Behavioral profiling of hippocampal grey matter in late childhood

Mingyeong Choi[1], Simon R. Steinkamp[2], Kathrine Skak Madsen[2], Sarah Genon[3], Angela R. Laird[4] & Anna Plachti[2,3]

[1] Institute of Social Science Research, Pusan National University, South Korea, [2]Danish Research Centre for Magnetic Resonance, Hvidovre, Denmark, [3]Institute of Neuroscience and Medicine (INM-7: Brain and Behaviour), Research Centre Jülich, Jülich, Germany, [4]Department of Physics, Florida International University, Miami, FL, USA.

annap@drcmr.dk

Introduction

- Meta-analytical studies examined the involvement of the hippocampal formation (HF) in several cognitive and emotional functions
- Recent work in adults showed no significant associations between HF volume and various tested functions (Clark et al., 2020), raising the question whether interindividual variability in hippocampal structure can account for interindividual variability in behavior

Methods

Sample:

- ABCD participants (N = 6391, age range: 8 -11 years)
- Hippocampus **VOI** from SPM Anatomy Toolbox & Harvard-Oxford Atlas
- **MRI**: T1-weighted images
  - Preprocessed with smriprep v0.8.3
  - Modulated with Jacobian determinants
  - Smoothed with a Gaussian FWHM 8mm kernel
- Regressing out covariates of no interest from HF voxels:
  - Age, sex, age-by-sex, handedness, caregiver education, income, family environment, neighborhood safety/crime, puberty, race or ethnicity, site, total cortical volume
  - Using generalized additive models

Statistics:

- Data-driven multivariate approach to characterize HF grey matter in relation to a variety of functions in the phase of late childhood
- Partial least square analysis performed on right and left HF separately (permutations = 10 000, bootstrap resampling = 10 000, split-half resampling = 250, $p<0.05$ for latent variables)

Behavior:

- Language: NIH toolbox picture vocabulary
- Working and episodic memory: NIH toolbox list sorting working memory, picture sequence memory tests
- Spatial and visual processing: mental rotation little man task
- Social: Youth prosocial behavior survey
- Reward: cash choice task
- Approach/motivation: BIS-BAS questionnaire
- Behavioral and emotional problems: Child Behavior Checklist (CBCL)

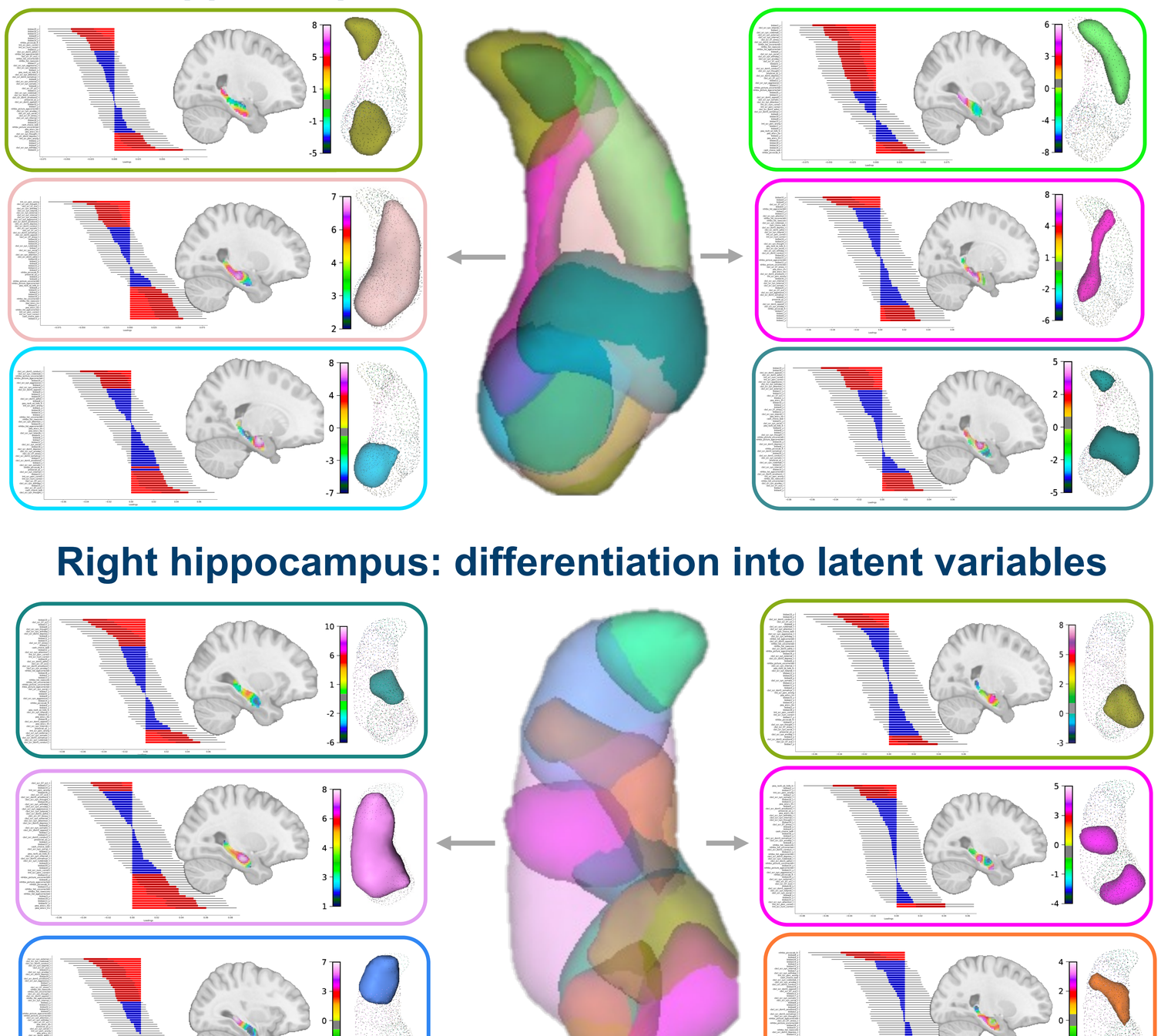
Results

Left hippocampus: differentiation into latent variables

Emotional-depressive
thought problems
depressive symptoms
"I do become fearful or nervous, when something bad happens to me. "

Motivated emotional and cognitive engagement
Delay discounting, mental rotation, working memory
"It would excite me to win a contest."

Internalizing behavior
Thought problems,
Depression,
daydreaming, difficulty initiating and sustaining effort,
internalizing behavior,
language



Motivated Pursuit of Goals and Novelty
mental rotation
"Nobody can stop me when I want something."
"I crave excitement and new sensations."

Anxiety, fear and worry
"I worry about making mistakes."
"I am very fearful compared to my friends."
language, anxiety, depression

Emotional sensitivity
"I feel pretty upset when I think that someone is angry with me.",
obsessive compulsive
working memory, anxiety disorder

Right hippocampus: differentiation into latent variables

Externalizing Behavior and Somatic concerns
conduct problems,
rule-breaking behaviour,
somatic problems
externalizing behavior

Cognitive and emotional engagement
Mental rotation,
working memory,
Language,
episodic memory,
"I get thrilled when good things happen to me."

Motivated Pursuit of Goals and Novelty
Delay-discounting
I am always willing to try
Working memory
"I crave excitement and new sensations."

Emotional Reactivity and Anxiety
"I am very fearful compared to my friends."
"I am hurt when people scold me or tell me that I do something wrong."

Mental rotation

Internalizing behavior
daydreaming, difficulty initiating and sustaining effort,
"I usually get very tense when I think something unpleasant is going to happen."

Emotional sensitivity
depression,
oppositional defiant problems,
"I feel pretty upset when I think that someone is angry with me."

Figure 1. Behavioral profiles related to left and right hippocampus grey matter voxels. Latent variables $p<0.05$.

Discussion

- Functional asymmetries were observed such that left HF was more involved in language processing, while right HF was more engaged in visual processing
- Latent variables were related to anxiety, depression or motivation
- mental rotation and working memory appeared to be associated with HF along the anterior-posterior dimension, suggesting that complex behavior may require the collaboration of multiple subregions within HF
- The findings highlight the significance of intact HF functioning for the (healthy) development of cognition and emotion in childhood

References: Clark, I. A., et al. (2020) Does hippocampal volume explain performance differences on hippocampal-dependant tasks? NeuroImage, 221, 117211. https://doi.org/https://doi.org/10.1016/j.neuroimage.2020.117211 ; Plachti, A., et al. (2019). Multimodal parcellations and extensive behavioral profiling tackling the hippocampus gradient. Cerebral cortex, 29(11), 4595-4612. https://doi.org/10.1093/cercor/bhy336 ; Robinson, J. L., et al. (2016) Functional connectivity of the left and right hippocampi: Evidence for functional lateralization along the long-axis using meta-analytic approaches and ultra-high field functional neuroimaging. NeuroImage, 135, 64-78. https://doi.org/10.1016/j.neuroimage.2016.04.022

Acknowledgments: This study was supported by the Capital Region of Denmark Research Fund 2021, Nr. A7118