Hypothyroidism is associated with prolonged COVID-19-induced anosmia: a case–control study

Since the onset of COVID-19 pandemic, an exponentially increasing body of data suggests that infection with SARS-CoV-2 affects multiple organs with short-term and long-term outcomes that remain still unknown. Viral effects on thyroid function can, inevitably, lead to multisystem involvement, as thyroid hormones affect the development and function of virtually all human cells, including neural maturation of olfactory receptor neurons. A recent prospective observational study by Lui et al found abnormal thyroid function tests, defined as deranged thyroid-stimulating hormone (TSH) and/or free thyroxine (fT4) and/or free triiodothyronine (fT3) in 25 patients (13.1%), suggesting that SARS-CoV-2 might directly induce viral thyroiditis. Moreover, low fT3 values were independently associated with an increased likelihood for clinical deterioration; the researchers concluded that 'there may be a direct effect of SARS-CoV-2 on thyroid function, potentially leading to exacerbation of pre-existing autoimmune thyroid disease'. However, it was not clear whether thyroid dysfunction was more frequent among patients with particular clinical features, that is, anosmia, or not.

Our multidisciplinary collaborative team has previously investigated the prevalence and neuroimaging findings in patients with COVID-19 presenting with olfactory disorders. We have used validated smell test (containing microencapsulated odorant strips) to quantitatively assess olfactory dysfunction in patients with COVID-19 and controls. The prevalence of normosmia was significantly lower in cases than controls (23% vs 64%). In addition, high-resolution brain MRI revealed that COVID-19-induced persistent (>40 days) anosmia/hyposmia was associated with olfactory bulb (OB) atrophy. However, to the best of our knowledge, there are no data regarding potential risk factors that may be associated with protracted olfactory dysfunction and development of OB atrophy in patients with COVID-19.

In view of the former considerations, we conducted a prospective case–control study comparing the prevalence of hypothyroidism in patients with prolonged COVID-19-induced hyposmia/anosmia (>40 days) versus age-matched and sex-matched patients with COVID-19 without subjective and objective olfactory disorders, at a referral centre in Athens, Greece between 22 May 2020 and 15 January 2021. Written informed consent was obtained by all participants and patients' data were handled under strict anonymity in agreement with the Helsinki Declaration. All subjects had a laboratory-confirmed COVID-19 infection, using real-time reverse transcriptase PCR on respiratory samples. Olfactory function was objectively assessed using the three-odorant test Quick Smell Identification Test (Q-SIT; Sensonics, Haddon Heights, New Jersey, USA), that consists of individual 5×5.5-inch tear-out cards, each of which contains three microencapsulated odorant strips. Q-SIT was selected on the basis of cost, convenience, format, standardisation and validation. A robust test, the SIT (32014), a comprehensive and accurate 40-item test in future larger multicentre studies.

The present preliminary findings are by no means confirmatory but support an intriguing hypothesis. SARS-CoV-2-induced smell dysfunction could be triggered by a direct viral insult of both the olfactory nerve and the thyroid gland. The absence or the slow recovery of olfaction may be impelled by the viral-induced downregulation of thyroid function that may blunt the effects of thyroid hormones into the maturation and regeneration of olfactory neuronal cells especially in patients with a history of thyroid dysfunction. This preliminary observation and hypothesis require confirmation in larger case–control studies that may control for other confounders including but not limited to those related to thyroid dysfunction (eg, family history, thyroiditis), and/or history of autoimmune.

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EK, MPaneta, KP and LP. Drafting and revising the manuscript were performed by GT, PCF and LP. Critical comments during manuscript revision were provided by EK, MPaneta, KP, CP, MPapathanasiou, SL, PPS and ST. All authors read and approved the final manuscript.

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