Journal of
Alzheimer's Disease & Parkinsonism

Masaoka and Phillips, J Alzheimers Dis Parkinsonism 2016, 6:3
DOI: 10.4172/2161-0460.1000232

Commentary Open Access

Does The Occurrence of Sleep Disorder or Deficits in Olfaction Provide an Early Indication of Neurodegeneration and Subsequent Dementia?

Yuri Masaoka[1]* and Anthony Phillips[2]

[1]*Department of Physiology, Showa University School of Medicine, Japan*
[2]*Department of Psychiatry, Djavad Mowafaghian Centre for Brain Health, University of British Columbia, Canada*

It is now well recognized that impairments in olfaction often provide the first sign of neurodegenerative disorders such as Alzheimer's (AD) and Parkinson's disease (PD) [1-5]. Recent studies have also revealed that olfactory deficits are observed in individuals living with psychiatric disorders including depression [6], and schizophrenia [7]. Accordingly, it is hypothesized that abnormalities in brain function may account for difficulties in the detection odor or identification of specific classes of odor. The first indications of an impairment in olfaction are often manifested as a difficulty in the recognition of specific odors whereas the detection threshold for odor does not differ from age-matched controls [5]. A subsequent progression to anosmia involves further impairment of the classification of odors, and finally an inability to detect the presence of an odor [5]. The ability to identify a specific odor is quite complex, involving as it does the capacity to encode and store in memory past perceptions of a unique volatile chemical signature, which can then be and recalled and categorized by a single name. Olfactory memory encoding and storage involves neural activity within the hippocampus and parahipppocampus, and recall and recognition of the memory of a specific odor engages a neural network linking between amygdala-hippocampus and orbitofrontal cortex [8,9]. As with other forms of prospective memory function, the process by which specific odors are identified may be referred to as "travelling back to the future."

The anatomical pathways involved in processing of odor are amongst the best characterized neural systems in the forebrain involving receptors on the terminal regions of olfactory within the nasal mucosa, which in turn project via the olfactory tubercle and piriform cortex, to structures within the limbic region including entorhinal cortex, amygdala and hippocampus [10]. It is now known that these olfactory limbic structures are damaged in the early stages of PD and AD, as well as psychiatric disorders also linked to neurodegenerative disorders [1-5, 6]. Accordingly, deficits in olfactory perception may reflect this underlying process of neurodegeneration. Related changes may include difficulty with the recall of emotional memory, a lack of appropriate emotional responses, as well as subsequent problems in cognition and social interactions.

In light of recent evidence, it is important to recognize that deficits in olfaction are often co-morbid with disturbances in sleep behavior including changes in the sleep cycle and insomnia [11]. Abnormalities in rapid eye movement (REM) sleep stage are observed in early stage of Parkinson's disease [12,13]. REM sleep is characterized by rapid eye movements, cortical activation, vivid dreaming, skeletal muscle paralysis and muscle twitches, and is mediated by a distributed network within the brainstem, hypothalamus and limbic regions, including a key role for the amygdala in the regulation of REM sleep [14]. Disturbance in the neural control of REM sleep is linked directly to REM sleep behavior disorder (RBD), characterized by dream-enacted behavior associated with skeletal muscle atonia during REM sleep [15]. Schenck et al. [13] report that 11 out of 29 patients with RBD developed a parkinsonian disorder at a mean interval of 3.7 years after RBD onsets. Other findings indicate that RBD may proceed dementia or PD in 66.7 % of patients [12]. When these observations are considered in conjunction with the finding that olfactory impairment has been observed within a similar time frame (7 years) prior to diagnosis of PD [16], it is tempting to speculate that both these impairments in olfaction and RBD may reflect common mechanisms of neurodegeneration.

In our previous case study, we examined decision-making skills, facial expression recognition which served as an index for social cognition, olfaction, and dopamine positron emission tomography imaging in RBD patients [17]. These detailed measures revealed a patient with impaired social cognition and decision-making skills, as well as impaired olfactory identification, and reduced dopamine positron emission tomography imaging indicating striatal terminal loss. Braak et al. [18] suggested that impairment of the amygdala and striatum occurs at the same stage as α-synucleinopathy, and we hypothesized that symptoms of RBD may follow the same progression as is the case for PD patients.

Given the role of amygdala in both REM sleep regulation [14,17] and deficits in olfaction [8,9,10] noted above, perhaps pathophysiological changes within the amygdala may contribute to abnormality in both RBD and olfaction. Indeed, Maquet et al. [19] postulate that activation of the amygdala complex during REM sleep contributes to memory processing that involves a functional link between the amygdala, the hippocampus formation and cortical areas. Accordingly, disturbance of REM sleep observed in RBD may be causally related to impairment of cognitive, social and memory tasks [17].

At this juncture it is difficult to specify whether the observed deficits in olfaction, as distinct from sleep disorder may provide the earliest signal of impending cognitive dysfunction. While 80% of PD, AD and other neuro generative disorders including patients with Type 1 Myotonic dystrophy have olfactory deficits, the majority are unaware of their condition [5]. In contrast, with respect to a sleep disorder, individuals who become self-aware of their condition or are informed by a family member often seek medical assistance. The extent of the co-occurrence of olfactory deficits and sleeps disorders such as RBD remains to be determined, and it must also be noted that the occurrence of olfactory deficits of unknown origin with or without RBD may precede PD. Nevertheless, proof of their co-occurrence may provide a more accurate and reliable indication of early stages of neurodegeneration and the possible co-occurrence of mild cognitive impairment.

***Corresponding author:** Yuri Masaoka, Department of Physiology, Showa University School of Medicine, Japan, Tel: +81 3 3784 8113; E-mail: faustus@med.showa-u.ac.jp

Received March 30, 2016; **Accepted** April 12, 2016; **Published** April 19, 2016

Citation: Masaoka Y, Phillips A (2016) Does The Occurrence of Sleep Disorder or Deficits in Olfaction Provide an Early Indication of Neurodegeneration and Subsequent Dementia? J Alzheimers Dis Parkinsonism 6: 232. doi: 10.4172/2161-0460.1000232

Acknowledgement

This study is supported by a JSPS KAKENHI Grant Number 15K00210.

References

1. Doty RL, Deems DA, Stellar S (1988) Olfactory dysfunction in parkinsonism: a general deficit unrelated to neurologic signs, disease stage, or disease duration. Neurology 38: 1237-1244.
2. Hawkes C (2003) Olfaction in neurodegenerative disorder. Mov Disord 18: 364-372.
3. Talamo BR, Rudel R, Kosik KS, Lee VM, Neff S, et al. (1989) Pathological changes in olfactory neurons in patients with Alzheimer's disease. Nature 337: 736-739.
4. Thompson MD, Knee K, Golden CJ (1998) Olfaction in persons with Alzheimer's disease. Neuropsychol Rev 8: 11-23.
5. Masaoka Y, Pantelis C, Phillips A, Kawamura M, Mimura M, et al. (2013) Markers of brain illness may be hidden in your olfactory ability: a Japanese perspective. Neurosci Lett 549: 182-185.
6. Zucco GM, Bollini F (2011) Odour recognition memory and odour identification in patients with mild and severe major depressive disorders. Psychiatry Res 190: 217-220.
7. Brewer WJ, Wood SJ, McGorry PD, Francey SM, Phillips LJ, et al. (2003) Impairment of olfactory identification ability in individuals at ultra-high risk for psychosis who later develop schizophrenia. Am J Psychiatry 160: 1790-1794.
8. Rolls ET (2001) The rules of formation of the olfactory representations found in the orbitofrontal cortex olfactory areas in primates. Chem Senses 26: 595-604.
9. Masaoka Y, Harding IH, Koiwa N, Yoshida M, Harrison BJ, et al. (2014) The neural cascade of olfactory processing: a combined fMRI-EEG study. Respir Physiol Neurobiol 204: 71-77.
10. Yeshurun Y, Sobel N (2010) An odor is not worth a thousand words: from multidimensional odors to unidimensional odor objects. Annu Rev Psychol 61: 219-241, C1-5.
11. Postuma RB, Lang AE, Massicotte-Marquez J, Montplaisir J (2006) Potential early markers of Parkinson disease in idiopathic REM sleep behavior disorder. Neurology 66: 845-851.
12. Boeve BF, Silber MH, Ferman TJ, Lucas JA, Parisi JE (2001) Association of REM sleep behavior disorder and neurodegenerative disease may reflect an underlying synucleinopathy. Mov Disord 16: 622-630.
13. Schenck CH, Bundlie SR, Mahowald MW (1996) Delayed emergence of a parkinsonian disorder in 38% of 29 older men initially diagnosed with idiopathic rapid eye movement sleep behaviour disorder. Neurology 46: 388-393.
14. International Classification of Sleep Disorders (2005) Diagnostic and Coding Manual (Edn 2) American Academy of Sleep Medicine, Westchester.
15. Fraigne JJ, Torontali ZA, Snow MB, Peever JH (2015) REM Sleep at its Core - Circuits, Neurotransmitters, and Pathophysiology. Front Neurol 6: 123.
16. Marras C, Goldman S, Smith A, Barney P, Aston D, et al. (2005) Smell identification ability in twin pairs discordant for Parkinson's disease. Mov Disord 20: 687-693.
17. Koyama S, Kobayakawa M, Tachibana N, Masaoka Y, Homma I, et al. (2012) Neuropsychological and radiological assessments of two cases with apparent idiopathic rapid eye movement sleep behaviour disorder. Eur Neurol 67: 18-25.
18. Braak H, Bohl JR, Müller CM, Rüb U, de Vos RA, et al. (2006) Stanley Fahn Lecture 2005: The staging procedure for the inclusion body pathology associated with sporadic Parkinson's disease reconsidered. Mov Disord 21: 2042-2051.
19. Maquet P, Péters J, Aerts J, Delfiore G, Degueldre C, et al. (1996) Functional neuroanatomy of human rapid-eye-movement sleep and dreaming. Nature 383: 163-166.