Study 3: ALPSAC cohort and genotyping

Individuals recruited via the wider ALSPAC sample [1, 2]. Briefly, Pregnant women resident in Avon, UK with expected dates of delivery 1st April 1991 to 31st December 1992 were invited to take part in the study. The initial number of pregnancies enrolled is 14,541 (for these at least one questionnaire has been returned or a "Children in Focus" clinic had been attended by 19/07/99). Of these initial pregnancies, there was a total of 14,676 foetuses, resulting in 14,062 live births and 13,988 children who were alive at 1 year of age. Participants were genotyped using the Illumina HumanHap550 quad chip genotyping platforms by 23andme subcontracting the Wellcome Trust Sanger Institute, Cambridge, UK and the Laboratory Corporation of America, Burlington, NC. Ethical approval for the study was obtained from the ALSPAC Ethics and Law Committee and the Local Research Ethics Committees. Consent for biological samples has been collected in accordance with the Human Tissue Act (2004). The genome-wide data were subjected to quality control as follows: individuals were excluded on the basis of sex mismatches; minimal or excessive heterozygosity; individual SNP missingness (>3%). Population stratification was assessed by multidimensional scaling analysis and compared with Hapmap II (release 22) European descent (CEU), Han Chinese, Japanese, and Yoruba reference populations; all individuals with non-European ancestry were removed. SNPs with a minor allele frequency of <1%, a call rate of <95% or evidence for violations of Hardy-Weinberg equilibrium (P < 5E-7) were removed. Cryptic relatedness was measured/excluded as proportion of identity by descent (IBD > 0.1). Related subjects that passed all other quality control thresholds were retained during subsequent phasing and imputation. Nine thousand one hundred fifteen subjects and 500527 SNPs passed these quality control filters. We combined 477482 SNP genotypes in common between the sample of mothers and sample of children. We removed SNPs with genotype missingness above 1% due to poor quality (11396 SNPs removed) and removed a further 321 subjects due to potential ID mismatches, resulting in a data set containing 465740 SNPs. We estimated haplotypes using ShapeIT (v2.r644) which utilizes relatedness during phasing. We obtained a phased version of the 1000 genomes reference panel (phase 1, version 3) from the Impute2 reference data repository (phased using ShapeIt v2.r644, haplotype release date Dec 2013). Imputation of the target data was performed using Impute V2.2.2 against the reference panel (all polymorphic SNPs excluding singletons), using all 2186 reference haplotypes (including non-Europeans). After quality control, a total of 8365 individuals were genotyped and underwent SCZ-PRS calculations. Please note that the study website contains details of all the data that is available through a fully searchable data dictionary and variable search tool available at http://www.bristol.ac.uk/alspac/researchers/our-data/.

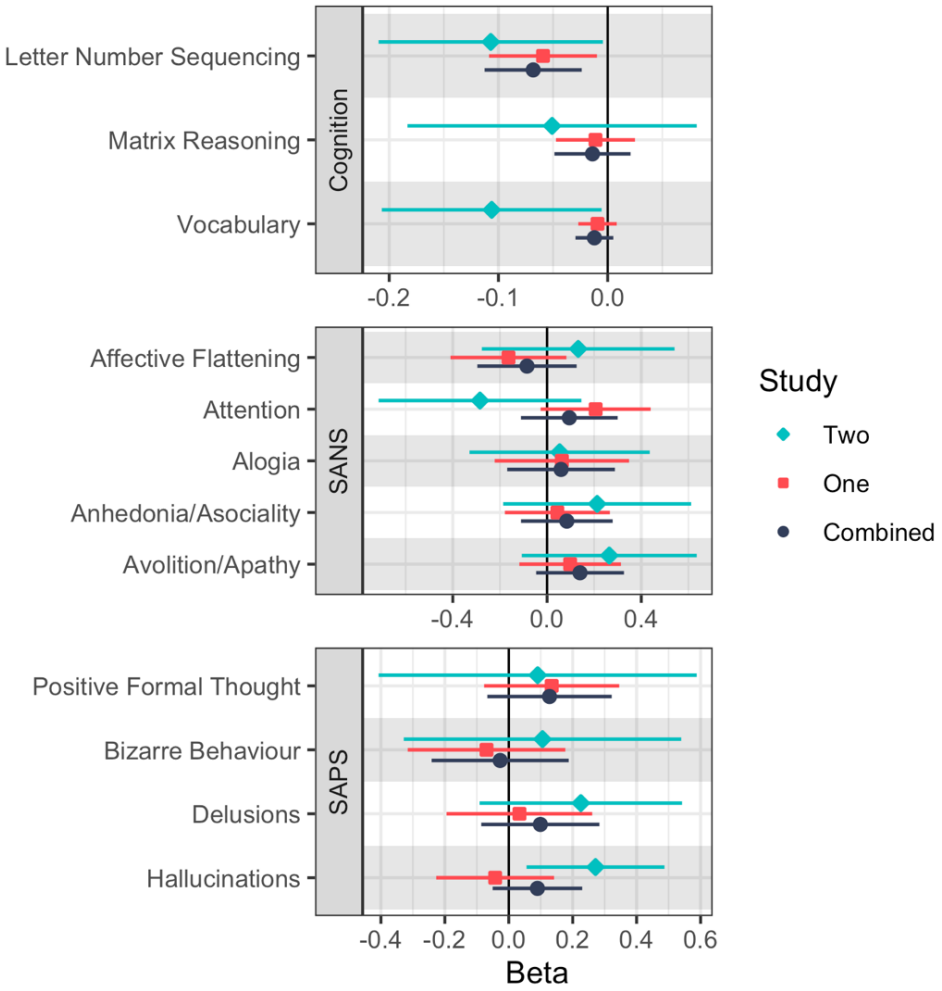
Supplementary Table 1. Effect sizes (Cohen's *d*), averaged across hemisphere for cortical thickness (_thickavg); cortical surface area (_surfavg) and volume for Schizophrenia (SCHZ, from [3, 4]) and Attention Deficits Hyperactivity Disorder (ADHD, from [5, 6]).

Region_of_interest	ADHD	SCHZ
Accumbensarea	-0.15	-0.25
Amygdala	-0.19	-0.31
Caudate	-0.11	0.02
Hippocampus	-0.11	-0.46
Pallidum	0.00	0.21
Putamen	-0.14	0.08
ThalamusProper	-0.03	-0.31
bankssts_thickavg	0.00	-0.3535

caudalanteriorcingulate_thickavg	-0.04	-0.1355
caudalmiddlefrontal_thickavg	-0.05	-0.34
cuneus_thickavg	0.02	-0.2145
entorhinal_thickavg	-0.08	-0.1765
frontalpole_thickavg	0.01	-0.2105
fusiform_thickavg	-0.10	-0.5135
inferiorparietal_thickavg	0.01	-0.355
inferiortemporal_thickavg	-0.03	-0.444
insula_thickavg	-0.05	-0.407
isthmuscingulate_thickavg	0.03	-0.3085
lateraloccipital_thickavg	0.03	-0.3365
lateralorbitofrontal_thickavg	-0.03	-0.378
lingual_thickavg	-0.02	-0.3675
medialorbitofrontal_thickavg	0.00	-0.2375
middletemporal_thickavg	-0.02	-0.4115
paracentral_thickavg	-0.05	-0.2345
parahippocampal_thickavg	-0.06	-0.281
parsopercularis_thickavg	-0.04	-0.3995
parsorbitalis_thickavg	-0.02	-0.329
parstriangularis_thickavg	0.01	-0.357
pericalcarine_thickavg	-0.01	-0.0815
postcentral_thickavg	-0.02	-0.271
posteriorcingulate_thickavg	-0.03	-0.304
precentral_thickavg	-0.11	-0.33
precuneus_thickavg	-0.03	-0.3025
rostralanteriorcingulate_thickavg	-0.01	-0.151
rostralmiddlefrontal_thickavg	0.00	-0.3375
superiorfrontal_thickavg	0.00	-0.411
superiorparietal_thickavg	0.01	-0.214
superiortemporal_thickavg	0.00	-0.439
supramarginal_thickavg	-0.02	-0.3905
temporalpole_thickavg	-0.12	-0.241
transversetemporal_thickavg	0.01	-0.2575
bankssts_surfavg	-0.07	-0.1755
caudalanteriorcingulate_surfavg	-0.09	-0.142
caudalmiddlefrontal_surfavg	-0.13	-0.161
cuneus_surfavg	-0.06	-0.1625
entorhinal_surfavg	-0.07	-0.1235
frontalpole_surfavg	-0.05	-0.0955
fusiform_surfavg	-0.12	-0.218
inferiorparietal_surfavg	-0.11	-0.1885
inferiortemporal_surfavg	-0.10	-0.2065

insula_surfavg	-0.12	-0.1175
isthmuscingulate_surfavg	-0.09	-0.053
lateraloccipital_surfavg	-0.11	-0.164
lateralorbitofrontal_surfavg	-0.12	-0.1645
lingual_surfavg	-0.07	-0.158
medialorbitofrontal_surfavg	-0.11	-0.144
middletemporal_surfavg	-0.10	-0.2055
paracentral_surfavg	-0.04	-0.102
parahippocampal_surfavg	-0.08	-0.121
parsopercularis_surfavg	-0.08	-0.1485
parsorbitalis_surfavg	-0.08	-0.1835
parstriangularis_surfavg	-0.12	-0.136
pericalcarine_surfavg	-0.08	-0.12
postcentral_surfavg	-0.10	-0.1845
posteriorcingulate_surfavg	-0.13	-0.121
precentral_surfavg	-0.08	-0.1905
precuneus_surfavg	-0.10	-0.1465
rostralanteriorcingulate_surfavg	-0.11	-0.1575
rostralmiddlefrontal_surfavg	-0.12	-0.1935
superiorfrontal_surfavg	-0.15	-0.222
superiorparietal_surfavg	-0.13	-0.18
superiortemporal_surfavg	-0.11	-0.1955
supramarginal_surfavg	-0.09	-0.131
temporalpole_surfavg	-0.11	-0.0995
transversetemporal_surfavg	-0.06	-0.1595

Supplementary Figure 1 / Table 2. Association between SCZ-MRS and Wechsler Adult Intelligence Scale (WAIS-IV) subsets and global factors for the Scale for the Assessment of Positive and Negative Symptoms (SANS, SAPS). All estimates are adjusted for covariates within sample. Error bars represent 95% confidence intervals of the beta estimate. Combined effects were estimated via fixed-effect meta-analysis.



COMBINED					
TRAIT	PHENOTYPE	BETA	SE	PVAL	P_{BON}
Cognition	Letter Number Sequencing	-0.068	0.023	0.003	0.032
Cognition	Matrix Reasoning	-0.014	0.018	0.434	1.000
Cognition	Vocabulary	-0.012	0.009	0.169	1.000
SANS	Affective Flattening	-0.085	0.108	0.429	1.000
SANS	Attention	0.094	0.105	0.367	1.000
SANS	Alogia	0.059	0.117	0.610	1.000
SANS	Anhedonia/Asociality	0.084	0.099	0.398	1.000
SANS	Avolition/Apathy	0.140	0.095	0.141	1.000
SAPS	Positive Formal Thought	0.128	0.099	0.199	1.000
SAPS	Bizarre Behaviour	-0.027	0.109	0.806	1.000
SAPS	Delusions	0.099	0.094	0.295	1.000
SAPS	Hallucinations	0.090	0.072	0.210	1.000

Supplementary References

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