Disputes & Debates: Editors' Choice

Editors' Note: Age-Related Changes in Neurologic Examination and Sensory Nerve Amplitude in the General Population

Dr. Taams et al. reported age-related differences in neurologic examination and nerve conduction studies in a cross-sectional population-based study of 4,179 participants in a suburb of Rotterdam, the Netherlands. They found 90.5% of participants did not have polyneuropathy based on a symptom questionnaire, neurologic examination, and nerve conduction studies that were classified by an expert panel. The frequency of "normal" examination features declined with age, most notably for vibration sense at the hallux, Achilles tendon reflexes, and sural sensory nerve action potential amplitudes. By contrast, superficial pain sensation and patellar tendon reflexes remained stable with age. The authors suggested that clinical interpretation of vibration sense, Achilles tendon reflexes, and sural nerve amplitudes should be viewed in the context of age. In response, Dr. Hodzelmans et al. counter that age may simply be an independent risk factor for the development of axonal damage, such that these "abnormal" findings may have clinical implications and support a diagnosis of axonal polyneuropathy. Responding to these comments, the authors acknowledge this possibility because they cannot exclude whether older patients with such findings in their cohort may progress to clinically apparent axonal polyneuropathy in the absence of longitudinal data. This exchange demonstrates the challenges of defining population-based norms for neurologic and electrophysiologic examination parameters, particularly when relying on cross-sectional findings.

Aravind Ganesh, MD, DPhil, FRCPC, and Steven Galetta, MD
Neurology® 2024;102:e209408. doi:10.1212/WNL.0000000000209408

Reader Response: Age-Related Changes in Neurologic Examination and Sensory Nerve Amplitude in the General Population

Jurriaan J.A. Hodzelmans (Maastricht, the Netherlands), Marcus L.F. Janssen (Maastricht, the Netherlands), Janneke G.J. Hoeijmakers (Maastricht, the Netherlands), and Nadia A. Sutedja (Maastricht, the Netherlands)
Neurology® 2024;102:e209409. doi:10.1212/WNL.0000000000209409

We read with interest the article by Taams et al.[1] who described age-related changes of features of peripheral nerve function. We compliment the authors on this large population-based study attempting to define the boundaries of normal aging using standardized methods and thorough screening procedures. Normal features were clearly less prevalent in older participants. The authors suggest that clinical interpretation of especially vibration sense, Achilles tendon reflex, and sural nerve amplitude, should be in the context of age and propose to accept lower values in older persons.

As a gold standard for distal axonal polyneuropathy is still lacking,[2] we would like to open the provocative discussion on whether we should indeed use age-dependent cutoff values in the diagnosis of polyneuropathy, of course, in the context of appropriate clinical findings.

While the currently most accepted view is to use cutoff values that are corrected for age,[3] age may merely be an independent risk factor for the development of axonal damage. Thus, deterioration

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

of some of the investigated features by Taams et al., especially a lower sural nerve amplitude, reflect (length-dependent) axonal degeneration.[4,5] Therefore, it is thinkable that, even in the elderly, abnormal findings may have clinical implications and support the diagnosis of axonal polyneuropathy.

1. Taams NE, Drenthen J, Hanewinckel R, Ikram MA, van Doorn PA. Age-related changes in neurologic examination and sensory nerve amplitude in the general population: aging of the peripheral nervous system. *Neurology*. 2023;101(13):e1351-e1358. doi:10.1212/WNL.0000000000207665
2. England JD, Gronseth GS, Franklin G, et al. Distal symmetrical polyneuropathy: definition for clinical research. *Muscle Nerve*. 2005;31(1):113-123. doi:10.1002/mus.20233
3. Vrancken AF, Kalmijn S, Brugman F, Rinkel GJ, Notermans NC. The meaning of distal sensory loss and absent ankle reflexes in relation to age: a meta-analysis. *J Neurol*. 2006;253(5):578-589. doi:10.1007/s00415-005-0064-0
4. Preston DC, Shapiro B. Electromyography and neuromuscular disorders: clinical electrophysiologic correlations. *Mcgill J Med*. 2006;9(2):173. doi:10.1016/C2010-0-68780-3
5. Callaghan BC, Price RS, Feldman EL. Distal symmetric polyneuropathy: a review. *JAMA*. 2015;314(20):2172-2181. doi:10.1001/jama.2015.13611

Author Response: Age-Related Changes in Neurologic Examination and Sensory Nerve Amplitude in the General Population

Pieter A. van Doorn (Rotterdam, the Netherlands) and Noor E. Taams (Rotterdam, the Netherlands)
Neurology® 2024;102:e209410. doi:10.1212/WNL.0000000000209410

We thank Hodzelmans et al. for their interest in our article describing age-related changes in neurologic examination and sensory nerve amplitude.[1] They question age-dependent values in the diagnosis of polyneuropathy, especially regarding sural nerve amplitude values. We provided values for features of the neurologic examination and sural nerve amplitude for different age categories in the general population that may be useful when interpreting diagnostic findings, for example, when investigating a person once in an outpatient clinic.[1] The association between lower sural sensory nerve amplitudes and older age may be part of normal aging variation or may be the first sign of (subclinical) axonal polyneuropathy.[1,2] Both possibilities were described in the discussion of our study, especially because the results were based on cross-sectional analysis and we cannot exclude that persons may progress to clinically apparent chronic axonal polyneuropathy. Eventually, with longitudinal data, we aim to elucidate whether lower sural nerve amplitude is the first sign of a mild or subclinical axonal polyneuropathy. In the meantime, we emphasize the importance of the multimodal process when diagnosing polyneuropathy by including symptoms, neurologic examination and nerve conduction studies while taking into account the effect of aging.[1,3]

1. Taams NE, Drenthen J, Hanewinckel R, Ikram MA, van Doorn PA. Age-related changes in neurologic examination and sensory nerve amplitude in the general population: aging of the peripheral nervous system. *Neurology*. 2023;101(13):e1351-e1358. doi:10.1212/WNL.0000000000207665
2. Vrancken AF, Franssen H, Wokke JH, Teunissen LL, Notermans NC. Chronic idiopathic axonal polyneuropathy and successful aging of the peripheral nervous system in elderly people. *Arch Neurol*. 2002;59(4):533-540. doi:10.1001/archneur.59.4.533
3. England JD, Gronseth GS, Franklin G, et al. Distal symmetrical polyneuropathy: definition for clinical research. *Muscle Nerve*. 2005;31(1):113-123. doi:10.1002/mus.20233

CORRECTIONS

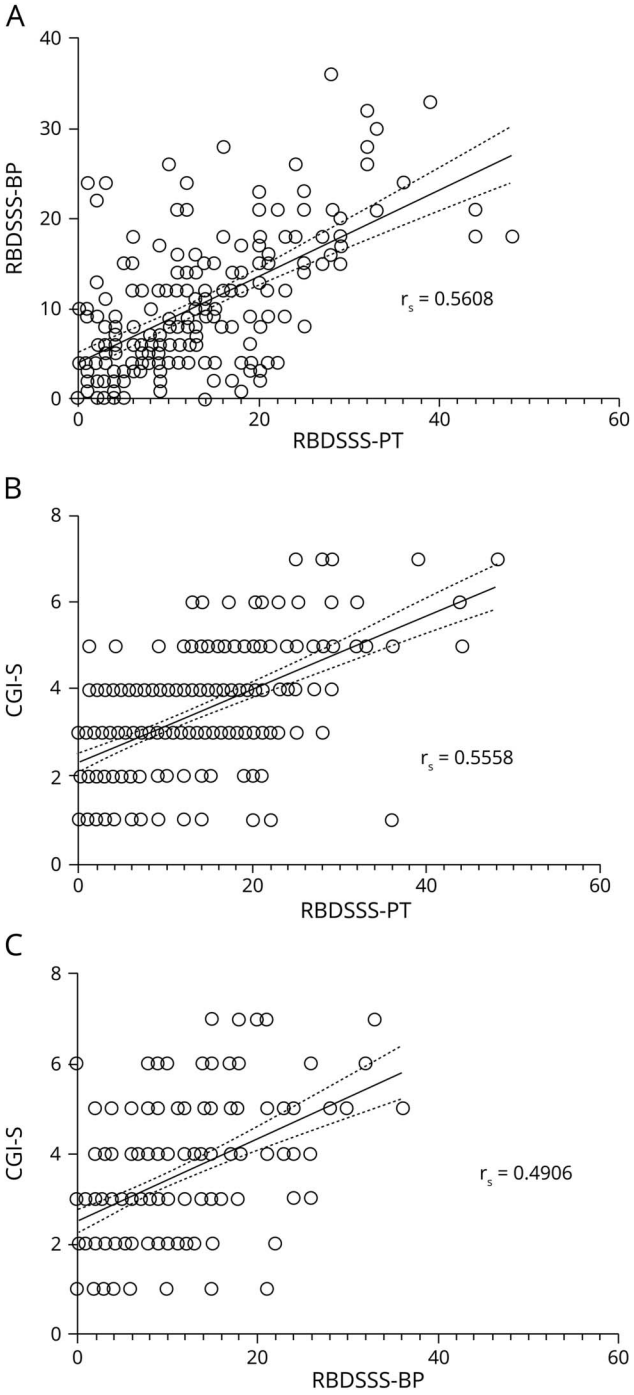
Validation of the RBD Symptom Severity Scale in the North American Prodromal Synucleinopathy Consortium

Neurology® 2024;102:e209355. doi:10.1212/WNL.0000000000209355

In the Research Article "Validation of the RBD Symptom Severity Scale in the North American Prodromal Synucleinopathy Consortium" by Choudhury et al.,[1] author Andrea Busicesu's

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

Figure 5 Correlations Between the RBDSSS-PT, RBDSSS-BP, and CGI-S



(A) Correlation between the RBDSSS-PT and RBDSSS-BP, r = 0.5608, n = 214. (B) Correlation between the RBDSSS-PT and CGI-S, r = 0.5558, n = 261. (C) Correlation between the RBDSSS-BP and CGI-S, r = 0.4906, n = 214. All correlations are significant with $p < 0.0001$. Solid line represents linear regression with dashed lines representing 95% CIs. CGI-S = Clinical Global Impression Scale of Severity; RBDSSS = RBD Symptom Severity Scale; RBDSSS-BP = RBD Symptom Severity Scale–bed partner version; RBDSSS-PT = RBD Symptom Severity Scale–participant version.

affiliation should be listed as "University of Arizona College of Medicine, Phoenix." The publisher regrets the error.

In addition, the x-axis of Figure 5C should be labeled "RBDSSS-BP." The corrected figure is below. The editorial office regrets the error.

Reference

1. Choudhury P, Lee-Iannotti JK, Busicescu AO, et al.; NAPS Consortium. Validation of the RBD Symptom Severity Scale in the North American Prodromal Synucleinopathy Consortium. *Neurology*. 2024;102(3):e208008. doi:10.1212/WNL.0000000000208008

Untangling the Landscape of Neurologic and Psychiatric Post-COVID-19 Conditions

Neurology® 2024;102:e209464. doi:10.1212/WNL.0000000000209464

In the Editorial "Untangling the Landscape of Neurologic and Psychiatric Post-COVID-19 Conditions" by Chow and Chopra,[1] the correspondence email should be listed as "erchow@kingcounty.gov." The editorial staff regret the error.

Reference

1. Chow EJ, Chopra A. Untangling the landscape of neurologic and psychiatric post-COVID-19 conditions. *Neurology*. 2024;102(5):e209211. doi:10.1212/WNL.0000000000209211

CORRECTION & REPLACEMENTS

Variation in Resting Metabolic Rate Affects Identification of Metabolic Change in Geographically Distinct Cohorts of Patients With ALS

Neurology® 2024;102:e209407. doi:10.1212/WNL.0000000000209407

In the Research Article "Variation in Resting Metabolic Rate Affects Identification of Metabolic Change in Geographically Distinct Cohorts of Patients With ALS" by Holdom et al.,[1] the ninth author's name should be listed as "Ruben P.A. van Eijk." The publisher regrets the error. In addition, the third sentence of the Results section in the Abstract was corrected from "Of the 22 predication equations…" to "Of the 22 prediction equations…." The complete sentence should read "Of the 22 prediction equations assessed, the Sabounchi Structure 4 (S4) equation performed relatively well across all control cohorts." The authors regret the error. The article has been replaced with a corrected version.

Reference

1. Holdom CJ, van Mantgem MRJ, He J, et al. Variation in resting metabolic rate affects identification of metabolic change in geographically distinct cohorts of patients with ALS. *Neurology*. 2024;102(5):e208117. doi:10.1212/WNL.0000000000208117

Baseline Clinical and Blood Biomarkers in Patients With Preataxic and Early-Stage Disease Spinocerebellar Ataxia 1 and 3

Neurology® 2024;102:e209455. doi:10.1212/WNL.0000000000209455

In the Research Article "Baseline Clinical and Blood Biomarkers in Patients With Preataxic and Early-Stage Disease Spinocerebellar Ataxia 1 and 3" by Tezenas du Montcel et al.,[1] the methods for spinocerebellar ataxia type 1 and 3 genetic testing were not supplied or referenced. The methods used for genotyping and determination of CAG repeat lengths are now listed in eAppendix 1. In addition, those developing the methods and working on the study in Europe

and the United States should have been listed as authors in the byline. Authors who contributed to genotyping include Karla P. Figueroa, Stefan M. Pulst, Anne-Laure Fauret-Amsellem, and Claudia Dufke. Among them, the omitted authors include Figueroa, Pulst, Fauret-Amsellem, and Dufke. The omitted authors and their disclosures are now listed with the article.

In addition, Appendix 2 listing the READISCA Consortium coinvestigators has been updated to include 2 previously omitted coinvestigators: William Ondo and Haris I. Sair.

The article has been replaced by a corrected version. The original version with the changes highlighted is available from a link in the corrected article. The authors regret the omissions.

Reference

1. Tezenas du Montcel S, Petit E, Olubajo T, et al. Baseline clinical and blood biomarkers in patients with preataxic and early-stage disease spinocerebellar ataxia 1 and 3. *Neurology*. 2023;100(17):e1836-e1848. doi:10.1212/WNL.0000000000207088