The Genetic Relationship Between Educational Attainment and Cognitive Performance in Major Psychiatric Disorders

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Introduction

Cognitive deficits are a core and robust feature of psychiatric disorders and predict long-term social and functional outcomes. Given the strong correlations on both a genetic and phenotypic level between educational attainment and intelligence, educational attainment has been proposed as a proxy-phenotype for cognition. Studies in the general population have already shown a higher polygenic score for educational attainment to be associated with higher performance on neurocognitive tests. This association in cohorts of patients with known cognitive deficits has been less studied and there is a need to explore this association across a range of cognitive domains.

Methods

Participants The selected sample comprised a total of 730 PsyCourse [1] participants with a DSM-IV diagnosis of schizophrenia, schizoaffective disorder or bipolar disorder (type I or II).

Cognitive performance psychometric instruments:

1. Mehrfachwahl–Wortschatz–Intelligenztest (MWT-B)
Crystallized intelligence

2. Trail-Making-Test (TMT)
Visual attention and task switching

3. Verbal digit span
Short term and working memory capacity

4. Digit-Symbol-Test (DST)
Processing speed, working memory, visuospatial processing and attention

5. Verbal Learning and Memory Test (VLMT)
Memory parameters

Table 1 Sample characteristics

	PsyCourse patients (n = 730)
Age at baseline	43.19 (13.01)
Sex (Male)	414 (56.7)
Diagnosis	
Schizophrenia	337 (46.2)
Schizoaffective	73 (10.0)
Bipolar-I disorder	256 (35.1)
Bipolar-II disorder	64 (8.7)
Education	
0	10 (1.4)
1	46 (6.3)
2	146 (20.0)
3	179 (24.5)
4	130 (17.8)
5	87 (11.9)
6	114 (15.6)
Missing	18 (2.5)
Duration of illness	12.93 (10.81)
Baseline treatment	
None	23 (3.2)
Outpatient	355 (48.6)
Day patient	38 (5.2)
Inpatient	310 (42.5)
Missing	4 (0.5)

Biological samples Peripheral blood samples were used for DNA extraction using standard techniques. DNA samples were then used to genotype patients using the Infinium PsychArray Beadchip from Illumina.

Statistical analyses

- Genome-wide polygenic scores for educational attainment (GPS_{EDU}) were calculated using summary statistics obtained from the SSGAC [2].
- Blockwise linear regression models were used to estimate the amount of variation in cognitive performance explained by the educational attainment genome-wide polygenic score at four SNP *p*-value thresholds ($pT < 5\times10^{-8}$, 0.05, 0.1, and 1) for each cognitive domain.
- All models were adjusted for confounding variables measured at the time of testing, i.e., age, age^2, sex, in/outpatient status, study center, PANSS sum scores and principle components.
- Multiple testing was corrected for using the False Discovery Rate (FDR) method correcting for the polygenic profiles at all four thresholds and for all phenotypes investigated.
- The effect of schizophrenia [3] and bipolar [4] polygenic risk scores on cognitive performance were tested.

Results

Educational attainment polygenic scores explained up to 2% of variance in domains related to linguistic learning and working memory.
These effects were robust to the influences of diagnosis, medication, and the genetic load of schizophrenia and bipolar disorder.
Furthermore, on their own, bipolar and schizophrenia polygenic risk scores did not explain variance in cognitive performance.

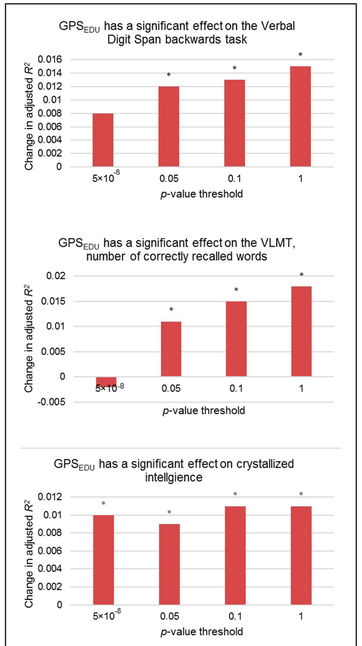

Figure 1
Effect of genome-wide polygenic risk scores for educational attainment (GPS_{EDU}) on cognitive performance (Significant *p*-value thresholds were labeled with an Asterix (* $p < 0.05$)).

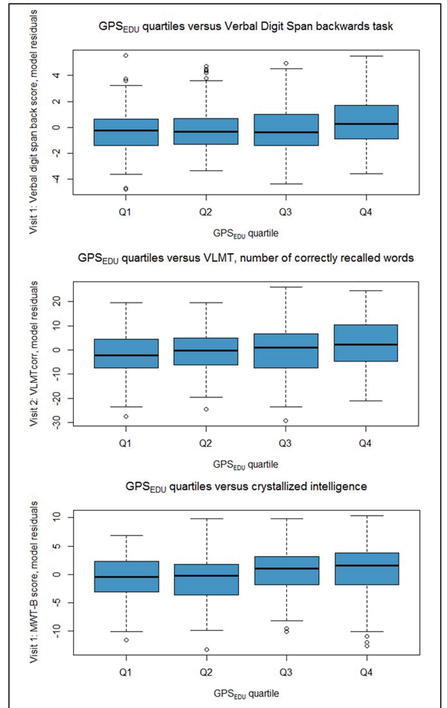

Figure 2
Cognitive performance model residuals plotted against quartiles of genome-wide polygenic risk score for educational attainment (GPS_{EDU}).

Conclusion

Identifying a genetic component related to distinct neurocognitive profiles has potential to identify a more burdened subgroup of patients that in turn might be at risk for lower levels of functioning and poor social outcomes.
Future studies, over the course of the disorder, would be informative to determine how this association changes over time. Polygenic estimates may in the future be part of predictive models for more personalized interventions.

References

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