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The Life Stories of Adults with Amnesia: Insights into the Contribution of the Medial Temporal Lobes to the Organization of Autobiographical Memory

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Abstract

Autobiographical memories are not stored in isolation but rather are organized into life chapters, higher-order knowledge structures that represent major themes conveying the arc of one's life. Neuropsychological studies have revealed that both episodic memory and some aspects of personal semantic memory are impaired in adults with medial temporal lobe (MTL) damage. However, whether such impairment compromises the retrieval and formation of life chapters is unknown. Therefore, we had 10 adults with MTL amnesia and 20 control participants narrate their life stories, and we extracted life chapters from these narratives using a novel scoring protocol. For the retrograde and anterograde time period separately, we evaluated the number of life chapters and assessed their quality, as indexed by measures of complexity and richness. Additionally, to investigate the idea that formation of life chapters occurs on a protracted time scale, we separated the amnesic participants into an early-life and a later-life onset subgroup. Results revealed that early-onset, but not later-onset, amnesic participants generated fewer retrograde life chapters than controls. The higher-order temporal relation among retrograde chapters, but not their thematic relation or the richness of individual life chapters, was impaired in both amnesic subgroups. The amnesic participants also generated fewer anterograde life chapters than controls, and the richness of their anterograde chapters was reduced in terms of content, but not self-reflection. Findings suggest that the organization of autobiographical content into life chapters is a protracted process that depends on the MTL, as does retrieval of higher order temporal relations among life chapters.

Keywords

Personal Semantic Memory; Autobiographical Memory; Amnesia; Medial Temporal Lobe

1. Introduction

Autobiographical memory, which is the repository of experiences and facts that are unique to each person, plays a central role in one's self-concept (Conway, 2005; Prebble et al.,

2013). It does so not only by virtue of storing the content of one's personal history, but also by functioning as an organizing structure in which that information is integrated. With regard to the content of autobiographical memories, a broad distinction can be made between episodic memories that capture singular life events and personal semantic memories, which include facts about one's life, knowledge of one's traits and roles, as well as personal beliefs (Grilli & Verfaellie, 2014; Renoult et al., 2012). Notably, it has been suggested that episodic and personal semantic memories are not stored as isolated mental representations, but rather are organized into hierarchical autobiographical knowledge structures that reflect associative networks of contents (Conway, 2005; Conway & Pleydell-Pearce, 2000; Thomsen, 2015). According to this idea, low in the memory hierarchy are knowledge structures that organize autobiographical contents around themes that capture general or repeated events, such as one's typical morning jog or holidays with family. High in the hierarchy are knowledge structures that organize autobiographical content around major life themes that reflect extended time periods, typically spanning months to years, such as childhood or one's career (McAdams, 2001; Thomsen, 2009). These latter knowledge structures, which we refer to as life chapters, are the focus of the present study.

Because life chapters reflect higher-order themes of one's life story, they can form links between autobiographical memories that are separated by years, and represent activities, people, and places that are drawn from diverse experiences (Thomsen, 2015). For example, the network of contents that represents a life chapter of "living in Boston" could include episodic memories of navigating a moving truck on the narrow city streets and attending a playoff game at Fenway Park, as well as personal semantic memories of friends, favorite restaurants, and weekend runs. Life chapters can overlap in autobiographical content (e.g., memories that occurred while living in Boston could be incorporated into multiple life chapters), but each life chapter is unique, and collectively they capture the milestones and turning points of one's life history. As such, it is thought that one of the essential functions of life chapters is to condense a lifetime of experience into a continuous and coherent life story (Prebble et al., 2013).

From this perspective, without life chapters, autobiographical memory would be fractionated, consisting of islands of memories from different points in one's life. Yet, this organizational framework does not need to be viewed as a simple, linear outline of one's personal history. Life chapters can overlap in time, reflecting distinct thematic focal points that are simultaneously operative. For example, the life chapter of living in Boston could partly overlap in duration with another life chapter that began sometime after moving to this location, such as "having a child." Life chapters also can be inter-related at higher-order conceptual levels because they share content themes (Thomsen, 2015). As an example, "living in Boston" and "living in Tucson" are two life chapters that are similar in their organization around living locations. Moreover, life chapters add meaning to autobiographical memory by binding contents that may have come from diverse contexts and time periods. For instance, the life chapter of living in Boston could take on greater personal significance after it becomes an organizing theme for memories of friends from work and other social spheres from that time period.

Neuropsychological studies of autobiographical memory have focused on the individual contents of autobiographical memory. An extensive literature has documented the impact of medial temporal lobe (MTL) lesions on episodic memory (Cermak & O'Connor, 1983; Corkin, 2002; Tulving, 1985), and more recently, it has become clear that retrieval of personal semantic memory is commonly impaired in adults with MTL lesions as well (Grilli & Verfaellie, 2014; Philippi et al., 2015). However, not all subtypes of personal semantic memory appear to be affected, as retrieval of personality trait knowledge (e.g., knowing that one is an organized person), which is thought to be a highly abstract form of personal semantic memory, has been found to be spared by MTL lesions (Klein et al., 2002; Tulving, 1993). Similarly, we recently showed that individuals with MTL amnesia are impaired in their retrieval of autobiographical factual knowledge that is associated with a spatiotemporal context (e.g., repeated-event derived facts, such as that one goes for long runs on Saturday mornings), whereas retrieval of abstract facts (e.g., names of family members and friends) is preserved (Grilli & Verfaellie, 2016; also see, Westmacott et al., 2004). Taken together, these findings suggest that MTL lesions may selectively impair autobiographical content that is “experience-near” (i.e., related to a spatiotemporal context), regardless of whether it is episodic or semantic.

A question that has not been addressed by neuropsychological studies is how impaired retrieval of experience-near content in MTL amnesia affects the higher-order organization of autobiographical memory. Life chapters consist of both experience-near and abstract contents, each of which is bound to the life theme (Thomsen, 2015). As such, it is possible that abstract contents attached to life themes are sufficient to maintain life chapters that were formed prior to the onset of amnesia, as retrieval of an abstract content could trigger retrieval of other abstract contents that share a thematic link, leading to the reconstruction of a life chapter. From this viewpoint, retrieval of retrograde life chapters may be largely spared by MTL lesions. Yet, theoretical models also suggest that such sparing may not apply to life chapters that capture life themes starting in the years immediately preceding the onset of amnesia. According to Thomsen (2015), life chapters are formed on a protracted time scale, such that autobiographical contents are associated to life themes after those individual contents are consolidated, a process that may unfold over the course of several years. These higher-order connections may be established through repeated retrieval of autobiographical contents and reflection on their associations to life themes and other contents, a type of relational processing that could depend on the MTL (Cohen & Eichenbaum, 1993; Konkel et al., 2008). Given that abstract contents are thought to be extracted from commonalities in life experiences, the binding of these contents to life themes may be particularly extended. Thus, to the degree that associating abstract contents around themes beginning proximal to the onset of amnesia is incomplete, such life chapters might be disrupted by MTL damage.

This raises the intriguing possibility that the impact of MTL damage on retrograde life chapter retrieval may vary as a function of age at amnesia onset. Namely, disrupted organization of life experiences leading up to the onset of amnesia may have a minor impact on retrograde life chapter retrieval in adults who incur amnesia later in life, as new themes typically emerge on the scale of years or decades in later adulthood. In other words, very few life chapters may be in a vulnerable state of organization when amnesia onset occurs in later life. In contrast, a high frequency of themes simultaneously start early in life, specifically

prior to age 30 (Thomsen & Bernsten, 2008; Thomsen et al., 2011). If the organization of autobiographical content is a protracted process, early adulthood may be a period of time during which many emerging life chapters are still in a state of formation, and as such are highly susceptible to disruption by MTL damage. Therefore, whereas retrograde life chapter retrieval may be largely spared in adults who sustain amnesia later in adulthood, it could be impaired in adults who incur amnesia in close proximity to this chapter-rich life period.

For retrograde life chapters that are maintained, whether experience-near content makes an essential contribution to the quality of a life chapter is not known. In regard to temporal complexity, the ability to maintain overlapping life chapters may be facilitated by the incorporation of experience-near contents that tag these knowledge structures with timestamps or spatial footprints (e.g., knowing that chapters overlapped in time because both started while one was a postdoctoral fellow). In regard to thematic complexity, experience-near contents may provide event-like details that enhance the likelihood of retrieval of life chapters that are associated on a thematic level (e.g., chapters that, although not overlapping in time, occurred while living in Boston). Experience-near contents also could add unique information and personal meaning, enhancing the richness of these knowledge structures. Therefore, examining the quality of retrograde life chapters generated by adults with amnesia may shed light on the degree to which the MTL is necessary to maintain the higher-order organizational features of autobiographical memory.

In addition to uncertainty regarding the contribution of the MTL to retrograde life chapter retrieval, the impact of amnesia on the formation of anterograde life chapters also is unknown. Prior research has revealed that the acquisition of personal semantic content is commonly compromised in individuals with amnesia (Grilli & Verfaellie, 2014). Therefore, the formation of new life chapters may be impaired by MTL damage because these knowledge structures might need to be formed on the basis of a limited repository of content from post-amnesia life. Moreover, if the ability to bind abstract contents to each other on a thematic level depends on the MTL, the formation of post-amnesia life chapters may be further compromised. Consistent with the latter idea, studies of adults with amnesia have shown that semantic learning in MTL amnesia is not flexible (Glisky, 2004) or well integrated into existing knowledge structures (Westmacott & Moscovitch, 2001), two mnemonic qualities that can be facilitated by relational processing. Therefore, regardless of the timescale on which autobiographical contents are organized in life chapters, it would not be surprising to find that MTL damage impairs the formation of anterograde life chapters. Further, to the extent that new life chapters can be formed, impaired storage of novel autobiographical content could diminish the complexity and richness of these knowledge structures.

To investigate these potential contributions of the MTL to the quantity and quality of life chapters, in the present study we asked adults with amnesia and healthy adults to narrate their life stories, and we applied a novel scoring protocol to extract life chapters from the narrative responses. To evaluate the idea that autobiographical contents are organized into life chapters on a protracted time scale, we separated the amnesic participants into two groups based on whether onset of amnesia occurred before or after age 30 and we assessed retrieval of both retrograde and anterograde life chapters. To investigate the contribution of

the MTL to complexity of life chapters, we assessed the thematic and temporal relations of these knowledge structures. We also sought to evaluate the richness of life chapters, which we assessed on the basis of the amount of knowledge and the extent of self-reflection incorporated into each life chapter.

We predicted that if links between thematically related abstract contents are sufficient to maintain life chapters, retrograde life chapter retrieval would be largely spared in later-life amnesic participants, given that these individuals had sufficient time to organize most pre-amnesia autobiographical contents into associative networks representing life themes. However, we also hypothesized that if organizing abstract contents into these knowledge structures occurs on a protracted time scale, retrograde life chapter retrieval would be impaired in early-life amnesic participants, given that these individuals had amnesia during a period of time when many emerging themes were serving as an organizing principle for autobiographical content. We also predicted that regardless of age of amnesia onset, the complexity (i.e., temporal and thematic relations) and richness (i.e., content and self-reflection) of retrograde life chapters would be diminished in amnesic participants, given that these qualitative aspects of life chapters may be enhanced by experience-near contents, the retrieval of which is disrupted by MTL lesions. In regard to anterograde memory, we predicted that both early-life and later-life amnesic participants would be impaired at updating the post-amnesia life story with new life chapters because of impaired acquisition of autobiographical content and disrupted relational processing, and if generated, the complexity and richness of new life chapters would be compromised, given the limited repository of autobiographical content available.

2. Methods

2.1 Participants

Ten adults with MTL amnesia participated in this study (see Table 1). Extensive neuropsychological testing confirmed that significant impairments were largely isolated to episodic memory in all participants (see Supplementary Table 1 for additional data regarding neuropsychological profiles). Etiology of amnesia included hypoxic-ischemic injury ($n = 6$), stroke ($n = 2$), encephalitis ($n = 1$), and status epilepticus followed by left temporal lobectomy ($n = 1$). MRI/CT scans confirmed MTL pathology for 8 participants and volumetric data was available for 6 of these participants. One of these participants (P02) had lesions that extended beyond the MTL into anterolateral temporal neocortex¹. Two participants (P04 and P07), who had suffered cardiac arrest, could not be scanned due to medical contraindications. MTL pathology for these participants was inferred based on etiology and neuropsychological profile.

Amnesic participants were separated into two subgroups on the basis of age of amnesia onset. P01, P02, and P03 suffered their injuries at ages 22, 26, and 23 respectively, and thus were included in the early-life amnesia subgroup ($M = 23.7$). The remaining seven amnesic participants suffered their injuries at later ages (range = 37 to 69 years old; $M = 51$) and were

¹P02's life chapter retrieval was similar to the other two early-life amnesics, and therefore differences between the early-life and later-life amnesic subgroups were not driven by this participant.

included in the later-life amnesia subgroup. The former subgroup was significantly younger than the latter subgroup not only at the time of amnesia onset ($p < .001$), but also at time of testing ($M = 51.7$ vs. 62.6), $p = .04$. The two amnesic subgroups did not significantly differ in regard to years of education, verbal intelligence or working memory, as measured by the Wechsler Adult Intelligence Scale, Third Edition, or episodic memory, as measured by the Wechsler Memory Scale, Third Edition, p 's $> .14$.

Twenty healthy adults also participated in the study. Control participants were separated into two groups, one for the early-life amnesic subgroup ($n = 6$) and one for the later-life amnesic subgroup ($n = 14$). Two controls of the same gender were selected for each amnesic participant such that on average they were within five years of age (greatest spread for controls relative to their amnesic participant was -5 to $+4$) and three years of education (greatest spread for controls relative to their amnesic participant was -4 to 0). The early-life control group was matched to the early-life amnesic subgroup on age, education, verbal intelligence, and working memory, p 's $> .60$. Similarly, the later-life control group was matched to the later-life amnesic subgroup on age, education, verbal intelligence, and working memory, p 's $> .26$.

All participants provided informed consent in accordance with the Institutional Review Board of the VA Boston Healthcare System.

2.2 Materials and Procedures

Participants were informed that they would be telling “their life story – from birth leading up to now.” The experimenter explained that telling one’s life story involves sharing “the unfolding of events that tell who you are.” Participants were encouraged to take at least 15 minutes to tell their life story. However, they were not obligated to do so, nor were they stopped if they spoke for longer than 15 minutes (i.e., there was no time limit). Participants were informed when 5, 10, and 15 minutes had passed by showing a card with the time displayed. This was done to ensure that participants did not feel rushed on this open-ended task. The experimenter provided a reorienting prompt whenever the participant lost his or her train of thought (e.g., you have told me about your life from when you were born to when you got your first job. What is next in your life story?). No additional prompting or specific cueing was provided. Responses were recorded.

2.3 Scoring

A segment of an amnesic participant’s and a control’s life stories, with scoring illustrated, are included in the Supplementary Materials.

2.3.1 Number of life chapters—Scoring of each participant’s life story began by segmenting the narrative into distinct life chapters. Based on current theoretical models, we defined life chapters as a time course of activities that must take place over more than 24 hours but typically spans months to years. We also conceptualized life chapters as consisting of multiple autobiographical contents describing a single theme. We used themes reported by prior studies as guides (e.g., living location, school, career, relationships, leisure activities, death/illness) (Thomsen & Bernsten, 2008; Thomsen et al., 2011), but we did not

restrict our scoring to them. After each life story was segmented into life chapters, the first level of scoring determined whether each life chapter was retrograde or anterograde based on follow-up interviews with informants of the amnesic participants and with the control participants. We interviewed informants of the amnesic participants to determine whether life chapters started pre-amnesia (i.e., prior to their age of injury or illness) or post-amnesia. For control participants, the interview focused on determining whether life chapters started prior to or since the age at which the matched amnesic participant became amnesic. For example, given that P01 was 22 years old when he suffered his injury, we determined how many life chapters started prior to and since that age for P01's two controls.

2.3.2 Quality of life chapters

2.3.2.1 Complexity: Complexity was scored on the basis of temporal and thematic relationships. A life chapter was scored as temporally related if it overlapped in time with at least one other life chapter, whereas a life chapter was scored as temporally unrelated if it did not overlap in time with any other life chapter. A life chapter that shared a content theme with at least one other life chapter was scored as thematically related (e.g., one chapter about one's first job and another chapter about one's current job), whereas a life chapter was scored as thematically unrelated if it did not share a theme with any other life chapter.

2.3.2.2 Richness: One measure of richness reflected the amount of knowledge incorporated into each life chapter. Based on theoretical models of life chapters (Conway, 2005; Thomsen, 2015), we scored the total number of people (e.g., a parent), places (e.g., the city where one grew up), and activities (e.g., walking to school) included per life chapter. A second measure focused on personal significance and reflected the total number of self-referential comments included per life chapter. Self-referential comments were defined as statements that connected the content of the life chapter with one's personal feelings, thoughts, or present situation.

2.4 Reliability

Inter-rater reliability was calculated based on 30 percent of the life stories. Life stories from 4 amnesic participants and 5 control participants were randomly selected. The secondary rater, but not the primary rater, was blind to subject status, in accordance with established scoring procedures (Levine et al., 2002; Verfaellie et al., 2014). Reliability was good to excellent for total number of life chapters (Cronbach's $\alpha = .91$), both complexity measures (Cronbach's α range = .79 to .92), and both richness subtypes (Cronbach's α range = .98 to .99).

2.5 Data Analyses

Given our prediction that the impact of amnesia on retrograde life chapter retrieval would differ in the amnesic subgroups, the number of retrograde and anterograde life chapters for each amnesic subgroup was compared to their respective control group. Because these amnesic subgroup/control group comparisons involved small sample sizes, a nonparametric approach was used, consistent with prior neuropsychological studies (Berryhill et al., 2007; Grilli & Verfaellie, 2016). In these nonparametric mixed models analysis of variance (ANOVA) the F statistic was first calculated in the standard way. Scores for between and

within-subject variables were then randomly rotated, and a new ANOVA was run with new F values. This was repeated 100,000 times to generate a nonparametric distribution of F values for main effects and the interaction. An effect in the original data was considered significant if the obtained F value fell in the top 5 percent of that effect's distribution. For measures of complexity and richness, the amnesic subgroups were combined into a single amnesic group and compared to a single control group, as there was no a priori reason to expect age of amnesia onset to impact these measures. Parametric analyses were used for these comparisons.

In order to directly compare the two amnesic subgroups, we expressed each amnesic participant's performance as a z-score based on their respective control group and compared z-scores in the two amnesic subgroups. This approach ensured that subgroup comparisons were not confounded by the fact that the number of years contributing to the retrograde and anterograde time period differed for the two amnesic subgroups. Consistent with the amnesic subgroup/control group analyses, these amnesic subgroup comparisons were done using nonparametric analysis of variance. Although we did not expect there to be subgroup differences for complexity and richness measures, for completeness we compared the two subgroups on these measures as well. For these comparisons, consistent with prior studies of small groups with neuropsychological populations (Berryhill & Olson, 2008; Grilli & Verfaellie, 2016), we used a permutation test analogous to a one-tailed t-test. In this approach, the t-test was first calculated on the observed values. Then two groups were randomly defined and a t-test was performed again. This was repeated 100,000 times. The reported p-values refer to the proportion of scores above the observed original value.

3. Results

3.1 Number of life chapters

Figure 1 depicts the mean number of retrograde and anterograde life chapters generated by amnesic participants and control participants. As can be seen in Figure 1, later-life amnesics show only a small numerical group difference for retrograde life chapter generation, and virtually no difference for anterograde life chapter generation, although the latter were infrequently included in the life stories of either later-life amnesic participants or their controls (i.e., participants of both groups). Consistent with this impression, a 2 (group: amnesic vs. control) X 2 (temporality: retrograde vs. anterograde) nonparametric ANOVA revealed no effect of group, $F(1, 19) = .16, p = .79$, a main effect of temporality, $F(1, 19) = 79.45, p = .001$, and no interaction, $F(1, 19) = .13, p = .81$.

For early-life amnesic participants and their controls, a different pattern of results emerged. As shown in Figure 1, the early-life amnesic participants generated fewer retrograde and anterograde life chapters than their control participants. A 2 X 2 nonparametric ANOVA revealed a main effect of group, $F(1, 7) = 11.23, p = .03$, a marginal effect of temporality, $F(1, 7) = 7.88, p = .06$, and no interaction, $F(1, 7) = .08, p = .85$.

The difference in pattern across the two amnesic subgroups was confirmed with a 2 (subgroup: early- vs. later-life) X 2 (temporality: retrograde vs. anterograde) nonparametric ANOVA, as there was only a main effect of amnesic subgroup, $F(1, 8) = 25.64, p = .003$

(main effect of temporality and interaction, $F_s < 1$). This indicates that in comparison to their respective control groups, early-life amnesic participants retrieved fewer retrograde and anterograde life chapters than did later-life amnesic participants.

3.2 Quality of retrograde life chapters

Table 2 shows the mean proportion of retrograde life chapters generated by amnesic participants and controls that were temporally related or thematically related to another life chapter, as well as the mean number of core elements of knowledge and self-referential comments included in each life chapter.

3.2.1 Complexity—In regard to temporal complexity, an independent samples t-test revealed that amnesic participants generated proportionally fewer life chapters that were temporally related to another chapter than did controls, $t(28) = 3.17, p = .004, d = 1.2$. In regard to thematic complexity, although the proportion of life chapters that were thematically related to another chapter was numerically smaller in amnesic participants than in control participants, this difference was not statistically significant, $t(28) = 1.84, p = .08, d = .70$. A comparison of temporal and thematic complexity z-scores showed that the difference between amnesic participants and controls was greater for temporal complexity than for thematic complexity (temporal $M = -1.36, SD = 1.12$; thematic $M = -.71, SD = .85$), $t(9) = 4.3, p = .002, d = 1.6$. Permutation t-tests comparing the amnesic subgroups showed no difference in their proportions of temporally related chapters, $p = .76$, or thematically related chapters, $p = .68$.

3.2.2 Richness—Independent samples t-tests revealed no effects of elements of knowledge, $t(28) = .85, p = .40$, or self-referential comments, $t(28) = 1.76, p = .09, d = .67$. Therefore, relative to controls, the amnesic participants were not impaired on these two measures of retrograde life chapter quality. Moreover, permutation t-tests comparing the amnesic subgroups showed no difference in their incorporation of elements of knowledge, $p = .36$, or self-referential comments, $p = .92$, per retrograde life chapter.

3.3 Quality of anterograde life chapters

The low number of anterograde chapters generated by the amnesic participants ($M = 1.3, SD = .95$) and controls ($M = 2.2, SD = 2.3$) precluded analysis of the complexity measures, but descriptive results are presented in Supplementary Table 2.

Richness measures were analyzed for the subset of participants who generated at least one anterograde life chapter (8 amnesic participants and 14 control participants). An independent samples t-test indicated that the amnesic participants incorporated fewer core elements of knowledge per life chapter relative to controls (amnesic $M = 2.69, SD = 1.10$; control $M = 4.52, SD = 1.79, t(20) = 2.61, p = .02, d = 1.17$). In contrast, the number of self-reflective elements per life chapter did not differ across groups (amnesic $M = 1.13, SD = .99$; control $M = 1.64, SD = 1.08$), $t(20) = 1.1, p = .28$. Given that two of the three early-life amnesic participants did not generate a single anterograde life chapter, we were not able to compare the amnesic subgroups.

4. Discussion

Life chapters are an important component of autobiographical memory as they organize a lifetime of content into a coherent story and facilitate a continuous sense of self. However, the cognitive and neural mechanisms that allow for the retrieval and formation of these knowledge structures are unknown. To shed light on these questions, we investigated the ability of adults with MTL amnesia to retrieve autobiographical memory in the form of life chapters. There were four main findings: 1) retrieval of retrograde life chapters was spared in later-life amnesic participants, but impaired in early-life amnesic participants; 2) complexity of retrograde life chapters was reduced in both amnesic subgroups, but richness was not; 3) anterograde life chapter retrieval was impaired in the early-life amnesic participants; and 4) for those amnesic participants who generated anterograde life chapters, richness of these chapters, as measured by the number of content elements, was reduced relative to controls.

The later-life amnesic subgroup retrieved as many retrograde life chapters as their controls. Given that these amnesic participants had sufficient time to organize most pre-amnesia autobiographical contents into higher-order themes, these results support the idea that life chapters, once firmly established, can be maintained independent of the MTL. In light of this finding, we postulate that the ability to reconstruct a consolidated life chapter can be supported by networks of abstract semantic memories that depend on neocortical regions for retrieval. Consistent with this idea, functional neuroimaging research has shown that the retrieval of content from higher-order autobiographical constructs, including life chapters, activates the lateral temporal lobe (Addis et al., 2012; Ford et al., 2011), a brain region implicated in the representation of abstract personal semantic contents (Renoult et al., 2012).

In contrast to the later-life amnesic participants, the early-life amnesic participants generated fewer retrograde life chapters than their controls. We also found that the performance of the early-life amnesic participants was more discrepant from that of their matched controls than was the case for the later-life amnesic participants, confirming that there was a significant difference in the performance of the two amnesic subgroups. Together, these findings support the notion that life chapters are particularly vulnerable to disruption when MTL damage is sustained in early adulthood, which is associated with the emergence of many new life themes in a short period of time. Notably, the retrieval of abstract autobiographical contents does not depend on the MTL (Klein et al., 2002; Grilli & Verfaellie, 2016), and even semantic knowledge acquired in the years immediately preceding onset of amnesia is spared (Verfaellie et al., 1995). Thus, we conclude that the paucity of retrograde life chapters in the later-life amnesic participants reflects impaired organization of autobiographical content rather than a reduction of autobiographical content per se. These results are therefore consistent with the idea that the formation of life chapters is a protracted process (Thomsen, 2015) that depends on MTL mechanisms to bind autobiographical contents, including abstract knowledge, to life themes and in the process forms associative networks of these representations. If the ability to organize autobiographical contents to form life chapters is disrupted, abstract autobiographical contents from the period proximal to the onset of amnesia may be stored as islands of autobiographical knowledge, no longer bound together to capture major life themes from before MTL damage was incurred.

With regard to the quality of retrograde life chapters, both amnesic subgroups were less likely than healthy controls to generate retrograde life chapters that were temporally overlapping and thus simultaneously operative. In other words, regardless of how many life chapters were retrieved, the pre-amnesia life story in the amnesic participants was told in a more serial fashion. Therefore, MTL damage affects the complexity of life chapters, a finding consistent with the notion that experience-near content is important for linking life chapters in time. However, certain organizational features of life chapters might be more dependent on experience-near content than others. In contrast to the retrieval of life chapters that were temporally overlapping, the retrieval of retrograde life chapters that were thematically connected to one another was only numerically, but not statistically reduced in the amnesic participants relative to controls, and the difference from controls was significantly smaller than it was for temporal complexity. The possibility that experience-near contents increase organizational complexity primarily by linking life chapters in time remains to be further explored. Whereas we examined temporal and thematic organization, life chapters also can be organized on the basis of their relevance to core aspects of personal identity (e.g., my self-concept of being a father could be supported by life chapters of family life and being a youth soccer coach). However, to capture this particular quality of the autobiographical memory hierarchy, more explicit reflection on identity statements might be required. Thus, multiple methods may be needed to further elucidate the contribution of the MTL to the organizational framework of life chapters.

In regard to the richness of individual life chapters, findings revealed that the amnesic participants, regardless of age at amnesia onset, included as many core elements of knowledge and self-referential comments in their retrograde life chapters as did controls. These results indicate that once a life chapter is completely organized, the core content appears to be largely maintained without reliance on the MTL, as does the ability to evoke the personal significance of these higher-order knowledge structures. It is important to note that whereas we measured richness through these two features of a life chapter, there may be other ways to capture the depth of such knowledge structures (e.g., goal relevance) (Conway, 2005). Nonetheless, based on the results of the present study we can conclude that once autobiographical content has been extracted and bound together on the basis of a life theme, the MTL is not necessary to retrieve the core content and personal significance of that higher-order knowledge structure.

Prior studies have shown that the acquisition of novel autobiographical content is commonly compromised in amnesia (Grilli & Verfaellie, 2014). The present finding that the early-life amnesic participants included fewer anterograde life chapters in their life stories than did their matched controls suggests that MTL lesions also disrupt the organization of anterograde autobiographical content into novel life chapters. Notably, this interpretation rests on the assumption that amnesia does not in itself preclude the opportunity to start new life chapters. We believe this notion is justified. Amnesia changes the trajectory of one's life story, and as such, marks the start of life changes that usually form life chapters (e.g., retirement, illness). Further, individuals with amnesia typically experience social, activity, and residential changes that normally are the sources of new themes (Thomsen & Bernsten, 2008; Thomsen et al., 2011). In fact, two of the three individuals in the early-life onset amnesia subgroup (P02 and P03), who were 25 and 34 years post-onset of amnesia, had

experienced changes to living locations, leisure activities, and social relationships; yet, they did not generate a *single* anterograde life chapter. In other words, their life stories abruptly stopped in a pre-amnesia chapter, without mentioning experiences from the decades that have unfolded since that time. Although P02's lesion extends into the anterolateral temporal lobe, P03's lesion is restricted to the hippocampus, casting doubt on the likelihood that extra-MTL damage is responsible for this impairment. Rather, the findings, albeit based on a small sample, indicate that hippocampal damage is sufficient to severely disrupt formation of new life chapters.

The deficit in anterograde life chapter retrieval in the early-life amnesic participants may reflect the contribution of the MTL both to updating the repository of autobiographical knowledge after incurring MTL damage and to binding post-amnesia autobiographical content into higher-order knowledge structures. The present study does not elucidate their respective contributions. With a primary focus on the retrieval of life chapters in adults with MTL amnesia, we did not investigate the integrity of individual autobiographical contents across the lifespan. Therefore, we do not know the status of abstract autobiographical content from the anterograde time period in the amnesic participants. This is a limitation of the present study, but the life story narrative is not an ideal approach to assess the integrity of isolated autobiographical memories, since this retrieval mode biases retrieval to core information of life chapters. Future research should assess both autobiographical contents and life chapters in the same study, as this could clarify the degree to which anterograde life chapter retrieval is impaired because of disrupted acquisition of content or relational processing.

In light of the anterograde memory performance of the early-life amnesic participants, at first glance it is surprising that the later-life amnesic participants were not also impaired in the generation of anterograde life chapters. However, given that new life themes typically arise over years in later adulthood, the relatively brief time frame since onset of amnesia in this subgroup ($M = 11.6$ years) likely restricted our ability to detect an impairment in anterograde life chapter formation. In fact, the controls for this amnesic subgroup also generated few new life chapters since the age of injury of their matched amnesic participant. Therefore, because anterograde life chapter retrieval was impaired in the early-life amnesic participants, it is reasonable to suspect that impairment to post-amnesia life chapter formation in the later-life subgroup might be more apparent in years to come.

In regard to the richness of anterograde life chapters that were generated, two contrasting results were found. On the one hand, amnesic participants' post-amnesia chapters were impoverished in terms of core elements of knowledge. This finding is consistent with the idea that the few anterograde life chapters that are organized by individuals with amnesia may be impoverished in content because they are built on a limited repository of knowledge. On the other hand, the incorporation into post-amnesia chapters of self-referential statements was not disrupted in the amnesic participants, suggesting that reflection on the meaning of new autobiographical content to one's conceptualization of the self does not depend on the MTL. Findings from fMRI studies have reliably implicated the ventral medial prefrontal cortex (vmPFC) in the ability to process information in relation to the self, including during the retrieval of autobiographical contents (Martinelli et al., 2013; Murray et al., 2015;

Svoboda et al., 2006). There also is evidence from neuropsychological studies that vmPFC damage can eliminate the advantage of self-referential processing in episodic learning (Philippi et al., 2011) and disrupt the ability to retrieve experience-near content from the perspective of the self (Kurczek et al., 2015). In light of these findings, the results of the present study raise the possibility that vmPFC may similarly support the assigning of personal meaning to autobiographical facts, as well as the ability to relate that content to the self during subsequent retrieval.

In conclusion, in the present study we sought to understand how damage to the MTL affects the higher-order organization of autobiographical memory. The results indicate that once life chapters are consolidated, the MTL is not necessary to retrieve life chapters themselves, nor to support their core content and personal meaning. Yet, MTL amnesia can interfere with retrieval of life chapters reflecting autobiographical information pertaining to life themes that emerge proximal to the onset of amnesia, suggesting that the formation of life chapters is a protracted process. Moreover, the organizational framework in which retrograde life chapters are embedded, in particular the temporal quality of this hierarchy, remains dependent on the MTL. The formation of new life chapters also critically relies on the MTL, likely because of the contribution of the MTL to the acquisition of autobiographical content as well as its role in binding contents into associative networks representing life themes. The amount of knowledge integrated into these life chapters also is impaired, which may reflect disrupted semantic learning of autobiographical information. Therefore, adults with amnesia can maintain at least some semblance of a life story prior to their injury, but the complexity of what remains is diminished by MTL damage, and the ability to update this timeline is largely severed. Whereas prior neuropsychological research has focused on the fate of autobiographical contents in adults with amnesia, here we demonstrate how MTL lesions affect the organization of such content. Additional cognitive neuroscience research into the organizational principles of autobiographical memory could shed further light on how a lifetime of personal experience is stored and bound to one's self-concept.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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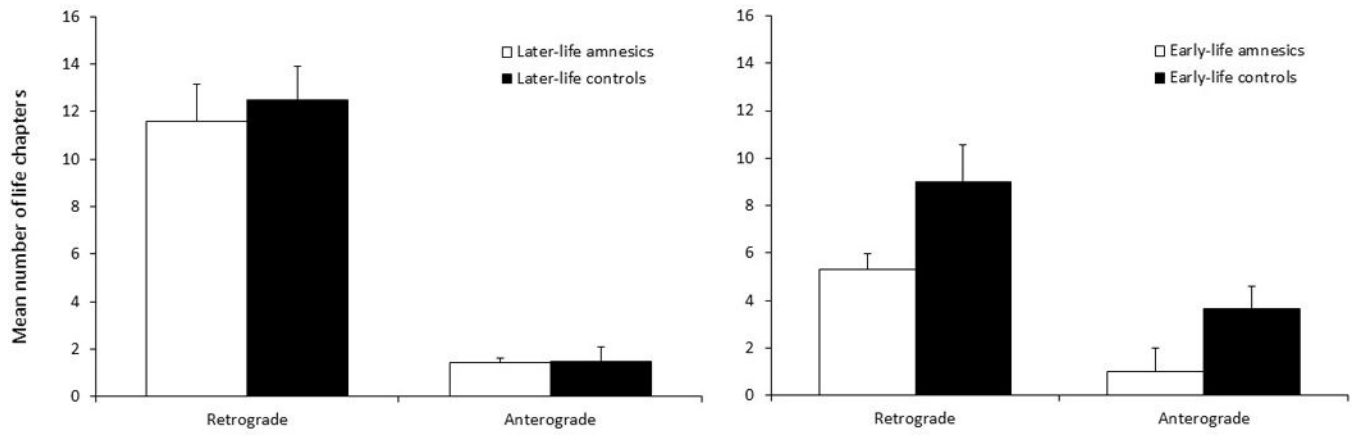


Figure 1. Mean number of retrograde and anterograde life chapters generated by later-life amnesic participants and their controls, and early-life amnesic participants and their controls. Error bars depict the standard error of the mean.

Table 1

Demographic information, neuropsychological data, and volumetric data

Etiology	Age	Edu	WAIS-III		WMS-III		Volume Loss (%)		
			VIQ	WMI	GM	VD	Hippocampal	Subhippocampal	
Early-Life Amnesics									
P01	47	12	103	97	59	68	55	L:45%; R:46%	-
P02	51	16	93	99	49	53	52	L: 89%; R:37%	60% ^a
P03	57	14	84	88	45	53	52	L: 76%; R:64%	-
<i>mean</i>	51.7	14	93.3	94.7	51	58	53		
Controls									
<i>mean</i>	49.3	14	98.7	100.5					
Later-Life Amnesics									
P04	63	17	131	128	86	78	86	N/A	N/A
P05	57	14	106	111	59	72	52	L: 18%; R:27%	-
P06	65	12	88	82	52	56	55	N/A	N/A
P07	65	16	100	88	86	78	83	N/A	N/A
P08	73	13	99	104	49	56	58	N/A	N/A
P09	51	20	111	104	60	65	58	L: 46%; R:40%	-
P10	62	18	117	88	67	75	55	L: 63%; R:62%	-
<i>mean</i>	62.6	15.7	107.4	100.7	65.6	68.6	63.9		
Controls									
<i>mean</i>	62.4	15.9	114.3	111.5					

Note: Age, age in years; Edu, education in years; WAIS-III, Wechsler Adult Intelligence Scale-III; WMS-III, Wechsler Memory Scale-III; VIQ, verbal intelligence quotient; WMI, working memory index (prorated); GM, general memory; VD, visual delayed; AD, auditory delayed; Hippocampal volume loss, L = left and R = right;

^aVolume loss in left anterior parahippocampal gyrus (i.e., entorhinal cortex, medial portion of the temporal pole, and the medial portion of perirhinal cortex; (see Kan et al., 2007 for methodology)

Table 2

Mean (SD) proportion of retrograde life chapters including temporal or thematic relations with other life chapters and number of core elements of knowledge and self-referential comments per chapter.

Quality Measures	Amnesics	Controls
<i>Complexity</i>		
Temporally related	.21 (.16)	.40 (.16)
Thematically related	.53 (.24)	.70 (.23)
<i>Richness</i>		
Content	4.63 (.93)	5.13 (2.25)
Self-reflection	1.14 (.61)	1.60 (.71)