Enhanced brain activity associated with memory access in highly superior autobiographical memory

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SUPPLEMENTARY INFORMATION

Methods

Participants: Seventy-three individuals contacted us claiming to possess HSAM. They were initially screened trough a telephone interview in which they were tested with the "Public event" quiz [1] (see below). Eight of those adults (5 males; mean age: 32.5 y.o.; range: 24-37 y.o.) scored well beyond the HSAM threshold of 24.0, with an average score of 59.2 (sd = 22.5; Table S1). The 24.0 threshold was estimated as the average score obtained by control individuals plus 3.09 standard deviations. This threshold corresponds to the value below which 99.9% of all observations collected in a random-sampled population would be found. In accordance with previous studies [1], the eight subjects that scored beyond the HSAM threshold were further tested with the even more challenging "Ten dates" quiz (see below). These subjects scored overall 75.4% at this test, well beyond the threshold established by the previous literature (65%; [1]) to confirm HSAM. Twenty-one control subjects (10 male; mean age: 32.5 y.o., range: 24-39 y.o.) were also included in the study. Their average score on the Public event quiz was 9.5 (SD = 4.7).

Specifically, the screening procedure consisted of the Public events quiz and the Ten dates quiz [1], both administered via telephone interviews, with no time limits.

The Public events quiz consisted of thirty questions, based on public events selected from five categories: sporting events, political events, notable negative events, events concerning famous people and holidays. For fifteen of these questions the subjects were requested to retrieve the date of a given significant public (national or international) event (e.g., "Please give the day of the week and precise date with day, month and year of when Federica Pellegrini, the famous Italian swimmer, won the gold medal at the Olympic game in Beijing"); the remaining fifteen questions requested participants to associate a given date with a highly significant public event (e.g., "What happened on the 25th of June 2009?"). All questions concerned events that took place when the subjects were at least 8 years old. The order of presentation of questions was randomised and counterbalanced. For each question, individuals were asked to name the day of the week the date fell on. One point was awarded for each correct response (i.e., the event, the day of the week, the month, the date and the year); the maximum total score was 88 points.

The Ten dates quiz consisted of ten computer-generated random dates, ranging from the individuals' age of fifteen to the day before the testing. Individuals were asked to provide three details for each date: (1) the day of the week; (2) a description of a verifiable event (i.e. any event that could be confirmed via a search engine) that occurred within one month before and after the generated date; (3) a description of a personal autobiographical event. One point each was awarded for the correct day of the week, a correct public event, and unverified personal autobiographical memory. A maximum of three points per date could be achieved (30 points total).

Task and stimuli: During scanning, participants were asked to retrieve autobiographical memories (AMs) [2]. To ensure that participants retrieved AMs with specific spatiotemporal coordinates, we requested them to locate either the "first" or the "last" time in which a specific event occurred (e.g., "The first time you drove a car" or "The last time you went to a restaurant"; see Table S2). Participants first confirmed the appearance of AM through a response button ("access" phase) and then continued to elaborate on the retrieved event in as much detail as possible for the remaining part of the trial ("reliving" phase). Thirty seconds after the onset of the auditory cue, participants were given auditory instructions to rate the amount of emotion and reliving associated with the memory. They were presented with two auditory sentences: "Emotional level: negative, mild negative, neutral, mild positive, positive" (duration = 13 sec) and "Reliving: low, medium, high" (duration = 9 sec). Participants pressed the response button corresponding to the appropriate level. A semantic recall condition was included to control for abstract knowledge retrieval [3]. Specifically, participants were presented with a given semantic category (e.g., "Examples of animals"; see Table S2) and instructed to mentally generate as many examples as possible of items belonging to that category and then press the response button when the first example of that given category came to their mind. Again, thirty seconds after the onset of the semantic auditory cue, participants were asked to rate the ease with which they were able to generate examples (very difficult, difficult, easy, very easy; duration = 11 sec) and the approximate number of examples they were able to generate (fewer than 5, between 5 and 10, more than 10; duration = 11 sec).
During scanning participants were instructed to keep their eyes closed. Along with the three functional runs related to the memory task we also acquired for each participant an additional run of resting state (8 min) for a separate report.

Post-scanning interview: Post-scanning, participants were asked to provide details about memories retrieved during the experiment (see, for a similar procedure, [3-4]). First, we asked participants to provide a detailed description of the AM they had retrieved during scanning, and to retrieve the emotional and reliving evaluation provided during scanning. We then asked them to date as accurately as possible the timing of the event and to state its emotional salience (no importance, important enough, important, very important). Richness of details reported in the AM description was quantified by following the procedure used by Levine et al. [5]. Briefly, we computed the mean number of details of the events retrieved by participants in the post-scanning interview according to the following categories: event (happenings, individuals present, weather conditions, physical/emotional actions, or reactions in others); time (year, season, month, day of week, time of day); place (localization of an event including the city, street, building, room, part of room); perceptual (auditory, olfactory, tactile, taste, visual and visual details, body position, duration);

thought/emotion (emotional state, thoughts, implications) (Fig. 1e). Moreover, we performed a qualitative evaluation of the retrieved events (Fig. S2), assigning from 0 (no mention of information) to 3 points (highly vivid description) according to the time, place, perceptual, and thought/emotion categories, plus two other categories: "time integration" (integration into a larger time scale as evidenced by inclusion of temporal contextual information or relation to other life periods) again on a 3 points scale, and "episodic richness" (the overall degree to which a feeling of re-experiencing was conveyed) on a finer grained 6 point scale. For SM trials, we asked participants to retrieve the examples generated during scanning and to estimate their confidence in having reported all the examples originally generated (low, medium, high).

Magnetic Resonance Imaging: A quadrature volume head coil was used for radio frequency transmission and reception. Head movement was minimized by mild restraint and cushioning. Thirty-two slices of functional MR images were acquired using blood oxygenation level-dependent imaging (3 x 3 mm, 2.5 mm thick, 50% distance factor, repetition time = 2.08 s, time echo = 30 ms), covering the entirety of the cortex.

fMRI Data Analysis: After having discarded the first 4 volumes of each run, all images were corrected for head movements. Slice-acquisition delays were corrected using the middle slice as reference. All images were normalized to the standard SPM12 EPI template, resampled to 2 mm isotropic voxel size, and spatially smoothed using an isotropic Gaussian kernel of 8 mm FWHM. Time series at each voxel for each participant were high-pass filtered at 220 s and pre-whitened by means of autoregressive model AR(1).

Statistical inference was based on a two-steps random effects approach: First-level multiple regression models estimating contrasts of interest for each subject, followed by the second-level analyses for statistical inference at the group-level (with non sphericity correction). The first-level models had separate regressors for the Cue, Access, Response, Reliving, and the Ratings in the task [4]. Stimuli functions varied between regressors as either zero duration Dirac delta functions (Cue and Response) or as fixed (Ratings, 22 sec) or variable duration box-car functions (Access and Reliving) that depended on the time of the motor response of each single subject. First-level models could also include a final regressor for those trials in which participants failed to retrieve the specific AM or SM (i.e., "no memory" trials, modelled as fixed duration box-car functions of 52 sec, i.e., whole trial length). The primary aim of the present study was to investigate neural activation associated with AM retrieval in HSAM subjects, compared to controls, and its specificity with regard to access to or reliving of autobiographic memories. Accordingly, for each subject we estimated contrast images that removed the activity associated with access to and reliving of SM (control condition) to the main AM conditions. (This was done after having verified the substantial overlap between SM mechanisms in each group; Fig. S3.) This resulted in 4 contrast images per group: "access to first AM > access to SM"; "reliving of first AM > reliving of SM"; "access to last AM > access to SM"; "reliving of last AM > reliving of SM". The single-subjects contrast images of parameter estimates were entered into a mixed design ANOVA with group (HSAM vs. control) as between-subjects variable and phase (access vs. reliving) and AM type (first vs. last) as within-subjects variables at the second-level group-analysis.

Functional connectivity analysis: To explore the functional connectivity of the three regions selectively involved in AM access in HSAM subjects we used analyses of inter-regional connectivity as implemented by the "Generalized Form of Context-Dependent Psychophysiological Interactions" SPM toolbox [6]. At the subject level, each psychophysiological interaction analysis included together with the first-level regressors corresponding to the psychological variables of interest (see above first-level analysis), the time course of the seed area (the physiological variable), and the critical crossproducts (i.e., the psychophysiological interaction term) between the six psychological variables of interest (phase X trial type) and time course of the seed area. The head motion realignment parameters were included as covariates of no interest. As in the main standard analysis, we estimated for each subject contrast images that removed the activity associated with access and reliving of SM (control condition) to the main AM conditions. The resulted four contrast images per group were entered into a mixed design ANOVA with the factors of group, AM phase and AM type. We then tested for changes of VMPFc, DMPFc, or TPJ connectivity with the rest of the brain, as a function of group (HSAM > control), with the additional constraint of considering only voxels showing a group x phase interaction (T-contrast, p-unc. = 0.001), ensuring that we selected only regions activated by access to AM in the HSAM group [7]. The statistical threshold was set to p = 0.05, FWE corrected at the voxel level, considering the whole brain as the volume of interest.

ROI correlations with memory access latencies and obssessiveness scores in HSAM subjects: We used two multiple regression models. The first one included the activity related to the access of remote AMs (i.e., "access to first AM > access to SM") and the mean individual latencies to access remote AMs as behavioral parameter. The second included the activity related to the access of recent AMs (i.e., "access to last AM > access to SM") and the mean individual latencies to access recent AMs as behavioral parameter. We tested these effects within the three ROIs (small volume correction [8]) showing enhanced activity during memory access in the HSAM group (i.e., the left VMPFc, the left DMPFc, and the left TPJ; Fig. 2B), plus the left hippocampus, showing increased functional connectivity with the VMPFc during memory access (Fig. 3). Any significant effect in HSAM individuals was compared with analogous multiple regression models based on control subjects data. The four ROIs were centred on the peak of activity related to controls. These peaks were selected by averaging, at the second level model, the activity across the four main conditions (AM phase x AM remoteness) in the control group, i.e., using an unbiased "all positive" t-contrast highlighting the overall brain activity [9]. Finally, we used similar multiple regression models to investigate whether the activity related to the access to remote or recent AMs covariates as a function of obsessive-compulsive traits in HSAM subjects. In this case, the multiple regression models included the activity related to the access of either remote or recent AMs plus the individual obsessivess score as behavioral parameter.

Table S1. Sex, age and mean score at the "Public Events" quiz [1] of the recruited participants.

	Sex	N.	Mean Age (y)	Mean Score (%)	Average Age (y)	Average Score (%)
HSAM	M	5	31.2 ± 6.2	68.6 ± 19.8	32.3 ± 5.0 y.o.	59.3 ± 22.3
	F	3	34.0 ± 2.0	43.7 ± 19.3		
Controls	M	10	30.9 ± 6.1	8.6 ± 4.7	32.5 ± 5.9 y.o.	9.5 ± 4.7
	F	11	33.9 ± 5.5	10.2 ± 5.1		

Table S2. Auditory sentences used as memory cues to trigger autobiographical ("first time" or "last time" events) and semantic memories ("example of", based on [10]).

The first time that you:	**The last time that you:**	**Example of:**
drove a car	had a fever	clothes
kissed someone	went to a theatre	furnitures
smoked a cigarette	went to a restaurant	kitchen utensils
have been at a stadium	swam in the sea	jobs
went to a concert	went to an amusement park	body parts
went to a funeral	gave or received a present	car brands
went to a wedding	have been on holidays	sports
went on a school trip	saw a sunset	animals
danced at a disco	took a train	metals
went to a foreign country	had an argument with someone	fabrics
took an airplane	cooked something	music instruments
had an accident	lodged at a hotel room	diseases
have been awarded a prize	celebrated your birthday	gemstones
went on a boat trip	stayed over at a friend's place	flowers
swam in a swimming pool	lost something	fruits
went skiing	went to a shopping mall	trees
rode a bicycle	cut your hair	working tools
practiced a sport	fixed something	vegetables

Figure S1. Mean ratings of AM and SM provided by the participants during fMRI scanning. a) Emotional level: negative (neg), mild negative (mNeg), neutral (neu), mild positive (mPos), positive (pos); b) Level of reliving: low (L), medium (M), high (H); c) Easiness of generating SM examples: very difficult (vD); difficult (D); easy (E); very easy (vE); d) Number of generated examples: low (L; i.e., less than 5), medium (M, i.e., between 5 and 10), high (H, i.e., more than 10).

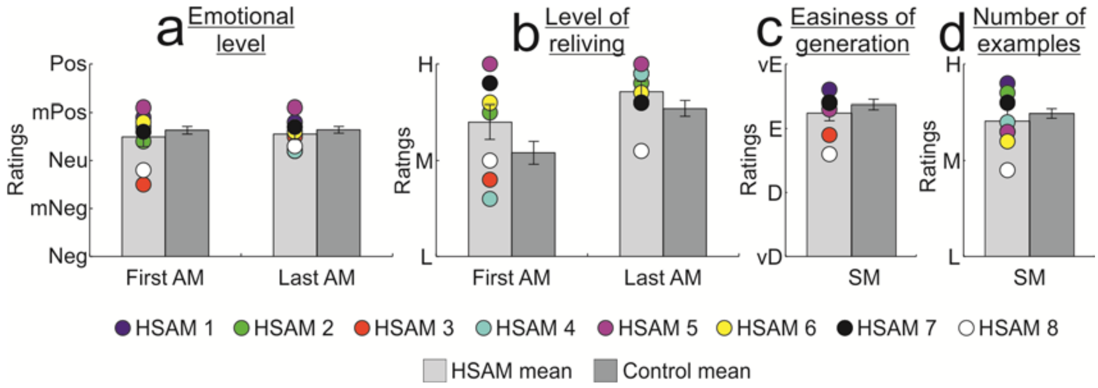


Figure S2. Qualitative evaluation of retrieved events according to Levine et al.'s [5] categories: episodic richness (ER), time, place, perceptual, thought/emotion (T/E), time integration (TI).

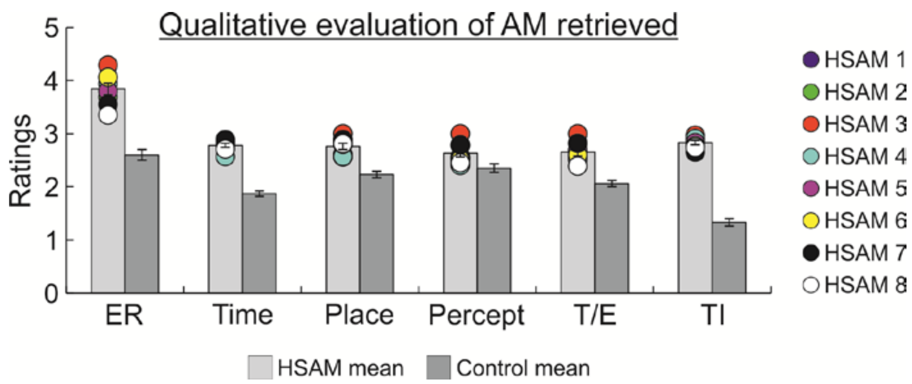
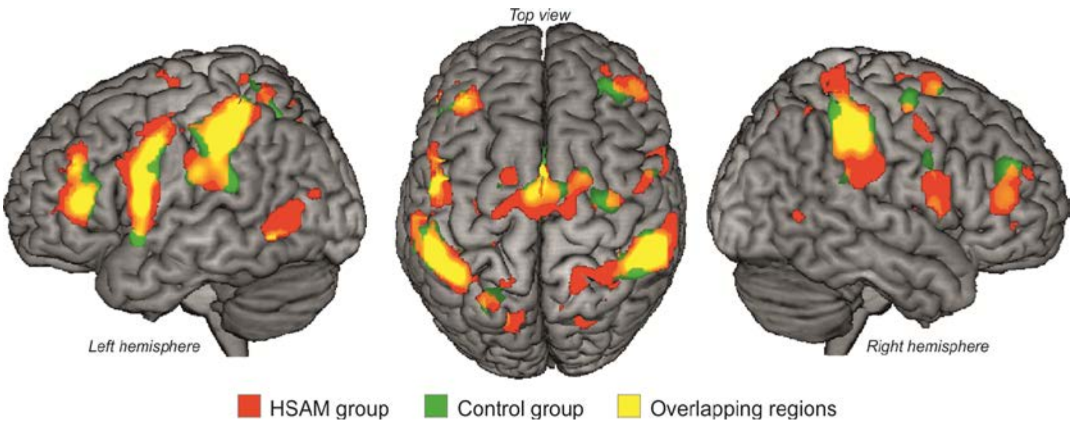


Figure S3. Regions activated by semantical vs. autobiographical memory – irrespective of the access or elaboration phase – showing overlapping regions between HSAM and control subjects. The maps are displayed at a threshold of p-FWE-corrected < 0.05.



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