Supplementary Material S1. Estimation of the morphometric measures.

Of 183 patients screened for the present study a sub cohort of 123 also underwent a magnetic resonance imaging (MRI) protocol. MRI was performed on a 3 Tesla scanner (Discovery MR750, General Electric, USA) at the University of Campania 'Luigi Vanvitelli'. Sixty of 183 patients did not undergo MRI because of ferromagnetic materials in their body or of other conditions (e.g., history of claustrophobia). All exams were performed during the morning and all patients were instructed to stay motionless and awake during the scanning procedure.

During the enrolment of the patients, a hardware upgrade was performed by changing the head-coil of the scanner, therefore an early group of 62 patients were acquired with a 16-channels head-coil while a late group of 61 patients were acquired with a 32-channels head-coil. Structural data of the early group was obtained using a three-dimensional T1-weighted sagittal images (gradient-echo sequence Inversion Recovery prepared Fast Spoiled Gradient Recalled-echo) with the following parameters: repetition time (TR)= 6988 ms, inversion time (TI)= 1100 ms, echo time (TE)= 3.9 ms, flip angle= 10, voxel size= 1x1x1.2mm3, duration ~ 10 minutes). Similarly, structural data of the late group was obtained with the same sequence but different parameters: TR = 6900 msec, TE = 3.0 msec, resolution = 1x1x1 mm3, matrix size = 256x256, TI = 650 msec, duration ~ 7 minutes.

All data were processed using FreeSurfer (FS) version 7.1.1 (https://surfer.nmr. mgh.harvard.edu/) on a Hewlett-Packard workstation equipped with two 8-core Intel Xeon Bronze 3106 @1.70 GHz, 128 GB RAM and Linux CentOS 7. For all data sets, raw data were imported in FS and submitted to the standard structural image pre-processing and reconstruction pipeline of FS via the 'recon-all' command (for a detailed description of this procedure please see https://surfer.nmr.mgh.harvard.edu/fswiki/recon-all).[1] Quality control of the resulting brain reconstructions was performed by using the Euler number (EN) that is a measure of reconstructed brain surface complexity calculated by FS itself.[2] The EN is a mathematical property of a polygonal tessellation (e.g., surface) that can be obtained by the number of its vertices and faces. FS estimates, separately for each hemisphere, the EN with the following formula:

$$EN = 2-2n \quad (1)$$

where *n* is the number of defects (e.g., holes and bridges). During its automated reconstruction procedure FS aims to maximize the EN to the value of 2 that corresponds to having a flat surface (i.e., no defects), thus, the higher is the resulting EN the better is the surface reconstruction.

Following the workflow described in previous studies,[3,4] for each patient the EN was obtained by averaging the EN values calculated for the two hemispheres and, considering the EN values across the whole group, patients were considered as outliers and excluded from the subsequent statistical analyses if their EN was lower than the following threshold (th):

$$th = Q1-1.5*IQR \quad (2)$$

where Q1 is the first quartile and IQR is the interquartile range.[5]

The exclusion of the outliers based on the EN has been recommended for studies including hippocampal subfields or cortical areas and it has been found to correlate with motion artifacts and manual quality-rating.[3]

The data from three patients, belonging to the group acquired with the 32-channels head-coil, did not pass the quality check and were discarded. The remaining data, obtained from 120 patients, were further visually inspected and, where needed, additional manual editing was performed.[6] Morphometric data such as cortical thickness (CT) and volume (VOL) were estimated, respectively, for a cortical representation of the Papez circuit[7] and three subregions of the hippocampus[8] that have been previously shown to play a critical role in mnemonic functions.[9]

First, considering the Papez circuit,[7] we focused our attention on a bilateral network of 12 cortical region-of-interest (ROIs) as (i) it is difficult to observe the whole Papez circuit with the resolution of the current imaging modalities (see e.g., Choi et al.[10] for a high-resolution diffusion imaging study) and (ii) there are no available atlases.[11] In particular, following the selection performed by Simeone and colleagues,[11] we considered the cortical segmentation available in the FS's atlas[12] and the CT values were estimated bilaterally for four regions in the cingulate area (i.e., caudal anterior, rostral anterior, isthmus and posterior regions), for the entorhinal cortex and the parahippocampal region.

Second, considering that the hippocampus is not a homogeneous structure, but it is divided into subfields with specific features, VOL data (after intracranial volume correction) were extracted for the three larger subfields as defined in the FS hippocampal subfields atlas, namely head, body, and tail.[8]

References

1. Fischl B. FreeSurfer. Neuroimage 2012; 62: 774-781.

2. Dale AM, Fischl B, Sereno MI. Cortical surface-based analysis. I. Segmentation and surface reconstruction. Neuroimage 1999; 9: 179-194.

3. Rosen AFG, Roalf DR, Ruparel K, et al. Quantitative assessment of structural image quality. Neuroimage 2018; 169: 407-418.

4. Monereo-Sánchez J, de Jong JJA, Drenthen GS, et al. Quality control strategies for brain MRI segmentation and parcellation: Practical approaches and recommendations - insights from the Maastricht study. Neuroimage 2021; 237: 118174.

5. Tukey JW. Exploratory Data Analysis, Addison-Wesley, Massachusetts, Reading, 1977.

6. Canna A, Russo AG, Ponticorvo S, et al. Automated search of control points in surface-based morphometry. Neuroimage 2018; 176: 56-70.

7. Papez JW. A proposed mechanism of emotion. 1937. J Neuropsychiatry Clin Neurosci 1995; 7: 103-112.

8. Iglesias JE, Augustinack JC, Nguyen K, et al. A computational atlas of the hippocampal formation using ex vivo, ultra-high resolution MRI: Application to adaptive segmentation of in vivo MRI. Neuroimage 2015; 115: 117-137.

9. Forno G, Lladó A, Hornberger M. Going round in circles-The Papez circuit in Alzheimer's disease. Eur J Neurosci 2021; 54: 7668-7687.

10. Choi SH, Kim YB, Paek SH, Cho ZH. Papez Circuit Observed by in vivo Human Brain With 7.0T MRI Super-Resolution Track Density Imaging and Track Tracing. Front Neuroanat 2019; 13: 17.

11. Simeone P, Auzias G, Lesimple B, et al. Memory impairment associated with Papez circuit lesions in patients with severe traumatic brain injury assessed by diffuse tensor imaging and volumetric MRI analysis., In Review, 2022.

12. Desikan RS, Ségonne F, Fischl B, et al. An automated labeling system for subdividing the human cerebral cortex on MRI scans into gyral based regions of interest. Neuroimage 2006; 31: 968-980.