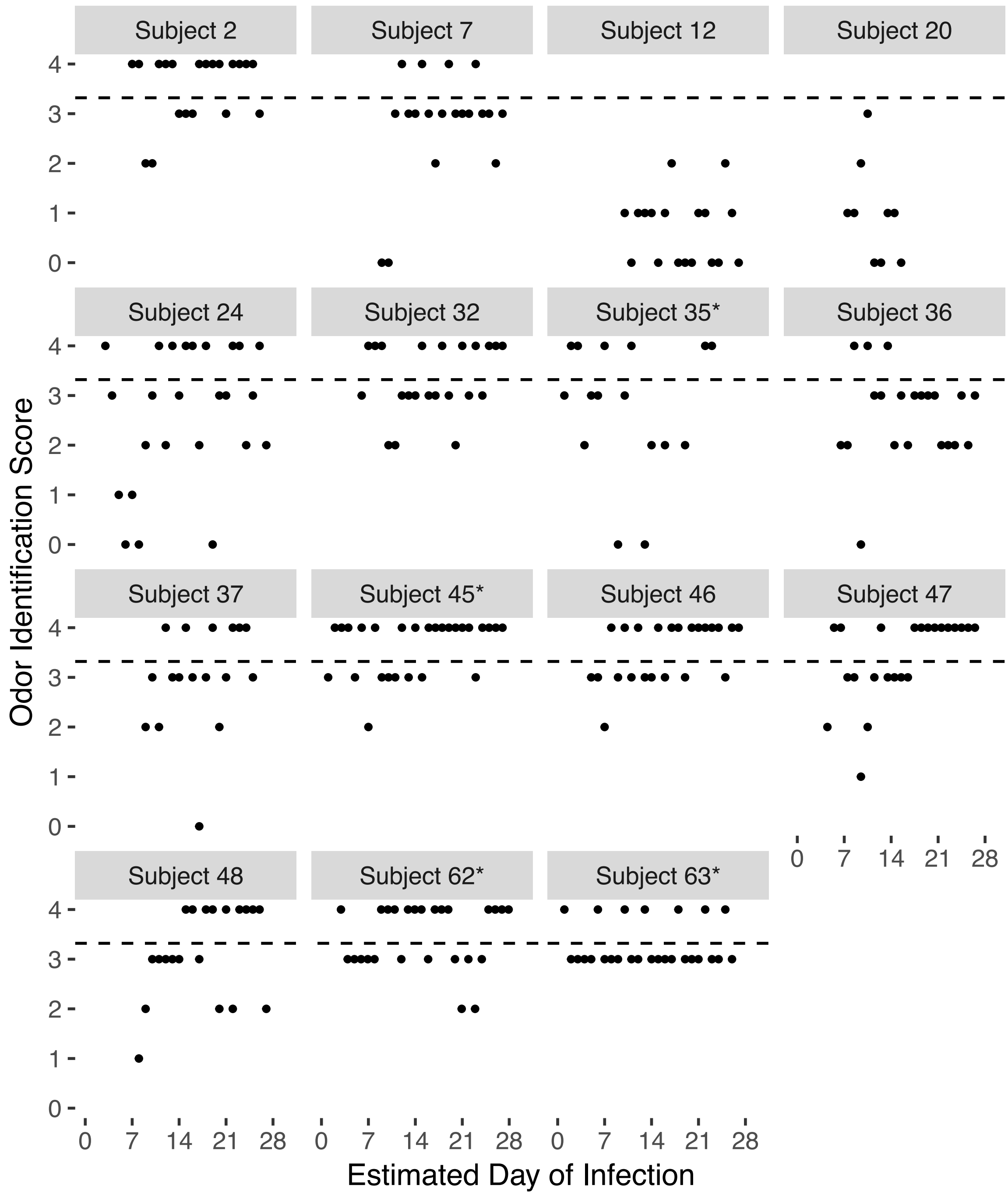
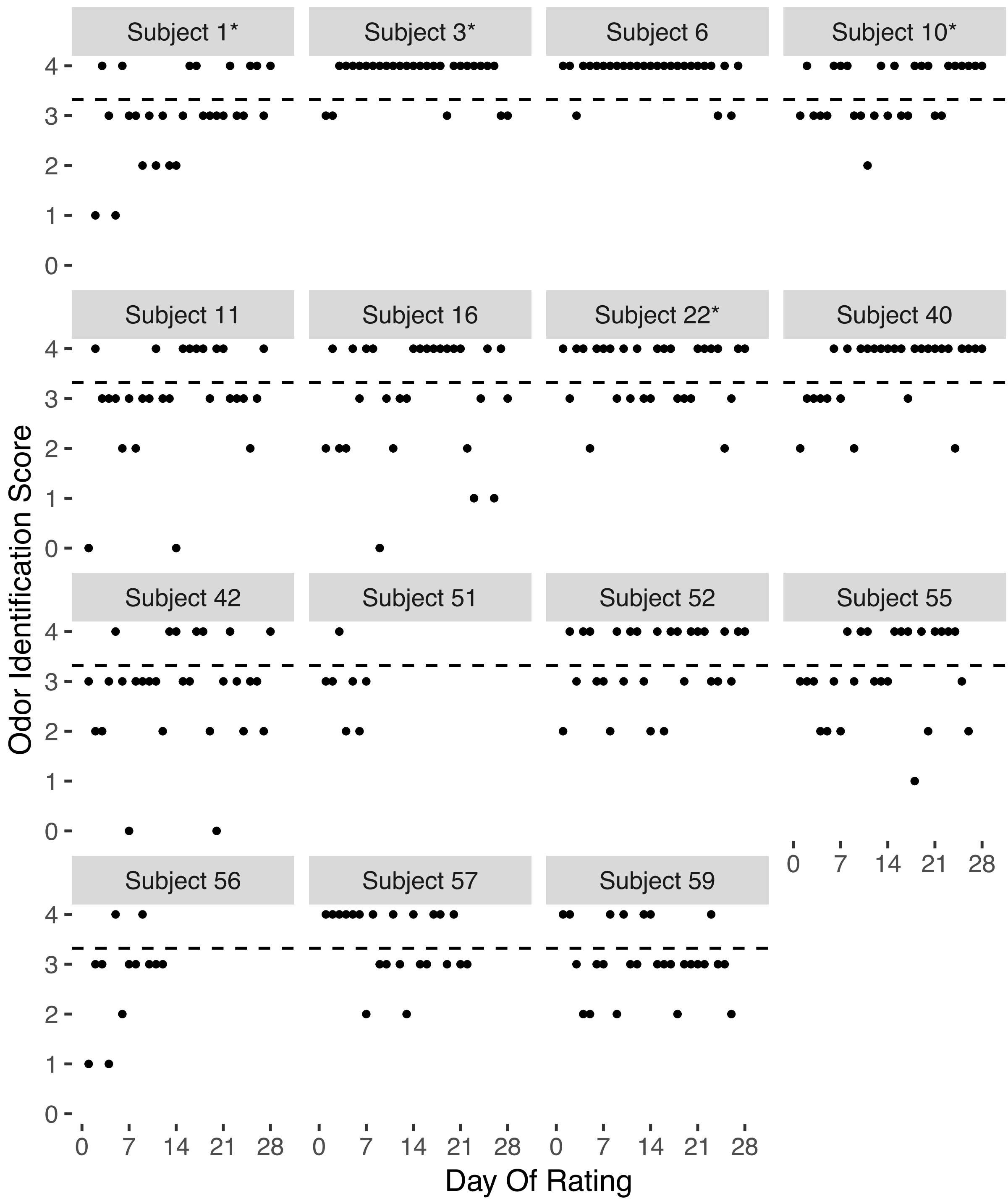
Supplemental Materials

Supplemental Figure 1



Raw daily odor identification scores from the ScentCheckPro cards over time for the COVID-19 cases (n=15) who entered the study on or before day 10 of their infection.

Supplemental Figure 2



Raw daily odor identification scores from the ScentCheckPro cards over time for the 15 controls.

Supplemental narrative and discussion of symptoms for the 4 cases

Subject 35

Subject 35 became a case during the study, enabling visualization of the falling and rising phases of her responses (see Figure 4). Her symptoms included cough, runny nose/congestion, sore throat, and headache. Regarding orthonasal scratch-n-sniff intensity ratings, daily means decreased through day 15 before recovering. OdorID scores showed a similar pattern, but data were noisier given the learning effect described above. Together, this suggests her orthonasal olfaction was transiently affected during active COVID-19 infection, as expected (e.g., [19, 71, 72]). Notably, she showed impaired smell even after nasal blockage resolved around Day 8, and her maximal smell loss and maximal nasal blockage were dyssynchronous. This is consistent with other reports showing COVID-19 smell loss is not associated with nasal blockage [4-7, 10], presumably because COVID-19-associated loss arises from ACE2 receptor-mediated disruption of the olfactory epithelium, and not the conductive losses seen with the common cold.

Her sourness ratings from the Sour Cherry jellybean declined until ~Day 15, when ratings began to increase, while sweetness declined until ~Day 6, before beginning to recover. The decline and subsequent rise of sweet and sour taste likely signifies normal recovery, although Figure 4 also shows dyssynchronous recovery of these tastes (i.e., sweetness did not recover as swiftly as sourness). These data indicate sweet and sour taste are each transiently affected with an active COVID-19 infection, and this was *not* merely a taste/flavor semantic confusion, as ratings were obtained while wearing nose clips. Subject 35 also showed large changes in burn from the Cinnamon jellybeans, suggesting oral chemesthesis is affected by COVID-19. The lack of burn from the Sour Cherry jellybeans serves as a negative control, indicating she was successful in discriminating between burn from a Cinnamon jellybean and a lack of burn from a Sour Cherry jellybean (a pattern also seen in the three other cases shown in Figure 4). These data indicate perception of oral burn can be affected by an active COVID-19 infection dyssynchronously from taste or smell. While patient anecdotes (including social media posts) have previously suggested nasal and/or oral chemesthesis may be affected by SARS-CoV-2 infection [39, 49, 73], the daily assessment and prospective design used here provide quantitative evidence of altered oral chemesthesis with COVID-19.

Subject 45

Subject 45 converted from being a close contact to an active COVID-19 case during the study, but unlike Subject 35, Subject 45 never reported any symptoms during her infection. Yet. despite being nominally asymptomatic, she still showed a clear drop in both OdorID performance and ratings of orthonasal intensity around Day 5 (with a bigger effect size for intensity). This highlights that some individuals infected with SARS-CoV-2 may be unaware of the impact on their sensory abilities, consistent with recent meta-analysis by Hannum and colleagues [8, 48]. Nor was this transient disruption in smell due to nasal blockage (as reported elsewhere [4-7, 10]). As her infection progressed, sourness from the Sour Cherry jellybean was variable, and sweetness from this jellybean steadily declined over the course of infection, again indicative of temporal dyssynchrony for different taste qualities. In contrast to burn rating from the Sour Cherry jellybean (which stayed near 0 across the study period, as expected), burn from the Cinnamon jellybean steadily increased in a monotonic fashion until a small drop was observed at the end of the study. Taken together with data from Subject 35, this indicates suggests oral chemesthesis is altered by active SARS-CoV-2 infection. Another study noted that during recovery from COVID-19, some patients report an increase in the ability to feel sensations in the mouth, including burning [49].

Subject 62

Subject 62's infection began 1 day before enrollment. Like Subject 45, he failed to self-report any symptoms, but unlike Subjects 35 and 45, his orthonasal intensity ratings and OdorID performance remained relatively constant throughout the study period, and his nasal blockage was generally low – while many individuals experience smell loss with COVID-19, some do not (e.g., [8, 48]). Regarding taste, noisy data make it hard to draw any strong conclusions, but it still seems he may have experienced substantial changes in sour and sweet taste. Regarding burn, he rated the burn from Sour Cherry jellybeans near zero for the entire study, suggesting he successfully distinguished burn from the Cinnamon jellybean from the lack of burn from the Sour Cherry jellybean (like the other cases). Two other values merit comment: in the 1st and 3rd week of testing, a sharp drop in sour taste intensity and sharp increase in burn intensity can be seen on two separate days; we suspect he may have misread the blinding codes, tasting the wrong sample on these days, as Sour Cherry jellybeans should be sour without any burn. Still, despite noise in his ratings, his panel plots for burn suggest he experienced transient changes in oral chemesthesis. If this case did in fact experience altered burn and altered taste without concomitant smell loss, this would emphasize that mechanisms of loss across all three modalities are distinct, with the caveat that the noise in these data should temper any strong inferences.

Subject 63

Subject 63 enrolled 2 weeks days before becoming a case. Because this greatly exceeds the expected incubation period of 5 to 7 days [37, 50], our study team contacted her via email. At that point, she reported a second exposure to an individual with COVID-19 – we assume this second exposure was the source of the infection documented here. Her data reveals changes in smell, taste, and chemesthesis as she transitioned from being a close contact to being a case, but the observation period only captures her initial illness without any recovery as she had enrolled after her first exposure that did not cause an infection. Consistent with this interpretation, she did not report any symptoms for the first 2 weeks, but then began reporting many symptoms (sore throat, fever or chills, dry cough, body aches, fatigue, diarrhea, nausea or vomiting, headache, and dry cough). Notably, her mean orthonasal ratings began to decline somewhat a few days before the estimated day of infection, but she indicated little to no nasal blockage, as expected [4-7, 10]. Also, her intensity ratings suggest she experienced hyposmia, rather than full anosmia, so it is unsurprising that her OdorID performance remained relatively constant across the study period, with some evidence of a slight learning effect near the beginning of the study. As discussed previously, this suggests rated smell intensity might provide more nuanced assessment of smell function versus odor identification. We have no obvious explanation for her unexpectedly low sourness ratings on the first two days of the study. Still, if her peak ratings during this initial (uninfected) period are tentatively treated as a baseline, we see a subsequent decline in sourness around the time her other symptoms appeared. For the rest of the study, her sour ratings remained relatively depressed, at least relative to the maximal values she reported pre-infection. In contrast, sweetness, while noisy, appeared more constant across the entire study. Tentatively, these plots suggest Subject 63 lost some taste function in a quality specific manner, as well as partial smell loss and loss of oral chemesthesis, with staggered timing of each, during her infection.