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A case of hyperthymesia: Rethinking the role of the amygdala in autobiographical memory

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Abstract

Much controversy has been focused on the extent to which the amygdala belongs to the autobiographical memory core network. Early evidence suggested the amygdala played a vital role in emotional processing, likely helping to encode emotionally charged stimuli. However, recent work has highlighted the amygdala's role in social and self-referential processing, leading to speculation that the amygdala likely supports the encoding and retrieval of autobiographical memory. Here, cognitive as well as structural and functional magnetic resonance imaging data was collected from an extremely rare individual with near-perfect autobiographical memory, or hyperthymesia. Right amygdala hypertrophy (approximately 20%) and enhanced amygdala-to-hippocampus connectivity (> 10 standard deviations) was observed in this volunteer relative to controls. Based on these findings and previous literature, we speculate that the amygdala likely charges autobiographical memories with emotional, social, and self-relevance. In heightened memory, this system may be hyperactive, allowing for many types of autobiographical information, including emotionally benign, to be more efficiently processed as self-relevant for encoding and storage.

Keywords

amygdala; hyperthymesia; superior memory; hypermnnesia; autobiographical memory

1. Introduction

The mysteries of human memory have intrigued philosophers, scientists, and society in general for centuries. Why is it that some memories endure the test of time, while others are seemingly lost within days or weeks? Understanding the neurophysiology of memory can help to elucidate the difference between these two scenarios. Autobiographical memory (AM) has received a great deal of attention over the past decade. Many believe AM to be uniquely human, allowing us to maintain a sense of self, as well as to simulate and predict future events (Schacter et al., 2007). More specifically, AM is a complex phenomenon, dependent on the delicate interaction of episodic memory for “what,” “where,” and “when”, semantic memory for factual knowledge, visual imagery, emotion, self-reflection, mental

time travel, and executive control functions (Cabeza & St. Jacques, 2007; Conway & Pleydell-Pearce, 2000), which collectively provoke the subjective perception of re-experiencing a past event (Conway, 2009). Clinically, AM abnormalities have been implicated early in neurodegenerative processes such as Alzheimer's disease and related geriatric cognitive disorders (Addis et al., 2009). As such, neuroscientists have attempted to elucidate the brain networks that support AM, with the motivation that a more thorough knowledge of AM would have broad relevance for understanding human brain function, and could translate to the clinic where memory disorders comprise a growing public health concern.

The majority of neuroimaging studies investigating AM suggest a large core brain network, involving hippocampus, parahippocampal gyrus, medial and ventrolateral prefrontal cortex, precuneus, retrosplenial and posterior cingulate cortices, lateral temporal cortex, and temporo-parietal junction (Cabeza & St. Jacques, 2007; Schacter et al., 2007). Additionally, the amygdala and sensory-perceptual areas, such as occipital cortex, are recruited during AM encoding and retrieval (Cabeza & St. Jacques, 2007; Maguire, 2001; Svoboda et al., 2006), but the significance of these additional structures to the core network has been debated (Markowitsch, 1992; Markowitsch & Staniloiu, 2011; Svoboda et al., 2006). Previous behavioral and neuroimaging investigations of AM have been performed over a range of individuals with normal or reduced AM performance. However, limited information is available regarding individuals with elevated AM performance. In fact, there has been only one case report in the literature of an individual with near-perfect AM, otherwise described as autobiographical hypermnesia or *hyperthymesia* (Parker et al., 2006). Parker et al. describe a female, AJ, in her 40s whose perfect AM dominates her life. AJ spends excessive amounts of time reliving past events with great detail and accuracy. Although there has been great media attention surrounding AJ, and possibly others with perfect autobiographical memory, there has been very little investigation into the structural and functional differences in the brains individuals with hyperthymesia relative to normals. Indeed, such a detailed examination of structural and functional brain differences may help to elucidate the underpinnings of healthy AM, and perhaps have relevance in translational studies by providing possible targets for therapy in patients with memory disorders.

Here, we performed intellectual, cognitive, and neuroimaging studies with HK, a 20-year old man with autobiographical hypermnesia. Aside from being only the second case reported in the scientific literature, HK's medical history makes the study of his superior AM unique. He was born prematurely at 27 weeks and suffered retinopathy of prematurity (ROP), resulting in complete blindness. Although visual imagery is thought to be at the core of autobiographical re-experiencing, patients born blind are believed to show relatively little differences in the quality or detail of their autobiographical memories (Eardley & Pring, 2006). To understand the underpinnings of HK's superior AM, we undertook three phases of investigation. First, HK underwent an extensive battery of intellectual and memory testing to understand the uniqueness of his AM performance relative to other cognitive functions. Second, to understand the accuracy of HK's AM, we queried at least four unremarkable dates from each year of his life. Events, which were multiple for any given date, were verified through diaries kept by HK's grandmother, interview with his family, electronic medical records at Vanderbilt University Hospital, and the Internet. We also developed an autobiographical memory interview based on previous work in the field to understand the episodic and semantic contributions to his AM, as well as a structured interview to understand HK's subjective experience of AM retrieval. Finally, to understand the anatomical and hemodynamic substrates underlying his AM, HK and healthy volunteers underwent structural and function connectivity neuroimaging analysis. To our knowledge, this is the first report of such a broad cognitive and neuroimaging examination of an

individual with superior AM, and the results of this investigation provide novel insight into the mechanistic origins of memory in humans.

2. Methods

2.1 Intellectual and Memory Assessment

To assess IQ/Intellect in HK, subtests that do not require vision from Wechsler Adult Intelligence Scales – IV were administered over one 2-hour session. Approximately one week later, the Wechsler Memory Scales – IV and California Verbal Learning Test – II were administered over one 2-hour session to assess HK's memory. Results were compared with well-known normative scores for these tests in age and sex-matched cohorts (Delis et al., 2000; Wechsler, 2008).

2.2 Autobiographical Memory Assessment

The AM assessment was broken into three parts. First, we collected at least four dates from every year of HK's life since his first memory in 1993. For each date, we gathered at least three facts from HK's family, medical records, and historical facts regarding the Nashville area, where HK resided. The entire interview consisted of 80 dates spanning two separate sessions, 10 of which were repeated across sessions to help assess consistency in HK's AM. Percent correct was calculated by dividing the total number of correct facts given by HK by the total number of facts for each event. Second, to assess the semantic and episodic contributions to his AM, we developed a semi-structured questionnaire based on the Autobiographical Memory Interview (AMI; Kopelman et al., 1990; Levine et al., 2002) and the Test Episodique de Mémoire du Passé autobiographique (TEMPau; Piolino et al., 2003). We selected three time periods, consisting of six-year blocks, beginning from the age of three (3–8, 9–14, 15–20). Cues were general events that had occurred in HK's life. For example, for the Adolescent time period, one of the cues was, "Tell me about an event that involved sports and your grandmother between in the ages of 9 and 14." HK's responses were recorded, transcribed, and scored for semantic and episodic details using previously established criteria (Levine et al., 2002). Finally, we administered a structured interview to understand HK's subjective experience of his AMs. For examples of questions and responses for each of the AM interviews, see Appendix.

2.3 Magnetic resonance imaging (MRI)

In addition to the above cognitive testing, we performed structural and functional MRI on HK and a group of age and sex-matched controls. All volunteers provided informed, written consent and were scanned at 3.0T (Philips Medical Systems, Best, The Netherlands) using volume body coil transmission and phased-array (8-channel) head coil reception.

2.3.1 Structural imaging—Standard T₁-weighted structural imaging (3D turbo gradient echo; 1×1×1 mm³; TR=9.1/TE=4.6 ms) was performed in both HK as well as a cohort (n=30) of approximately age-matched (29 ± 4 years) healthy male volunteers. Additionally, T₂-weighted (2D turbo spin echo; 0.5×0.5×4 mm³; TR=3000/TE=80 ms) and T₂-weighted FLuid Attenuated Inversion Recovery, FLAIR (turbo inversion recovery; 1×1×5mm³; TR=9000/TE=120 ms), sequences were performed on HK for pathology classification.

2.3.2 Functional connectivity imaging—HK, as well as a sub-group of the control volunteers (n=10; age=29 ± 5 years) were scanned using a baseline blood oxygenation level-dependent, BOLD (gradient echo; 3×3×4 mm³; TR/TE=3000/35 ms; 120 time points), approach. Volunteers were instructed to lie in the scanner awake, with their eyes closed. These data were acquired with the intent of assessing functional connectivity within and

between cortical and subcortical structures. Owing to HK being born blind, and the corresponding difficulty in performing memory encoding tasks in the scanner, for this study memory encoding tasks were not specifically performed.

2.4 Analysis

2.4.1 Volumetric analysis—Total gray matter (GM), white matter (WM) and cerebrospinal fluid (CSF) volume were quantified in mL from T₁-weighted structural scans using a hidden Markov random field model and an associated Expectation-Maximization algorithm (Zhang et al., 2001) and routines provided by the Oxford Functional MRI of the Brain (FMRIB) software library (FSL). Additionally, the volume of subcortical structures believed to have relevance to memory networks, including hippocampus, amygdala, thalamus, caudate, putamen and palladium, were quantified separately in left and right hemispheres using model-based segmentation algorithms available within the FMRIB integrated registration and segmentation tool, FIRST (Patenaude et al., 2011). For intersubject comparison, subcortical volumes were normalized by total intracranial tissue volume to reduce bias from head size discrepancies. Finally, vertex analyses (Patenaude et al., 2011) were performed to identify the spatial locations of volumetric differences between HK's subcortical structures and controls.

2.4.2 Functional connectivity imaging—BOLD data were corrected for motion, baseline drift, and co-registered to a standard space brain atlas (Montreal Neurological Institute atlas; 2 mm). Seven known network hubs (Tomasi & Volkow, 2010) comprising PCVP, inferior parietal, cuneus, postcentral cortex, cerebellum, thalamus, and amygdala were detected on an individual subject basis using a seed voxel analysis (Table 2; seed voxel coordinates). Voxel-wise t-scores, describing the extent to which a given voxel time course significantly correlates with the seed voxel time course, were calculated. A composite map was created by summing the t-scores from all subject-specific maps and thresholding at the 99% confidence interval (robust range). This mask was then applied to all volunteer data and t-values were recorded within the mask for each volunteer, thereby giving a measure of intranetwork connectivity. Next, connectivity, measured as t-score, between each voxel and the functional hub seed voxel were determined. Voxels in which the t-score of HK's map was more than four standard deviations from the mean control t-score map value were defined as significant. Therefore, connectivity within major functional hubs as well as between the functional hubs and all voxels were determined.

2.5 Case study considerations

The exceptional nature of HK's memory clearly warrants a thorough investigation of any possible unique brain anatomy and/or neurophysiology. However, the unique nature of HK is such that AM characterization must be accomplished within the limitations of a case study, as it is not possible to perform group-level comparisons owing to the small number of individuals with hyperthymesia. Therefore, extreme care must be taken to ensure identical scanner hardware and gradient configuration, pulse sequence parameters, and co-registration performance when evaluating changes between a single volunteer and a control group. The former two requirements were ensured by scanning all volunteers on the same scanner and software version (Rel. 2.6.3.4). For co-registration, 12-parameter affine transformations were used and care was taken, through both detailed visual inspection and ensuring similar cost and similarity function values for HK and controls, to ensure that co-registration of HK's structural and low-resolution gradient echo data were of comparable quality as the control data.

3. Results

3.1 Intellectual and Memory Assessment

Table 1 demonstrates that HK performed within the average range of intelligence. On the Wechsler Adult Intelligence Scales – Fourth Edition, his Verbal Comprehension Index Score was 97 and his Working Memory Index Score was 95 (mean = 100, standard deviation = 15). He also performed in the average range on measures of episodic memory. On the Wechsler Memory Scales – Fourth Edition, HK performed within ± 0.5 standard deviations from the group mean on the Auditory Memory, Immediate Memory, and Delayed Memory Indices. He was also within ± 0.5 standard deviations on all measures of the California Verbal Learning Test – II. For intellectual and memory performance data, please see Table 1.

3.2 Autobiographical Memory Assessment

The AM assessment was broken into three parts to examine the development, accuracy, and quality of HK's AMs. HK reported his first autobiographical recollection to be from December 17th, 1993, when at the age of 3.5 years, his father put him in a red satchel and carried him around the house like Santa Claus. As can be seen in Figure 1, for dates between this first memory until his tenth year of life, HK shows a relatively steady increase in accuracy for autobiographical events. Accuracy takes a noticeable jump to near 90% in 2001 at age 11. From that point forward, HK's recollection of autobiographical events is near perfect. Additionally, 10 dates were re-queried in a second session. HK's answers were extremely similar for these dates across sessions, with no missed events or content, placing his consistency across a month-long delay at 100%. Related to the development and quality of HK's AMs, we developed a semi-structured questionnaire based on the AMI (Kopelman et al., 1990; Levine et al., 2002) and the TEMPau (Piolino et al., 2003). Three time periods of HK's life were explored: 3 to 8 years old (childhood), 9 to 14 years old (adolescence), and 15 to 20 years old (recent). Results, using previously established scoring criteria to examine the contribution of semantic and episodic information (Levine et al., 2002) to HK's AM, reveal a significant increase in episodic details for the adolescent and recent AMs compared to the childhood AMs (see Figure 2). It should be noted here that in addition to semantic-based memories from his childhood years, there is likely contamination from external sources (e.g., family member rehearsing memories). For example, although HK could perceive light and some color information in his right eye very early in his life, it is likely that the description of the satchel as "red" in his first memory was gathered from an external source while rehearsing with family members. This type of contamination has been referred to as *suggestibility* (Schacter, 1999), and is common in children where the actual memory is accurate, but embellishment has been provided due to suggestibility (see Ceci, 1995 for review).

In addition to the objective measure of the quality of HK's AMs, we also developed an interview to understand HK's subjective experience of his AMs. He reports that he is able to relive memories in his mind as if they just happened. HK stated that everything about his memory, including sounds, smells, and emotions, are vividly re-experienced when he remembers a particular event in time, and he described his AMs as being in the first person approximately 90% of the time. He stated that there is no difference in the vividness of his recollection between events that occurred when he was five and events that he experienced within the past month. HK also reported that sounds, smells, emotions, and news events act as cues for his AM, triggering the retrieval of past events with similar contexts. He claims that he does not dwell on his memories, but it becomes part of his daily routine to wake up and think about that particular date in his own history. HK reported that he cannot stop AMs from coming into consciousness, and bad memories are recalled just as often as good

memories. However, HK stated that he can stop thinking about his memory at any given time, and he tends to focus on only the positive memories. For examples of questions and responses for each of the AM interviews, see Appendix.

3.3 Magnetic resonance imaging (MRI)

The results of the neuroimaging studies reveal a pattern of structural and functional connectivity uniqueness that likely contributes to HK's heightened AM. Figure 3 shows a subsample of slices from the structural scanning of HK; the colored arrows show regions of pathology, presenting primarily as white matter pathology and damage to the optic radiations as a result of his prematurity. A more detailed volumetric analysis (Figure 4) reveals significantly reduced total tissue volume in HK (1019 mL) relative to controls (1249 ± 29 mL). Additionally, a volumetric analysis of subcortical structures shows general reduction in subcortical volumes, with the noted exception of the right amygdala, which is fractionally larger ($18 \pm 6\%$) than the control volume. This finding is for an approximately age-matched ($n=30$; age= 29 ± 4 yrs) cohort of male volunteers, however we found this trend to be preserved when structural data from a larger ($n=74$) mixed-sex cohort was analyzed as well (right amygdala fractional increase = $15 \pm 5\%$). Volume renderings of the amygdala are shown in Figure 4c.

Table 2 shows the seven hubs used for functional connectivity analysis, which include both cortical and subcortical networks, and were selected for analysis based on the robust presence of these networks in functional connectivity density mapping procedures (Tomasi & Volkow, 2010). The seed voxel coordinates used for map generation (Figure 5) are displayed, as well as the functional connectivity, reported as t-score, for the control population and HK. Notice that the postcentral and thalamic networks have increased connectivity in HK, which may be attributed to heightened somatosensory awareness concurrent to blindness (Shu et al., 2009). Alternatively, the posterior cingulate/ventral precuneus (PCVP) network, which is comprised of regions that constitute the default mode network (DMN), was reduced in HK relative to controls.

To further understand the amygdala volumetric finding and any potential unique functional role of the amygdala in HK, we investigated functional connectivity between the amygdala and other brain structures. Figure 6 shows the regions where the connectivity between the amygdala network hub is significantly increased in HK relative to the control population. Notice that the connectivity is most different in the right hippocampus, as well to a lesser extent in more distal white matter regions.

4. Discussion

A detailed examination of AM performance in an individual with hyperthymesia, as well as structural, functional, and metabolic neuroimaging has helped to possibly elucidate underpinnings of heightened AM. With respect to the development of AM, HK demonstrated an increase in both accuracy and episodic detail during the transition from childhood to adolescence. Specifically, from the period of 9 to 12 years of age, we observed a sharp increase in the accuracy of HK's AMs, as well as an increase in episodic details compared to semantic details in his AMs for the 9 to 14 year adolescent time period. These findings are generally consistent with work examining the development of AM. Specifically, while evidence suggests that children as young as three exhibit a capacity for episodic memory, they tend to only recollect semantic fact-stating narratives from their pasts (Fivush, 2011; Nelson & Fivush, 2004). It has been speculated that the mental time-travel aspect of AM does not develop until around the age of 11 (Piolino et al., 2007), and that autobiographical recollections from children this age struggle to meet criteria for true AM (Fivush, 2011). Supporting this hypothesis, others have found that not until the age of 12 can

children link events in their life to an accurate autobiographical timeline (Habermas & de Silveira, 2008). In fact, eight-year-old children are slightly above chance at accurately judging the order of the events that occurred more than a few months in the past (Friedman, 2003). These behavioral findings are also consistent with neuroimaging work revealing that brain regions associated with the AM network lack functional connectivity until seven to nine years of age (Fair et al., 2008). Further, DMN, which heavily overlaps with the AM network, has been reported not to fully develop until nine to 12 years of age (Thomason et al., 2008).

The development of HK's AM is also very similar to that of AJ, the first individual with autobiographical hypermnesia presented in the literature (Parker et al., 2006). AJ reported her first memory as being from when she was 18 to 24 months in age, and she vividly remembers autobiographical details from late in her 3rd year of life. AJ recalls that her memory "changed" at the age of eight, when she was traumatized by the move of her family. At this point, she began organizing and recording her memories, and stated that she constantly forced herself to relive her experiences. AJ first became aware of her superior memory around the age of 12. She can recall most, but not all days between the ages of 8 and 13. For events at the age of 14 and beyond, her AM is almost automatic (Parker et al., 2006). Similarly, HK can vividly remember events as early as three years of age, and reports first becoming aware of his superior memory at age 11, with near automaticity by the age of 14.

Cognitive neuroscientists report structural and connectivity changes associated with brain development may be responsible for changes in AM performance (Bauer et al., 2007). Longitudinal studies suggest a steady increase in cortical gray matter volume in memory-related areas until approximately the age of 16 (Giedd et al., 1999). Limbic subcortical areas also show developmental growth (albeit much slower), with recent work suggesting a sharp increase in amygdalar volume between the ages of 11 and 13 associated with increased testosterone during puberty (Neufang et al., 2009). This time period is highly consistent with when a noticeable jump in HK's AM accuracy was observed. Researchers also highlight a dramatic increase in white matter volume and connectivity, particularly to and from memory-related limbic areas, during the first 10 years of life (Pfefferbaum et al., 1994). Two findings from the current neuroimaging study stand out with respect to the structure and functional connectivity within the AM network. First, HK's right amygdala is significantly larger in volume compared to control subjects. Second, the functional connectivity between the amygdala and hippocampus, as well as distal cortical and subcortical regions in HK, is significantly increased compared to controls (greater than 10 standard deviations above control group mean).

Although there has been debate as to whether the amygdala falls in the AM core network (Markowitsch, 1992; Markowitsch & Staniloiu, 2011; Svoboda et al., 2006), recent work has certainly highlighted the importance of the amygdala to *encoding* AMs (Greenberg et al., 2005; Spreng & Mar, 2010). Most recently, it has been shown that amygdala activity at encoding predicts the subjective vividness of an episodic memory, regardless of its emotional valence or arousal (Kensington et al., 2011; Phelps & Sharcot, 2008), leading to the hypothesis that the amygdala is critical in relaying biological and social significance to AM (Markowitsch & Staniloiu, 2011). Indeed, it has been proposed that the subjective sense of remembering invariably involves an emotional re-experiencing of an event (Rubin & Berntsen, 2003; Welzer & Markowitsch, 2005), and this emotional aspect serves as the foundation for episodic AMs (Piolino et al., 2009). Further, emotionally benign information may be processed in an affective manner due to its self-relevance (Markowitsch & Staniloiu, 2011; Rameson et al., 2010). Consequently, it has been posited that the amygdala acts as the hub for processing sensory information of biological, social, and self-importance for

encoding and subsequent storage in neocortical areas (Markowitsch & Staniloiu, 2011). It is likely that the enhanced functional connectivity between amygdala and hippocampus in HK allows for information to be easily processed as self-relevant and bundled by amygdala-hippocampal interaction for encoding and storage.

The interactions of amygdala and cortical areas has been highlighted by studies of functional connectivity, which show that the amygdala is connected to nearly 90% of all cortical areas (Cole et al., 2010; Young et al., 1994), making it an excellent candidate for increasing the likelihood that memories are properly stored and *retrieved* (Ritchey et al., 2008). Indeed, right amygdala-hippocampal connectivity to medial prefrontal regions has been shown to support memory encoding of high self-relevance or self-involvement (Muscatell et al., 2010). Moreover, in a study comparing the retrieval of true AMs and the retrieval of fictitious episodes, the right amygdala was activated when retrieving the true AMs, whereas the retrosplenial/precuneus area was activated during the retrieval of the fictitious episodes (Markowitsch et al., 2000). This right lateralized effect has also been seen in the retrieval of *field memories*, or memories experienced in the first person (Eich et al., 2009). Similarly, HK, whose right amygdala is enlarged compared to controls, reports that approximately 90% of his AMs are experienced in the first person. This is in comparison to the general population, who report approximately 66% of AMs being in the first person (Sutin & Robins, 2008). It has been argued that the increase in right amygdala activity during first person retrieval perspective reflects the higher degree of subjective emotionality (Eich et al., 2009).

Of course, changes in structure and function of amygdala have also been linked to other pathologic changes in memory. For example, amygdalar volumes are increased in individuals who are exposed to chronic stress due to posttraumatic stress disorder (PTSD) (Roosendaal et al., 2009), and right amygdala over-activation has been implicated in the retrieval of traumatic memories in these patients (Driessen et al., 2004). Memories associated with PTSD are persistent and commonly rehearsed by these individuals, despite their desire to end the rumination. It has been proposed that hypermnnesia, particularly for emotional events, may be amygdala-dependent and varies as a function of noradrenergic-glucocorticoid input into the amygdala (Hurlemann et al., 2005). In contrast, individuals with right medial temporal lobectomies produced fewer emotional AMs compared to individuals with left medial temporal lobectomies (Buchanan et al., 2005). These studies provide further evidence that the amygdala is critically involved in encoding and retrieval of AMs, but our understanding of the mechanism of such retrieval is relatively limited.

While HK's structural and connectivity results may enhance our understanding of superior AM, we would be remiss to not acknowledge his unique situation and inherent limitations of the current study. HK's occipital regions are highly active and well connected during rest, and studies of blind individuals have shown recruitment of occipital areas on tasks of episodic memory (Raz et al., 2005). Though there have been few studies of AM in the blind, recent literature suggests that blind participants demonstrated no differences in memory specificity compared to sighted individuals, even if the retrieval cue is dependent on visual imagery (Eardley & Pring, 2006). Future work could potentially recruit born blind individuals with normal AM to compare HK's structural and functional differences compared to this control group. We also acknowledge that unique case studies such as HK are not easily translated or generalizable to the normal population. The current results should be interpreted with caution, but continue to provide evidence that the amygdala is heavily involved in autobiographical memory. Further, perhaps the present findings can help to guide future regions of brain stimulation in memory-disordered populations, with the goal of improving memory function. Indeed, brain stimulation to deep, subcortical memory-related structures has shown very early promise in patients with AD (Laxton et al., 2010).

In conclusion, we provided a detailed examination of AM performance as well as structural and functional neuroimaging in an individual with hyperthymesia with the motivation of elucidating the mechanistic origins of AM. The behavioral data show an increase in accuracy and episodic contribution associated with AM, paralleling the course of AM development proposed in normal individuals. However, there was a sharp increase in accuracy and the number of episodic details associated with the transition from childhood to adolescence, which could indicate the time interval associated with pathologic developmental changes related to brain structure and physiology. The neuroimaging data reveal HK's right amygdala to be nearly 20% fractionally larger than normals, in the face of significantly reduced gray and white matter volumes. Additionally, HK has significantly increased connectivity between his right amygdala and hippocampus, as well as distal cortical and subcortical regions. We posit that the amygdala, particularly the right amygdala, plays a vital role in AM encoding and retrieval, likely by charging AMs with emotion or social and self-relevance (Markowitsch & Staniloiu, 2011). We further speculate that in HK, this system is hyperactive, resulting in emotionally benign information being processed in a self-relevant affective manner (Rameson et al. 2010). While the results of this unique case study do not provide direct evidence for the underpinnings of normal memory function, the present investigation provides significant support for previous hypotheses as to the role of the amygdala in autobiographical memory performance as well as provides the basis of potential future targeted therapies for patients with memory disorders.

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References

- Addis DR, Sacchetti D, Ally BA, Schacter DL, Budson AE. Episodic simulation of future events is impaired in mild Alzheimer's disease. *Neuropsychologia*. 2009; 47:2660–2671. [PubMed: 19497331]
- Bauer PJ, Burch MM, Scholin SE, Guler OE. Using cue words to inform the distribution of autobiographical memories in childhood. *Psychol Sci*. 2007; 18:910–916. [PubMed: 17894609]
- Buchanan TW, Tranel D, Adolphs R. Emotional autobiographical memories in amnesic patients with medial temporal lobe damage. *Journal of Neuroscience*. 25:3151–3160. [PubMed: 15788772]
- Cabeza R, St Jacques P. Functional neuroimaging of autobiographical memory. *Trends in Cognitive Sciences*. 2007; 11:219–227. [PubMed: 17382578]
- Ceci, SJ. False beliefs: Some development and clinical considerations. In: Schacter, DL., editor. *Memory distortion: How minds, brains, and societies reconstruct the past*. Cambridge, MA: Harvard University Press; 1995. p. 91-128.
- Cole MW, Pathak S, Schneider W. Identifying the brain's most globally connected regions. *NeuroImage*. 2010; 49:3132–3148. [PubMed: 19909818]
- Conway MA. Episodic memories. *Neuropsychologia*. 2009; 47:2305–13. [PubMed: 19524094]
- Conway MA, Pleydell-Pearce CW. The construction of autobiographical memories in the self-memory system. *Psychol Rev*. 2000; 107:261–88. [PubMed: 10789197]
- Delis, DC.; Kramer, JH.; Kaplan, E.; Ober, BA. *California Verbal Learning Test*. 2. San Antonio, TX: Pearson Publishing; 2000.

- Driessen M, et al. Different fMRI activation patterns of traumatic memory in borderline personality disorder with and without additional posttraumatic stress disorder. *Biological Psychiatry*. 2004; 55:603–611. [PubMed: 15013829]
- Eardley AF, Pring L. Remembering the past and imagining the future: A role for nonvisual imagery in the everyday cognition of blind and sighted people. *Memory*. 2006; 14:925–936. [PubMed: 17077028]
- Eich E, Nelson AL, Leghari MD, Handy TC. Neural systems mediating field and observer memories. *Neuropsychologia*. 2009; 47:2239–2251. [PubMed: 19524090]
- Fair DA, Cohen AL, Dosenbach NUF, Church JA, Miezin FM, Barch DM, Raichle ME, Petersen SE, Schlaggar BL. The maturing architecture of the brain's default network. *Proc Natl Acad Sci U S A*. 2008; 105:4028–4032. [PubMed: 18322013]
- Fivush R. The development of autobiographical memory. *Annu Rev Psychol*. 2011; 62:559–582. [PubMed: 20636128]
- Friedman WJ. The development of a differentiated sense of the past and the future. *Adv Child Dev Behav*. 2003; 31:229–269. [PubMed: 14528663]
- Giedd JN, Blumenthal J, Jeffries NO, Castellanos DX, Liu H, Zijdenbos A, Paus T, Evans AC, Rapoport JL. Brain development during childhood and adolescence: a longitudinal MRI study. *Nature Neuroscience*. 1999; 2:861–863.
- Greenberg DL, Rice JJ, Cabeza R, Rubin DC, Labar KS. Co-activation of the amygdala, hippocampus, and inferior frontal gyrus during autobiographical memory retrieval. *Neuropsychologia*. 2005; 43:659–674. [PubMed: 15721179]
- Habermas T, de Silveira C. The development of global coherence in life narratives across adolescence: temporal, causal, and thematic aspects. *Dev Psychol*. 2008; 44:707–721. [PubMed: 18473638]
- Hurlmann R, et al. Noradrenergic modulation of emotion-induced forgetting and remembering. *Journal of Neuroscience*. 2005; 25:6343–6349. [PubMed: 16000624]
- Kensinger EA, Addis DR, Atapattu RK. Amygdala activity at encoding corresponds with memory vividness and with memory for select episodic details. *Neuropsychologia*. 2011; 49:663–673. [PubMed: 21262244]
- Kopelman, MD.; Wilson, AE.; Baddeley, A. *The Autobiographical Memory Interview*. Thames Valley Test Co; Bury St. Edmunds: 1990.
- Laxton AW, Tang-Wai DF, McAndrews MP, Zumsteg D, Wennberg R, Keren R, et al. A phase I trial of deep brain stimulation of memory circuits in Alzheimer's disease. *Annals of Neurology*. 2010; 68:521–534. [PubMed: 20687206]
- Levine B, Svoboda E, Hay JF, Winocur G, Moscovitch M. Aging and autobiographical memory: dissociating episodic from semantic retrieval. *Psychol Aging*. 2002; 17:677–689. [PubMed: 12507363]
- Maguire EA. Neuroimaging studies of autobiographical event memory. *Philos Trans R Soc Lond B Biol Sci*. 2001; 356:1441–51. [PubMed: 11571035]
- Markowitsch, HJ. *An historical perspective*. Hogrefe & Huber Publishing; Toronto, ON, CA: 1992. Intellectual functions and the brain.
- Markowitsch HJ, Thiel A, Reinkemeier M, Kessler J, Koyuncu A, Heiss WD. Right amygdala and temporofrontal activation during autobiographic, but not during fictitious memory retrieval. *Behavioural Neurology*. 2000; 12:181–190. [PubMed: 11568430]
- Markowitsch HJ, Staniloiu A. Amygdala in action: Relaying biological and social significance to autobiographic memory. *Neuropsychologia*. 2011; 49:718–733. [PubMed: 20933525]
- Muscatell KA, Addis DR, Kensinger EA. Self-involvement modulates the effective connectivity of the autobiographical memory network. *Social, Cognitive and Affective Neuroscience*. 2010; 5:68–76. [PubMed: 20007242]
- Nelson K, Fivush R. The emergence of autobiographical memory: A social cultural developmental theory. *Psychological Review*. 2004; 111:486–511. [PubMed: 15065919]
- Neufang S, Specht K, Hausmann M, Gunturkun O, Herpertz-Dahlmann B, Fink GR, Konrad K. Sex differences and the impact of steroid hormones on the developing human brain. *Cereb Cortex*. 2009; 19:464–473. [PubMed: 18550597]

- Parker ES, Cahill L, McGaugh JL. A case of unusual autobiographical remembering. *Neurocase*. 2006; 12:35–49. [PubMed: 16517514]
- Patenaude B, Smith SM, Kennedy DN, Jenkinson MA. Bayesian model of shape and appearance for subcortical brain segmentation. *Neuroimage*. 2011; 56:907–922. [PubMed: 21352927]
- Pfefferbaum A, Mathalon DH, Sullivan EV, Rawles JM, Zipursky RB, Lim KO. A quantitative magnetic resonance imaging study of changes in brain morphology from infancy to late adulthood. *Arch Neurol*. 1994; 51:874–887. [PubMed: 8080387]
- Phelps EA, Sharot T. How (and why) emotion enhances the subjective sense of recollection. *Current Directions in Psychological Science*. 2008; 17:147–152. [PubMed: 21399743]
- Polino P, Belliard S, Desgranges B, Perron M, Eustache F. Autobiographical memory and auto-noetic consciousness in a case of semantic dementia. *Cognitive Neuropsychology*. 2003; 20:619–639. [PubMed: 20957587]
- Polino P, Desgranges B, Eustache F. Episodic autobiographical memories over the course of time: Cognitive, neuropsychological and neuroimaging findings. *Neuropsychologia*. 2009; 47:2314–2329. [PubMed: 19524095]
- Polino P, Hisland M, Ruffevelle I, Matuszewski V, Jambaque I, Eustache F. Do school-age children remember or know the personal past? *Consciousness and Cognition*. 2007; 16:84–101. [PubMed: 16464615]
- Rameson LT, Satpute AB, Lieberman MD. The neural correlates of implicit and explicit self-relevant processing. *NeuroImage*. 2010; 50:701–708. [PubMed: 20045472]
- Raz N, Amedi A, Zohary E. V1 activation in congenitally blind humans is associated with episodic retrieval. *Cereb Cortex*. 2005; 15:1459–1468. [PubMed: 15647525]
- Ritchey M, Dolcos F, Cabeza R. Role of amygdala connectivity in the persistence of emotional memories over time: An event-related fMRI investigation. *Cerebral Cortex*. 2008; 18:2494–2504. [PubMed: 18375529]
- Roosendaal B, McEwen BS, Chattarji S. Stress, memory and the amygdala. *Nature Reviews Neuroscience*. 2009; 10:423–433.
- Rubin DC, Berntsen D. Life scripts help to maintain autobiographical memories of highly positive, but not highly negative, events. *Memory and Cognition*. 2003; 31:1–14.
- Schacter DL. The seven sins of memory. Insights from psychology and cognitive neuroscience. *The American Psychologist*. 1999; 54:182–203. [PubMed: 10199218]
- Schacter DL, Addis DR, Buckner RL. Remembering the past to imagine the future: the prospective brain. *Nat Rev Neurosci*. 2007; 8:657–661. [PubMed: 17700624]
- Shu N, Liu Y, Yonghui L, Chunshui Y, Jiang T. Altered anatomical network in early blindness revealed by diffusion tensor tractography. *PLoS One*. 2009; 4:e7228. [PubMed: 19784379]
- Spreng RN, Mar RA. I remember you: A role for memory in social cognition and the functional neuroanatomy of their interaction. *Brain Research*. (in press). 10.1016/j.brainres.2010.12.024
- Sutin AR, Robins RW. When the “I” looks at the “me”. Autobiographical memory, visual perspective, and the self. *Consciousness and Cognition*. 2008; 17:1386–1397. [PubMed: 18848783]
- Svoboda E, McKinnon MC, Levine B. The functional neuroanatomy of autobiographical memory: a meta-analysis. *Neuropsychologia*. 2006; 44:2189–2208. [PubMed: 16806314]
- Thomason ME, Chang CE, Glover GH, Gabrieli JDE, Greicius MD, Gotlib IH. Default-mode function and task-induced deactivation have overlapping brain substrates in children. *Neuroimage*. 2008; 41:1493–1503. [PubMed: 18482851]
- Tomasi D, Volkow ND. Association between functional connectivity hubs and brain networks. *Cerebral Cortex*. Mar 21.2011 (in press). 10.1002/hbm.21252
- Wechsler, D. Wechsler Adult Intelligence Scales. 4. San Antonio, TX: Pearson Publishing; 2008.
- Welzer H, Markowitsch HJ. Towards a bio-psycho-social model of autobiographical memory. *Memory*. 2005; 13:63–78. [PubMed: 15724908]
- Young MP, Scannell JW, Burns GA, Blakemore C. Analysis of connectivity: neural systems in the cerebral cortex. *Rev Neurosci*. 1994; 5:227–250. [PubMed: 7889215]

Zhang Y, Brady M, Smith S. Segmentation of brain MR images through a hiddenMarkov random field model and the expectation-maximization algorithm. *IEEE Trans Med Imaging*. 2001; 20:45–57. [PubMed: 11293691]

Appendix

A) From the Dates in History Autobiographical Questionnaire

Examiner: *"Can you tell me what happened during your day on January 2nd, 2001?"* **HK:** "Laughs. I got up around 10:15 that morning, my grandmother cut my hair, we got dressed, and my grandmother went to work. She had the 4–8 shift that night. But Mr. James Biddeford, my friend and mentor, picked me up and we went to the Jeff Fisher show. Jeff Fisher had a two-hour show a couple of days, 5 days I think, before the Titans played the Baltimore Ravens in the playoffs. The Titans ended up getting beat 24-10. I got to sit in Jeff Fisher's lap and I had my picture taken with him. I also got an autograph from Frank Wycheck and I met Dwight Lewis. Dwight Lewis is was a columnist for the Tennessean. We ended up eating dinner there, at Applebee's. James' wife, Bridgette, had to leave early because she was expecting a call from Julia, her daughter. Around 8:00 everyone left, and then we went back to the house to meet my grandmother. She and I watched the nightly news, I listened to Sean Hannity on talk radio, and I ended up going to bed around 10:00 pm. It was an exciting day."

Examiner: *"Can you tell me what happened during your day on March 19th, 2003?"* **HK:** "Oh, that's when the war in Iraq started. I had spent the night at the Tennessee School for the Blind the night before, in the cottage. That was a Wednesday night. After my grandmother picked me up from school, we had dinner at home. Spinach Alfredo and noodles. After dinner, I was watching Star Search on Channel 5. At around 8:45 pm they broke in and said that US troops were shooting in target houses thinking Saddam Hussein might have been in there. Three civilians ended up being killed that day, Iraqi civilians."

Examiner: *"Can you tell me what happened during your day on September 22nd, 2003?"* **HK:** "Well, nothing exciting happened that day. I went to school, then went to therapy at Vanderbilt. Ellen Diamano had me walking on the treadmill and working on my flexibility on this big ball all night. We ate dinner in the Vanderbilt Courtyard Café. I had spinach casserole. That night I watched Everybody Loves Raymond. I was excited because it was the first episode of the new season. I think it was the eighth season. I think there might have also been a report on the news of a suicide bomber in Baghdad. There was a car explosion near the UN. **Examiner:** *"Do you think you could tell me what happened on the episode of Everybody Loves Raymond?"* **HK:** "Yeah, Ray and Debra went golfing. So they could spend more time as a couple. They ended up getting in this big fight on the 13th green, and Ray accused Debra of coming just so she could ruin the only thing he loves to do. They end up making up and Debra admits that she hates golf and Ray can just do it alone or with his brother Robert."

Examiner: *"Can you tell me what happened during your day on February 5th, 2008?"* **HK:** "There were tornadoes that day in Macon and Sumner Counties, and we were under a watch in Nashville. During the storms, there was a natural gas explosion at a plant in Sumner County that night. I remember being at school. I was scared. We were in the closet under shelter for two periods of time. The first one was during school between 9:15 to 10:00 for the first tornado warning. Then we were up again in shelter at the cottage from 12:00 am to 3:00 am for the second tornado warning. The siren was screaming and I remember being really hot. It was also Super Tuesday in Tennessee. Mike Huckabee ended up winning the Republican Primary and Hillary Clinton won the Democratic Primary. I really wanted to

vote that day, but it was a couple months before my 18th birthday, so I couldn't. When my grandmother asked me what I wanted for my 18th birthday, I told her all I wanted was to vote!"

B) From the Autobiographical Memory Interview based on the TEMPau

Example response from a memory from Adolescence (9–14 years old):

Examiner: *"Tell me about a day involving sports from when you were between the ages of 9 and 14."*

HK: "Well, the first year I made it to the Junior Olympics was in 1999. It was Wednesday October 13th, and it was kind of warm in Kentucky for that time of the year, like 70 degrees. I ran the 60 meter dash and the standing long jump, where I basically jumped into this big sandpit, and I also threw the softball throw. I was so happy, I did really good. I was 2nd place in the 60 meters, 3rd place in the standing long jump, and 3rd place in the softball throw. A friend's dad brought me back to my school, where my grandmother and her friend Janey picked me up. My grandmother was so proud of me, she let us stop at McDonald's on the way back home. I had chicken nuggets with fries, and then we went straight home. We had to rush because Janey was leaving to go back to Florida the next day. I was tired and went straight to bed."

C) Structured Interview to understand HK's subjective AM experience

1) How do you remember dates and events that happened to you?

HK: "They just come into my mind. I can just picture it as if I was there again. Especially when anniversaries come around. That day of the anniversary, I just think back to what I was doing, what the weather was like, who I was with, and so-and-so. I just remember it."

2) Do you remember only things that interest you or do you seem to remember just about anything that happened on a particular date regardless of whether you are interested in it?

HK: "No, I remember everything that happens during my day. All of it is easy to remember. I feel like I am a walking computer sometimes. The information just gets stored in my brain. It can get distracting, but I can let it go too."

3) Do you ever think about bad things?

HK: I remember bad things too. I just don't dwell on the bad things. My grandmother has always taught me to focus on the positive, and that's what I do."

4) Do you think about memories that happened to you a lot?

HK: "Well, I think about them quite a bit. Especially if it is something that affects me. A lot of times, when someone mentions something to me, it triggers a memory. I like telling my grandmother what certain anniversaries are. Like I'll think about what we did 5 years ago. You know, she also takes me to her appointments so that I can help her to remember her stuff too (laughs)."

5) What percentage of the time do you think that you are thinking about your memories?

HK: "I'd say about 30 percent of the time. I've gotten better about it. I think when I was younger I used to do it more than now. It would get me in trouble in school."

6) When these events come to you mind, how do you experience them? Do you experience them as just a fact or do you actually feel like you are experiencing the event all over again?

HK: “Well, kind of both. I can remember all kinds of facts. But when I think about something from the past, and event or something, I fell like I am right back in that situation. There really is no difference in when it happened and when I remember it.”

7) When you are experiencing these memories, are you right back inside your own eyes, or are you maybe looking down on the scene.

HK: “I am usually experiencing it just like it happened, right through my own eyes. (laughs) Of course, I’m blind, so I don’t see it, but it feels like I am right back there. I can sort of see thing in my mind though.”

8) What percentage of time are you looking through your own eyes?

HK: “I would say 80 to 90 percent of the time. I do have the experience like I am another person seeing something else happen. Like I am sitting there reliving a memory outside of my body. But it is usually like I am there again.

9) If I were to ask you to remember something that happened when you were 5 or 6, does your memory experience differ from something that happened last month?

HK: “No. Really there is no difference.”

10) You know, there is another person that has perfect memory too. She says that sometimes she feels like there is two television sets in her head. One playing back memories, and one where she is in the present. Do you ever feel like this?

HK: “Yes, Jill Price. And I think there is some guy in Wisconsin or something. Yes, sometimes I feel like that. Mostly it is one or the other though.”

11) Some research has shown that maternal reminiscing or reliving about the past with their children influences memory. Did you ever relive your experiences with your grandmother when you were little?

HK: (laughs) “Funny you should ask that. When I was little, my grandmother would ask me every night in bed to tell her everything about my day. So every night, I would tell her everything from the time I woke up to the time that I was going to bed. It was our thing.”

12) You seem to get the day of the week right every time we ask you about a particular date in history. Do you ever use math to calculate what day of the week a certain date fell on or do you simply know it?

HK: “No, I just know it.”

13) You also seem to know the weather for a particular date. How is it that you can remember the weather so well?

HK: Well, that is the first thing I do when I wake up, listen to the weather on talk radio. I have always liked the weather. We actually used to watch the Weather Channel in science class. I always wanted to learn about weather.”

14) At what age did you start to realize that you could remember dates and events like you do?

HK: “About 10 years old. I remember I was sitting in my chair listening to sports radio and my grandmother asked me why I was smiling. I told her that 3 years earlier on that date, we went to the Brentwood Rotary Club and had breakfast with everyone. She looked it up on her calendar and I was right. I guess my memory started to get really good when I was 10, 11, or 12.”

15) Do things like smells or sounds ever trigger memories for you?

HK: “Oh yeah, they all do. Sounds, smells, even when I feel something or taste something it can bring back a memory of a similar time. The news really acts as a trigger for me.”

16) Do you collect anything?

HK: “Well, I guess I collect events and memories (laughs). I have had a collection of coins in the past.”

HK Autobiographical Memory Performance

Figure 1.

Accuracy of HK's autobiographical memory performance. Bars represent percent correct for autobiographical events. Numbers in parentheses report HK's age for the year above, starting at 3 years of age in 1993.

Figure 2.

Quality of HK's autobiographical memory performance. Bars represent the proportion of episodic details to the overall number of details for the three periods of HK's life.

Figure 3. Structural Neuroimaging. Representative slices from FLAIR, T2-weighted and T1-weighted structural MRI acquisitions in HK. Blindness is secondary to damage to the optic radiations (blue arrow). Cystic encephalomalacia is present in the left dorsal lateral thalamus (red arrow) and slight periventricular leukomalacia (yellow arrow) is observed. These findings are consistent with an individual born >10 weeks premature.

Figure 4.

Volumetric Analysis. Volumetric analysis reveals smaller cortical (a) and subcortical (b) volumes in HK. Subcortical fractional volumes are defined as structure volume normalized to total brain tissue volume. Notice the increased right amygdala fractional volume relative to all other subcortical structures analyzed. (c) Volume rendering (below) of statistical variation in amygdala volume inlaid on standard space brain atlas. The color bar describes the F-statistic for which HK's amygdala volume is larger than that of the control population. On right, the right amygdala rendering is shown (three views), with cooler colors describing regions of increased growth relative to the control population.

Figure 5.

Within-network functional connectivity. The seven functional network hubs analyzed, corresponding to (a) posterior cingulate/ventral precuneus (PCVP), (b) inferior parietal, (c) cuneus, (d) postcentral, (e) cerebellum, (f) thalamus, and (g) amygdala. The color bar represents the cumulative t-score distribution, thresholded at the 99 percentile robust range over all volunteers. All colored voxels shown were used for defining the network masks, and each mask was applied separately to each volunteer to assessing intranetwork functional connectivity within the specified network hub.

Figure 6. Functional connectivity from HK's right amygdala. Coronal and sagittal slices are shown above, as well as representative axial slices below. The color bar describes the number of standard deviations HK's t-scores vary from those of the control population. Notice the increased connectivity to the right hippocampus.

Table 1

Results of HK's Intellectual and Memory Testing

	IQ/Scaled Score	Percentile	SS
Verbal Comprehension Index	95	37	-0.33
Similarities	9	37	-0.33
Vocabulary	8	25	-0.67
Comprehension	10	50	0.00
Working Memory Index	97	42	-0.28
Digit Span	10	50	0.00
Arithmetic	9	37	-0.33
Letter-Number Sequencing	9	37	-0.33

	IQ/Scaled Score	Percentile	SS
Auditory Memory Index	102	55	+0.25
Logical Memory I	11	63	+0.33
Logical Memory II	11	63	+0.33
Verbal Paired Associates I	9	37	-0.33
Verbal Paired Associates II	11	63	+0.33
Immediate Memory Index	100	50	0.00
Delayed Memory Index	107	68	+0.45
California Verbal Learning Test-II	Raw Score	Percentile	SD
Trial 1 Free Recall	6/16	31	-0.5
Trial 2 Free Recall	9/16	31	-0.5
Trial 3 Free Recall	11/16	50	0.0
Trial 4 Free Recall	12/16	50	0.0
Trial 5 Free Recall	14/16	69	+0.5
Trail 1-5 Total Recall	52	58	+0.2
List B Free Recall	5/16	16	-1.0
Short Delay Free Recall	13/16	69	+0.5
Short Delay Cued Recall	14/16	84	+1.0
Long Delay Free Recall	13/16	50	0.0
Long Delay Cued Recall	14/16	69	+0.5
Long Delay Recognition	16/16	69	+0.5

HK's performance on the WAIS-IV intellectual testing. (mean Index score = 100, SD = 15; mean Scaled Score = 10, SD = 3)

HK's performance on the WMS-IV and the CVLT-II memory testing. (mean Index score = 100, SD = 15; mean Scaled Score = 10, SD = 3)

Voxel coordinates (MNI) used for seed voxel analysis in defining each of the separate network hubs, along with within network connectivity (t-scores) for controls and HK.

Table 2

	x	y	z	t-score _{Control}	t-score _{HK}
PCVP	4	-55	29	12.9 ± 1.7	8.8*
Inferior Parietal	-38	-57	39	11.0 ± 5.2	8.9
Cuneus	-24	-83	15	12.2 ± 7.9	9.2
Postcentral	20	-48	59	9.9 ± 6.6	50.1*
Cerebellum	-9	-56	-27	7.4 ± 2.4	10.0
Thalamus	-12	-20	8	8.0 ± 2.1	26.9*
Amygdala	24	-5	-18	14.8 ± 13.5	14.7

* Regions where HK's t-scores are significantly (> 2 standard deviations) different from those of controls.