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Single Case Report

Lifelong impairment in episodic re-experiencing: Neuropsychological and neuroimaging examination of a new case of Severely Deficient Autobiographical Memory

Matilde Conti [a,*], *Alice Teghil* [a,b], *Antonella Di Vita* [c] *and Maddalena Boccia* [a,b]

[a] *Department of Psychology, Sapienza University of Rome, Rome, Italy*
[b] *Cognitive and Motor Rehabilitation and Neuroimaging Unit, IRCCS Fondazione Santa Lucia, Rome, Italy*
[c] *Department of Human Neuroscience, Sapienza University of Rome, Rome, Italy*

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ABSTRACT

Autobiographical memory (AM) represents a complex and multimodal cognitive function, that allows an individual to collect and retrieve personal events and facts, enabling to develop and maintain the continuity of the self over time. Here we describe the case of DR (acronym of the fictional name Doriana Rossi), a 53-year-old woman, who complains of a specific and lifelong deficit in recalling autobiographical episodes. Along with an extensive neuropsychological assessment, DR underwent a structural and functional MRI examination to further define this impairment. The neuropsychological assessment revealed a deficit in episodic re-experiencing of her own personal life events. DR showed reduced cortical thickness in the Retrosplenial Complex in the left hemisphere, and in the Lateral Occipital Cortex, in the Prostriate Cortex and the Angular Gyrus in the right hemisphere. An altered pattern of activity in the calcarine cortex was detected during ordering of autobiographical events according to her own personal timeline. The present study provides further evidence about the existence of a severely deficient autobiographical memory condition in neurologically healthy people, with otherwise preserved cognitive functioning. Furthermore, the present data provide new important insights into neurocognitive mechanisms underpinning such a developmental condition.

1. Introduction

Autobiographical memory (AM) – namely, the memory systems that encode, consolidate and retrieve personal events and facts (Fossati, 2013) – is an ensemble of events and knowledge integrated into a coherent story of the self, that allows individuals to create meaning and purpose in life (Fivush & Graci, 2016). This is possible because autobiographical memory is deeply intertwined with autonoetic consciousness, that enables to be aware of subjective time in

* *Corresponding author*. Department of Psychology, "Sapienza" University of Rome, Via dei Marsi, 78, 00185 Rome, Italy.
E-mail address: matilde.conti@uniroma1.it (M. Conti).
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which events happened, and to mentally travel back to past episodes to retrieve them in a recollective way (Tulving, 2002; Wheeler et al., 1997). According to Bluck (2003) the importance of autobiographical memory in everyday life functioning lies in three main aspects: AM guarantees the development and continuity of the self (self function); facilitates empathic processes and social interactions (social function); contributes to problem solving and to guide behavior through the prediction of future events (directive function) (Bluck, 2003). Autobiographical memory can be distinguished into an episodic and a semantic component: episodic autobiographical memory (EAM) refers to events that are situated in a specific spatial and temporal context and recollected with sensory-perceptual details, thoughts and emotions. Instead, semantic autobiographical memory (SAM) concerns knowledge about the self (Levine, 2004) and involves personal information detached from the context of acquisition, namely abstracted and generalized forms of personal semantics (PS; e.g., I am a PhD student) (Renoult et al., 2012). However, specific categories of PS, such as autobiographical facts, are considered "experience-near" (enPS; e.g., I am a PhD student at the Department of Psychology since 2022 and every day I reach the Department by train), since they are more strongly associated with a spatiotemporal context compared to general semantic knowledge, that is devoid of contextual features (Grilli & Verfaellie, 2014, 2016).

Neuroimaging studies identified a set of brain areas involved in this complex and multimodal cognitive function. In a meta-analysis Svoboda et al. (2006) identified a "core" AM network consisting in medial and ventrolateral prefrontal cortices, medial and lateral temporal cortices, the temporoparietal junction, the retrosplenial/posterior cingulate cortex and the cerebellum (Svoboda et al., 2006). Cabeza and St Jacques (2007) described activations according to the main components of the AM retrieval network. In particular, search and controlled processes involve the left lateral prefrontal cortex; self-referential processes rely on the medial PFC and recollection engages the hippocampus and the retrosplenial cortex (Cabeza & St Jacques, 2007). Autobiographical memory functioning spans along a distribution of different performances in healthy individuals; within this distributions, two conditions, respectively named Highly Superior Autobiographical Memory (HSAM, LePort et al., 2012) and Severely Deficient Autobiographical Memory (SDAM), represent the extremes of the continuum (Palombo et al., 2015, 2018). HSAM refers to the ability to recall personal events with a high degree of details and accuracy, without the apparent use of mnemonic skills (LePort et al., 2012), while SDAM concerns a lifelong and selective impairment in re-experiencing personal events (Palombo et al., 2015). Even if the paucity of group-studies and case reports prevents any definite conclusion, these two conditions have been tentatively associated with specific patterns of alterations in the brain network of autobiographical memory. Specifically, HSAM has been associated with increased activation of the prefrontal/hippocampal circuit (Santangelo et al., 2018). On the other hand, little is known about the brain correlates of SDAM. Indeed, the only few cases have been reported by Palombo et al. (2015). In a small sample of three individuals, they found that the deficit in autobiographical memory was associated with reduced activation in the core autobiographical memory network, including the prefrontal cortex and the precuneus.

In this paper we provide an extensive neuropsychological and neuroimaging examination of DR, a woman who complains of a lifelong severe deficit in reliving autobiographical events.

2. Methods

No part of the study procedures or analyses was preregistered prior to the research being conducted. We report how we determined our sample size, all data exclusions (if any), all inclusion/exclusion criteria, whether inclusion/exclusion criteria were established prior to data analysis, all manipulations, and all measures in the study.

2.1. *Case presentation*

DR, a 53-year-old woman, came to our observation for the first time in 2017, complaining of lifelong memory difficulties. She referred a main impairment in retrieving past autobiographical events and public events. Also, she reported difficulties in episodic memory and slow learning since she can remember. For instance, DR reported to be unable to freely recall specific events occurred during a holiday; she referred to be unable to recall such events also when cues were provided by significant others. She reported to have difficulty in linking events in her memory, to have patchy and "abstracted" memories, and to be completely unable to relive events occurring during her own life. Instead, she reported to be able to learn sequences of movements, such as during dancing. Nevertheless, DR holds a Master's degree and is fully independent in her social and work activities. She reported to have spontaneously developed a sort of hierarchical strategy to recall events, using a lifetime period as an index to deepen the search of a specific memory. Parallel to this process, she used personal information to "jump" from one event to the others, looking for a specific event, without a systematic searching procedure. There is no evidence of neurological disease in her history. Radiological examination, performed in the context of the present study, confirmed the absence of any brain malformation or damage. There was no evidence in her history of a psychiatric condition at the time of the investigation. She has a high socio-economic condition, satisfying relationships and an active lifestyle. She does not report conflicts in her family of origin. Her problem in recalling events from her own past has not limited her achievement in life. Nonetheless she refers a sense of frustration regarding this deficit, especially when is brought out in social environments (e.g., when a friend is astonished because she does not remember a trip taken together). DR underwent an extensive neuropsychological and neuroimaging examination (see below) to investigate the difficulties mentioned above. Control samples were derived from our previous datasets, if possible, or enrolled ad hoc for the present study (see below for further information). Subsamples were always matched for gender and age, with the exception of the fMRI study, in which age was entered as a covariate. All control participants were right-handed, without a previous or current history of neurological or psychiatric

disorders. These inclusion criteria were established prior to data collection and analyses. Sample size was determined based on the previous case reports of developmental deficits (see for example Nemmi et al., 2015; Palermo, Piccardi, et al., 2014) and single-case methodology (Crawford & Garthwaite, 2006; Crawford & Howell, 1998). She gave written informed consent to the study, that was approved by ethical committee of the IRCCS Fondazione Santa Lucia.

2.2. Neuropsychological assessment

In 2017, DR underwent a first neuropsychological assessment. The assessment included an extensive investigation of attention, memory, working memory and constructional praxis (see Table 1 for specific information about tasks administered). As a part of the neuropsychological examination, a psychological assessment was performed through a

Table 1 – Scores obtained by DR in the neuropsychological assessment.

Test	DR's score	ES[a]/Cut-off[b]/SD[c]
Attention		
Test of everyday attention (Cantagallo & Zoccolotti, 1998; Robertson et al., 1996)		
Map search	79	−.05[c]
Elevator counting	7	0[c]
Elevator counting with distraction	10	.47[c]
Visual elevator	10	.66[c]
Auditory elevator with reversal	8	.26[c]
Telephone search	2.95	−.75[c]
Telephone search dual task	1.03	.1[c]
Lottery task	9	−1.1[c]
Memory		
Rey auditory verbal learning test (Carlesimo et al., 1996; Rey, 1964)		
Immediate recall	59	4[a]
Delayed recall	11	4[a]
Recognition	15	
Prose memory test (Novelli et al., 1986)	20	4[a]
Digit span (Monaco et al., 2013, 2015)		
Forward	7	4[a]
Backward	5	4[a]
Corsi block tapping task (Corsi, 1972; Monaco et al., 2013, 2015)		
Forward	5	2[a]
Backward	4	2[a]
Rey complex figure test (Carlesimo et al., 2002; Rey, 1941)		
Immediate recall	13.5	2[a]
Delayed recall	15.5	2[a]
Corsi supra-span (Capitani et al., 1980; Piccardi et al., 2013)		
Learning	157	1.18[c]
Delayed recall	8	.71[c]
Famous events questionnaire 1966–1997 (Budriesi et al., 2002)		
1994–1997	**3**	3.573[b]
1990–1993	**4**	3.911[b]
1986–1989	**2**	3.526[b]
Recognition of names of famous people (Bizzozero et al., 2007)		
Name recognition	7926	3[a]
Personal identification	268	
Famous people (correct answers)	56	
Semantic score	**4.77**	0[a]
Working memory		
Paced auditory serial addition task (Ciaramelli et al., 2006; Gronwall, 1977)		
Stimulus interval 4000	1	3.7[b]
Stimulus interval 3000	6	7[b]
Stimulus interval 2600	2	6[b]
Stimulus interval 2200	**16**	9[b]
Stimulus interval 1800	**11**	10[b]
Constructional praxis		
Rey complex figure test (Carlesimo et al., 2002; Rey, 1964)		
Copy	35	3[a]

Pathological scores are marked in bold.
[a] equivalent scores adjusted for sex, age and years of education.
[b] cut-off.
[c] standard deviation.

clinical interview. No signs of an ongoing psychopathological process were detected during the interview, including mood, anxiety, or psychotic disorders. DR came spontaneously to our laboratory to explore her lifelong impairment; she was highly motivated and collaborative. At the time of the assessment, she was not involved in any legal litigation nor requesting a claim of disability linked to her job.

2.3. Autobiographical memory assessment

In April 2022 DR underwent an extensive assessment of autobiographical memory through the administration of the Autobiographical Interview (Levine et al., 2002). The Autobiographical Interview is a semi-structured interview in which the subject is asked to choose and retrieve an event occurred in a specific spatio-temporal context, from each of five life periods: childhood (ages 0–11), adolescence (ages 11–18), early adulthood (ages 18–30), adulthood (ages 30–55) and the last year. Retrieval is manipulated by increasing structure in three conditions: free recall, general probe and specific probe. During free recall the subject is asked to describe the event in as much detail as possible without any interruption from the examiner, until a natural ending point is reached or five minutes had passed (for similar procedure see also Palombo et al., 2015). After retrieval of an event, the examiner can use general probes to encourage greater recall of details. Finally, the specific probe consists in a structured interview designed to elicit additional details that were not spontaneously retrieved and is administered at the end of the recall condition. Questions in specific probe are organized into five categories: event (happenings, weather, other people and their behavior), time (year, month or season, date, day of the week, time of day), place (country, province, city, street, address, building, room within building, and location within room), other sensory information (visual images, colors, tastes, smells, sounds, physical sensations, body position and event duration), and emotion/thought (feelings and thoughts at the time of the event). The interview is audio-recorded and subsequently transcribed for scoring. Each memory is then segmented into informational bits or details, which are defined as a unique occurrence, observation or thought typically expressed as a grammatical clause. There are two broad categories of details: internal and external. Internal details are those pertaining directly to the main event, specific to time and place, and considered to reflect episodic re-experiencing; external details are semantic (facts or extended events that do not require recollection of a specific time and place), repetitions or other details.

2.3.1. Autobiographical Interview analysis

We first tallied and summed details for each category, forming an Internal and an External composites. We then calculated the ratio of internal-to-total details, which reflects episodic re-experiencing unbiased by the total verbal output (Levine et al., 2002). We computed this index to control for individual variability in spontaneous speech, specifically to avoid potential confounds associated with verbosity (for similar procedures see Setton et al., 2022; Spreng et al., 2018). In line with Levine et al. (2002), scores were analyzed cumulatively across the different levels of recall. Since we aimed to test episodic re-experiencing, as a first step we focused on the ratio of internal-to-total details in overall DR's production. Then, we computed this ratio for each period separately, in order to disclose a possible gradient. Given the lack of normative data for the Italian population, scores obtained by DR in the Autobiographical Interview were compared to those of a control group specifically enrolled for the purpose of the present study ($n = 7$, all females), by using a *t*-test modified procedure (SinglimsEX.exe; https://homepages.abdn.ac.uk/j.crawford/pages/dept/abnolims.htm; Crawford et al., 2010). The control group was matched with DR for age ($t = .097$, $p = .46$) and education ($t = .79$, $p = .23$). All control participants gave written informed consent to participate to the study.

2.4. Imaging protocol

In 2018 DR underwent an MRI scanning at IRCCS Fondazione Santa Lucia, in Rome. Later, in 2022, she further participated in a task-based fMRI protocol, developed in the context of an independent study investigating brain correlates of temporal ordering of autobiographical information (Teghil et al., 2022). The study was designed in accordance with the principles of the Declaration of Helsinki and was approved by the Ethical Committee of IRCCS Fondazione Santa Lucia. Informed consent was obtained from the patient and from all control participants (see below).

2.5. Structural MRI examination

Images were collected using a Philips Achieva scanner, operating at 3T. A three-dimensional, high-resolution T1-weighted structural image (TR = 13,000 msec, TE = 5.8 msec, flip angle = 8°, 256 × 228 image matrix, .5 × .5 mm in-plane resolution, 342 contiguous .5 mm thick sagittal slices) was acquired.

2.5.1. Structural MRI analyses

Surface-based morphometry analyses were performed on T1-weighted structural images, using the Computational Anatomy Toolbox (CAT12, http://dbm.neuro.uni-jena.de/cat12/), an extension to SPM12 (http://www.fil.ion.ucl.ac.uk/spm/).

T1 images were manually checked for scanner artefacts and gross anatomical abnormalities. Images were normalized using high-dimensional Diffeomorphic Anatomical Registration Through Exponentiated Lie Algebra (DARTEL) normalization, and segmented into grey matter (GM), white matter and cerebrospinal fluid (CSF). Cortical thickness (CT) was estimated in native space before any spatial normalization. CT was estimated automatically using the projection-based thickness (PBT) method (Dahnke et al., 2013), and performing topological correction (Yotter, Dahnke, et al., 2011), spherical mapping (Yotter, Nenadic, et al., 2011), and spherical registration. Data were quality-checked and smoothed using a 15-mm FWHM kernel.

We performed a ROI-based morphometry analysis. Estimated values of CT were extracted according to the surface-based atlas parcellation by Glasser et al. (2016), included in CAT12. Individual CT values of DR in the ROIs were then compared to those extracted from a sample of healthy individuals ($n = 5$, all females, mean age = 48.8, all holding a master's degree) that were specifically recruited for the purpose of this investigation and underwent the same MRI

protocol. All control participants gave written informed consent to participate to the study. CT values were compared between DR and the control group using the modified t-test procedure proposed by Crawford and Howell (1998).

2.6. *fMRI paradigm*

In 2022, DR took part in a task-based fMRI protocol, developed in the context of an independent study investigating brain correlates of temporal ordering of autobiographical information (Teghil et al., 2022). Data acquired from DR were not included in the original study. More in detail, the previous study investigated brain regions supporting the ordinal organization into lifetime periods along the personal timeline for different types of personal knowledge, namely episodic autobiographical memories (EAMs), and experience-near personal semantic memories (enPS), that correspond to conceptual knowledge about the self that is more strongly associated with a spatiotemporal context compared with general semantic knowledge (Grilli & Verfaellie, 2014, 2016) (Teghil et al., 2022). Stimuli presented during the fMRI task were collected using a modified version of the Autobiographical Fluency Task (Dritschel et al., 1992). Stimuli were collected outside the scanner, immediately before the fMRI acquisition.

In brief, for each of 5 life periods (5–11 yrs, 11–14 yrs, 14–19 yrs, >19 years excluding the last 12 months, last year) DR was asked to report personal events (EAMs) and names of friends, teachers, schoolmates or colleagues (enPS) corresponding to those periods. The instructions specified that she had to report as many items as possible for each period and category, and to provide a label uniquely identifying the specific EAM or enPS. Also, she was asked to report only events occurred at a specific time and place, and names of persons not associated to multiple life periods. 90 sec were given for each combination of period and category (EAM or enPS) (Dritschel et al., 1992). Finally, DR was asked when the events occurred (EAMs) and when she met the persons (enPS) for the first time.

The task performed by DR during fMRI is described in detail in Teghil et al. (2022). It involved a 2 × 2 factorial design, with the factors "Memory category" (EAM and enPS) and "Task condition" (compatible *vs* non-compatible with the mental timeline, see below) and was developed as a block-design. During fMRI, labels corresponding to the EAMs and enPS collected as described above were shown one at a time, in an unbroken sequential manner in four serially balanced sequences (one for each Memory category and Task condition), in which each stimulus preceded and followed every other stimulus the same number of times (Aguirre, 2007; Nonyane & Theobald, 2007).

In each trial, DR was asked to decide whether the currently presented stimulus preceded or followed the previously shown stimulus along her personal timeline, i.e., in chronological order (Fig. 1). Responses were provided using a 2-button MRI-compatible keypad. In the compatible condition, participants had to press the "Backward" button if the current stimulus temporally preceded the previous one, and the "Forward" button if it followed the previous one; they were asked to do the opposite in the non-compatible condition (i.e., to provide backward/forward responses when the stimulus followed/preceded the previous one) (Teghil et al., 2021, 2022).

A total of four runs was acquired. Task conditions (compatible and non-compatible) were presented across runs; at the beginning of each run, written instructions were presented. Within each run, labels referring to EAMs and enPS were presented in different blocks, following an ABBA order. There were 10 blocks in each run. Each block lasted 25,000 msec. Within each block, 10 labels were presented for 2000 msec, followed by a fixation point lasting 500 msec. A fixation point was also presented during inter-block intervals, lasting 15,000 msec. Stimuli were presented using E-Prime 3.0 (Psychology Software Tools, Pittsburgh, PA).

DR performed a short familiarization session with the same structure of the experimental task immediately before fMRI, outside the scanner.

2.6.1. *Images acquisition*

Images were collected using a Siemens MAGNETOM Prisma scanner (Erlangen, Germany), operating at 3T and equipped with a 32-channel head coil. Functional, whole brain MR images were acquired with a T2*-weighted gradient-echo echo-planar imaging (EPI) sequence, a multiband factor of 4, and an isotropic voxel size of 2.4 mm^3 (60 slices, Field of View [FOV] 208 × 208 mm^2, TR = 1100 msec, TE = 30 msec, flip angle = 65°, no in-plane acceleration) (Feinberg et al., 2010; Moeller et al., 2010; Xu et al., 2013). 370 fMRI volumes were acquired in each run, including 6 dummy scans before each run that were

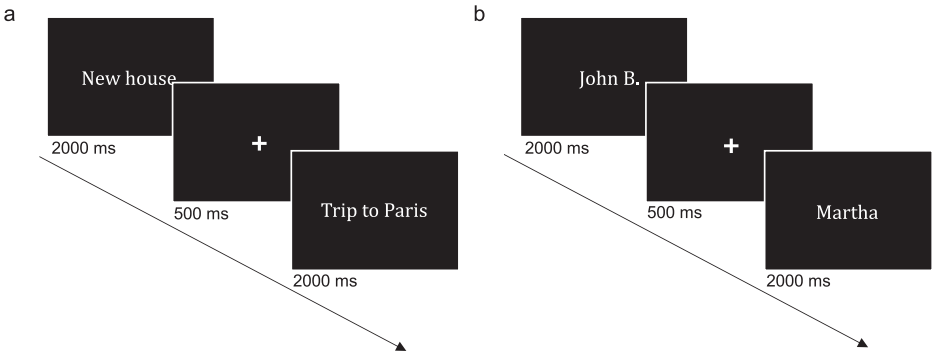

Fig. 1 – Example of stimuli presented to DR during the fMRI task (adapted from Teghil et al., 2022). a) Episodic autobiographical memory (EAM) condition; b) experience-near personal semantics (enPS) condition (please note that stimuli showed here do not correspond to actual labels provided by DR).

discarded. Two spin-echo EPI volumes with phase encoding in opposite direction, no multiband acceleration and the same geometrical and sampling properties of functional runs were also acquired for field mapping (TE = 80 msec, TR = 7000 msec). T1-weighted structural images were also acquired using an MPRAGE (Magnetization Prepared Rapid Gradient-Echo) sequence with perspective motion correction and selective reacquisition of data corrupted by motion based on interleaved 3D EPI navigators (Hess et al., 2011; Tisdall et al., 2012) (176 slices, isotropic resolution 1 mm^3, TR = 2500 msec, TE = 2 msec, TI = 1070 msec, flip angle = 8°).

2.6.2. *Analysis of performance during the fMRI task*

Regarding behavioral data collected during fMRI task, DR's accuracy in Memory category (EAM and enPS) was analyzed comparing her performance to a control group ($n = 19$, all females) from our previous study (Teghil et al., 2022). Given that control participants were younger than LD, analyses were performed using a t-test modified procedure including age as a covariate (BTD_Cov.exe; https://homepages.abdn.ac.uk/j.crawford/pages/dept/Single_Case_Covariates.htm; Crawford et al., 2011). The control group was matched for education ($t = .22$, $p = .41$) with DR.

2.6.3. *Analysis of fMRI data*

Preprocessing and analyses were performed using SPM12 (http://www.fil.ion.ucl.ac.uk/spm/). A field map was computed from the spin-echo EPI images. All fMRI images were simultaneously corrected for head movements and B0-distortion, including motion × field interaction (realignment and unwarping, Andersson et al., 2001) using the first volume as reference. Images were slice-timing corrected, coregistered onto the respective T1-weighted image, and normalized to the standard MNI-152 template using the T1 as a source (voxel size: $2.4 \times 2.4 \times 2.4$ mm^3). Images were then smoothed using a 6-mm full-width at half-maximum (FWHM) isotropic Gaussian kernel.

In line with our previous fMRI study using this paradigm (Teghil et al., 2022), a 2 × 2 ANOVA with the factors Memory category and Task condition showed no significant interaction between these factors in the present sample, either at the behavioral level [accuracy: Memory category: $F(1,18) = 3.886$, $p = .064$, $\eta_p^2 = .178$; Task condition: $F(1,18) = 4.560$, $p = .047$, $\eta_p^2 = .202$; Memory category × Task condition: $F(1,18) = .0472$, $p = .830$, $\eta_p^2 = .003$; response times: Memory category: $F(1,18) = 15.55$, $p = .001$, $\eta_p^2 = .447$; Task condition: $F(1,18) = 12.68$, $p = .002$, $\eta_p^2 = .413$; Memory category × Task condition: $F(1,18) = 1.39$, $p = .830$, $\eta_p^2 = .072$] or in voxel-wise analyses. Given the lack of interaction with Task condition and since we were interested in assessing activation patterns showed by DR in ordering EAMs and enPS, regardless of possible compatibility effects, only the factor Memory category was considered in following analyses.

Functional images were analyzed on a voxel-by-voxel basis, according to the general linear model (GLM). Neural responses during EAM and enPS blocks were modeled as boxcar functions, convolved with a canonical hemodynamic response function and used as separate predictors in the GLM (one for each experimental condition). Inter-block intervals were also modeled in relation to the nature of the previous block (EAM-rest or enPS-rest) and treated as baseline.

We first performed voxel-wise analyses to identify brain regions supporting the temporal organization of memories according to their category (EAM or enPS). Given the possibility that the presence of a developmental deficit has resulted in compensatory mechanisms, this analysis was performed on the whole sample of participants, including both the control group and DR.

Contrast maps resulting from the contrasts EAM − enPS and enPS − EAM at the first level analysis were entered into second-level random effects analyses, and a one-sample t-test was performed for each contrast. Since participants of the control group were significantly younger than DR, age was included as a covariate in second-level analyses. The resulting statistical parametrical maps were thresholded using $p < .05$ FWE at the peak level, and a cluster size $k > 30$ voxels.

3. Results

3.1. *Neuropsychological examination*

DR performed within the normal range in tasks assessing attention in ecological contexts (TEA, Cantagallo & Zoccolotti, 1998; Robertson et al., 1996), verbal and visuo-spatial short term memory (Digit span, Monaco et al., 2013, 2015; CBT, Corsi, 1972; Monaco et al., 2013, 2015), learning and long term memory (RAVLT, Carlesimo et al., 1996; Rey, 1964; Prose memory test, Novelli et al., 1986; Rey complex figure, Carlesimo et al., 2002; Rey, 1941; Corsi supra span, Piccardi et al., 2013; Capitani et al., 1980). We found a slight impairment in a working memory test (PASAT, Ciaramelli et al., 2006; Gronwall, 1977) and a deficit in memory for public events (Famous events questionnaire 1966–1997, Budriesi et al., 2002) and knowledge about famous people (Recognition of names of famous people, Bizzozero et al., 2007).

3.2. *Autobiographical Interview*

We found a significant inferior ratio in overall DR's production ($t = -2.04$, $p = .04$) compared to the control group. Concerning the different life periods, we found in DR a significant reduction in the ratio for the childhood ($t = -3.11$, $p = .01$) and adolescence ($t = -2.02$, $p = .05$) periods. No significant difference was found for early adulthood, adulthood and last year lifetime periods (all $p > .05$) (Fig. 2).

Given that ratio is calculated between internal to total details, we further investigated which kind of external details determined the reduction observed in DR's performance by using a two-tailed t-test modified procedure (SinglimsES.exe; Crawford et al., 2010). This analysis showed only a significant increase in semantic details for DR ($t = 5.92$, $p = .001$) compared to the control group; any other comparison was not significant (all $p > .05$).

3.3. *Structural MRI analysis*

Results of the surface-based morphometry analysis showed that DR had significantly reduced CT compared to the control

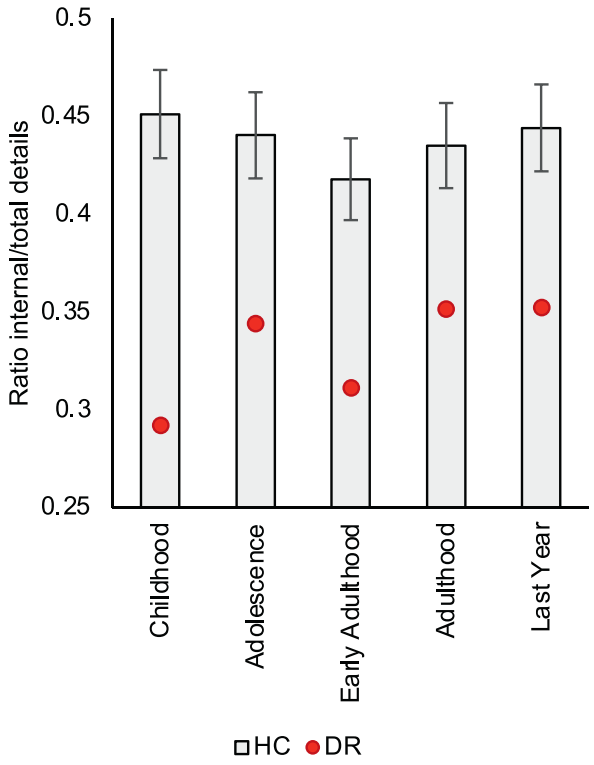

Fig. 2 – Episodic re-experiencing. Bars indicate mean ratio of the internal to total details in the control group, for each period tested by using AI, whereas red dots represent DR's performances. Control group is shown with 95% confidence intervals.

group in four ROIs (Fig. 3 and Table 2): lRSC (left RetroSplenial Complex), rLO1 (right Lateral Occipital Cortex), rProS (right Prostriate Cortex) and rPFm (in the right Angular Gyrus).

3.4. *fMRI paradigm*

3.4.1. *Behavioral results*

No significant difference was found for DR's accuracy compared to the control group in the enPS condition (z-score = .08, $p = .22$) and only a trend for DR to perform worse than controls in the EAM condition (z-score = −1.01, $p = .07$).

3.4.2. *fMRI analysis*

At the group level, the contrast EAM > enPS highlighted a cluster in the left calcarine cortex (peak at MNI −4, −88, 14, 89 voxels) that was more strongly activated during EAM than enPS. The reverse contrast (enPS > EAM) highlighted stronger activation of the precuneus (two clusters, peak at MNI 1, −54, 43, 36 voxels and 6, −57, 28, 62 voxels), middle temporal gyrus (peak at MNI 49, −64, 21, 36 voxels) and medial orbitofrontal cortex (peak at MNI 4, 58, −12, 104 voxels) in the right hemisphere.

BOLD signal change resulting from the two contrasts within the clusters reported above was then compared between DR and the control group, using the modified two-tailed t-test procedure proposed by Crawford et al. (2011). Mean and standard deviation in the control group were extracted based on individual estimates of the contrasts in control participants. Concerning the contrast enPS > EAM, no significant difference in brain activation was found between DR and controls. Conversely, activation of the left calcarine cortex for the contrast EAM > enPS was significantly higher for DR than for controls ($t = 3.622$, $p = .002$) (Fig. 4).

4. Discussion

When we met DR for the first time, she complained of a lifelong impairment in recalling autobiographical events. The absence of any neurological disease, or developmental conditions that could have explained her complaints, makes it possible to exclude a secondary deficit due to brain damage, such as developmental amnesia following hippocampal damage in early age (Cooper et al., 2015). A radiological examination confirmed the absence of any brain damage. There was no evidence of an ongoing or past psychiatric disorder, nor stressful condition that could support a dissociative amnesia. Also, there were no ongoing legal litigations or external incentives that suggested an exaggeration of symptoms or malingering (Sherman et al., 2020).

Neuropsychological assessment highlighted a slight impairment in working memory and in memory for public events and knowledge about famous people, while performances in tasks assessing attention, verbal and visuo-spatial STM and LTM fell within the normal range. Regarding AM, she underwent a specific assessment with the Autobiographical Interview (Levine et al., 2002). Results showed a significant reduction in the ratio of internal-to-total details, a measure that reflects episodic re-experiencing – which is a key factor in AM, that allows an individual to retrieve an episode in a recollective way (Tulving, 2002; Wheeler et al., 1997) – unbiased by the total verbal output (Levine et al., 2002; Setton et al.,

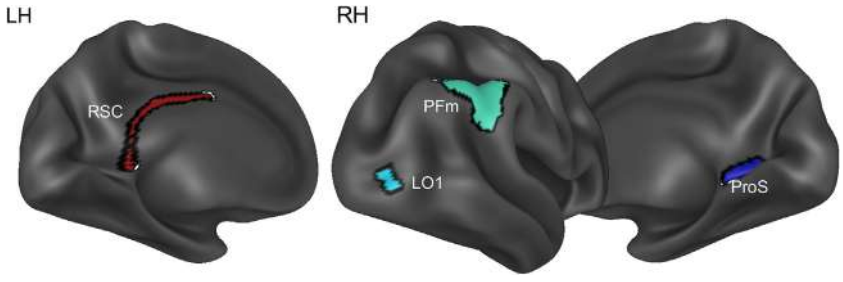

Fig. 3 – ROIs showing a significant reduced CT in DR. LH = left hemisphere, RH = right hemisphere, RSC = RetroSplenial Complex, LO1 = Lateral Occipital Cortex, ProS = Prostriate Cortex, PFm = Angular Gyrus.

Table 2 – Significant CT values of DR compared to a control group.

ROIs	Crawford *t*	Crawford *p*
lRSC (left RetroSplenial Complex)	−2.5260346	.0428608
rLO1 (right Lateral Occipital Cortex)	−2.924661	.03063228
rProS (right Prostriate Cortex)	−3.1697061	.02524605
rPFm (Angular Gyrus)	−2.8907011	.03148852

2022; Spreng et al., 2018). As a side note, among external details, DR produced more semantic details than controls, supporting her own report that her memories are "abstracted" and patchy in nature. We further tested whether a gradient would be observed in her performance. To investigate this point, the ratio of internal-to-total details was analyzed separately for each lifetime period. We found a significant reduction in this index for childhood and adolescence, while no differences were noticed for the periods of early adulthood, adulthood and last year. Interestingly, this result mirrors findings by Palombo et al. (2015) in patients with SDAM; actually, as a group, patients with SDAM performed worse than controls in recollecting events from childhood and adolescence. At the same time, this result definitively excludes the possibility that DR's performance was affected by cognitive decline associated with pathological aging. Also, the lack of a deficit in verbal and visual learning rules out the possibility that the observed pattern resulted from a deficit in acquiring novel information. Even if symptom validity tests were not performed during the neuropsychological assessment, the cognitive profile showed by DR is coherent with her report of a selective lifelong impairment in recalling autobiographical events.

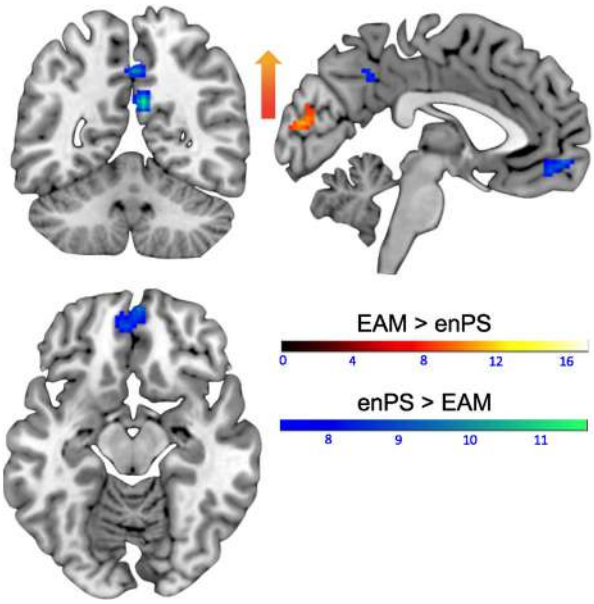

Fig. 4 – Clusters of activation found in EAM > enPS (red scale) and enPS > EAM (blue scale) contrasts in coronal, sagittal and axial views. The arrow points out activation of the left calcarine cortex for the contrast EAM > enPS that was significantly higher for DR.

DR underwent both a structural MRI examination and a task-based fMRI protocol; the latter was aimed to investigate brain correlates of temporal ordering of autobiographical information (Teghil et al., 2022). The fMRI investigation was performed using a paradigm previously developed by our group, for which data have already been collected during a previous study. Here we re-analyzed data from a subset of participants (female only) involved in the previous study (Teghil et al., 2022) in order to compare their activations to those of DR. Surface-based morphometry showed a reduced cortical thickness in four ROIs: lRSC (left RetroSplenial Complex), rLO1 (right Lateral Occipital Cortex), rProS (right Prostriate Cortex) and rPFm (in the right Angular Gyrus). Previous neuroimaging studies have implicated the retrosplenial and occipital cortices in the AM network (Cabeza & St Jacques, 2007), as well as the angular gyrus (Boccia et al., 2019). Even though a causal relationship between reduced CT and ratio of internal-to-total details cannot be established in the present study, it is interesting to notice that DR shows a reduction in areas that are known to be implied in autobiographical memory. Regarding fMRI, behavioral data showed a non-significant trend in ordering stimuli according to her personal timeline less well than controls in the EAM condition, while no significant difference was found in the enPS condition. Even if these data must be considered carefully, they suggest a slight difficulty exclusively in ordering autobiographical events. Here we found that DR showed a significant higher activation of the calcarine cortex compared to controls for the contrast EAM > enPS. It is worth noting that the calcarine cortex has been implicated in detailed episodic memory (Bone & Buchsbaum, 2021). Also, in a recent study exploring eye movements, Armson et al. (2021) reported evidence of a link between the visual system and the recollection of episodic autobiographical memories. Indeed, their results showed that participants' number of fixations were positively associated with the number of internal details recalled. Moreover, a staged event experiment showed that individual differences in autobiographical memory moderate the effect of fixation rate on internal details, with a greater effect in participants reporting a high, rather than low, episodic autobiographical memory trait (Armson et al., 2021). Another set of evidence come from studies on blindness. Tekcan et al. (2015) found that blind participants were less proficient than sighted participants in retrieving autobiographical memories, even if they had a stronger belief in the accuracy of events recalled and reported higher narrative and auditory imagery at retrieval (Tekcan et al., 2015).

In this light, a stronger recruitment of the calcarine cortex during a task involving EAM might thus reflect the fact that this condition is more demanding for DR than for controls (Jung et al., 2021). Together with findings that DR performed slightly worse than controls in ordering events from the same condition, this pattern may suggest a compensatory mechanism that, nonetheless, is not sufficient to support a performance fully within the normal range. Notably, this result cannot be due to working memory demands involved in the task, since the EAM and enPS conditions were directly compared in the fMRI analyses. The presence of a compensatory mechanism in DR is further in line with findings of a significant reduction of re-experiencing of early lifetime

events. We may speculate that a compensatory mechanism has been implemented by DR during her early adulthood, allowing her to achieve educational and working goals. This tentative interpretation fits DR's reports about her own strategy to access events.

The fMRI paradigm used here was designed to assess a specific feature of AM, namely the ordinal representation of autobiographical information along the personal timeline (Teghil et al., 2022). Thus, although findings of the fMRI investigation are suggestive of an alteration of neural mechanisms involved in this process in DR, the specificity of the paradigm limits conclusions that can be drawn concerning more general AM alterations in the patient. Notably, although DR's performance in ordering EAMs was slightly lower than that of controls, she could overall perform the task, suggesting that her ordinal representation of AMs was somewhat preserved. Whereas DR could have not been able to perform a task involving the detailed recollection of episodic autobiographical memories, the use of the present task allowed us to characterize brain patterns associated with the temporal organization of AMs in this case report. Although conclusions of the fMRI investigations have thus to be limited to a specific feature of AM, these findings tie well with those of the structural neuroimaging protocol and with those of the neuropsychological and autobiographical memory investigation in suggesting a complex and subtle pattern of alterations in episodic components of AM.

This is the very first report about a deficit in memory for public events in an individual with a lifelong impairment in autobiographical memory. It is difficult to draw definite conclusions about the relation between SDAM and deficit in memory for public events, due to the paucity of SDAM reports. Nevertheless, it is worth to note that individuals with highly superior autobiographical memory (HSAM), which may correspond to the opposite dimension of SDAM on a continuum (Palombo et al., 2015), show higher performances on tests tapping knowledge about public events (Santangelo et al., 2018). Thus, considering the report by Santangelo and colleagues, this association is not surprising; on the contrary we should expect such an association. On the one hand, finding that DR showed a deficit in memory for public events supports the idea by Palombo and colleagues that SDAM may be the opposite dimension of HSAM along a continuum. On the other hand, it provides the first report that these two dimensions, i.e., episodic autobiographical memory and memory for public events, which are associated in individuals with HSAM, may be associated in SDAM as well. However, this interpretation is still tentative and future studies should explore the frequency of the association between SDAM and deficit in memory for public events. Finally, the three cases described by Palombo and colleagues showed a common visual memory deficit, with one patient also showing deficit in the copy trial of the Rey Complex Figure Test. Taken together with the results by Palombo and colleague, our finding may suggest that SDAM has different – almost unexplored – facets.

In sum, the present results point towards a specific deficit in vividly re-experiencing autobiographical events, associated with a reduced CT in brain areas involved in AM. This profile seems to be similar to that characterizing other developmental conditions – consisting of selective life-long inability in presence of otherwise normal cognitive functions, and in the absence of a cerebral injury/malformation or other neurological condition – such as developmental topographical disorientation (Bianchini et al., 2010, 2014; Conson et al., 2018; Iaria et al., 2009; Iaria & Barton, 2010; Kim et al., 2015; Nemmi et al., 2015; Palermo, Foti, et al., 2014; Palermo, Piccardi, et al., 2014). Thus, the memory deficit in DR may be reasonably described as a developmental autobiographical memory deficit. This condition must be distinguished from developmental amnesia (Adlam et al., 2009; Cooper et al., 2015) resulting from early brain damage or congenital issues, which impair the development of memory skills.

Noteworthy, people who complain of a reduced or absent lifelong ability to mentally create images – a condition named "aphantasia" – also report difficulties to recall autobiographical events (Zeman et al., 2015). In a recent study, individuals with aphantasia produced significantly less internal details for remote and recent periods in the Autobiographical Interview, compared to control and hyperphantasia groups; the same pattern emerged when the ratio of internal to total details was analyzed (Milton et al., 2021). It has been thus suggested that SDAM and aphantasia could be at least partially overlapping syndromes (Watkins, 2018). However, to date there is no study formally testing mental imagery in individuals with SDAM. Thus, future studies should test the possible association between SDAM and deficit in mental imagery.

Importantly, a pervasive impairment in episodic autobiographical memory is also the key feature of dissociative amnesia, namely the inability to consciously recall autobiographical information in the absence of significant brain damage, and which assumes dissociation as the primary pathogenetic mechanism. This condition does not always follow Ribot's law, can occur suddenly and is associated with functional impairment (Markowitsch & Staniloiu, 2016; Staniloiu & Markowitsch, 2014). Given the dynamic nature of episodic autobiographical memory, it has been proposed that a widespread blockade of such memories can occur in presence of highly stressful events, leading in pathological cases to dissociative amnesia or memory block syndrome (Markowitsch & Staniloiu, 2022). Psychogenic amnesia may manifest in a global form, in which the entirety of a person's life is affected and personal identity can be implicated, or can be situation-specific, with memory gaps for specific events, such as those occurring in post-traumatic stress disorder or in victims of a crime (Kopelman, 2019). In DR there was no evidence of an ongoing or past psychiatric disorder, nor stressful condition that could support a dissociative amnesia, thus we have to exclude the possibility that memory deficit is due to psychogenic amnesia.

Since only three previous cases of SDAM or developmental autobiographical memory deficit have been described to date, reporting evidence for new cases is of key importance to better characterize this condition. There are obvious limitations due to the use of single case approach, which inevitably limits generalization. However, we used a statistical approach specifically developed for testing differences in a single case, increasing the reliability of the present results. Notably, autobiographical memory is not routinely assessed in clinical neuropsychological practice. Thus, it is possible that the

presence of such a developmental memory deficit is underestimated in the population. Future group studies, besides providing further information about the epidemiology of SDAM, will provide a more fine-grained characterization of the phenomenology of this condition.

CRediT author statement

Matilde Conti: Conceptualization, Methodology, Formal analysis, Investigation, Writing - original draft, Writing - review & editing. **Alice Teghil**: Conceptualization, Methodology, Formal analysis, Investigation, Writing - review & editing. **Antonella Di Vita**: Conceptualization, Methodology, Investigation, Writing - review & editing. **Maddalena Boccia**: Conceptualization, Methodology, Formal analysis, Investigation, Writing - review & editing, Supervision, Funding acquisition.

Data availability

The conditions of our ethics approval do not permit public archiving of data when – also in an anonymized form – it is not possible to rule out any link to the individual's identity. Here we reported data belonging to an extremely rare individual. For these reasons, data anonymization cannot be fully guaranteed. Readers seeking access to the data should contact the lead author M. C., mailto: matilde.conti@uniroma1.it. Access will be granted to named individuals in accordance with ethical procedures governing the reuse of clinical data, including completion of a formal data sharing agreement and approval of the local ethics committee.

All the analyses mentioned in the manuscript were performed using standard pipelines implemented by the cited software, and no in-house software or code was used.

The script of the fMRI task is available at the following link: osf.io/5xycq.

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