

## Sniffing for Parkinson Disease

Dogs are known as man's best friend, and the benefits of dog ownership are enormous, including aiding people with special needs, being deployed in search-and-rescue operations, and tracking down criminals. Given their sophisticated olfactory function, dogs can potentially be used for medical screening.

A sniffer dog or detection dog is trained to use its sense of smell to detect a variety of substances. Volatile organic compounds (VOCs) generated during the pathological process enable sniffer dogs to identify human diseases.<sup>1</sup> Recently, sniffer dogs have been utilized in the coronavirus disease 2019 (COVID-19) pandemic, and they may be potentially employed as a fast and cost-effective screening tool for coronavirus disease 2019 infection.<sup>2</sup> The immune response of the body to the viral infection gives rise to VOCs, and the chemicals that constitute the VOCs can be identified using metabolomics.<sup>3</sup>

Many countries are experiencing the silver tsunami, with the rapid rise of aging-related neurodegenerative diseases, such as Alzheimer disease and Parkinson disease. There are estimated 6.5 million people in America living with Alzheimer disease, and the numbers are projected to reach 13.8 million in 2060,<sup>4</sup> whereas Parkinson disease affects 1%-2% of the population older than 65 years of age globally.<sup>5</sup> As such, there is a mounting need to develop a fast and easy-to-use screening tool to identify people at risk or patients at early stage of these diseases for early intervention. Some people, known as super smellers, are able to differentiate the odor released by patients with Parkinson disease.<sup>6</sup> Considering their superb olfactory system, sniffer dogs were trained to identify Parkinson disease with high sensitivity and specificity in a recent double-blind study.<sup>7</sup> The study involved 109 patients with Parkinson disease who were on medications, 654 subjects without Parkinson disease, 37 patients with drug-naïve Parkinson disease, and 185 non-Parkinson's

disease controls. The authors found that most of the sniffer dogs were able to identify patients with Parkinson disease who were on medications, with 91% index test sensitivity, 95% specificity, and excellent positive and negative likelihood ratios. For drug-naïve patients the sensitivity was 89%, and the specificity was 86%. These observations suggest that sniffer dogs can potentially be used to conduct noninvasive, fast, and cost-effective screening of patients with Parkinson disease in the community. This is the first reported study using sniffer dogs to detect Parkinson disease successfully.

Despite the interesting findings, the study needs to be replicated independently. For example, similarly trained sniffer dogs have to be tested in independent cohorts of patients with Parkinson disease to validate the generalizability of its broad application. In addition, the capability of sub-breeds of the dogs needs to be further tested and investigated. The diverse genetic background between dogs of the same species may make it hard to select an appropriate breed. In addition, the well-being of the dogs is another concern. Discomfort has been complained by the super smeller following smell detection for 2 hours.<sup>6</sup> As dogs cannot verbalize, studies into the workload, stress, and diet that could affect the olfactory performance will be useful.<sup>8</sup> Personal hygiene in Parkinson disease can be a potential confounder because difficulty in daily activities may lead to odors that can be confused with those produced by medications for Parkinson disease. Therefore, healthy subjects with poor personal hygiene habits or other diseases that may hamper daily living activities (such as stroke and other neurodegenerative diseases) can be used as controls in future studies.

It has been found that compounds in the sebum may account for the smell unique to patients with Parkinson disease in whom seborrhea is more common and severe than in age-matched subjects.<sup>9</sup> A spectrometric study analyzing sebum samples has demonstrated that metabolites are different between patients with Parkinson disease and healthy subjects.<sup>10</sup> Such analysis in patients with Parkinson disease and controls that have been initially identified by the dogs will be useful to determine the exact metabolite variances. The samples recognized by the sniffer dogs have a higher chance to contain VOCs specific to Parkinson disease. If we can pinpoint the nature of the smell, which is likely a metabolic signature that has yet to be established, the chemicals can be collected through a skin swab to quantify its level as a biomarker. Alternatively, an "electric nose" model has been developed to

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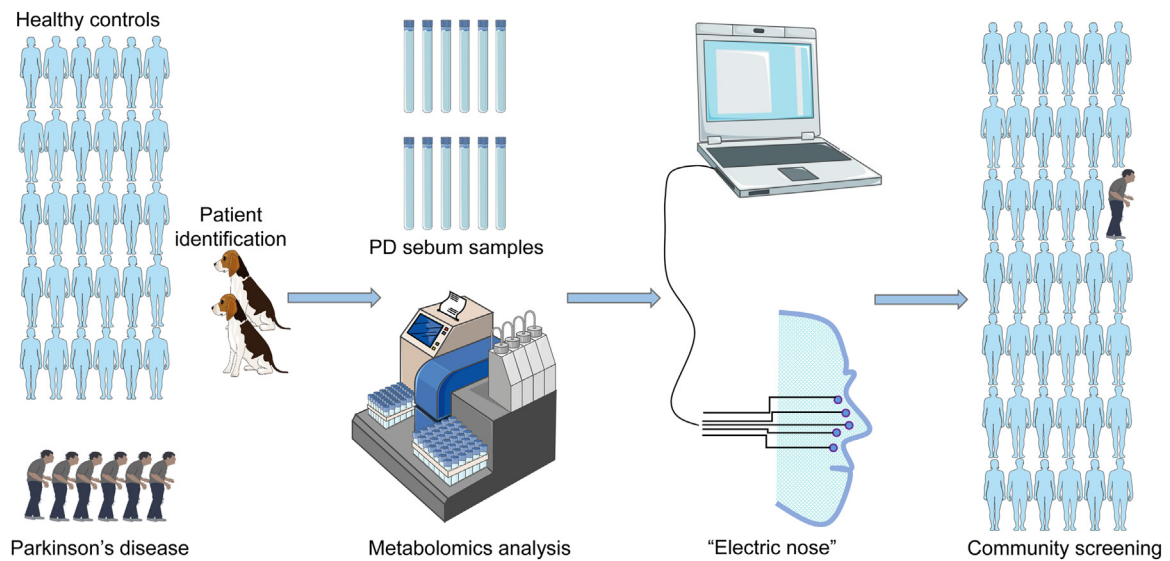
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**Figure 1** Role of sniffer dogs in identifying Parkinson disease. In a case control study, skin swabs from medicated or patients with drug-naïve Parkinson disease and age- and sex-matched controls were sniffed by trained dogs. The dogs identified Parkinson disease from among the study subjects with a high degree of sensitivity and specificity. The chemical compounds secreted by patients with Parkinson disease could be identified by metabolomics studies. This suggests that Parkinson disease-specific odor signatures can potentially be used to establish an “electric nose” model to facilitate screening for Parkinson disease in the community. Figure was partially generated using templates from Servier Medical Art, which is licensed under a Creative Commons Attribution 3.0 Unported License.

facilitate recognition of specific odors during cooking and other activities. Thus, it may be utilized to screen for Parkinson disease or other diseases, with proper sensors detecting identifiable Parkinson disease odor and an algorithm recognizing a relevant smell pattern for Parkinson disease (Figure 1). The electric nose can obviate the need for repeated training of the dogs, and the reliability can be significantly enhanced.

Dogs are excellent human companions, and ideal for old folks with physical and mental disabilities. Sniffer dogs can potentially serve multiple functions in patients with Parkinson disease and at-risk individuals if their ability to identify and differentiate Parkinson disease and its subtypes can be independently demonstrated and confirmed.

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