Acquired amnesia in childhood: A single case study

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Abstract

We report the case of C.L., an 8-year-old child who, following the surgical removal of an ependymoma from the left cerebral ventricle at the age of 4 years, developed significant difficulties in retaining day-to-day events and information. A thorough neuropsychological analysis documented in C.L. a severe anterograde amnesic syndrome, characterised by normal short-term memory, but poor performance on episodic long-term memory tests. In particular, C.L. demonstrated virtually no ability to recollect new verbal information several minutes after the presentation. As for semantic memory, C.L. demonstrated general semantic competencies, which, depending on the test, ranged from the level of a 6-year-old girl to a level corresponding to her actual chronological age. Finding a patient who, despite being severely impaired in the ability to recollect new episodic memories, still demonstrates at least partially preserved abilities to acquire new semantic knowledge suggests that neural circuits implicated in the memorisation of autobiographical events and factual information do not overlap completely. This case is examined in the light of growing literature concerned with the dissociation between episodic and semantic memory in childhood amnesia.

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1. Introduction

Human memory, which is generally defined as the capacity to acquire, retain and recall experiences and/or information, is no longer considered as a unitary cognitive function. Functional dissociations in healthy subjects and neuropsychological dissociations in brain-damaged patients suggest that memory is fragmented into a series of functionally independent, but clearly interacting, systems and subsystems. Squire (1987) presented a cognitive model of the amnesic function that has proved to be theoretically and practically useful. In agreement with Atkinson and Shiffrin (1971), the author’s first distinction is between short-term memory (STM) and long-term memory (LTM). The functional independence of the two memory systems was confirmed by the description of a neuropsychological double dissociation. There are reports of patients with severe impairment of episodic LTM, but essentially normal STM performance (e.g., Baddeley & Warrington, 1970) and, on the other hand, of patients with severe reduction of verbal span (a measure of STM capacity) and nearly normal performance on episodic LTM tests (e.g., Basso, Spinelli, Vallar, & Zanobio, 1982). In LTM, the model distinguishes between explicit or declarative memory, and implicit or procedural memory. Explicit memory is involved in intentional and/or conscious recall and recognition of experiences and information. Implicit memory is manifested as a facilitation (i.e., performance improvement) in perceptual, cognitive and motor tasks, without any conscious reference to previous experiences. The amnesic impairment profile observed in patients with pure amnesia is the strongest evidence supporting the dichotomy between implicit and explicit memory.
systems. It has often been reported that these patients, although seriously deficient in intentionally recalling previously acquired information, show normal procedural learning, and have a normal repetition priming level (Schacter, Chiu, & Ochsner, 1993).

Tulving (1972) first proposed to distinguish two different forms of declarative memory: episodic and semantic. Episodic memory is responsible for storing and recalling information and experiences, mainly autobiographical, which can be placed in the spatial and temporal context in which they were acquired. What happened when we married or graduated, which clothes we were wearing, or whether it was raining or not are clear examples of episodic memory. Semantic memory, instead, is involved in acquiring and recalling information constituting our cultural heritage (language, historical and geographical knowledge, etc.) and, as such, is not generally referable to the spatial–temporal context in which it was acquired. Our knowledge of the brain, the way it works, how memory is organized and writing about all this in English, instead of Italian, are also relevant to semantic memory, a system, which we tend to take for granted.

Although it is generally accepted that both semantic and episodic memory entail explicit processes, the relationship between these two different forms of memory is still controversial. According to Squire (Squire, 1992; Squire & Zola, 1998), a unitary memory system underlies episodic and semantic learning. In this view, semantic memory is simply the amassing of several episodic memories, for which the contextual cues were missed, and only the generic features persist. However, other authors hold the alternative view that separate memory systems, subtended by at least partially distinct neural circuits, underlie the learning of new episodic and semantic data (Tulving, Hayman, & Macdonald, 1991; Vargha-Khadem et al., 1997). Particularly relevant in this debate is the hypothesis that individuals with organic amnesia suffer from a disproportionately more severe deficit in the learning of new episodic information than of semantic information. Indeed, the finding that these patients have updated their semantic memory through the acquisition of a substantial number of new words and semantic facts during a period in which they were severely impaired in storing new personal events would support the claim that semantic and episodic information follow at least partially independent routes to memorisation (Tulving & Markowitsch, 1998).

Data from the neuropsychological literature regarding patients who became amnesic as adults are controversial on this issue. Indeed, while earlier attempts to demonstrate post-morbid vocabulary learning in densely amnesic patients were unsuccessful (Gabrieli, Cohen, & Corkin, 1988; Reed & Squire, 1998; Verfaellie, Reiss, & Roth, 1995), more recent data suggest that, at least in some patients, new semantic learning may occur despite profound loss of episodic memory (Kitcner, Hodges, & McCarthy, 1998; McKenna & Gerhard, 2002). Instead, data from patients who became amnesic following a cerebral damage occurred during childhood more clearly document a dissociation between the severely compromised ability to acquire new episodic information and the at least partial sparing of the ability to acquire new semantic information. The first detailed case of a child with acquired amnesia was reported by Ostergaard in 1987. C.C. was a 10-year-old boy, who developed amnesia after an episode of anoxia, which determined a multifocal brain damage also involving the hippocampal regions, bilaterally. General intelligence and procedural memory were normal but the deficit in declarative memory was evident. Specifically, both semantic and episodic memory difficulties were reported. However, C.C. was able to progress in academic skills, thus suggesting at least partially spared ability to store new data in his semantic memory. Similar findings were observed in T.C., described by Wood, Brown and Felton (1989), in M.S. reported by Broman, Rose, Hotson, and Casey (1997), and in A.V., more recently documented by Brizzolara and Casalini (2002). Preserved ability to store new semantic memories despite a severe impairment of episodic memory were clearly demonstrated by Vargha-Khadem et al. (1997) in a study reporting amnesic abilities in three children who had suffered from severe anoxia within the first days of life. More recently, Gadian et al. (2000) added three new cases with a similar clinical history and memory profile. With respect to previously reported cases, children described by Vargha-Khadem et al. were better characterised as for the localisation of cerebral damage. In particular, a thorough morphovolumetric analysis of mesio-temporal structures on high-resolution brain MR images documented, in all these children, a bilateral atrophy of the hippocampus (ranging from 0.43 to 0.71 of the mean value for normal individuals), but a normal representation of associative neocortex in the parahippocampal gyrus. Based on these findings, the authors advanced a neuroanatomical model of declarative memory in which the hippocampus proper and the parahippocampal region play a differential role, the former being responsible for storing new episodic, context-related information, and the latter in the learning of new semantic, context-free data.

Squire and Zola (1998) objected to the possibility of inferring the existence of two separate episodic and semantic memory systems from the above reported cases of childhood amnesia. According to these authors, in order to conclude that these individuals acquired new semantic data through a memory system which is independent from that involved in episodic learning, two conditions should be satisfied: first, no preserved ability to acquire new episodic information should be demonstrated in these patients; second, their ability to acquire new semantic data should be completely preserved. In these authors’ opinion, since in no one of the previously reported cases these two conditions could be verified (because some residual ability of acquiring new episodic memories was still evident, and because semantic and academic skills were never at the expected level in relation to chronological age), there is no unequivocal reason to reject the alternative view that these patients acquired new semantic data via the residual memory capacities of a unitary declarative memory system. In fact, since “...no formula exists for determining what level of school achievement should in fact be expected, given an impairment in moment-to-moment [i.e., episodic] memory...” then “...there is no basis for judging whether the amount of semantic knowledge eventually acquired by these patients is unusual or simply what would be expected after repeated effort over many years” (Squire & Zola, 1998; p. 206 and 210).
Here, we report a new case of childhood amnesia. A detailed neuropsychological investigation of this young girl demonstrated virtually no preserved ability to acquire new episodic information on laboratory-based tests. Despite that, she appeared to have acquired a substantial amount of new semantic data and academic skills during the 4 years elapsing from the onset of cerebral pathology (an ependymoma of the left ventricle, which was surgically removed) to the time of our investigation.

2. Case report

C.L., an 8-year-old girl, was admitted to our clinic to assess long-term effects on neuropsychological and behavioural functioning of a surgically removed cerebral ependymoma.

C.L. is an only child, born full-term (40 weeks) by a normal delivery, after a normal pregnancy. Weight, height and cranial circumference at birth were 3820 g, 50 cm and 33 cm, respectively; Apgar index was 9/10. Early development progressed normally: sleep/awake rate was normal; she produced her first words at 10 months and started walking at 14 months. She was leading a normal life and was in good health until the age of 3 years and 9 months, when, abruptly, she presented with difficulties in walking and balance disorders. When admitted to the hospital, the neurological exam showed ataxia, hypotonia, and reduced strength of the lower left limb. A brain MRI exam documented the presence of a tumour in the left lateral and third ventricles, with associated hydrocephalus and signs of intracranial hypertension. Nine days later C.L. underwent surgical resection of the tumour, with placement of an external shunt for draining the hydrocephalus. Because of a considerable intraoperative bleeding, the resection was only partial. Histology was performed and showed that the tumour was an ependymoma. Intracranial pressure was monitored in the following days and it always resulted within the normal range. Thus, a month later the external shunt was removed. In the following days, C.L. started a therapeutic protocol, consisting of an intensive chemotherapy regimen, followed by systemic high-dose chemotherapy and local radiotherapy. Fourteen months after the tumour resection, she and her family had spent their last summer vacations. From a questionnaire (modified from Sunderland, Harris, & Baddeley, 1983) which asked her parents to rate how often C.L. had forgotten each of 28 prototypical daily events on a scale ranging from 1 (never occurred in the past 6 months) to 9 (occurring more than once a day), the vast majority of the ratings were 7 (occurring more than once a week).

4. Neuroradiological examination

An MRI brain scan was obtained when C.L. was 8 year and 4-month old. Magnetisation Prepared Rapid Gradient Echo (MPRAGE) T1-weighted images (TR = 11.4 ms, TE = 4.4 ms, flip angle = 15°) were obtained with a Siemens Vision Magnetom MR system (Siemens Medical Systems, Erlangen, Germany) operating at 1.5 T. The high spatial resolution brain sampling of 1.25 by 0.98 by 0.98 mm³, allowing images to be rotated by small angles in the three orthogonal planes, facilitated the identification of anatomical landmarks for the selection of the regions of interest. This sequence produced 128 contiguous slices of 1.25 mm thickness, which covered the whole brain.

As shown in Fig. 1, the left ventricle was significantly enlarged in all its extension. An area of cortical–subcortical damage, resulting from surgical access to the ventricles, was clearly visible at the level of the caudal portion of the left frontal lobe (panels a–c). At a cortical level, the lesioned area involved the superior gyrus (BAs 8 and 9) and the cingulate gyrus (BAs 24, 32 and 33). At a subcortical level the lesion, in addition to involving the corpus callosum, and the white matter surrounding the frontal horn of the left lateral ventricle, also affected the caudate nucleus, the thalamus, the superior colliculus and the fornix. In particular, sagittal section of C.L.’s brain conducted 3 mms on the left of the midline (panel a), and a coronal section at the level of the anterior commisure (panel b) revealed the sectioning of the fornical body in its anterior portion, and no trace of the right and left fornical columns. Since the enlargement of the temporal horn of the left lateral ventricle caused a downward dislocation of the left mesial temporal lobe structures, the left hippocampus appeared to be slipped down in relation to the contralateral hippocampus, with consensual twisting of the left fornix (panel d).

In order to obtain volumetric measurements of anatomical structures in the MTL, we have performed a manual segmentation of C.L.’s hippocampal formation and parahip-
Fig. 1. MRI of C.L.’s brain. Panel a: left sagittal slice \((x = -3)\) showing damage in the fronto-medial surface including the superior frontal gyrus, the cingulate gyrus, the corpus callosum, and the caudate nucleus. The arrow indicates the locus of sectioning of the body of fornix. Panel b: coronal slice \((y = 0)\) revealing no trace of the fornical body and columns in the context of third and lateral ventricles. Panel c: the two most rostral coronal slices \((y = 37, y = 31)\) show the lesion in the superior frontal gyrus (dorsolateral view). The most caudal slice \((y = 15)\) shows the sufferance of the white matter surrounding the frontal horn of left lateral ventricle. Panel d: coronal slice \((y = 38)\) showing the downward dislocation of the left compared to the right hippocampus (arrows), and the twisting of the left fornix.

The hippocampal gyrus (including perirhinal, entorhinal and parahippocampal cortices) in both the cerebral hemispheres according to Insausti et al. (1998) and Pruessner et al. (2000, 2002), using the interactive program DISPLAY (J.D. McDonald, Brain Imaging Center, Montreal Neurological Institute; http://www.bic.mni.mcgill.ca/software/Display). Due to a lack of a control group of healthy children, these volumes could be not interpreted based on normative data. However, a comparison of MTL volumes in the C.L.’s lesioned left hemisphere against analogous volumes in the contralateral, macroscopically intact, right hemisphere revealed only marginal differences. In fact, the volumes of the hippocampal formation and of the parahippocampal gyrus (non-corrected for the intracranial volume) were 2615 mm\(^3\) and 5136 mm\(^3\) on the right side and 2450 mm\(^3\) and 5098 mm\(^3\) on the left side (a difference of about 7% in both cases).

5. Neuropsychological examination

5.1. General intelligence

The examination was carried out when C.L. was 8-year old. On the WISC-R (Orsini, 1993; Wechsler, 1991) C.L. obtained a full scale IQ of 80, corresponding to a mental age (MA) of 6 years and 4 months, with a slight difference between Verbal IQ (84; verbal MA = 6.6) and Performance IQ (80; non-verbal MA = 6.4).

Verbal MA was also evaluated with the Peabody Picture Vocabulary Test (PPVT; Dunn & Dunn, 1981). On this test C.L. obtained a raw score of 58, which corresponds to a MA of 6.6 years and to a IQ of 80.

5.2. Memory

C.L.’s MA was about 18 months lower than her chronological age (CA). In order to get a better insight about the development of her memory capacities, C.L.’s performances on tests of memory functioning were compared with scores expected based on MA and CA. When normative data were available, C.L.’s performance scores were first adjusted according to CA (8 years) or MA (6.5 years). The two normalized scores were then considered as normal or pathological if they fell above or below the 5‰ of the score distribution in the normative population. As regards tests for which norms were not available, C.L.’s performance scores were directly contrasted with those from two control groups of healthy children, the first composed of nine 8-year-old children (CA matches), the latter consisting of ten 6-year-old children (MA matches), using the Crawford and Garthwaite’s procedure (2002).

5.2.1. Short-term memory

Verbal short-term memory abilities were evaluated with the Digit Forward test (Orsini et al., 1987). C.L.’s span was 6, which is above the 90‰ for both her CA and MA. C.L. was also given a
Word span test (Brizzolara & Casalini, 2002) for lists of words, which differ in length (two versus four syllables), acoustic similarity (similar versus dissimilar) and frequency (high versus low). In all lists C.L. obtained spans above the 50‰ for both her CA and MA.

Visual spatial STM abilities were evaluated with the Corsi’s Block Tapping task (Orsini et al., 1987). C.L.’s score was 3, which corresponds to the 8‰ for her CA and to the 36‰ for her MA.

In summary, C.L. had fully preserved verbal STM. Her performances in a visual spatial STM task were somewhat poor, but yet within the normal range.

5.2.2. Episodic verbal memory

Episodic verbal LTM was evaluated by means of tests of free-recall of word lists and a short story, a probe recall test for word pairs, and two recognition tests (y/n and Forced-Choice) for word lists. Performance scores obtained on these tests by C.L. and her CA and MA matched controls are reported in Table 1.

Two Word-list learning tests (Vicari, Pasqualetti, Marotta, & Carlesimo, 1999) were administered. The first list is composed of 16 nouns of concrete objects semantically unrelated. The second list is composed of 16 nouns of concrete objects, 4 for each of four semantic categories (animals, fruits, body parts, and tools), randomly arranged. For each list the test consists of five consecutive immediate free-recall trials, during which the examiner orally presents the 16 words and immediately afterwards the subject is asked to recall as many words as possible, and of a delayed recall trial 15 min after the last immediate recall. C.L. did not show clear signs of learning in any of the two lists. Indeed, as shown in Fig. 2 (panel a), the overall number of words recalled in the immediate recall trials of the semantically unrelated list was within the normal range but the learning rate was deficient: in fact, the number of words recalled by C.L. across trials 1–5 did not increase as it does in normal subjects. As revealed by plotting the recall accuracy of individual words in the list as a function of serial position in the list, almost all of the words recalled (19 out of 22) came from the last four positions in the list, thus suggesting their transient storage in a short-term memory system (Koppenaal & Glanzer, 1990). As a matter of fact, C.L. was not able to recall any word after a 15 min delay.

Substantially the same pattern of results was observed for the semantically related list (Fig. 2, panel b). Here C.L. immediately recalled a number of words below the range of both CA and MA matched controls, and failed to show any improvement of accuracy across the five trials of immediate recall. In this case, all words recalled in the immediate trials were from the last three serial positions in the list. Finally, she did not recall any word after the delay.

The sum of informative units recalled by C.L. in the immediate trial of the Short Story memory test did not significantly differ from that of CA matched (t = 1.29; p > 0.10) and MA matched (t = 0.9; p > 0.10) controls. However, in the delayed recall trial she was able to recall only a single informative unit, a performance well below that of both the CA and MA matches (t = 2.57 and 1.78; p = 0.02 and 0.05, respectively).

<table>
<thead>
<tr>
<th>Test</th>
<th>C.L.</th>
<th>Lower limit of 95% tolerance interval for C.L.’s chronological age norms (8 years)</th>
<th>Lower limit of 95% tolerance interval for C.L.’s mental age norms (6 years)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Related word-list recall</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Immediate</td>
<td>15/80 a,b</td>
<td>26.1</td>
<td>17.8</td>
</tr>
<tr>
<td>Delayed</td>
<td>0/16 a,b</td>
<td>5.4</td>
<td>3.0</td>
</tr>
<tr>
<td>Unrelated word-list recall</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Immediate</td>
<td>21/80 a</td>
<td>26.6</td>
<td>18.3</td>
</tr>
<tr>
<td>Delayed</td>
<td>0/16 a,b</td>
<td>5.0</td>
<td>2.9</td>
</tr>
<tr>
<td>Short story</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Immediate</td>
<td>4/28</td>
<td>10.4 (4.8)</td>
<td>6.1 (2.2)</td>
</tr>
<tr>
<td>Delayed</td>
<td>1/28 a,b</td>
<td>11.2 (3.8)</td>
<td>8.6 (4.1)</td>
</tr>
<tr>
<td>Word pair learning</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Associates</td>
<td>13/18</td>
<td>14.0 (2.4)</td>
<td>11.7 (2.2)</td>
</tr>
<tr>
<td>Non-associates</td>
<td>3/12</td>
<td>5.9 (3.1)</td>
<td>4.4 (2.5)</td>
</tr>
<tr>
<td>Yes/No word recognition</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Immediate</td>
<td>35/40 a,b</td>
<td>39.3 (1.1)</td>
<td>39.7 (0.5)</td>
</tr>
<tr>
<td>Delayed</td>
<td>24/40 a,b</td>
<td>38.2 (1.6)</td>
<td>37.0 (2.0)</td>
</tr>
<tr>
<td>Forced-Choice word recognition</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Immediate</td>
<td>20/20</td>
<td>19.9 (0.3)</td>
<td>19.9 (0.3)</td>
</tr>
<tr>
<td>Delayed</td>
<td>14/20 a,b</td>
<td>19.6 (1.0)</td>
<td>19.7 (0.5)</td>
</tr>
</tbody>
</table>

For each test, depending on the availability of normative data, the lower limit of the 95% tolerance interval for the normative population, or mean scores and S.D. of CA and MA matched control groups are also reported.

a Significantly poorer than CA matched healthy children.

b Significantly poorer than MA matched healthy children.
C.L. received two Word Recognition tests. During the study phase of both tests, the subject is presented with 20 black-and-white photos of unknown faces, and is requested to express his/her opinion about their likeability on a five-point scale. Recognition memory for the two face lists is tested by means of two distinct procedures, a Yes/No, and a Forced-Choice recognition test. Moreover, each list is tested twice, immediately following the study phase, and 10 min later. In the Yes/No recognition test, each previously studied word is presented randomly, alternated with 20 new words. The subject is requested to say whether or not the presented word has been previously studied. In the Forced-Choice test, the subject has to recognize each studied word, which is presented side-to-side with an unstudied word. Compared with the groups of CA and MA matched controls, C.L.’s performance was significantly poorer on the immediate Yes/No test ($t = 3.67$ and $8.96$, respectively; $p < 0.01$ in both cases), on the delayed Yes/No test ($t = 8.23$ and $6.01$, respectively; $p < 0.01$ in both cases), and on the delayed Forced-Choice test ($t = 5.22$ and $11.32$, respectively; $p < 0.001$ in both cases). However, she performed equally to CA and MA matched controls in the immediate Forced-Choice test ($t < 1$ in both cases). Interestingly, in the delayed trials of both the Yes/No and the Forced-Choice recognition tests, C.L.’s ability to discriminate between studied and unstudied words was not significantly different from chance ($\chi^2 = 0.81$ and $1.67$, respectively; $p > 0.10$ in both cases).

In summary, C.L. did not exhibit any clear evidence of the ability to recover recently presented verbal data from her episodic long-term memory. Indeed, while she frequently performed within or only slightly below the normal range when learning was tested immediately following stimulus presentation (e.g., see the Word Pair learning), in delayed tests her performance was consistently lower, irrespective of whether a recall or a recognition procedure was used. Good performance on immediate tests likely benefited from her intact verbal short-term memory. This was particularly evident in word list recall tests, for which a normal or near-normal performance score was reached exclusively thanks to the ability to recall words from the last serial positions in the lists.

5.2.3. Episodic visual-spatial memory

Episodic visual-spatial memory was tested by means of immediate and delayed reproduction of the Rey’s Figure B (Di Nuovo, 1979; Rey, 1959), multitrail learning of a supraspan sequence in the Corsi block tapping test (Spinelli & Tognoni, 1987), and recognition tests with pictures of unknown faces, images of concrete objects, and spatial positions. Performance scores obtained on these tests by C.L. and her CA and MA matches are reported in Table 2.

In the 3 min-delayed reproduction of the Rey Figure B (Di Nuovo, 1979; Rey, 1959), C.L. scored 11.5, which corresponds to the 20‰ of the normal distribution in CA matches, and to the 30‰ of the distribution in MA matched normal controls. C.L. failed to learn an eight-block spatial sequence in the Corsi’s supraspan task (Spinelli & Tognoni, 1987). Indeed, she obtained a score considerably below the range of both MA and CA matched controls in the immediate test ($t = 3.17$ and $2.68$, respectively; $p = 0.01$ in both cases), and did not exhibit any memory for the spatial sequence after a 5 min-delay.

C.L. was given two Face Recognition tests. During the study phase of both tests, the subject is presented with 20 black-and-white photos of unknown faces and is requested to express his/her opinion about their likeability on a five-point scale. Recognition memory for the two face lists is tested by means of two distinct procedures, a Yes/No, and a Forced-Choice test. In the Yes/No procedure, studied faces are presented randomly, alternated with 20 new faces, and the subject is requested to say whether the face, which is being presented has already been encountered or not. In the Forced-Choice test, the subject is presented with 20 pairs of faces, each comprising a studied and an unstudied face, and is requested to choose, between the two alternatives, the one that had been previously studied. Both the Yes/No and the Forced-Choice procedures are given twice, immediately following the study phase, and after a 10 min-delay.
C.L.’s performance in the Yes/No immediate test was in the average of MA matched controls ($t = 0.26; p > 0.10$) but 2 S.D.s below the average of CA matched controls ($t = 3.66; p < 0.01$). However, in the Yes/No delayed test she performed below the level of both CA ($t = 4.75; p < 0.01$) and MA ($t = 2.41; p = 0.02$) matched controls, and actually not differently from chance ($\chi^2 = 0.81; p > 0.10$). In the Forced-Choice test, C.L.’s performance did not significantly differ from that of MA matched controls in both the immediate test ($t = 0.01$), and the delayed test ($t = 1.09; p > 0.10$). As compared to CA matches, however, her performance was poor. Indeed, while in the immediate test a direct comparison is prevented by a ceiling effect of performance in the healthy group, in the delayed test C.L. scored more than 2 S.D.s below the mean of controls ($t = 5.77; p < 0.01$), and actually not differently from chance ($\chi^2 = 2.67; p = 0.10$).

Recognition memory for images of concrete objects was tested with the Visual-object learning test (Vicari, Bellucci, & Carlesimo, 2005). In each of three consecutive trials, fifteen images of common objects (e.g., a tree, a knife, a flower) are shown. Immediately afterwards, fifteen pages, each reporting one of the studied items, and three other physically different versions of the same object (e.g., four trees, four knives, four flowers) are presented and the subject is requested to discriminate the studied from the unstudied items. A final recognition task, in this case pages are divided into four quadrants (Vicari et al., 2005). Differently from the visual-object learning test, in this page cases are divided into four quadrants and during each trial of the study phase, one of 20 figures is positioned in one of the quadrants. During the testing phase, which immediately follows the study phase, target stimuli are presented and the subject is asked to indicate the position occupied by the figure on an empty page sub-divided into four quadrants. Also in this case, the administration of the entire test is repeated three times, and a delayed test is given 15 min after the last immediate trial. As compared to the CA matched controls, C.L.’s performance was significantly poorer in all the immediate and delayed tests ($t$ consistently $>2.0; p < 0.05$ in all cases). Instead, her performance did not significantly differ from the MA matched controls in the two first immediate trials ($t = 1.12$ and $1.30$, respectively; $p > 0.10$ in both cases). Moreover, C.L.’s accuracy in the delayed trial did not significantly differ from chance ($\chi^2 = 0.56; p > 0.10$).

Finally, C.L. was administered the Visual-spatial learning test (Vicari et al., 2005). Differently from the visual-object learning task, in this case pages are divided into four quadrants and during each trial of the study phase, one of 20 figures is positioned in one of the quadrants. During the testing phase, which immediately follows the study phase, target stimuli are presented and the subject is asked to indicate the position occupied by the figure on an empty page sub-divided into four quadrants. Also in this case, the administration of the entire test is repeated three times, and a delayed test is given 15 min after the last immediate trial. As compared to the CA matched controls, C.L.’s performance was significantly poorer in all the immediate and delayed tests ($t$ consistently $>2.0; p < 0.05$ in all cases). Instead, her performance did not significantly differ from the MA matched controls in the two first immediate trials ($t = 1.12$ and $1.30$, respectively; $p > 0.10$ in both cases). However, she performed at a significantly lower level than MA matched controls in the last immediate trial ($t = 4.23; p = 0.01$). Finally, C.L.’s performance on the delayed test did not significantly differ from chance ($\chi^2 = 0.56; p > 0.10$).
In summary, similarly to what observed in the verbal domain, C.L.’s episodic visual-spatial memory was severely compromised. In this case, however, some evidence of the ability to retrieve recently presented visual information from long-term memory was observed in the delayed reproduction of the Rey Figure B (Di Nuovo, 1979; Rey, 1959). In all the other tests, no clear sign of learning was revealed in the delayed testing trials. Moreover, impaired performances were also observed in some cases in which memory for spatial positions (Corsi block test) or human faces was tested immediately after stimulus presentation.

5.2.4. Language and semantic memory

Performance scores obtained by C.L. on tests of semantic memory are reported in Table 3.

C.L.’s score on the Boston Naming Test (Nicholas, Brookshire, McLennan, Schumacher, & Porrazzo, 1989; Riva, Nichelli, & Devoti, 2000) was significantly poorer than expected based on CA but in the 50% of MA matched normal population.

As a measure of morphology/syntax comprehension, C.L. was administered the Grammar Comprehension Test (Rustioni, 1994). On this test, subjects are requested to listen to sentences of variable grammar difficulty, and to point, for each sentence, to the corresponding picture among four alternatives. C.L.’s score on this test corresponds to a chronological age of 6 years.

On WISC-R Information and Vocabulary subtests, which are usually considered as reliable indices of factual knowledge in children, C.L.’s standard scores were 6 and 9, respectively. Although performance on the Information subtest was lower than we may expect based on her CA, vocabulary score was in the average.

In the Category Word Fluency test (Riva et al., 2000) C.L. was requested to generate as many nouns as she could within a specified category (animals, clothes, fruits and toys) in 1 min. Her score on this test was consistently above the performance range observed in CA and MA matched controls.

Finally, a questionnaire exploring semantic knowledge of a series of common objects, foods or animals was administered (Laiacona, Barbarotto, Trivelli, & Capitani, 1993). Example of questions are: “Orange” is: an object, an animal or a vegetable? Is it a fruit, a flower, or a tree? Has it a stone, seeds or a shell? Is its skin thinner than that of a lemon? Do you eat it underdone, cooked or is a jam prepared with it? It grows on a small plant, directly on the land, or on palms?” On this test C.L. obtained a score in the range of CA matched healthy children ($t = 0.78; p > 0.10$) but significantly higher than the mean observed in MA matches ($t = 2.51; p = 0.02$).

In conclusion, in language tests exploring naming and comprehension abilities, C.L.’s performances were poorer than expected based on her CA (and actually in the range of her MA). In tasks exploring more directly semantic competencies, however, C.L. performed in the high range of CA matches (with the only exception of the Information subtest of WISC-R).

5.2.5. Academic skills

In order to exclude that good performance on the above described tests of semantic memory may be just the effect of a preserved retrograde memories – i.e., of information acquired before the onset of the disease – we tested C.L.’s academic skills. Indeed, when she started primary school, the tumour had already been removed and treated. Thus, all the scholastic learning was necessarily achieved after the tumour removal. C.L. was able to read single words in a list, but her performance as for speed and accuracy was lower than the normal cut-off for her class grade (Sartori, Job, & Tressoldi, 1995). Instead, her ability to point to the picture corresponding to a written word or sentence was in the normal range (13 out of 15 correct responses) (Cornoldi & Colpo, 1998). Moreover, her writing abilities, tested with a word dictation task (Sartori et al., 1995), were impaired, since she was able to write down only single and simple words (CVCV). In summary, C.L. was able to read and to write, although with some difficulties.

5.2.6. Follow-up

We had the opportunity to test C.L. again 10 months after the first evaluation, when she was 8 year and 10-month old. At that time, C.L. showed improved academic skills. Indeed, she was able to read short passages and to write individual words fluently, even though with spelling mistakes. She had also improved her lexical knowledge as measured by PPVT (Dunn & Dunn, 1981). Indeed, at that time she obtained a row score corresponding to her CA.

<table>
<thead>
<tr>
<th>Test</th>
<th>C.L.</th>
<th>CA matched controls ($n = 9$), mean (S.D.)</th>
<th>MA matched controls ($n = 10$), mean (S.D.)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Boston Naming Test</td>
<td>22/60*</td>
<td>36.0 (6.2)</td>
<td>25.4 (5.9)</td>
</tr>
<tr>
<td>Categorical Word Fluency</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Animals</td>
<td>17</td>
<td>13.1 (2.3)</td>
<td>10.2 (3.5)</td>
</tr>
<tr>
<td>Clothes</td>
<td>16</td>
<td>9.3 (1.8)</td>
<td>7.4 (1.3)</td>
</tr>
<tr>
<td>Fruits</td>
<td>15</td>
<td>9.4 (2.3)</td>
<td>8.3 (1.7)</td>
</tr>
<tr>
<td>Toys</td>
<td>11</td>
<td>7.4 (2.3)</td>
<td>5.9 (1.6)</td>
</tr>
<tr>
<td>Total</td>
<td>59</td>
<td>39.3 (5.9)</td>
<td>31.8 (5.4)</td>
</tr>
<tr>
<td>Questionnaire of semantic knowledge</td>
<td>55/60</td>
<td>52.3 (3.3)</td>
<td>46.3 (3.3)</td>
</tr>
</tbody>
</table>

For each test, depending on the availability of normative data, the lower limit of the 95% tolerance interval for the normative population or mean scores and S.D. of the CA and MA matched control groups are also reported.

* Significantly poorer than CA matched healthy children.
6. Discussion

We reported the case of a young girl, C.L., who at the age of 3 years and 9 months underwent surgical removal of an ependymoma of the left lateral ventricle. A further surgical intervention for the removal of a gliotic area at the head of the left caudate nucleus was performed when C.L. was about 5-year old. As a result of these two surgical interventions, cerebral MRI revealed an asymmetry of the ventricular system due to a considerable enlargement of the left ventricle. Areas of focal damage in the left cerebral hemisphere involved cortical and subcortical structures, mainly in the mesial surface of the posterior portion of the frontal lobe. Most likely, the involvement of left hippocampal formation and fornix was critical for the genesis of the amnesic syndrome. Indeed, even though the left hippocampus was only slightly reduced in volume with respect to the contralateral hippocampus, it was considerably dislocated downward, with consensual twisting of the left fornix at its origin. Moreover, the body of the fornix appeared sectioned along its course in the third ventricle, thus resulting in an anatomical disconnection between both the hippocampal formations and the diencephalic structures.

When C.L. came to our observation, at 8 years of age, her main complaint was a severe memory disorder characterised by a difficulty in retaining day-to-day events and information. Despite that, informal assessment revealed verbal abilities adequate to her chronological age. Indeed, C.L.’s spontaneous language was well articulated, fluent, syntactically correct, and with a seemingly adequate lexical repertoire. Laboratory tests, as well as academic accomplishments demonstrated linguistic and general semantic competencies, which, depending on the particular test, ranged from the level of a 6-year-old girl to a level corresponding to her actual chronological age. In fact, C.L.’s I.Q. was between one and two standard deviations below the mean and her verbal MA was 6.6. Performance scores compatible with a MA of about 6 years were also obtained in tests of visual naming and sentence comprehension, in the Information sub-test of the WISC, and in tests of visual-spatial ability. C.L.’s reading and spelling abilities were also likely to be at the level of a first-grade student (but in this regard, we do not have a formal evaluation). However, in the WISC Vocabulary subtest, in a Categorical Word Fluency test, and in a questionnaire exploring general semantic knowledge about the world, C.L.’s performances were indistinguishable from those of CA matched healthy children. Verbal abilities had further increased at a follow-up examination performed 1 year after our first observation. At that time, C.L.’s reading and spelling competencies had clearly improved and her naming abilities were now at the level of her CA.

A maturation of linguistic and semantic competencies, which is clearly higher than the level presumably achieved at the time of the pathological event, but does not reach the level expected for the CA, is the rule in the cases of childhood amnesia reported so far. So, in all of these cases [with the only exceptions of Jon (Vargha-Khadem et al., 1997) and A.V. (Brizzolara, Casalini, Montanaro, & Posteroara, 2003)], verbal MA (mainly an expression of lexical-semantic competencies) was 1 year (case 3 of Gadian et al., 2000) to 6 years (Broman et al., 1997) lower than the actual age. On the other side, even when intelligence scales documented a normal MA, a thorough evaluation revealed incomplete maturation of semantic competencies. So, Jon’s spelling abilities were significantly lower than predicted from his CA (Vargha-Khadem et al., 1997) and A.V. showed a significant delay relative to her actual school level in understanding the meaning of a text (Brizzolara et al., 2003). The incomplete maturation of lexical-semantic competencies is one of the two arguments advanced by Squire and Zola (1998) to reject the claim that childhood amnesia would support the hypothesis of functionally independent episodic and semantic memory systems. The other argument arises from the evidence that, although the ability to retrieve new information from the declarative memory system was deeply compromised in these children, it was never completely abolished. So, for example, it is true that the three patients reported by Vargha-Khadem et al. (1997) revealed very poor or also absent delayed retention of verbal and visual information when tested by means of recall procedures; nevertheless, these patients performed normally on a number of recognition tests for recently presented information, thus revealing residual episodic memory abilities. Analogously, A.V. was able to recall 3 out of 16 words in a list following a 15 min delay from presentation, and she also scored in the normal range in tests of episodic recognition (Brizzolara et al., 2003). Based on these evidences, Squire and Zola (1998) claimed that residual declarative memory abilities were responsible for the acquisition of new lexical and semantic data after the onset of the amnesic syndrome, most likely facilitated by repeated exposures to the same information (as it is the rule in semantic learning). However, the memory deficit did not allow for a normal storage of new semantic information, thus accounting for the deficient maturation of semantic competencies.

Although the case of C.L. is consistent with Squire and Zola’s first criterion for defining the status of episodic-semantic memory abilities in amnesic children (i.e., semantic competencies higher than those presumably achieved at the time of the pathological event but not fully normal for her CA), a thorough neuropsychological analysis of C.L.’s anterograde memory functioning provided little support for Squire and Zola’s second argument, i.e., that residual episodic memory abilities are needed for the acquisition of new lexical and semantic knowledge following the onset of the amnesic syndrome. Indeed, not only did the neuropsychological assessment confirm the clinical diagnosis of an anterograde amnesic syndrome (i.e., normal short-term memory but poor performance on explicit long-term memory tests as compared to both CA and MA healthy children), but it also documented that, at least in the verbal domain, residual episodic memory abilities were almost undetectable in C.L. In fact, in all verbal memory tests involving a delay between stimulus presentation and retrieval, C.L.’s performance was at floor or, in the case of recognition tests, indistinguishable from chance. So, she did not remember any word from the semantically related and unrelated lists, and only one out of 28 informative units of a short story following a 15 min delay. Moreover, her accuracy in discriminating studied from unstudied words did not significantly differ from chance either when a Yes/No or a Forced-Choice recognition paradigm was used. In the visual domain C.L. was not able to reproduce any frag-
ment of the supraspan spatial sequence in the Corsi paradigm following a 5 min delay, and her performance in 15 min delayed recognition tests involving human faces or images of concrete objects did not significantly differ from chance. Some uncertainty about possible residual abilities in learning new visual material come from C.L.’s performance in the 3 min delayed memory reproduction of the Rey Figure B, where she scored in the lower limit of the normal range. Also at variance with the general impression of completely lost ability to acquire new verbal data is the patient’s normal performance in the immediate recall of unrelated word pairs. For this kind of material, however, we do not have a delayed recall test, so we could not make any definitive conclusions about a long-term consolidation of the memory trace. Finally, we did not administer other, more ecological, memory tests to C.L. (such as the Rivermead Behavioral Memory Test) which in previous studies were able to document some residual memory abilities in children with amnesia (e.g., Vargha-Khadem et al., 1997).

As for the basic deficit underlying C.L.’s poor episodic memory performance, most of the data suggest that her main problem was inability to consolidate new episodic memory traces in the episodic memory system. Indeed, not only did she generally show a significant performance decrement passing from immediate to delayed recall tests, but her ability to access studied material did not improve when specific retrieval cues were provided (as in the recognition tests). However, in view of the fact that in most instances C.L.’s immediate recall was below the average performance of both CA and MA matched controls and in some cases (Corsi block and Face recognition tests) it was clearly pathological, an impairment of also the ability to encode new memory traces could be not excluded.

In view of the reduced concentration capacities clinically manifested by C.L., one could also question whether the episodic/semantic dissociation was at least in part the effect of discrepant attentional resources involved in the two kinds of tests. In fact, some of the episodic memory tests utilised (such as related word-list and prose recall) are likely more effortful than most semantic memory tasks (e.g., the semantic questionnaire or the Boston Naming Test). However, in some other cases the relative contribution of attentional resources is likely reversed, with greater involvement in semantic (e.g., word fluency) than in episodic tests (e.g., item recognition). Since C.L.’s performance pattern consistently indicated poor (or also absent) access to episodic memory traces and relatively (or also absolutely) normal access to semantic knowledge (irrespective of the attentional demands of each individual test), an account of C.L.’s memory performance as due to reduced concentration capacities seems very unlikely.

The neuropsychological evidence of a dissociation between virtually lost ability to retrieve recently presented information from the episodic memory system, and at least partial sparing of the ability to acquire new semantic knowledge clearly supports the hypothesis that autobiographical events and factual information follow at least partially independent routes to memorisation. The distinction between these two kinds of learning has been variously theorised. According to the majority of authors, the critical difference consists in the role played by memory for the spatial and temporal context in which the information was acquired, which is critical in the case of autobiographical events (episodic memory) but is negligible for factual knowledge (semantic memory). The different role relational (or associative) memory plays in these two cases would account for the different neural substrates implicated (Tulving & Markowitsch, 1998). Another view posits the critical difference in the time needed for synaptic changes underlying memory storage to occur. Holdstock, Mayes, Isaac, Gong and Roberts (2002) postulated the existence of a fast learning system, subtended by rapid synaptic changes (typically following a single exposure to information), followed by equally rapid forgetting. Another system, based on synaptic changes which occur slowly as a result of cumulation of repeated experiences, would underlie a type of learning which needs repeated exposure to the same information to occur, and which is more resistant to forgetting. In the opinion of these authors, the dichotomy slow/fast learning does not fully conform to the distinction between episodic and semantic memory. In fact, both autobiographical events and factual knowledge could be acquired following a single experience and, as a consequence, be subject to rapid forgetting or, alternatively, be learned via repeated exposure and therefore give rise to more durable memory traces. However, since typically autobiographical events occur only once, while acquisition of lexical and factual knowledge generally results from repeated exposure to the same information, then it is more likely that episodic memory is mainly subtended by the functioning of the fast learning system, while semantic learning occurs via the slow learning system.

Both the above-mentioned theories agree in positing the hippocampal formation as crucial for episodic learning. In particular, according to the first theory the hippocampus is critically implicated in associative learning (Cohen, Poldrack, & Eichenbaum, 1997), and following the second theory it would be the site of rapid synaptic changes underlying fast learning (Holdstock et al., 2002). The cortical area implicated in semantic learning is more debated. According to Varga-Khadem et al. (1997; see also Tulving & Markowitsch, 1998), since in the reported cases of childhood amnesia the hippocampal formation was severely atrophic but the parahippocampal gyrus was of normal morphology and size, a putative role for semantic learning could be attributed to the neocortex adjacent to the hippocampal formation (particularly the perirhinal cortex). Other authors (e.g., Holdstock et al., 2002; Kapur, 1994), based on the evidence in focal brain damaged patients and in patients with semantic dementia of a dissociation, which is opposite to the one observed in the cases of childhood amnesia (i.e., semantic memory more severely compromised than episodic memory), localised the cortical substrate for semantic (or slow) learning at the level of the inferior-lateral surface of the temporal lobe, contiguous to the temporal pole.

In the case of C.L., damage in left hippocampus and a sectioning of the fornix disconnecting the mesial temporal structures from the diencephalic nuclei (mammillary bodies and anterior thalamic nuclei) were likely to be responsible for the episodic memory deficit. As for the partially spared ability to store new semantic information, the results of MRI investigation did not...
help to identify the possible contribution of putative cortical regions in the temporal lobe. Indeed, in both temporal lobes the neocortical regions were substantially spared. In particular, a morphovolumetric analysis did not demonstrate any significant difference in size between the parahippocampal gyri in the left and right hemispheres, and no sign of cortical damage in the more antero-lateral regions of the temporal pole was detected at visual inspection of MR images. However, the poor performances exhibited by C.L. in recognition memory tests suggests a possible dysfunction of the parahippocampal cortices too. Indeed, there is neuropsychological evidence in amnesic patients (e.g., Turriziani, Fadda, Caltagirone, & Carlesimo, 2004) and functional neuroimaging evidence in healthy subjects (Kohler, Danckert, Gati, & Menon, 2005) that the parahippocampal regions are able to support episodic recognition of individual items. In particular, some patients with mesial temporal lobe damage confined to the hippocampal formation (but sparing the parahippocampal cortices) have been reported with severely impaired performance on recall tests but normal ability to recognize individual items (e.g., Turriziani et al., 2004; Vargha-Khadem et al., 1997). Based on this kind of evidence, we conclude that C.L.’s proficient semantic learning was more likely subsumed by operations of neocortical associative regions in the inferior/anterior regions of the temporal lobes.

A final comment should be made about the reason for incomplete maturation of lexical and semantic competencies in C.L., despite the substantial sparing of neocortical areas, which are thought to be implicated in semantic memory. As a first remark, such a defective maturation of semantic competencies could be attributed to a more general delay in the cognitive maturation related to the extension of the brain damage to various subcortical structures in the left hemisphere. However, since a partial deficit of semantic knowledge was also present in other cases of childhood amnesia, in which a thorough neuroradiological investigation had revealed a cerebral damage strictly confined to the hippocampal formation (Gadian et al., 2000; Vargha-Khadem et al., 1997), we could also assume that semantic learning would not be completely independent from the hippocampal formation. A similar view was indeed espoused by Holdstock et al. (2002). In the opinion of these authors, multiple exposures to a piece of information allowing the slow learning system to consolidate new memory traces can be obtained either by repeatedly experiencing the same event, or by internally rehearsing the critical information deposited in the hippocampal-dependent system. This is also the reason why “...in the absence of a normally functioning hippocampus, learning through repeated trials would result in above chance, but not necessarily normal, levels of memory performance (memory would be acquired by repetition only, rather than repetition and rehearsal).” (Holdstock et al., 2002, p. 751).

In conclusion, the case of C.L. adds to the growing literature demonstrating, in children with an organic memory disorder, a preserved ability to store new lexical and semantic information despite a severe episodic memory deficit. A peculiarity of this case is the demonstration of virtually absent ability to store new memory traces following a single exposure to novel verbal material. Despite that, in a 4-year period since the onset of cerebral pathology, C.L. was able to significantly enrich her factual knowledge and, in some cases, to reveal a lexical-semantic repertoire, which was indistinguishable from that of healthy CA matched children. In our opinion, such an evidence is strongly suggestive of at least partially independent routes to memorisation for episodic events and semantic information. Further studies are needed to better comprehend the intrinsic nature of such independence. As previously noted, it could be related to the fundamental associative nature of episodic memory as opposed to the non-associative nature of semantic knowledge, or, alternatively, it could pertain to the operations of two distinct learning systems, a first one which, due to the rapid formation of new synaptic connections following a single exposure to the critical event, is better suited for storing autobiographical events, and a second one which, being based on slow plastic changes resulting from repeated exposures to the same information, seems to be more appropriate to the needs of semantic learning.

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References


