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Review

Measuring forgetting: A critical review of accelerated long-term forgetting studies

Gemma. Elliott [a,b], Claire L. Isaac [a,c] and Nils Muhlert [c,d,*]

[a] Clinical Neuropsychology Services, Royal Hallamshire Hospital, Sheffield, UK
[b] Department of Psychology, University of Sheffield, Sheffield, UK
[c] Neuropsychology Department, Lincolnshire Partnership NHS Foundation Trust, Lincoln, UK
[d] Cognitive Neuroscience, School of Psychology, Cardiff University, Cardiff, UK

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ABSTRACT

Accelerated long-term forgetting (ALF) refers to abnormal forgetting over hours to weeks despite normal acquisition or initial consolidation. Since standardised assessments of memory typically only test at delays of up to 40-minutes, ALF may go undetected in clinical practice. The memory difficulties associated with ALF can however cause considerable distress to patients. It is important therefore that clinicians are aware that ALF may represent a distinct phenomenon that will require additional and careful assessment to aid patients' understanding of the condition and assist in developing strategies to address its effects. At the same time, ALF may also provide insight into long-term memory processes. Studies of ALF in patients with epilepsy have so far demonstrated mixed results, which may reflect differences in methodology. This review explores the methodological issues that can affect forgetting, such as the effects of age, general cognitive function, test sensitivity and initial learning. It then evaluates the extent to which existing studies have considered these key issues. We outline the points to consider when designing ALF studies that can be used to help improve their validity. These issues can also help to explain some of the mixed findings in studies of ALF and inform the design of standardised tests for assessing ALF in clinical practice.

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1. Introduction

Accelerated long-term forgetting (ALF) refers to the phenomenon whereby memories are encoded and retained normally over delays of up to 30-min, but are then forgotten at an abnormally rapid rate over delays of days to weeks thereafter. The phenomenon was first described in a case study by De Renzi and Lucchelli (1993), and greater forgetting over days in people with epilepsy was first reported by Martin et al. (1991). Since then several further case studies have been published (Butler & Zeman, 2008a; Cronel-Ohayon et al., 2006; Holdstock, Mayes, Isaac, Gong, & Roberts, 2002; Jansari, Davis, McGibbon, Firminger, & Kapur, 2010; Kapur et al., 1997, 1996; Kemp, Illman, Moulin, & Baddeley, 2012; Lucchelli & Spinnler, 1998; Mayes et al., 2003; O'Connor, Sieggreen, Ahern, Schomer, & Mesulam, 1997). Whilst these cases of ALF are associated

* *Corresponding author*. Cognitive Neuroscience, Department of Psychology, Cardiff University, 60 Park Place, Cardiff CF10 3AT, UK.
E-mail address: muhlertN@cardiff.ac.uk (N. Muhlert).
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with a range of aetiologies, the fact that the majority experienced temporal lobe epilepsy (TLE) resulted in a focus on group studies of people with TLE. The phenomenon was originally labelled "long-term amnesia" (Kapur et al., 1997, 1996). However, the term accelerated long-term forgetting was introduced by Blake, Wroe, Breen, and McCarthy (2000) and has subsequently become the most widely used label.

Abnormal forgetting has often been attributed to a failure of memory consolidation (e.g., Isaac & Mayes, 1999a). This is the hypothetical process in which memories become stabilised within long-term storage, through processes of both synaptic and systems level changes (McGaugh, 2000), allowing later retrieval. Whilst consolidation may continue for weeks, months or even years (Squire & Alvarez, 1995) it is generally assumed that its efficacy can be evaluated after relatively short delays, explaining the use of 30-min delays in standardised memory tests. The neurobiological underpinnings of ALF are poorly understood but may benefit from considering theories of long-term memory (LTM). The main theory of consolidation, the Standard Model (Alvarez & Squire, 1994; Squire, 1992; Squire & Alvarez, 1995; Squire, Cohen, & Nadel, 1984), proposes that the Medial Temporal Lobe (MTL) is involved in the initial stages of consolidation but that, over time, memories are reorganised so as to become supported by the neocortex and, eventually, independent of the MTL. Mayes et al. (2003) distinguish 'fast' from 'slow' LTM consolidation processes. The 'fast' consolidation process involves interactions between a number of cortical systems which is thought to be mediated by MTL structures, such as the hippocampus. If ALF reflects a failure of this consolidation system then this could result from subtle MTL damage or abnormal activity, in which functional disconnection between hippocampal and cortical systems prevents memories from becoming established. ALF would therefore represent a mild form of amnesic syndrome. In contrast, the 'slow' consolidation process is thought to depend on a stable environment in the temporal neocortex, allowing for repeated and synchronous activation of hippocampal–neocortical connections. In this case, ALF may result from failed slow transfer of information into neocortical storage sites resulting either from structural neuropathology preventing establishment of memories or from disrupted transfer due to epileptiform activity (e.g., Kapur et al., 1997). An alternative theory, the Multiple Trace Theory (Nadel & Moscovitch, 1997), proposes that the MTL is always involved in the stabilisation and retrieval of memories. In this model each reactivation of a memory produces a new trace within the MTL and neocortical regions. Forgetting occurs when memories are not re-activated and so do not benefit from the formation of multiple traces in the MTL and neocortex, or when these processes of stabilisation are compromised (Nadel & Moscovitch, 1997).

Both theories of LTM predict that structural damage and/or seizure activity may disrupt consolidation/stabilisation processes (Mayes et al., 2003). Improved definition of the nature and underlying causes of abnormal forgetting may therefore have important implications for theories of normal memory functioning. To date however, the evidence for ALF in TLE has been mixed (Bell & Giovagnoli, 2007; Butler & Zeman, 2008b; Fitzgerald, Mohamed, Ricci, Thayer, & Miller, 2013), with ALF reported in some TLE studies (Blake et al., 2000; Butler et al., 2007; Mameniskiene, Jatuzis, Kaubrys, & Budrys, 2006; Manes, Graham, Zeman, de Lujan Calcagno, & Hodges, 2005; Martin et al., 1991; Muhlert et al., 2011; Muhlert, Milton, Butler, Kapur, & Zeman, 2010; Tramoni et al., 2011) but not others (Bell, 2006; Bell, Fine, Dow, Seidenberg, & Hermann, 2005; Giovagnoli, Casazza, & Avanzini, 1995). Another issue for studies of ALF, is that patients may show accelerated forgetting over immediate and short delays (e.g., 30 min) as well as very-long delays. In these cases, it is necessary to use procedures which match participants for initial learning and immediate recall.

One serious challenge for assessing ALF routinely is that standardised tests of memory do not assess performance at delays greater than 40 min. As ALF, by definition, occurs beyond this time point, some patients' memory impairment may go undetected. In the absence of standardised tests, researchers have created their own materials and procedures for assessing forgetting over extended delays. The mixed findings in studies of ALF could therefore be explained by differences in methodological approaches and the significant difficulties encountered when comparing normal and pathological forgetting. These methodological problems associated with studying ALF are the same as those encountered when studying any form of forgetting. Considering methodological issues from the wider literature on forgetting (e.g., Isaac & Mayes, 1999a) may therefore help to inform this debate.

This review aims to evaluate methodological problems within forgetting research in general and ALF in particular. In contrast to previous reviews of ALF (Bell & Giovagnoli, 2007; Butler & Zeman, 2008b; Fitzgerald, Mohamed, et al., 2013), this review primarily focusses on the impact of methodology on forgetting rates, rather than the clinical features of patients who show ALF. Revisiting this literature is timely when many researchers are developing new assessments and procedures to study ALF. In Part I, the literature addressing methodological issues in the assessment of forgetting rates is summarised. Rather than trying to resolve the complex theoretical and mathematical debates, this review aims to summarise the different opinions on studying forgetting, evaluate their implications and provide a reference point for issues that should be tackled when assessing ALF. In Part II, we review existing case reports and group studies of ALF with emphasis on experimental design. We evaluate the extent to which key methodological issues have been addressed in each study and describe findings that take into account these quality-related issues.

1.1. *Search strategy*

The initial search strategy is summarised in Table 1 (searches resulting in zero matches are not shown). Broad search terms were used for Part I to avoid biasing the selection of methodological issues. Searches were limited to peer-reviewed, human studies for which the full text was available in English.

Following initial searches, titles and available abstracts were examined for relevance and reference lists were trawled to identify reports which were not indexed. Trawling references proved to be the source of many articles identified for Part I, since their publication dates preceded indexing. Only papers considering methodological factors that could be controlled for in studies of ALF were included. This process

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