ADHD and theta/beta power ratio

No evidence that ADHD explains any variance in TBR

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Background

ADHD...
- Highly prevalent (~7%) and heritable (~75%) childhood psychiatric disorder
- Three subtypes: inattention, hyperactivity/impulsivity and combined
- Diagnosis is complex process - aptitude tests, parent/teacher questionnaires, RTV tests and more

Theta/Beta Power Ratio (TBR) is...
- Electroencephalography (EEG) based, FDA approved diagnostic aid for ADHD (2013)
- Costs ~$425 per test
- Recent studies unable to confirm diagnostic accuracy

Aims
1. Estimate TBR heritability
2. Examine the relationship between TBR and ADHD measures
3. Examine the relationship between genetic liability for clinical ADHD in children and TBR

Data and Methods

Data
- Brisbane Adolescent Twins (Table 1)
- TBR - EEG theta/beta power (eyes open an closed)
- ADHD variables were collected using 3 measures: SWAN (mothers & self report) and ASRS (Adult self report), with scores available for 3 subtypes
- Polygenic Risk Scores (PRS) - Demontis 2019 GWAS Data were calculated using Plink 2.0. We excluded: MAF < 1%, R² <0.6, Strand ambiguous SNPs and Indels. For PRS scores we partitioned GWAS results into 8 P-value thresholds

Table 1 - Shows the sample size overlap from the Brisbane Adolescent Twin Study for each variable across eyes open and eyes closed data

	Eyes open (%female)	Eyes closed (%female)
SWAN (self-report)	581 (58%)	722 (58%)
SWAN (mothers report)	515 (51%)	636 (51%)
ASRS	370 (63%)	454 (64%)
PRS scores	838 (52%)	1036 (51%)

Methods
- TBR Heritability was estimated with a Twin Design using a Structural Equation Modelling approach using MZ and DZ twins (and up to two sibs) to partition phenotypic variance into latent variance components A, C, D and E. We used the R software package OpenMx to fit a twin model under Full information maximum likelihood.
- For the prediction of TBR we estimated variance explained by each predictor using Linear Mixed Models in GCTA. This allowed us to include a Genetic Relationship Matrix to take into account the high relatedness of our twin sample. We also included 4 principal components and age and sex as covariates.

Results and Conclusions

- TBR is **highly heritable** in both eyes open (0.87%) and eyes closed (0.86%) measurements (Table 2)
- **No significant TBR variance explained** by ADHD measures (fig. 1a and 1b)
- **No significant TBR variance explained** by ADHD Polygenic risk (fig. 1c and 1d)
- **Further research** is required to justify the use of NEBA as a biomarker for ADHD

Table 2 - Variance estimates for ACDE in TBR (eyes open and eyes closed), based on the best fitting model. AIC – Akaike Information Criterion, -2LL Log Likelihood, Df = degrees of freedom, ACDE – Additive genetic, Shared environment, Dominant genetic, Unshared environmental variation respectively

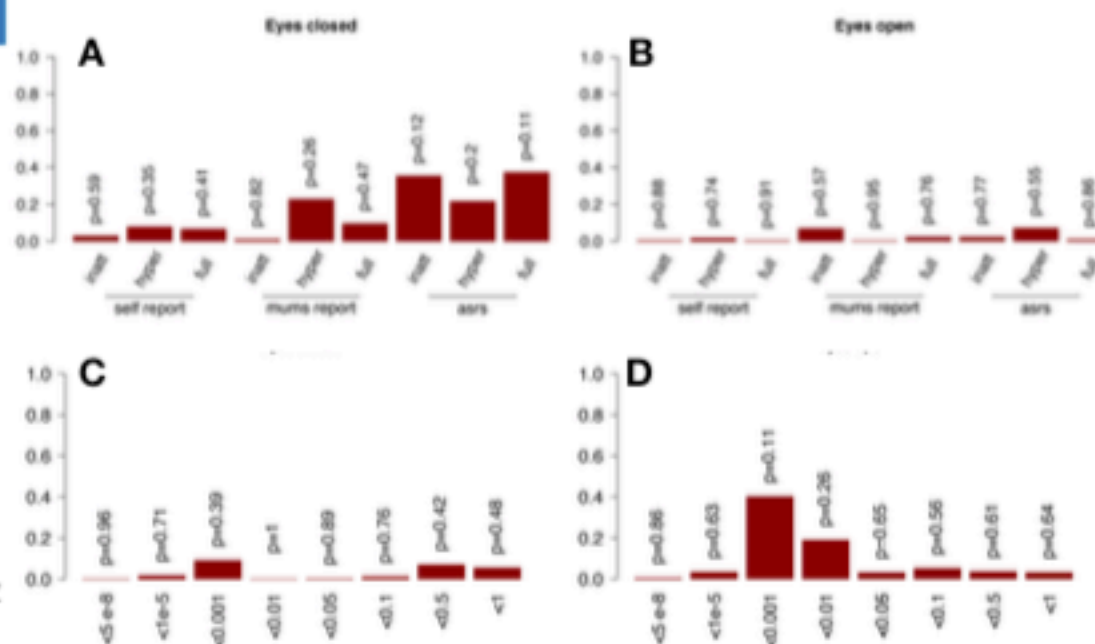|		AIC	-2LL	Df	A	C	D	E	h²
Theta/ beta	EO	1560	3340	890	2.92(2.57,3.31)	-	-	0.45(0.36,0.56)	0.87
	EC	-1266	944	1105	0.16(0.15,0.18)	-	-	0.027(0.022,0.033)	0.86

Figure 1 - Figures A, B, C, D, show results of LMM using GCTA. % Variance explained (R2) by independent variable. P–value of variance explained displayed over each bar. A. Represents variance explained in Eyes closed TBR by 9 ADHD measures. Inatt = Inattention, Hyper = Hyperactivity/Impulsivity, Full = Combined subtype. Self report = SWAN questionnaire, Mums report = SWAN questionnaire, asrs = Adult Self Report Scale Questionnaire. B. Same as A but for eyes open TBR C. Variance explained in eyes closed TBR by ADHD PRS scores within 8 p-value thresholds. D. Same as C but for eyes open TBR