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**EVALUATING AUTOBIOGRAPHICAL MEMORY IN
TEMPORAL LOBE EPILEPSY PATIENTS**

by

Tara Tamny-Young

A dissertation submitted to the Graduate Faculty in Psychology in partial fulfillment of the requirements for the degree of Doctor of Philosophy, The City University of New York.

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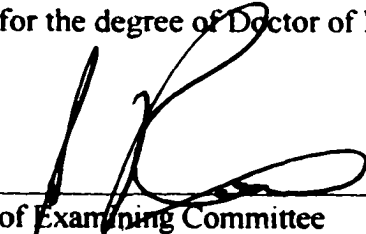
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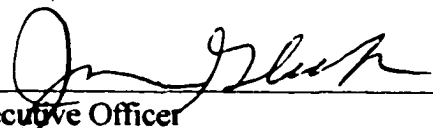
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This manuscript has been read and accepted for the Graduate Faculty in Psychology in satisfaction of the dissertation requirement for the degree of Doctor of Philosophy.

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Abstract**EVALUATING AUTOBIOGRAPHICAL MEMORY IN
TEMPORAL LOBE EPILEPSY PATIENTS****by****Tara Tamny-Young****Advisor: Professor Jeffrey J. Rosen**

Individuals with medically intractable Temporal Lobe Epilepsy (TLE) often undergo surgical treatment for seizure control, which typically involves removal of the anterior portion of the temporal lobe including medial structures. Although surgery is frequently successful in eliminating or reducing seizure activity, patients are at risk for memory decline because medial temporal structures play a critical role in learning and memory. Furthermore, many TLE patients who undergo temporal lobe resection report memory problems and complain primarily of poor memory for personal events, e.g., forgetting vacations or conversations. However, conventional neuropsychological measures do not appear to assess these patients' concerns and experiences, and instead focus on memory for impersonal material. Therefore, this investigation added autobiographical memory measures to pre- and post-operative neuropsychological evaluations and to Wada testing to determine whether these measures better evaluate patients' complaints.

This study additionally examined the underlying neurological substrates of autobiographical memory. Autobiographical memory function was tested and compared under conditions of confirmed neuroanatomical damage, temporary anesthesia of brain regions, and resective brain surgery. An examination of the underlying neuroanatomy of confabulatory responding (i.e., false memory production) was also attempted.

A small group of TLE patients was tested pre- and post-operatively and found to perform worse one year after surgery than before surgery on the incident items of the Autobiographical Memory Inventory. Although this was the predicted finding, further examination of the data revealed that declines were found in patients who underwent right AMTL, whereas patients who underwent left AMTL improved slightly on autobiographical measures.

In addition, Wada test findings for 16 TLE patients with unilateral medial temporal damage revealed poorer recall of recent autobiographical events than of remote events during temporary bilateral medial temporal dysfunction. These findings support the consolidation theory of memory.

In contrast, the current investigation failed to reveal any significant differences between left and right hemisphere dysfunction and autobiographical memory retrieval during Wada testing. It is likely that the perfusion of amobarbital to a large portion of each hemisphere confounded the comparison. In addition, an examination of the underlying neuroanatomy of confabulatory responding was attempted, but confabulations were insufficiently frequent for empirical analysis.

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Chapter 1

OBJECTIVES AND BACKGROUND

1.1.1 Primary Objectives: Evaluating Autobiographical Memory in Temporal Lobe Epilepsy Patients

Individuals with medically intractable Temporal Lobe Epilepsy (TLE) often undergo surgical treatment for seizure control. This surgery typically involves removal of the anterior portion of the temporal lobe including medial structures (i.e., removal of the “seizure focus”). Although surgery is frequently successful in eliminating or reducing seizure activity, patients are at risk for memory decline because the medial temporal structures play a critical role in learning and memory. Accordingly, many patients who undergo temporal lobe resection report memory decline postoperatively (Bergin, Thompson, Baxendale, Fish, & Shorvon, 2000; Guerreiro, Jones-Gotman, Andermann, Bastos, & Cendes, 2001).

Studies in which objective memory tests are administered before and after surgery have shown significant declines in some patients. Most of these tests, however, assess memory for “impersonal” material, such as words or pictures. However, patients

complain primarily of poor memory for personal events, e.g., forgetting vacations or conversations. Thus, conventional neuropsychological measures might not provide an assessment that addresses patients' actual concerns (and experiences). Furthermore, several studies have demonstrated that deficits in autobiographical memory (i.e., personal memory) can be differentiated from memory abilities for impersonal material.

There are several reasons why conventional memory test results might fail to coincide with memory functioning outside the clinical setting. Some reasons pertain to the nature of the tests. For instance: (1) they involve paradigms that are rarely encountered outside the laboratory (e.g., paired associate learning); (2) they attempt to assess 'pure' aspects of memory (e.g., verbal versus visual); (3) they tend to tap only relatively short-term memory; (4) the information to be learned is often trivial; and (5) contextual cues are usually minimized. This differs from "real life" in which many external aids are available (e.g., diaries; cues from other people), information to be learned involves multiple modalities (e.g., memory for holidays), contextual cues often facilitate recall, and events to be remembered are often very pertinent to the individual (Bennett-Levy & Powell, 1980). Finally, autobiographical memory might involve a somewhat different neurological substrate than does memory for impersonal material.

In addition to neuropsychological assessments, TLE patients considering surgical treatment undergo other procedures to determine whether brain regions to be resected are critical for cognitive function. The Wada test, also known as the Intracarotid Amobarbital Procedure (IAP), is used to determine whether the hemisphere contralateral to the seizure focus can support learning and memory. One of the main goals of the procedure is to

predict whether the patient will experience significant memory decline after surgery.

Amobarbital injection into the internal carotid artery effectively simulates the proposed surgery by briefly “inactivating” the brain structures to be resected (i.e., primarily the temporal region). This enables examination of function in the other hemisphere.

Currently, most Wada test protocols are structured as follows. Discrete, usually concrete, items are presented immediately following injection of Amobarbital to the hemisphere of the seizure focus. Memory for these common objects and pictures is assessed upon full recovery. This procedure is then repeated following injection to the other hemisphere. A strong performance in the expected direction (i.e., better recall by the “healthy” hemisphere compared to that demonstrated by the “unhealthy” hemisphere) suggests that the patient will have adequate memory functioning following surgery.

Similar to conventional neuropsychological assessments, such Wada test protocols often assess only “impersonal” memories. These “impersonal” memories include the learning and retention of presented objects and pictures, which may fail to assess the ability of patients to recall meaningful events from their personal past. It is this loss of autobiographical memories (e.g., the inability to recall a conversation one had, the failure to remember a vacation one took) that patients report as distressing, rather than the inability to remember impersonal objects. At the Columbia Comprehensive Epilepsy Center, most Wada memory items are “impersonal” (i.e., objects, pictures), although a limited number of autobiographical items are included as well. However, comparisons between performances involving these two item types have not yet been performed, nor

has the relationship between Wada performance and post-operative autobiographical memory been assessed.

To date, no epilepsy surgery programs have used a standardized objective measure of autobiographical memory in assessment of individuals with TLE undergoing surgical treatment. In addition, this project was the first systematic investigation of the utility of autobiographical memory items during Wada testing. Previous research at the Columbia Presbyterian Medical Center has shown that 'traditional' Wada items are sometimes recognized without awareness of the context in which they were learned (Hamberger & Hirsh, 1999). The addition of autobiographical Wada items allows for the assessment of both recent and remote memories that are pertinent to the individual, and may require that individuals rely more strongly upon their awareness of the context in which the memories were acquired. For instance, autobiographical memories almost always include contextual characteristics about the perceived physical environment. The environmental characteristics may include the location, time period, actions, and people (Brewer, 1988). In contrast, conventional Wada test items are "impersonal" objects which are made to represent a particular, orchestrated episode (e.g., "Do you remember any of the objects you were shown during this last injection?"). The current study attempted to establish and document a more sensitive, reliable method of assessing and predicting real-life memory abilities following temporal lobe resection through the addition of objective autobiographical memory testing.

In this study autobiographical memory was assessed pre- and post-operatively using items from the Autobiographical Memory Interview (AMI) created by Kopelman,

Wilson, and Baddeley (1990). The AMI measures personal semantic and episodic memories from different time periods (childhood, early adulthood, and recent past) and has been found to provide reliable measures. For instance, inter-rater reliability for the AMI has high correlations between pairs of testers, varying between .75 and .86 (Kopelman, Wilson, & Baddeley, 1989; Kopelman, 1989; Viskontas, McAndrews, & Moscovitch, 2000). The AMI has also been found to be a valid measure of the ability to remember personal experiences (Kopelman et al., 1989); it has discriminated between healthy controls and in individuals with memory impairments resulting from dementia, head injury, stroke, and TLE (Kopelman et al, 1989; Kopelman, 1989; Kopelman, Stanhope, & Kingsley, 1999; Viskontas et al., 2000). In addition, patients with memory deficits showed impaired remote memory when assessed on the AMI, as well as on other existing remote memory tests (e.g., News Recall Test), producing product-moment coefficients in the .27 to .76 range, with most .40 or above. Another advantage of the AMI is that it tests information that any person is likely to possess: the events of one's own life. In contrast, other measures have relied on public knowledge (e.g., news events) which is likely to differ from one person to the next, as such knowledge is dependent upon one's interest in current events and accessibility to media. One problem, however, with the use of personal recollections of one's past, is that of verifying accuracy. Kopelman et al. tested patients on the AMI with memory dysfunction, as well as frontal lobe dysfunction, a combination that has been suggested to underlie confabulatory responding. They found that the amount of inaccuracies and confabulations that occurred were quite small relative to the magnitude of the deficit between patients and controls.

They therefore concluded that detailed checking of AMI responses with relatives is probably unnecessary.

A recent investigation of individuals with TLE with known medial temporal damage (e.g., mesial temporal sclerosis¹, surgical resection) found that damage to medial temporal structures is related to significant impairment in autobiographical memory performance on the AMI (Viskontas et al., 2000). This study was the first to show that the AMI can be used to discriminate memory impairment in TLE patients from normal controls. However, memory performances on conventional memory measures were not compared to performances on the AMI. In addition, the between-subject design (comparing performances of TLE patients with known medial temporal damage to normal controls) did not allow for the assessment of perceived, predicted, or actual memory declines in TLE patients following surgery.

The current investigation was designed to examine potential changes in episodic autobiographical recall in patients with either intact or damaged medial temporal structures after unilateral temporal lobe resection. Episodic autobiographical memory function was also assessed during Wada testing to further investigate consolidation versus multiple trace theories, as well as strategic retrieval models (discussed below in Background section).

Subjective ratings for levels of saliency, emotion, surprise, frequency (occurred,

¹ Mesial temporal sclerosis is a pathological process in which there is marked neuronal loss and gliosis particularly in the CA1 sector of the hippocampus, as well as in other medial temporal structures (Blumenfeld, 2002).

thought about, told to another), vividness, and accuracy were obtained for each episodic autobiographical memory revealed on the AMI. These characteristics of autobiographical memories were chosen because some types of autobiographical memories appear to be more memorable than others, due possibly to different underlying functional/structural mechanisms. For example, most Americans can recall where they were and what they were doing when they learned that Neil Armstrong had taken his first step on the moon, or when planes had flown into the World Trade Center. These “flashbulb” memories are thought to be the result of the surprise, meaning, or emotion experienced at the time of the event and are theorized to be the result of a limbic system “now print” mechanism (Brown & Kulik, 1977). The “now print” neuro-physiological mechanism is thought to begin with the reticular formation area of the brain, which becomes activated when there is recognition of novelty or unexpectedness. A diffusely projecting reticular formation discharge, conceived to be a “now print” order for memory, is then distributed throughout both hemispheres. Finally, all recent brain events (recent conduction activities) are printed. Brown and Kulik also suggest that the flashbulb memory is not a narrative or verbal form, but one of images. However, other researchers have found that flashbulb memories are often inaccurate and thus less likely the result of an exact encoding of the moment, and more likely due to the repetitive telling and repetitive thinking one does about a salient event (Neisser, 1988). The event is repeated, rehearsed, and reconstructed as one rethinks or retells where one was and what one was doing when a the salient event occurred. These repetitive reconstructions strengthen the neural networks associated

with the event. Whether autobiographical memories are created at encoding or during a process of reconstruction, these features of saliency, surprise, emotion, frequency of occurrence, frequency thought about, and frequency retold all seem crucial in determining whether the memory is constructed and retrieved.

In the current investigation, subjects' memory concerns were also obtained and evaluated pre- and post- operatively using a structured interview, a subjective memory rating scale, and the Short Inventory of Memory Experiences (SIME) created by Herrmann, Neisser, and Gotlieb (1978). Unlike other self-report measures, the SIME measures various kinds of everyday memory problems (e.g., rote memory, conversations, people, errands, places) and assesses how well recent and remote memories are thought to be recalled.

Selected items from the AMI, as well as questions about more recent events and photographs of significant people in the patients' lives, were presented during the Wada test and compared to traditional Wada test items for accuracy in predicting both actual and perceived post-operative memory outcome. The items chosen from the AMI included questions about remote autobiographical events (childhood) and more recent autobiographical events (within the last 5 years). Additional recent autobiographical event memory questions were included to assess memory for events that occurred both within the previous 12 hours and for upcoming events that would occur later that day. Very remote, somewhat remote, and recent autobiographical memory items were developed to examine different neuroanatomical models of autobiographical memory (e.g., consolidation versus multiple trace models). Photographs of the patient's physician and

of a family member were added to the autobiographical memory items for a more visually-based autobiographical memory item. Previous research with conventional memory items has shown material-specific deficits. For instance, after left temporal lobe resection, patients show deficits on verbal memory tasks; after right temporal lobe resection, memory is impaired for stimuli that are more visual in nature.

1.1.2 Background: Finding Memory Impairment Following Medial Temporal Resection

Since the 1950's, surgical removal of part of the temporal lobe has been the treatment for patients with epileptic seizures not controlled by medication. Early on, bilateral medial temporal resection was performed on a handful of these patients, and resulted in the development of a severe anterograde amnesia postoperatively. In 1953, surgeon William Scoville and neuropsychologist Brenda Milner examined one patient, H.M., who underwent the bilateral surgery. Although his memory for events prior to the surgery was intact (he recalled incidents from his school days and jobs he had held in his teens and early 20's), H.M. was unable to recall events that occurred following the surgery. Milner (1966) gave the following description of H.M.'s deficits:

He could no longer recognize the hospital staff, apart from Dr. Scoville himself, whom he had known for many years; he did not remember and could not relearn the way to the bathroom, and seemed to retain nothing of the day-to-day happenings in the hospital. A year later, H.M. had not yet learned the new address, nor could he be trusted to find his way home alone (p. 113).

Due to the profound deficits H.M. incurred, this bilateral surgical procedure is no longer performed. Instead, unilateral anteromesiotemporal resection (removal of 3-6 centimeters of the basal and lateral temporal gyri and associated white matter from the temporal pole) with amygdalohippocampectomy (amygdaloid body, and the parahippocampal formation, which is the parahippocampal gyrus, hippocampus, and the uncus) is currently the standard surgical treatment for temporal lobe epilepsy that is refractory to medical treatment. Approximately 70 to 80 percent of TLE patients with medial temporal onsets are seizure free at one year follow-up, but serious potential deficits in memory are possible (Jack, Nichols, Sharbrough, Marsh, & Peterson, 1988). In addition, standard anteromesiotemporal resection (AMTL) may lead to less favorable surgical outcome in patients with lateral neocortical temporal onsets (Spencer, Spencer, Williamson, & Mattson, 1990). Deficits similar to H.M.'s were sustained as a result of unilateral hippocampectomy to a patient, P.B., a civil engineer, who had a unilateral AMTL, but was found at autopsy to have mesial temporal sclerosis contralateral to the resected temporal lobe. After his surgery, his remaining sclerotic medial temporal structures could not support new learning, leaving P.B. with a severe anterograde amnesia for the remaining 15 years of his life. Although this level of impairment is rare, more subtle memory declines appear to be common.

1.1.3 Conventional Assessment of Memory Functions

Studies confirm these declines through conventional neuropsychological memory tests that are administered to TLE patients before and after surgery (Seidenberg et al., 1998; Hermann & Wyler, 1988; Chelune, 1994; Dodrill, Hermann, Rausch, Chelune, & Oxbury, 1993; Hermann, Wyler, Bush, & Tabatabai, 1992). However, these tests evaluate memory for “impersonal” material, such as words or pictures, whereas in contrast, patients complain of poor memory for personal events (Bennett-Levy, Polkey & Powell, 1980). Thus, as mentioned, conventional neuropsychological measures might not provide an adequate, comprehensive assessment of pre- and post-surgical memory ability in TLE patients. There is a growing awareness in the field of memory research that the memory skills and processes measured conventionally may be rather different from those needed for functioning in everyday life (Neisser, 1978; Bennett-Levy & Powell, 1980).

Several investigators have administered subjective memory rating scales, in addition to conventional objective neuropsychological memory tests, to assess memory function in TLE. Subjective memory rating scales measure functional memory complaints by asking people to indicate how well they recognize or recall knowledge or events. Memory complaints are thought to reflect the memory problems that people experience in everyday life (Gilewskil & Zelinski, 1986). However, findings from these investigations have been inconsistent across surgery programs. For instance, Sawrie et al. (1999) operationalized objective memory as change on a list learning test, the California Verbal Learning Test (CVLT), and subjective memory as outcome scores on the memory

subscale of the Quality of Life in Epilepsy Survey (QOLIE-89). The memory subscale of the QOLIE-89 consists of six items. The first question assesses the degree to which the patient has experienced memory problems over the past four weeks. The next four questions assess the degree to which the patient has experienced specific memory problems (e.g., forgetting names, details of conversations). The sixth question assesses the degree to which the difficulties trouble the patient. The correlations between change on the QOLIE-89 memory subscale and change on the CVLT were not statistically significant. Interestingly, they found far greater declines on CVLT measures than indications of self-perceived memory loss on the QOLIE-89. In contrast, Perrine et al. (1997) found a significant correlation between another list-learning test (Rey Auditory Verbal Learning Test) and the memory subscale of the QOLIE-89. It is notable, however, that both groups of investigators suggest that responses on the memory subscale of QOLIE-89 often relate more to mood than to memory. For instance, Sawie et al. found that self-reported memory decline on the QOLIE-89 was predicted best by higher preoperative levels of self-reported depression on the Profile of Mood States in patients who underwent left temporal lobe resection. Perrine et al. also found that mood, as measured by the Profile of Mood States, was the strongest predictor of ratings on the QOLIE-89 memory scale. Bennett-Levy et al. (1980) also examined self-reports of memory skills from patients who underwent TLE surgery. However, they used their Subjective Memory Questionnaire (SMQ) and compared TLE patients to normal controls. The SMQ is a 43-item questionnaire asking subjects how they rate their memories for a number of different everyday memory situations (e.g., “How good is your

memory for giving messages?” “How good is your memory for faces?”). They found that patients as a group saw themselves as having poorer memories than normal controls and were “reasonably accurate in their judgment about their ‘real-life’ memory abilities.” In contrast, Helmstaedter, Hauff, and Elger (1998) found that performance on German translations of the Rey Auditory Verbal Learning Test and the SMQ were not significantly correlated.

Because studies relating performance on conventionally utilized memory tests have shown poor correlation in general with questionnaires of self-perceived memory function (which have been found to relate more to emotional status than objective memory performance), Dodrill and Ojemann (1997) suggested using an open-ended interview process to assess self-perception of memory loss after TLE surgery. However, these investigators did not justify how an open-ended interview process avoids the confounding variable of emotional status. Others agree that the strength of validity data is too low to warrant using self-perceived memory questionnaires as the sole method of assessment, but suggest that questionnaires might nonetheless be useful to check manipulations and conclusions involving objective memory measures (Herrmann, 1982).

1.1.4 The Utility of Autobiographical Memory Testing

As stated, many researchers have found little validity to self-report memory questionnaires. Perrine et al. (1997) and Sawrie et al. (1999) argue that self-report measures of function have more to do with patients' depressed mood than their actual memory performance. Other researchers argue that the self-report questions may not be

sufficiently clear about the memory tasks that are at issue, causing confusion in the subject and an inaccurate response (Herrmann, Grubs, Sigmundi, & Grueneich, 1986). Still, other investigators state that the questionnaire design is sound and that validity tests are appropriate, but that people simply do not hold accurate beliefs about their everyday memory performance (Herrmann, 1982). However, for the current investigation, it was hypothesized that the validity problems involved the conventional memory measures (that might not assess patients' actual concerns), rather than problems with self-report questionnaires. For instance, it is conceivable that while successfully recalling a number of "impersonal" words or geographic designs, a patient may still report valid memory problems with everyday recall (e.g., "Did I schedule that appointment while I was talking to her?" "Where did I go on my last vacation?"). Therefore, the hypotheses for the present investigation were as follows: (1) the addition of measures of autobiographical memory would provide an ecologically valid measure of everyday memory function, (2) autobiographical memory measures would better correlate with self-reported memory responses, and (3) autobiographical memory measures would better predict and assess post-surgical memory status in individuals with TLE than would conventional measures.

There has been limited research using more ecologically valid measures of memory in individuals with TLE. For instance, Barr, Goldberg, Wasserstein, and Novelly (1990) investigated retrograde amnesia following left and right AMTL in a pairwise-matched sample of six left and six right temporal lobe resection patients. Because they were investigating retrograde memory function, patients were all over age 30 and had an onset of seizures that began after age 15. The patients were matched by age, sex, education

level, age of onset of seizures, and pre-surgical Full-Scale Intelligence Quotient (FSIQ). In addition, a group of six normal controls were matched by age, sex, education level, and estimated FSIQ. Patients and normal controls were administered an extensive battery of remote memory tests, including the Famous Faces test (48 photographs of politicians and/or celebrities whose fame is associated with a specific decade), the Television test (72 self-administered multiple choice questions for programs that were broadcast for no more than 1 year), and the Goldberg-Barnett Remote Memory Battery, which includes questions about generic factual knowledge (e.g., “When do flowers bloom?”), specific factual knowledge (e.g., “What is the Sahara?”), public chronological knowledge (e.g., “Who was Winston Churchill?”), and autobiographical knowledge (e.g., “What is your mother-in-law's first name?”). There were no significant differences on test performances between right temporal resection and normal control groups. However, significantly lower scores were evident for the left temporal resection group on tests of “non-episodic” factual and autobiographical knowledge. Because there were no significant correlations between remote memory performance and confrontation naming performance, Barr et al. (1990) denied that poor performance by the left temporal resection group was due to verbal memory deficits. Instead, Barr et al. suggest that left medial temporal regions may underlie the generation of retrieval functions and storage processes related to remote memory. However, these findings are limited to semantic memory processes, as even autobiographical memory items were limited to semantic information (e.g., “How old is your oldest grandchild?”). Autobiographical semantic information may be more

ecologically valid than general information, but it does not assess memory for episodic autobiographical events.

Viskontas et al. (2000) were the first to publish results from the use of the AMI (which includes both semantic and episodic autobiographical memory measures) with individuals with TLE. Their study included a sample of 25 subjects tested pre- and post-surgically, all of whom had documented medial temporal damage, and a group of normal controls matched for age and education. On the AMI, the TLE subjects were found to perform significantly worse than controls, but only on the episodic items (e.g., “What memorable event occurred in high school?”). In contrast to findings by Barr et al. (1990), Viskontas et al. did not find a deficit on semantic autobiographical items (e.g., “What was your address when you were in high school?”) in their TLE group. However, Viskontas et al. did not differentiate between left and right temporal patients. Of note, TLE patients' poor episodic memories lacked the characteristic temporal gradient (i.e., poor memory for recent events, with memory improving as memories become more remote). Instead, impairment was noted for memories as far back as early childhood, with slightly better performances revealed for more recent time periods. Conventional memory test findings and AMI results were not compared. Instead, the conventional memory test findings were simply presented to show the constitution of the patient group. The left TLE group showed impairment on story memory (as assessed on the delayed logical memory subtest of the Wechsler Memory Scale), but the right TLE group had equivalent difficulty with both memory for stories and for visual material (as assessed on the delayed visual reproduction subtest of the Wechsler Memory Scale). In addition, this

between-subject design (patients compared to normal controls) did not assess individual memory change pre- to post-surgically. Because autobiographical memory retrieval of the TLE patient group was poor for all time periods, Viskontas et al. suggested that episodic autobiographical memory retrieval remains dependent on the hippocampal formation and perihippocampal structures as long as the memory exists. This finding is in contrast to consolidation models in which the medial temporal region performs some time-limited function and eventually allows memory storage and retrieval to proceed without participation from this area (Squire, 1987; Squire & Zola-Morgan, 1991; McClelland, McNaughton, O'Reilly, 1995). Viskontas et al. suggest a life-long dependency for episodic autobiographical memory on medial temporal areas of the brain, and specifically postulate a multiple trace model of memory (Nadel & Moscovitch, 1997). The core notion of the multiple trace model is that the hippocampal components remain a necessary part of episodic memory as long as the memory traces are viable. Episodic memory traces consist of linked ensembles of the hippocampal complex (which includes the hippocampus proper, the dentate gyrus, the subiculum, entorhinal cortex, the perirhinal cortex, and the parahippocampus gyrus) and neocortical neurons. More specifically, Nadel and Moscovitch suggest that the spatial and temporal contextual information that characterizes autobiographical memory depends upon the continuing involvement of the hippocampal complex (for spatial context) and the frontal cortex (for temporal context). Although a multiple trace model recognizes that autobiographical memories are more distributed in nature, this model fails to consider the additional higher cortical processes that control the strategic retrieval of autobiographical memories

(detailed below). Nevertheless, if medial temporal structures remain important in memory retrieval for remote events, then there is concern for retrograde, in addition to anterograde, amnesia following epilepsy surgery.

The current investigation added episodic memory testing on the AMI to conventional pre- and post-surgical neuropsychological evaluations. This allowed for a within (pre-post) subject design and a comparison of autobiographical and conventional neuropsychological memory tests with self-report measures. In addition, episodic autobiographical memory items added to the Wada test were systematically analyzed to assess whether these items were useful in predicting memory decline after surgery.

1.1.5 Expanding Memory Assessment During the Wada Test

The Wada test is used in order to help the neurosurgeon determine whether the proposed surgery is likely to result in functional deficits in language and memory for the particular individual. The Wada test refers to a class of procedures that assess cognitive function during temporary anesthesia of one hemisphere of the brain achieved through the injection of sodium amobarbital into the internal carotid artery or, when necessary because of poor vasculature, into the common carotid artery. Results are used to determine whether the hemisphere contralateral to the proposed resection can support memory functions. If the patient fails to remember a sufficient number of stimuli presented following the injection ipsilateral to seizure onset, the patient is believed to be at risk for amnesia following surgery. Although a central component of the evaluation for

epilepsy surgery, Wada test procedures remain unstandardized, and vary from center to center (Hamberger & Walczak, 1995).

As is traditional in science, there has been a reductionistic approach in the investigation of memory. Beginning with Ebbinghaus and his “pure” study of memory through the use of nonsense syllables, many investigations of memory have become so well controlled that the experiences hardly resemble the phenomena of life that they propose to explain. The trend of emphasizing methodology, rather than theory and observation, occurs in Wada protocols in that the typical protocol includes discrete item presentation. The to-be-remembered stimuli are presented during the drug effect, and recall or recognition of these common objects, pictures, or words (e.g., hat, dollar) is assessed upon neurological recovery. Jones-Gotman (1987) explains that “simple tests are sufficient because when an injection disables the hemisphere that has been supporting memory alone or in part, memory capacities become so marginal that very little new material should be retained, regardless of its simplicity” (p. 204). Milner (1997), who designed the original Wada memory test, explains that she was looking for a task that an amnesic patient (H.M.) would fail, but that an aphasic patient would be able to pass. Because amnesiacs do poorly on both recall and recognition tasks, but aphasic patients can successfully complete recognition tasks, line drawings of common objects were used and adequate recognition memory was accepted as a pass. Another concern of investigators is that the effect of the dose lasts only four to five minutes, and language, in addition to memory, must also be assessed during that time. Because object-naming errors have become the gold standard for assessing language at many centers (Dodrill,

1993), due to time constraints, it makes sense to use these items for later memory evaluation. However, few would consider the development of a rote skill (such as recalling or recognizing a few items) an adequate measure of autobiographical memory ability, since these conventional stimuli do not encompass the organization that emerges from real, complex, methodologically messy experiences in life (Brewer, 1988). As noted earlier, these discrete-item tests attempt to assess 'pure' aspects of memory (e.g., verbal versus visual), they tend to tap only relatively short-term memory, the information to be learned is often trivial, and contextual cues are usually minimized. Also, in "real-life," many external aids are available (e.g., diaries; cues from other people), information to be learned cuts across all modalities (e.g., memory for holidays), contextual cues often lead to recall, and events to be remembered are often very pertinent to the individual (Bennett-Levy & Powell, 1980). Thus, by cleaning up real-life experiences and extracting them down to single objects, conventional Wada protocols may not adequately assess the processes of search and retrieval of meaningful and complex events.

Individuals undergoing the Wada procedure often report that they do not recall being shown the items, but then correctly select the same items when the items are presented among distractor items. Though they have selected the correct item, the patients often report that they are guessing. This ability relies on implicit memory systems, which do not include the conscious experience of familiarity with the event. In everyday life, an individual would not generally be satisfied with being able to pick out a correct item without having a conscious memory of its presentation. Therefore, traditional Wada procedures often assess only semantic memories and fail to measure the

episodic personal recollections they aim to preserve. Semantic memory is the intricate network of concepts, associations and facts that constitutes one's general knowledge about the world (Schacter, 1996). Semantic memory is responsible when an individual has item recognition during a Wada procedure but, at the same time, fails to recollect the episode in which the item was acquired. Exposure to an item (e.g., a watch) is thought to result in an excitation of the semantic representation of that item (Schacter, 1996), but it is episodic memory that allows an individual to recall that he saw the item in a particular context, setting, and under particular circumstances.

Hamberger and Hirsh (1999) assessed the confidence with which individuals undergoing the Wada test evaluate their response choices. After recognizing one of the presented items among a set of distractors, the individual is asked how certain (e.g., very sure, medium sure, or guessing) he is that he was presented with the item during a specific time period (e.g., after the last injection). These ratings are incorporated into the individual's overall score for the procedure, thus revealing whether episodic memory functions were intact. Other investigators fail to make this assessment, leaving it completely unclear whether episodic memory functions remained functional, or if the individual simply guessed correctly due to intact semantic memory processes (e.g., primed semantic representations).

As noted, the Wada procedure plays an important role in the presurgical identification of patients who are at risk for cognitive declines in language and memory abilities. However, many variations of the procedure exist that are rarely compared, and

few investigators have examined patients' recall for autobiographical memory events while undergoing a Wada test.

Dodrill and Ojemann (1997) were one of the few investigators who reported what patients can recall about their personal experience during the Wada test. Their non-traditional post-injection assessment involves an interview procedure that queries the patient for five basic events that occurred during the injection phase of the Wada procedure. The questions assess recall for: (1) absence versus presence of speech arrest; (2) whether motor weakness occurred; (3) whether errors were made in object naming; (4) whether errors were made in reading sentences, and; (5) whether errors were made when recalling the objects. Correct recall of four or more items is the criterion for passing this "interview test." Their injection phase of the Wada procedure is a more traditional technique in that impersonal items are presented. For instance, the patient first names an impersonal object, then reads a sentence, and then short term memory is assessed by having the patient recall the object named before the presentation of the sentence. This procedure is continuously repeated with different objects and sentences presented. Passing the injection phase of the Wada requires that the patient have an error rate no greater than 49 percent during a five-minute period beginning either two minutes after the injection or following the return of speech and correct item naming. Using the Wada methods described, Dodrill and Ojemann found that performances during the injection phase of the Wada procedure (which involved the traditional impersonal items) correctly classified 76 percent of individuals (11 individuals with memory loss, 8 individuals with no memory loss), while the performances during the non-traditional post-injection

interview test only correctly classified 52 percent of individuals (5 individuals with memory loss, 8 individuals with no memory loss). In Dodrill & Ojemann's study, memory loss was determined post-surgically when patients' performances were at least 40 percent lower on at least two of the three conventional verbal memory measures, and when patients' reported memory declined since surgery. Subjective assessment is done during an interview by asking the individual, "Have you noticed any change in your memory since surgery? If so, in what way?" Dodrill and Ojemann chose conventional verbal memory decline to determine memory loss because of "the general agreement that this is the area of greatest concern rather than non-verbal memory or visual spatial memory" (p. 213). They suggested that the failure of the interview test to allow for better predictions of memory function may reflect the patient's lack of awareness during the injection phase, and suggested that the interview is measuring inattention rather than memory. This is likely to be the case since many investigators have reported that patients under the effect of the amobarbital are unaware of their dysphasia and hemiplegia and believe they obey the various commands successfully (Wada & Rasmussen, 1960). Because Dodrill and Ojemann did not assess patient awareness of these events (dysphasia, hemiplegia) during the injection phase, it is unknown if the results are due to forgetting or to a lack of awareness/encoding at time of injection. They also only assessed memory for recent events (those occurring during the period following the injection) and did not assess patients' memory for remote autobiographical events.

In the present study, following the administration of traditional Wada test items (e.g., objects and pictures), autobiographical memories were elicited during the injection

phase (e.g., “What memorable event occurred during high school?”). Subsequently, during the post injection phase, subjects were asked to recall which traditional items were presented, as well as which autobiographical items (e.g., “I asked you about a past event. What event did I ask you about?”) were assessed during the injection phase. Subjects also provided confidence ratings for both traditional and autobiographical response choices. These procedures allowed for episodic autobiographical memory assessment both during the injection phase and during the post-injection phase. This procedure best mimics memory demands outside the laboratory because patients were required to search, retrieve, evaluate, and share their autobiographical memories. It was hypothesized that performance on autobiographical memory items during the Wada procedure would better predict memory changes after surgical treatment than would conventional Wada items. Memory changes after surgery were measured by objective memory-change scores on autobiographical and conventional memory measures, as well as by self-reported memory changes.

1.2.1 Secondary Objectives: Using Wada Findings to Test Neuroanatomical Models of Autobiographical Memory

Although many investigators use the Wada procedure to assess whether a post-surgical anterograde amnesia will result, no one has attempted to examine the relationships between neuroanatomical systems and autobiographical memory function (both recent and remote) using this procedure.

In the current study, the Wada test, in addition to being a clinical measure, was used to investigate the neuroanatomy of autobiographical memory. Although the areas affected by each injection were large (most of one hemisphere), the differences in each arterial perfusion pattern, as well as the difference in known areas of damage in each individual, produced different patterns of dysfunction, which could then be compared. Because the neuroanatomical relationships between structure and autobiographical memory function remain unclear, these findings provided some insights into the proposed systems of autobiographical memory.

1.2.2 Perfusion Patterns

Perfusion patterns from an injection of the Internal Carotid Artery (ICA) generally include the Middle Cerebral Artery (MCA)² and Anterior Cerebral Artery (ACA)³. The Posterior Cerebral Artery (PCA) is rarely perfused during an ICA injection, because in most individuals it is supplied via the vertebrobasilar system. However, in approximately nine percent of patients, the PCA originates from the ICA, and in another small percentage of patients the PCA fills from the ICA by way of the Posterior Communicating Artery (Gotman, Bouwer, & Jones-Gotman, 1992). Since the

² The MCA supplies the following structures: putamen, globus pallidus, anterior temporal lobe, orbital frontal lobe, pre and post central gyri, superior and inferior parietal lobules, and posterior temporal lobe (Parent, 1996).

³ The ACA supplies the following structures: caudate, putamen, internal capsule, inferior frontal cortex, pars orbitalis, medial frontal lobe, corpus callosum, and cingulate gyrus (Parent, 1996).

PCA rarely is perfused and supplies medial temporal structures including the hippocampal formation, the parahippocampal gyrus, and at least half of the inferior temporal gyrus as well as the posterior temporal lobe and the occipital lobes (Jack et al., 1988), many investigators question whether the Wada is a valid test for predicting postoperative memory impairment (Morton, Polkey, Cox, & Morris, 1996). Blumenfeld (2002) explains that the injection that perfuses the ACA and MCA indirectly inhibits the medial temporal lobe by cutting off its major sources of input including hemispheric cortex, white matter (tracts of nerve fibers within a hemisphere), and corpus callosum (a bundle of nerve fibers connecting the cerebral hemispheres). Others add that because the Anterior Choroidal Artery is perfused from an ICA injection and supplies the anterior one-third of the hippocampus, the amygdala, and the uncus, the Wada test provides a valid assessment (Perrine, Devinsky, Luciano, Choi, & Nelson, 1995). In approximately 30 percent of patients the Wada test is further complicated by contralateral ACA perfusion due to filling across the Anterior Communicating Artery (Silfvenius, Fagerlund, Saisa, Olivecrona, & Christianson, 1997). However, this percentage might be slightly high, as it was unclear whether the authors were referring to machine versus hand injections during the angiogram. During the Wada Test the injection of the amobarbital is performed with a hand injection, which has been documented as having less force than the machine injection generally used during the contrast run which produces the angiogram. Therefore, the perfusion of amobarbital may be somewhat overestimated by the ratings from the angiogram. The combination of temporary dysfunction of brain structures from the effects of the amobarbital and areas of damage (e.g., unilateral mesial temporal

sclerosis) revealed on MRI allowed for the examination of temporary bilateral medial temporal dysfunction, bilateral frontal dysfunction, and unilateral frontal dysfunction on autobiographical memory retrieval in various patients. The roles of these structures in autobiographical memory are reviewed below.

1.2.3 Background

The medial temporal structures are believed to play an important role in memory. Some memory theorists suggest that the medial temporal structures initially play a critical part in memory, but that a subsequent consolidation process results in the formation of remote cortical memories that no longer rely on medial temporal structures (Squire, 1987; McClelland et al., 1995). Others have provided evidence of a multiple trace theory in which the hippocampus (a segment of the medial temporal structures) remains an important part of remembering indefinitely (Nadel & Moscovitch, 1997; Viskontas et al., 2000). In addition, recent discoveries through imaging research suggest frontal lobe connections play an important role in the search, evaluation, and cue elaboration necessary to retrieve an autobiographical memory (Conway & Turk, 1999; Conway, Pleydell-Pearce, & Whitecross, 2001).

1.2.4 The Role of the Frontal Lobes in Autobiographical Memory Construction

A number of imaging studies have revealed differential hemispheric activations in prefrontal regions during memory tasks. These findings led to a proposed model of hemispheric encoding/retrieval asymmetry (HERA). The assertions of the HERA model

are that (1) right prefrontal cortical areas are more involved in episodic retrieval than are left prefrontal areas, and that (2) left prefrontal areas are more involved in semantic retrieval and episodic encoding than are right prefrontal areas (Nyberg, Cabeza, & Tulving, 1996; Buckner, 1996). However, the so called “episodic” procedures used in these HERA studies consisted of subjects learning a list of 'impersonal' words, then completing word-stems with words only from that word list. Although this task may add a level of complexity to the semantic memory task of simple word stem completion (e.g., produce any word that begins with the following three letters), it remains debatable whether such a task is comparable to recalling events from one's life.

In contrast to HERA assertions, Conway and Turk (1999) suggest that autobiographical memories are more complex and initially require processes of a “working self” system for retrieval that is based on left frontal function. Imaging studies reveal that areas in the left frontal cortex activate during autobiographical memory retrieval to cue words (Conway & Turk, 1999; Craik et al., 1999). Similarly, Conway et al. (2001) found during a slow cortical potential study that autobiographical memory began in left frontal networks and terminated with a shift of activation in posterior temporal and occipital networks of the right hemisphere. Conway suggests that this left frontal activation early in retrieval reflects the operation of the “working self.” He defines the “working self” as a retrieval verification network against which outputs are evaluated and, if necessary, additional searches are generated.

Fink et al. (1996) also used imaging to examine how an autobiographical event is remembered. They, like the HERA researchers, found a network of primarily right

prefrontal cortex activation (among other right hemisphere regions), but no left frontal activation during autobiographical memory retrieval. However, in Fink's task subjects were provided with a distinct detail from a previously recalled memory, then asked to imagine what happened next. This procedure bypassed the generative retrieval phase, as the provided memory detail activated event-specific knowledge in the knowledge base, and a stable pattern of activation was formed without the need for cue elaboration (Conway & Turk, 1999).

It appears that autobiographical memory may rely on left frontal networks during a process of search, evaluation, and cue elaboration. These processes may not be necessary, or as complex in memories for other types of information (e.g., word lists). In autobiographical memory, frontal networks operate in parallel with additional posterior and medial areas of the brain.

In the current study, autobiographical memory was assessed during the Wada test using a general cue (e.g., "What memorable event occurred in high school?"). This general cue requires the patient to formulate a search for a memory. This procedure likely required what Conway et al. (1999) term a "working self" process that appears to be related to left frontal lobe function. When no memory was found, or an unverified memory was provided, more detailed cues were provided by the examiner. This cue elaboration provided a functional external "working self" (similar to the methodology found in the Fink et al. (1996) study). Thus, the current study's design allowed for comparisons between left and right hemisphere dysfunction (i.e. ACA and MCA perfusion) and autobiographical memory retrieval under different circumstances (i.e., with

a general cue and after elaborated cues). It was hypothesized that patients with functional left hemispheres (i.e., patients with right hemisphere seizure onsets following right amobarbital injections) would successfully retrieve autobiographical memories from general cues, more so than would patients with dysfunctional left hemispheres (i.e., patients with left hemisphere seizure onsets following left amobarbital injections). However, it was also hypothesized that with the provision of elaborated cues given to the patients by the examiner, patients with dysfunctional left hemispheres would perform as well as those with functional left hemispheres.

1.2.5 The Role of Medial Temporal and Neocortical Connections in Autobiographical Memory Construction

As mentioned, many researchers suggest that it takes some time after initial encoding for a memory to become fully established or organized in the brain. This process is called consolidation. One type of consolidation operates over short time periods of seconds or minutes, converting short-term memories into long-term memories. Another kind of consolidation operates over longer time periods of months or years. This second type of consolidation appears more resistant to disruption over time. In some cases, patients have great difficulty remembering experiences from relatively recent time periods, but less difficulty remembering experiences from the distant past. This temporal gradient has been demonstrated in numerous groups of amnesic patients with medial temporal damage. For instance, researchers presented cue words to amnesic patients with hippocampal damage and asked them to remember episodes from before and after

childhood. The patients remembered the same number of remote (e.g., childhood memories), but remembered fewer recent experiences (e.g., adulthood memories) compared to normal controls (MacKinnon & Squire, 1989).

This process of the formation of memory is thought to include cortical and subcortical memory circuits that engage in feedback with each other (Mishkin & Appenzeller, 1987; Moscovitch, 1995). For instance, after a processed sensory stimulus activates the hippocampus, the memory circuits play back on the cortical sensory areas. This feedback presumably strengthens and perhaps stores the neural representation of the sensory event. This neural assembly might undergo changes leading to the preservation of the connection pattern, and transform the perception into a durable cortical memory (Mishkin & Appenzeller, 1987).

Consolidation begins after this initial cohesion. When it is complete, the memory trace (i.e., the reactivated pattern of sensory areas) can be maintained without the involvement of the hippocampal complex. For instance, at recollection, an exogenously or endogenously generated cue interacts automatically with the memory trace. Because the information that the cue contains overlaps with that in the memory trace, the neural activity associated with the cue primes the memory trace. If retrieval occurs before consolidation is complete, the cue primes the memory trace via the hippocampal code. Once consolidation is complete, the involvement of the hippocampus and related structures is no longer necessary, and the cue interacts directly with the memory trace (Moscovitch, 1995).

In summary, some researchers report that the role of the hippocampal system is time limited (Moscovitch, 1995; Squire & Zola-Morgan, 1991; McClelland et al., 1995). The hippocampal system binds together the relevant cortical sites that together represent memory for a whole event. These memories gradually become reorganized (consolidated), so that over time the memory is no longer dependent on medial temporal structures. For instance, H.M. could not recall events that occurred shortly before the date of his surgery, suggesting medial temporal structures involvement in retrieving recent memories. While memory for very remote information remained spared, suggesting remote memories had been consolidated in cortical sensory areas and were no longer dependent on medial temporal structures (Milner, 1966).

Another theory is that medial temporal structures remain involved in all memories, both recent and remote (Nadel & Moscovitch, 1997). This multiple trace theory suggests that the hippocampal complex rapidly binds novel information and experience into a coherent memory trace composed of hippocampal elements and of neocortical elements that represent the event's features or components activated at the time of encoding. Each autobiographical memory trace consists of this ensemble of neurons in both the hippocampal complex and neocortex for as long as it exists. No long-term consolidation process is postulated in which the hippocampal contribution is relinquished. Thus, damage to the hippocampal complex would result in the loss of even remote episodic memories. In this model, newly acquired autobiographical memories are particularly vulnerable, because the neural traces have not yet proliferated within the medial temporal structures to the extent that older neural traces have proliferated. Therefore, this theory

explains the temporal gradients reported in bilateral medial temporal damage (e.g., as in H.M.'s memory) to be the result of partial damage rather than complete damage of the hippocampal complex.

A recent study that tested a group of TLE patients with known unilateral medial temporal damage on the AMI reported findings consistent with a multiple trace theory of memory. Their patients had difficulties retrieving memories from all time periods, especially that for the most remote memories (Viskontas et al., 2000). Therefore, unlike what was demonstrated with H.M. (i.e., poor recent recall with intact remote memory), TLE patients with unilateral damage recalled recent events with more clarity than they recalled remote events.

In the current investigation, episodic memory questions were presented during the Wada test. The Wada test allowed for the examination of proposed memory models by briefly anesthetizing medial temporal structures in patients with contralateral sclerotic medial temporal structures. Not only do the items of the AMI seem more ecologically valid for predicting post-operative memory problems, they also provide a method of assessing accessibility of autobiographical memory retrieval in different conditions of neuroanatomical inactivation (e.g., left mesial temporal sclerosis and right hemisphere inactivation). One tacit assumption associated with the Wada procedure is that, "if medial temporal structures contralateral to the injection are sufficiently dysfunctional, a temporary bilateral amnesic state will be produced and predict an amnesic syndrome postsurgically" (Loring, Lee, Meador, & King, 1991). The current investigation examined a subgroup of patients with unilateral MTS during amobarbital injections contralateral to

their damage (thus producing bilateral medial temporal dysfunction) and determined whether their autobiographical memory dysfunction was for only recent events (supporting a consolidation theory) or for both recent and remote events (supporting a multiple trace memory theory).

1.3.1 Tertiary Objective: The Examination of Confabulatory Behavior During the Wada Test

The role of anterior structures in memory have not been examined during the Wada test. Instead, poor memory performances that are believed to result from cross-flow of the ACA are often reported as invalid due to inattentiveness or obtundation (Perrine et al., 1995). It is suggested here that ACA cross-flow does not simply result in inattention, but can result in a confabulation syndrome. Confabulation is distinguished from classical amnesia in that the patient may produce “memories” that have no basis in actual events or occurrences. This report of fallacious memories is not simply due to error or lying, and is usually in connection with amnesia (Fischer, Alexander, D’Esposito, & Otto, 1995). For instance, all “errors of commission” which remain uncorrected by the individual are confabulations. Some models of confabulation suggest only a dysexecutive syndrome is necessary to elicit confabulations, but other models of confabulation suggest a dual model that includes both amnesia and executive dysfunction. The Wada test provided a procedure in which dysexecutive and dual model hypotheses could be tested.

In the present investigation, recent autobiographical memory items were used to assess for possible confabulation. These autobiographical memory questions had accurate

answers known to the examiners. For instance, during the Wada test, patients were asked, "What did you have for breakfast?" As patients are told not to eat anything the morning of their procedure, an accurate answer would be "nothing," whereas a confabulation might be, "steak and eggs." These particular items were also used for the assessment of neuroanatomical regions underlying confabulation.

1.3.2 Background

Kopelman (1987) proposed two types of confabulation, provoked and spontaneous. Provoked confabulations are transient elaboration responses in reaction to direct questioning. Spontaneous confabulation is the persistent, often unprovoked, generation of spectacular false memories. For example, Kapur & Coughlan (1980) describe one patient, R.J., who sustained a severe head injury in an accident and remained unresponsive for several weeks. A Computerized tomography (CT) scan showed intracerebral hemorrhages in both frontal lobes. On one occasion, he asked his wife, "Why do you keep telling people we are married?" She explained that they were married and had children, to which he replied that children did not necessarily imply marriage. At this point she showed him wedding pictures. R.J. admitted that the person marrying her looked like him, but denied that it was he. Provoked and spontaneous confabulations have been observed from patients with Korsakoff syndrome, Alzheimer's disease, epilepsy, anterior communicating artery (ACoA) aneurysms, head injury, dementia, and stroke. These disparate etiologies often have in common the presence of both amnesia and executive deficits. However, investigators question whether confabulatory

responding is an outcome of an executive disorder alone (Baddeley & Wilson, 1986; Johnson, Hastroudi & Lindsay, 1993), or both an executive disorder and amnesia (Fischer et al., 1995; DeLuca, 1993).

Baddeley and Wilson (1986) are proponents of an executive disorder model of confabulation. They suggest that the “central executive” is malfunctioning in confabulating patients. In the normal subject the determinant of neural activity would be the central executive, whereas in these patients the absence of such control allows the neural system to be captured by any available stimulus. The malfunction of the “central executive” may result in some patients not initiating behavior to search memory, in some patients having no capacity for retrieval of personal incidents in response to general cueing, and in some patients having difficulty initiating a search and evaluating its outcome.

In an examination of a Korsakoff’s patient with a severe amnestic-confabulatory syndrome, hypoperfusion in the orbital and medial frontal regions and the medial diencephalic area on single-photon emission computerized tomography (SPECT) scan was revealed. However, four months later, the patient’s amnesia remained but confabulatory responses ceased. Repeat SPECT showed a return to normal perfusion in the frontal brain areas, but little improvement in the medial diencephalic region, suggesting that confabulation results from dysfunction of orbital and medial frontal cortex (Benson et al., 1996). In another examination of nine confabulatory patients following the rupture and recovery from ACoA aneurysms, patients who produced spontaneous confabulations were found to have multiple lesions to the medial basal forebrain, the ventral frontal lobe,

and the striatum. Patients who produced provoked confabulations, however, had more limited lesions to the basal forebrain or orbital frontal cortex (Fischer et al., 1995).

DeLuca and Cicerone (1991) suggest that both frontal lobe and basal forebrain infarcts are necessary to elicit confabulations. Support for this is provided by DeLuca (1990) who presented an ACoA patient with involvement limited to frontal structures who did not confabulate and was not amnesic. DeLuca suspects that basal forebrain damage underlies confabulation. The basal forebrain is part of the telencephalon, structures located near the surface of the brain that include the septal area, the olfactory tubercle, parts of the amygdala, and the area under the anterior commissure known as the substantia innominata.

In summary, some models of confabulation suggest only a dysexecutive syndrome is necessary to elicit confabulations, but other models of confabulation suggest a dual model that includes both amnesia and executive dysfunction.

In the present study, the Wada test provided a procedure in which the neuroanatomical regions underlying confabulation could be investigated because in approximately 30 percent of patients, the Wada test is complicated by contralateral ACA perfusion due to filling across the Anterior Communicating Artery (Silfvenius et al., 1997). If patients with bilateral perfusion of the ACA (and thus the ACoA), or patients with perfusion contralateral to a frontal lesion (bilateral frontal dysfunction), demonstrated more confabulatory responses than did patients without bilateral dysfunction, then a dysexecutive syndrome model would have been supported. If, however, patients demonstrated more confabulatory responses when bilateral ACAs are

perfused (and thus the ACoA) and the contralateral medial temporal lobe was sclerotic (thus producing bilateral medial temporal dysfunction), then a dual model of confabulation would have been supported.

1.4.1 A Summary of the Present Objectives

To summarize, this investigation was three-fold. Primary objectives were to examine whether autobiographical memory measures provide a more ecologically valid assessment than do conventional neuropsychological measures in addressing patients' post-operative complaints of memory problems, and to investigate whether the neurological substrates that underlie autobiographical memory are different from those that underlie memory for impersonal material. Secondary objectives were to investigate the roles of right and left anterior brain regions in the search, elaboration, and reconstruction of autobiographical memory, and to test whether temporarily produced bilateral medial temporal dysfunction resulted in performances that supported the consolidation model of memory or the multiple trace model of memory. A tertiary objective was to assess whether confabulatory responding during the Wada test occurred only as the result of a dysexecutive syndrome or as the result of dual dysfunction (i.e., both frontal and medial temporal dysfunction).

Chapter 2

METHODS

2.1.1 Subjects

All participants were recruited from the Columbia Comprehensive Epilepsy Center from 2000 to 2002. Patients were invited by their physicians to participate. Patients who agreed were contacted and informed that participation involved 20-30 minutes of additional outpatient testing both pre- and post-operatively, and that their consent to participate permitted collection of routine clinical data for research purposes. Signed, informed consent was obtained prior to testing. Patients with Wechsler Adult Intelligence Scale Revised, or Third Edition, FSIQ scores below 70 were excluded from the study.

Over a period of 24 months, 36 surgical candidates participated in this study. Thirty had TLE (17 Left TLE, 12 Right TLE, 1 Bilateral TLE), and six had exclusively extratemporal seizure onsets. Seventeen patients went on to have surgery, however, the other 19 patients did not proceed to surgery (see Appendix A for explanations). Of the 17 patients that had surgery: five had right AMTL; four had left AMTL; one had a left anterior temporal lobe resection without removal of medial structures; one had tailored

resection of a left temporal tumor that pathology results indicated was a grade III glioma⁴; one had a right tailored resection of fronto-temporal areas due to cortical dysplasia;⁵ one had a corpus callosotomy⁶; one had a left frontal lobe resection; and one had a tailored resection of a left parietal tumor. Nine of the 17 patients who proceeded to surgery returned for post-operative testing. Three of these nine patients underwent left AMTL, one underwent left anterior temporal lobe resection without the removal of medial temporal structures, four underwent right AMTL, and one underwent right superior temporal and inferior frontal resection for cortical dysplasia. The other eight patients who underwent surgery had not returned because: one was living in London; one had an increase in seizures since surgery; one had terminal cancer; and five were not yet one-year post-operative (see Appendix B).

Demographic information (e.g., seizure focus, gender, age, age of onset of continuous seizures, duration of epilepsy, MTS status, handedness, hemisphere language dominance, seizures since surgery, education) and pre-operative prorated Full Scale intelligent quotients (Wechsler Adult Intelligence Scale-Revised or Wechsler Adult Intelligence Scale-III) for the nine patients who were tested pre- and post-operatively are presented in Table 1. Although an attempt was made to assess patients' pre-operative

⁴ A grade III glioma is a malignant brain tumor.

⁵ Cortical dysplasia is a developmental malformative disorganization of the cytoarchitecture of the cortical neurons.

⁶ Corpus Callosotomy is a surgery that severs a posterior portion of the corpus callosum.

Table 1. Demographic Information for Nine Patients Tested Pre- and Post- Operatively

Patient Number and Seizure Focus	Age (yrs) at Pre-Operative Evaluation	Gender	Age of Onset (yrs)	Duration of Epilepsy (yrs)	MTS	Handedness	HLD	Post-Operative Seizure Outcome (Engel scale)	Education (yrs)	WAIS FSIQ
19 LT	34	F	32	2	N	R	L	CS (1D)	10	88
9 LT	35	M	31	4	Y	R	L	CS (1C)	18	117
12 LT	45	F	<1	44	Y	R	L	SF (1A)	12	72
5 LT*	41	F	23	18	Y	AMB	R	SF (1A)	12	90
25 RT	24	M	19	5	Y	R	L	CS (1D)	16	111
1 RT	34	F	2	32	Y	AMB	L	CS (1C)	19	112
3 RT	33	M	12	21	Y	R	L	CS (1B)	12	80
18 RT	30	F	7	23	Y	R	L	SF (1A)	13	79
8 RT+	46	M	26	20	N	R	L	SF (1C)	18	115

LT, left temporal; LT*, left temporal but right hemisphere language dominance; RT, right temporal; RT+, right temporal plus right frontal; F, Female; M, Male; Age of Onset, age of onset of continuous seizures; MTS, Mesial Temporal Sclerosis as assessed by radiologist, if MTS is present it is on the same side as the seizure focus; HLD, Hemisphere language dominance determined during Wada test; Post-Operative Seizure Outcome, SF, Seizure Freedom, CS, Continued Seizures, Seizures continuing after surgery and classification of postoperative outcome (Engel, Vauness, Rasmussen, & Ojoniour, 1993): 1A- Completely free of disabling seizures, 1B- Non-disabling simple partial seizures only since surgery, 1C- Some disabling seizures initially after surgery, but free of disabling seizures for at least 2 years, 1D- Generalized convulsion with antiepileptic drug withdrawal only; WAIS FSIQ, Preoperative Wechsler Adult Intelligence Scale-R/III Full Scale Intelligence Quotient.

seizure frequency, many patients had difficulty reporting seizure frequency because they were reportedly often asleep during the events or amnesic for them. Therefore, seizure frequency data was not included as demographic information or analyzed as a subject variable.

2.1.2 Procedures

Phase 1. Pre-Operative Autobiographical Memory Testing

Patients received the Autobiographical Memory Inventory (Kopelman, Wilson, & Baddeley, 1990) which required approximately 20 minutes of testing. The Autobiographical Memory Inventory (AMI) assesses recall of autobiographical incidents and factual knowledge about a person's own past across three broad time periods, i.e., childhood, early adulthood, and recent years. Administration and scoring procedures as described in the AMI test manual (Kopelman et al., 1990) were followed. Patients were asked to provide incidents that occurred during childhood, early adulthood, and recently⁷. Temporal and spatial contextual information for each incident was also requested. Three incidents for each time period were elicited with probes. The childhood probes were for recall of the patient's first memory from the period before starting school, to recall an incident that occurred while at grammar school, and to recall an incident that occurred while at high school. The early adulthood probes were for the patient to recall either an

⁷ In addition to autobiographical incident questions, the AMI also includes personal semantic questions. This semantic memory measure was not of interest for the current investigation, but is part of the administration of the AMI. Therefore, patients were also asked these questions, which included names and locations of schools attended, home addresses, and names of friends. The personal semantic questions are also divided into the three time periods.

incident from college or from the patient's first job, to recall an incident that occurred at the patient's wedding (or if not married, a wedding they attended), and to recall the patient's first encounter with someone when the patient was in his twenties. The recent probes were to recall an incident that occurred at the hospital in the past five years, to recall an incident involving a relative or visitor in the last year, and to recall an incident which took place while on any vacation within the past five years. Responses were transcribed on the scoring sheets as close to verbatim as possible. Each incident was scored out of a possible score of three, based on the descriptive richness and specificity in time and place of the response. The maximum score per time period was nine and the maximum total score was 27. One rater scored each of the questions. To check reliability of the scores, an independent rater blind to subject and original ratings scored 40 percent of the memory incidents.

In addition, the experimenter developed a rating scale for patients to rate each autobiographical incident they provided on the AMI for how salient, emotional, surprising, frequently occurring, frequently thought about, frequently shared, vivid, and accurate it was. These ratings were all four-point likert scales and were presented after the completion of the entire AMI (see Appendix C).

Patients also completed the Herrmann, Neisser & Gottlieb's (1978) Short Inventory of Memory Experiences (SIME) which is a rating scale assessing how well they remembered certain memories from early childhood and daily life (e.g., "How well do you remember the first day you went to school?") and how often they experience various kinds of everyday forgetting (e.g., "How often are you unable to find something that you

put down only a few minutes before?”). Scores on the remembered items were summed for each patient, resulting in a remembered total score. Items were then divided into two groups, recent and remote remembered events. Seven recent items (e.g., “How well do you remember what you did on your last birthday?”) were summed for each patient resulting in a recent remembered event score. Eight remote items (e.g., “How well do you remember a time when you were sick or hurt as a young child?”) were summed for each patient resulting in a remote remembered event score. Scores on the forgetfulness items were summed for each patient, resulting in a forgetfulness total score. In addition, forgetfulness items were divided into eight specific memory abilities based on the factor analyses conducted by Herrmann and Neisser (1979), which revealed each patient's score for rote memory, absent mindedness, names, conversations, errands, people, retrieval and places.

The AMI and rating scales were administered during a routine office visit close to the date of the patient's standard pre-operative neuropsychological evaluation. The standard neuropsychological evaluation included measures of overall intellectual function, language, visuospatial perception, verbal and nonverbal memory, attention and concentration, executive function, achievement, clinical scales, and self-perceived ratings of memory function. The critical performances for this investigation included long delay free recall on a list-learning task (California Verbal Learning Test or Rey Auditory Verbal Learning Test), logical memory delayed recall, visual reproduction delayed recall, and ratings from the Epilepsy Surgery Inventory-55 (ESI-55, the memory trouble item, and the scale score for “role limitation due to memory problems”). Two of the patients (case

1 and case 9) received either their pre- or post-neuropsychological evaluation outside of Columbia Presbyterian Medical Center due to insurance issues. Their testing reports and raw data were forwarded for inclusion in the study.

Phase 2. The Wada Test

At Columbia Presbyterian Medical Center, prior to the injection of sodium amobarbital a machine injection of contrast is injected and angiography reveals each individual's perfusion pattern. The radiologist rates the perfusion of the contrast into the ipsilateral and contralateral PCA, Posterior Communicating Artery, MCA, and ACA. These ratings are on a scale from 3 to 0. A score of 3 represents a full filling of the artery with the contrast, a 2 represents a partial filling, a 1 represents a flash filling, and 0 represents no filling (M. Hamberger, personal communication). It is notable that the Wada Test (the injection of the amobarbital) is performed with a hand injection, which has been documented as having less force than a machine injection, therefore the perfusion of amobarbital may be somewhat overestimated by the ratings from the angiogram. The remainder of the Wada procedure at Columbia Presbyterian Medical Center has been reported previously (Hamberger, Walczak, & Goodman, 1996) and is as follows:

The Internal Carotid Artery (ICA) ipsilateral to the suspected seizure focus is injected first, and the interval between ipsilateral and contralateral injections ranges from 30 to 45 minutes, with the second injection only initiated after full clinical recovery. Patients are administered 100-125 mg of sodium amobarbital in 10 ml normal saline over a period of five seconds,

with contralateral hemiplegia and EEG slowing of the injected hemisphere used as evidence for desired drug effect. If hemiplegia is not obtained, an additional bolus of 20 mg of sodium amobarbital is injected immediately (pp. 1089-1090).

Following ICA injection, ten conventional “impersonal” items (two verbal commands, two real objects, four object drawings, and two abstract designs) and five autobiographical items are presented. During the presentation of the conventional items grip strength is tested after every two items to check for the continuation of the desired drug effect. If the patient's strength returns, conventional items are stopped and the presentation of autobiographical items begins. If the patient's grip strength remains poor during all conventional items, the grip strength is tested once more before the presentation of the autobiographical items. Because autobiographical memory testing requires language abilities, autobiographical items were presented after conventional items. The mean time elapsed from initial injection to the presentation of autobiographical memory items was 257.4 seconds following left injection, and 200.32 seconds following right injection⁸.

Two autobiographical items assess memory for same day events (e.g., “What did you have for breakfast today?”), one assesses memory for an event that occurred during the last year (e.g., “What memorable event occurred during your last vacation?”), and one assesses memory for a remote event (e.g., “What memorable event occurred during grammar school?”). In addition, patients are presented with a photograph of a familiar

⁸ These means were calculated from 25 patients who underwent Wada testing during which timing from injection to autobiographical memory items was accurately performed.

person (e.g., family member or physician) and are asked to recognize the person in the photo. Autobiographical memory function is assessed both during and following the injection phase. Recall and recognition of conventional items are assessed only following the injection. During memory testing that follows the injection, patients are asked after each response whether they are “very sure,” “medium sure,” or “just guessing.” The same protocol is performed with an injection of the contralateral ICA, although different items are used.

Scoring During the Period of Anesthesia

Performance on autobiographical memory items presented during the period of anesthesia were scored as follows. Correct responses were considered to be those that matched recalled episodes on the AMI at pre-operative testing and were given a score of 3. If an alternative, probable event had been recalled, patients were provided more specific cueing. For instance, if a patient recalled an event from the his freshman year rather than the specific graduation event he had recalled on the AMI, the examiner would ask if the patient could recall a memorable event from his senior year. If the specific event was then recalled, the patient received a score of 2⁹. If patients provided a vague response (e.g., graduation), and failed to elaborate with cueing from the examiner, they

⁹ When patients recalled different, yet valid, events from those provided pre-operatively it was reasoned that the autobiographical memory responses given by patients on their pre-operative AMIs should be primed by recent recall, as well as assessable to explicit memory systems as demonstrated by previous recall. Therefore, patients were given poorer scores for these memories and further cued for the events originally presented.

received a score of 1. Patients received a score of 0 for responses of “don’t know” or “don’t recall” and for confabulatory responding (i.e., improbable and incorrect responses).

Scores attained during ipsilateral and contralateral injections were divided into same day events (i.e., recalling what they had for breakfast, what time they work up that morning, what they would do that day, and what they would do that evening), recent events (i.e., an event that occurred during their last vacation, or an event that occurred during their video/EEG monitoring) and remote events (i.e., an event that occurred during grammar school, or an event that occurred during high school).

Scoring Following the Period of Anesthesia

Responses following recovery from anesthesia were scored as correct if patients either recalled or recognized from multiple choice the items with which they had been presented earlier. Separate ratio scores for autobiographical memory items and traditional items were then calculated using the Hamberger and Hirsch procedure (1999) which incorporates confidence ratings. The procedure is as follows:

For each item, an incorrect response is 0 points; a correct response reported to be a “pure guess” is 1 point; a correct response with level of confidence reported as “medium sure” is 2 points; and a correct response with level of confidence reported as “very sure” is 3 points (p. 1288).

Hemispheric asymmetry scores for responses after recovery were obtained for autobiographical and traditional memory Wada testing using Hamberger and Hirsh's (1999) scoring procedures which are as follows:

For each side of testing, sum the points and divide the number of valid items presented, then calculate the asymmetry ratio by dividing the higher hemispheric score by the lower hemispheric score. Asymmetry ratios of greater than or equal to 1.5 were considered significant (p. 1288).

Phase 3. Post-Operative Follow-up Testing

Nine individuals returned approximately one year after surgery for a routine office visit close to the date of the patients' standard post-operative neuropsychological evaluation. At this time, each individual additionally underwent a brief interview concerning experiential memory loss, re-administration of the AMI, re-administration of ratings for the AMI incidents (for levels of saliency, emotional reaction, surprise, frequently occurring, frequently thought about, frequently shared, vividness, and accuracy), and re-administration of the SIME.

2.1.3 Data Analysis

2.1.3.1 Testing Primary Objectives: Testing the Relationship Between Autobiographical and Conventional Memory Performances and Subjective Memory Complaints

Small sample sizes precluded planned correlational comparisons assessing whether autobiographical memory measures would better correlate with self-reported memory

responses, and whether autobiographical memory measures would better predict and assess post-surgical memory status in individuals with TLE, than would conventional measures. Instead, paired t-tests comparing objective memory test (e.g., AMI, WMS: Logical Memory, Visual Reproduction, and list learning) performance before surgery to performance after surgery, and Wilcoxon tests comparing subjective memory (ESI-55, SIME) reports before surgery to reports after surgery were performed. Differences between right TLE group data and left TLE group data was examined. Fisher's exact probability tests were used to test whether area of dysfunction (i.e., right or left temporal) and performance on memory testing (i.e., improvement or decline) were related.

Inter-Rater Reliability of the AMI

Because the AMI scoring system requires subjectivity on the part of the scorer, inter-rater reliability analysis was performed. A Pearson correlation was used to evaluate inter-rater reliability for AMI incident responses scored by two individuals. The resulting coefficient was .67.

Subject Variables

Data were further explored to assess whether the group differences (right temporal dysfunction, left temporal dysfunction) found on objective and subjective memory measures might be due to confounding subject variables. Subject variables included age, education, age of onset, and duration of epilepsy. However, small, uneven sample sizes precluded the use of independent sample t-tests. Instead, the data is presented

descriptively. Pre- and post-surgical Wechsler Adult Intelligence Scales (WAIS-R/III) IQ indices and the selected indices from the Symptom Checklist-90 item-revised (SCL-90-R) were compared via related pairs t-tests, and scores on the pre-and post-surgical memory characteristic ratings (e.g., level of saliency) were compared via Wilcoxon tests.

Subsequently, group differences were examined. Fisher's exact probability tests were used to assess performance differences between left and right temporal groups on IQ, SCL-90-R indices, and memory characteristic ratings.

Testing the Relationship Between Autobiographical and Traditional Memory

Performance on the Wada Test and Post-Operative Outcome

Because only nine patients returned for post-operative memory testing, small sample sizes precluded planned correlational comparisons to assess whether autobiographical memory measures would better correlate with self-reported memory responses, and whether autobiographical memory measures would better predict and assess post-surgical memory status in individuals with TLE, than would conventional measures. Instead, the data for the nine subjects is presented descriptively. In addition, the three different Wada methods (i.e., traditional memory items presented following recovery, autobiographical items presented during the drug effect, autobiographical memory items presented following recovery) were compared for 28 patients who underwent Wada testing and were deemed good surgical candidates. The traditional and autobiographical memory items that were presented following recovery were scored with the incorporation of confidence ratings (e.g., a 3 for reporting being very sure, a 2 for

being medium sure, and a 1 for guessing about a correct response) and were represented as a ratio as described earlier. Scores for the autobiographical memory items that were presented during the period of anesthesia were also represented as ratio scores, however, rather than incorporating confidence values, the ratings described earlier for autobiographical memory recall were incorporated (e.g., 3 points for accurate recall, 2 points for accurate recall after further cueing, 1 point for vague recall, and 0 points for don't know/unlikely responses). Confidence ratings were not assessed during the period of anesthesia due to the limited time of the drug effect.

2.1.3.2 Testing Secondary Objectives: Comparing the Roles of Left and Right Anterior Brain Regions in Autobiographical Memory Retrieval

The data from a subgroup of patients with known unilateral seizure onsets and left hemisphere language dominance was used to compare the role of the right versus the left anterior hemisphere in autobiographical memory retrieval. A between-subject comparison using a chi square test allowed for the examination of whether left anterior hemisphere function (i.e., performance of patients with right hemisphere seizure onsets during ipsilateral sodium amobarbital injection) outperforms right anterior hemisphere function (i.e., performance of patients with left hemisphere seizure onsets during ipsilateral sodium amobarbital injection) on a test of autobiographical memory recall from general cues (i.e., spontaneously correct or not correct spontaneously). A chi square was also used to test whether once given an elaborated cue (i.e., correct with cue, or not

correct after a cue), right anterior hemisphere function would result in equal-to-better recall of autobiographical memories than would left anterior hemisphere function.

Comparing Recent Versus Remote Memory During the Wada Test: Support for Consolidation or Multiple Trace Models of Memory

The data from a subgroup of patients with known unilateral mesial temporal sclerosis (or other medial temporal damage) who underwent contralateral injections during the Wada procedure (thus producing bilateral medial temporal inactivation) were used to determine whether memory dysfunction occurred for only recent events (supporting a consolidation theory) or for both recent and remote events (supporting a multiple trace memory theory).

Scores for two types of autobiographical memory items (recent and remote) attained during conditions of temporary bitemporal dysfunction/inactivation were compared via matched pairs t-tests. Scores attained on tests of same day events/memories (e.g., “What did you have for breakfast this morning?”) were excluded from this analysis, as they were not thought to characterize the memorable episodic autobiographical memories that the recent (e.g., “What memorable event occurred during your last vacation?”) and remote (e.g., “What memorable event occurred during grammar school?”) items had. To show that significant findings during temporary bitemporal dysfunction were due to the condition (i.e., bitemporal dysfunction), rather than the type (recent or remote) of memory compared, additional matched pairs t-tests were performed.

These comparisons included recent versus remote memory performance during unilateral dysfunction, and bilateral versus unilateral performance during recent memory.

2.1.3.3 Testing a Tertiary Objective: Comparing Conditions Underlying Confabulation

It was hypothesized that if during the Wada test patients with bilateral perfusion of the ACA (filling of the contralateral ACA with a rating of 3 by the neuroradiologist) or if patients with a frontal lesion who were injected on the contralateral side (thus also producing a bilateral frontal dysfunction) demonstrated more confabulatory responses than did patients without bilateral frontal dysfunction, then a dysexecutive syndrome model would be supported. If, however, patients demonstrated more confabulatory responses when bilateral medial temporal dysfunction was produced (i.e., injecting contralateral to dysfunctional medial temporal structures) and bilateral ACAs were perfused (filling of the contralateral ACA with a rating of 3 by the neuroradiologist), then a dual model of confabulation would be supported. Scores for number of confabulations produced during two conditions of inactivation (bifrontal only and bifrontal/bimedial temporal) were compared via chi square tests.

Chapter 3

RESULTS

Results are presented in the order of the most salient findings, not necessarily in the order presented in the methods section. Given the small number of patients that proceeded to surgery at this point, the primary hypotheses are not yet fully answerable, but interesting trends in patient performance that are already evolving are described. Because the hypotheses examined during Wada testing were statistically analyzable due to the greater number of patients that underwent this procedure, these secondary objectives are discussed first. Primary findings comparing pre- to post-operative memory function and, subsequently, the tertiary findings investigating neurosubstrates that underlay confabulatory responding are then described.

3.1.1 Recent Versus Remote Autobiographical Memory During the Wada Test: Support for a Consolidation Model of Memory

The data from a subgroup of patients with known unilateral MTS (or other medial temporal damage) who underwent contralateral injections during the Wada procedure

(thus producing bilateral medial temporal inactivation) were used to determine whether problems with memory were only for recent events (supporting a consolidation theory) or for both recent and remote events (supporting a multiple trace memory theory). Scores for two types of autobiographical memory items (recent and remote) attained during conditions of bitemporal inactivation were compared via matched pairs t-tests.

Subjects

Eighteen patients had known medial temporal damage prior to the Wada test, as evidenced on MRI and/or EEG monitoring. However, two patients were excluded from the analysis because they were not tested on recent or remote autobiographical memory items during their Wada tests. Of the remaining 16 patients, 11 had MTS, one had high signal in the region of the left anterior hippocampus with minimal volume loss, one had a mass in the left temporal lobe that involved the entire hippocampus and adjacent tissue, one had a calcified lesion in the right medial temporal region, one had a cavernous malformation¹⁰ involving the right hippocampal tail, and one had right medial temporal onsets on EEG and later was found to be seizure free after a right AMTL. This latter patient was both included and excluded from the analyses because of questionable medial temporal dysfunction prior to surgery. Because the outcome of the analyses were similar, the patient's data were included in the group data and are reported.

¹⁰ Cavernous malformations are abnormally dilated vascular cavities which are lined by only one layer of flat cells (Blumenfeld, 2002).

Demographic information for the sixteen TLE patients tested with recent and remote autobiographical memory items during the Wada test are as follows: 11 patients had left temporal onsets, five had right temporal onsets; seven were males, nine were females; 13 were right handed, two were left handed, one was ambidextrous; 15 were left hemisphere language dominant, one was right hemisphere language dominant. Means and standard deviations were calculated for patients' age, age of onset of continuous seizures, years of education, intelligence quotients (WAIS-R/III), and conventional neuropsychological memory findings from their pre-operative evaluations (e.g., delayed recall trials of logical memory and visual reproduction) and are presented in Table 2.

Recent and Remote Autobiographical Memory Items

Autobiographical memory items were grouped into recent items and remote items. Recent items queried memory for events that occurred in recent years (e.g., last vacation, recent seizure monitoring). Remote items queried memory for events that occurred long ago (e.g., grammar school, high school). Each patient was asked about one recent and one remote event following each injection (i.e., ipsilateral to medial temporal damage and contralateral to medial temporal damage).

When temporary bilateral medial temporal dysfunction was produced (i.e., sodium amobarbital was injected contralateral to the side of damaged medial temporal structures), patients demonstrated poorer recall of recent autobiographical events than of remote ones ($t = 2.33, p < .04$). In contrast, when the same patients were injected ipsilateral to their known medial temporal damage (resulting in unilateral medial temporal dysfunction),

Table 2. Demographic Information for Sixteen Patients Who Underwent Recent and Remote Autobiographical Memory Wada Testing

Measures	M (SD)
Age (yrs)	33.93 (7.20)
Age of Onset of continuous seizures (yrs)	16.45 (11.52)
Education (yrs)	14.67 (2.58)
WAIS R/III VIQ	98.44 (27.87)
WAIS R/III PIQ	95.56 (13.57)
WAIS R/III FSIQ	96.94 (16.64)
WMS-R/III Logical Memory delayed recall scaled score	7.20 (1.21)
WMS-R/III Visual Reproduction delayed recall scaled score	10.00 (3.38)

there was no significant difference between their recent and remote autobiographical memory recall. The difference between recent autobiographical memory recall during the period of bilateral versus unilateral medial temporal dysfunction was also significant ($t = 3.87, p < .01$). Descriptive data are presented in Table 3.

3.1.2 Comparing the Roles of Left and Right Anterior Brain Regions in Autobiographical Memory Retrieval

Between-subject comparisons of left versus right hemisphere function during the Wada test (i.e., injections ipsilateral to the side of suspected seizure focus) under different conditions of autobiographical memory recall (i.e., with a general cue and after elaborated cues) allowed for the examination of right versus left hemisphere roles in autobiographical memory retrieval.

Autobiographical memory performance during the period of anesthesia was analyzed for the 22 patients with unilateral seizure onsets, left hemisphere language dominance, and who received recent and remote memory items (e.g., “What memorable event do you recall from your last vacation?” “What memorable event do you recall from high school?”). Mean age at time of Wada testing was 36.77 (SD, 8.55) and mean pre-operative FSIQ as assessed by the WAIS-R/III was 97.36 (all > 70 ; SD, 16.44). Chi square analyses of left-versus-right hemisphere performance during general cues and elaborated cues were not significant.

Table 3. Recent Versus Remote Autobiographical Memory Recall During Temporary Conditions of Medial Temporal Dysfunction

Injection Side	Autobiographical Memory Recall		
	Recent M (SD)	Remote M (SD)	
Contralateral to known medial damage Bilateral Medial Temporal Dysfunction	.75 (1.13)	1.69 (1.25)	p < .04
Ipsilateral to known medial damage Unilateral Medial Temporal Dysfunction	1.75 (1.29)	1.50 (1.21)	ns
	p < .01	ns	

3.2.1 Results for Primary Objectives

Findings on the objective and subjective memory measures for the nine patients that were tested both pre- and post-operatively are discussed below. Means and standard deviations, as well as significant findings for paired t-tests comparing pre- to post-operative performance are displayed in Table 4.

3.2.2 Objective Tests

AMI

Performances on the AMI significantly changed across patients following surgery, and some significant differences between patient groups were revealed as well. On the total incident recall score of the AMI, six of the nine patients demonstrated declines in autobiographical memory performance. A paired t-test revealed that the mean AMI total incident score one year after surgery tended to be worse than before surgery ($t = 2.02, p < .08$). Seven of the nine patients showed a decline on the AMI for childhood and recent incident recall. Paired t-tests revealed that performances on the AMI childhood incident recall ($t = 2.98, p < .02$) and recent incident recall ($t = 2.93, p < .02$) were significantly worse one year after surgery than before surgery. Performance on early adulthood memory items on the AMI resulted in improvement of six of nine patients. However, a paired t-test comparing the AMI early adulthood incident score before and one year after surgery was not significant.

Table 4. Pre- and Post- Operative Memory Measure Data

Memory Measures	Preoperative M (SD)	Postoperative (1 year) M (SD)	
AMI Total Score (range 0 - 27)	18.06 (2.26)	16.44 (3.16)	p < .08
AMI Childhood Incident Score (range 0 - 9)	5.81 (1.03)	4.67 (1.50)	p < .02
AMI Early Adulthood Score (range 0 - 9)	5.25 (1.27)	5.72 (1.27)	ns
AMI Recent Incident Score (range 0 - 9)	7.00 (.70)	6.28 (1.19)	p < .02
Logical Memory Delayed Recall* (t score)	46.44 (8.06)	50.44 (11.90)	ns
List Learning Delayed Free Recall** (t score)	31.67 (9.35)	37.38 (15.70)	ns
Visual Reproduction* (t score)	52.83 (12.48)	50.00 (10.92)	ns
ESI-55 Memory Trouble Item (range 1 - 4)	2.67 (1.11)	3.33 (.71)	ns
ESI-55 Role Limitations Index (range 0 - 100)	39.98 (13.42)	52.61 (11.51)	p < .03
SIME Remembered Total Score (range 15 - 105)	49.00 (13.10)	51.78 (18.31)	ns
SIME Remembered Remote Events Score (range 8 - 56)	23.63 (9.40)	21.00 (6.28)	ns
SIME Remembered Recent Events Score (range 7 - 49)	18.13 (6.27)	17.00 (6.50)	ns
SIME Forgetfulness Total Score (range 24 - 168)	87.50 (33.59)	67.86 (19.25)	p < .07

***WMS-R/III, **CLVT and Rey Auditory Verbal Learning Test**

Number of Pairs: AMI, N = 9; Logical Memory, N = 9; List Learning, N = 8; Visual Reproduction, N = 6; ESI-55, N = 9; SIME, N = 8.

The data for the AMI were subsequently divided into two patient groups, those with right temporal (RT) resections and those with left temporal (LT) resections. Although patient 5 had a left temporal resection, she demonstrated RHLA during the Wada test, and was therefore considered to be more similar to the right temporal patient group. However, because it remains unclear how the brain reorganizes (e.g., switched dominance versus crowding hypotheses¹¹), all analyses were performed both with patient 5 considered right temporal and with patient 5 excluded. Because the outcome of the analyses were similar, results presented include patient 5 as part of the right temporal group.

On the AMI total incident recall score, the RT group consistently showed a decline one year after surgery from their pre-operative performance. For example, prior to surgery, when case 3 (a RT patient) was asked to recall an event from a recent vacation, he responded, "Going to Pennsylvania Dutch Country, I remember noticing people still driving a horse and buggy. There was a parking lot with cars and horse and buggies at K-Mart. You don't forget that." In contrast, one year after surgery, when asked to describe a recent vacation, he stated vaguely, "Sesame Place last year in August. It's in Pennsylvania. We went for the day. We saw shows, went to the pools and rides." When asked if he could recall anything in particular about the day, he reported that he could not.

¹¹ The crowding hypothesis suggests a decline non-verbal abilities associated with a shift in language dominance to the right cerebral hemisphere following early left hemisphere damage. This shift occurs at the expense of non-verbal abilities, which are thought to be crowded out (Loring, 1999).

In contrast, the LT group consistently showed a slight improvement post-operatively (see Figure 1). For example, case 19 (a LT patient) gave the following response before surgery, when asked about a memorable event from high school: "I remember Glenn had a big party at his parent's house and we had a food fight in his kitchen and it was a mess." A year after surgery, she gave the following response regarding a memorable event that occurred during high school:

I got pregnant. I had terrible periods all the time and my mom took me to the gynecologist and I was pregnant. My mom was in the room, she was shocked. I was very upset. My parents said, "get rid of the baby," then they were like, "you can keep it." Me and my dad didn't get along while I was pregnant. I was 14. The office was in _____, not too far from where I live now. The doctor's son works there now. He's better than his dad. He was rude and not too gentle.

A Fisher's exact probability test showed a significant relationship between the area of dysfunction (i.e., right or left temporal) and performance (i.e., decline or increase) on the AMI incident memory total score ($p < .02$). However, when the group (i.e., RT, LT) findings on the AMI were divided into time periods (i.e., childhood, early adulthood, and recent), Fisher's exact probability tests were not significant. Nevertheless, interesting patterns of performance were revealed. On the childhood incident items the RT patients consistently demonstrated a decline after surgery, whereas performance of the LT group after surgery was evenly divided between improved, declined, and unchanged (see Figure 2). On the recent incident items, five of the six RT patients and two of the three LT

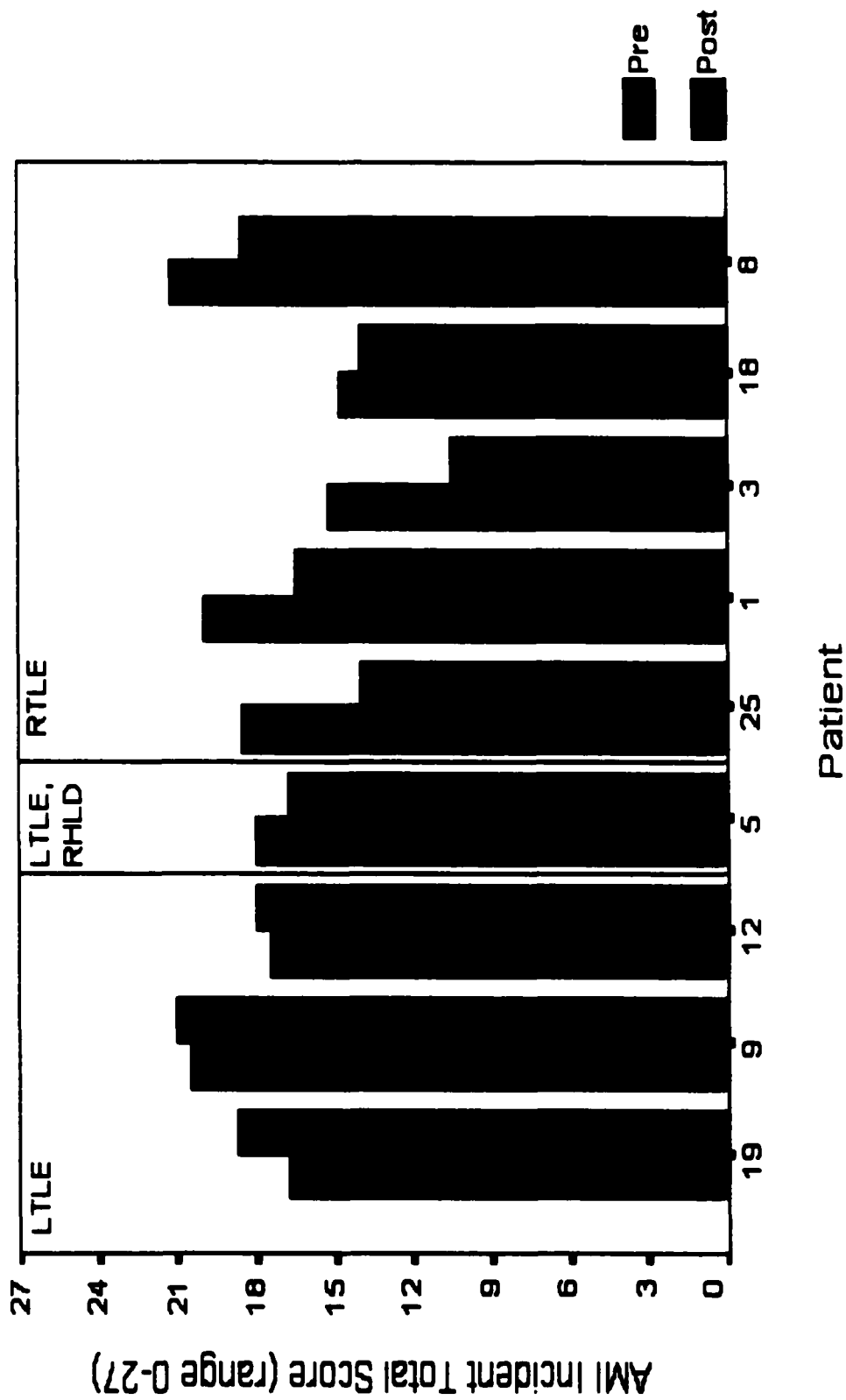


Figure 1. AMI Incident Total Scores Pre and Post Surgery.

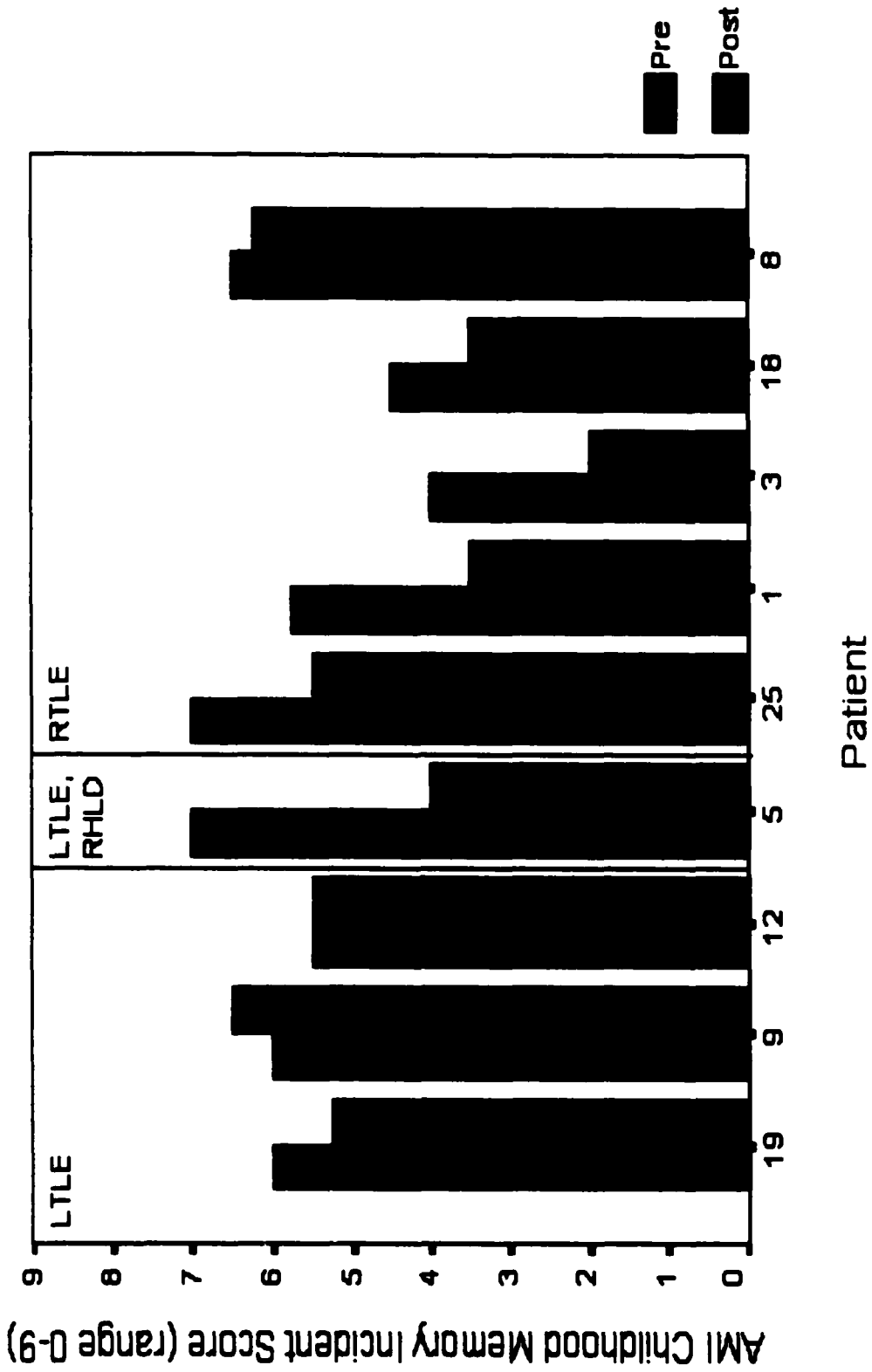


Figure 2. AMI Childhood Incident Scores Pre and Post Surgery.

patients demonstrated a decline after surgery (see Figure 3). On the early adulthood items the RT group post-operatively was evenly split between improvement and decline, while the LT group all improved post-operatively (see Figure 4).

Conventional Neuropsychological Memory Measures

Across patients, performance on conventional neuropsychological memory measures did not change significantly following surgery, however, some interesting group differences were revealed.

List learning was assessed pre- and post-operatively with the California Verbal Learning Test for eight of the nine patients. However, one patient (case 18) received the Rey Auditory Verbal Learning Test pre- and post-operatively. Therefore t scores were calculated based on normative reference data provided in test manuals. The delayed free-recall trial was used to measure rote verbal memory, and a matched pairs t-test showed that performance was not significantly different from before surgery to one year postoperatively. However, when the group data are examined, five of the RT patients showed improvement on the list learning subtest post-operatively, while the two of the three patients from the LT group showed a decline post-operatively (see Figure 5). A Fisher's exact probability test showed a significant relationship between laterality of dysfunction (i.e., right or left temporal) and performance (i.e., improvement or decline) on the delayed recall trial of list-learning tests ($p < .05$).

Because different versions of the logical memory subtest of the Wechsler Memory Scale (WMS-R and WMS-III) were used across patients, t scores were calculated based

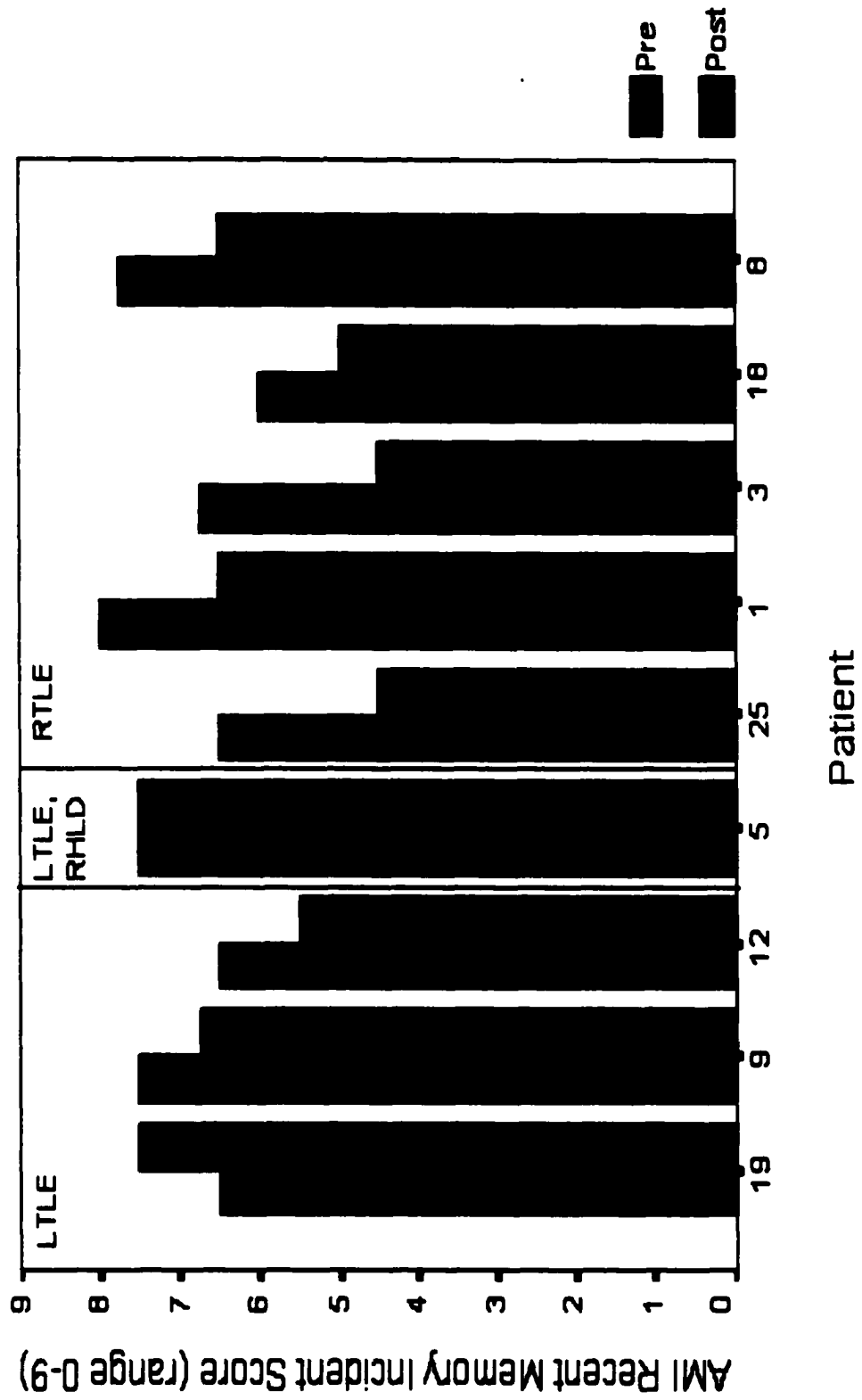


Figure 3. AMI Recent Incident Scores Pre and Post Surgery.

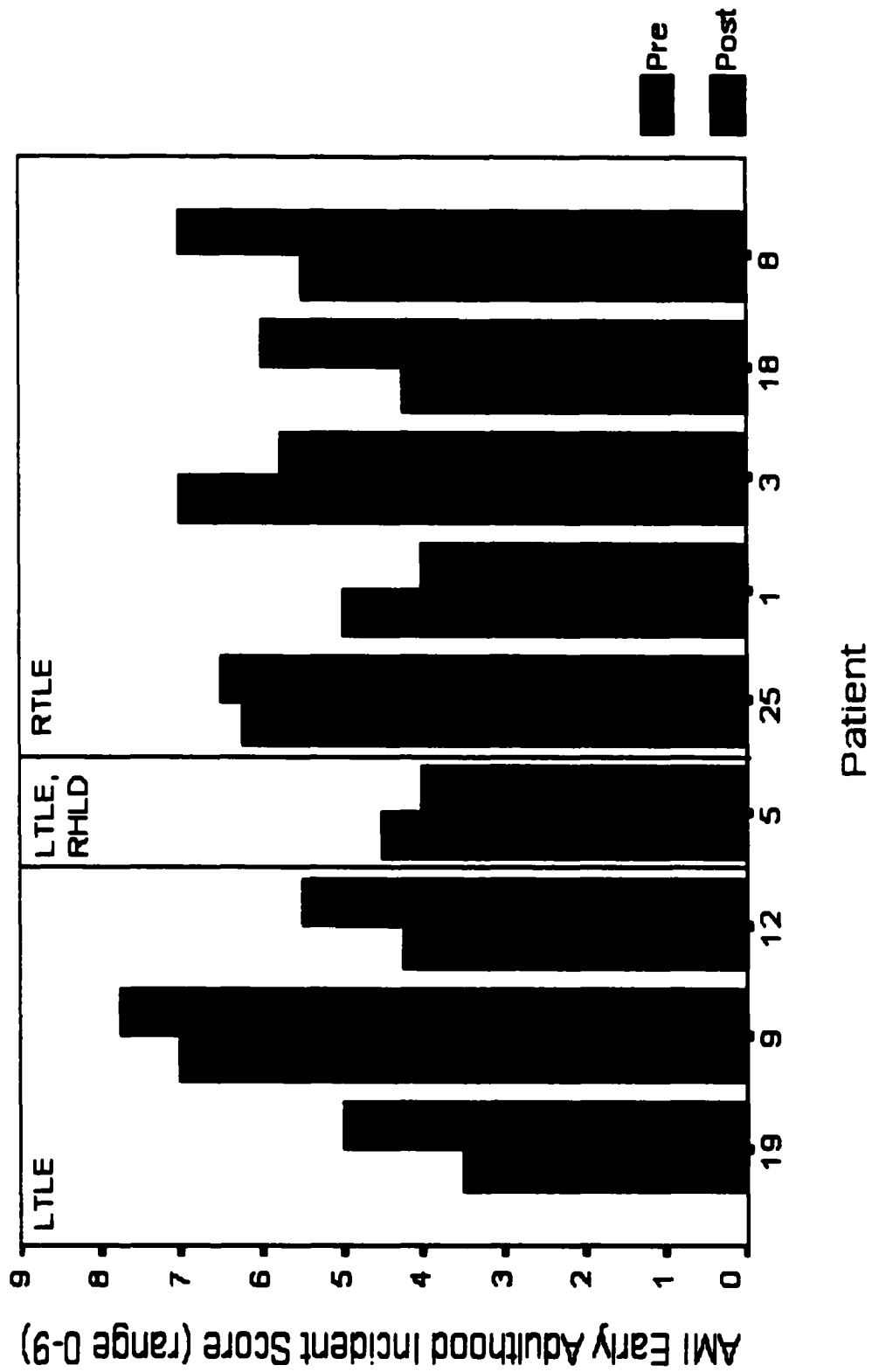


Figure 4. AMI Early Adulthood Incident Scores Pre and Post Surgery.

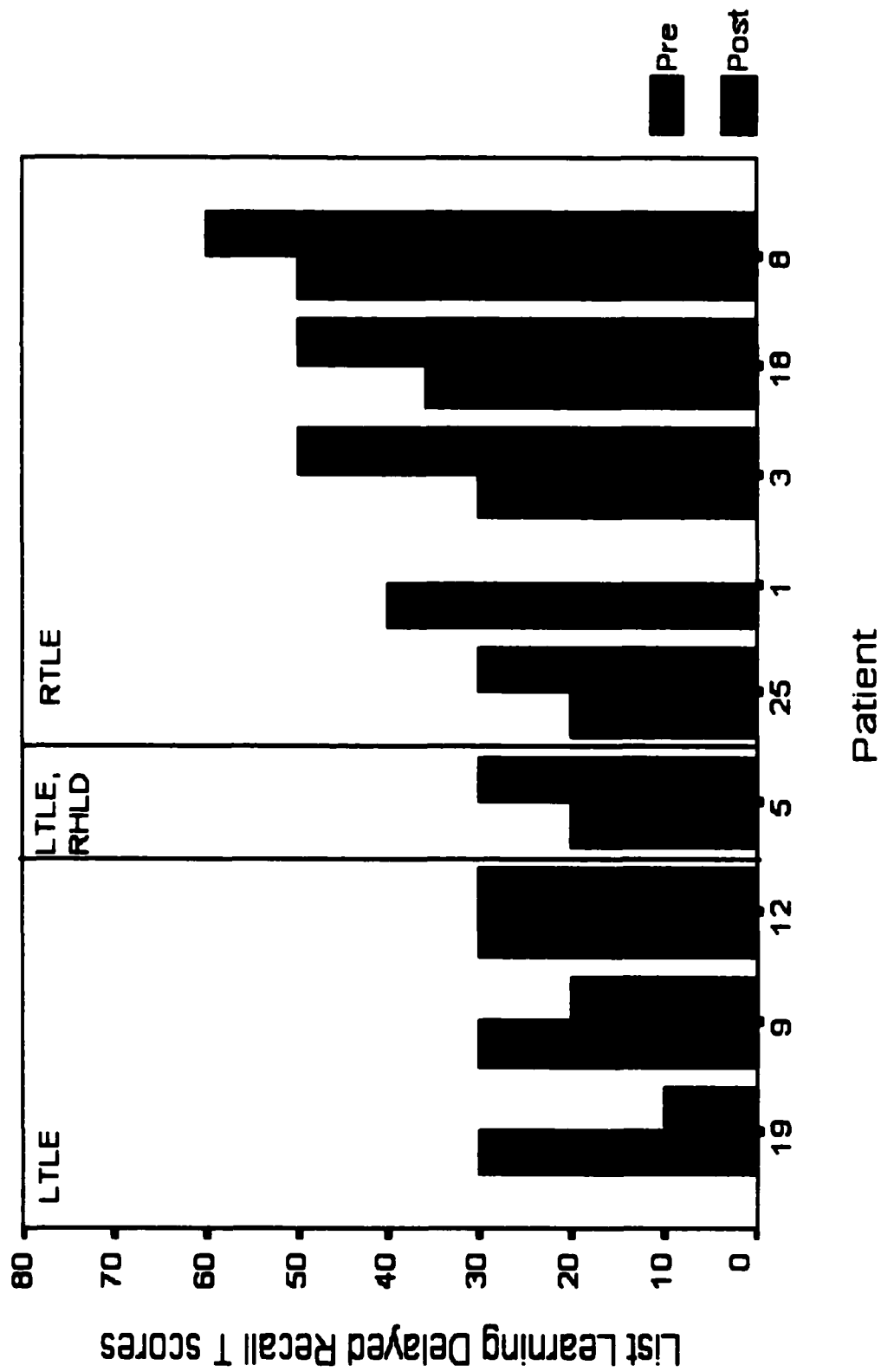


Figure 5. List Learning Delayed Free Recall T Scores Pre and Post Surgery₀

on normative reference data provided in test manuals. The mean scores were compared via paired t-tests and were not found to be significantly changed one year post-operatively from before surgery. However, a Fisher's exact probability test ($p = .08$) revealed a trend in the group data, in which the RT group showed an improvement on the logical memory subtest post-operatively, while the LT group tended to show a decline post-operatively (see Figure 6).

Only six (five RT and one LT) of the nine patients received the visual reproduction subtest of the Wechsler Memory Scale (WMS-R and WMS-III). Because different versions of the visual reproduction subtest of the Wechsler Memory Scale (WMS-R and WMS-III) were used across patients, t scores were calculated based on normative reference data provided in test manuals. The mean scores for the six patients were compared via paired t-tests and were not found to be significantly changed one year post-operatively from before surgery. Due to the small number of patients tested, group data could not be compared and is therefore described. There was an improvement in performance one year after surgery for three of the RT patients, and a decline in performance one year after surgery was evident for two of the RT patients and the one LT patient tested.

3.2.3 Subjective Memory Measures

ESI-55

Memory complaints as assessed by the ESI-55 memory trouble item were not significantly changed pre- to post-operatively (see Figure 7). Two of the three LT

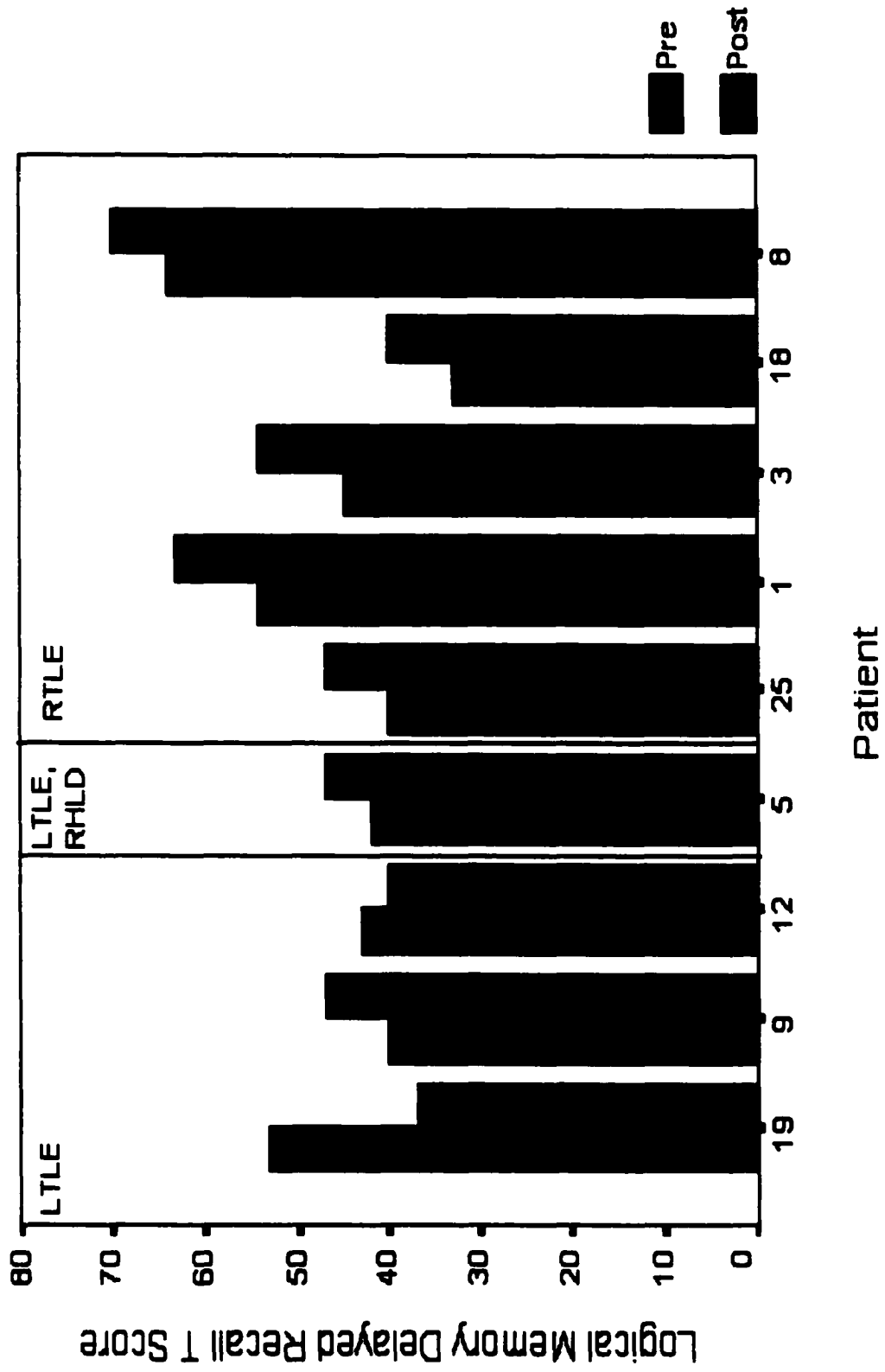


Figure 6. Logical Memory Delayed Recall T Scores Pre and Post Surgery. 72

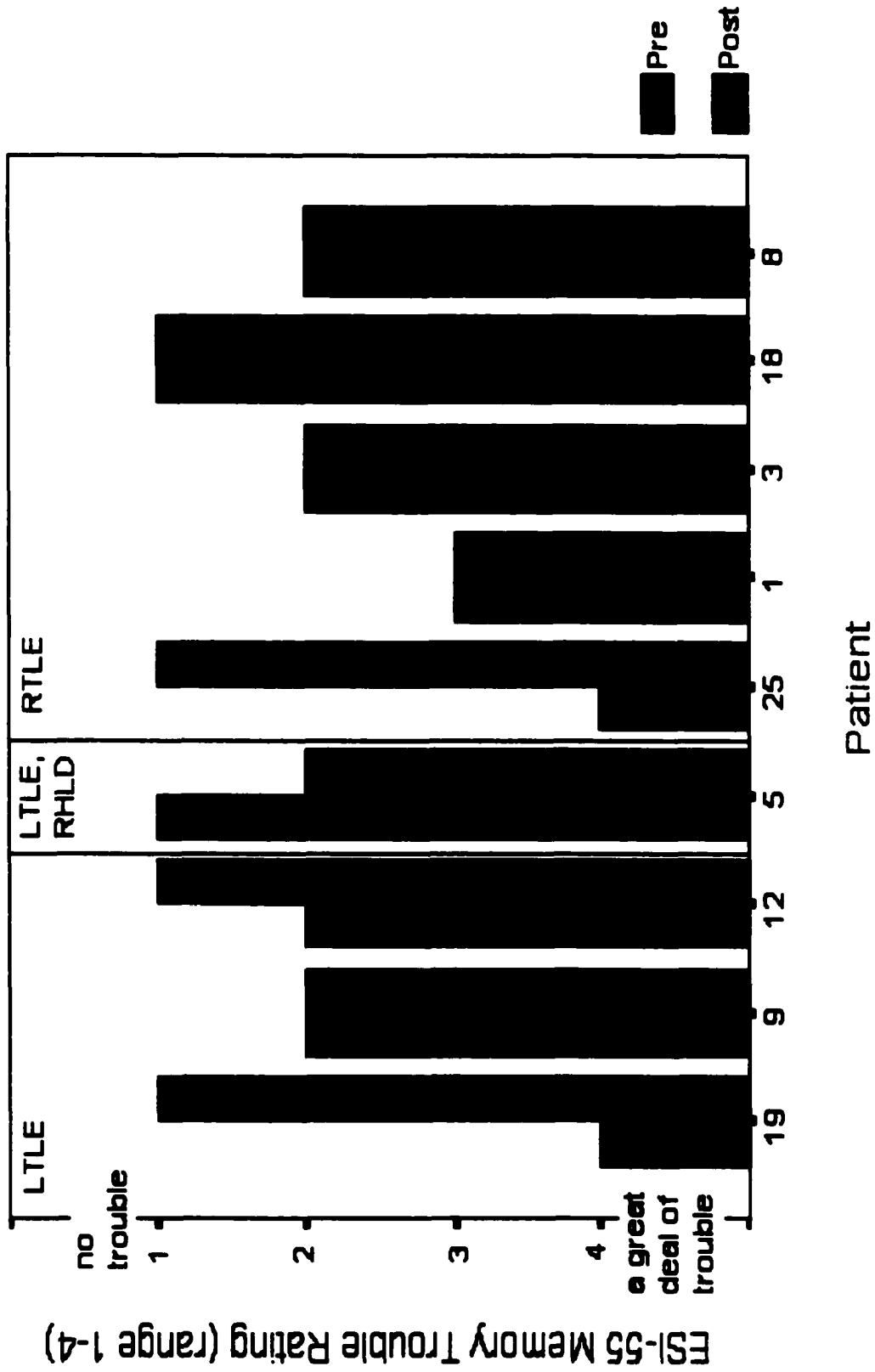


Figure 7. ESI-55 Memory Trouble Rating Item Pre and Post Surgery.

patients reported less memory trouble one year after surgery than before surgery, and one LT patient reported no change in his memory difficulties. These subjective reports were inconsistent with objective findings reported above that LT patients' memory performances tended to decline on conventional memory measures. However, the LT patients' reports of experiencing less memory trouble were consistent with their tendency to improve on autobiographical memory measures. RT patients indicated the following about their memory difficulties: four reported no change, one reported an increase and one reported a decline. This was also notable, as RT patients were found to decline on objective autobiographical memory measures, but improve on conventional neuropsychological verbal memory measures.

A Wilcoxon test comparing scores pre- and post-operatively on the role limitations due to memory problems scale of the ESI-55 revealed significant reports of improvement one year after surgery ($z = 2.02, p < .04$). Although one LT patient did not receive this measure pre-operatively, the group data showed that after surgery the remaining two LT patients indicated no change, one RT indicated no change, and five RT indicated improvement (i.e., less role limitations due to memory problems, see Figure 8). A Fisher's exact probability test revealed that this pattern of group performance was not significant. Because this memory item includes limitations also caused by speech and language, it is consistent that RT patients who improved on verbal memory measures would also report fewer role limitations due to memory, speech and language problems, as they showed poor performances on verbal memory measures one year after surgery. Because two LT patients showed poor performances on verbal memory measures one

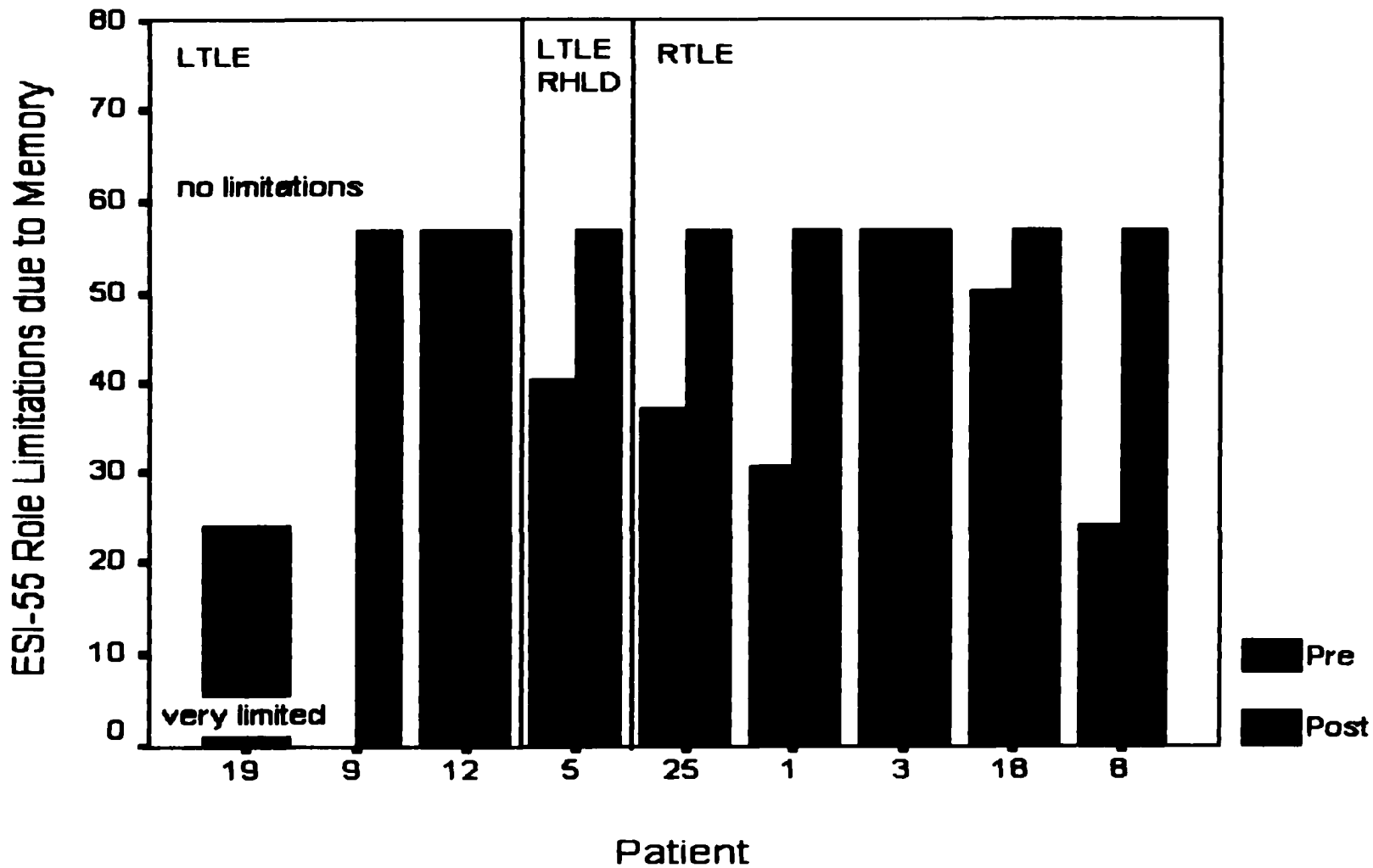


Figure 8. ESI-55 Limitations Due to Memory Scale Pre and Post Surgery.

year after surgery, it is remarkable that they did not indicate declines in role limitations due to memory, speech, and language problems.

SIME

One RT patient failed to complete the SIME pre-operatively. Of the remaining eight patients, six indicated a decline in memory for personal events one year after surgery on the SIME (see Figure 9). However, a Wilcoxon test did not reveal a significant change in patients' reports pre- to post-operatively on the SIME remembered- events total score. Subsequently, the SIME remote personal event items were separated from the recent personal event items. On the remote personal items of the SIME, six patients indicated a decline in memory for remote personal items one year following surgery (see Figure 10), but a Wilcoxon test revealed that this also was not significant. Scores on the SIME recent personal event items showed even greater variability. Four patients indicated improvement and four indicated poorer memory for recent personal events one year after surgery (see Figure 11).

Fisher exact probability tests analyzing the group data on the remembered event items of the SIME did not reveal any consistent patterns of group performance pre- to post-operatively. However, it was notable that on the total score and the remote events score of the SIME, four of five RT patients tested indicated a decline in their ability to remember personal events one year after surgery, which was consistent with their performance on the AMI. In contrast, only two of five RT patients indicated a decline in their ability to remember recent personal autobiographical events. Two of the three LT

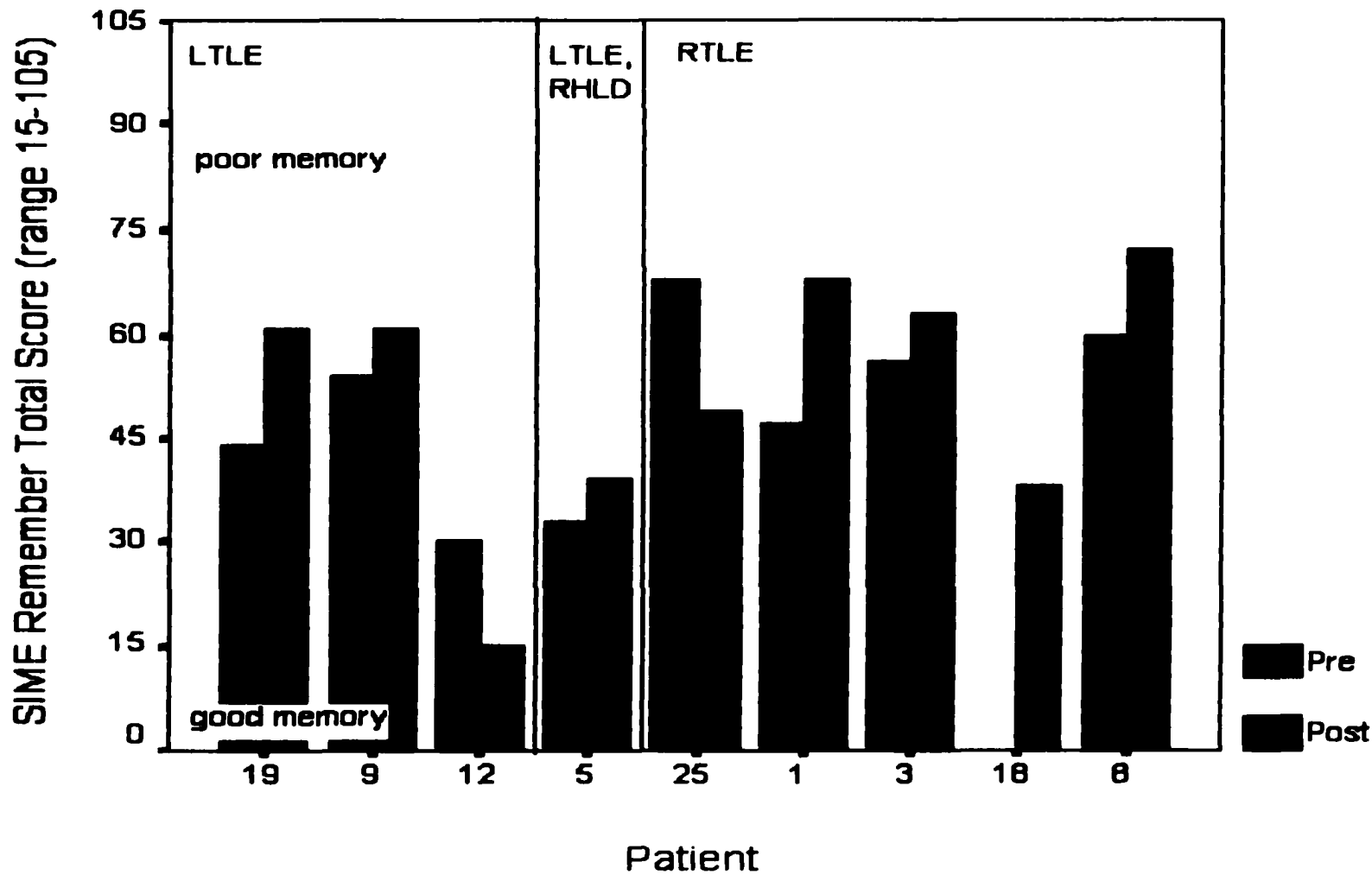


Figure 9. SIME Remembered Items Total Scores Pre and Post Surgery.

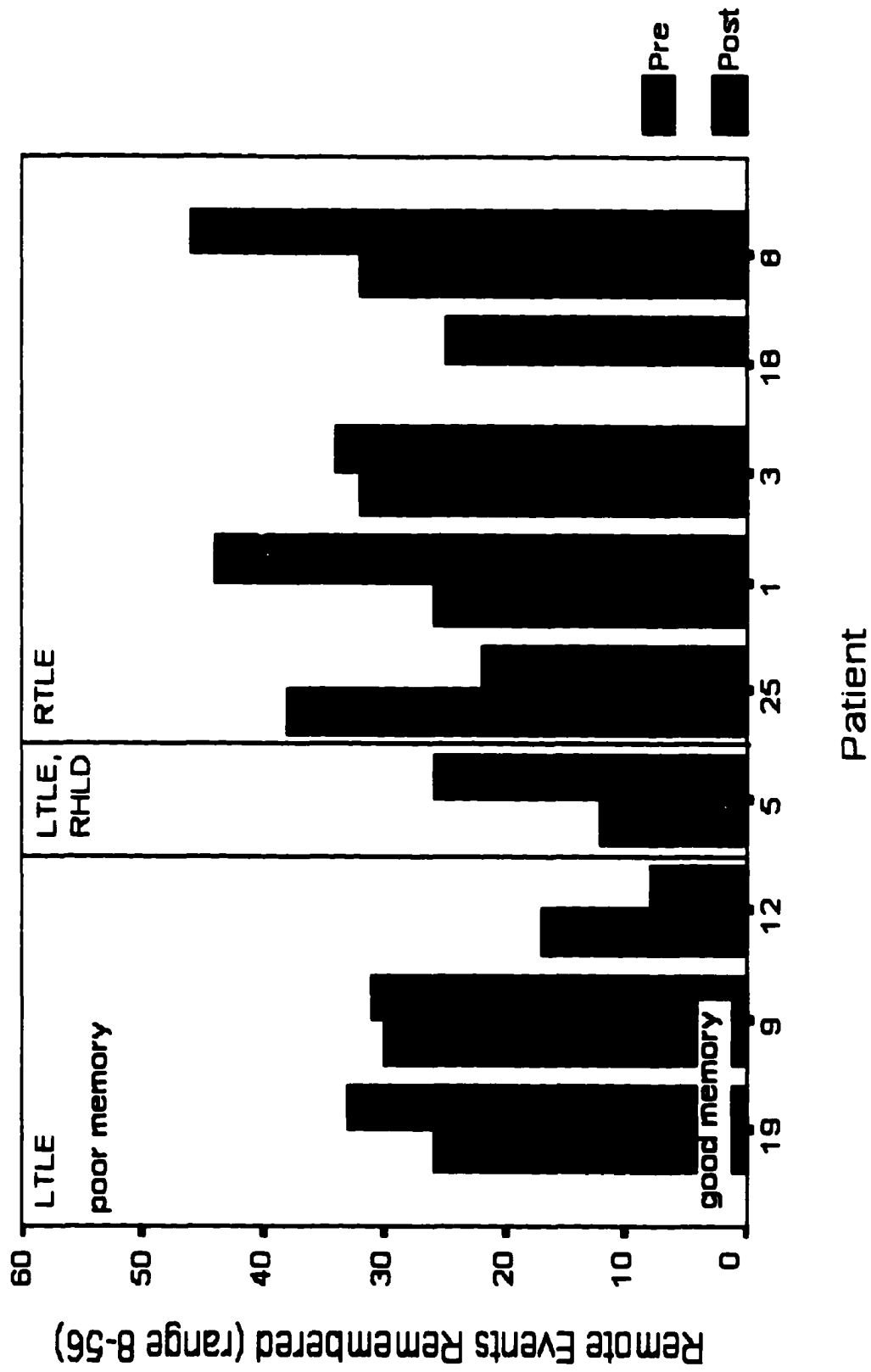


Figure 10. SIME Remote Remembered Items Score Pre and Post Surgery. ⁷⁸

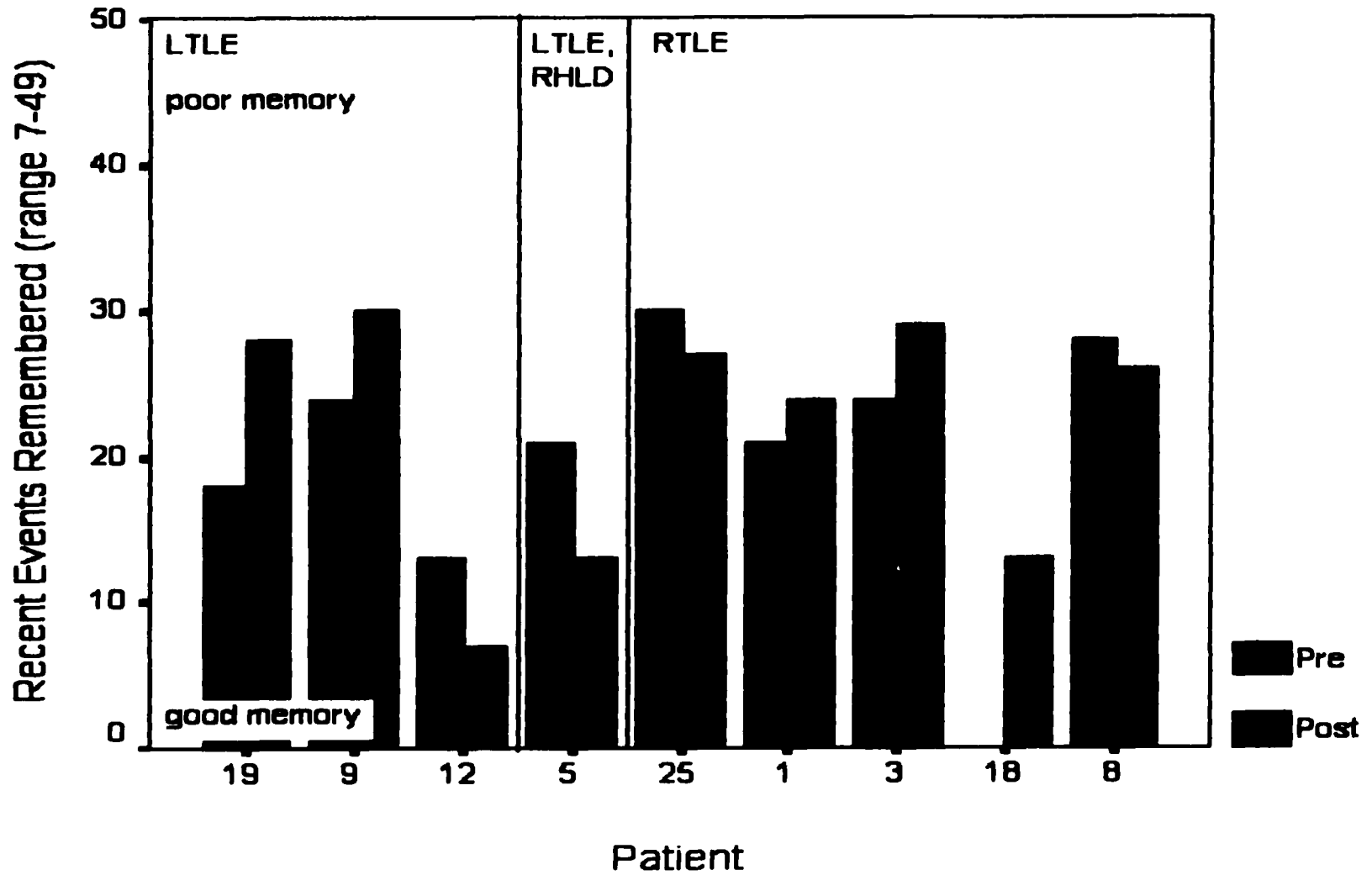


Figure 11. SIME Recent Remembered Items Score Pre and Post Surgery.

patients indicated a decline in their ability to remember remote and recent personal events one year after surgery, which was inconsistent with the slight improvement in autobiographical memory they demonstrated on the AMI.

A trend was found for the total forgetfulness score on the SIME ($z = 2.21, p < .07$). Overall, patients tended to be less forgetful one year after surgery than prior to surgery (see figure 12). However, a Fisher's exact probability test was not significant for RT and LT group performance differences. All three LT patients indicated a decrease in their everyday forgetfulness, and four of five RT patients also indicated a decline in their everyday forgetfulness. Subsequently, the forgetfulness items were separated into eight factors (i.e., rote memory, names, conversations, people, places, errands, absentmindedness, and retrieval). Wilcoxon tests revealed no significant change pre- to post-surgery in any of the eight forgetfulness factors. There were also no significant patterns of group (RT, LT) change pre- to post-operatively on forgetfulness factors as revealed by Fisher's exact probability tests.

3.2.4 Potential Influences on Memory Performance

Subject variables were examined to ascertain whether there were significant differences in age, education, age of seizure onset, duration of epilepsy, IQ, mood, or memory characteristics that were underlying RT versus LT group differences. Because there were so few patients tested both pre- and post-operatively, sample t-tests comparing the RT to the LT for age, education, age of seizure onset, and duration of epilepsy were not informative. Instead, the data are reported descriptively. Paired t-

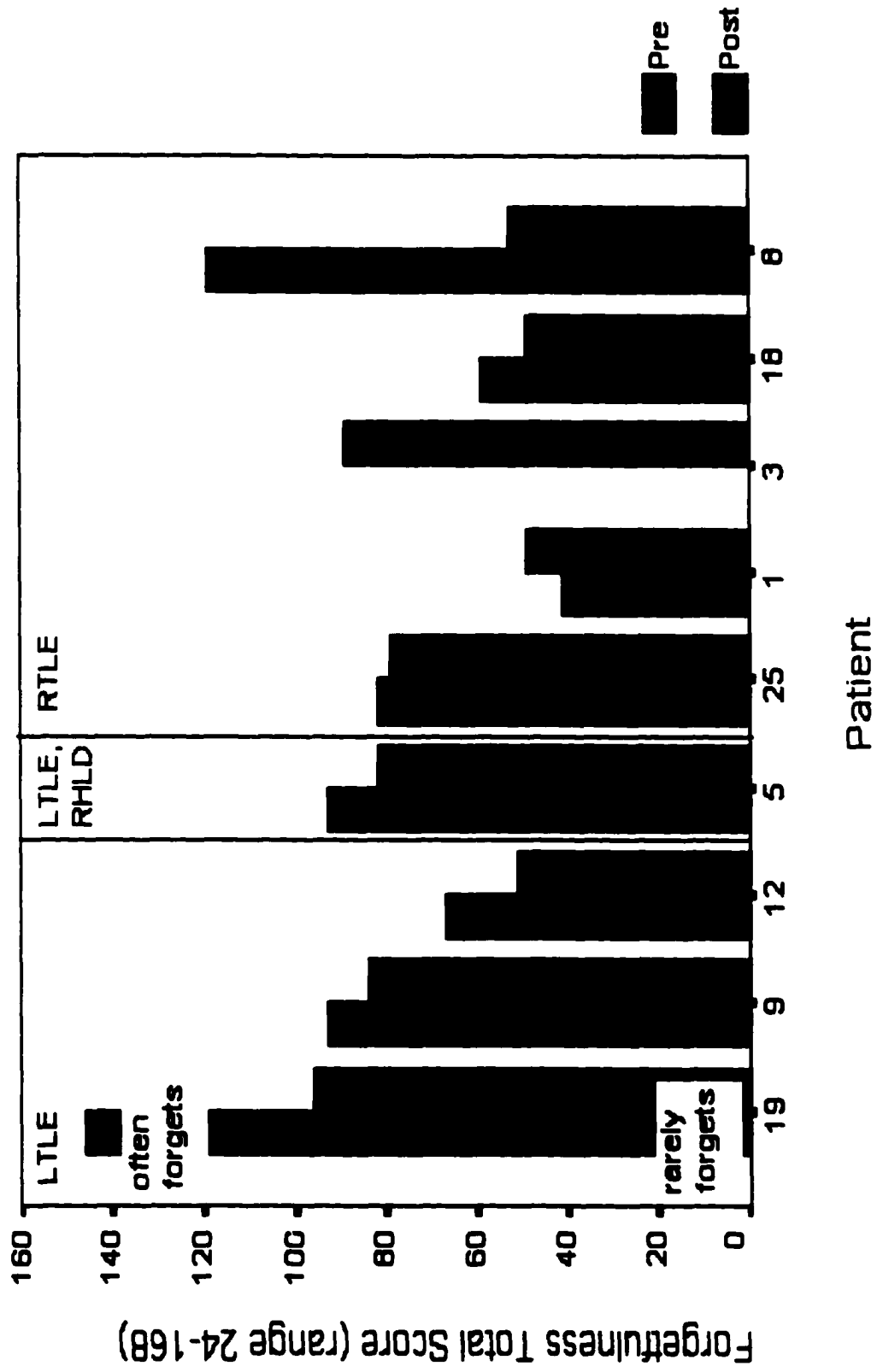


Figure 12. SIME Forgetfulness Items Total Scores Pre and Post Surgery.[∞]

tests for IQ, mood, and memory characteristics are reported and Fisher's exact tests were used to compare RT and LT performances on these measures.

Patient Variables

Table 5 presents the mean age, years of education, age of seizure onset, and duration of Epilepsy for the nine patients that were tested both pre- and post-operatively. There appeared to be no differences between RT and LT patients in age, years of education, age of seizure onset, or duration of Epilepsy.

IQ

Matched pairs t-tests revealed a significant improvement in patients' general intelligence as measured by the WAIS R/III FSIQ indices ($t = -2.78, p < .05$) and Performance IQ indices ($t = -3.50, p < .01$) from pre-operatively to one year post-operatively. There was no significant difference in Verbal IQ indices pre- to post-operatively. Descriptive data for IQ are displayed in Table 6. When the data was examined for group differences in IQ change pre- to one year post-operatively, Fisher's exact probability tests showed no significant differences between the RT and LT groups on measures of IQ.

Table 5. Patient Variables

	RT Patients (N = 6)	LT Patients (N = 3)	Total Patients (N = 9)
	M (SD)	M (SD)	M (SD)
<u>Patient Variables in Years</u>			
Age	34.67 (7.84)	38.00 (6.08)	35.78 (7.10)
Education	15.00 (3.10)	13.33 (4.16)	14.44 (3.32)
Age of Onset of Continuous Seizures	14.83 (9.41)	21.25 (17.76)	16.97 (12.02)
Duration of Epilepsy	19.83 (8.75)	16.67 (23.69)	18.78 (13.81)

Table 6. Pre- and Post- Operative IQ Data

<u>IQ Measures</u>	<u>Preoperative M (SD)</u>	<u>Postoperative (1 year) M (SD)</u>	
FSIQ (N= 8)	93.38 (16.94)	98.75 (17.08)	p <.05
VIQ (N= 8)	94.00 (18.33)	96.50 (19.50)	
PIQ (N= 9)	95.89 (14.62)	102.78 (12.86)	p <.01

Mood

Matched pairs t-tests that compared t scores pre- and post-operatively on a detailed questionnaire (SCL-90-R) regarding current symptoms were significant for anxiety ($t = 3.88, p < .02$) and global severity ($t = 2.92, p < .05$), but not significant for depression scales. Overall, patients were less anxious and demonstrated less global severity one year after surgery (see Figures 13 and 14). Fisher's exact probability tests revealed no significant differences between the RT and LT groups on the SCL-90-R measures.

Memory Characteristics

Wilcoxon tests showed that patients' mean ratings of their autobiographical memories on the AMI for saliency, surprise, emotion, accuracy, frequency of occurrence, and frequency reconstructed did not significantly change pre- to post-operatively. However, mean ratings for ability to picture events did change in that patients reported a significant increase in vividness of their autobiographical memories on the AMI one year after surgery ($z = 2.20, p < .03$). Memory rating characteristic means were separately calculated for memories during three broad time periods (i.e., childhood, early adulthood, and recent). Wilcoxon tests revealed that memory rating characteristics for vividness of childhood memories were also significantly improved one year following surgery from before surgery ($z = 2.02, p = <.05$). Wilcoxon tests revealed that memory rating characteristics for saliency of early adulthood memories were rated as significantly less salient ($z = 2.02, p = <.05$), one year post-operatively than pre-operatively.

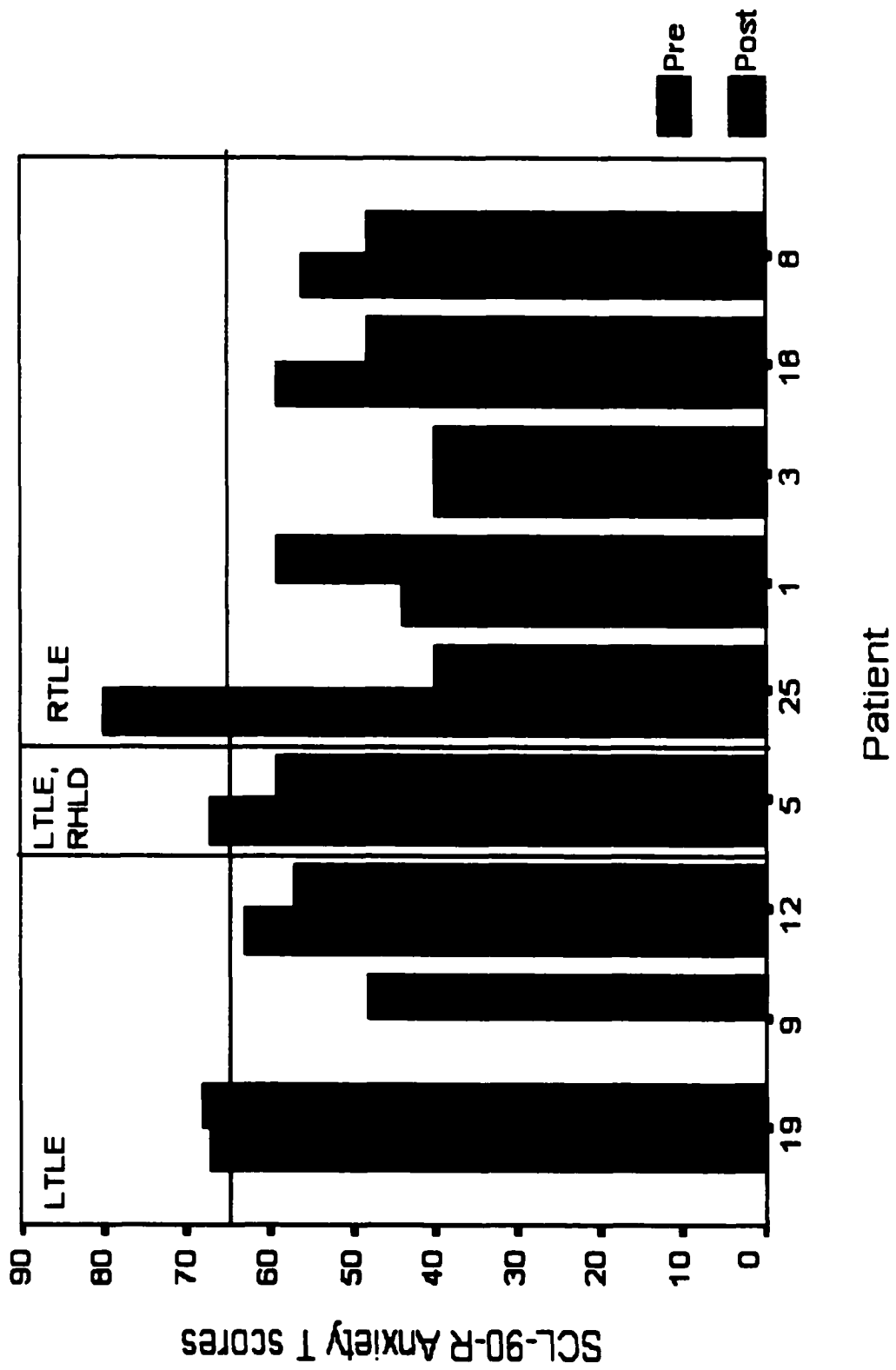


Figure 13. SCL-90-R Anxiety Index Pre and Post Surgery.

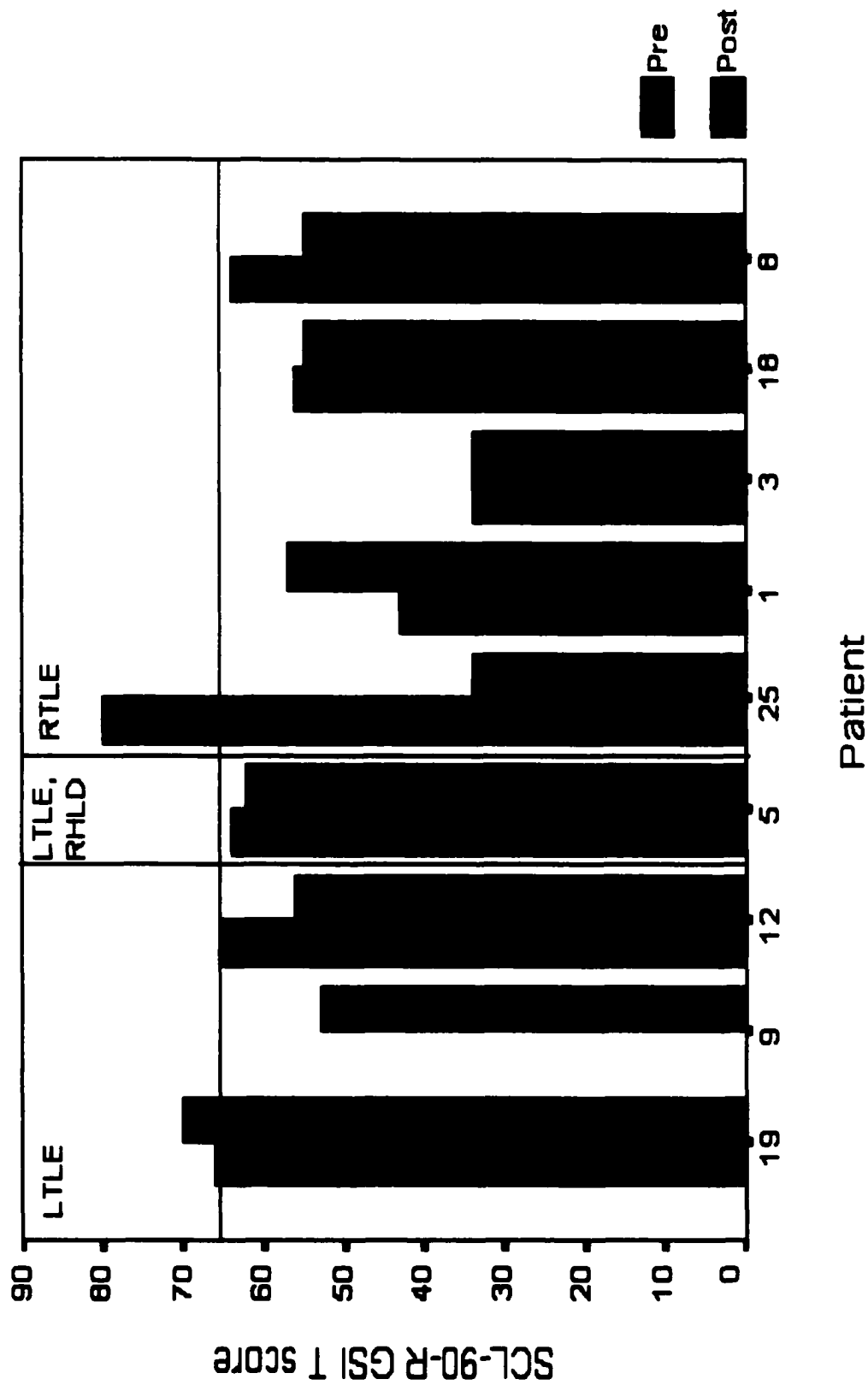


Figure 14. SCL-90-R Global Severity Index Pre and Post Surgery.

Wilcoxon tests revealed a trend in memory rating characteristics for recent memories such that memories were rated as less surprising ($z = 1.94$, $p < .06$) and more vivid ($z = 1.75$, $p = < .08$) one year after surgery than before surgery. Small sample sizes precluded comparisons between RT and LT memory characteristic ratings. Fisher's exact probability tests revealed a significant difference between the RT and LT groups for their ratings for saliency of early adulthood memories. LT patients' ratings for saliency were unchanged, while decreased levels of saliency were indicated by all RT patients for early adulthood memories. However, RT and LT patients' performances were variable on tests of early adulthood autobiographical memory on the AMI. There were no other group differences found for memory ratings.

3.2.5 Performance on the Wada Test and Post-Surgical Memory Outcome

For the nine patients who returned post-operatively, Wada test methods were compared to each other. A correct lateralization was found when a patient's contralateral "healthy" hemisphere outperformed based on the scoring criteria the ipsilateral "affected" hemisphere from which the seizures were thought to originate. Three patients (cases 5, 12, and 25) were correctly lateralized using the traditional Wada method, two patients (cases 3 and 12) were correctly lateralized using the autobiographical memory following recovery Wada method, and no patients were correctly lateralized using the autobiographical memory during anesthesia Wada method. For the nine patients, none of the three methods produced incorrectly lateralized findings (i.e., the "affected" hemisphere outperformed the "healthy" hemisphere), but many patients were reportedly

nonlateralized (i.e., no significant difference between the “affected” and “healthy” hemisphere). Overall, there was not a consistent difference in post-operative memory performance between the four patients (cases 3, 5, 12, and 25) who had lateralized findings on their Wada tests and those patients who did not. What is notable, however, is that patient 12, who was found to have lateralized findings on both traditional and autobiographical memory Wada test methods, showed little to no change after surgery on a number of memory outcome measures (see Figures 1, 2, 5, 6, and 8). This pattern of findings (little to no change) is consistent with what would be expected following surgery of an already dysfunctional region.

Wada test data was subsequently compared for the 28 patients deemed good surgical candidates. Mean age at time of Wada testing was 36.25 (SD, 8.26) and mean pre-operative FSIQ as assessed by the WAIS- R or III was 98.46 (all > 70; SD, 15.25). One patient was right hemisphere language dominant, four patients had bilateral language, and 23 were left hemisphere language dominant. Table 7 shows lateralization results elicited by three Wada testing methods (traditional memory testing following the injection, autobiographical memory testing following the injection, and autobiographical memory testing during anesthesia). The traditional memory testing method was the most accurate in that it elicited lateralized scores for 13 of the 15 patients and that all were in the correct direction. Both the traditional testing method and autobiographical memory testing method that followed the injection were similar in that they tested memory for what was presented during the injection period. However, asymmetrical performance for autobiographical memory items was poorer than that for traditional items.

Table 7. Calculations For Each Wada Test Method

Wada Method	Asymmetry Score
<u>Following Recovery</u>	
Traditional Wada with Memory Confidence Ratings	13 = correct lateralization 0 = false lateralization 15 = nonlateralized
Autobiographical Wada with Memory Confidence Ratings	7 = correct lateralization 3 = false lateralization 18 = nonlateralized
<u>During Anesthesia</u>	
Autobiographical Wada with Response Score Ratings	3 = correct lateralization 3 = false lateralization 22 = nonlateralized

Autobiographical memory items lateralized fewer patients (10/28) than the traditional method (13/28), and in three cases autobiographical items lateralized to the wrong side (i.e., the hemisphere opposite the side of suspected seizure onset). The findings for the autobiographical memory test method that occurred during the period of anesthesia were even less lateralizing (6/28), and three of those patients were lateralized incorrectly. However, it should be noted that the latter procedure was unlike the other two methods in that it combined performances on items that elicited very recent memories (for that day), recent memories (for last year), and remote memories (for childhood). Therefore, lateralized findings for this method may have been obscured by recall for different time periods.

3.3.1 Results for a Tertiary Objective: Conditions Underlying Confabulation

Conditions supporting a dysexecutive syndrome model and dual model of confabulation could not be compared due to the infrequency with which confabulatory responses occurred, the infrequency with which bilateral frontal dysfunction occurred, and the still greater infrequency of bilateral frontal and bilateral medial dysfunction.

Chapter 4

DISCUSSION

Many patients who undergo temporal lobe resection report memory problems and complain primarily of poor memory for personal events, e.g., forgetting vacations or conversations. However, conventional neuropsychological measures do not appear to provide an appropriate assessment addressing patients' actual concerns and experiences, and instead focus on memory for impersonal material. Therefore, autobiographical memory measures were added to pre- and post-operative neuropsychological evaluations and to Wada testing to determine whether autobiographical memory measures better evaluate patients' complaints. Autobiographical memory items from the AMI were used to measure memories for specific personal events that occurred across the life span. Personal event memories involve the recall of a circumscribed, moment-in-time event that includes thoughts, feelings, and sensory experiences (i.e., sensory images including visual, auditory, and olfactory images, or bodily sensations), as well as other specific details (e.g., date, place). In addition, a newly constructed self-report rating scale was added to assess autobiographical memory characteristics (e.g., saliency, vividness, emotion) and the

SIME was used to measure self-reported difficulties with autobiographical memory retrieval.

In addition to investigating the clinical utility of autobiographical memory assessment, this study examined the underlying neurological substrates of autobiographical memory. Autobiographical memory function was tested and compared under conditions of confirmed neuroanatomical damage, temporary anesthesia of brain regions, and resective brain surgery. An examination of the underlying neuroanatomy of confabulatory responding was also attempted, but confabulations were insufficiently frequent for empirical analysis.

4.1.1 Wada Test Findings Support a Consolidation Model of Memory Function

The findings of this study support the most widely held view, known as consolidation theory, that long-term memories initially occur in the medial temporal structures, and that as a result of voluntary and involuntary rehearsal over long periods of time, storage changes occur gradually so that retrieval becomes independent of these structures (Squire, 1987; Squire & Zola-Morgan, 1991; Squire, 1992; McClelland et al., 1995). Initial evidence for consolidation came from the study of H.M., a patient who after bilateral mesial temporal resection showed a selective memory deficit for material acquired shortly before the date of his lesion, suggesting medial temporal structures' involvement in retrieving recent memories. However, memory for very remote information was spared, suggesting remote memories had been consolidated in cortical sensory areas and were no longer dependent on medial temporal structures (Milner,

1966). This shift of structures is important in a memory system as explained by McClelland et al. (1995) who suggest a model of consolidation of memory that involves complimentary learning systems of the neocortex and hippocampal region. The neocortical processing system is a widely distributed pattern of neural activity that subtly changes in response to single experiences, whereas the hippocampal memory system is a sparsely distributed pattern of neural activity in which single experiences result in stable changes. McClelland et al. suggest that these subtle changes in the neocortical system do not generally lead to explicit knowledge of the processed information. Rather, the information processed in the neocortical system is generally responsible for implicit knowledge including acquired skills, perceptual representations, affective sensations, and semantic knowledge. In contrast, the information processed in the hippocampal system is the rapidly and explicitly learned contents of specific episodes.

In this model, the hippocampus is viewed as the teacher of the neocortical processing system. This teaching is a result of “interleaved learning” in which a particular item is acquired gradually, through a series of presentations interleaved with exposure to other examples from the domain. This allows for the generalization from one concept to another through a process that assigns each concept an internal representation that captures its conceptual similarity to other concepts. Therefore, the neocortex slowly learns to discover the structure in a group of experiences, while the hippocampal system permits rapid learning of new items without disrupting this structure. The hippocampal system permits the reinstatement of new memories and interleaves them with whole

structures of generalized experience in the neocortical memory systems. These structures of generalized experience are what Bartlett (1932) referred to as schemata. Percepts that are related to already constructed (cortically based) schemata are assimilated more rapidly and remembered more accurately, than those that are contrary to existing schemata.

Without the hippocampal system, contrary experiences and information could result in "catastrophic interference," where a single event could break down whole structures of generalized experiences (e.g., schemata) in the neocortex. Thus, the hippocampal system can rapidly learn the contents crucial for specific episodes and events, while changes (e.g., accommodations) in the neocortical system take a long time. Once a memory is stored in the hippocampal system it can be reactivated and reinstated in the neocortex. This reinstatement process may lead to the memory's consolidation in the neocortex. Thus, the role of the hippocampus is time limited in the formation of neocortical representations.

Additionally, McClelland et al. (1995) suggest that over time there is a decay of hippocampal traces. If the rate of decay is rapid in comparison with the rate of consolidation, much of the idiosyncratic content of individual episodes and events might not be consolidated at all. This race between hippocampal delay and interleaved learning therefore provides the mechanism that leads to the loss of idiosyncratic information (e.g., specific events), while what is common to many episodes and experiences tends to remain (e.g., semantic memories). However, if the idiosyncratic information is reinstated in the neocortical system frequently enough, it too will be recalled.

Even more important than the frequency with which events are reinstated are the relationships between the features of the events and the existing schematic structures. In autobiographical memory, schematic structures are thought to maintain continuity and coherence by categorizing and organizing aspects of experience (Bartlett, 1932).

Autobiographical schematic categories begin early in development (e.g., infancy) and lead to the development of a self-concept. The primary motivation for the organization of experience and memory becomes the maintenance of identity, continuity, and meaning (Bartlett, 1932). Schemas develop and result in a sense of predictability that allows for generalizations. Remembered autobiographical events are often those that are closely related to and maintain the integrity of existing self-schemas. Thus, autobiographical memory is a subsystem of episodic memory that contains self-related schema (Brewer, 1986). One aspect of self-schema is thought to develop from adults engaging children in memory talk, which indicates to the child the desired form and content of autobiographical memory. In this way, care-givers provide a scaffold for the structure and content of children's memory narratives. In addition, the sociocultural context in which these interactions occur bias perception and the reconstruction of autobiographical memory (Bartlett, 1932; Wang, 2001). Self-schema is theorized to allow for a sense of subjective experience of congruence and is constructed from self-knowledge, life themes, and sense of self (Reviere, 1996). Self-schema is also suggested to guide and facilitate retrieval of autobiographical memories, and studies find that material which is encoded with reference to self is generally more easily recalled (Strauman, 1990). Studies have also shown that autobiographical memories that are congruent with self-reported beliefs about

oneself are more readily recalled, while inconsistent details may be distorted or omitted in the interest of self-preservation (Loftus, 1993). In addition, our remembered past selves are colored by the current self that does the remembering. For instance, one often remembers oneself as more similar to who one is in the present (Engel, 1998). These findings suggest that schema bias perception and memory, and serve to maintain general themes or assumptions that provide a thread of continuity regarding the self throughout the lifetime.

In this investigation, recent and remote autobiographical memory items were presented during the Wada test for the first time. During conditions of temporary bilateral medial temporal dysfunction patients recalled remote events better than they recalled recent events. More specifically, when patients received injections contralateral to known mesial temporal sclerosis, they recalled events that occurred during childhood better than they recalled events that occurred during the last five years. In addition, recent events remained intact under conditions of unilateral temporal dysfunction and remote memories remained intact under conditions of both bilateral and unilateral dysfunction. These findings suggest that bilateral medial temporal structures play a temporary role in autobiographical memory retrieval of specific personal events, and that over long periods of time the retrieval of these memories eventually ceases to be dependent upon this region.

Numerous case study reports support consolidation theory, revealing that individuals with bilateral medial temporal damage exhibit a temporally graded retrograde memory loss with sparing of remote memories (Scoville & Milner, 1957; Penfield &

Milner, 1958; Butters & Cermak, 1986; MacKinnon & Squire, 1989; Squire, 1992; Squire & Alvarez, 1995; Rempel-Clower, Zola, Squire, & Amaral, 1996). However, a recent review (Nadel & Moscovitch, 1997) of additional case studies suggests the existence of a flat temporal gradient to autobiographical memories (Cermak & O'Conner, 1983; Damasio, Eslinger, Damasio, & Van Hoesen, 1985; Tulving, Schacter, MacLachlan, & Moscovitch, 1988; Barr, Goldberg, Wasserstein, & Novelly, 1990; McCarthy & Warrington, 1992; Warrington & Duchon, 1992). A flat temporal gradient shows that remote events are as poorly recalled as recent events. These latter case studies appear to suggest that medial temporal structures remain involved for as long as the memory exists. However, damage extending beyond the medial temporal structures of the patients studied (Damasio et al., 1985; Tulving et al., 1988) and the different methods used likely account for the disparity in the findings. For example, many cases that were reviewed by Nadel and Moscovitch examined public event memories (e.g., public events test, famous faces test) and personal semantic information (e.g., "Who was the best man at your wedding?") rather than autobiographical memories of specific personal events (Barr et al., 1990; McCarthy & Warrington, 1992; Warrington & Duchon, 1992). As described above, personal and non-personal semantic information that does not contain idiosyncratic content or is not related to self-schemata (e.g., details of when and where one learned the information, or the sensory perceptions, bodily sensations, and feelings associated with the event) rapidly decays in hippocampal structures and is either rapidly accommodated by existing schemas in neocortical areas or forgotten. If this is the case, then medial temporal damage should not affect non-personal or personal semantic memories that were

encoded prior to the damage because these memories are mediated by neocortical areas. Additionally, when using public events or materials as cues, it remains unclear when the subject learned the material because this information is subsequently read in books and viewed on television (Malamut, 1989).

Also, though some of the studies described by Nadel and Moscovitch (1997) did elicit autobiographical memories of specific personal events, they used a technique developed by Crovitz and Schiffman (1974) in which participants are given cue words and asked to produce a specific autobiographical memory in response to each word. This technique lacks the face validity of the AMI because the technique requires patients to respond to an artificial list of cue words (e.g., train, book, car), rather than to cues related to the organization of autobiographical memory. Findings from reaction time studies investigating the organization of autobiographical memory suggest that individuals integrate memories of specific personal events into extended-time lines (Anderson & Conway, 1993; Barsalou, 1988). These extended-time lines have been shown to have similar themes across individuals and include those life time periods found on the AMI, e.g., events from grammar school, events from the first job, events from a recent vacation. In addition, the arbitrary cues used by Crovitz and Schiffman do not contain cues for events that occurred across the life span (Kopelman et al., 1989). A number of investigations using Crovitz and Schiffman's technique revealed that memories were not recalled from all decades with equal frequency (Malamut, 1989). Therefore, findings based on the Crovitz and Schiffman technique failed to adequately sample recall of events

from both recent and remote time periods. This truncated sampling of events likely explains why the investigators found a flat temporal gradient.

4.1.2 The Clinical Utility of Autobiographical Memory Items During Wada Testing

In this investigation, the utilization of autobiographical memory items during the Wada test supported the consolidation theory of memory. However, autobiographical memory testing during the Wada test did not appear to be a useful clinical measure because it did not lateralize memory dysfunction to the side of suspected seizure onset. In retrospect, this was likely due to the multiple types of autobiographical memory items that were included in the final autobiographical memory Wada score. Specifically, the remote memories were found to be dependent upon cortical areas rather than on the medial temporal structures that the Wada test aims to assess. Additionally, the items which asked about events from that morning (e.g., “What did you have for breakfast today?” “What time did you wake up today?”) were likely less meaningful to the patients than were specific personal events (e.g., “What memorable event occurred during your last vacation?”). For instance, information about what one had for breakfast and what time he awoke on a particular morning is likely trivial and, thankfully, more susceptible to forgetting than a salient personal event; it would be overwhelming if individuals could recall these trivial events with the same kind of clarity that they recalled salient personal event memories. Most individuals can recall what they had for breakfast this morning, but few people who vary what they eat can recall what they had for breakfast last Tuesday. For the most part, everyday habits are shallowly processed and quickly

forgotten. The hippocampal traces rapidly decay and what is common to many meals or "wake-ups" will be consolidated in neocortical areas to form semantic memories.

Additionally, these trivial memories have little to do with ones self-concept. However, if some meaningful event, like food poisoning, occurred then the idiosyncratic information would be reinstated in the neocortical system frequently enough to be recalled and features of the event may be related to part of ones self-schemata (e.g., times I was sick).

In the future, these trivial event items and the remote items should be eliminated from autobiographical memory testing for clinical purposes and replaced by a larger number of meaningful recent autobiographical memories. The consolidation model of memory suggests that it is the meaningful recent autobiographical memories that are initially supported by the medial temporal lobes. Therefore, future Wada testing for lateralization of memory function should assess memory specifically for these items.

In addition, the consolidation findings of this investigation suggest that the photographs of familiar people in the patients' lives should also be modified. During one injection patients were shown a picture of their neurologist and during the other injection the same patients were shown a picture of a family member. The family member was often someone the patient had known for several years (e.g., a spouse, a parent), however, the neurologist was someone they had met only recently or someone they had also known for years. Additionally, semantic memory is more likely responsible for recognition of pictured individuals presented during the Wada procedure. Exposure to the pictures likely results in the excitation of a semantic representation of that item, but not

necessarily in an episodic memory that includes a particular context, setting, and circumstance.

In summary, the use of recent and remote autobiographical memory items in this investigation supported a consolidation theory of memory. However, because salient, recent autobiographical memories were found to be more dependent on medial temporal structures than were remote memories, future Wada testing should increase the number of meaningful recent autobiographical memory items presented during the amobarbital effect. This new method will allow for a more ecologically valid clinical technique, as it would test those recent specific personal event memories with which, post-surgically, patients report difficulty (e.g., recent vacations and conversations).

Another methodological problem inherent in the testing of autobiographical memory was that the testing required both verbal comprehension (e.g., “What memorable event occurred during high school?”) and verbal expression (e.g., “I fell off the roof and broke my arm two or three weeks before going on spring break”). Because the dominant hemisphere injection results in the temporary loss of language (both expressive and receptive), autobiographical memory testing began after the patient regained language abilities, at which time the drug effect had diminished substantially. On average, the time between injection to the left hemisphere and presentation of autobiographical memory items exceeded the time between right injection and presentation of those items by one minute. This suggests that patients were under a greater medication effect during autobiographical testing following right injections than they were following left injections. Nevertheless, chi square analyses comparing left versus right hemisphere performance

during autobiographical memory testing were not significant, suggesting that patients remained under sufficient drug effect with both injections. In addition, post-operative findings in this study suggest that right medial temporal structures might play a greater role in autobiographical memory than left medial temporal structures. Nevertheless, autobiographical memory performances were not significantly better following left injections than were performances following right injections.

This lack of difference between left and right hemisphere performance may have been due to the effect of the amobarbital on anterior regions of the brain's circulation. The complexity of autobiographical memory retrieval appears to require evaluative processes that have been found to depend on left frontal functions (Conway et al., 1999). Although the patients in this study received elaborated cues when they failed to retrieve the target memory on their own, the cues may not have been distinctly detailed enough to bypass the generative retrieval phase. Further research with the provision of more distinctive cues is necessary. Alternatively, on rare occasions patients receive selective injections during Wada test procedures in which a tiny balloon is inserted to occlude the perfusion of the amobarbital into the anterior circulation. This procedure allows the neuropsychologist to test memory function while only the medial temporal regions are anesthetized and other areas remain relatively unaffected. Therefore, even with a left injection, language and the proposed generative system of autobiographical memory would remain intact while the medial temporal areas that correspond more closely to areas to be resected would be temporarily dysfunctional. Because selective injections carry a substantially higher risk they are performed only unilaterally, and therefore differences

between memory performances of the left and right hemispheres would have to be assessed between individuals rather than within the same person.

Another flaw in the current study's methodology was the failure to counterbalance the order of recent and remote items presented during the Wada test. Patients in this study were asked first about something that occurred that morning, then about a recent event, and finally about a remote event. Since the drug effect was diminishing over time, one might conclude that remote events were better recalled because patients were under less of an effect from the anesthesia. However, it was notable that when injections were ipsilateral to known mesial temporal damage, there was no difference between patients' ability to recall recent and remote events. If the difference found between recent and remote event memory during temporary bilateral medial temporal dysfunction was simply due to the diminished drug effect, the same difference should have been found with the ipsilateral injection.

4.2.1 The Effect of TLE Surgery on Autobiographical Memory

Another purpose of this study was to examine autobiographical memory processes in patients with TLE. The AMI was used to measure autobiographical memory pre- and post-surgery for events that occurred throughout an individual's lifetime. The underlying assumption was that, following surgery, patients' complaints for memory problems were related to declines in autobiographical memory not detected by conventional neuropsychological memory measures. It was shown that autobiographical memory performances one year after surgery tended to be worse than performance had

been before surgery. Although this was the predicted finding, further examination of the data revealed that declines were found in the larger group of patients who underwent right AMTL, while the few patients who underwent left AMTL improved slightly on autobiographical measures. Therefore, until more patients are tested post-operatively, it remains unclear whether autobiographical memory declines following AMTL or whether autobiographical memory relies primarily on non-linguistic memory features, the latter indicating a material-specific decline following right AMTL.

4.2.2 Limitations of Self-Report Measures

There were not enough patients tested post-operatively to establish whether the self-reported memory problem measures from the ESI-55 and SIME correlated better with autobiographical or conventional objective memory measures. However, two of the three LT patients' reports of experiencing less memory trouble post-operatively were consistent with their tendency to improve on autobiographical memory measures, but were inconsistent with their decline on conventional memory measures. Until more LT patients are evaluated post-operatively, it is difficult to know what the findings mean. The larger group of RT patients generally indicated no change in their memory difficulties following surgery. It may be that their self-appraisal of no change in memory problems was a balancing out of improvement in verbal memory and decline in autobiographical memory. Another possibility is that, following right resections, patients have been found to be more indifferent to problems and difficulties (Bear & Fedio, 1977; Davidson, Smith, Tamny, & Fedio, 1996). In this investigation, the patients who underwent right AMTL

reported no change in their memory difficulties, while on objective testing there were declines in autobiographical memory. This may suggest that the patients minimized the change in their difficulties.

The ESI-55 “role limitations due to memory problems” scale suggested improvement in memory one year after surgery. These improvements were seen in five of the six RT patient reports. However, because this memory item includes role limitations also caused by speech and language, it makes sense that RT patients who improved on verbal memory measures would also report fewer role limitations due to speech, language, and memory problems.

In contrast to ESI-55 self-reports, self-reports elicited on the SIME (e.g., “Rate how well you can recall the first time you earned your own paycheck”) by RT patients following surgery indicated a decline in their ability to remember personal events, particularly those that were remote (e.g., “Rate how well you can recall your first friend”). This finding was consistent with their performance on the objective autobiographical memory measure (AMI). The SIME, like the ESI-55, requires patients to evaluate their memory function, but the SIME might better help the patients to consider their memory function because it provides specific circumstances under which to make these judgements. This provision might have helped the patients to make more accurate judgements about their memory function.

4.3.1 Autobiographical Memory Relies Strongly on Non-Linguistic Functions

All six patients with right temporal dysfunction showed a decline one year after surgery from pre-operative performance. In contrast, the few LT patients tested post-operatively showed a slight improvement. Although this group finding was unanticipated, if it is reliable (shown with a larger number of post-operative patients) it may be consistent with Brown and Kulik's (1977) theory that autobiographical memories are not primarily a narrative or verbal form, but one of images. Brown and Kulik termed these autobiographical memories "flashbulb memories" because of their long lasting and highly vivid qualities that are almost perceptual and contain event-specific sensory-perceptual details that are typically lost from memories of other, less consequential experiences. However, personal event memories are not limited to visual-perceptual images, but include additional sensory experiences such as sounds, smells, and bodily sensations. For example, when asked about a memorable event that occurred during a recent hospital visit, a patient who was status post left AMTL provided the following autobiographical memory:

Being awakened during surgery. I think I woke up early, earlier than they expected, and they were still actually working on my head. And I remember, because of the meds, how dry my mouth was, and I had a hard time talking. I think the funniest thing was that while they were testing me they had the ear plug in my right ear, and the thing in front of me, and I guess the testing was going well because the doctor starting talking above me. And I had to actually stop altogether. Because when they were doing

the testing with the earplug, I couldn't hear what was coming into my right ear, cause they were talking into my left ear. And I couldn't shout out, or call out, so I just stopped answering altogether. And they actually rolled the camera away and they said, "Is everything okay?" It was Dr. Hamberger, and I said, "They have to stop talking 'cause I can't hear anything." So they asked everyone to be quiet and oh god I remember it all.

In contrast to this detailed, momentous response, a patient who underwent right AMTL provided the following vague response when asked about a memorable event that occurred during his last vacation: "I went to Italy. I spent the whole time on the beach, and I became close with my cousins that I didn't really know." When asked whether he could recall any particular event that occurred while he was in Italy, he responded that he could not. This was remarkable, because before surgery the patient had described the following experience from the trip: "I saw Mount Etna. It was interesting, unbelievable, to see it erupting in front of us. It was guzzling and the floor was warm."

These phenomenological features of memory, e.g., seeing, feeling, experiencing, might depend upon right medial temporal structures. Researchers using imaging techniques have found that autobiographical memories appear to be represented in those sensory-perceptual regions of the brain involved in their original processing which, for the most part, appear to be in the posterior right hemisphere (Fink et al., 1996; Conway & Turk, 1999; Nyberg et al., 1996).

Some investigators have suggested that the right medial temporal areas are related to spatial and object representations (Pigott & Milner, 1993; Breier et al., 1996), and it is argued that these types of associations are necessary for represented scenes (Mayes & Roberts, 2002). Kopelman and Kapur (2002) have suggested case study evidence reveals that the retrieval of autobiographical incidents depends more upon the integrity of right temporal lobe structures. They point to a study by O'Connor, Butters, Miliotis, Eslinger, and Cermak (1992) in which a patient who had extensive damage to the right medial temporal structures following a herpes encephalitis was found to have a severe autobiographical memory impairment. The patient also had visuoperceptual deficits, which was argued to have led to a particular difficulty conjuring up the visual images necessary for the retrieval of past autobiographical experiences.

Therefore, it may be that autobiographical memory taps into non-linguistic, sensory-perceptual memory abilities in a way that conventional neuropsychological tests have failed to do. While many researchers have found a material-specific decline in verbal memory on conventional neuropsychological measures following left temporal resection, few have found substantial change to visual memory using conventional neuropsychological measures following right temporal resection (Loring, Hermann, Lee, Drane, & Meador, 2000; Barr et al., 1997; Chelune, Naugle, Luders, & Awad, 1991; Gleibner, Helmstaeder, & Elger, 1998; Loring, Lee, Martin, & Meador, 1988). For instance, Barr et al. (1997) reported that findings from their multi-center retrospective study revealed no difference between left and right temporal lobe epilepsy patients' performances on conventional figural memory tests (e.g., WMS-R visual reproduction,

Rey Complex Figure Test). Lack of a decline in memory for unfamiliar faces and memory for nonsense figures following right AMTL has also been documented (Hermann, Connell, Barr, & Wyler, 1995). Additionally, a study investigating the relationship between hippocampal MRI volumes and visual memory performance on the visual reproduction test of the WMS showed no correlation between the two (Martin et al., 1999). These findings taken together suggest that conventional non-verbal memory tests fail to measure the memory functions of the right medial temporal structures.

The current study revealed that following right AMTL autobiographical memory diminishes further, whereas following left temporal resection autobiographical memory slightly improves. This finding suggests that personal event memories may rely more on right than on left medial temporal structures. If this turns out to be the case with a larger post-operative patient group, then material-specific declines for the right hemisphere will be demonstrated in a way that conventional neuropsychological testing has failed to demonstrate thus far.

A contradictory finding in the current investigation was that patients reported an increase following surgery in their ability to picture or imagine autobiographical events on a newly constructed self-report rating scale. This self-reported finding is inconsistent with the explanation posed above that resection of right medial temporal regions leads to a particular difficulty in conjuring up the visual images necessary for the retrieval of past autobiographical experiences. However, most of the self-reported memory characteristics (e.g., saliency, level of emotion, surprise, frequency thought about) failed to match up with scores on the AMI. Therefore, patients were likely unable to be introspective in the

way the examiner had hoped. In the future, initial training items will be added so that patients will have some understanding of what the examiner believes the ratings are meant to assess. For instance, prior to obtaining self-reported rating characteristics of personal events, the examiner would discuss events, such as the space shuttle Challenger explosion, and provide examples of what a rating of 1, 2, 3, or 4 on the vividness scale, or some other scale (e.g., emotion, surprise) would imply.

4.4.1 Suggestions of Validity in Findings

Whereas many of the performances by patients in this investigation were expected, they are worth pointing out as an indicator that there was nothing unusual about the group of patients assessed in this study.

Performance on the AMI

On pre- and post-operative testing, patients with unilateral damage to the temporal lobes demonstrated difficulty with remote memories. However, they showed improvement in their recall of an event the closer in time to the present it occurred. Whereas, overall, patients performed poorer than normal controls, the difference between remote and recent scores were similar in both groups. The AMI presents cut-off scores based on the performance of 34 healthy controls in which a score of six out of a possible nine points for childhood memory items is in the acceptable range, while for young adulthood and recent memory items, a score of six out of nine points is in the borderline range (Kopelman, 1989). It was expected that patients with unilateral temporal damage

would perform in a pattern similar to, although poorer overall than, normal controls. It is reasoned that only under conditions of bilateral medial temporal damage would patients show better remote than recent memory retrieval.

In contrast to this investigation's findings on the AMI, studies have emerged in which TLE patients with unilateral dysfunction were reported to demonstrate flat temporal gradients on autobiographical memory measures such that impairment in autobiographical memory for remote as well as recent memories was evident (Barr et al., 1990; Vitkontas et al., 2000). However, as noted, flat temporal gradient findings may be attributable to the assessment of personal semantic memories, only remote personal event memories, or personal event memories from truncated life-time periods. Also, though the findings of Vitkontas et al. (2000) were reported as representing a flat temporal gradient, the graph of their findings revealed a positive slope where patient performance was better on recent than on remote items. This pattern of findings was similar to that found with current testing. The current findings, along with the findings of Vitkontas et al., suggest that left and right temporal lobe epilepsy patients show a similar pattern to, although poorer performance overall than, normal controls on tests of autobiographical memory.

Conventional Memory Measures Reveal Material-Specific Declines for Verbal Material

In the current study, RT patients improved on conventional neuropsychological memory measures including list learning and story memory, whereas the LT patients declined in those conventional neuropsychological verbal memory measures. This difference between performances of patients with left and right temporal dysfunction on

conventional verbal neuropsychological measures was consistent with material-specific memory deficits. Material-specific difficulties is a common finding in individuals with dominant (left) medial temporal dysfunction or temporal lobe resection. The literature shows that verbal memory function changes after left AMTL surgery. Verbal memory has been found to improve following right AMTL and to decline following left AMTL (York et al., 2003; Rausch et al., 2003). As noted above, comparable decrements in visual memory on conventional neuropsychological measures have been less consistent after right AMTL (Loring et al., 2000; Gleibern et al., 1998; Barr et al., 1997; Chelune et al., 1991). When improvements have been shown post-operatively, they have been attributed to (1) a reduction in 'interictal' EEG abnormalities that disrupted their ability to attend and encode material pre-operatively, (2) reduced AEDs, and (3) the role of practice effects on cognition. Additionally, Rausch (1991) suggested that the often reported lack of increased deficiencies after right temporal lobe resection may indicate greater functional plasticity of the right temporal lobe.

FSIQ and PIQ Improves Post-Operatively

Another common finding in TLE patients following resection, regardless of side of surgery, is improvement in PIQ and FSIQ (Chelune, 1991). This finding was evident in this investigation as well.

Findings Do Not Appear to Be Due to Confounding Subject Variables

A number of factors are suggested to influence neuropsychological outcome after AMTL. Factors include subject variables such as age, age at onset of continuous seizures, duration of epilepsy, level of cognitive function, continued seizures after surgery, and mood (Hermann, Seidenberg, Haltiner, & Wyler, 1995). Though the subject group was too small for empirical analysis, the data were examined for patterns between subject and grouping variables. There was variability in age, age of seizure onset, and mood for individuals in both the LT and RT groups. There did not appear to be a difference between the LT and RT groups in pre-operative IQ. In addition, there was no apparent difference in LT and RT patient groups in their continued epileptic activity after surgery. Such a finding may have suggested that current epileptic activity caused impaired retrieval of earlier encoded memories. Regarding mood, Kopelman and Kapur (2002) raise the question of whether autobiographical memory loss in individuals is related to their current emotional states (e.g., extreme arousal or depression). They suggest that if the stress is severe, the individual's sense of self and identity is diminished, resulting in a lack of autobiographical awareness. The change of autobiographical memory recall abilities for patients in this investigation did not appear to be related to change in emotional state. Measures of anxiety and global severity on the SCL-90 were generally diminished one year after surgery for both LT and RT patient groups.

4.5.1 Inconclusive Findings for the Role of Anterior Structures in Autobiographical Memory Function.

Although some research supports the involvement of right prefrontal cortical areas in autobiographical memory retrieval (Nyberg et al., 1996; Buckner, 1996; Fink et al., 1996), other investigations support the involvement of left frontal areas in autobiographical memory retrieval (Conway & Turk, 1999). It was hypothesized that better autobiographical memory retrieval would be demonstrated during right injections, since left anterior structures remained functional and theoretically underlie the generative processes of search, evaluation, and cue elaboration. However, the current investigation failed to reveal any significant differences between left and right anterior hemisphere dysfunction (i.e. ACA and MCA perfusion) and autobiographical memory retrieval under different circumstances (i.e., with a general cue and after elaborated cues). It is likely that the perfusion of amobarbital to a large portion of each hemisphere confounded the comparison of the role of right and left anterior structures. Because posterior (and apparently medial) temporal sections of the right hemisphere appear to play an integral role in autobiographical memory reconstruction, right injections may have been especially problematic since autobiographical memory retrieval has been suggested to terminate with a shift of activation in posterior temporal and occipital networks of the right hemisphere (Conway & Turk, 1999).

4.6.1 Concluding Comments

Autobiographical memories were first examined by a group of philosophers and psychologists (e.g., Dewey, Bartlett, Neisser, Linton, Winograd, Rubin, Brewer and others) who had become discouraged by the nature of memory research conducted in the majority of laboratories. They believed that though perceptual, emotional, cognitive, and social aspects of autobiographical memories may seem separate, they are not, but rather integral parts of the same phenomenon. Autobiographical memory processes include an integration of conditions of the physiology, the physical environment, sociological influences, and cultural systems. The historical separation of these features for examination has resulted from the failure in psychology to recognize that these concepts, when reduced, are no longer related to the phenomenon being examined. Autobiographical memory, in contrast, allows us to examine this organization of experience under ordinary conditions. The study of autobiographical memory is a meaningful way to examine the process of actively constructing models of one's experienced world. However, it remains one of the least well-developed areas in the study of human memory (Brewer, 1988).

Based on this understanding of autobiographical memory, conventional neuropsychological memory measures were thought inadequate to address self-reported autobiographical memory declines. This investigation utilized the AMI to examine autobiographical memory retrieval in TLE patients undergoing brain surgery to reduce epileptic seizures. Findings supported consolidation theories and suggested that autobiographical memory may rely on nonverbal memory mechanisms in the right medial temporal structures.

Appendix A

Patients that have not proceeded to surgery

<u>Patient #</u>	<u>Reason for not proceeding to surgery</u>
17	good candidate, to be scheduled for surgery
26	good candidate, to be scheduled for surgery
27	good candidate, to be scheduled for surgery
36	good candidate, to be scheduled for surgery
33	good candidate, to be scheduled for surgery
6	good candidate, seizure frequency decreased
10	good candidate, seizure frequency decreased
21	good candidate, seizure frequency decreased
32	good candidate, unsure about surgery
4	good candidate, not interested in surgery
29	localized but cognitive concerns regarding surgery
16	needs implants for localization
34	needs implants for localization
11	lost insurance during evaluation process not pursuing surgery
20	refused implants for localization
2	both epileptic and non-epileptic seizures
23	non-surgical, non-lateralizing seizures
7	non-surgical, memory problems only
30	poor candidate, bilateral onsets

Appendix B

Surgical patients not tested post-operatively

<u>Patient #</u>	<u>Type of surgery</u>	<u>Reason for lack of post-operative neuropsychological evaluation and AMI</u>
24	Right AMTL	to be tested 6/03
28	Left frontal resection	to be tested 6/03
31	Left Gamma Knife surgery	to be tested 10/03
13	Left AMTL	to be tested 10/03
35	Right hippocamal resection	to be tested 11/03
22	Left partial DNT low grade	living in London
14	Corpus Callosotomy	increased seizures since surgery
15	Left grade III tumor resection	poor prognosis

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