



# Reply to Bos and De Jonge: Between-subject data do provide first empirical support for critical slowing down in depression

With interest we read the response of Bos and De Jonge (1) to the paper by van de Leemput et al. (2). They argue that our paper (*i*) rests on illegitimate generalization of group level results to the individual level and (*ii*) statistically mixes up between-subject and within-subject variability.

With respect to *i*, we indeed provided support for an intraindividual model through individual differences data. The logic behind our analysis is simply that, if individual people display early warning signals when closing in on a transition, then individuals who are closer to a tipping point should show higher levels of autocorrelation and variance. In our data, the subsamples of individuals who proved to be in a different state on follow-up indeed showed such warning signals. Although the tested statistical hypothesis concerns the population distribution of autoregressive coefficients, as Bos and De Jonge note, that hypothesis is derived directly from a theory on the structure of intraindividual processes; this derivation was made consciously and with care, as testified by our supporting information. Thus, we did not mix up levels of analysis. However, we do agree with Bos and De Jonge that time series assessments obtained while individuals undergo a transition would be ideal, because these would allow for direct intraindividual tests of our hypothesis.

With respect to *ii*, the authors suggest that between- and within-effects were not properly disaggregated in our multilevel models for autocorrelation. This suggestion is incorrect. We used the strategy of person-mean centering, which unambiguously disaggregates these effects (3). As stated in our paper, the effect of the mean is indeed one of the

issues with analyzing variances (4); however, we addressed this issue through the analysis of the coefficients of variation (see ref. 2, supporting information). This analysis shows effects of the means but also reveals that the elevated variation in mood as an early warning of an upcoming depression in the general population is robust against correction for the mean. Thus, the data do not support the alternative explanation of the results as put forward by Bos and De Jonge. This defuses the argumentation underlying their conclusion that the evidence presented is weak.

We agree with the authors that we cannot exclude the possibility that individual transitions may have been gradual or minimal. Future within-subject designs may further elucidate the presence of relevant transitions in this regard. However, the current group-based findings were consistent with expectations following from the principles of dynamic systems, and our paper reports empirical results compatible with the idea that depression behaves as a complex system. Naturally, we are aware of the limitations of between-subject findings and strongly agree that future research should aim to examine intraindividual changes in early warning signals and whether these anticipate clinically relevant intraindividual transitions in depression.

**Marieke Wichers<sup>a,1</sup>, Denny Borsboom<sup>b</sup>, Francis Tuerlinckx<sup>c</sup>, Peter Kuppens<sup>c,d</sup>, Wolfgang Viechtbauer<sup>a</sup>, Ingrid A. van de Leemput<sup>e</sup>, Kenneth S. Kendler<sup>f,g</sup>, and Marten Scheffer<sup>e</sup>**

<sup>a</sup>Department of Psychiatry and Psychology, School for Mental Health and Neuroscience,

Maastricht University, 6200 MD, Maastricht, The Netherlands; <sup>b</sup>Department of Psychology, Psychological Methods, University of Amsterdam, 1018 XA, Amsterdam, The Netherlands; <sup>c</sup>Faculty of Psychology and Educational Sciences, KU Leuven, University of Leuven, 3000 Leuven, Belgium; <sup>d</sup>Melbourne School of Psychological Sciences, University of Melbourne, Melbourne, VIC 3010, Australia; <sup>e</sup>Aquatic Ecology and Water Quality Management, Wageningen University, 6700 AA, Wageningen, The Netherlands; <sup>f</sup>Virginia Institute for Psychiatric and Behavioral Genetics and Department of Psychiatry, Virginia Commonwealth University, Richmond, VA 23298; and <sup>g</sup>Department of Human and Molecular Genetics, Medical College of Virginia, Virginia Commonwealth University, Richmond, VA 23298

**1** Bos EH, De Jonge P (2014) "Critical slowing down in depression" is a great idea that still needs empirical proof. *Proc Natl Acad Sci USA* 111:E878.

**2** van de Leemput IA, et al. (2014) Critical slowing down as early warning for the onset and termination of depression. *Proc Natl Acad Sci USA* 111(1):87–92.

**3** Curran PJ, Bauer DJ (2011) The disaggregation of within-person and between-person effects in longitudinal models of change. *Annu Rev Psychol* 62:583–619.

**4** Dakos V, van Nes EH, D'Odorico P, Scheffer M (2012) Robustness of variance and autocorrelation as indicators of critical slowing down. *Ecology* 93(2):264–271.

Author contributions: M.W., D.B., F.T., P.K., W.V., I.A.v.d.L., K.S.K., and M.S. wrote the paper.

The authors declare no conflict of interest.

<sup>1</sup>To whom correspondence should be addressed. E-mail: m.wichers@maastrichtuniversity.nl.