Reply to 'Mechanisms underlying resilience in ageing'

Roberto Cabeza, Marilyn Albert, Sylvie Belleville, Fergus I. M Craik, Audrey Duarte, Cheryl L. Grady, Ulman Lindenberger, Lars Nyberg, Denise C. Park, Patricia A. Reuter-Lorenz, Michael D. Rugg, Jason Steffener and M. Natasha Rajah

In their Correspondence, Stern et al. commented on our Opinion article (Maintenance, reserve and compensation: the cognitive neuroscience of healthy ageing. *Nat. Rev. Neurosci.* **19**, 701–710 (2018))[1] concerning the concepts of reserve, maintenance and compensation (Mechanisms of resilience in ageing. *Nat. Rev. Neurosci.* https://doi.org/10.1038/s41583-019-0138-0 (2019))[2]. Our article summarized the consensus among 13 researchers working primarily in the cognitive neuroscience of healthy ageing. Achieving a broader consensus will require dialogue across different domains in the neuroscience of ageing, including clinical researchers (such as Stern and colleagues) and researchers working with animals. Thus, we see the debate with Stern et al. as an important step towards a general consensus.

Stern et al. note three points of disagreement with our definitions of reserve, maintenance and compensation. Regarding reserve, they disagreed with our suggestion to merge the terms 'brain reserve' and 'cognitive reserve' into a single 'neurocognitive reserve' term, a suggestion that we based on the widely accepted proposition that all cognition is brain-based. Although explicitly agreeing with this proposition, Stern et al. emphasize the heuristic value of distinguishing between brain reserve to refer to aspects of brain structure (such as volume) and cognitive reserve to refer to variables moderating the effects of brain decline (which includes pathology) on cognitive performance (which includes clinical status). We believe that limiting brain reserve to structural brain measures is problematic because cognition and behaviour result from complex interactions of brain chemistry, structure and function, which may occur at various temporal and spatial scales. The term cognitive reserve is also problematic because proxies of cognitive reserve, such as education, need to result in robust and lasting brain changes to serve as a buffer against decline, albeit perhaps at levels of analysis and complexity not yet measurable by current methods. We are optimistic that scientific progress will unravel the cerebral manifestations of what is currently called cognitive reserve. We therefore believe that the use of the single term neurocognitive reserve, or 'reserve' for short, is parsimonious and stresses the point that cognitive reserve invariably has a cerebral basis.

Regarding maintenance, Stern et al. criticize our use of the term 'maintenance' without the 'brain' qualifier. We agree with Stern et al. that the notion of maintenance refers to the brain and it was not our intention for this term to be understood in any other way. By maintenance we refer to domain-general or function-specific components of the brain whose maintenance helps to postpone and minimize cognitive decline[1].

Finally, regarding compensation, Stern et al. argue that compensation is not at the same level of abstraction as reserve and maintenance. We see all three phenomena, reserve, maintenance and compensation, as mediating some (but not all) of the effects of interacting genetic and environmental factors on cognitive ageing (see Figure 1a in REF.[1]). In our view, reserve and maintenance set the stage for compensation but do not necessarily cause it, and minimum levels of reserve and maintenance can be seen as necessary (but not sufficient) conditions for compensation. We assume that compensation shows important individual differences that cannot be subsumed under individual differences in reserve or maintenance. Thus, we propose that clarifying compensation mechanisms might provide insights into how to boost resilience by attenuating the adverse effects of normal and pathological ageing on behaviour.

In sum, our disagreements with Stern et al. primarily concern the proposal to abandon the distinction between brain reserve and cognitive reserve, and the proposition that compensation might contribute to resilience. We welcome the comments from Stern et al. and we look forward to feedback from researchers in our field that can help advance current models of cognitive ageing.

Roberto Cabeza[1], Marilyn Albert[2], Sylvie Belleville[3], Fergus I. M Craik[4], Audrey Duarte[5], Cheryl L. Grady[4], Ulman Lindenberger[6], Lars Nyberg[7], Denise C. Park[8], Patricia A. Reuter-Lorenz[9], Michael D. Rugg[8], Jason Steffener[10] and M. Natasha Rajah[11]*

[1]*Center for Cognitive Neuroscience, Department of Psychology and Neuroscience, Duke University, Durham, NC, USA.*

[2]*Departments of Psychiatry and Neurology, John Hopkins University, Baltimore, MD, USA.*

[3]*Research Center of the Institut Universitaire de Gériatrie de Montréal, Montreal, Quebec, Canada.*

[4]*Rotman Research Institute, Baycrest Health Sciences, Toronto, Ontario, Canada.*

[5]*School of Psychology, Georgia Tech, Atlanta, GA, USA.*

[6]*Max Planck Institute for Human Development and Max Planck UCL Centre for Computational Psychiatry and Ageing Research, Berlin, Germany.*

[7]*Departments of Radiation Sciences and Integrated Medical Biology, UFBI, Umeå University, Umeå, Sweden.*

[8]*Center for Vital Longevity, University of Texas, Dallas, TX, USA.*

[9]*Department of Psychology, University of Michigan, Michigan, Ann Arbor, MI, USA.*

[10]*Interdisciplinary School of Health Sciences, University of Ottawa, Ottawa, Ontario, Canada.*

[11]*Department of Psychiatry, McGill University, Montreal, Quebec, Canada.*

*e-mail: cabeza@duke.edu

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1. Cabeza, R. et al. Maintenance, reserve and compensation: the cognitive neuroscience of healthy ageing. *Nat. Rev. Neurosci.* **19**, 701–710 (2018).
2. Stern, Y. et al. Mechanisms of resilience in ageing. *Nat. Rev. Neurosci.* https://doi.org/10.1038/s41583-019-0138-0 (2019).

Competing interests
The authors declare no competing interests.