PREPARE Challenge Data Access and Data Processing Summary

1. A public link to the dataset and a description of how it can be accessed (if not public)

- The link to access the data: https://ida.loni.usc.edu/ (pending approval)
- The data processed for the PREPARE Challenge belongs to Alzheimer's Disease Neuroimaging Initiative (ADNI). Researchers interested in using the ADNI data need to submit a data access request to ADNI, which is reviewed by the ADNI Data and Publications Committee (DPC; https://adni.loni.usc.edu/data-samples/access-data/#access_data). ADNI indicates that the review process does not judge the merit of the scientific question, but largely exist to ensure compliance that the data is being shared with the scientific community; thus, the review process is used to check whether the applicant is affiliated with a scientific or educational institution, or has a legitimate reason to request the data. Being part of this competition should meet the requirement for data access.
- Once the researcher is approved by the DPC, they will be provided with a login to access the IDA https://ida.loni.usc.edu/. After logging in, the researcher is free to access the relevant data. The functional network products produced by our project team, as well as the relevant target/predictor data, and meta-data will be available via the ADNI-LONI data access portal.

2. If relevant, information about any data processing you did including:

a. How and where raw data were accessed

Raw neuroimaging data and clinical data matching to the MRI sessions were accessed via ADNI-LONI (see above for procedure to request data access)

b. A description of the processing

The structural and functional neuroimaging data underwent rigorous preprocessing and quality checking to attenuate variance related to several sources of known artifacts, using methods developed by both our laboratory and others. Description of data cleaning below is focused on both structural and functional (resting-state) brain images**.**

i. *Pre-processing of structural and functional images*

To obtain measures of functional connectivity, accurate measurement of brain structure is also necessary (i.e., to map the cortical surface, to identify sub-cortical regions of interest, etc.). As such, the description below begins with our procedures for processing structural magnetic resonance imaging (MRI) images, followed by details on pre-processing functional MRI images.

The processing of structural images (T1-weighted MRI images) was performed using FreeSurfer 6.0 to create cortical surface images. Structural processing included brain extraction, tissue segmentation, generation of white matter and pial surfaces, inflating surfaces to a sphere, and surface shaped-based spherical registration for the participant's native surface to fsaverage surface (Dale et al., 1999; Fischl et al., 1999). A single deformation map was created for each participant. The map combined two different deformation maps: one was generated when registering an individual's native surface to FreeSurfer's fsaverage atlas, and the other was generated through registering fsaverage-aligned data to a hybrid left–right fsaverage surface (fs_LR; (Van Essen et al., 2012)). Each individual's native FreeSurfer generated output was registered to fs_LR using the single deformation map in a one-step resampling procedure.

Resting-state fMRI images (blood oxygen dependent imaging; BOLD) were processed using a standard fMRI preprocessing pipeline using Nipype 0.8.0. The preprocessing steps included the following: (1) slice-timing correction because of interleaved slice acquisition; (2) rigid body correction for estimating and correcting head movement between frames; and (3) realignment to the T1-weighted image from the same session. All steps were performed using FSL 6.0, except for realignment between frames and rigid body correction. SPM8 was used for realignment and rigid body correction, as it provided more accurate estimates in our processing stream.

After initial fMRI preprocessing, resting-state functional correlation (RSFC) processing was applied to the preprocessed fMRI data using the following steps: (i) demean/detrend, (ii) multiple regression of tissue signal (grey matter [global signal regression], white matter, ventricle) and Friston 24 motion regressor (Friston et al., 1996), (iii) motion "scrubbing" (Power et al., 2014) where motion-contaminated frames were interpolated and replaced (contaminated frames were identified as having > 0.3mm frame-wise displacement [FD; a measure of head-motion from one volume to the next, calculated as the sum of the absolute values of the differentiated realignment estimates] or were between two contaminated frames that were less than 5 frames apart), (iv) bandpass filtering (0.009-0.8Hz), and (iv) removal of interpolated frames used for preserving time series during bandpass filtering in step (iii).

Considerable evidence has shown that older age is associated with greater amounts of head movement (Mowinckel et al., 2012; Savalia et al., 2017; Van Dijk et al., 2012), which has been shown to systematically alter the correlation structure of resting-state signals (Power et al., 2014, 2015; Satterthwaite et al., 2013; Van Dijk et al., 2012; Yan et al., 2013; Zeng et al., 2014). To this end, while a part of the global signal may contain variance related to general levels of arousal and neural activity (Keller et al., 2013; Schölvinck et al., 2010), a

major component of the global signal includes spatially nonspecific signal artifacts related to head motion, cardiac signals and breathing (Satterthwaite et al., 2013; Power et al., 2014, 2015, 2017). Removing the global signal thus helps control these known influences of artifact (Power et al., 2014, 2017; Yan et al., 2013). As no method presently exists for denoising known artifactual signals while retaining all remaining "real" signals, the alternate option of retaining the global signal in each participant is likely to result in misestimation of correlations and the resultant network measures. Based on these considerations, the RSFC processing description above includes a series of motion-processing procedures, including global signal regression (GSR) together with data- censoring ("scrubbing") and signal-processing procedures, as these procedures have been shown to best reduce global and distance-dependent artifacts (Ciric et al., 2017; Power et al., 2014). As such, the resulting RSFC data have been processed to greatly reduce variance attributable to motion-, respiration- and cardiac-related signals that could artifactually inflate functional correlation between brain areas that are close to each other in acquisition space (i.e., 3D voxel space).

ii. Quality control

Quality control (QC) for structural images was performed by manually inspecting images for skull-stripping quality, functional to anatomical registration, and anatomical to group-atlas registration. Any scans with subpar skull-stripping or registration were reprocessed with custom parameters. Structural data that failed skull-stripping or registration were excluded from further processing/analysis.

QC for functional images include checking the quality of signal by calculating the mean, standard deviation, and signal to noise ratio (SNR) for each voxel (across time) for each scan session. This step detects the outliers of fMRI signal in voxel-level signal. After removing of head motion related artifacts (i.e., scrubbing), only sessions with at least 100 BOLD frames remaining were retained for further analysis.

After functional data were mapped to the brain surfaces, surface-mapping QC included manual inspection of the mapped image. Data that did not contain full converge of the cortex or failed the mapping process were excluded.

iii. Construction of RSFC network matrices

Brain networks were constructed using the preprocessed resting-state data, for each individual(s) MRI session(s) that passed quality checks (as described above).

Our generation of brain networks are based on first defining biologically plausible brain network nodes (Wig et al., 2011). In the case of the functional MRI data we are processing, these nodes correspond to brain areas and plausible sub-divisions of brain areas. We have led and been involved with the development of methods to achieve this parcellation task (Chan et al., 2014; Han et al., 2018; Power et al., 2011; Wig, Laumann, Cohen, et al., 2014; Wig, Laumann, & Petersen, 2014).

For the present dataset, a functional correlation matrix was constructed for each participant. The correlation matrix was generated with 441 surface-based cortical nodes that were defined with boundary-based analyses (Chan et al., 2014; Wig, Laumann, & Petersen, 2014), and 61 volume-based subcortical nodes (Seitzman et al., 2020). Cortical nodes were generated with the following steps: (1) identifying putative area centers that were the local

minima of a previously published RSFC-boundary map (Cohen et al., 2008; Wig, Laumann, & Petersen, 2014) (2) creating disks with a radius of 3 mm around the identified area centers to avoid area borders that may exhibit more variance between individuals. Subcortical nodes were 4.5mm radius sphere created using MNI coordinates provided by Seitzman et al. (2020), resulting in the following 61 subcortical and cerebellar nodes: hippocampus (4), amygdala (2), basal ganglia (16), thalamus (12), cerebellum (27).

The pairwise Fisher's z-transformed correlation of all nodes was computed to create a correlation matrix (brain network). The first 100 cleaned RSFC frames were used for this analysis, to limit the bias introduced by using unequal number of frames in derivation of resting-state matrices (Han et al., 2024).

Each cortical/subcortical node was assigned to a large-scale functional system (Power et al., 2011). For cortical nodes, all vertices within a node disk were identified based on their spatial overlap with an a priori vertex-wise community map in the same fs_LR space (Power et al., 2011), where each disk was labeled with a functional system based on a winner-take-all approach. The subcortical nodes were assigned to the same a priori vertex wise community map (Power et al., 2011) based on the similarity of their patterns of resting-state correlations to the cortical systems. Specifically, functional timeseries of the voxels in the subcortex (Morel, 2013) and cerebellum (Diedrichsen et al., 2009) were correlated with the mean cortical network timeseries (after partialing out the other networks), and assigned to a specific cortical network (Seitzman et al., 2020). The anatomical parcel was assigned to a cortical network based on a winner-take-all approach, and sphere regions of interest (ROIs) were created in those parcels and labeled based on the same cortical network.

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