**Supplementary Information (Appendix)**

**Supplementary notes**

Supplementary notes 1: Olfactory evaluations and SARS-CoV-2 virologic assessments.

Supplementary notes 2:Neuroradiological magnetic resonance imaging (MRI) data acquisition.

Supplementary notes 3: Smell training via the electronic portable aromatic rehabilitation (EPAR) diffusers.

**Supplementary tables**

Supplementary table 1: Sino-nasal outcome test (SNOT-22) of patient 1, before olfactory treatment.

Supplementary table 2: Sino-nasal outcome test (SNOT-22) of patient 1, after 4-weeks of olfactory treatment.

Supplementary table 3: Sino-nasal outcome test (SNOT-22) of patient 2.

Supplementary table 4: Functional connectivity (FC) of the left and right caudate and the olfactory cortical network (OCN) regions.

Supplementary table 5:Volume of the olfactory bulb and tract.

Supplementary table 6: Cerebral blood flow (CBF) in the olfactory cortical network (OCN) regions.

Supplementary table 7: Butanol threshold test (BTT).

**Supplementary figures**

Supplementary figure 1 | Magnetic resonance (MR) spectroscopy of the gyrus rectus and superior frontal cortex. (A) The position of the single voxel Point Resolved Spectroscopy (PRESS) was placed at the gyrus rectus and superior frontal cortex. (B) Healthy control. (C) Patient 2. Cho, choline; Cr, creatine; mI, myo-inositol; NAA, N-acetylaspartate.

**Supplementary materials**

Supplementary material 1: Olfactory function questionnaire.

Supplementary material 2: Electronic portable aromatic rehabilitation (EPAR) diffuser–Instruction guide.

Supplementary material 3: Electronic portable aromatic rehabilitation (EPAR) diffuser–Set up and refill.

**References**

**Supplementary notes 1**: Olfactory evaluations and SARS-CoV-2 virologic assessments.

**Patients and controls**

All participants completed a detailed olfactory questionnaire at study recruitment (Supplementary Material 1).1 2

**Olfactory evaluations**

Subjective olfactory performance was assessed using Sino-Nasal Outcome Test (SNOT-22; Supplementary Tables 1–3).3 Quantitative olfactory function was measured using butanol threshold test (BTT; prepared in-house; Supplementary table 7) and smell identification test (SIT; Sensonics International, New Jersey, USA).4 5 Nasoendoscopic examinations were performed for COVID-19 patients, as described previously.1

**SARS-CoV-2 reverse transcription polymerase chain reaction (RT-PCR) tests**

COVID-19 patients were diagnosed by RT-PCR of pooled nasopharyngeal and throat swab specimens targeting the SARS-CoV-2 envelope gene (TIB Molbiol, Berlin, Germany). Control subjects were tested negative for SARS-CoV-2 by commercial PCR assays (Xpert® Xpress SARS-CoV-2, Sunnyvale, California, United States; or RT-PCR COVID-19 Test, Prenetics, Hong Kong, China) at the time of MRI evaluation.

**SARS-CoV-2 serological assessments**

All study participants received SARS-CoV2 serological assessments by enzyme immunoassay (EIA) tests for SARS-CoV-2 nucleoprotein (NP) and spike protein receptor binding domain (RBD); furthermore, microneutralization assays (MN) were performed, as previously described (Table 1).6 7

**Supplementary notes 2:** Neuroradiological magnetic resonance imaging (MRI) data acquisition.

All subjects underwent MRI brain scans using a 1.5T MR scanner (SIGNA; GE Healthcare, Chicago, Illinois, United States) with a standard 16-channel head coil. Structural MRI brain images were acquired with fast and high-resolution three-dimensional (3D) sequences (BRAVO\_3D sagittal, TI=450ms, Flip angle=13o, voxel size=1×1×1.2mm3, FOV=256×256mm2). The parameters of the 3D arterial spin labeling (ASL) were TR=4885ms, TE=10.5ms, labeling-duration=1800ms, post-labeling delay=2025ms, 40 slices with spatial resolution of 1.9×1.9×4mm3.

Volumetric analyses of the olfactory bulbs and tracts included a sagittal 3D T2 FLAIR (TR=6000ms, TI=1858ms, FOV=24cm) with 1.4mm interleaved scans. After reformatting, the coronal plane was obtained with 1.5mm spacing. The 3D volumetric processing of the bilateral olfactory bulbs and tracts were performed on GE workstation (AW server 3.2; GE Healthcare, Chicago, Illinois, United States). The olfactory bulbs were located at the anterior cribriform plate, while the olfactory tracts extended posteriorly to enter the brain below the rostrum of the corpus callosum.8

MR spectroscopy was performed using the single voxel Point Resolved Spectroscopy (PRESS), TE=136ms, TR=1500ms, voxel size=2×2×2cm3.9 The voxel was placed at gyrus rectus (GR) and superior frontal cortex.

Resting state functional magnetic resonance imaging (rs-fMRI) of the brains were collected using a gradient-echo echo-planar sequence (parameters: TR=2000ms, TE=30ms, flip angle=90o, voxel size=3×3×4mm3) sensitive to blood-oxygen-level-dependent (BOLD) contrast. During the rs-fMRI scanning, the participants were instructed to open their eyes to look at the cross presented within the MR scanner and not to think of anything.

The pre-processing of the rs-fMRI data were performed using the DPABI toolbox (http://rfmri.org/dpabi) based on the SPM12 software (https://www.fil.ion.ucl.ac.uk/spm/software/spm12/). The first ten images were discarded to account for the spin saturation effects and acclimatization of scanning noise by the subjects. The differences in image acquisition time of the remaining rs-fMRI images were corrected between slices. Head motion corrections were performed to adjust the images in the same position. Images were excluded from further analyses if the head movements were greater than 3mm in any dimensional planes of x, y, or z; or over 3o of deviation. Nuisance signals, including Friston-24 head motion parameters, mean white matter (WM), and cerebrospinal fluid (CSF) time series within brain masks were regressed out from the time courses in each voxel. Then the images were spatially normalized to the standard Montreal Neurological Institute (MNI) space and resampled to 3×3×3mm3 using the transformation parameters that were estimated through DARTEL segmentation.10 After normalization, the data were band-pass filtered (0.01<f<0.1Hz) to reduce the high-frequency respiratory and low-frequency cardiac noise drifts.

Hypothesis-driven region of interest (ROI) approach was applied in the evaluation of the rs-fMRI images. The center of the seed regions were located at the MNI coordinates for the left (-14, 14, 2) and right (14, 12, 9) caudate nuclei, respectively.11 12 We defined the seed regions for functional connectivity (FC) analyses with a sphere of 10 mm radius. We then calculated the correlations between the ROI series and the whole brain for each individual subject in a voxel-wise manner. To normalize the distribution of correlation coefficient (Pearson correlation, *r*), the values were transferred to standard z scores based on Fisher transformation. The connectivity maps of patients and healthy controls of similar age groups were calculated.

Based on the Automated Anatomical Labeling (AAL) template, the pre-processed rs-fMRI data were segmented into 90 regions.11 Twenty-eight out of the 90 regions were associated with the functional olfactory cortical networks (OCN). The primary OCN areas included the bilateral piriform gyrus and amygdala; while the secondary OCN areas included the superior orbitofrontal cortex (OFC), inferior OFC, medial OFC, GR, insula, anterior cingulate cortex, hippocampus, parahippocampus, caudate nucleus, putamen, as well as the superior and middle temporal poles.12-14 We created a mask which included both primary and secondary OCN processing areas (Fig. 1). The results provided spatial maps of the olfactory network FC within the created mask. The threshold was set at 0.2 and maximum z value was standardized to 1.

Based on the ROIs of olfactory regions reported, the connectivity between seed regions (left and right caudate) and other ROIs were obtained by extracting the average time series from each ROI and calculating the correlation.15-17 The average FC values between seeds and other regions of the OCN were calculated.

We also studied the gustatory, somatosensory, and integrative networks of COVID-19 patients and healthy controls. The gustatory network included bilateral insula, frontal operculum, postcentral gyrus, inferior OFC, pregenual anterior cingulate, medial orbitofrontal gyrus and thalamus.18 19 The center coordinates of the gustatory seed regions (a sphere of 6mm radius) were at the (1) -36, 6 -2 (left insula) and (2) 38, 20, 2 (right insula).

Furthermore, the somatosensory and integrative networks were evaluated. The somatosensory network included primary and secondary somatosensory cortices and insula, while the integrative network comprised of the OFC, insula, inferior parietal lobule, middle and superior temporal gyrus.12 The size of ROIs were 10mm radius spheres. The center coordinates of the seed ROIs in the somatosensory network were (1) -58, -42, 36 (left supramarginal) and (2) 58, -32, 34 (right supramarginal). For the integrative network, the center coordinates of the seed ROIs were (1) -34, 22, 10 (left insula) and (2) 39, 6, 2 (right insula). After the seed-based FC calculations, we overlapped the masks of the three networks with the FC maps. The threshold was set at 0.2 and maximum z value was standardized to 1.

**Supplementary notes 3:** Smell training via the electronic portable aromatic rehabilitation (EPAR) diffusers.

Four categories of essential oils [lemon (Citrus limon), eucalyptus (Eucalyptus radiata), geranium (Pelargonium graveolens), and cedarwood (Juniperus virginiana)] were used for smell training (ST), which were individually stored in four different EPAR diffuser units. Patients were instructed to conduct ST at a seated position, where the EPAR diffuser was placed at an arm’s length with the stream of aerosolized essential oil directed upwards (see Supplementary material 2 and 3 for video demonstrations). During ST sessions, all four categories of essential oils were delivered via the EPAR diffusers for 20 seconds sequentially, providing a total of 80 seconds of olfactory stimulation three times per day.

**Supplementary table 1**: Sino-nasal outcome test (SNOT-22) of patient 1, before olfactory treatment.

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| (1) Considering how severe the problem is when you experience it and how often it happens, please rate each item below on how "bad" it is by circling the number that corresponds with how you feel using this scale: 🡪 | No Problem | Very Mild Problem | Mild or slight Problem | Moderate Problem | Severe Problem | Problem as bad as it can be | 5 Most Important Items |
| 1. Need to blow nose | 0 | × | 2 | 3 | 4 | 5 |  |
| 2. Nasal Blockage | × | 1 | 2 | 3 | 4 | 5 |  |
| 3. Sneezing | × | 1 | 2 | 3 | 4 | 5 |  |
| 4. Runny nose | 0 | × | 2 | 3 | 4 | 5 |  |
| 5. Cough | × | 1 | 2 | 3 | 4 | 5 |  |
| 6. Post-nasal discharge | × | 1 | 2 | 3 | 4 | 5 |  |
| 7. Thick nasal discharge | × | 1 | 2 | 3 | 4 | 5 |  |
| 8. Ear fullness | 0 | 1 | × | 3 | 4 | 5 |  |
| 9. Dizziness | × | 1 | 2 | 3 | 4 | 5 |  |
| 10. Ear pain | 0 | × | 2 | 3 | 4 | 5 |  |
| 11. Facial pain/pressure | 0 | × | 2 | 3 | 4 | 5 |  |
| 12. Decreased Sense of Smell/Taste | 0 | 1 | 2 | 3 | 4 | × | ■ |
| 13. Difficulty falling asleep | × | 1 | 2 | 3 | 4 | 5 |  |
| 14. Wake up at night | × | 1 | 2 | 3 | 4 | 5 |  |
| 15. Lack of a good night’s sleep | × | 1 | 2 | 3 | 4 | 5 |  |
| 16. Wake up tired | 0 | 1 | × | 3 | 4 | 5 |  |
| 17. Fatigue | × | 1 | 2 | 3 | 4 | 5 |  |
| 18. Reduced productivity | × | 1 | 2 | 3 | 4 | 5 |  |
| 19. Reduced concentration | × | 1 | 2 | 3 | 4 | 5 |  |
| 20. Frustrated/restless/irritable | × | 1 | 2 | 3 | 4 | 5 |  |
| 21. Sad | × | 1 | 2 | 3 | 4 | 5 |  |
| 22. Embarrassed | × | 1 | 2 | 3 | 4 | 5 |  |

(2) Please mark the most important items affecting your health (maximum of 5 items)

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**Supplementary table 2**: Sino-nasal outcome test (SNOT-22) of patient 1, after 4-weeks of olfactory treatment.

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| (1) Considering how severe the problem is when you experience it and how often it happens, please rate each item below on how "bad" it is by circling the number that corresponds with how you feel using this scale: 🡪 | No Problem | Very Mild Problem | Mild or slight Problem | Moderate Problem | Severe Problem | Problem as bad as it can be | 5 Most Important Items |
| 1. Need to blow nose | 0 | 1 | × | 3 | 4 | 5 |  |
| 2. Nasal Blockage | 0 | 1 | 2 | × | 4 | 5 |  |
| 3. Sneezing | 0 | × | 2 | 3 | 4 | 5 |  |
| 4. Runny nose | 0 | 1 | × | 3 | 4 | 5 |  |
| 5. Cough | × | 1 | 2 | 3 | 4 | 5 |  |
| 6. Post-nasal discharge | 0 | × | 2 | 3 | 4 | 5 |  |
| 7. Thick nasal discharge | 0 | 1 | × | 3 | 4 | 5 |  |
| 8. Ear fullness | 0 | 1 | 2 | × | 4 | 5 | ■ |
| 9. Dizziness | × | 1 | 2 | 3 | 4 | 5 |  |
| 10. Ear pain | 0 | × | 2 | 3 | 4 | 5 |  |
| 11. Facial pain/pressure | × | 1 | 2 | 3 | 4 | 5 |  |
| 12. Decreased Sense of Smell/Taste | 0 | 1 | 2 | 3 | × | 5 | ■ |
| 13. Difficulty falling asleep | 0 | × | 2 | 3 | 4 | 5 | ■ |
| 14. Wake up at night | 0 | 1 | × | 3 | 4 | 5 |  |
| 15. Lack of a good night’s sleep | 0 | × | 2 | 3 | 4 | 5 |  |
| 16. Wake up tired | 0 | 1 | × | 3 | 4 | 5 | ■ |
| 17. Fatigue | 0 | × | 2 | 3 | 4 | 5 |  |
| 18. Reduced productivity | 0 | × | 2 | 3 | 4 | 5 |  |
| 19. Reduced concentration | × | 1 | 2 | 3 | 4 | 5 |  |
| 20. Frustrated/restless/irritable | × | 1 | 2 | 3 | 4 | 5 |  |
| 21. Sad | × | 1 | 2 | 3 | 4 | 5 |  |
| 22. Embarrassed | × | 1 | 2 | 3 | 4 | 5 |  |

(2) Please mark the most important items affecting your health (maximum of 5 items)

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**Supplementary table 3**: Sino-nasal outcome test (SNOT-22) of patient 2.

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| (1) Considering how severe the problem is when you experience it and how often it happens, please rate each item below on how "bad" it is by circling the number that corresponds with how you feel using this scale: 🡪 | No Problem | Very Mild Problem | Mild or slight Problem | Moderate Problem | Severe Problem | Problem as bad as it can be | 5 Most Important Items |
| 1. Need to blow nose | × | 1 | 2 | 3 | 4 | 5 |  |
| 2. Nasal Blockage | × | 1 | 2 | 3 | 4 | 5 |  |
| 3. Sneezing | × | 1 | 2 | 3 | 4 | 5 |  |
| 4. Runny nose | × | 1 | 2 | 3 | 4 | 5 |  |
| 5. Cough | × | 1 | 2 | 3 | 4 | 5 |  |
| 6. Post-nasal discharge | × | 1 | 2 | 3 | 4 | 5 |  |
| 7. Thick nasal discharge | × | 1 | 2 | 3 | 4 | 5 |  |
| 8. Ear fullness | × | 1 | 2 | 3 | 4 | 5 |  |
| 9. Dizziness | 0 | 1 | × | 3 | 4 | 5 | ■ |
| 10. Ear pain | × | 1 | 2 | 3 | 4 | 5 |  |
| 11. Facial pain/pressure | × | 1 | 2 | 3 | 4 | 5 |  |
| 12. Decreased Sense of Smell/Taste | 0 | 1 | 2 | 3 | × | 5 | ■ |
| 13. Difficulty falling asleep | 0 | × | 2 | 3 | 4 | 5 |  |
| 14. Wake up at night | × | 1 | 2 | 3 | 4 | 5 |  |
| 15. Lack of a good night’s sleep | × | 1 | 2 | 3 | 4 | 5 |  |
| 16. Wake up tired | 0 | × | 2 | 3 | 4 | 5 |  |
| 17. Fatigue | 0 | 1 | × | 3 | 4 | 5 |  |
| 18. Reduced productivity | 0 | 1 | × | 3 | 4 | 5 |  |
| 19. Reduced concentration | 0 | × | 2 | 3 | 4 | 5 |  |
| 20. Frustrated/restless/irritable | 0 | 1 | 2 | 3 | × | 5 | ■ |
| 21. Sad | 0 | 1 | 2 | 3 | × | 5 | ■ |
| 22. Embarrassed | 0 | 1 | 2 | 3 | × | 5 | ■ |

(2) Please mark the most important items affecting your health (maximum of 5 items)

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**Supplementary table 4**: Functional connectivity (FC) of the left and right caudate and the olfactory cortical network (OCN) regions.

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | **Left caudate seed** | | | **Right caudate seed** | | |
| **Subjects** | **Primary**  **OCN regions** | **Secondary**  **OCN regions** | **Combined**  **OCN regions** | **Primary**  **OCN regions** | **Secondary**  **OCN regions** | **Combined**  **OCN regions** |
| C–1 | 0.55 | 0.40 | 0.40 | 0.46 | 0.37 | 0.35 |
| C–2 | 0.50 | 0.42 | 0.41 | 0.37 | 0.26 | 0.25 |
| P1–1 | 0.35 | 0.22 | 0.19 | 0.28 | 0.11 | 0.09 |
| P1–2 | 0.28 | 0.17 | 0.17 | 0.24 | 0.15 | 0.14 |
| P1–3 | 0.26 | 0.23 | 0.21 | 0.26 | 0.14 | 0.15 |
| P2–1 | 0.11 | 0.08 | 0.06 | 0.20 | 0.23 | 0.20 |

C–1: Control 1; C–2: Control 2; P1–1: Patient 1–baseline; P1–2: Patient 1–2 weeks of vitamin A and smell training; P1–3: Patient 1–additional 2 weeks of smell training, after 2 weeks of combination treatment with vitamin A and smell training; P2–1: Patient 2–baseline.

**Supplementary table 5**:Volume of the olfactory bulb and tract.

|  |  |  |
| --- | --- | --- |
|  | **Volume of the olfactory bulb and tract (mm3)** | |
| **Subjects** | **Left side** | **Right side** |
| C–1 | 49.5 | 45 |
| C–2 | 84 | 79.5 |
| P1–1 | 37.5 | 22.5 |
| P1–2 | 36 | 37.5 |
| P1–3 | 42 | 49.5 |
| P2–1 | 39 | 27 |

C–1: Control 1; C–2: Control 2; P1–1: Patient 1–baseline; P1–2: Patient 1–2 weeks of vitamin A and smell training; P1–3: Patient 1–additional 2 weeks of smell training, after 2 weeks of combination treatment with vitamin A and smell training; P2–1: Patient 2–baseline.

**Supplementary table 6**: Cerebral blood flow (CBF) in the olfactory cortical network (OCN) regions.

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  | **Cerebral blood flow (mL/100g/min)** | | | | |
| **Anatomical area** | **Healthy mean** | **P1–1** | **P1–2** | **P–3** | **P2–1** |
| **Primary OCN areas** | | | | | |
| Piriform cortex (left) | 49.87 | 54.38 | 57.35 | 63.86 | 56.39 |
| Piriform cortex (right) | 53.18 | 53.13 | 59.04 | 58.97 | 54.69 |
| Amygdala (left) | 44.74 | 59.98 | 47.92 | 49.52 | 49.34 |
| Amygdala (right) | 40.47 | 46.01 | 45.12 | 38.83 | 49.99 |
| **Secondary OCN areas** | | | | | |
| Orbitofrontal cortex (left, superior) | 63.26 | 50.53 | 66.02 | 70.25 | 61.28 |
| Orbitofrontal cortex (right, superior) | 62.34 | 53.94 | 70.49 | 67.14 | 60.77 |
| Orbitofrontal cortex (left, inferior) | 55.94 | 51.10 | 60.49 | 66.21 | 57.65 |
| Orbitofrontal cortex (right, inferior) | 55.27 | 50.71 | 57.40 | 58.67 | 58.01 |
| Orbitofrontal cortex (left, medial) | 62.64 | 70.97 | 66.07 | 69.77 | 58.96 |
| Orbitofrontal cortex (right, medial) | 59.12 | 69.12 | 63.18 | 65.14 | 57.19 |
| Gyrus rectus (left) | 61.58 | 49.56 | 68.72 | 71.38 | 65.71 |
| Gyrus rectus (right) | 63.02 | 56.72 | 67.40 | 68.51 | 63.57 |
| Insula (left) | 52.99 | 55.65 | 53.30 | 58.20 | 54.73 |
| Insula (right) | 50.39 | 54.33 | 55.64 | 57.37 | 56.63 |
| Anterior cingulate cortex (left) | 54.73 | 58.90 | 64.33 | 66.02 | 61.20 |
| Anterior cingulate cortex (right) | 49.70 | 52.99 | 61.13 | 62.61 | 55.39 |
| Hippocampus (left) | 47.15 | 67.60 | 49.28 | 54.93 | 58.04 |
| Hippocampus (right) | 47.60 | 59.68 | 50.13 | 49.71 | 55.48 |
| Parahippocampus (left) | 50.23 | 53.69 | 52.72 | 62.24 | 57.06 |
| Parahippocampus (right) | 51.59 | 56.29 | 55.22 | 55.26 | 57.28 |
| Caudate nucleus (left) | 42.09 | 52.50 | 43.47 | 46.79 | 40.82 |
| Caudate nucleus (right) | 44.28 | 51.27 | 50.23 | 46.83 | 41.06 |
| Putamen (left) | 43.36 | 53.85 | 50.22 | 49.20 | 44.65 |
| Putamen (right) | 43.03 | 50.49 | 50.21 | 45.00 | 46.97 |
| Temporal pole (left, superior) | 53.38 | 53.34 | 46.97 | 56.03 | 47.49 |
| Temporal pole (right, superior) | 51.57 | 56.95 | 50.10 | 54.18 | 51.57 |
| Temporal pole (left, middle) | 55.09 | 48.98 | 56.79 | 61.64 | 54.66 |
| Temporal pole (right, middle) | 51.33 | 54.18 | 55.71 | 58.94 | 57.11 |

C–1: Control 1; C–2: Control 2; P1–1: Patient 1–baseline; P1–2: Patient 1–2 weeks of vitamin A and smell training; P1–3: Patient 1–additional 2 weeks of smell training, after 2 weeks of combination treatment with vitamin A and smell training; P2–1: Patient 2–baseline.

**Supplementary table 7:** Butanol threshold test (BTT).

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Step** | **Dilution step** | **1-butanol (mL)** | **Deionized water (mL)** | **1-butanol concentration (%)** |
| 1 | 1 | 20mL of 99.9% 1-butanol | 480 | 4 |
| 2 | 2 | 50mL of dilution step 1 | 150 | 1 |
| 3 | 3 | 50mL of dilution step 2 | 150 | 0.25 |
| 4 | 4 | 50mL of dilution step 3 | 150 | 0.0625 |
| 5 | 5 | 50mL of dilution step 4 | 150 | 0.01563 |
| 6 | 6 | 50mL of dilution step 5 | 150 | 0.00391 |
| 7 | 7 | 50mL of dilution step 6 | 150 | 0.00098 |
| 8 | 8 | 50mL of dilution step 7 | 150 | 0.00024 |
| 9 | 9 | 50mL of dilution step 8 | 150 | 0.00006 |
| 10 | 10 | 50mL of dilution step 9 | 150 | 0.00002 |

10-steps serial dilution of 99.9% 1-butanol. Each BTT bottle contained 100mL of solutions, excess volume was discarded.

**Supplementary figure 1 |** Magnetic resonance (MR) spectroscopy of the gyrus rectus and superior frontal cortex. (A) The position of the single voxel Point Resolved Spectroscopy (PRESS) was placed at the gyrus rectus and superior frontal cortex. (B) Healthy control. (C) Patient 2. Cho, choline; Cr, creatine; mI, myo-inositol; NAA, N-acetylaspartate.

**Supplementary Material 1**: Olfactory function questionnaire.

|  |  |
| --- | --- |
| **Basic patient characteristics** | |
| Level of education |  |
| Occupation |  |
| Smoking status | ꙱ Non-smoker  ꙱ Ex-smoker  ꙱ Smoker  Detailed smoking history   * Age of first exposure to cigarette smoking: **\_\_\_\_\_\_\_\_\_\_** (years) * How many cigarettes smoked per day: **\_\_\_\_\_\_\_\_** (pack per day) * Any exposure to vaping or cigar smoking:yes ꙱ or no ꙱ * Any self-perceived alterations in the ability to smell during the period of smoking: **yes** ꙱ or **no** ꙱, comments: **\_\_\_\_\_\_\_\_\_\_** * Age of smoking cessation (if applicable): **\_\_\_\_\_\_\_\_\_\_** (years) * Any self-perceived alterations in the ability to smell after cessation of smoking: **yes** ꙱ or **no** ꙱, comments: **\_\_\_\_\_\_\_\_\_\_** |
| Drinking status | ꙱ Non-drinker  ꙱ Occasional drinker  ꙱ Social drinker  Detailed drinking history   * Frequency of alcohol consumption: **\_\_\_\_\_\_\_\_** (glasses per week) * Type of alcohol consumed: **\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_** |
| Recreational drug use | ꙱ No  ꙱ Yes, comments: **\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_** (cannabis, cocaine) |
| Chemical exposure | ꙱ No  ꙱ Yes, comments: **\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_** |
| Past Medical history | ꙱ No  ꙱ Yes, comments: **\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_** (nasal polyps, allergic rhinitis, diabetes mellitus, hypothyroidism, rheumatological conditions) |
| History of head trauma | ꙱ No  ꙱ Yes, comments: **\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_** |
| History of neurosurgery or maxillofacial surgery | ꙱ No  ꙱ Yes, comments: **\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_** |
| History of primary varicella zoster virus infection | ꙱ No  ꙱ Yes, comments: **\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_** (age of onset), any history of zoster reactivation **\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_** (area affected). |

|  |  |
| --- | --- |
| **Smell History** | |
| Self-perceived smell impairments | ꙱ No  ꙱ Yes, date of onset: **\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_** (dd / mm / year) |
| Anosmia | ꙱ No  ꙱ Yes |
| Hyposmia | ꙱ No  ꙱ Yes, comments: **\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_** |
| Parosmia | ꙱ No  ꙱ Yes, comments: **\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_** |
| Cacosmia | ꙱ No  ꙱ Yes, comments: **\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_** |

|  |  |
| --- | --- |
| **Smell History (administered to COVID-19 patients with olfactory dysfunction)** | |
| Self-perceived improvements in smell function | ꙱ No  ꙱ Yes  Details of improvements   * Date of onset of improvements: **\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_** (dd / mm / year) * Comments: **\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_** |
| Persistent smell impairments | ꙱ No  ꙱ Yes  Details of improvements   * Change in appetite: **yes** ꙱ or **no** ꙱   Comments: **\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_**   * Change in mood: **yes** ꙱ or **no** ꙱   Comments: **\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_** |

**Supplementary material 2:** Electronic portable aromatic rehabilitation (EPAR) diffuser–Instruction guide.

**Supplementary material 3:** Electronic portable aromatic rehabilitation (EPAR) diffuser–Set up and refill.

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