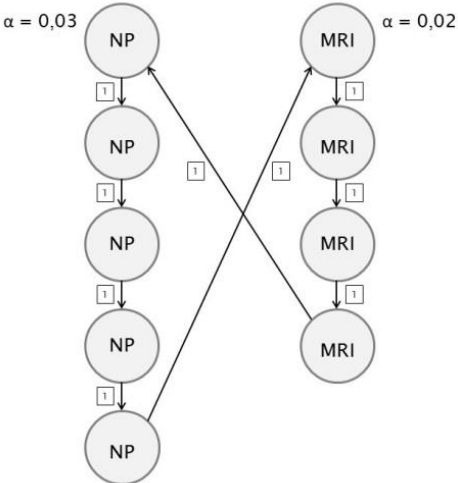


SUPPLEMENTARY MATERIAL

Since multiple outcome measures will be studied, correction for this is applied using the sequentially rejective multiple testing procedure described in Bretz *et al.* (2008)(69). As we are highly interested in both the neuropsychological tests and the MRI parameters, the MRI parameters and the neuropsychological parameters are clustered. A significance level of 0.05 is used, and an alpha level of 0.03 is allocated to the neuropsychological tests and 0.02 to the MRI parameters. The neuropsychological tests and neuroimaging tests will be tested with a multiple testing procedure (supplementary figure 1). The neuropsychological tests will initially be tested at 3/5 of the overall type I error rate (i.e. 0.03 two-sided) and neuroimaging parameters at 2/5 of it (i.e. 0.02 two-sided). Alpha will be reallocated when shown that the corresponding hypothesis is rejected. Based on the literature a specific hypothesis sequence will be tested (the sequence for the neuropsychological tests is: digit span, TAP flexibility task, story immediate/delayed recall, verbal fluency and MoCA; for the MRI parameters: DTI parameters, ASL measures, BOLD response of the Stroop test and grey and white matter volumes). Within each test separately correction for multiple testing will be included, for example for multiple brain areas analysed within a MRI parameter.



Supplementary figure 1. Multiple testing sequence. NP: neuropsychological tests, MRI: MRI parameters.