Statistical modelling to identify neural networks responsible for becoming neurological superagers

Introduction

Superagers are defined as adults more that 80 years old who have a memory performance similar or superior to that of middle-aged adults [1-2]. Understanding the reasons for this superior cognitive aging and the neurological markers in superagers is paramount to understanding the resilient brain areas necessary for memory maintenance in later life.

Evidence to date suggests that specific neural networks differentiate superagers from age-matched controls [3]. Differences in the default mode network (DMN) and the salience network (SN) have been noted in superagers which are not present in age-matched controls [3-4]. The DMN network is known to be active when a person is not focused on the outside world e.g. when an individual is thinking about others, thinking about themselves, remembering the past or planning for the future. Disruption in the DMN occurs in people with Alzheimer's disease and the autism spectrum disorder. The salience network contributes to a variety of complex functions, including communication, social behaviour and self-awareness. Dysfunction in the salience network has been observed in various psychiatric disorders, including Alzheimer's diseases, schizophrenia and dementia.

Project

This project will seek to identify whether networks additional to the DMN and SN may also differentiate between superagers and age-matched controls. We will use functional magnetic resonance (f-MRI) data from ~600 adults over 80 years old from a number of European neurological centers. Statistical analysis on the data will explore differences in the resting-state functional connectivity between superagers and age-matched controls and identify the most discriminative networks as well as the within-network nodes that can predict superagers. In addition to the DMN and SN, we will also include both executive control networks (executive control network left =ECN_L and executive control network right =ECN_R) and the hippocampal and language networks. All of these networks play an important role in the healthy functioning of brain activity.

Within the six networks, Regions of Interest (ROIs) will be identified. The statistical analysis will comprise of:

a. Developing a statistical model using penalized regression analysis [5-6] across all ROIs within all networks – but clustered per network- to identify which of the six networks are statistically different in superagers compared to age-matched controls and quantify this difference.
b. Within each of the six networks a separate penalized regression analysis will explore nodes that are statistically different in superagers compared to age-matched controls and quantify this difference.

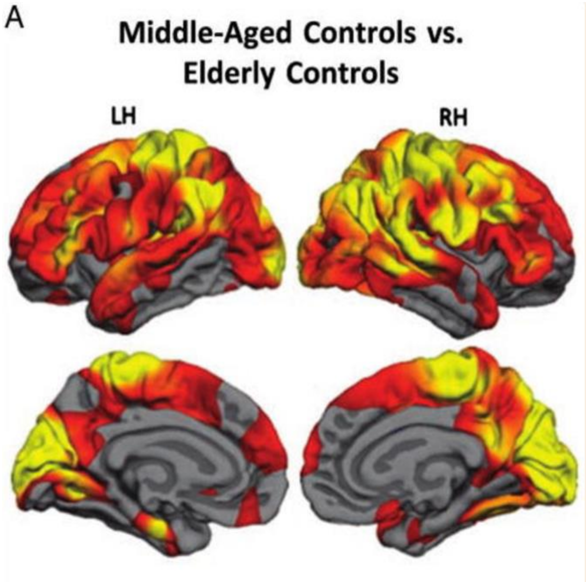

Figure 1: Cortical thickness differences in average cognitive agers and cognitive superagers from [2]. The red and yellow regions show significant cortical thinning across both hemispheres in average cognitive agers compared to cognitive superagers.

Prerequisites

An interest in learning how to read and write, understand and interpret numerical code for statistical analysis in either R, Stata or Python. Support will be given and existing codes can be shared which can be adapted, extended and expanded for the purposes of this project.

Interest in neurological aging and in interdisciplinary translational work with ability to communicate analysis and results with medical professionals such as neurosurgeons and radiologists as well as mathematicians and statisticians.

Reading

[1] De Godoy LL, Studart-Neto A, de Paula DR, Predicting superagers by brain networks and nodes using resting-state functional magnetic resonance imaging, Clinical Neuroimage, in submission, June 2022 (supervisor is senior author and can share the manuscript)

[2] Rogalski EJ, Gefen T, Shi J, et al. Youthful memory capacity in old brains: anatomic and genetic clues from the Northwestern SuperAging Project. *J Cogn Neurosci*. 2013;25(1):29-36. doi:10.1162/jocn_a_00300

[3] Betzel RF, Byrge L, He Y, Goñi J, Zuo XN, Sporns O. Changes in structural and functional connectivity among resting-state networks across the human lifespan. *Neuroimage*. 2014;102 Pt 2:345-357. doi:10.1016/j.neuroimage.2014.07.067

[4] Geerligs L, Renken RJ, Saliasi E, Maurits NM, Lorist MM. A Brain-Wide Study of Age-Related Changes in Functional Connectivity. *Cereb Cortex*. 2015;25(7):1987-1999. doi:10.1093/cercor/bhu012

[5] Greenwood CJ, Youssef GJ, Letcher P, Macdonald JA, Hagg LJ, et al. (2020) A comparison of penalised regression methods for informing the selection of predictive markers. PLOS ONE 15(11): e0242730. https://doi.org/10.1371/journal.pone.0242730

[6] Penalized regression introduction
https://statweb.stanford.edu/~jtaylo/courses/stats203/notes/penalized.pdf