

Editors' Note: Grabenhenrich and Roll critique the methodology and design in the study by Kerti et al. on the association between glucose metabolism and memory performance. The authors conduct additional statistical analysis to support their results. *Neurology's* sometime neuromythologist and historian, William Landau, cites quotations from Parkinson's historical monograph to comment on the article by Bohnen et al. on gait speed in Parkinson disease. The authors respond.

—Chafic Karam, MD, and Robert C. Griggs, MD

HIGHER GLUCOSE LEVELS ASSOCIATED WITH LOWER MEMORY AND REDUCED HIPPOCAMPAL MICROSTRUCTURE

Linus B. Grabenhenrich, Stephanie Roll, Berlin: Kerti et al.¹ attempted to establish an association between glucose metabolism and memory performance. They concluded that higher blood glucose levels negatively influenced cognition. We believe that the design and methodology is inadequate to draw these conclusions.

The bivariate approaches do not consider that confounding factors might be related to both glucose metabolism and memory (e.g., age). The hippocampus as a potential mediator is stated to lose significance upon adjustment for even the most basic confounders. Presenting raw and adjusted models would allow the assessment of the role of confounders.

In addition, we could not interpret the standardized regression coefficients for sex as a dichotomous trait. Measures of precision (e.g., confidence intervals [CIs]) for associations were not reported. To translate the authors' results to real-world quantities, we do not see how to use many significant test results without adjustment for multiple testing. We were not able to derive a meaningful adjusted measure of association between HbA1c and the presented memory tests.

The authors should provide a comprehensible magnitude adjusted for potential confounders, for example: "5 mmol/mol higher HbA1c levels were associated with an average of 1.5 (0.5–3.0) fewer words remembered in the delayed recall test."

Author Response: Lucia Kerti, A. Veronica Witte, Ulrike Grittner, Agnes Floeel, Berlin: The authors thank Drs. Grabenhenrich and Roll for their comments. We reported significant associations of markers of

glucose metabolism with memory performance in 141 older adults.¹ In addition to bivariate analyses, we reported adjusted multiple regression models, which were controlled for confounding factors including age and sex using a stepwise selection method.

We have conducted alternative models using the "enter" method for age and sex variables and obtained similar results to those we reported, thus supporting our original conclusions. HbA1c remained significantly associated with the primary outcome (delayed recall) and the other 2 subtests of memory performance ($p < 0.05$). If a Bonferroni correction for multiple testing is applied, the associations between HbA1c and delayed recall and between HbA1c and learning ability remained significant. According to the regression model, a difference in HbA1c levels of 5 mmol/mol was associated with a reduction of 1.4 remembered words (95% CI 0.4–2.3) in the delayed recall task.

In our study, we outlined strengths and weaknesses of a cross-sectional design and highlighted the necessity of future longitudinal trials. A recent epidemiologic survey of glucose levels and dementia revealed that higher glucose levels may be a risk factor for dementia, even in those without diabetes.²

© 2014 American Academy of Neurology

1. Kerti L, Witte AV, Winkler A, Grittner U, Rujescu D, Floel A. Higher glucose levels associated with lower memory and reduced hippocampal microstructure. *Neurology* 2013; 81:1746–1752.
2. Crane PK, Walker R, Hubbard RA, et al. Glucose levels and risk of dementia. *N Engl J Med* 2013;369:540–548.

GAIT SPEED IN PARKINSON DISEASE CORRELATES WITH CHOLINERGIC DEGENERATION

William M. Landau, St. Louis: The authors of the article concerning gait speed in Parkinson disease (PD)¹ seem to be unaware of a pertinent earlier clinical observation.² Further quotations from that text:

As the malady proceeds the propensity to lean forward becomes invincible, and the patient is thereby forced to step on the toes and the forepart of the feet, whilst the upper part of the body is thrown so far forward as to render it difficult to avoid falling on the face. In some cases, when this state of the malady is attained, the

Neurology[®]

Higher glucose levels associated with lower memory and reduced hippocampal microstructure

Linus B. Grabenhenrich, Lucia Kerti, Stephanie Roll, et al.

Neurology 2014;83;102

DOI 10.1212/WNL.0000000000000558

This information is current as of June 30, 2014

Updated Information & Services	including high resolution figures, can be found at: http://n.neurology.org/content/83/1/102.1.full
References	This article cites 2 articles, 1 of which you can access for free at: http://n.neurology.org/content/83/1/102.1.full#ref-list-1
Errata	An erratum has been published regarding this article. Please see next page or: /content/83/10/950.full.pdf
Permissions & Licensing	Information about reproducing this article in parts (figures, tables) or in its entirety can be found online at: http://www.neurology.org/about/about_the_journal#permissions
Reprints	Information about ordering reprints can be found online: http://n.neurology.org/subscribers/advertise

Neurology® is the official journal of the American Academy of Neurology. Published continuously since 1951, it is now a weekly with 48 issues per year. Copyright © 2014 American Academy of Neurology. All rights reserved. Print ISSN: 0028-3878. Online ISSN: 1526-632X.



fatal since the ORs for infection and hospitalization for stroke were similar across racial groups. Several reviews of randomized controlled trials evaluating vitamin D for the prevention of infection have indicated conflicting results.^{4,5} There is no conclusive evidence that vitamin D is related to the incidence of infection. The hypotheses that vitamin D may contribute to stroke deaths in black patients after acute infection is intriguing but untested.

© 2014 American Academy of Neurology

1. Levine DA, Langa KM, Rogers MA. Acute infection contributes to racial disparities in stroke mortality. *Neurology* 2014;82:914–921.
2. Grant WB, Peiris AN. Possible role of serum 25-hydroxyvitamin D in black-white health disparities in the United States. *J Am Med Dir Assoc* 2010;11:617–628.
3. Brøndum-Jacobsen P, Nordestgaard BG, Schnohr P, Benn M. 25-hydroxyvitamin D and symptomatic ischemic stroke: an original study and meta-analysis. *Ann Neurol* 2013;73:38–47.
4. Jolliffe DA, Griffiths CJ, Martineau AR. Vitamin D in the prevention of acute respiratory infection: systematic review of clinical studies. *J Steroid Biochem Mol Biol* 2013;136:321–329.
5. Yamshchikov AV, Desai NS, Blumberg HM, Ziegler TR, Tangpricha V. Vitamin D for treatment and prevention of infectious diseases: a systematic review of randomized controlled trials. *Endocr Pract* 2009;15:438–449.

CORRECTION

Higher glucose levels associated with lower memory and reduced hippocampal microstructure

In the WriteClick® Editor's Choice correspondence regarding "Higher glucose levels associated with lower memory and reduced hippocampal microstructure" by L.B. Grabenhenrich and S. Roll (*Neurology*® 2014;83:102), there is an error in the byline of the Author Response. The fourth author's name is misspelled and should read "Agnes Flöel." The editorial staff regrets the error.

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