Smith et al. (2015). A positive-negative mode of population covariation links brain connectivity, demographics and behavior. *Nature Neuroscience*. doi:10.1038/nn.4125

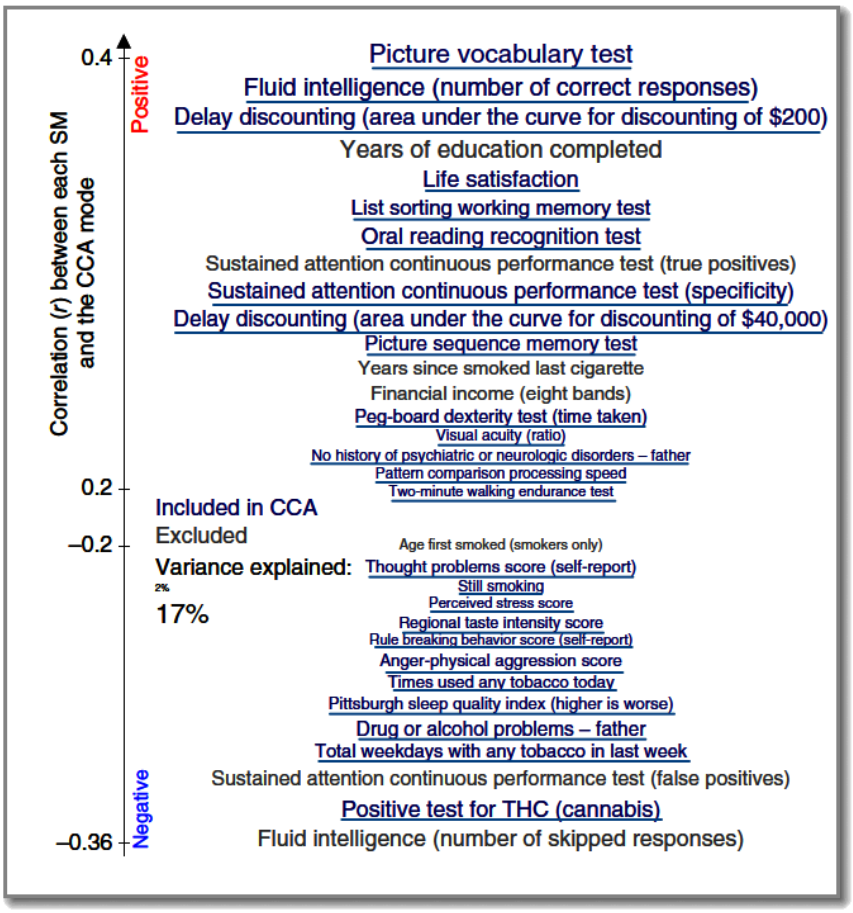
Abstract. ***We investigated the relationship between individual subjects' functional connectomes and 280 behavioral and demographic measures*** in a single holistic multivariate analysis relating imaging to non-imaging data from 461 subjects in the ***Human Connectome Project***. We identified one strong mode of population co-variation: subjects were predominantly spread along ***a single 'positive-negative' axis*** linking lifestyle, demographic and psychometric measures to each other and to a specific pattern of brain connectivity. (Emphases added).

We wanted to discover whether any specific patterns of brain connectivity are associated with specific sets of correlated demographics and behavior, as brain-behavior modes of population co-variation.

To date, data sets from 500 subjects have been publicly released [by the Human Connectome Project (HCP)], including imaging data measuring functional and structural brain connectivity, as well as 280 non-imaging subject measures (SMs), including demographics (age, sex, income, education level, drug use, etc.), psychometrics (IQ, language performance, etc.) and other behavioral measures such as 'rule-breaking behavior'…We used resting-state functional magnetic resonance imaging (fMRI) data from 461 HCP subjects….Separately, 158 behavioral and demographic non-imaging SMs from the same set of subjects were formed into a subject measure matrix.

A natural choice of method for investigating underlying relationships between two sets of variables is canonical correlation analysis (CCA), a procedure that seeks maximal correlations between combinations of variables in both sets. Using CCA, we estimated pairs of canonical variates along which sets of SMs and patterns of brain connectivity co-vary in a similar way across subjects. We refer to each such pair of variates as a mode of co-variation…This analysis revealed a single highly significant CCA mode that relates functional connectomes to subject measures ($r = 0.87$, $P < 10-5$ corrected for multiple comparisons across all modes estimated).

This mode of population co-variation resembles descriptions of a general intelligence *g* factor, but extends it to include key aspects of real-life function, including years of education, income and life satisfaction. This can be considered a one-dimensional positive-negative axis, insofar as nearly all the positively correlated SMs are commonly considered as positive personal qualities or indicators (for example, high performance on memory and cognitive tests, life satisfaction, years of education, income), and all negatively correlated SMs relate to negative traits (for example, those related to substance use, rule-breaking behavior, anger). One notable example is the strongly negative position of cannabis usage on the scale (although this is not on its own driving the overall results, which are almost unchanged if cannabis users are excluded from the CCA; Online Methods). High-scoring subjects (top-right points in the scatter plot) have high relative values for positive SMs (at the top of the SM list) and low relative values for negative SMs (at the bottom). In low-scoring subjects (bottom-left points), the pattern is reversed, with high values for negative SMs and low values for positive ones.

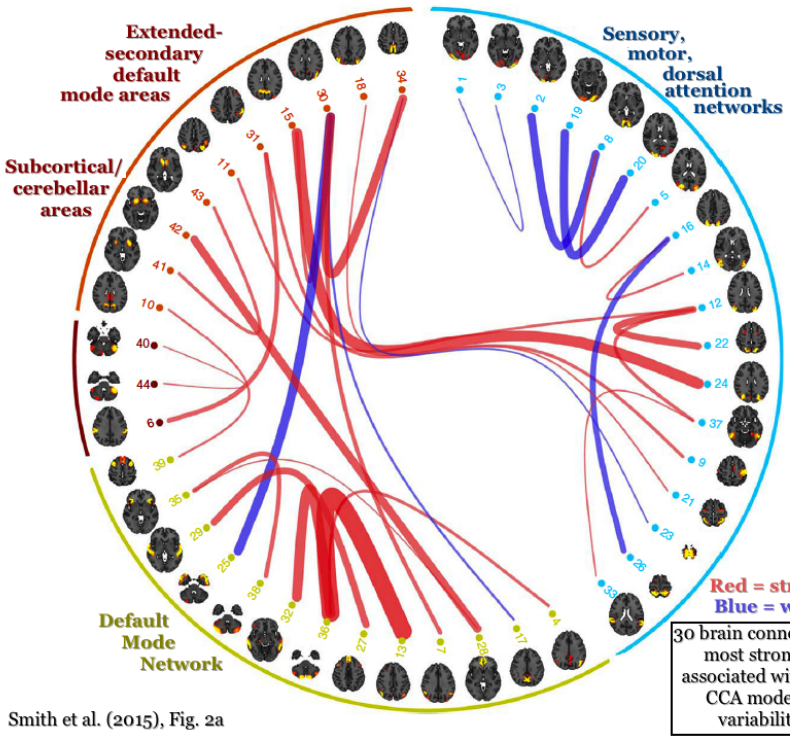


SMs most strongly associated with the CCA mode of population variability.

SMs in blue were included in the analysis.

SMs in grey were correlated with the CCA mode post hoc.

Vertical position is according to correlation with CCA mode & font size indicates SM variance explained by CCA mode.



Smith et al. (2015), Fig. 2a