

Association of polygenic risk scores with ADHD trajectories and brain structural features

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Background

Attention-deficit/hyperactivity disorder (ADHD) has been associated with several altered brain regions. Although traditionally defined as a neurodevelopmental disorder with a childhood-only onset, ADHD across lifespan has been focus of several discussions, with recent evidences challenging this concept. For example, cohorts and longitudinal studies have demonstrated both late-onset of symptoms and age-independent remission.

ADHD, such as most psychiatric disorders, has a multifactorial etiology, where common genetic variants contribute to its susceptibility with minor effect sizes. This polygenic genetic architecture of psychiatric disorders frequently has been assessed with Polygenic Risk Scores (PRS).

Methods

This study included adults with ADHD from a follow-up study, assessed from HCPA. Patients were diagnosed with ADHD in adulthood (between 2003 and 2007, n = 344), reassessed about 7 years later (n = 223) and current assessed now, 13 years after diagnosis. In this third wave of evaluation all subjects eligible to perform Magnetic Resonance Imaging (MRI) underwent in a Siemens Spectra 3.0T scanner at Radiology Clinic Serdil. Structural images were processed using FreeSurfer 5.3.

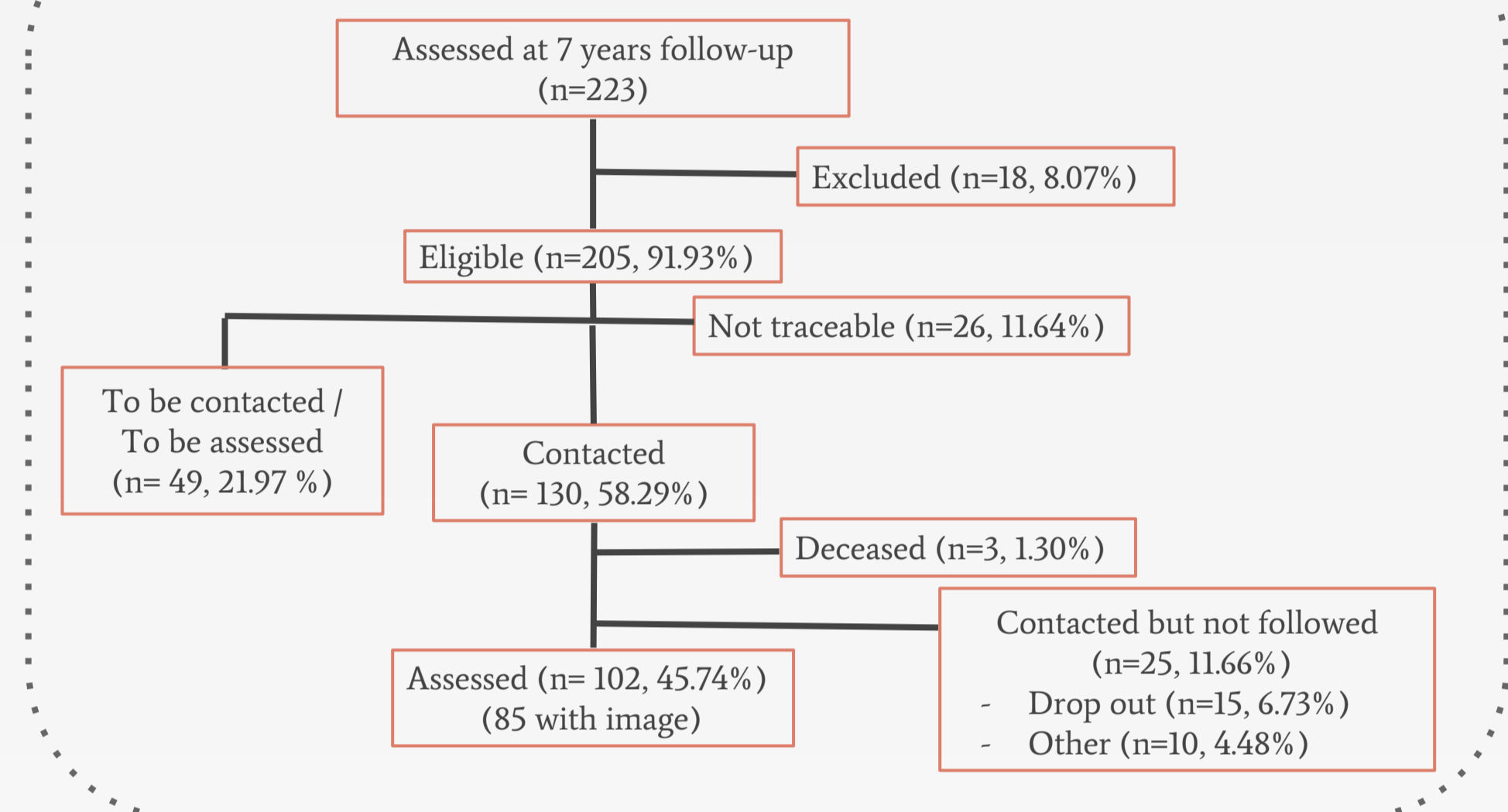
All samples were genotyped through Illumina PsychChip Array, and imputed through Ricopile Pipeline. The PRS were performed using the PRSice 2.0 software, with the effect sizes weighted by the PGC-ADHD 2017 (19,099 cases and 34,194 controls).

Objective

- To compare the genomic profile (PRS) between ADHD adults who had remitted or not (i.e persistent)
- To evaluate the relationship between ADHD genomic risk profiles with brain structures (accumbens, amygdala, caudate, hippocampus, putamen and intracranial volume).

Results and Discussion

Flowchart of the Assessment



From the 223 subjects assessed at the 7-year follow-up, we have assessed so far 102 subjects, of which 85 underwent on the scanner for imaging acquisition (details on the Flowchart above). This are preliminary data, 21.97% of the sample remain to be evaluated, however up to now we have a retention rate of 51.22% (i.e 102 assessed + 3 deceased / 205 eligible).

In the PRS analysis, 3643285 variants were included from base file, 152611 remain after clumping. The ADHD PRS was not associated with neither ADHD outcome (i.e remission/persistence) nor with brain volumes. Since patients are still being collected, these results are preliminary and have to be confirmed in the total sample. Comorbidities, medication use or severity have also to be considered in further analysis. Also, we have to be aware of some limitations of this study, more importantly the ADHD PRS was weighted considering a sample composed mainly by children. Also, it is possible that other brain regions have a larger effect, the regions to be evaluated here were selected based on results from ENIGMA ADHD mega-analyses, which sample is also composed most by children and young-adults.