Electroconvulsive Therapy related Autobiographical Amnesia: A review and case report.

Lomas, Matthew. [a, b*], *Rickard, Victoria.* [a], *Milton, Fraser.* [c], *Savage, Sharon.* [c, d*], *Weir, Andrew* [e], *Zeman, Adam*** [a].

[a] College of Medicine and Health, College House, University of Exeter, EX1 2LU, United Kingdom.

[b] Centre for Ecology and Conservation, University of Exeter, Penryn, TR10 9FE, United Kingdom.

[c] School of Psychology, College of Life and Environmental Sciences, Washington Singer, University of Exeter, EX4 4QG, United Kingdom.

[d] School of Psychology, University of Newcastle, Newcastle, NSW 2308, Australia.

[e] Institute of Neurological Sciences, Langlands Drive, University of Glasgow, G51 4LB, United Kingdom.

* Present address.

**Corresponding Author (a.zeman@exeter.ac.uk)

Abstract

Introduction: While short-term cognitive impairment following electro-convulsive therapy (ECT) is well described and acknowledged, the relationship between ECT and persistent memory impairment, particularly of autobiographical memory, has been controversial.

Methods: We describe the case of a 70 year old consultant neurophysiologist, AW, who developed prominent, selective autobiographical memory loss following two courses of ECT for treatment-resistant depression.

Results: His performance on standard measures of IQ, semantic and episodic memory, executive function and mood was normal, while he performed significantly below controls on measures of episodic autobiographical memory.

Conclusions: Explanations in terms of mood-related memory loss and somatoform disorder appear unlikely. We relate AW's autobiographical memory impairment, following his ECT, to reports of similar autobiographical memory impairment occurring in the context of epilepsy, and emphasise the importance of using sensitive approaches to AbM assessment.

Keyword: Electroconvulsive Therapy

Abbreviations:

AbA = Autobiographical Amnesia

AbM = Autobiographical Memory

ECT = Electroconvulsive Therapy

1. Introduction

Electroconvulsive therapy (ECT) involves the induction of an epileptic seizure by passing an electric current across the brain. In use for nearly 90 years, it remains a controversial but common treatment for severe mental health disorders including major depressive disorder (MDD), especially where other treatments have failed (Ferrier, 2019). The UK ECT Review Group (2003) states that "ECT remains an important treatment option for the management of severe depression" (p. 807).

ECT is known to cause widespread changes in the brain (Cowen, 2019), however the precise mechanism remains unclear. Potentially relevant findings include modulation of neurochemicals including GABA, glutamate, dopamine, serotonin, noradrenaline and brain derived neurotrophic factor; structural changes in the limbic system including an increase in the volume of the hippocampus and amygdala (Ousdal et al., 2019; Wilkinson, Sanacora, & Bloch, 2017); and amelioration of the 'hyper-connected state' revealed in functional imaging studies of depression (Perrin et al., 2012).

The early cognitive side-effects of ECT are uncontroversial (Finnegan & McLoughlin, 2019). The induced seizure and associated anaesthetic cause immediate disorientation, impairment of attention and amnesia for the period of the treatment and some minutes afterwards. Recovery of orientation generally occurs within around half an hour. A degree of anterograde memory impairment on standard tests, particularly affecting verbal memory, is common over the days to weeks after completion of the course of ECT. Retrograde memory, especially for events occurring close to the onset of the ECT, is also often affected during this recovery period (Finnegan & McLoughlin, 2019). There is, however, disagreement in the literature about the frequency and severity of more persistent retrograde amnesia, especially affecting episodic autobiographical memory (AbM), the ability to recollect, and to some degree 're-experience', salient life events. Table S1 (supplementary materials) summarises papers examining remote memory loss occurring after ECT. Although this literature describes both subjective and objective evidence of prolonged impairment of AbM following ECT (e.g. Squire & Slater, 1983; Verwijk et al., 2012), Finnegan and McLoughlin (2019) conclude that there is no high quality evidence indicating that retrograde amnesia persists after ECT. Alternative explanations for complaints of prolonged AbM impairment following ECT include depression-related memory impairment (Dalgliesh & Werner-Seidler 2014, Semkovska & McLoughlin, 2014) and somatoform disorder (Fink, 2007).

There has, to date, been little dialogue between studies of autobiographical amnesia (AbA) following ECT and the now extensive literature on AbA related to epilepsy (Butler & Zeman, 2008; McAndrews, 2012; but see Soderlund, Percy & Levine, 2012 for an exception). This latter literature indicates that disproportionate AbA can occur in patients with epilepsy, especially temporal lobe epilepsy, who

perform normally or near normally on standard memory assessment. This work has highlighted the key importance of using sufficiently sensitive measures of AbM in patients complaining of AbM loss (Zeman, Kapur, & Jones-Gotman, 2012). As ECT involves the induction of what are effectively epileptic seizures, and is often induced by temporal lobe stimulation, it is a plausible hypothesis that there is some common ground between AbA occurring in the contexts of epilepsy and ECT.

Here we report the case of a man (AW) who developed a severe AbA following two courses of ECT despite making a good recovery from his depressive illness. We used approaches to assessment which have proved revealing in studies of AbA occurring in patients with epilepsy (Butler & Zeman, 2008; Milton et al. 2010), to corroborate his subjective complaint. Given his account of his symptoms, we hypothesized that AW would show an impairment on sensitive measures of autobiographical memory, with preserved performance on standard measures of general cognitive ability and anterograde memory.

2. Methods

2. 1. Participants

2. 1. 1. Case AW

AW is a 70-year-old retired Consultant Clinical Neurophysiologist, with a family history of bipolar disorder in his maternal grandfather. He experienced an episode of depression as a student aged 21, treated with Amitriptyline. He was generally well until his mid-forties, when rare episodes of mood disturbance began to occur. Intermittent treatment with SSRIs was successful, with a few periods off work. His professional life was successful and demanding, involving varied senior clinical, academic and administrative roles and extensive travel. Relapses in 1998 and 2001 were treated effectively with venlafaxine, with little response to Cognitive Behaviour Therapy (CBT) and Eye Movement Desensitisation and Reprocessing (EMDR). He retired from NHS practice in 2007, continuing to consult privately for 5 further years. Following stressful life events, a more severe deterioration in his mood occurred in 2007. Between 2008 and 2014 he was treated primarily with venlafaxine and lamotrigine as a mood stabiliser, with periods of unsuccessful adjunctive treatment with lithium (one year), quetiapine and aripiprazole. During these years his mood fluctuated but he continued to perform in a range of demanding roles until 2013, when his mood deteriorated further and he was diagnosed as having ‘drug resistant major depressive disorder’ (MDD). Between February and April 2014 he received 14 treatments with brief pulse bilateral temporal Electroconvulsive Therapy (ECT), with considerable improvement in his mood. Despite continuing treatment with venlafaxine and lamotrigine, his mood again declined after 6 months, and he received a further 26 ECT treatments

between December 2014 and August 2015. While these were less effective than the first series, his mood has substantially recovered on maintenance treatment with venlafaxine (525 mgs/day) and lamotrigine (300 mgs/day). At the time of our assessments (November 2017 and March 2018), AW regarded his mood as content, was able to take pleasure in life, felt energetic, could concentrate normally and was sleeping and eating well.

During both periods of ECT treatment, AW was aware of significant difficulties with day-to-day memory, confirmed by his wife, which he had been warned to expect. After the completion of ECT, however, AW also noticed a marked and persistent loss of memory for salient autobiographical events, particularly from the preceding two decades. He could no longer recall numerous family holidays abroad, memorable lecturing trips, for example to China, Russia, many to the USA, as well as highly salient personal events (e.g. speaking at his parents' funerals and attending social events with royalty). AW remarked that it seemed the 'centre part of my life had disappeared'; reviewing photographs was like 'looking into somebody else's life'. Whilst the densest loss was from the 1990's to 2014, prior memories also lacked vivid details. Occasional experiential memories, however, appeared to be preserved, for example a visit to the US in the 1980s, and fragments of a holiday to the Caribbean in 2014. He also found that he could no longer use visual imagery to recall familiar routes and landmarks. During and for around one year after the second course of ECT treatment, AW experienced occasional short-lived olfactory hallucinations lasting for seconds, generally of a 'drains-like smell', but also more persistent unpleasant experiences of smell triggered by smells encountered in his surroundings which continue to the present day. His past medical history included an episode of thyrotoxicosis (1980); prostate surgery and regular migraine with aura. He is at most a light drinker and has never used recreational drugs.

Clinical neuropsychological assessment performed locally as a result of these autobiographical memory symptoms in 2016 revealed high average to superior performance in all cognitive domains that were formally assessed including attention, memory, language, executive function and general intellectual ability. A focussed assessment of autobiographical memory performed by his clinical team in 2017 revealed normal performance on a measure of personal semantic memory, with normal performance on an unspecified routine measure of episodic autobiographical memory for the childhood and adult periods, but borderline performance for recent events.

On assessment by AZ (author) in November 2017, AW had a normal neurological examination and scored with the normal range (95/100) on the Addenbrooke's Cognitive Examination III (Hodges & Larner, 2017), a 'bedside' measure of cognition. At this time, AW was taking Tamsulosin (400mg p/d),

Amoldipine (10mg p/d) and low-dose aspirin to be taken daily in addition to the drugs mentioned above.

2. *1. 2.* *Healthy controls*

Data from two groups of age-matched healthy control participants were used to evaluate AW's cognitive performance on a set of research measures previously found to be sensitive to autobiographical memory disturbance. These groups were previously recruited to our study of memory impairment occurring in epilepsy, the TIME project (http://projects.exeter.ac.uk/time/). Group 1 (used to evaluate AW's anterograde memory performance) involved 7 age-matched healthy control participants (5m/2f; range = 54 to 76; mean age = 67.42). Performance on remote memory was compared with group 2, a set of 12 healthy control participants (4m/8f; range = 51 to 77; mean age = 64.58) originally reported in Milton et al. (2010).

No control participants reported a history of neurological or psychiatric disorder. All participants provided informed consent.

2. 2. *Measures*

Face-to-face testing of AW was conducted over two sessions: remote memory was assessed in the first (November 2017), anterograde memory in the second (March 2018). Tests of general cognition and mood measurements were split across these two sessions. Long-term retention of anterograde memory was assessed by follow-up testing over telephone.

2. 2. 1. *General Cognition, Memory and Mood*

Standard cognitive tests of general intellectual ability and executive function were administered. To estimate IQ, AW and group 2 completed subtests from the Wechsler Abbreviated Scale of Intelligence (WASI; Wechsler, 1999), whereas group 1 were administered the Wechsler Test of Adult Reading (WTAR; Holdnack, 2001). All groups completed the Controlled Oral Word Association Test (using letters F, A, S and animal category) for verbal and semantic fluency (COWAT; Steinberg, Bieliauskas, Smith, and Ivnik, 2005; Tombaugh, Kozak, and Rees, 1999) and the Trail Making Test (TMT; Steinberg et al., 2005) for executive function (speed difference between tests A and B). The new words test (Milton et al., 2010) was employed for AW and group 2 to assess semantic memory. This test requires respondents to give definitions of 42 modern words (e.g. A-bomb, Wi-Fi), followed by a multiple choice test for definition of the same words (see supplementary 1 for further detail).

All groups completed tests of anterograde memory, including the logical memory subtest from the WMS-III (Wechsler, 1997) and the Rey Complex Figure test (RCFT; Meyers and Meyers, 1995).

Standard 30-minute delay intervals were used. Visual and verbal recognition memory were evaluated using the Warrington Recognition Memory test (WRMT; Warrington, 1984).

All participants completed the Hospital Anxiety and Depression Scale (HADs; Zigmond and Snaith, 1983) to evaluate mood.

2. 2. 2. *Visual Imagery*

AW completed a version of the Vividness of Visual Imagery Questionnaire (VVIQ; Marks, 1973), using reversed scoring (see supplementary 2).

2. 2. 3. *Olfactory Function*

With regards to AW's report of olfactory disturbance, the University of Pennsylvania Smell Identification Test (UPSIT; Doty, Frye, & Agrawal, 1989) was administered (see supplementary 3).

2. 2. 4. *Accelerated Long Term Forgetting (ALF)*

Two tests were used to evaluate memory performance over a three-day interval, to assess accelerated long-term forgetting: a modified Memory for Design test (mMFD; Butler et al., 2007); and a modified version of the Rey Auditory Verbal Learning Test (mRAVLT; Schmidt, 1996) (see supplementary 4).

2. 2. 5. *Topographical Memory*

The Four Mountains Test (4MT; Chan et al., 2016) was used to assess topographical memory (see supplementary 5).

2. 2. 6. *Autobiographical Memory*

Two tests were used to assess autobiographical memory: the Autobiographical Interview (AI; Levine, Svoboda, Hay, Winocur, and Moscovitch, 2002), and the personal semantics test (Milton et al., 2010). Both tests sampled five life periods: childhood (up to 9), youth (10–19), young adult (20–29), middle-age (30 to the most recent decade), and the most recent decade (see supplementary 6).

2. 3. *Statistical Analysis*

To compare AW's performance to the healthy controls, Crawford's modified *t*-tests for single case studies was utilised (Crawford & Garthwaite, 2002). *T*-tests were two tailed. To correct for multiple comparisons, a Bonferroni correction was applied to the measures of general cognition, short-term memory and mood (28 comparisons). Significance for these measures was inferred at $p = 0.002$. Separately, where the overall analysis was significant for the Autobiographical Interview measures (the number of internal details, and the qualitative ratings) we performed follow-up pairwise

comparisons on the individual time periods. Bonferroni corrections were applied to the 5 pairwise comparisons in each case meaning significance for the analysis of these measures was inferred at p = 0.01.

3. Results

3. 1. General Cognition, Memory and Mood

See Table 1 for general cognition, memory and mood scores across all groups. AW's IQ was within the very superior range and higher than that of the anterograde memory control group (group 1, p = .003), and of the remote memory control group (group 2, p = .304), but not significantly so in either case after correcting for multiple comparisons. No differences were detected on measures of executive function, verbal fluency, semantic memory, depression or anxiety in comparison to either control group.

While no differences were detected in free recall of the WMS-III logical memory story, AW's score on the recognition element of this test was lower than control group 1, despite his superior overall cognitive ability. However, AW's score was not significantly different to the performance of either control group on this element of the WMS-III. AW performed similarly to controls on visuospatial tasks (RCFT) and on word (WRMT – Words) and face recognition (WRMT – faces).

3. 2. Visual Imagery

AW's ability to create vivid mental pictures was at the high end of the average range, with a VVIQ score of 72/80 (as compared to participants in Zeman, Dewar & Della Sala, 2015).

3. 3. Olfactory Function

AW scored in the 58th percentile for his age and gender on the UPSIT, indicating normal olfactory function at the time of testing.

3. 4. Accelerated Long Term Forgetting (ALF)

AW did not display accelerated forgetting of material on the mMFD and mRAVLT tasks. Stimuli were learned at the same rate as controls, and lost at a similar rate over time. Table 2 shows the results for these tasks.

3. 5. Topographical Memory

AW correctly identified alternative perspectives of mountains in the 4MT on fewer trials than controls (AW score = 17, Control M = 23.57, SD = 2.37, p = .041), suggesting difficulties in spatial memory.

3. 6. *Autobiographical Memory*

Figure 1 shows autobiographical memory performance for AW and controls on the Levine AI and Personal Semantics Test across the five time periods. AW had significantly reduced overall recall for both the number of internal details provided (AW *M* = 31.86, Control *M* = 60.98, *SD* = 16.28, p = .005) and the qualitative ratings (AW *M* = 43, Control *M* = 71.8, *SD* = 34.12, *p* < .001) on the Levine AI. Furthermore, AW recalled fewer internal details in the youth and middle-age time periods than the control groups, however the significance threshold was not met after corrections for multiple comparisons. The qualitative rating of memory was significantly impaired for youth, middle age and recent memories, but not for memories of childhood and his 20s-30s. AW did not differ in the number of external details provided for any individual time period. Personal semantic memory was not significantly impaired for any of the individual time periods.

4. Discussion

We describe a case of disproportionate or focal autobiographical amnesia (AbA), occurring in a middle aged man as a result of extended bitemporal ECT which was effective for his mood disorder. His case is worthy of note for two reasons. First, although there is suggestive evidence for a link between autobiographical memory (AbM) impairment and ECT (see Table S1), a recent chapter in a widely-used textbook of ECT states that "there is no high level evidence for persisting retrograde amnesia after ECT" (p112; Finnegan & McLoughlin, 2019). This report, which uses a measure highly sensitive to AbM loss, may help provide evidence for this relationship. Second, while there has been extensive research in recent years into AbA occurring in epilepsy, and in ECT, there has been surprisingly little interaction between the two related literatures. Analogies between AbA occurring in patients with epilepsy and following ECT suggest that, while AbA post-ECT might sometimes reflect a somatoform disorder (Fink, 2007) or a persistence of depression-related AbA (Semkovska & McLoughlin, 2014; Semkovska, Noone, Carton, & McLoughlin, 2012), in other cases it is likely to be a more direct neurobiological consequence of ECT. Further, the study of AbA in epilepsy has highlighted the critical importance of using the appropriate memory measures in patients who complain of selective or disproportionate AbA: 'standard' memory assessments can fail to capture severe autobiographical memory impairment with an 'organic' basis (Butler & Zeman, 2008; McAndrews, 2012; Zeman, Byruck, Tallis, Vossel, & Tranel, 2018). We discuss each of these points below.

The key neuropsychological features of AW's case comprise his well-preserved general cognition, and performance on measures of semantic and episodic memory, alongside a marked impairment of AbM which first became apparent during and after his second course of ECT. This is in keeping with AW's subjective report, corroborated by his spouse. The mild impairment on a measure of topographical

memory, the 4MT, may point to a subtle anterograde hippocampal memory impairment, in addition to his AbM impairment, but this test is not yet a standard part of neuropsychological assessment, and the reduction in AW's score was not significant after correction for multiple comparisons. AW scored at the 20th percentile on the trail making measure of executive function (Strauss, Sherman & Spreen, 2006), an unexpectedly poor performance. However, the poorer average performance of control group 2, AW's normal performance on measures of verbal fluency, and his competence in everyday life, suggests this single area of underperformance does not reflect significant executive dysfunction. Low imagery vividness has been associated with AbM impairment (Rubin & Greenberg, 1998), but despite AW's report of diminished imagery vividness during and following ECT, there was no evidence of continuing reduction in his ability to imagine a variety of mental scenes, as measured by the VVIQ. Whilst AW's performance on the personal semantics test was no different to that of controls, the high performance of controls points to a ceiling effect that could have concealed any impairment. However, his normal score on the new words test suggests that his general verbal semantic memory is not impaired. Thus the neuropsychological picture is indeed one of 'focal' or 'disproportionate' retrograde amnesia.

Given AW's substantial recovery from his depressive illness, confirmed by his normal score on a measure of depression and the lack of any evidence for depression on mental state assessment at the times of examination, there is no reason to attribute his AbM impairment to his depressive illness itself. Although we did not systematically examine the emotional characteristics of AW's AbM impairment, there was no evidence of the 'biased recollection of negative memories' or selective depletion of positive memories that have been described as typical features of AbM due directly to depression (Dalgliesh & Werner-Seidler 2014). The relatively abrupt change in his previously rich autobiographical recollection (as noted by AW himself and corroborated by his spouse) over the period of his ECT clearly suggests a causative role for the latter.

Similarly, there is little reason to suspect a functional or somatoform explanation. Markowitsch and Staniloiu (2013) suggest 6 features that support a diagnosis of selective functional retrograde amnesia: a selective pattern of retrograde amnesia (including preservation of most other intellectual functions), loss of personal identity, onset related to trauma or stress, lack of relationship to a known medical disorder, a background of a mood disorder, and a 'belle indifference' (p. 1502). Besides his selective retrograde amnesia, AW satisfies only one, or possibly two of these criteria: the presence of a prior history of mood disorder, and, arguably, an onset related to psychological trauma or stress. The most obvious explanation for AW's AbA is therefore a direct effect of his ECT. We note his history raises the outside possibility that the ECT kindled subtle TLE, manifested by his olfactory hallucinations: such

kindling has been reported to occur occasionally (Bryson, Gardner, Wilson, Rolfe, & Archer, 2016), and provides an additional mechanism that might link ECT with autobiographical amnesia.

There is agreement that ECT causes short-lived cognitive sequelae but there has been disagreement about its longer-term cognitive side effects (Calev et al., 1991; Meeter et al., 2011). AbM is the cognitive domain that has most often been implicated as a potential long-term casualty of ECT. In a number of past studies, there has been a discrepancy between the high frequency of subjective reports of AbM difficulties following ECT and relatively normal performance on objective measurement (Fraser, O'Carroll, & Ebmeier, 2008; Ingram, Saling, & Schweitzer, 2008; Prudic, Peyser, & Sackeim, 2000). This may in part be due to mood-related misperception of memory function but the use of relatively insensitive measures of AbM provides an alternative or additional explanation. Studies of AbA in other contexts, particularly the context of epilepsy, discussed further below, have revealed the vital importance of using appropriately sensitive measures in studying AbM function (Butler & Zeman, 2008; McAndrews, 2012; Zeman et al., 2018). Where the literature has pointed to AbA as a side effect of ECT (e.g. Coleman et al., 1996; Napierala et al., 2019), its persistence and severity has been linked to many relevant variables, including site (McLoughlin, Kolshus, & Jelovac, 2017; Semkovska et al., 2016), waveform (Loo et al., 2008; Mayur, Byth, & Harris, 2013), patient age at the time of ECT (Berman et al., 2008; Brus et al., 2017), individual baseline cognitive function and reorientation time following the procedure (Martin et al., 2015; Sobin et al., 1995).

Remote memory loss, in particular loss of autobiographic episodic memories, has recently been described as a moderately common occurrence among patients with temporal lobe epilepsy. The contexts include chronic refractory epilepsy (Addis, Moscovitch, & McAndrews, 2007; Lah, Lee, Grayson, & Miller, 2006; Viskontas, McAndrews, & Moscovitch, 2000), the aftermath of temporal lobectomy (Lah, Grayson, Lee, & Miller, 2004; Noulhiane et al., 2007), adult onset drug sensitive TLE (Tramoni et al., 2011), including subtle TLE (Jansari, Davis, McGibbon, Firminger, & Kapur, 2010), and, as a prodromal phenomenon, preceding the clinical onset of epilepsy (Hornberger et al., 2010). AbA is particularly common in transient epileptic amnesia (TEA), a sub-type of TLE occurring in two thirds of patients (Butler et al., 2007). It occurs among patients with normal or near normal anterograde memory on standard tests, and is often, but not always, associated with accelerated long-term forgetting (Butler et al., 2007; Butler & Zeman, 2008). Particularly characteristic of epilepsy-related AbM loss is the depletion of fine grain, perceptual and contextual information which underlie detailed autobiographical recollection (McAndrews, 2012). The lifelong depletion of AbM, with relative preservation of general and personal semantic memory, detected in these studies of epilepsy bares a clear resemblance to the memory loss documented in AW's case. The importance of using sensitive

measures of AbM is a recurring theme in these studies (Butler et al., 2007; Butler & Zeman, 2008; Levine et al., 2002; McAndrews, 2012).

The choice of instrument to assess autobiographical memory is wide, with variations in the approach to eliciting, probing, scoring and validating memories (Butler & Zeman, 2008; Kopelman et al., 1989; Levine et al., 2002; Piolino et al., 2009). In our own previous work with patients with TEA (Butler 2007, Milton 2010; see also Manes et al 2001), while both a modified version of the AMI (Kopleman 1989) and the AI (Levine et al 2002) demonstrated autobiographical memory impairment in the patient group, the AI, which has also been used by others in studies of AbM impairment in people with epilepsy (e.g. Hornberger et al. 2010), has proved especially sensitive. This is likely to be the result both of the detailed probing of memories, designed to ensure that as many recollected details as possible are described, and the meticulous and highly detailed approach to scoring, intended in particular to discriminate between 'semantic' and genuinely 'episodic' aspects of the recollection.

There are a number of mechanisms by which ECT might give rise to an 'organic' AbA, analogous to the AbA occurring in association with epilepsy. First, there is strong evidence that ECT affects the hippocampus, including evidence for hippocampal volume increase post-ECT and experimental evidence for immediate effects of ECT on hippocampal metabolism (Wilkinson et al., 2017). The influential multiple trace theory of AbM would predict that alteration of hippocampal function would be likely to impact episodic AbM (Moscovitch, 2012). Second, there is evidence that ECT reorganizes brain connectivity and brain network interactions which are clearly of key importance in memory processing (Perrin et al., 2012). It could be that the reduction in the over-connected state that is thought to be responsible for depression by ECT disrupts aspects of connectivity required for AbM function. Thirdly, it could be that the seizure activity induced by ECT has a direct effect on widely distributed cortical engrams, degrading memory representations. Fourthly, ECT modulates neurotransmitter systems which in turn modulate memory function. Clearly these possibilities are not mutually exclusive and it may well be that a combination of mechanisms underlie the effects of ECT on AbM revealed by this case. Further studies are required to determine their relative contributions.

5. Acknowledgements

We thank the Department of Clinical Psychology of Forth Valley Health Board for their initial assessments of AW. The other authors thank AW for making initial contact with them, after he noted the similarity between his memory loss post-ECT and memory loss described in the context of temporal lobe epilepsy.

6. Declaration of Interest

This work was supported by the Dunhill Medical Trust [R322/1113]. The authors declare no conflict of interest.

7. References

Addis, D. R., Moscovitch, M., & McAndrews, M. P. (2007). Consequences of hippocampal damage across the autobiographical memory network in left temporal lobe epilepsy. *Brain, 130*(9), 2327-2342. doi:10.1093/brain/awm166

Åsberg, M., Montgomery, S., Perris, C., Schalling, D., & Sedvall, G. (1978). A comprehensive psychopathological rating scale. *Acta Psychiatrica Scandinavica, 57*(S271), 5-27.

Barbizet, J. (1970). *Human Memory and Its Pathology*. San Francisco: W. H. Freeman.

Berman, R. M., Prudic, J., Brakemeier, E.-L., Olfson, M., & Sackeim, H. A. (2008). Subjective evaluation of the therapeutic and cognitive effects of electroconvulsive therapy. *Brain Stimulation, 1*(1), 16-26. doi:https://doi.org/10.1016/j.brs.2007.08.005

Brus, O., Nordanskog, P., Båve, U., Cao, Y., Hammar, Å., Landén, M., Lundberg, J., & Nordenskjöld, A. (2017). Subjective Memory Immediately Following Electroconvulsive Therapy. *The Journal of ECT, 33*(2), 96-103. doi:10.1097/yct.0000000000000377

Bryson, A., Gardner, H., Wilson, I., Rolfe, T., & Archer, J. (2016). Temporal lobe epilepsy following maintenance electroconvulsive therapy—Electrical kindling in the human brain? *Epilepsia, 57*(11), e216-e220. doi:10.1111/epi.13565

Butler, C. R., Graham, K. S., Hodges, J. R., Kapur, N., Wardlaw, J. M., & Zeman, A. Z. J. (2007). The syndrome of transient epileptic amnesia. *Annals of Neurology, 61*(6), 587-598. doi:10.1002/ana.21111

Butler, C. R., & Zeman, A. Z. (2008). Recent insights into the impairment of memory in epilepsy: transient epileptic amnesia, accelerated long-term forgetting and remote memory impairment. *Brain, 131*(9), 2243-2263. doi:10.1093/brain/awn127

Calev, A., Nigal, D., Shapira, B., Tubi, N., Chazan, S., Ben-Yehuda, Y., Kugelmass, S., & Lerer, B. (1991). Early and long-term effects of electroconvulsive therapy and depression on memory and other cognitive functions. *Journal of Nervous and Mental Disease, 179*(9), 526-533. doi:10.1097/00005053-199109000-00002

Chan, D., Gallaher, L. M., Moodley, K., Minati, L., Burgess, N., & Hartley, T. (2016). The 4 Mountains Test: A Short Test of Spatial Memory with High Sensitivity for the Diagnosis of Pre-dementia Alzheimer's Disease. *JoVE*(116), e54454. doi:doi:10.3791/54454

Coleman, E. A., Sackeim, H. A., Prudic, J., Devanand, D. P., McElhiney, M. C., & Moody, B. J. (1996). Subjective memory complaints prior to and following electroconvulsive therapy. *Biol Psychiatry, 39*(5), 346-356. doi:10.1016/0006-3223(95)00185-9

Cowen, P. J. (2019). Mechanism of Action of ECT. In I. N. Ferrier & J. Waite (Eds.), *The ECT Handbook* (4th ed., pp. 13-23). Cambridge, UK: Cambridge University Press.

Crawford, J. R., & Garthwaite, P. H. (2002). Investigation of the single case in neuropsychology: confidence limits on the abnormality of test scores and test score differences. *Neuropsychologia, 40*(8), 1196-1208. doi:https://doi.org/10.1016/S0028-3932(01)00224-X

Crovitz, H. F. (1979). Memory Retraining in Brain-Damaged Patients: The Airplane List. *Cortex, 15*(1), 131-134. doi:https://doi.org/10.1016/S0010-9452(79)80013-1

Dallenbach, K. M. (1951). A Puzzle-Picture with a New Principle of Concealment. *The American Journal of Psychology, 64*(3), 431-433. doi:10.2307/1419008

Doty, R. L., Frye, R. E., & Agrawal, U. (1989). Internal consistency reliability of the fractionated and whole University of Pennsylvania Smell Identification Test. *Perception & Psychophysics, 45*(5), 381-384. doi:10.3758/bf03210709

Ferrier, I. N. (2019). ECT in the Treatment of Depression. In I. N. Ferrier & J. Waite (Eds.), *The ECT Handbook* (4th ed., pp. 24-31). Cambridge, UK: Cambridge University Press.

Fink, M. (2007). Complaints of Loss of Personal Memories After Electroconvulsive Therapy: Evidence of a Somatoform Disorder? *Psychosomatics, 48*(4), 290-293. doi:https://doi.org/10.1176/appi.psy.48.4.290

Finnegan, M., & McLoughlin, D. M. (2019). Cognitive Side Effects of ECT. In I. N. Ferrier & J. Waite (Eds.), *The ECT Handbook* (4th ed., pp. 109-120). Cambridge, UK: Cambridge University Press.

Fraser, L. M., O'Carroll, R. E., & Ebmeier, K. P. (2008). The Effect of Electroconvulsive Therapy on Autobiographical Memory: A Systematic Review. *The Journal of ECT, 24*(1), 10-17. doi:10.1097/YCT.0b013e3181616c26

Goldberg, E. (1985). The Goldberg-Barnett remote memory questionnaire. *New York: Albert Einstein Medical College*.

Hodges, J. R., & Larner, A. J. (2017). Addenbrooke's cognitive examinations: Ace, ace-r, ace-iii, aceapp, and m-ace. In *Cognitive screening instruments* (pp. 109-137): Springer.

Holdnack, H. (2001). Wechsler test of adult reading: WTAR. *San Antonio, TX: The Psychological Corporation*.

Hornberger, M., Mohamed, A., Miller, L., Watson, J., Thayer, Z., & Hodges, J. R. (2010). Focal retrograde amnesia: Extending the clinical syndrome of transient epileptic amnesia. *Journal of Clinical Neuroscience, 17*(10), 1319-1321. doi:https://doi.org/10.1016/j.jocn.2010.03.005

Ingram, A., Saling, M. M., & Schweitzer, I. (2008). Cognitive side effects of brief pulse electroconvulsive therapy: a review. *J ect, 24*(1), 3-9. doi:10.1097/YCT.0b013e31815ef24a

Jansari, A. S., Davis, K., McGibbon, T., Firminger, S., & Kapur, N. (2010). When "long-term memory" no longer means "forever": Analysis of accelerated long-term forgetting in a patient with temporal lobe epilepsy. *Neuropsychologia, 48*(6), 1707-1715. doi:https://doi.org/10.1016/j.neuropsychologia.2010.02.018

Kopelman, M. D. (1989). Remote and autobiographical memory, temporal context memory and frontal atrophy in Korsakoff and Alzheimer patients. *Neuropsychologia, 27*(4), 437-460. doi:https://doi.org/10.1016/0028-3932(89)90050-X

Lah, S., Grayson, S., Lee, T., & Miller, L. (2004). Memory for the past after temporal lobectomy: impact of epilepsy and cognitive variables. *Neuropsychologia, 42*(12), 1666-1679. doi:https://doi.org/10.1016/j.neuropsychologia.2004.04.008

Lah, S., Lee, T., Grayson, S., & Miller, L. (2006). Effects of Temporal Lobe Epilepsy on Retrograde Memory. *Epilepsia, 47*(3), 615-625. doi:10.1111/j.1528-1167.2006.00476.x

Levine, B., Svoboda, E., Hay, J. F., Winocur, G., & Moscovitch, M. (2002). Aging and autobiographical memory: Dissociating episodic from semantic retrieval. *Psychology and Aging, 17*(4), 677-689. doi:10.1037/0882-7974.17.4.677

Manes, F., Hodges, J. R., Graham, K. S., & Zeman, A. (2001). Focal autobiographical amnesia in association with transient epileptic amnesia. *Brain, 124*(3), 499-509. doi: https://doi.org/10.1093/brain/124.3.499

Markowitsch, H. J., & Staniloiu, A. (2013). The impairment of recollection in functional amnesic states. *Cortex, 49*(6), 1494-1510. doi:https://doi.org/10.1016/j.cortex.2012.05.020

Marks, D. F. (1973). Visual imagery differences in the recall of pictures. *British Journal of Psychology, 64*(1), 17-24. doi:10.1111/j.2044-8295.1973.tb01322.x

Martin, D. M., Gálvez, V., & Loo, C. K. (2015). Predicting Retrograde Autobiographical Memory Changes Following Electroconvulsive Therapy: Relationships between Individual, Treatment, and Early Clinical Factors. *International Journal of Neuropsychopharmacology, 18*(12). doi:10.1093/ijnp/pyv067

Mayur, P., Byth, K., & Harris, A. (2013). Autobiographical and Subjective Memory With Right Unilateral High-Dose 0.3-millisecond Ultrabrief-Pulse and 1-millisecond Brief-Pulse Electroconvulsive Therapy: A Double-blind, Randomized Controlled Trial. *The Journal of ECT, 29*(4), 277-282. doi:10.1097/YCT.0b013e3182941baf

McAndrews, M. P. (2012). Remote memory and temporal lobe epilepsy. In A. Z. Zeman, N. Kapur, & M. Jones-Gotman (Eds.), *Epilepsy and Memory* (1st ed., pp. 227-243). Oxford, Uk: Oxford University Press.

McElhiney, M. C., Moody, B., & Sackeim, H. (1997). The Autobiographical memory interview–Short form. *New York: New York State Psychiatric Institute*.

McLoughlin, D. M., Kolshus, E., & Jelovac, A. (2017). Systematic review and meta-analysis of randomised controlled trials of bitemporal versus high-dose right unilateral ECT for depression. *Brain Stimulation, 10*(2), 358. doi:https://doi.org/10.1016/j.brs.2017.01.054

Meeter, M. (2003). *Long-term memory disorders: Measurement and modeling.* University of Amsterdam.

Meeter, M., Kloomps, P., & Borsboom, D. (2000). *Amsterdamse Media Vragenlijst. Public events test for retrograde amnesia*. Unpublished research report. University of Amsterdam.

Meeter, M., Murre, J. M. J., Janssen, S. M. J., Birkenhager, T., & van den Broek, W. W. (2011). Retrograde amnesia after electroconvulsive therapy: A temporary effect? *Journal of Affective Disorders, 132*(1), 216-222. doi:https://doi.org/10.1016/j.jad.2011.02.026

Meyers, J. E., & Meyers, K. R. (1995). Rey complex figure test under four different administration procedures. *The Clinical Neuropsychologist, 9*(1), 63-67. doi:10.1080/13854049508402059

Milton, F., Butler, C. R., Benattayallah, A., & Zeman, A. Z. J. (2012). The neural basis of autobiographical memory deficits in transient epileptic amnesia. *Neuropsychologia, 50*(14), 3528-3541. doi:https://doi.org/10.1016/j.neuropsychologia.2012.09.027

Milton, F., Muhlert, N., Pindus, D. M., Butler, C. R., Kapur, N., Graham, K. S., & Zeman, A. Z. J. (2010). Remote memory deficits in transient epileptic amnesia. *Brain, 133*(5), 1368-1379. doi:10.1093/brain/awq055

Moscovitch, M. (2012). The contribution of research on autobiographical memory to past and present theories of memory consolidation. In D. C. Rubin & D. Berntsen (Eds.), *Understanding Autobiographical Memory: Theories and Approaches* (pp. 91-113). Cambridge: Cambridge University Press.

Naphade, N. M., Gupta, N. S., & Shetty, J. V. (2017). Electroconvulsive Therapy in Severe Depression: Is Amnesia a Problem? *Journal of Dental and Medical Sciences, 16*, 71-77.

Napierala, M., Bodnar, A., Chlopocka-Wozniak, M., Permoda-Osip, A., & Rybakowski, J. (2019). Electroconvulsive therapy and autobiographical memory in patients with treatment-resistant depression. *Psychiatr Pol, 53*(3), 589-597. doi:10.12740/pp/85787

Noulhiane, M., Piolino, P., Hasboun, D., Clemenceau, S., Baulac, M., & Samson, S. (2007). Autobiographical memory after temporal lobe resection: neuropsychological and MRI volumetric findings. *Brain, 130*(12), 3184-3199. doi:10.1093/brain/awm258

Ousdal, O. T., Argyelan, M., Narr, K. L., Abbott, C., Wade, B., Vandenbulcke, M., . . . Sienaert, P. (2019). Brain Changes Induced by Electroconvulsive Therapy Are Broadly Distributed. *Biological Psychiatry*. doi:https://doi.org/10.1016/j.biopsych.2019.07.010

Perrin, J. S., Merz, S., Bennett, D. M., Currie, J., Steele, D. J., Reid, I. C., & Schwarzbauer, C. (2012). Electroconvulsive therapy reduces frontal cortical connectivity in severe depressive disorder. *Proceedings of the National Academy of Sciences, 109*(14), 5464-5468. doi:10.1073/pnas.1117206109

Piolino, P., Desgranes, B., Belliard, S., Matuszewski, V., Lalevée, C., De La Sayette, V., & Eustache, F. (2003). Autobiographical memory and autonoetic consciousness: triple dissociation in neurodegenerative diseases. *Brain, 126*(10), 2203-2219. doi: 10.1093/brain/awg222

Prudic, J., Peyser, S., & Sackeim, H. A. (2000). Subjective memory complaints: a review of patient self-assessment of memory after electroconvulsive therapy. *J ect, 16*(2), 121-132. doi:10.1097/00124509-200006000-00004

Rubin, D. C., & Greenberg, D. L. (1998). Visual memory-deficit amnesia: a distinct amnesic presentation and etiology. *Proc Natl Acad Sci U S A, 95*(9), 5413-5416. doi:10.1073/pnas.95.9.5413

Schmidt, M. (1996). *Rey auditory verbal learning test: A handbook*: Western Psychological Services Los Angeles, CA.

Semkovska, M., Landau, S., Dunne, R., Kolshus, E., Kavanagh, A., Jelovac, A., . . . McHugh, C. (2016). Bitemporal versus high-dose unilateral twice-weekly electroconvulsive therapy for depression (EFFECT-Dep): a pragmatic, randomized, non-inferiority trial. *American Journal of Psychiatry, 173*(4), 408-417.

Semkovska, M., & McLoughlin, D. M. (2014). Retrograde Autobiographical Amnesia After Electroconvulsive Therapy: On the Difficulty of Finding the Baby and Clearing Murky Bathwater. *The Journal of ECT, 30*(3), 187-188. doi:10.1097/yct.0000000000000122

Semkovska, M., Noone, M., Carton, M., & McLoughlin, D. M. (2012). Measuring consistency of autobiographical memory recall in depression. *Psychiatry Research, 197*(1), 41-48. doi:https://doi.org/10.1016/j.psychres.2011.12.010

Sobin, C., Sackeim, H. A., Prudic, J., Devanand, D. P., Moody, B. J., & McElhiney, M. C. (1995). Predictors of retrograde amnesia following ECT. *Am J Psychiatry, 152*(7), 995-1001. doi:10.1176/ajp.152.7.995

Soderlund, H., A., P., & Levine, B. (2012). Electroconvulsive therapy for depression and autobiographical memory. In A. Z. Zeman, N. Kapur, & M. Jones-Gotman (Eds.), *Epilepsy and Memory* (1st ed., pp. 244-258). Oxford, Uk: Oxford University Press.

Squire, L. R. (1974). Remote memory as affected by aging. *Neuropsychologia, 12*(4), 429-435. doi:https://doi.org/10.1016/0028-3932(74)90073-6

Squire, L. R., & Cohen, N. (1979). Memory and amnesia: resistance to disruption develops for years after learning. *Behavioral and Neural Biology, 25*(1), 115-125. doi:https://doi.org/10.1016/S0163-1047(79)90841-0

Squire, L. R., & Slater, P. C. (1983). Electroconvulsive Therapy and Complaints of Memory Dysfunction: A Prospective Three-Year Follow-up Study. *British Journal of Psychiatry, 142*(1), 1-8. doi:10.1192/bjp.142.1.1

Steinberg, B. A., Bieliauskas, L. A., Smith, G. E., & Ivnik, R. J. (2005). Mayo's Older Americans Normative Studies: Age- and IQ-Adjusted Norms for the Trail-Making Test, the Stroop Test, and MAE Controlled Oral Word Association Test. *The Clinical Neuropsychologist, 19*(3-4), 329-377. doi:10.1080/13854040590945210

Stevens, M. (1979). *Famous personality test: A test for measuring remote memory.* Paper presented at the Bulletin of the British Psychological Society.

Strauss, E., Sherman, E. M., & Spreen, O. (2006). *A compendium of neuropsychological tests: Administration, norms, and commentary*: American Chemical Society.

The UK ECT Review Group (2003). Efficacy and safety of electroconvulsive therapy in depressive disorders: a systematic review and meta-analysis. *The Lancet, 361*(9360), 799-808.

Tombaugh, T. N., Kozak, J., & Rees, L. (1999). Normative Data Stratified by Age and Education for Two Measures of Verbal Fluency: FAS and Animal Naming. *Archives of Clinical Neuropsychology, 14*(2), 167-177. doi:10.1093/arclin/14.2.167

Tramoni, E., Felician, O., Barbeau, E. J., Guedj, E., Guye, M., Bartolomei, F., & Ceccaldi, M. (2011). Long-term consolidation of declarative memory: insight from temporal lobe epilepsy. *Brain, 134*(3), 816-831. doi:10.1093/brain/awr002

Verwijk, E., Comijs, H. C., Kok, R. M., Spaans, H.-P., Stek, M. L., & Scherder, E. J. A. (2012). Neurocognitive effects after brief pulse and ultrabrief pulse unilateral electroconvulsive therapy for major depression: A review. *Journal of Affective Disorders, 140*(3), 233-243. doi:https://doi.org/10.1016/j.jad.2012.02.024

Viskontas, I. V., McAndrews, M. P., & Moscovitch, M. (2000). Remote episodic memory deficits in patients with unilateral temporal lobe epilepsy and excisions. *Journal of Neuroscience, 20*(15), 5853-5857.

Warrington, E. K. (1984). *Recognition memory test: Manual*: Nfer-Nelson.

Wechsler, D. (1997). Wechsler Memory Scale—III San Antonio. *TX: Psychological Coorporation*.

Wechsler, D. (1999). Weschler abbreviated scale of intelligence. *San Antonio TX: The Psychological Corporation*.

Wilkinson, S. T., Sanacora, G., & Bloch, M. H. (2017). Hippocampal Volume Changes Following Electroconvulsive Therapy: A Systematic Review and Meta-analysis. *Biological Psychiatry: Cognitive Neuroscience and Neuroimaging, 2*(4), 327-335. doi:https://doi.org/10.1016/j.bpsc.2017.01.011

Zeman, A., Byruck, M., Tallis, P., Vossel, K., & Tranel, D. (2018). Touching the void – First and third person perspectives in two cases of autobiographical amnesia linked to temporal lobe epilepsy. *Neuropsychologia, 110*, 55-64. doi:https://doi.org/10.1016/j.neuropsychologia.2017.07.007

Zeman, A., Dewar, M., & Della Sala, S. (2015). Lives without imagery – Congenital aphantasia. *Cortex, 73*, 378-380. doi:https://doi.org/10.1016/j.cortex.2015.05.019Zeman, A., Kapur, N., & Jones-Gotman, M. (2012). *Epilepsy and Memory* (A. Z. Zeman, N. Kapur, & M. Jones-Gotman Eds. 1st ed.). Oxford, Uk: Oxford University Press.

Zigmond, A. S., & Snaith, R. P. (1983). The Hospital Anxiety and Depression Scale. *Acta Psychiatrica Scandinavica, 67*(6), 361-370. doi:10.1111/j.1600-0447.1983.tb09716.x

Tables

Table 1

AW performance compared to control on General Cognition, Memory and Mood

Instrument	**Measure**	**AW Result (max score)**	**Group 1 Control Result (SD)**	***P***	**Group 2 Control Result (SD)**	***P***
WASI/WTAR	IQ	134	112.14 (4.34)*	.003	119.33 (13.1)	.304
COWAT	FAS	47	56.86 (14.44)	.547	43.67 (13.36)	.851
	Animals	20	22.86 (4.78)	.596	18.00 (6.15)	.761
TMT (B-A seconds)	Executive Function	54.19	29.43 (9.58)	.052	80.04 (65.17)	.710
New Words Test	Free Recall	78 (84)	-	-	61.32 (12.6)	.165
	Recognition	42 (42)	-	-	39.96 (2.94)	.121
WMS-III (Logical Memory)	Immediate	14 (25)	14.57 (4.12)	.901	13.67 (5.25)	.953
	Delayed	7 (25)	13.00 (4.08)	.218	11.75 (4.97)	.378
	Recognition	11 (15)	13.43 (0.78)	.027	12.33 (2.10)	.555
RCFT	Copy	35 (36)	32.86 (3.19)	.553	32.96 (3.56)	.593
	Delayed	23 (36)	16.50 (6.29)	.371	16.71 (6.98)	.405
WRMT	Words	46 (50)	47.57 (1.72)	.426	46.73 (3.80)	.857
	Faces	48 (50)	39.14 (3.34)	.048	43.00 (3.98)	.253
HADs	Depression	3 (21)	3.14 (3.23)	.968	2.00 (2.45)	.450
	Anxiety	6 (21)	5.00 (3.00)	.766	3.58 (2.97)	.702

Note: *The WTAR was used to assess IQ in this group, and WASI in all others. Significance was inferred at p = 0.002.

Table 2

AW performance compared to control on measures of ALF and Topographical Memory

Instrument	**Measure (max)**	**AW Result**	**Mean Control Result (SD)**	***P***
mMFD	# Trials (10)	4	5.57 (1.61)	.397
	40s Recall (21)	12	16.29 (3.04)	.235
	30 min Recall (21)	15	15.43 (2.99)	.897
	3day Recall (21)	11	14.43 (3.31)	.370
	Recognition (7)	3	4.71 (1.38)	.290
mRAVLT	# Trials (10)	5	3.57 (0.98)	.221
	40s Recall (15)	9	11.43 (1.40)	.156
	30 min Recall (15)	8	10.43 (1.62)	.210
	3day Recall (15)	5	7.57 (2.87)	.434
	Recognition (15)	10	12.14 (1.68)	.278
	False Positives (15)	2	2.00 (1.15)	.999

Note: Significance was inferred at $p = 0.05$.

Figures

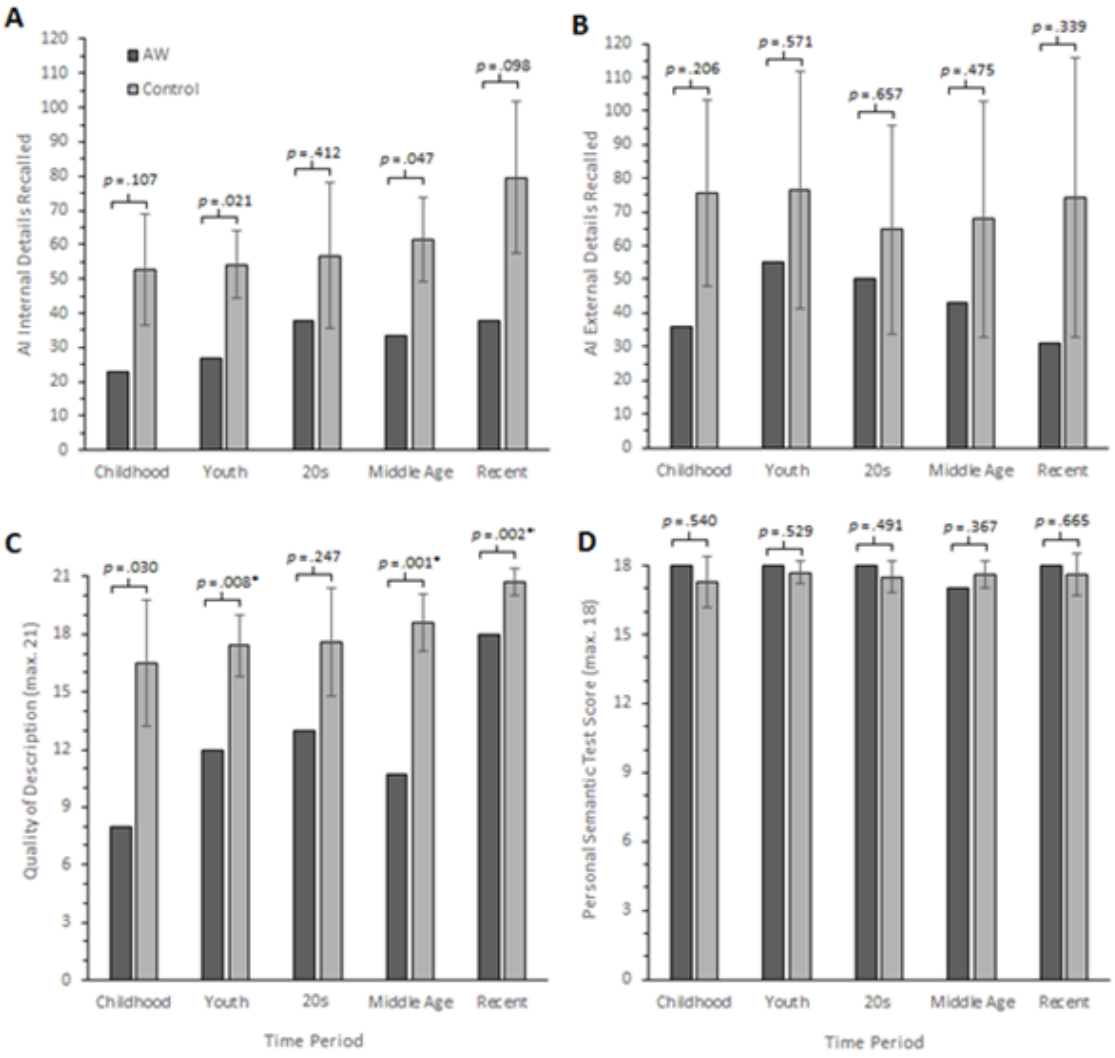

Figure 1. Mean control performance compared to AW scores on Levine AI (panels A to C) and Personal Semantics Test (panel D) across all five probed time periods. **(A)** Mean number of internal details recalled. **(B)** Mean number of external details provided. **(C)** Mean quality of description for internal details. **(D)** Personal semantics test scores. * = $p < .01$.