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# Aging and the Resting State: Cognition is not Obsolete

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We were pleased to see that our opinion paper generated so many thoughtful comments, and while there was some disagreement as to the role resting state data should play going forward, there was also much agreement. In reply, we briefly touch on some of the keys issues brought up by the authors and reiterate our view that task-based studies offer a greater opportunity to advance the field.

Our original paper questioned the utility of the resting state approach for neurocognitive aging, but Davis, Stanley, Moscovitch, and Cabeza (2016) extended this criticism to the entire field of cognitive neuroscience, the goal of which is to "understand the neural mechanisms of cognition" (p1). They point out that resting state networks are commonly assumed to determine or constrain 'cognitive function networks' (or networks active during cognitive tasks) and outline a number of problems with this assumption. Mainly, resting state networks are similar to, but not quite the same as, cognitive function networks because regions dynamically shift alliances in response to cognitive demands and as such, the same region can contribute to a number of different cognitive processes. Extending this notion of 'process specific alliances' to aging, we know that age affects some cognitive functions and not others; and indeed, it may affect some regions and not others. But more complex still, age may affect some process specific alliances, but not others. This question can only be addressed through cross-task comparisons. For instance, we recently showed that older adults underactivate the frontoparietal network (FPN) when it works in conjunction with other attentional control and visual networks during a fluid intelligence task (an ability that declines with age), but not when the FPN works in conjunction with the frontotemporal network during language comprehension (an ability that is preserved with age; Samu, Campbell, Tsvetanov, Shafto, Cam-CAN, & Tyler, submitted). Determining why certain process specific alliances (and associated cognitive processes) decline with age while others do not is a critical question for neurocognitive aging. Davis and colleagues argue that resting state data will not help in this endeavor and that its contributions to cognitive neuroscience in general "have been exaggerated" (p3).

One reason this contribution may be exaggerated is that resting state data have given rise to some admittedly impressive results. For instance, in their commentary, Iordan and Reuter-Lorenz (2016) point to a paper by Tavor and colleauges (2016, *Science*) showing that the shape and extent of an individual's task-evoked activity can be predicted from their resting state data alone after training a model to map resting state to task data on 97 other subjects.

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The key implication is that with your resting state data I can create a relatively accurate map of how your brain would look while performing a number of tasks from the Human Connectome Project (HCP). This is admittedly an impressive result, but there are a few issues that limit our enthusiasm. First, at its most accurate, the mean correlation between predicted and actual activity was ~0.8, with many tasks in the 0.5–0.6 range, thereby leaving appreciable differences between predicted and actual activity maps in some cases (see their Figures S1–S3 and S4). Some of these differences may be meaningful. Further, these analyses were based on healthy young adults from the HCP and it is uncertain whether they would hold up when tested on a more diverse sample, such as older adults who tend to show greater within- and between-person variability (MacDonald, Li, & Bäckman, 2009; Nyberg, Lövdén, Riklund, Lindenberger, & Bäckman, 2012). Finally and most importantly, even if we could predict a person's task-evoked activity with high accuracy, where would that leave us? In the absence of the corresponding task data, we would be left wondering 1) whether our prediction was accurate, 2) how these activations relate to performance on a trial-wise basis, and 3) how activation would be affected by some yet untested cognitive manipulation. Much time and effort has been dedicated to demonstrating the correspondence between resting state and task data (e.g., Cole, Bassett, Power, Braver, & Petersen, 2014; Finn et al., 2015; Smith et al., 2009; Tavor et al., 2016), and clearly functional connectivity at rest reflects some stable aspect of functional architecture that is also present during task. But the overlap is not perfect, so why look at proxies for task-based connectivity when we could look directly at the real thing?

Some of the other authors pointed out additional advantages of the resting state that we did not discuss in our original paper. For instance, Damoiseaux and Huijbers (2016) suggested that resting state data may be particularly useful for longitudinal studies in that, unlike task-based studies, resting state should be immune to practice effects. Putting aside potential repeat testing effects that may even affect rest (e.g., participants may feel calmer their second time in the scanner), there are a number of steps that can be taken to minimize practice effects on tasks. First, a number of tasks show minimal practice effects (e.g., object recognition, language comprehension) and offer the dual advantage of constraining participants' mental activity and allowing one to test specific hypotheses (e.g., do object representations become less distinct with age?). Further, longitudinal imaging research could benefit from adopting the same procedures as longitudinal behavioural work to minimize practice effects, such as introducing a new cohort of naïve participants at timepoint 2 (Schaie, 1983) or using additional practice sessions outside the scanner to allow practice effects to asymptote prior to scanning. We strongly agree that longitudinal data are critical to our understanding of true age effects, but that is only all the more reason to use these opportunities for task-based experiments that enable one to say something about the specific neurocognitive mechanisms that are changing with age.

Another potential use for resting state data, discussed by Grady (2016), is to examine changes in functional connectivity following a particular task. For instance, post-encoding rest data have been used to study memory consolidation and reactivation (Schlichting & Preston, 2015; Staresina, Alink, Kriegeskorte, & Henson, 2013; Stevens, Buckner, & Schacter, 2010; Tambini, Ketz, & Davachi, 2010) and we recently showed a change in hippocampal resting state connectivity following a specificity induction known to increase retrieval of episodic details (Madore, Szpunar, Addis, & Schacter, 2016). Admittedly, resting state data may offer the best opportunity to capture these subtle after-effects, as scanning during another task would likely interfere with detection. This may be a case where resting state data are preferable to task data, though it is worth noting that these studies are motivated by a clear cognitive hypothesis and thus do not fall into the class of "exclusively resting state studies" that we were initially criticizing.

Finally, Geerligs and Tsvetanov (2016) discussed previous work showing that resting state data can be used to correct for physiological artefact in task-based data. Tsvetanov and colleagues (2015) previously showed that resting state fluctuation amplitude (RSFA; or BOLD variability) is more closely related to measures of vascular health (i.e., blood pressure, resting heart rate variability) than measures of neural variability (quantified using MEG). They went on to show that voxelwise RSFA can be used to remove physiological artefact from task-based data to give a more accurate picture of true age differences in task-based neural activity. These findings are important, and RSFA-correction should likely be adopted as standard practice in fMRI studies of aging. However, this approach may represent the best way to *integrate* resting state with task data (which is what Geerligs and Tsvetanov argue for throughout their commentary), because it is unclear how can one argue that resting state data are largely made up of physiological signals that need to be corrected for but also constitute signals of interest that are worth studying in their own right. We are fully in favour of adopting a more integrative approach to neurocognitive aging, but as we argued in our original paper, we think that comparisons between tightly controlled experimental tasks will lead to greater advances than comparisons between tasks and the unconstrained resting state.

In conclusion, our commentary elicited a range of responses, with some people coming down strongly against the resting state approach and others still singing its praises. The fact that resting state scans are now commonly included in most small and large-scale fMRI projects suggests that this approach is likely here to stay and indeed, resting state data have their uses. But we would like to close with one final argument against using the resting state in isolation, and it is based on consideration of the steps that we as scientists ought to be taking to move research forward: asking questions, reading up on existing evidence, formulating a hypothesis, developing an experiment to test said hypothesis, analyzing data and drawing conclusions, refining ones' question/hypothesis, and testing again. If one's "experiment" is always the same and involves scanning people while they lie awake in the scanner with nothing to do, one is necessarily limited in the number and type of questions that can be addressed.

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