Disputes & Debates: Editors' Choice

Steven Galetta, MD, FAAN, Section Editor

Editors' note: Olfaction and incident Parkinson disease in US white and black older adults

In "Olfaction and incident Parkinson disease in US white and black older adults," authors Chen et al. found that hyposmia was a risk factor for Parkinson disease (PD) even beyond 5 years of follow-up. Mahlknecht et al. confirmed these results using a different cohort of patients with PD. Author Chen notes that even with relatively small sample sizes in both studies, the results were notably consistent, especially in regard to temporality and a potential sex difference. Future studies could focus on whether hyposmia is predictive of PD beyond 10 years.

Megan Alcauskas, MD, and Steven Galetta, MD Neurology[®] 2018;90:940. doi:10.1212/WNL.00000000005514

Reader response: Olfaction and incident Parkinson disease in US white and black older adults

Philipp Mahlknecht, Stefan Kiechl, Johann Willeit, Werner Poewe, and Klaus Seppi (Innsbruck, Austria) *Neurology*[®] 2018;90:940. doi:10.1212/WNL.00000000005511

We read the article by Chen et al.¹ that reported hyposmia as a risk factor for incident Parkinson disease (PD) in the ABC Health Study with interest. While, in the short term, this association had been established in other cohorts,^{2,3} Chen et al. could show that smell loss is associated with incident PD beyond 5 years of follow-up. This is an important detail, as the identification of PD risk cohorts heavily relies on the temporal course of the markers in relation to the development of defining motor symptoms.⁴ We sought to replicate the findings of Chen et al. in the cohort of the prospective population-based Bruneck Study of the 2005 assessment (n = 539 without PD or secondary parkinsonism; median age 67.2 [25th–75th percentile; 61.4–76.2] years; 290 females).⁵ Participants underwent the 12-item Sniffin' Sticks test at baseline. Cases of incident PD were identified by in-person examination after 5 and 10 years using the United Kingdom Parkinson's Disease Society Brain Bank criteria (11 and 9 cases, respectively).⁵ The relative risk for hyposmic participants to develop PD was 2.99 (95% confidence interval 0.89–10.06) over the first 5 years, 4.06 (1.03–15.91) over the second 5 years, and 3.60 (1.48–8.78) over the entire follow-up (4.54 [1.25–16.51] in men and 2.79 [0.78–9.96] in women), corroborating the observations of Chen et al.

- 4. Mahlknecht P, Seppi K, Poewe W. The concept of prodromal Parkinson's disease. J Parkinsons Dis 2015;5:681-697.
- Mahlknecht P, Gasperi A, Djamshidian A, et al. Performance of the Movement Disorders Society criteria for prodromal Parkinson's disease: A population-based 10-year study. Mov Disord 2018;33:405–413.

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Author disclosures are available upon request (journal@neurology.org).

Chen H, Shrestha S, Huang X, et al. Olfaction and incident Parkinson disease in US white and black older adults. Neurology 2017;89: 1441–1447.

Ross GW, Petrovitch H, Abbott RD, et al. Association of olfactory dysfunction with risk for future Parkinson's disease. Ann Neurol 2008; 63:167–173.

Berg D, Godau J, Seppi K, et al. The PRIPS study: screening battery for subjects at risk for Parkinson's disease. Eur J Neurol 2013;20: 102–108.

Author response: Olfaction and incident Parkinson disease in US white and black older adults

Honglei Chen (East Lansing) *Neurology*[®] 2018;90:941. doi:10.1212/WNL.000000000005515

We reported that hyposmia predicted the risk of Parkinson disease (PD) in both the short and intermediate term.¹ We are glad that Mahlknecht et al. were able to quickly confirm our findings in their independent study population. Interestingly, despite relatively small sample sizes (in both studies) and some differences in study populations and methods, the results were remarkably consistent, including the temporal relationship and the suggestion for a potential sex difference. These findings, as noted by Mahlknecht et al., are important because such details (e. g., temporality, specificity) will eventually determine the clinical usefulness of hyposmia as an early marker for PD. As both studies only assessed the sense of smell once and had a defined length of follow-up, future studies should evaluate whether hyposmia predicts PD risk beyond 10 years.

The importance of hyposmia and other prodromal symptoms in PD risk characterization has been well received by the clinical community.² We see this as an excellent opportunity to understand early stages of PD development and beyond.³ For example, future studies may use these symptoms as intermediate phenotypes to identify factors that contribute to prodromal neurodegeneration and factors that affect later progression to clinical PD.

2. Berg D, Postuma RB, Adler CH, et al. MDS research criteria for prodromal Parkinson's disease. Mov Disord 2015;30:1600–1611.

 Chen H, Burton EA, Ross GW, et al. Research on the premotor symptoms of Parkinson's disease: clinical and etiological implications. Environ Health Perspect 2013;121:1245–1252.

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Editors' note: Teaching Video NeuroImages: Palsy of conjugate horizontal gaze and face due to isolated abducens nuclear infarction

In reference to "Teaching Video NeuroImages: Palsy of conjugate horizontal gaze and face due to isolated abducens nuclear infarction," Dr. Miller points out that the title may mislead readers into thinking that both the horizontal gaze palsy and the facial nerve palsy were caused by the abducens nuclear infarction, rather than the ipsilateral facial palsy being caused by damage to the facial nerve fascicles bordering the abducens nucleus. Author Kim agrees with Dr. Miller's concerns and has issued a correction to the title, changing it to "Palsy of conjugate horizontal gaze and face due to a restricted infarction involving the abducens nucleus." The correction appears on page 942.

Megan Alcauskas, MD, and Steven Galetta, MD Neurology[®] 2018;90:941. doi:10.1212/WNL.000000000005510

Author disclosures are available upon request (journal@neurology.org).

Chen H, Shrestha S, Huang X, et al. Olfaction and incident Parkinson disease in US white and black older adults. Neurology 2017;89: 1441–1447.

Reader response: Teaching Video NeuroImages: Palsy of conjugate horizontal gaze and face due to isolated abducens nuclear infarction

Neil R. Miller (Baltimore) Neurology[®] 2018;90:942. doi:10.1212/WNL.000000000005513

I read and viewed with interest the Teaching Video NeuroImage by Kim et al.¹ Clearly, the reported patient did not have an "isolated" abducens nuclear infarction, as that would have caused a truly isolated ipsilateral horizontal gaze palsy. The ipsilateral facial palsy was caused by damage to the facial nerve fascicles adjacent to the abducens nucleus. Although the authors indicate this in the body of the text,¹ the title of the article suggests that both the horizontal gaze palsy and the facial palsy were caused by the abducens nuclear infarction. I would hate for those who simply read the title of the otherwise excellent vignette to think that facial nerve fibers are somehow located within the abducens nerve nucleus. It is confusing enough for physicians to remember that the nucleus contains both axons destined for the ipsilateral lateral rectus and axons of the medial longitudinal fasciculus destined for the contralateral medial rectus so that abducens nuclear lesions cause an ipsilateral horizontal gaze palsy rather than a sixth nerve palsy.

 Kim JS, Jeong SH, Choi JY, Kim HJ. Teaching Video NeuroImages: palsy of conjugate horizontal gaze and face due to isolated abducens nuclear infarction. Neurology 2017;89:e180–e181.

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Author response: Teaching Video NeuroImages: Palsy of conjugate horizontal gaze and face due to isolated abducens nuclear infarction

Ji-Soo Kim (Seongnam, South Korea) *Neurology*[®] 2018;90:942. doi:10.1212/WNL.000000000005512

I thank Dr. Miller for the interest in our article, ¹ and for raising an issue on the title. I agree that the title may provide a misconception that the facial nerve fibers are located within the abducens nucleus. Thus, the title may be better stated as "Palsy of conjugate horizontal gaze and face due to a restricted infarction involving the abducens nucleus."

 Kim JS, Jeong SH, Choi JY, Kim HJ. Teaching Video NeuroImages: Palsy of conjugate horizontal gaze and face due to isolated abducens nuclear infarction. Neurology 2017;89:e180–e181.

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CORRECTION

Teaching Video NeuroImages: Palsy of conjugate horizontal gaze and face due to isolated abducens nuclear infarction

Neurology[®] 2018;90:942. doi:10.1212/WNL.000000000005533

In the Teaching Video NeuroImages "Palsy of conjugate horizontal gaze and face due to isolated abducens nuclear infarction" by Kim et al.,¹ the title is misleading with regards to etiology of the ipsilateral facial palsy. The title should read "Palsy of conjugate horizontal gaze and face due to a restricted infarction involving the abducens nucleus." The authors regret any confusion caused by the original title.

Reference

 Kim JS, Jeong SH, Choi JY, Kim HJ. Teaching Video NeuroImages: palsy of conjugate horizontal gaze and face due to isolated abducens nuclear infarction. Neurology 2017;89:e180–e181.

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Teaching Video NeuroImages: Palsy of conjugate horizontal gaze and face due to isolated abducens nuclear infarction Neurology 2018;90;942 DOI 10.1212/WNL.000000000005533

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