Functional connectivity is both a state-of-mind and a stable trait

In response to, Brain Age: A State-Of-Mind? On the Stability of Functional Connectivity across Behavioral States, by J. Dubois.

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In our recent study in The Journal of Neuroscience (Geerligs et al., 2015), we examined the relative contributions of state and trait components to individual differences in functional connectivity. In a Journal Club review of our paper, Dubois made some interesting suggestions for additional analyses to further clarify the role of these state and trait effects. First, Dubois suggested that some connections may be more trait-like (stable across our three tasks), whereas others may be more state-dependent (differing across our tasks). To investigate this, we computed the intra-class correlation coefficient (ICC) to measure the consistency of individual differences, both within sessions (using a split-half analysis as in our original paper) and between different sessions (see figure 1). We observed that some connections are indeed more trait-like. The connections that were most stable between states were primarily the connections between networks involved in higher-order cognitive functions, whereas connections between sensorimotor networks showed lower consistency across sessions. This may be due to the nature of the three states we used, for which there was a lot of variation in the visual and auditory input that participants received. These regional differences in ICC were not solely due to differences in signal-to-noise, as the split-half ICC was high in sensorimotor regions (figure 1A) and the ratio of between-state ICC to split-half ICC showed a similar pattern (figure 1C).

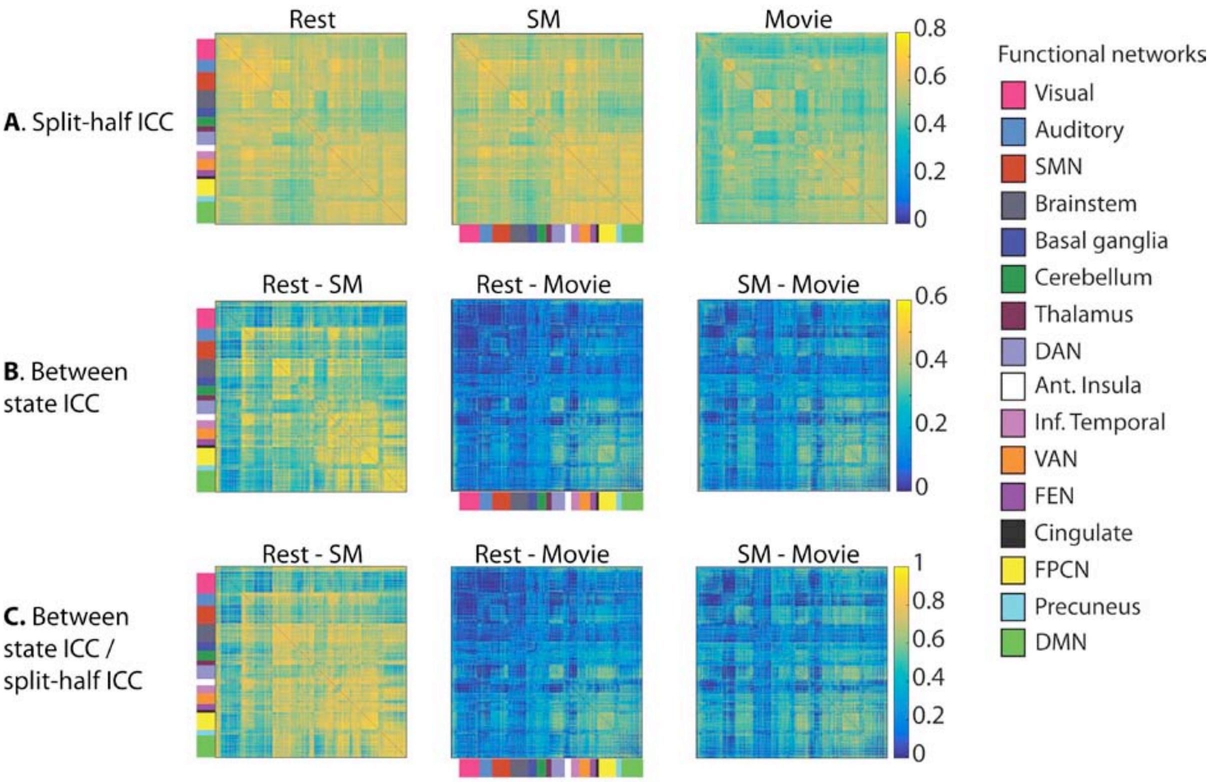

*Figure 1: For each connection the figures show: **A)** The ICC between two halves of the same scanning session; **B)** The ICC between different states; **C)** The between-state ICC divided by the split-half ICC.*

Colours on the left and bottom of the matrices indicate functional networks (see figure 1 in Geerligs et al., 2015).

A second point by Dubois was that it may have been better to use a predictive framework to see if a multivariate model based on one state could predict age in another state. To address this point, we used relevance vector machine regression (RVMR, Tipping, 2001) to predict each participant's age based on the full set of functional connections between regions. We scaled the values of each connection such that the minimum and maximum values across participants were between -0.5 and 0.5 in order to give them equal weight in the RVMR (Crone et al., 2006). We used 10-fold cross-validation across participants for training and testing, where we tested the obtained relevance vectors both on data from the same state and data from different states. In line with our previous results, we found that the RVMR performed best when training and testing was done on data from the same state (see figure 2).

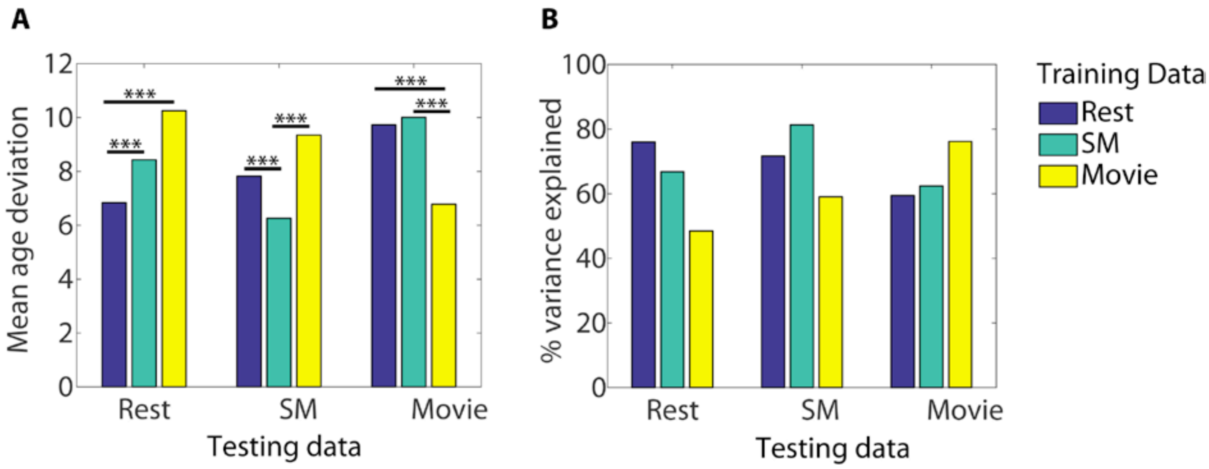

*Figure 2: Results of the relevance vector machine regression, where training and testing of the RVMR was done in the same or in different behavioural states (while training and testing was always on different participants). The mean age deviation of the predictions is shown in panel **A** (lower is more accurate), while panel **B** shows the % variance in the true age that could be explained by the predicted age (higher is more accurate). *** p<0.001*

The improvement in age prediction (based on mean age deviation) varied between 23-50% when the same state was used for training compared to when a different state was used. These new analyses demonstrate that also in a predictive framework, there is evidence for considerable variability between behavioural states, leading to lower performance of the RVMR when different behavioral states are used for training and testing. Nevertheless, the overall high levels of performance of the RVMR (> 48% variance explained in each of the combinations) also demonstrate that there is a substantial trait aspect to these functional connections.

In conclusion, these new analyses support our original results, suggesting that while some connections may be stable across states, others show considerable variability. To understand how brain function is affected by important dimensions of individual differences, such as aging and disease, it is important to study functional connectivity across a wider range of mental states.

References

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