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Examining the Enantiopathic Effect of Covid-19 on Olfactory Sensitivity: A Case Report

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Abstract

Objective: Pathophysiology behind reduced olfactory ability in hyperosmic individuals.

Background: Covid-19 infection as an enantiopathy to hyperosmia has not been described.

Design/Methods: A 63 year-right-handed male presented with hyperosmia of 150% of normal whereby aromas appeared distorted and disgusting. Shortly, he tested positive for Covid-19 which led to a resolution of his hyperosmia. Alcohol Sniff Test scores fluctuated between zero and three (anosmia). Gradually, his smell improved from 80% and 100% of normal. However, post Covid-19 infection, it returned to 130% of normal.

Results: Neurological abnormalities, Olfatory testing, Odor discrimination memory test, Total 7/12 (hyposmia). Bilateral olfactory threshold testing to phenylethyl alcohol 3 (hyposmia). Taste Threshold and Suprathreshold Testing: Mild hypogeusia to Sucrose. Ageusia to Hydrochloric acid, urea and propothiocarbamide. Olfactometer Identification Testing: Left nostril: 10 (anosmia), Right nostril: 8 (anosmia).

Conclusion: The mechanism whereby Covid-19 acts to reduce olfactory ability in normosmic individuals has been postulated as viral involvement of olfactory nerve at olfactory bulb, pathology of sustentacular cells, olfactory receptor site destruction vasculopathy/arteriopathy of cranial nerve or central connections of olfactory nerve or inflammatory response induced destruction of lamina propria and olfactory nerve apoptosis. The same may have incited a reduced olfaction in hyperosmic individuals-such may be under grouped as understanding the pathophysiology of this subject's hyperosmia. Perceived hyperosmia is often objectively hyposmic pathology of inhibiting the inhibitory olfactory discharges that result in enhancement of perceived odor. Elimination of hyperosmia reduces functionality of remaining normosmic neurons which then became relatively hyposmic, but were perceived as normal due to lack of the inhibitory factors. Recovery of hyperosmia upon recovery of olfactory function from Covid-19 would be consistent with such a postulation. Of those with preexisting chemosensory dysfunction, query as to impact of Covid-19 on remaining sensory function is warranted.

Keywords: Enantiopathy • Chemosensory dysfunction • Covid-19 and olfactory changes • Hyperosmia • Hyposmia

Introduction

One disease acting to alleviate another disease, yclept enantiopathy, has been described among myriad neurological disorders, including bradyphagia for burning mouth syndrome, upper respiratory infection for burning mouth syndrome, cerebellar hemorrhage for stereotypy, nasal congestion for phantosmia, anosmia for palinageusia, alcohol dependence for both cataplexy and essential tremors [1-6]. Parkinson's disease induces hyposmia for snatiation, heroin dependence for quetiapine-induced restless leg syndrome and chemosensory dysfunction for gustatory rhinitis [7-9].

While head trauma induced hyposmia as an enantiopathy for odor induced migraines has been described and Covid-19 hyposmia. Odor induced migraine with Covid-19 induced hyposmia as an enantiopathy to odor induced migraine [1,10]. While hyperosmia has been induced by Covid-19, Covid-19 infection as an enantiopathy to hyperosmia has not heretofore been described. Two such cases are presented [11].

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Case Study 1

A 63 year-right-handed male with a past history of muscle contraction headaches presented with ten days of metallic taste resolving with eating. This taste would begin an hour before waking in the morning, persist throughout the day, and recur immediately after eating. Despite this metallic taste, food would taste normal to him.

Approximately 3 months later, he noted that he had an increase in the intensity of his smell to 120% of normal. Some odors were more intense than others for him. Initially, this increase in his ability to smell intermittently over months became persistent. And his perceived ability to smell gradually increased to 150% of normal, such that aromas were overpowering him and some were causing his nostrils to be irritated. Some days it was his right nostrils, and some days his left nostrils were worse. He also noted that some odors were bothersome, such as cardboard aromas, which were disgusting. He observed that his metallic taste was so strong that he found he had to suck lemon heads or chew gum all day long to relieve it. Over several months, he also developed the perception that some odors were distorted and smelled disgusting, such that his hand soap and some perfumes smelled too chemical like. Some tastes began to taste different, such that they were distorted and bad. Chocolate tasted greasy and disgusting, and toothpaste smells disgusting. The patient developed a scratchy throat and noted the next day he could not smell garlic and tested positive for Covid. His taste also dropped to 20% of normal, where he could taste sugar but nothing else. His other chemosensory symptoms resolved during this time. Bimonthly testing of his olfaction with the Alcohol Sniff Test revealed a score of zero. Gradually, over the next few months, his smell did not improve, and his taste began to be able to detect initial flavors like lemon, brown sugar, and fried eggs. One and a half months after developing Covid-19 his sense of smell improved to 80% of normal from 150% prior to Covid-19. After Covid-19 his smell was 80% normal but felt like it was too

strong. His taste, however, also improved to 80% of normal, but he felt like he could taste everything less intensely. At that time, his Alcohol Sniff Test improved from 0 to 3 (anosmia). Gradually, his sense of smell returned, such that he was able to smell soup, for instance, and his sense of smell continued to gradually improve, correlating with an improved perception of taste. 3 months after Covid-19 his smell returned to 100% of normal, as did his taste, but the greasy taste of chocolate persisted, as did the distorted smell. His Alcohol Sniff Test at the time was one. By 8 months after Covid, his smell returned to 130% of normal, and his Alcohol sniff test fluctuated between one and two and returned to a level of two. And his perceived taste improved to level three, and his taste returned to 100% of normal.

Results

Abnormalities in the Neurological Test: Mental Status Examination: Able to recall 7 digits forward and 3 digits backward. Neuropsychiatric testing: Animal fluency test: 15 (normal) Go-No-Go Test: 6/6 (normal). Cranial nerve examination: CN I: CN II: Visual acuity 20/400 OU without correction. Reflexes: 1+ both upper extremities (BUE), 0 B lower (L) E.

Chemosensory Testing: Olfaction: Quick Smell Identification Test: 3/3 (normosmia). Odor Discrimination Memory Test: 10 seconds 3/4, 30 seconds 2/4, 60 seconds 2/4, Total 7/12 (hyposmia). Bilateral Olfactory Threshold Testing for Phenylethyl Alcohol: 3 (hyposmia).

Alcohol Sniff Test: 1 (anosmia), Retronasal Olfactory Testing: Retronasal Smell Test: 9 (normosmia). Propylthiouracil Disc Test: 10 (normogeusia). Suprathreshold Amyl Acetate Odor Hedonic Testing: Normal Pattern Suprathreshold Amyl Acetate Odor Intensity Testing: Normal Pattern Taste Threshold and Suprathreshold Testing: Normogeusia to Sodium Chloride. Mild hypogeusia to Sucrose. Ageusia to Hydrochloric acid, urea, and propothiocarbamide (PTC). Waterless Empirical Taste Test: Sweet: 3 (hypogeusia), Sour: 7 (normogeusia), Salty: 6 (normogeusia), Bitter: 0 (ageusia), Brothy: 0 (ageusia), Total: 29 (normogeusia). Olfactometer Identification Testing: Left nostril: 10 (anosmia); Right nostril: 8 (anosmia). Taste Quadrant Testing to NaCl, sucrose, citric acid, quinine hydrochloride, and alcohol: No R to L difference, no front to back difference. Taste weakness to sucrose: Throughout and NaCl. Fundiform papilli: 14R, 16L (normal). The results are presented in Table 1.

Table 1. Results from Case Study 1

Test	Result
Mental status examination	Recall: 7 digits forward, 3 digits backward
Neuropsychiatric testing	Animal Fluency Test: 15 (normal), Go-No-Go Test: 6/6 (normal)
Cranial nerve examination	CN I: Normosmia, CN II: Visual acuity 20/400 OU without correction
Reflexes	1+ Both Upper Extremities 0 Both Lower Extremities
Chemosensory testing	Olfaction: Quick Smell Identification Test: 3/3 (normosmia), Odor Discrimination Memory Test: 10 seconds 3/4, 30 seconds 2/4, 60 seconds 2/4, Total 7/12 (hyposmia), Bilateral Olfactory Threshold Testing for Phenylethyl Alcohol: 3 (hyposmia), Alcohol Sniff Test: 1 (anosmia), Retronasal Smell Test: 9 (normosmia), Propylthiouracil Disc Test: 10 (normogeusia)
Suprathreshold Amyl Acetate Odor Hedonic testing	Normal pattern
Suprathreshold Amyl Acetate Odor Intensity testing	Normal pattern
Taste Threshold and Suprathreshold Testing	Normogeusia to Sodium Chloride, Mild hypogeusia to Sucrose, Ageusia to Hydrochloric acid, Urea, and Propothiocarbamide (PTC)
Waterless Empirical Taste Test	Sweet: 3 (hypogeusia), Sour: 7 (normogeusia), Salty: 6 (normogeusia), Bitter: 0 (ageusia), Brothy: 0 (ageusia), Total: 29 (normogeusia)
Olfactometer Identification Testing	Left nostril: 10 (anosmia), Right nostril: 8 (anosmia)
Taste Quadrant Testing to NaCl, Sucrose, Citric Acid, Quinine Hydrochloride, and Alcohol	No Right to Left difference, No front to back difference, Taste weakness to Sucrose throughout and NaCl
Fundiform Papilli	14 Right, 16 Lower (normal)

Case Study 2

A 63-year-old right-handed male presented with gradual onset of chemosensory conditions of idiopathic origin, including phantosmia, palinosmia, cacosmia, phantogeusia, and myriad odor induced disorders such as panic attacks, migraines, somatization, and flavorful eructation. His sense of smell was 130% normal until January 2022, when, despite having both initial and booster Covid-19 vaccinations, the patient developed Covid. Initially, he presented with rhinorrhea without a fever. Within 24 hours of onset, his sense of smell and taste dropped to 50% of normal, followed by a total loss of smell and taste. The patient underwent treatment with Molnupiravir, a protease inhibitor, and within 5 days his smell and taste returned to 50% of normal and gradually recovered to 90% of normal. He could smell and taste everything, but not strongly as prior to Covid.

Results

Abnormalities in physical examination: General: 1+bilateral pedal edema. Neurologic Examination: Mental Status Examination: Immediate recall: 6 digits forwards and 3 digits backward. Cranial Nerve (CN) Examination: CN II: Visual field: patchy loss, temporal region OS. CN III, IV, VI: Bilateral ptosis. CN VIII: Hearing absent AD to Calibrated Finger Auditory Screening Test: strong 35. Ambassador Hear Pen: Absent AD. Motor: Bilateral intrinsics of hand: 4/5. Drift test: Mild left (L) pronator drift with L abductor digiti minimi sign. Gait: Mild foot drop on right (R). Sensory: Decreased light touch and pinprick bilateral lower extremities, distally. Rydel-Seiffer Vibratory Sense Evaluation: Absent in both lower extremities. Reflexes: Areflexia. Chemosensory Test: Olfaction: Quick Smell Identification Test: 3 (normosmia). Pocket Smell Test: 3 (normosmia). Odor Memory Test: 1 at 10 seconds, 0 at 30 seconds, 1 at 60 seconds; Total: 2/12 (anosmia). Alcohol Sniff Test: 23 (normosmia). Sniff Magnitude Test: Sniff Magnitude Ratio:

1.87 (anosmia).

Suprathreshold Amyl Acetate Odor Intensity Test: Crossed Pattern (Abnormal) Suprathreshold Amyl Acetate Odor Hedonic Test: Crossed Pattern (Abnormal). Olfactometer Identification Test: L 9.0, R 10.0 (hyposmia). Olfactometer Butanol Threshold: L 8.0 (normosmia), R 3.5 (anosmia). Sniff-n-Sticks: Threshold: L<1, R<1, Dirhinous<1 (anosmia), dirhinous discrimination: 8 (hyposmia), dirhinous identification: 6 (anosmia).

Brief Smell Identification Test: 9 (normosmia). Retronasal Smell Test: Retronasal Smell Index: 4 (abnormal). Gustation: Taste Threshold Test: Normogeusic to Urea, Sucrose, Phenylthiocarbamide; Mild hypogeusia of 10%-30% to sodium chloride and hydrochloric acid. Taste Quadrant Test: Decreased anterior tongue bilaterally to sodium chloride, sucrose, citric acid, quinine hydrochloride, and alcohol. Whole mouth weakness to sodium chloride.

Electrogustometry Test: Posterior tongue: L 34, R 30 (abnormal); Anterior tongue, L 34, R 34 (abnormal); palate: L 12, R 14 (normal). Neuropsychiatric Test: Semantic Fluency Test: 29 (normal). Zung Anxiety Scale: 56 (minimal-moderate anxiety). Beck Depression Inventory: 11 (normal). Center for Neurological Studies Lability Scale: 10 (normal). Other: Candida Culture: Negative. Saxon Test: 4 grams (Normal). Piesesthesiometry: Normal. Fungiform Papillae Count: L 24, R 22 (normal). CT scan of brain and sinuses: Normal. The results are presented in Table 2.

Table 2. Results from Case Study 2

Physical Examination Abnormalities	Results
General	1+bilateral pedal edema
Neurologic Examination	
Mental status examination	Immediate recall: 6 digits forwards and 3 digits backward
Cranial nerve examination	CN II: Visual field: Patchy loss, temporal region OS, CN III, IV, VI: Bilateral ptosis, CN VIII: Hearing absent AD to Calibrated Finger Auditory Screening Test: Strong 35, Ambassador Hear Pen: Absent AD
Motor	Bilateral intrinsics of hand: 4/5, Drift test: Mild left (L) pronator drift with L abductor digiti minimi sign, Gait: Mild foot drop on right (R)
Sensory	Decreased light touch and pinprick bilateral lower extremities, distally. Rydel-Seiffer Vibratory Sense Evaluation: Absent in both lower extremities, Reflexes: Areflexia
Chemosensory Test	
Olfaction	Quick Smell Identification Test: 3 (normosmia), Pocket Smell Test: 3 (normosmia), Odor Memory Test: 1 at 10 seconds, 0 at 30 seconds, 1 at 60 seconds; Total: 2/12 (anosmia), Alcohol Sniff Test: 23 (normosmia)
Sniff Magnitude test	Sniff Magnitude Ratio: 1.87 (anosmia), Suprathreshold Amyl Acetate Odor Intensity Test: Crossed Pattern (Abnormal), Suprathreshold Amyl Acetate Odor Hedonic Test: Crossed Pattern (Abnormal)
Olfactometer test	L 9.0, R 10.0 (hyposmia), Olfactometer Butanol Threshold: L 8.0 (normosmia), R 3.5 (anosmia), Sniff-n-Sticks: Threshold: L <1, R <1, Dirhinous <1 (anosmia), dirhinous discrimination: 8 (hyposmia), dirhinous identification: 6 (anosmia), Brief Smell Identification Test: 9 (normosmia)
Gustation	Taste Threshold Test: Normogeusic to Urea, Sucrose, Phenylthiocarbamide; Mild hypogeusia of 10%-30% to sodium chloride and hydrochloric acid, Taste Quadrant Test: Decreased anterior tongue bilaterally to sodium chloride, sucrose, citric acid, quinine hydrochloride, and alcohol. Whole mouth weakness to sodium chloride. Electrogustometry Test: Posterior tongue: L 34, R 30 (abnormal); Anterior tongue, L 34, R 34 (abnormal); palate: L 12, R 14 (normal)
Neuropsychiatric test	Semantic Fluency Test: 29 (normal), Zung Anxiety Scale: 56 (minimal-moderate anxiety), Beck Depression Inventory: 11 (normal), Center for Neurological Studies Lability Scale: 10 (normal)
Other	Candida Culture: Negative, Saxon Test: 4 grams (Normal), Piesesthesiometry: Normal, Fungiform Papillae Count: L 24, R 22 (normal), CT Scan of brain and sinuses: Normal

Discussion

The exact mechanism whereby Covid-19 acts to reduce olfactory ability in normosmic individuals has been postulated to be due to either direct viral involvement of the olfactory nerve at the olfactory bulb, pathology of sustentacular cells, olfactory receptor site destruction, vasculopathy/arteriopathy of the cranial nerve or central connections of the olfactory nerve or acute cytokine mediated inflammatory response with destruction of lamina propria and olfactory nerve apoptosis [12-15]. The same mechanisms may have acted on those patients with hyperosmia, to reduce the olfactory ability from enhanced to normal. Peradventure, this may be under grouped based on understanding the pathophysiology of this subject's hyperosmia.

Perceived hyperosmia is often objectively hyposmic: The hyperosmia may represent the pathology of inhibitory olfactory discharges, thus disinhibiting olfactory discharges; this release phenomenon enhances the intensity of perceived odor [16]. The elimination of hyperosmia may have been due to the reduced function of the remaining normosmic neurons, which then became relatively hyposmic but were perceived as normal due to the lack of other inhibitory factors. Recovery of hyperosmia upon recovery of olfactory function from Covid-19 would be consistent with such a postulated. Of those with preexisting chemosensory dysfunction, query as to impact of Covid-19 on remaining sensory function is warranted.

Conclusion

Covid-19's impact on olfactory ability in normosmic individuals is postulated to involve viral involvement of the olfactory nerve at the olfactory bulb, sustentacular cell pathology, olfactory receptor site destruction, vasculopathy/arteriopathy of the cranial nerve or central connections, and inflammatory response-induced destruction of the lamina propria and olfactory nerve apoptosis. The same mechanisms may have contributed to reduced olfaction in hyperosmic individuals, as their perceived hyperosmia is often objectively hyposmic. Understanding the pathophysiology of

hyperosmia is crucial in comprehending the subject's condition. Elimination of hyperosmia reduces functionality of remaining normosmic neurons, leading to relative hyposmia perceived as normal due to lack of inhibitory factors. The recovery of hyperosmia upon Covid-19 recovery aligns with this postulation. For individuals with preexisting chemosensory dysfunction, further investigation into the impact of Covid-19 on remaining sensory function is necessary.

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Conflict of Interest

The authors declare that they have no competing interests.

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