LETTER

Reply to Newman: Quantification of biological aging in young adults is not the same thing as the onset of obesity

Newman (1) highlights a challenge faced by studies seeking to measure aging: How to distinguish the process of aging from its causes. This is simple enough when causes originate outside the organism (e.g., environmental toxicants). But what about conditions inside the organism? Are age-related diseases the cause of biological changes in aging? Or is aging the root cause of age-related diseases?

Our study (2) attempted to: (*i*) disentangle aging from age-related disease by studying young people in their 20s and 30s, decades before age-related disease onset; and (*ii*) disentangle aging from specific pathologies of individual organ systems by tracking coordinated change over time across several different organ systems. We tracked 18 biomarkers of the cardiovascular, metabolic, and immune systems, kidneys, liver, lungs, gums, and DNA integrity in 954 humans in the Dunedin Study. Even though study members were all aged 26 y at baseline, we detected aging-related biomarker changes over the ensuing 12 y. Those changes showed coordinated decline in functioning of multiple organ systems, as predicted by theories of aging. Moreover, study members with faster change, what we called accelerated "Pace of Aging," showed signs of aging that gerontologists test in individuals with advanced chronological age: diminished physical functioning, cognitive decline, self-perception of poorer health, and aged facial appearance. Our findings argue that individual differences in aging are already established years before age-related disease onset. One implication is that early intervention to slow aging could postpone onset of age-related diseases.

Newman's (1) concern is that our measurements of aging may be overly influenced by weight gain during the middle years of the life course. This weight gain, Newman argues, is a cause of aging, not a sign of it. And yet, metabolic changes, including changes thought to cause weight gain, are among the so-called "hallmarks of aging" (3).

Whether weight gain is a sign of aging or a cause, the two measures of aging that we studied (Biological Age and Pace of Aging) are more than weight gain. First, our *Supporting Information* (2) shows that change in body mass index (BMI) accounts for only a fraction of variance in change among the other 17 biomarkers used to calculate Pace of Aging (table S2 in ref. 2). Second, the *Supporting Information* shows that leaving BMI out of Pace of Aging did not change findings (figure S2 in ref. 2).

Third, in response to Newman's letter (1), we reanalyzed our data. We repeated analysis to validate Biological Age and Pace of Aging, this time adding statistical control for weight gain (BMI change from 26 to 38). This new analysis shows weight gain does not account for our original results (Fig. 1). In sum, our study was not "fundamentally flawed," as Newman (1) claims.

The goal of our research is to furnish human studies with measurement tools that quantify aging-related biological changes before the onset of age-related disease. New methods are emerging in genomics and metabolomics to measure biological aging. The hypothesis that all methods measure the same thing needs to be tested. We hope the measurement tools we studied will prove useful for research on lifelong aging.

Daniel W. Belsky[a,b,1]

[a]*Department of Medicine, Center for the Study of Aging and Human Development, Duke University School of Medicine, Durham, NC 27710; and* [b]*Social Science Research Institute, Duke University, Durham, NC 27708*

1 Newman AB (2015) Is the onset of obesity the same as aging? *Proc Natl Acad Sci USA* 112:E7163.

2 Belsky DW, et al. (2015) Quantification of biological aging in young adults. *Proc Natl Acad Sci USA* 112(30): E4104–E4110.

3 López-Otín C, Blasco MA, Partridge L, Serrano M, Kroemer G (2013) The hallmarks of aging. *Cell* 153(6): 1194–1217.

Author contributions: D.W.B. wrote the paper.

The author declares no conflict of interest.

[1]Email: dbelsky@duke.edu.

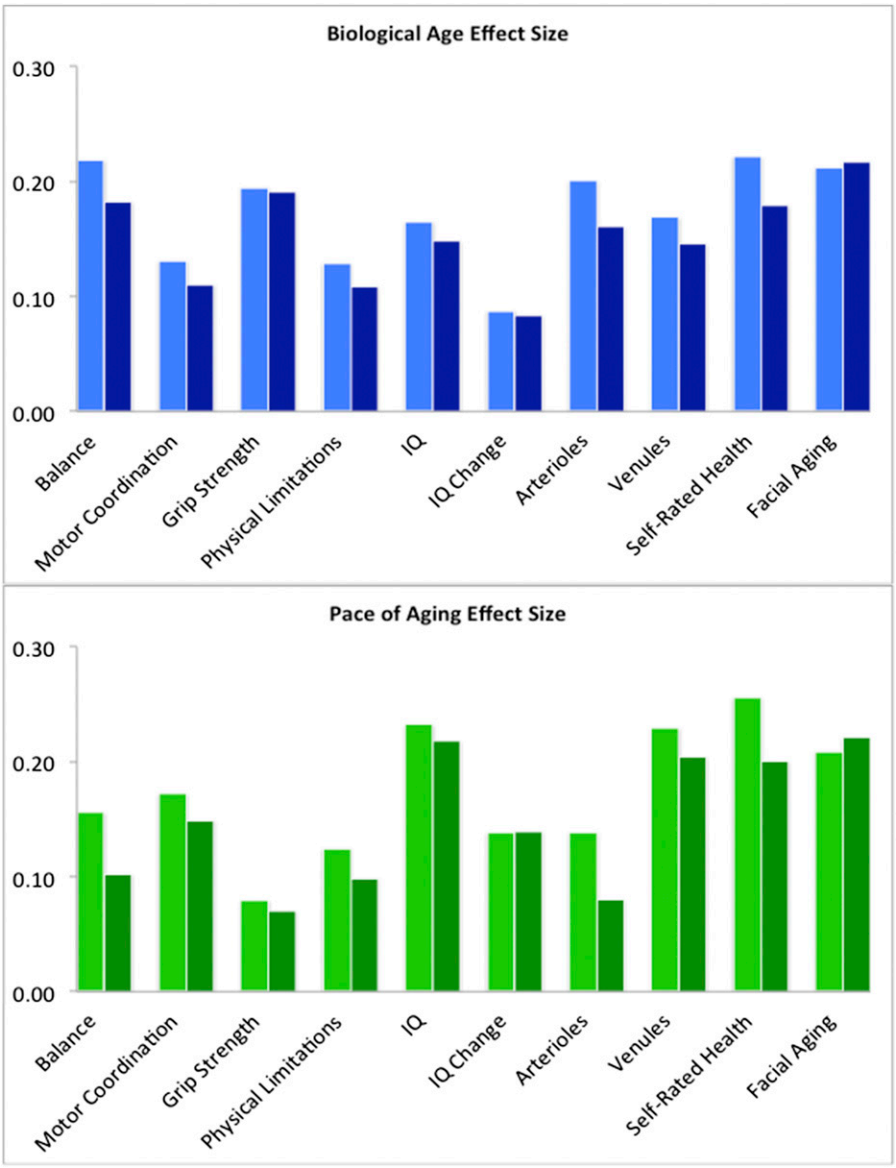

Fig. 1. Effect sizes for associations of the Biological Age and the Pace of Aging with the 10 validation metrics analyzed in our original article (2). The lighter bars graph the original effect sizes we reported in our article (2). The darker bars graph effect sizes after adding a statistical control for weight gain (change in BMI from ages 26–38 y). All effect sizes are statistically significant at $P < 0.05$, except for the association between Pace of Aging and arterioles ($P = 0.050$).