Epilepsy & Behavior 45 (2015) 205–211

Contents lists available at ScienceDirect

Epilepsy & Behavior

journal homepage: www.elsevier.com/locate/yebeh

Old dogs with new tricks: Detecting accelerated long-term forgetting by extending traditional measures

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ARTICLE INFO

Article history:
Received 3 December 2014
Revised 19 January 2015
Accepted 21 January 2015
Available online 29 March 2015

Keywords:
Epilepsy
Memory
Normative data
Recall

ABSTRACT

Accelerated long-term forgetting (ALF) is a condition in which normal memory performance is displayed after short delays, but significant memory loss is detected when memory is tested after several days or weeks. This condition has been reported in patients with epilepsy, but there are few normative scores available for its detection in clinical practice. In the present study, we assessed 60 healthy control subjects 18–60 years of age on three memory measures [Rey Auditory Verbal Learning (RAVLT), Logical Memory (LM), and Aggie Figures] at delays of 30 min and 7 days. With these normative values, we determined cutoff scores to look for ALF and then categorized the performance of 15 patients with focal epilepsy on the same tasks. Seven of the patients showed ALF, and, in four of these, no other memory deficits (i.e., deficits at 30 min on at least one task) were detected. Of the several demographic and epilepsy factors examined, only higher estimated IQ and older age predicted ALF (and only on one task: RAVLT). The findings provide a useful set of data to be applied in the clinic and some insight into the factors that influence retention within the first week.

1. Introduction

Accelerated long-term forgetting (ALF) [1,2], also known as long-term amnesia [3–5], is a condition in which a person shows normal memory in the short run (i.e., 20–30 min postpresentation) but significant loss of material after longer delays (e.g., days or weeks). Because neuropsychological tests usually only involve assessment of memory at shorter intervals, this condition cannot be detected under standard conditions. However, when special efforts are made to measure memory over longer periods, ALF has frequently been reported in studies of patients with both temporal lobe epilepsy (TLE) [6–8] and transient epileptic amnesia (TEA) [9]. Recently, it has also been identified in patients with extratemporal foci [10]. Furthermore, patients' complaints with regard to everyday memory have been found to better correlate with impairments in long-term delayed recall than with deficits in recall at 30 min [9,11,12], emphasizing the importance of capturing longer term memory deficits as part of the clinical assessment.

Many of the previous investigations of ALF have employed "in-house" material specifically designed to address particular study questions (e.g., [5,12–18]). In the subset of studies that have tested long-term performance on routinely presented clinical material [e.g., Rey Auditory Verbal Learning Test (RAVLT), Rey Complex Figure Test, and Wechsler Memory Scale subtests], normative values from matched control subjects either are based on a small sample (e.g., [12,19–21]) or have yielded no significant differences between the control group and the patient group [22]. However, in 1997, Geffen et al. [23] provided norms for the RAVLT word list, including mean recall scores after 7 days, from a large normative sample. They found that younger (20–39 years of age) and older (40–59 years of age) groups performed similarly on both learning and 7-day delayed recall. They also determined that long-term recall results obtained over the telephone were not different from those obtained in face-to-face testing.

In a recently published critical review of ALF studies, Elliott et al. [24] concluded that the creation of a set of standardized clinical ALF tests that involve both verbal stimuli and nonverbal stimuli and have suitable sensitivity would be ideal. Although the RAVLT and the Logical Memory (prose passages) subtests of the Wechsler Memory Scale are commonly used to assess verbal memory in epilepsy centers (at least at short delays), there is more variability in the tests used to assess nonverbal memory [25,26]. Jones-Gotman and colleagues [26–28] introduced the use of lists of abstract designs (e.g., Aggie Figures) for learning and retention as a visual analogue to the RAVLT. For this sort of material,

Abbreviations: ALF, accelerated long-term forgetting; EEG, electroencephalography; ETE, extratemporal epilepsy; FSIQ, Full Scale Intelligence Quotient; NC, normal control; MRI, magnetic resonance imaging; RAVLT, Rey Auditory Verbal Learning Test; TEA, transient epileptic amnesia; TOPF, Test of Premorbid Functioning; TLE, temporal lobe epilepsy; WMS, Wechsler Memory Scale.

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http://dx.doi.org/10.1016/j.yebeh.2015.01.024
1525-5050/

patients with large right hippocampal removals show deficits in (1) learning over the first few presentation trials and (2) percent retention over a 24-hour period [28]. Longer delays were not considered. The first goal of this study was to provide normative data for long-term (i.e., 7 days) recall of three memory tests: RAVLT, WMS-IV Logical Memory, and Aggie Figures.

Interestingly, in healthy subjects, sex effects have been found on tests of anterograde verbal memory. On the RAVLT, Geffen et al. [23] found that women outperformed men in memory for words at both 30-min and 7-day recall. Women also tend to show better memory for stories (at least until 30-min delay) [21,29], but, to our knowledge, sex differences in story retention over longer intervals have not been studied. With regard to memory for visual material, in one study, women performed better than men at remembering the position of an object in an array [30], but no one has found evidence of sex differences on tasks involving memory for abstract designs. For the present study, we considered possible effects of sex, along with age and education level when determining normative values for the target tasks.

With respect to identifying ALF in patients with focal epilepsy, previous investigations have tended to compare the mean score achieved by the patient group with that achieved by the control group to determine whether the patients with epilepsy (as a group) show pattern characteristic of ALF (e.g., [7,19,31,32], see also [19]). Hence, it is not clear whether (and how often) one would detect ALF in individual patients with focal epilepsy using cutoff scores. This could be done by establishing a quantitative definition of ALF (i.e., normal memory initially with greater-than-expected loss over time) based on normative values. The second goal of this study was to examine rates of ALF in patients with focal epilepsy.

Several factors have been found to contribute to ALF. In a review paper [33], we concluded that older age and higher IQ seem to be linked with this diagnosis. In adults with epilepsy, ALF has primarily been identified in those with a temporal lobe focus [3–5,8,34–36] but is not necessarily linked to hippocampal abnormalities [9,22,37]. Consistent with this, Lah et al. [32] reported a steep decline in memory over a 24-hour period in patients with TLE with hippocampal pathology on MR imaging but a more gradual decline in memory over several days in patients with TLE with no hippocampal abnormalities. Side of lesion has also not been found to predict its occurrence in a material-specific fashion [22,31]. That is, there is little evidence that left-sided epilepsy results in selective ALF for verbal material and that right-sided epilepsy causes ALF for visual material (which would be suggested from patterns seen after shorter intervals) [38–41]. Instead, there is some indication that patients with left-sided epilepsy have more pervasive memory deficits (i.e., affecting both verbal retention and nonverbal retention), whereas patients with right-sided foci have shown ALF limited to memory for designs (sparing long-term verbal memory) [6,12]. The third aim of the present study was to consider the possible influence of these factors in a prospective sample of patients with focal epilepsy who presented to our clinic for assessment. Finally, we looked at the overlap and the differences between patients found to have ALF and those who showed memory defects at 30 min. We hypothesized that the presence of a hippocampal lesion might be more likely in the latter case.

2. Method

2.1. Subjects

Sixty healthy normal control (NC) subjects were recruited as a sample of convenience from amongst friends and relatives of the three investigators as well as relatives of patients seen at the Neuropsychology Unit at Royal Prince Alfred Hospital. Subjects were asked to participate if they met the following criteria: spoke English as their best language and had no psychiatric or neurological history (including no previous seizures). We intentionally sought equal numbers of males and females evenly distributed in older (40–60 years of age) and younger (18–39 years of age) groups. In addition to age, subjects were divided according to gender (male or female) and education level (less than or equal to 12 years of education or post-high school education). Participants with *any* post-high school education were not divided further because analyses indicated no differences between those with postgraduate qualifications and those without postgraduate qualifications on any of the memory measures. Two NC participants failed to return the Aggie Figures response sheet after one week, so those data points are missing.

A prospective sample of 23 patients thought to have epilepsy who presented to the seizure clinic for neuropsychological evaluation also underwent assessment on all three long-term memory measures described below. These subjects met the same criteria listed above with the exception of having a history of seizures. Nine of these patients were eliminated from this study either because epilepsy was not confirmed or because they had primary generalized as well as focal-onset seizures. The 15 patients with EEG-confirmed focal epilepsy who were tested in this study included 8 women and 7 men between 18 and 61 years of age (mean = 37). See Table 1 for information on the distribution of the NC and patient participants with regard to demographics.

On the basis of imaging, EEG studies, and clinical history, the side and site of epileptic focus were determined without knowledge of the neuropsychological results. There were 9 patients with TLE and 6 patients with extratemporal epilepsy (ETE). Eight patients had left-sided foci, 6 patients had right-sided foci, and, in 1 patient, lateralization of seizure focus had not been determined. Five patients had hippocampal lesions, 1 patient had undergone hippocampal removal as part of a temporal lobectomy, and the other 4 patients had hippocampal sclerosis. The remaining 10 patients had no visible hippocampal abnormality on MRI. A Supplemental Table is provided with all of the patient details.

All subjects gave their informed consent, and the project was approved by both the University of Sydney and the Royal Prince Alfred Hospital Human Ethics Committee.

2.2. Materials

Three memory tests were used in this investigation. The stimuli for all three were administered as part of a larger study in a session that lasted approximately 90 min. In all three cases, the intervals between immediate recall and 30-min delayed recall were filled with other tests, as typically occurs in a clinical assessment. The intervening material was of a different modality than the test material. Tests were administered in the order presented below. Following standard protocol, subjects were not forewarned about any of the recalls. Although often included in a clinical assessment, for this study, recognition memory was not tested at 30 min to avoid the representation of the material serving as a reminder. At the end of the standard in-office assessment, arrangements were made for a convenient time and telephone number at which a follow-up interview could be performed 7 days post-assessment, and the subject was provided with a self-addressed stamped envelope and a blank piece of paper (unbeknownst to them, for the long-term Aggie Figures recall).

2.2.1. Rey Auditory Verbal Learning Test (RAVLT)

The Rey Auditory Verbal Learning Test is a well-known clinical measure of verbal learning and memory [42]. A 15-item word list (List A) is presented over five learning trials. In each trial, the list is read aloud to the subjects, and they are asked to recall as many words as possible. A distractor list of 15 items (List B) is then read by the examiner and recalled by the subject in a similar fashion (but only once), and an unprompted ("immediate") recall of List A follows. Twenty to 30 min later, delayed recall of List A is requested. For this study, subjects were also called 7 days later, and long-term recall of List A was collected over the telephone. Scores used in this evaluation were the recall at 30 min and the Percent Change score: [(30-min recall − 7-day recall) / 30-min recall] × 100.