Behavioral, Anatomical and Genetic Convergence of Affect and Cognition in Superior Frontal Cortex

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Study Aim

- Individual variation of affective and cognitive traits, as well as brain structure, has been shown to partly underlie genetic effects (Davies et al. 2011; Okbay et al. 2016; Zheng et al. 2016; Grasby et al. 2020).
- However, whether cognition and trait affect have a shared genetic relation to brain structure is incompletely understood.
- Here, we studied the relationship of cognitive abilities and trait affective self-reports in behavior and local brain structure and evaluated whether these traits share a genetic basis.

Methods

- Data were obtained from **Human Connectome Project** (S1200 release; Glasser et al. 2013; Van Essen et al., 2013). Our sample (N=1083, 585 women) was composed of monozygotic (N=281) and dizygotic (N=164) twins, siblings and unrelated individuals (N=638).
- Behavioural measures:
  - **Cognitive scores** and **affective self-reports** from NIH toolbox:

Category	*Domain*	*Sub-domain*	*Test*
Cognition	Fluid cognition	Executive function – cognitive flexibility	Dimensional Change Card Sorting (DCCS)
		Executive function – Inhibition and attention	Flanker
		Episodic memory	Picture Sequence Memory
		Processing speed	Pattern Comparison
		Working memory	List Sorting
	Crystallized cognition	Language	Picture Vocabulary
			Reading Recognition
Emotion	Positive affect/ psychological well-being	Life satisfaction	Self-report
		Meaning and purpose	
		Positive affect	
	Negative affect	Anger-affect	Self-report
		Anger-hostility	
		Fear-affect	
		Perceived stress	
		Sadness	

- Brain measures at 3T: **Subcortical volumes**, **cortical thickness** and **surface area**: Segmentation of T1w and T2w images and surface reconstruction using FreeSurfer version 5.3-HCP (Glasser et al. 2013)
- Preprocessing and quality control by **HCP minimal preprocessing pipeline** (Glasser et al. 2013; Van Essen et al., 2013)
- Parcellation scheme: Cortical brain measures were extracted within the **Schaefer-7-networks-200 parcels** solution (Schaefer et al., 2018)
- SOLAR 8.4.1.b (http://solar-eclipse-genetics.org) was used for **heritability** and **genetic correlation** analyses using the twin structure of HCP

Results

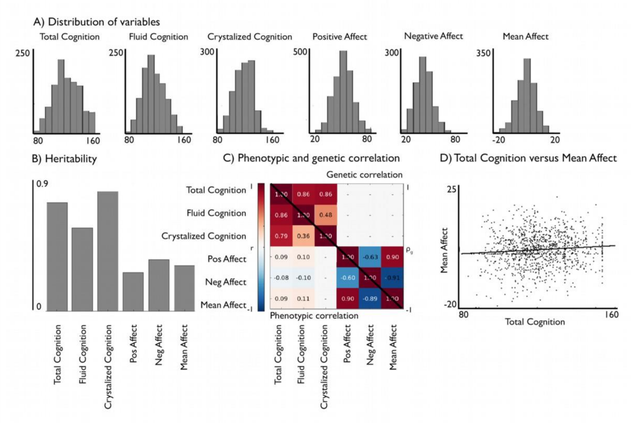

Fig 1. Phenotypic and genetic relation of cognition and affect
A) Distribution of variables; B) Heritability; C) bottom triangle: behavioral correlation (FDRq<0.05) and upper triangle: genetic correlation of the cognitive and affective scores (FDRq <0.05).

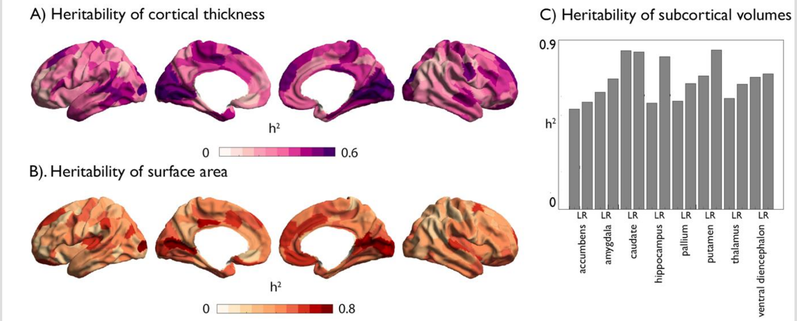

Fig 2. Heritability of local cortical thickness, surface area and subcortical volumes
Heritability of local cortical thickness, surface area and subcortical volumes. A) Heritability of local cortical thickness per parcel (200 parcel solution Schaefer, 2018); B) Heritability of local surface area per parcel. C) Heritability of subcortical volumes per FreeSurfer-segmented region.

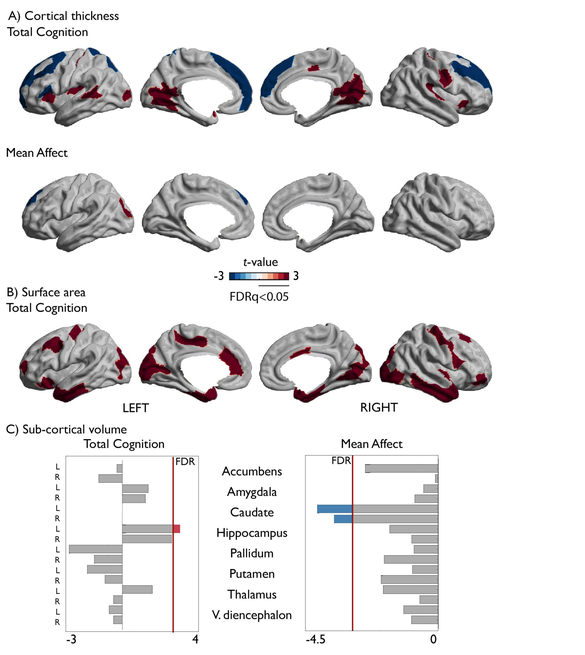

Fig. 3. Associations between cognition, affect and local brain structure
A) Correlation between total cognition and local cortical thickness; Second row: Correlation between mean affect and local cortical thickness B) Correlation between total cognition and local surface area. C) Correlations between cognition / affect and sub-cortical regions volumes. Red indicates a positive association, and blue a negative association between cognition / affect and local brain structure. Only FDRq<0.05 corrected findings are reported.

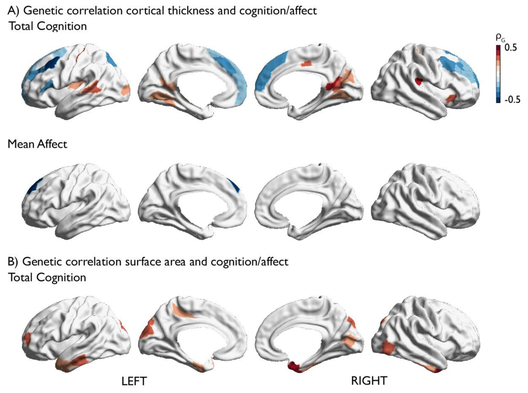

Fig. 4. Whole-brain genetic correlation between local cortical structure and cognition or affect
A) Results for cortical thickness. B) Results for surface area. Positive correlation is depicted in red, negative in blue. Only FDRq<0.05 corrected findings are depicted. FDR-corrected subcortical volumes were only significant for the association of mean affect with bilateral caudate volumes (left: r_g = -0.25, p=0.00, right: r_g = -0.27, p=0.00

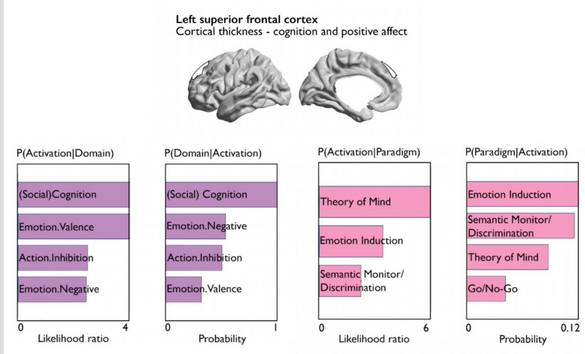

Fig. 5. Quantitative functional decoding of region showing association with both cognition and affect
Both forward inference and reverse inference of activation-domain and paradigm-domain contrasts are reported for the left superior frontal cortex which showed evidence of shared phenotypic and genetic association for cognition and affect scores.

Summary

- Both affective and cognitive trait scores were highly heritable and showed significant phenotypic correlation on the behavioral level (Fig. 1).
- Local brain structure measures (cortical thickness, surface area and subcortical volumes) were also highly heritable (Fig. 2).
- Following, we assessed the correlation between cognitive and affective traits on the one hand, and macroscale brain anatomy on the other. Whereas cognition had widespread associations with local cortical thickness and surface area, trait affect showed only sparse associations (Fig. 3).
- We found that most phenotypic behavior-brain associations were driven by shared genetic effects (Fig.4).
- Finally, we evaluated whether total cognition and mean affect were embedded in a common brain structural correlate and found that both measures showed a shared phenotypic and genetic association with cortical thickness of left superior frontal cortex (Fig. 5).
- Quantitative functional decoding further indicated that this region is involved in both cognitive and emotional functioning (Fig. 5).
- By combining multi-level analysis within the HCP dataset and ad-hoc meta-analytical functional decoding, this study provides converging evidence for a shared biological basis of inter-individual differences in cognitive abilities and affective traits in superior frontal anatomy.
- Follow-up work on the biological basis of complex behaviors may take a similar approach and integrate behavioral assessments with neuroimaging, behavioral genetics, and functional decoding to outline the specific biological mechanisms of the relationship between thoughts and feelings.
- Preprint available here: https://doi.org/10.1101/2020.12.03.401414

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