Data Request form YOUth (version 6.0, February 2020)

Introduction

The information you provide here will be used by the YOUth Executive Board, the Data Manager, and the Data Management Committee to evaluate your data request. Details regarding this evaluation procedure can be found in the Data Access Protocol.

All data requests will be published on the YOUth researcher's website in order to provide a searchable overview of past, current, and pending data requests. By default, the publication of submitted and pending data requests includes he names and institutions of the contact person and participating researchers as well as a broad description of the research context.

After approval of a data request, the complete request (including hypotheses and proposed analyses) will be published. If an applicant has reasons to object to the publication of their complete data request, they should notify the Project Manager, who will evaluate the objection with the other members of the Executive Board and the Data Management Committee. If the objection is rejected, the researcher may decide to withdraw their data request.

Section 1: Researchers

In this section, please provide information about the researchers involved with this data request.

- Name, affiliation and contact information of the contact person
- Name and details of participating researchers (e.g. intended co-authors)
- Name and details of the contact person within YOUth (if any)

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Section 2: Research context

In this section, please briefly describe the context for your research plans. This section should logically introduce the next section (hypotheses). As mentioned, please note that this section will be made publicly available on our researcher's website after submission of your request.
Please provide:

- The title of your research plan
- A very brief background for the topic of your research plan
- The rationale for and relevance of your specific research plan
- The specific research question(s) or aim(s) of your research (Please also provide a brief specification)
- A short description of the data you request

References can be added at the end of this section (optional).

Title of the study
Individual variability in the spatial distribution of fMRI activation patterns in adolescence

Background of the topic of your research plan, rationale, relevance (max. 500 words)

In neuroscience it is common practice to almost exclusively report averaged group results and rely on aggregate statistics. This is often done under the assumption that there is uniformity in the spatio-temporal dynamics of brain functions in a population. Deviation from a grouped mean is discarded as noise. For fMRI this means that individual activation maps are averaged to a single group map, and that information on variation across individuals is lost.

Variability can be seen as a mostly overlooked fundamental dimension of neuroimaging results. Studies that have focused on individual variability in fMRI signal patterns have shown that these can vary greatly within a single task, sometimes even lacking any overlap between paradigms[1]. Several studies have found unique and systematic individual patterns of brain activity across different tasks [2-5]. Research into variability has demonstrated that small fluctuations of neural activity can even be more informative than peak or mean BOLD activation [6,7]. Furthermore, variability in brain activation in terms of resting-state connectivity was shown to be, for a large part, heritable [8].

There is ample evidence showing a developmental shift from variable spatial activity to more focused patterns in the brain [9,10]. However, evidence for this shift comes solely from studies using average levels of brain activation, instead of using within-subject variability [11]. Structurally, this focalization of task-related activation may be driven by synaptic pruning [12].

There are two ways in which individual variability can be studied; **spatially** and **temporally**. **Spatial variability** refers to variance in the distribution of activation patterns across the brain – i.e. whether activation is centralized and focal, or more diffuse and scattered. This measure may serve as an indication of how specialized a given region is for a particular process, or alternatively as a proxy of a general underlying developmental measure that affects brain regions non-specifically. Generally speaking, this variance of individual results compared to group statistics in fMRI is interpreted as nuisance or noise. It is commonly assumed that by averaging over subjects the noise-related part of the signal is diminished, allowing true effects to emerge [13]. **Temporal variability** can provide us insights in how signal that is otherwise averaged, varies over time. As individuals mature, neural computations underlying task-specific actions may become more consistent, and therefore be less variable over time [14]. Over time, variability can even increase again due to age-relate decline in dopamine levels leading to noisier signal processing [15].

One study has recently measured variability of the BOLD signal in children, and found that increasing age was associated with both reduced spatial and temporal variability [11]. These effects were specifically linked to regions underlying the development of emotion regulation. The present study will use two distinct fMRI tasks, targeting emotion processing and behavioral inhibition, to study spatial and temporal variability in children. This enables us to investigate whether variability is a trait-like individual characteristic that spans paradigms. We will test whether this variability is related to age and both cognitive and emotional development.

The specific research question(s) or aim(s) of your research

1) Does neural variability as measured with functional MRI decrease with age, both spatially and temporally?

2) Is this variability an individual trait that is consistent across tasks and related to measures of cognitive and emotional development?

Summary of the data requested for your project: Please indicate which data you request to answer your research question.

We request all of the following data of the currently available "around 9" group:

- Anatomical MRI scans (for co-registration purposes)
- fMRI inhibition task (with behavioral data for QC purposes)
- fMRI emotion task (with behavioral data for QC purposes)
- Demographics (age, sex, parental IQ/SES)
- IQ
- EATQ questionnaire as a proxy of self-regulatory abilities
- Emotion regulation questionnaire

References (optional)

1. Miller, M. B. *et al.* Unique and persistent individual patterns of brain activity across different memory retrieval tasks. *NeuroImage* **48,** 625–635 (2009).
2. Miller, M. B., Donovan, C.-L., Bennett, C. M., Aminoff, E. M. & Mayer, R. E. Individual differences in cognitive style and strategy predict similarities in the patterns of brain activity between individuals. *NeuroImage* **59,** 83–93 (2012).
3. Bolt, T., Nomi, J. S., Yeo, B. T. T. & Uddin, L. Q. Data-Driven Extraction of a Nested Model of Human Brain Function. *J. Neurosci.* **37,** 7263–7277 (2017).
4. Bolt, T., Nomi, J. S., Bainter, S. A., Cole, M. W. & Uddin, L. Q. The situation or the person? Individual and task-evoked differences in BOLD activity. *Hum. Brain Mapp.* **40,** hbm.24570–12 (2019).
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7. Nomi, J. S., Bolt, T. S., Ezie, C. E. C., Uddin, L. Q. & Heller, A. S. Moment-to-Moment BOLD Signal Variability Reflects Regional Changes in Neural Flexibility across the Lifespan. *J. Neurosci.* **37,** 5539–5548 (2017).
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9. Dehaene-Lambertz, G., Monzalvo, K. & Dehaene, S. The emergence of the visual word form: Longitudinal evolution of category-specific ventral visual areas during reading acquisition. *PLoS Biol* **16,** e2004103–34 (2018).
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11. Moreira, J. F. G., McLaughlin, K. A. & Silvers, J. A. Spatial and Temporal Cortical Variability Track with Age and Affective Experience During Emotion Regulation in Youth. **34,** 1242–63 (2018).

12. DuPre, E. & Spreng, R. N. Structural covariance networks across the life span, from 6 to 94 years of age. *Network Neuroscience* **1,** 302–323 (2017).
13. Seghier, M. L. & Price, C. J. Interpreting and Utilising Intersubject Variability in Brain Function. *Trends in Cognitive Sciences* **22,** 517–530 (2018).
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15. Samanez-Larkin, G. R., Kuhnen, C. M., Yoo, D. J. & Knutson, B. Variability in Nucleus Accumbens Activity Mediates Age-Related Suboptimal Financial Risk Taking. *Journal of Neuroscience* **30,** 1426–1434 (2010).
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17. Vink, M. *et al.* Frontostriatal activity and connectivity increase during proactive inhibition across adolescence and early adulthood. *Hum. Brain Mapp.* **35,** 4415–4427 (2014).
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20. Guassi Moreira, J. F., McLaughlin, K. A. & Silvers, J. A. Spatial and temporal cortical variability track with age and affective experience during emotion regulation in youth. *Developmental Psychology* **55,** 1921–1937 (2019).

Section 3: Hypotheses

In this section, please provide your research hypotheses. For each hypothesis:

- Be as specific as possible
- Provide the anticipated outcomes for accepting and/or rejecting the hypothesis

Hypotheses

1. **Both spatial and temporal variability decrease with age**
   This between-person relationship will be assessed using independent regression analyses with spatial and temporal variability as DV, respectively, and age as an IV.
2. **Spatial and temporal variability are stable across tasks**
   As the underlying process of neural specialization is assumed to be a stable trait-like characteristic at a specific point in time, the inhibition and emotion task should yield comparable results. This can be tested by performing a rank-order correlation on spatial and temporal variability for the two tasks.
3. **Both spatial and temporal variability are related to cognitive and emotional development**
   This relationship, and whether spatial and temporal variability contribute additively or through interaction, will be assessed using independent regression analyses with spatial and temporal variability as DV, respectively, and the following measures as an IV: IQ, EATQ (behavioral control), Social competence.

Section 4: Methods

In this section, you should make clear how the hypotheses are tested. Be as specific as possible. Please describe:

- The study design and study population (Which data do you require from which subjects?)
- The general processing steps (to prepare the data for analysis)
- The analysis steps (How are the data analysed to address the hypotheses? If possible, link each description to a specific hypothesis)
- Any additional aspects that need to be described to clarify the methodological approach (optional)

Study design, study population and sample size (e.g. cross-sectional or longitudinal; entire population or a subset; substantiate your choices)

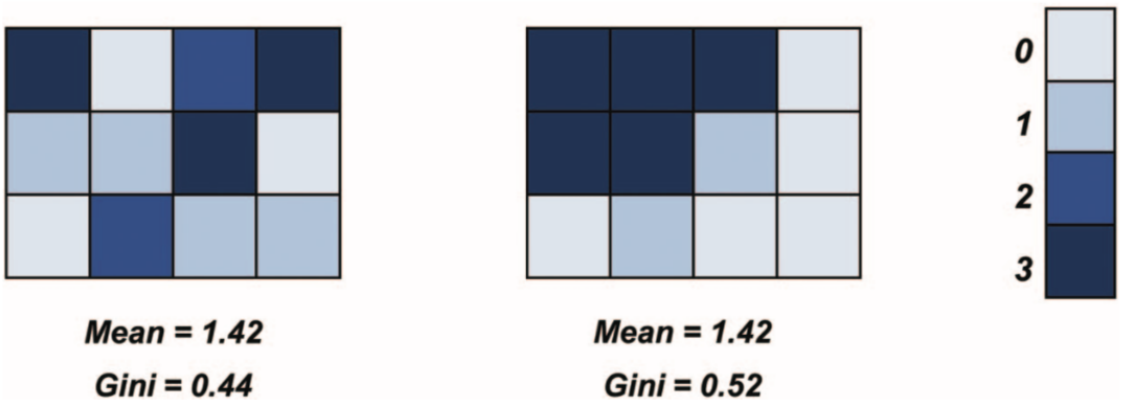
Cross-sectional, group with age spanning 8.5 to 11.5 years.

General processing steps to prepare the data for analysis

To prepare for the analysis of variability, image data for the task-related fMRI will be analyzed using SPM12 (http://www.fil.ion.ucl.ac.uk/spm). In brief, preprocessing will involve slice timing correction, realignment correcting for motion, spatial normalization to the Montreal Neurological Institute template brain. Functional data will be co-registered to the anatomical image (T1-weighted), and this image will not be used for any additional analyses.

For the initial task-specific analyses the data will also be spatially smoothed. For both tasks two contrasts will be created. For the inhibition task these are: 1) successful stops versus go trials with a stop-signal probability of zero percent, 2) successful stops versus go trials with a stop-signal probability of 20 and 33 percent (from here on referred to as >0% stop-signal probability). For the face processing task, two contrasts will be created as well: 1) images of faces versus rest, 2) images of faces versus images of houses. A recent reliability study of YOUth MRI acquisitions showed that these contrasts produce strong and relatively stable activation patterns at group level (Buimer et al., in preparation). Six realignment parameters will be added as regressors of no interest to correct for head motion. All data will be high-pass filtered with a cutoff of 128 seconds to control for low-frequency drifts. These analyses will produce four (two contrasts per task) t-maps for each participant.

For all contrasts a set of ROIs will be chosen from the automated anatomical labelling (AAL) template [16]. For the inhibition task, these are bilateral ROIs based on previous research [17,18], spanning the putamen, motor cortex, and frontal and parietal lobe. As the face/house task is aimed at activating face processing areas in the brain, we look at the variability of occipital, parietal and temporal regions [19].

Specific processing and analysis steps to address the hypotheses
Goal of the following analysis is to generate statistics for all participants for spatial and temporal variability of fMRI signal in both tasks for each region of interest. Spatial variability will be estimated after performing the task-specific statistical analysis, resulting in a number of contrasts. Univariate estimation estimates from voxels in pre-defined ROIs are used to calculate GINI-coefficients (specifics on this procedure, see Moreira and colleagues[20]). These coefficients serve as a measure of 'BOLD inequality' – with greater inequality of activation implying that a smaller subset of voxels account for a larger portion of BOLD signal within the ROI during a particular psycho-physiological process. Temporal variability will be estimated by taking the standard deviation of the voxels over time. This procedure will yield a set of coefficients for a set of ROIs indicating the degree of 'signal variability' for each subject.      **Figure 1.** Illustration of how a Gini coefficient used to characterize spatial variability. Both the pattern on the left and the right show a hypothetical distribution of activated voxels within a region of interest, where both yield the same mean activation level. However, the distribution on the left is more diffuse than the more focused activation pattern on the right, resulting in different Gini coefficients. *Adapted from Moreira et al., 2018* Temporal variability will be estimated by taking the standard deviation of a beta-series for a set of ROIs, with the method taken from Moreira and colleagues [20].

Additional methodological aspects (optional)

Section 5: Data request

In this section, please specify as detailed as possible which data (and from which subjects) you request.

Data requested
We will only use complete datasets. In other words, we will use data from subjects who have fMRI data from both tasks and an anatomical scan. The reason for this is that if one part of a set is missing, the data cannot be analyzed. Imputation is not possible.

Significant artefacts that yield one of the scans unusable will also lead to the exclusion of the subject.

Data request for the purpose of:

☒ Analyses in order to publish
☐ Analyses for data assessment only (results will not be published)

Publication type (in case of analyses in order to publish):

☐ Article or report
☐ PhD thesis
☒ Article that will also be part of a PhD thesis

Would you like to be notified when a new data lock is available?

☐ Yes
☐ No

Upon approval of a data request, the complete request will be made publicly available on our researcher's website by default.

Do you agree with publishing the complete request on our researcher's website after it is approved?

☐ Yes
☐ No. Please provide a rationale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