Smell: The Secret Super Sense

By Jason Rehg

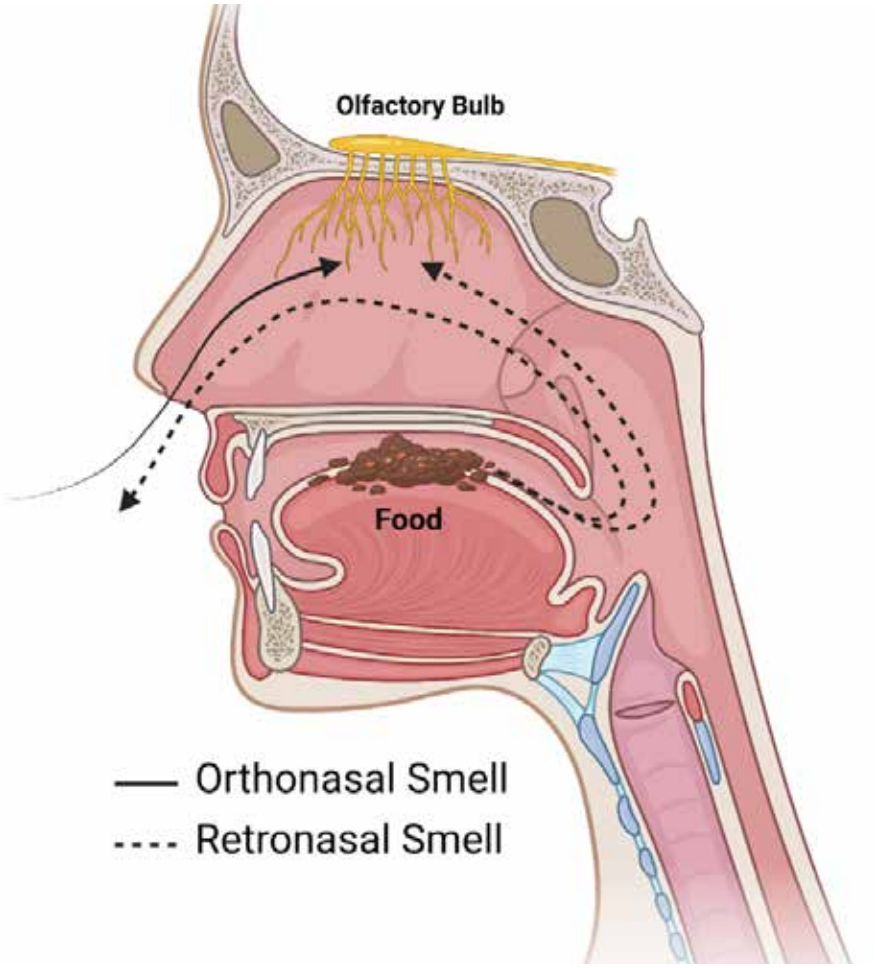
If you had to choose one sense to give up, which one would it be? Two years ago, Katherine Hansen might have responded "smell", but her answer is undoubtedly different today. Hansen, a real estate agent from Seattle, contracted COVID-19 in March of 2021 and awoke one morning to find that everything tasted of cardboard. Her keen sense of smell, once a source of pride, had vanished overnight. Now unable to tolerate eating most things, she relies on a diet of soups and shakes [1].

For millions of people around the world who contracted COVID-19, Hansen's experience is a familiar one. In addition to the classic array of symptoms associated with an upper respiratory infection - fever, cough, sore throat, etc. - a partial or complete loss of smell has emerged as a hallmark of the disorder. Called anosmia, this dimension has called new attention to a sense that is often overlooked. Fortunately for most, their sense of smell eventually recovers as they overcome the virus. But a minority of individuals, such as Hansen, are still waiting on its return [2].

While neuroscientists have been conducting in depth research into our sense of smell for decades, in the last three years COVID-19 has thrust our noses into the limelight. For individuals with anosmia, the impact of losing their smell is more than they would have expected, causing significant disruptions in their eating habits and mood. Who would have thought that our humble sense of smell could have such power?

Tasting with Your Nose

In our everyday speech, we use the words "taste" and "flavor" almost interchangeably. After all, taste is the sense that we associate most closely with the flavor of the food they consume. As a result, many are surprised to learn that taste contributes a relatively small piece to what we perceive as flavor. In reality, our sense of smell is the real star of the show and our taste but a supporting character. But how is smell so important if we mostly experience flavor once our food is already in our mouths?



The two smell pathways. Created by Jason Rehg in Biorender.

When we think about using our smell, we generally think of inhaling air from outside our bodies into our nose, allowing us to detect odors contained in the air we inhale. This type of smelling is called orthonasal smell - literally "straight smell". This type of smell allows us to detect desirable or dangerous odors in the environment around us, such as flowers, food aromas, and smoke. However there is a second way in which we smell without even realizing it most of the time.

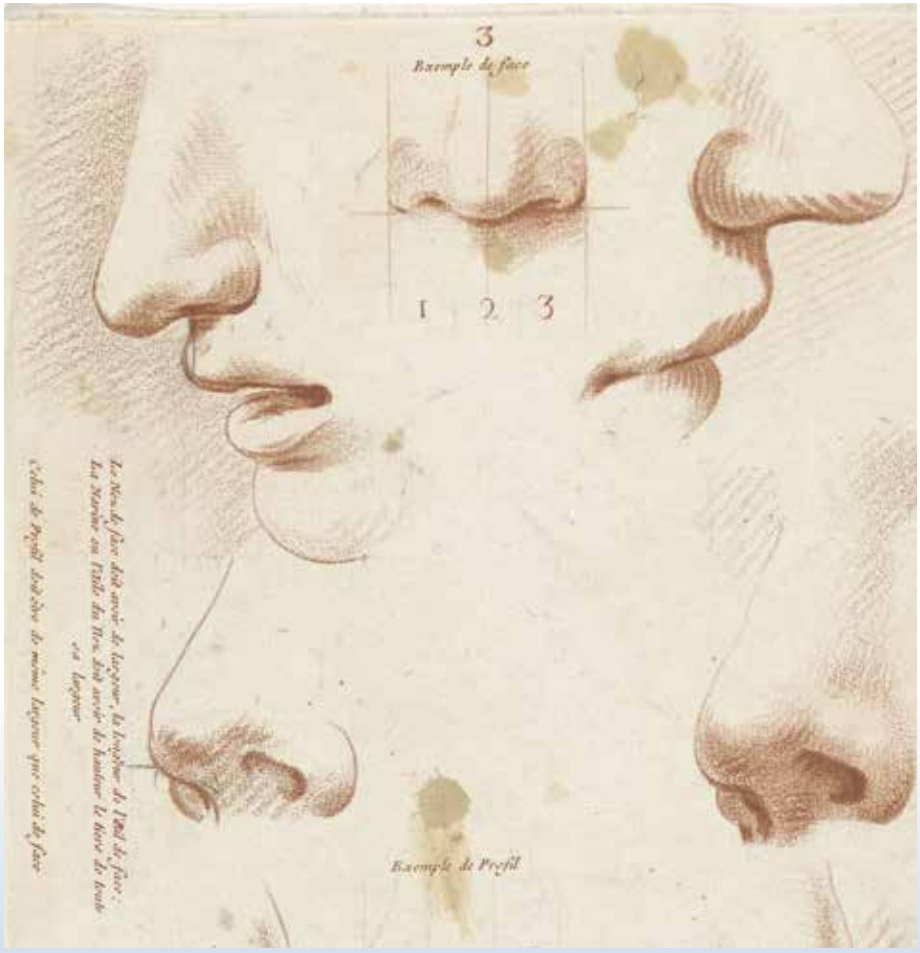
As our food breaks down in our mouths, it is released into the air, becoming vaporized. This vaporized food travels up from the back of our mouths into the nasal cavity, where we perceive it with our sense of smell. Called retronasal smell - or "back smell" - this action allows us to detect food odor in much more detail than orthonasal smell. Indeed, our smell detectors are specialized to detect different odors depending on which pathway - orthonasal or retronasal - they are traveling, a feature that allows us to perceive incredibly minute differences in the composition of our food as it travels through the retronasal pathway [3]. So how exactly does

smell differ from taste in the way it senses flavor?

How We Detect Odor

Taste and smell are both classified as "chemical senses"; that is—they involve specialized structures, called receptors, that can interpret the chemical composition of food or other substances in the environment. There are five types of taste receptors, each of which perceive a different flavor dimension. These receptors, located on cells called "taste buds", tell us if what we are eating is sweet, salty, sour, savory, or bitter. The specialization of our taste buds is directly shaped by survival needs. For example, our "sweet" receptors detect sugars and carbohydrates that provide efficient energy for our body, while "bitter" receptors tell us if there are chemical compounds that could be toxic. This function means that taste is designed to detect broad categories of compounds with a limited number of receptor types. By contrast, our smell is designed to detect high levels of specificity [4].

Inside our nose is a complex mosaic of smell receptors that extend like hairs into the nasal cavity. Each of these receptors is specialized to detect particular structures that may be part of an odor molecule. When an odor enters the nose, it binds to the set of receptors that correspond to each of its parts. Like a fingerprint, odor molecules possess individual characteristics that allow us to detect incredibly minute differences between molecules. Most foods and smells contain many different molecules, meaning that in addition to each molecule having its own "fingerprint", each food has a unique set of "fingerprints" based on which molecules make it up. The processing of smell, however, doesn't stop in the nose.

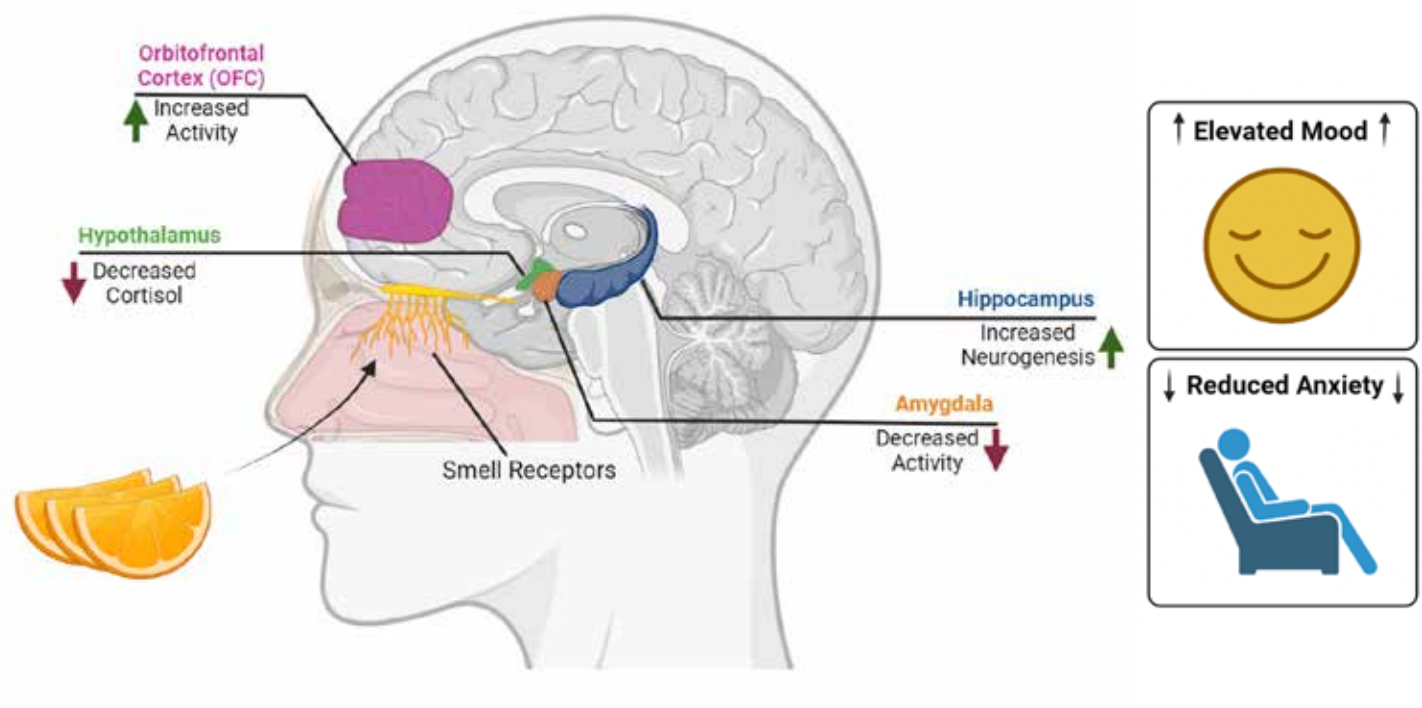


The information from our smell receptors is passed up directly into the olfactory bulb, the first stop in smell processing. The unique set of receptors to which each odor binds gives rise to an equally unique pattern of activation in this area, called an odor map. The olfactory bulb is organized in such a way that closely related smells are grouped together. For example, molecules that produce a "fruity" flavor all activate cells nearby each other. As a result, just looking at the pattern of activation in the olfactory bulb can tell you exactly what the flavor being perceived is.

This complex system of identification is what allows us to perceive so much variation, even in incredibly similar stimuli, such as different types of red wine. While there is some room for personal interpretation giving rise to perceived variation in closely related flavors, brain imaging studies of the olfactory bulb have confirmed that different activation patterns do indeed arise. Thus, a pinot noir from California produces a slightly different odor map than a pinot noir from France, allowing us to tell them apart. Indeed, studies have even shown that we can detect differences in food odors as small as a single atom in some cases [3].

Feeling with Your Nose

Incredibly acute perception is not the only thing that makes our sense of smell so special, but also the way it affects the rest of our brain. As it turns out, our smell



Pleasant smells cause changes in several regions of the brain responsible for emotional processing, elevating mood and reducing anxiety. Created by Jason Rehg in BioRender.

is wired differently than any of our other senses. The olfactory bulb directly connects the limbic system, a set of structures that are primarily responsible for memory and emotion processing in the brain. This means that odors are able to manipulate our memory, mood, and emotion much more readily than other senses, which are more indirectly connected to this region. This is no surprise when considering just how potent memories of smell are.

As an example, think about your favorite comfort food growing up. For me, this is the wild blueberry pie I had each summer in Maine. Each time I smell it again, especially after being deprived of it for quite some time, I am transported back to memories of warm days on the coast and enveloped in the joy of this recollection. I can almost smell the salt water and pine in the air. If, as for me, you still have your comfort food on occasion (or often), you are probably familiar with this sensation. After all, there is a reason we call these foods "comfort" foods - it is for the comforting sensation that they offer.

The key to smell's power to evoke memory and directly influence our emotional state is in its rewarding properties. When we smell pleasant odors, it directly activates the reward system in our brains. Brain imaging studies in humans have shown that the orbitofrontal cortex (OFC), a region of the brain that encodes how rewarding or pleasurable stimuli are, is directly activated by smell. Sensing pleasurable smells resulted in activation of the same areas that responded to methamphetamine and monetary rewards [5]. Unsurprisingly, the rewarding aspects of smell also involve the neurotransmitter dopamine. Dopamine levels, which are regulated by rewarding stimuli, elevate in response to pleasant smells. Increased dopamine levels drive us to seek out rewards. This makes sense when you think about how smell often affects our appetite, with attractive food smells making us more hungry [3]. Likewise, it is dopamine that motivates you to get out of bed in the morning when you smell coffee wafting in from the kitchen.

Beyond momentary enjoyment, these rewarding properties can have long lasting effects, altering our general mood. Neuroscientists often distinguish emotion from mood, with the former being more transient and situational while the latter is longer lasting. Roughly speaking, emotion and mood map onto each other like weather to climate. The weather is influenced by the climate, but can vary, and climate is ultimately defined by the weather. At the psychological level, there is a good deal of evidence that supports the positive effects of pleasant smells on mood. For example, studies examining the effects of daily cologne use on the mood of men and women found that those using cologne had significantly more

positive scores on depression and anxiety scales when compared to those using a placebo [6].

Important biological findings that support the behavioral effects of smells have been identified in mice, which have a very similar olfactory system to humans. Depression and anxiety have been closely linked to a decrease in neurogenesis, a process specific to the hippocampus, involving the creation of new neurons. In one study, researchers used lavender to enrich the environment of mice with a pleasant scent. After 3 weeks in this environment, the researchers looked at the hippocampus, an important structure that regulates mood and memory. Interestingly, mice that had been living in the lavender scented environment showed increased hippocampal neurogenesis, suggesting that this smell had improved their mood at a biological level [7]. Yet another study used green odor, a smell that emanates from green leaves and is associated with healing effects in humans and other animals. In this study, mice exposed to green odor showed similar improvements in behavioral tests of depression to others that were given an antidepressant, specifically a selective-serotonin reuptake inhibitor (SSRI). SSRIs produce their mood-enhancing effects by increasing the amount of serotonin in the brain. Likewise, blocking serotonin prevented the positive effects of green odor, suggesting that this smell enhances mood via a similar biological mechanism [8].

The power of smell over our mood and emotion, however, is a two way street. Pleasant smells can even make us less anxious, decreasing levels of cortisol, a hormone that becomes elevated when we are stressed [6]. As much as the enjoyment of pleasant smells can make us happy, repulsive smells can ruin our day. The same researchers that demonstrated the positive effects of cologne on mood found that those living in proximity to swine operations, which produce many unpleasant odors, had higher rates of anxiety and depression, along with generally lower average mood [9]. Even odors that are subtle enough to often be subconscious, such as air pollution and body odor, have been shown to lower mood. In our brains, unpleasant smells increase activity in the center of the amygdala, which regulates fear and anxiety [6]. With these findings in mind, it's no wonder there's such a large industry for scented candles.

Given such an important connection between smell and emotion, it is no surprise that loss of smell was so distressing for Katherine Hansen. Without her sense of smell, she was robbed of all of the rewarding and mood-boosting effects it offers. The food aromas that normally generated an appetite were gone, likely making it difficult to eat. Indeed eating itself was a chore without the enjoyment of flavor. Hansen's psychological distress mirrors many others who have lost their smell from COVID-19, but some have been painfully aware of the consequences of anosmia since long before the pandemic.

A Gift and a Curse: When Smell Goes Wrong

When the first cases of COVID-19 reported a loss of smell amongst the symptoms, many understandably glossed over it in favor of worrying about the virus' other symptoms. But researchers who had been studying anosmia and other olfactory disorders for years knew well how significant this dimension of COVID could be, if it stuck around. When the pandemic began, the negative psychological effects of a loss of smell were already well established. A review of the impact of olfactory disorders on quality of life, published in 2014, reported that olfactory disorders disrupted several aspects of psychological well being. Anhedonia, impairment of the ability to experience pleasure, was commonly reported, which often was accompanied by reduced appetite. Some reported experiencing social isolation due to self-ostracization, unable to experience the world like those around them do, an effect that likely interacts with significant disruptions in mood. Indeed, up to one-third of those with olfactory disorders meet criteria for clinical depression [10]. Furthermore, while those with anosmia experienced these symptoms, the review identified another disorder in which they may be even more severe.

While anosmia is no walk in the park, those with phantosmia may wish they couldn't smell anything. In phantosmia, so called because of the "phantom" odors those with the disorder perceive, the world is not completely devoid of smell, but it's hardly pleasant. Everyday smells become miswired, turning from pleasant odors to repulsive ones; the daily breakfast of eggs and toast tastes rotten, while laundry detergent smells of ammonia. Some evidence suggests that those with phantosmia experience the lowest quality of life amongst olfactory disorders. When we consider the ways in which unpleasant smells impact our mood and our brain, this makes sense. Individuals with this disorder are not only robbed of the rewarding effects of pleasant odors, they are also constantly exposed to unpleasant stimuli that drag down their mood

even further.

The relationship between smell and mood is reciprocal - just as olfactory disorders can disrupt mood, mood disorders can disrupt smell. Many psychiatric disorders in which mood is significantly dysregulated also involve altered sense of smell. Anhedonia is a core feature of clinical depression, and many with this disorder experience decreased sensitivity to smell, along with lower appetite and enjoyment of food [11]. Likewise, the restrictive eating disorder anorexia nervosa also entails decreased sensitivity to smell. Deficits in the reward processing system of the brain are believed to be at the center of anorexia, meaning that smells that normally drive appetite and enjoyment of food don't have quite the same effect on those with the disorder [12].

Harnessing the Other Senses

Although many more have had to experience the distressing consequences of losing one's smell as a result of COVID-19, there is an important silver lining. The increased attention on olfactory disorders that has resulted from the pandemic has inspired more efforts to find ways to improve quality of life for those with this deficit. A new cookbook, authored by chefs Ryan Riley and Kimberly Duke and titled "Taste and Flavour", contains recipes that are specifically designed to enhance the eating experience of those whose senses have been limited by COVID-19. The book capitalizes on the ways in which the other senses contribute to our perception of flavor. For example, many retain or regain their sense of taste, even if smell is impaired. As a result, they are still able to perceive basic flavors, like sweet, salty, sour, and savory. Riley describes how one of his favorite recipes, the miso butter potatoes with green herb vinegar, uses intense savory flavors from the miso, vinegar tartness, and pepper spiciness to create a stimulating experience for those who cannot rely on their nose to perceive flavor. In addition to taste, the dishes also capitalize on visual appeal and texture, both of which can enhance flavor [13].

Riley and Duke's work fits into a broader emerging field called "neurogastronomy", which seeks to use our understanding of how our brain processes flavor to compensate for many health-related food restrictions and sensory deficits. Within this field, chefs and neuroscience researchers have already been working together for years to compensate for olfactory deficits in patients with Alzheimer's disease and cancer, glucose intolerance in diabetics, and many more conditions.

Thanks to the hard work of these individuals, there is reason to be optimistic for Katherine Hansen and others facing the same predicament. Even so, their experience demonstrates just how important our sense of smell is, and how thankful most of us should be that it works properly, as we never know if it could become altered. In the meantime, it's worth taking an extra minute each day to stop and smell the roses, quite literally.

References

1. Rabin, R. C. (2021, January 2). Some Covid Survivors Haunted by Loss of Smell and Taste. The New York Times. https://www.nytimes.com/2021/01/02/health/coronavirus-smell-taste.html

2. Burges Watson, D. L., Campbell, M., Hopkins, C., Smith, B., Kelly, C., & Deary, V. (2021). Altered smell and taste: Anosmia, parosmia and the impact of long Covid-19. PLoS ONE, 16(9), e0256998. https://doi.org/10.1371/journal.pone.0256998

3. Shepherd, G. M. (2006). Smell images and the flavour system in the human brain. Nature, 444(7117), Article 7117. https://doi.org/10.1038/nature05405

4. Birkett, M. A., & Carlson, N. R. (2017). Physiology of behavior. Pearson. https://lib.hpu.edu.vn/handle/123456789/33486

5. Kringelbach, M. L. (2015). The pleasure of food: Underlying brain mechanisms of eating and other pleasures. Flavour, 4(1), 20. https://doi.org/10.1186/s13411-014-0029-2

6. Kontaris, I., East, B. S., & Wilson, D. A. (2020). Behavioral and Neurobiological Convergence of Odor, Mood and Emotion: A Review. Frontiers in Behavioral Neuroscience, 14. https://www.frontiersin.org/articles/10.3389/fnbeh.2020.00035

7. Rusznák, Z., Sengul, G., Paxinos, G., Kim, W. S., & Fu, Y. (2018). Odor Enrichment Increases Hippocampal Neuron Numbers in Mouse. Experimental Neurobiology, 27(2), 94–102. https://doi.org/10.5607/en.2018.27.2.94

8. Nakatomi, Y., Yokoyama, C., Kinoshita, S., Masaki, D., Tsuchida, H., Onoe, H., Yoshimoto, K., & Fukui, K. (2008). Serotonergic mediation of the antidepressant-like effect of the green leaves odor in mice. Neuroscience Letters, 436(2), 167–170. https://doi.org/10.1016/j.neulet.2008.03.013

9. Schiffman, S. S., Miller, E. A., Suggs, M. S., & Graham, B. G. (1995). The effect of environmental odors emanating from commercial swine operations on the mood of nearby residents. Brain Research Bulletin, 37(4), 369–375. https://doi.org/10.1016/0361-9230(95)00015-1

10. Croy, I., Nordin, S., & Hummel, T. (2014). Olfactory Disorders and Quality of Life—An Updated Review. Chemical Senses, 39(3), 185–194. https://doi.org/10.1093/chemse/bjt072

11. Burón, E., & Bulbena, A. (2013). Olfaction in affective and anxiety disorders: A review of the literature. Psychopathology, 46(2), 63–74. https://doi.org/10.1159/000338717

12. Rapps, N., Giel, K. E., Söhngen, E., Salini, A., Enck, P., Bischoff, S. C., & Zipfel, S. (2010). Olfactory deficits in patients with anorexia nervosa. European Eating Disorders Review: The Journal of the Eating Disorders Association, 18(5), 385–389. https://doi.org/10.1002/erv.1010

13. Rothman, S. (2021, April 10). Lost taste and smell from COVID-19? A new cookbook aims to help. ABC News. Retrieved November 18, 2022, from https://abcnews.go.com/Health/loss-taste-smell-covid-19-cookbook-aims/story?id=76887711