelling of recovery curves. The BMJ. https://doi.org/10.1136/bmj-2021-069503.

Tana, C., Bentivegna, E., Cho, S.-J., Harriott, A.M., García-Azorín, D., Labastida-Ramirez, A., Ornello, R., Raffaelli, B., Beltrán, E.R., Ruscheweyh, R., Martelletti, P., 2022. Long COVID headache. J. Headache Pain 23, 93. https://doi.org/10.1186/s10194-022-01450-8.

Taquet, M., Dercon, Q., Luciano, S., Geddes, J.R., Husain, M., Harrison, P.J., 2021. Incidence, co-occurrence, and evolution of long-COVID features: a 6-month retrospective cohort study of 273,618 survivors of COVID-19. PLoS Med. 18. https://doi.org/10.1371/journal.pmed.1003773.

Torrell, G., Puente, D., Jacques-Aviñó, C., Carrasco-Ribelles, L.A., Violán, C., López-Jiménez, T., Royano, V., Cantón, A.M., Medina-Perucha, L., Rodríguez-Giralt, I., Berenguera, A., 2024. Characterisation, symptom pattern and symptom clusters from a retrospective cohort of Long COVID patients in primary care in Catalonia. BMC Infect. Dis. 24. https://doi.org/10.1186/s12879-023-08954-x.

Trott, M., Driscoll, R., Pardhan, S., 2022. The prevalence of sensory changes in post-COVID syndrome: a systematic review and meta-analysis. Front. Med. https://doi.org/10.3389/fmed.2022.980253.

Tsuda, T., Hanada, Y., Wada, K., Fujiwara, E., Takeda, K., Nishimura, H., 2023. Efficacy of intratympanic glucocorticoid steroid administration therapy as an initial treatment for idiopathic sudden sensorineural hearing loss during the COVID-19 pandemic. Ear Nose Throat J. 102. https://doi.org/10.1177/01455613211032534.

Tsukahara, T., Brann, D.H., Datta, S.R., 2023. Mechanisms of SARS CoV-2 associated anosmia. Physiol. Rev. 103. https://doi.org/10.1152/PHYSREV.00012.2023.

Uncini, A., Foresti, C., Frigeni, B., Storti, B., Servalli, M.C., Gazzina, S., Cosentino, G., Bianchi, F., Del Carro, U., Alfonsi, E., Piccinelli, S.C., De Maria, G., Padovani, A., Filosto, M., Ippoliti, L., 2021. Electrophysiological features of acute inflammatory demyelinating polyneuropathy associated with SARS-CoV-2 infection. Neurophysiol. Clin. 51. https://doi.org/10.1016/j.neucli.2021.02.001.

Uncini, A., Vallat, J.M., Jacobs, B.C., 2020. Guillain-Barré syndrome in SARS-CoV-2 infection: an instant systematic review of the first six months of pandemic. J. Neurol. Neurosurg. Psychiatry. https://doi.org/10.1136/jnnp-2020-324491.

Vahratian, A., Saydah, S., Bertolli, J., Unger, E.R., Gregory, C.O., 2024. Prevalence of post–COVID-19 condition and activity-limiting post–COVID-19 condition among adults. JAMA Netw. Open 7, e2451151. https://doi.org/10.1001/jamanetworkopen.2024.51151.

Vaira, L.A., De Vito, A., Lechien, J.R., Chiesa-Estomba, C.M., Mayo-Yàñez, M., Calvo-Henrìquez, C., Saussez, S., Madeddu, G., Babudieri, S., Boscolo-Rizzo, P., Hopkins, C., De Riu, G., 2022. New onset of smell and taste loss are common findings also in patients with symptomatic COVID-19 after complete vaccination. Laryngoscope 132. https://doi.org/10.1002/lary.29964.

Vaira, L.A., Deiana, G., Fois, A.G., Pirina, P., Madeddu, G., De Vito, A., Babudieri, S., Petrocelli, M., Serra, A., Bussu, F., Ligas, E., Salzano, G., De Riu, G., 2020. Objective evaluation of anosmia and ageusia in COVID-19 patients: single-center experience on 72 cases. Head Neck 42. https://doi.org/10.1002/hed.26204.

Verma, A.K., Zheng, J., Meyerholz, D.K., Perlman, S., 2022. SARS-CoV-2 infection of sustentacular cells disrupts olfactory signaling pathways. JCI Insight 7. https://doi.org/10.1172/jci.insight.160277.

Vihta, K.D., Pouwels, K.B., Peto, T.E.A., Pritchard, E., House, T., Studley, R., Rourke, E., Cook, Duncan, Diamond, I., Crook, Derrick, Clifton, D.A., Matthews, P.C., Stoesser, N., Eyre, D.W., Walker, A.S., Thomas, T., Cook, D., Ayoubkhani, D., Black, R., Felton, A., Crees, M., Jones, J., Lloyd, L., Sutherland, E., Crook, D., Wei, J., Howarth, A., Doherty, G., Kavanagh, J., Chau, K.K., Stephanie, H.B., Ebner, D., Martins Ferreira, L., Christott, T., Marsden, B.D., Dejnirattisai, W., Mongkolsapaya, J., Cameron, S., Tamblin-Hopper, P., Wolna, M., Brown, R., Hoosdally, S., Cornall, R., Jones, Y., Stuart, D.I., Screaton, G., Lythgoe, K., Bonsall, D., Golubchik, T., Fryer, H., Bell, J., Paddon, K., James, T., Newton, J., Robotham, J., Birrell, P., Jordan, H., Sheppard, T., Athey, G., Moody, D., Curry, L., Brereton, P., Jarvis, I., Godsmark, A., Morris, G., Mallick, B., Eeles, P., Hay, J., Lee, J., Sean, W., Evans, T., Bloemberg, L., Allison, K., Pandya, A., Davis, S., Conway, D.I., Macleod, M., Cunningham, C., 2023. Omicron-associated changes in severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) symptoms in the United Kingdom. Clin. Infect. Dis. 76. https://doi.org/10.1093/cid/ciac613.

Voruz, P., Cionca, A., Jacot de Alcàntara, I., Nuber-Champier, A., Allali, G., Benzakour, L., Lalive, P.H., Lövblad, K.O., Braillard, O., Nehme, M., Coen, M., Serratrice, J., Reny, J.L., Pugin, J., Guessous, I., Ptak, R., Landis, B.N., Adler, D., Griffa, A., Van De Ville, D., Assal, F., Péron, J.A., 2023. Brain functional connectivity alterations associated with neuropsychological performance 6–9 months following SARS-CoV-2 infection. Hum. Brain Mapp. 44. https://doi.org/10.1002/hbm.26163.

Weng, L.M., Su, X., Wang, X.Q., 2021. Pain symptoms in patients with coronavirus disease (COVID-19): a literature review. J. Pain Res. https://doi.org/10.2147/JPR.S269206.

Woltsche, J.N., Horwath-Winter, J., Dorn, C., Boldin, I., Steinwender, G., Heidinger, A., Woltsche, N., 2023. Neuropathic corneal pain as debilitating manifestation of LONG-COVID. Ocul. Immunol. Inflamm. https://doi.org/10.1080/09273948.2022.2090963.

Yamamoto, T., Koyama, Y., Ujita, T., Sawada, E., Kishimoto, N., Seo, K., 2023. SARS-CoV-2 recombinant spike protein induces cell apoptosis in rat taste buds. J. Dent. Sci. 18. https://doi.org/10.1016/j.jds.2022.08.016.

Yan, Q., Qiu, D., Liu, X., Guo, X., Hu, Y., 2021. Prevalence of smell or taste dysfunction among children with COVID-19 infection: a systematic review and meta-analysis. Front Pediatr. https://doi.org/10.3389/fped.2021.686600.

Yao, Q., Doyle, M.E., Liu, Q.-R., Appleton, A., O'Connell, J.F., Weng, N., Egan, J.M., 2023. Long-term dysfunction of taste papillae in SARS-CoV-2. NEJM Evidence 2. https://doi.org/10.1056/evidoa2300046.

Yener, A.Ü., 2021. COVID-19 and the eye: ocular manifestations, treatment and protection measures. Ocul. Immunol. Inflamm. https://doi.org/10.1080/09273948.2021.1977829.

Zazhytska, M., Kodra, A., Hoagland, D.A., Frere, J., Fullard, J.F., Shayya, H., McArthur, N.G., Moeller, R., Uhl, S., Omer, A.D., Gottesman, M.E., Firestein, S., Gong, Q., Canoll, P.D., Goldman, J.E., Roussos, P., tenOever, B.R., Jonathan, B.O., Lomvardas, S., 2022. Non-cell-autonomous disruption of nuclear architecture as a potential cause of COVID-19-induced anosmia. Cell 185. https://doi.org/10.1016/j.cell.2022.01.024.