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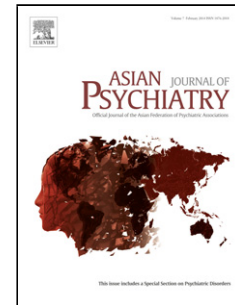
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Title: Correlates of self-reported, autobiographical, and mini-mental status examination defined memory deficits following electroconvulsive therapy in south India

Authors: Anto P. Rajkumar, Cheryl P. Petit, Arun Rachana, Funmi Deinde, G. Shyamsundar, P. Thangadurai, Kuruthukulangara S. Jacob



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Authors' names and affiliations:

Anto P. Rajkumar, M.D., M.R.C.Psych., Ph.D., Ph.D.^{a-c},

Cheryl P. Petit, M.D.^c,

Arun Rachana, M.P.H., M.D.^c,

Funmi Deinde, M.B.B.S.^b,

G. Shyamsundar, M.D.^c,

P. Thangadurai, D.P.M., D.N.B.^c,

Kuruthukulangara S. Jacob, M.D., F.R.C.Psych., Ph.D.^c

^a Department of Old Age Psychiatry, Institute of Psychiatry, Psychology, & Neuroscience, King's College London, 16, De Crespigny Park, London-SE5 8AF, United Kingdom

^b South London and Maudsley NHS foundation Trust, Bethlem Royal Hospital, Monks Orchard Road, Beckenham BR3 3BX, United Kingdom

^c Department of Psychiatry, Christian Medical College, Vellore-632002, India.

Corresponding author:

Dr. Anto Praveen Rajkumar Rajamani, M.D., D.N.B., M.R.C.Psych., Ph.D., Ph.D.,

Academic Clinical Lecturer,

Department of Old Age Psychiatry,

Institute of Psychiatry, Psychology, & Neuroscience,

King's College London,

16, De Crespigny Park,

London - SE5 8AF, United Kingdom.

Email: Anto.Rajamani@kcl.ac.uk

Phone: +44 02032289520

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Highlights

- Self-reported, MMSE-defined, and autobiographical memory deficits are common following ECT.
- Agreement between these memory deficits is poor, and their correlates are discrete.
- Serum cortisol levels correlate significantly with self-reported memory complaints.
- People receiving ECT need periodic assessments evaluating multiple cognitive domains.

Abstract

Background: Cognitive deficits, self-reported or found following electroconvulsive therapy (ECT), and their correlates are diverse. Despite the characteristics of people receiving ECT in Asia differ widely from the west, pertinent research from Asia remains sparse.

Methods: We investigated the correlates of self-reported, mini-mental status examination (MMSE) defined, and autobiographical memory deficits in a cohort that received ECT in a south Indian tertiary-care setting. 76 consecutive consenting people were recruited within seven days of completing their ECT course. Memory was assessed by a subjective Likert scale, MMSE, and an autobiographical memory scale (AMS). Psychopathology was assessed by brief psychiatric rating scale, and serum cortisol levels were estimated by chemiluminescence immunoassays. Relevant sociodemographic and clinical data were collected from the participants, and their medical records. The correlates were analysed using generalised linear models after adjusting for the effects of potential confounders.

Results: Self-reported, MMSE-defined, and autobiographical memory deficits were present in 27.6% (95%CI 17.6-37.7%), 42.1% (95%CI 31.0-53.2%), and 36.8% (95%CI 26.0-47.7%) of participants, respectively. Agreement between the memory deficits was poor. Age, less education, duration of illness, hypothyroidism, and past history of another ECT course were

significantly associated with MMSE-defined deficits. Age, anaemia, past ECT course, and pre-ECT blood pressure were significantly associated with autobiographical memory deficits, while residual psychopathology and cortisol levels were significantly associated with self-reported memory deficits.

Conclusion: Self-reported, MMSE-defined, and autobiographical memory deficits are common at the completion of ECT course, and their correlates differ. All service users receiving ECT need periodic cognitive assessments evaluating multiple cognitive domains.

Key words: Electroconvulsive therapy; Memory; Cognition; Cortisol; Schizophrenia

1. Introduction

Assessment of memory deficits following electroconvulsive therapy (ECT) is complex. Firstly, cognitive deficits following ECT are not global, but discrete. Routine cognitive assessment instruments like mini-mental status examination (MMSE) may fail to elicit the deficits in specific domains such as autobiographical memory (Sackeim, 2014). Secondly, psychiatric disorders necessitating ECT *per se* can contribute to the cognitive deficits, and it is difficult to disentangle the effects of the disorders and their treatment. Thirdly, opinions regarding ECT are often strong and polarised (Carney and Geddes, 2003). Many service users have reported severe enduring memory deficits following ECT (Chakrabarti et al., 2010; Rose et al., 2003). However, studies employing objective cognitive assessments have corroborated only acute and brief memory deficits (Semkovska and McLoughlin, 2010; UK-ECT-Review-Group, 2003; Versiani et al., 2011; Wang et al., 2015). The findings of service users-led and professionals-led assessments differ widely, and inherent observer bias is one of the potential explanations (Rose et al., 2003). Professionals

tend to focus on laboratory evidence for brain damage and objective memory assessment findings (Fink, 2007). They may fail to address the distress and disability, reported by some service users (Rose et al., 2004). Studies evaluating self-reported and objective memory deficits in a cohort of service users that received ECT are sparse (Rajkumar et al., 2006).

Available studies have mostly evaluated the correlates of memory deficits, defined by standard cognitive assessments, following ECT (Andrade and Bolwig, 2014; McCall et al., 2000; Neylan et al., 2001; Sackeim et al., 2000; Shapira et al., 2000; Sobin et al., 1995). They have principally investigated the associations with many treatment-related variables, such as electrode placements, treatment schedules, electrical dosing, wave pattern, seizure duration, and anaesthesia. Bilateral ECT (UK-ECT-Review-Group, 2003), sine-waveform (Pisvejc et al., 1998), more frequent ECT schedules (Shapira et al., 2000), and higher suprathreshold electrical dosing (McCall et al., 2000) can increase the risk for memory deficits. Moreover, individual-related factors such as advancing age, female gender, and lower premorbid intelligence have been associated with memory deficits (Sackeim et al., 2007; Sobin et al., 1995). Higher cortisol levels have been reported to increase the risk for memory deficits following ECT (Neylan et al., 2001), and pertinent glucocorticoid mechanisms have been hypothesised (Nagaraja et al., 2007). A multifactorial model for the neurocognitive effects of ECT including various individual, illness, and treatment-related variables has been proposed recently (McClintock et al., 2014).

Systematic studies investigating the correlates of self-reported and autobiographical memory deficits remain sparse. Investigating the associations of these memory deficits with various individual, illness, and treatment-related variables may help to broaden our understanding of these deficits, to identify people at risk of developing these deficits, and to develop potential approaches minimising these memory deficits following ECT (McClintock et al., 2014). Besides, majority of service users receiving ECT are older women with

depression in Europe and USA, but ECT is mostly used for younger men with schizophrenia in Asia (Leiknes et al., 2012). This limits the generalisability of the findings of western studies investigating ECT-related memory deficits to Asian settings, and relevant systematic studies from Asia remain few (Leiknes et al., 2012). Hence, we aimed to investigate the self-reported, MMSE-defined, and autobiographical memory deficits in a cohort that completed a course of ECT in a south Indian tertiary-care psychiatric facility.

2. Material and Methods

2.1. Study design: We adopted a case-control design for investigating the study objectives.

2.2. Setting: The department of psychiatry, Christian Medical College (CMC), Vellore, India, is a tertiary psychiatric facility providing mental health services for service users from India. This 122-bed hospital has a daily outpatient clinic, and provides short-term inpatient care. Service users and their family members stay in independent cottages during the period of hospitalisation, which often ranges from four to eight weeks. The emphasis is on a multi-disciplinary approach using a wide variety of pharmacological and psychological therapies.

2.3. Practice of ECT: The department has a dedicated ECT suite, and follows twice weekly ECT schedule (Mondays and Thursdays). Bilateral fronto-temporal electrode placement is the norm, and all ECTs are completed under intravenous sodium thiopental (2-3 mg/kg) anaesthesia, and intravenous suxamethonium chloride (0.5-1 mg/kg) muscle relaxation. Nivique versatile ECT system (Nivique Meditech Private Limited, Bengaluru, India) is used to deliver brief-pulse constant current electrical stimuli. A multi-disciplinary team including two psychiatrists, one anaesthetist, and 2-4 psychiatric nurses delivers all ECTs. Motor seizure duration is monitored using the “cuff” method (Chung, 2000). During the first ECT session of all service users, stimulus intensity is empirically titrated to elicit at least 25 seconds of motor seizures. This electrical dose is continued on subsequent sessions, except

when there are specific indications to change the stimulus intensity. Following ECT, all service users are monitored in a recovery room within the ECT suite. Therapeutic decision on using ECT is made through consensus among the treating team. The treating psychiatrists explained the details of ECT, and its risks and benefits to the service users and to their family, and obtained written informed consent. The treating team decided the number of ECTs, ECT methods, and when to stop the ECT course. The authors did not influence any of these decisions.

2.4. Participants: All consecutive inpatients or outpatients, who were at least 18 years old, and completed or withdrew from a course of ECT in the department were invited to participate. All consenting eligible service users were recruited in this study. Service users with severe medical comorbidity, intellectual disability, sensory impairment, or severe psychopathology precluding the assessment were excluded. The nature and purpose of this study, involved procedures, expected duration of involvement, and potential risks and benefits of this study were explained to all participants and their nearest relatives, and written informed consent was obtained from all participants. The protocol of this study was approved by the institutional review board of CMC, Vellore, India.

2.5. Assessment: All participants were assessed by two independent investigators in two sessions within one week after completing or withdrawing from their ECT course. Each assessment session lasted for approximately forty-five minutes. One investigator assessed the service users' memory by the following, (i) A Likert scale: each service user subjectively rated his/her memory deficits following ECT on a six-point Likert scale. The responses included no, minimal, mild, moderate, severe, and extremely severe memory deficits; (ii) MMSE: It is a 30-item screening measure of general cognitive ability (Folstein et al., 1975). Its psychometric properties have been extensively studied (Lopez et al., 2005; Tombaugh and McIntyre, 1992); (iii) Autobiographical Memory Scale (AMS): Autobiographical memory

was assessed by a culturally adapted 25-item AMS, which has already been used to investigate autobiographical memory deficits in an earlier cohort that received ECT in the department (Mohan et al., 2009). The AMS included major domains of a person's life, such as schooling, place of work, neighbourhood, and family events. Knowledgeable collateral source information from the next of kin was used as the criterion standard for evaluating the degree of recall of the participants (Dreyfus et al., 2010; Viswanath et al., 2013). Each AMS item was scored on a three-point scale from 0 (cannot remember anything) to 2 (can remember everything), and the total score of AMS ranged from 0 to 50.

Another independent investigator, blind to the results of memory assessment, assessed the psychopathology of all participants using 18-items Brief Psychiatric Rating Scale (BPRS). The BPRS is a short clinician-rated scale for measuring the severity of psychopathology, and it covers a broad range of areas including thought disturbance, emotional withdrawal, anxiety, depression, hostility, and suspiciousness (Overall and Gorham, 1962). The 18 items are rated from one to seven with a total score ranging from 18 to 126. The investigator interviewed all participants and their relatives using a structured proforma (Supplementary material) to collect data on individual-related variables including age, gender, marital status, urbanicity, education, and occupation. Moreover, three ml of peripheral blood sample was collected from all participants at 8 am (\pm 30 minutes) within one week after their course of ECT. Serum cortisol level was estimated using this sample by chemi-luminescence immunoassay on ADVIA Centaur XP immunoassay system (Siemens Medical Solutions USA, Inc., Malvern, PA, USA) in the department of clinical biochemistry, CMC, Vellore, India (Miller and Crapo, 1994).

2.6. Review of medical records: The department maintains comprehensive medical records, and ECT records for all services users receiving ECT. The investigator, blind to the results of memory assessment, accessed the records of the participants with their written informed

consent. Data on illness-related variables including clinical diagnosis, family history of neuropsychiatric morbidity, pre-ECT suicidal risk, age of onset of illness, duration of current episode of illness, total duration of illness, duration of untreated psychosis, pre-ECT MMSE scores, axis-II comorbidity, and medical co-morbidity, and on treatment-related variables including previous courses of ECT, co-medications, hospitalisation, pre-ECT cognitive function, pre-ECT physical examination, and number of ECTs in the current course of ECT were collected from the records. Data on the dose of anaesthesia, dose of muscle relaxant, pre-ECT blood-pressure (BP) and oxygen saturation, post-ECT BP and oxygen saturation, post-ictal confusion, electrical stimulus (millicoulombs), motor seizure duration, and post-ECT recovery were collected for each ECT session of all participants. When there were any discrepancies, the illness and treatment-related data were verified with the participants' relatives and their treating team with their consent.

2.7. Case definition of memory deficits: Self-reported memory deficit was defined by the participant reporting at least moderate severity of memory deficits in the Likert scale. MMSE-defined memory deficit was defined by the participant failing at least seven items of MMSE following ECT. Autobiographical memory deficit was defined by the participant scoring less than the median value of total AMS score of the cohort following ECT.

2.8. Statistical analyses: Participants' characteristics and their clinical and treatment profiles were initially analysed by descriptive statistics. Differences between subgroups were analysed by appropriate tests of statistical significance. Agreement between the self-reported, MMSE-defined, and autobiographical memory deficits were assessed by kappa statistics. The associations of the memory deficits with various individual, illness, and treatment-related variables were analysed by generalised linear models with binomial distribution and log-link function. Each model included the memory deficit as the dependent variable, a hypothesised explanatory variable, and age and number of ECTs as covariates. Adjusted risk ratios (ARR)

were derived from the exponentiated estimates of the regression coefficients of these models. ARR were preferred over the odds ratios, because the outcome event, memory deficits, were common (>10%). Robust standard errors were estimated to calculate the 95% confidence intervals (CI) of ARR. Considering multiple testing, Benjamini-Hochberg false discovery rate (5%) correction was done. All analyses were performed using the statistical software STATA 13.1 (StataCorp, TX, USA), and SPSS 21.0 (Armonk, NY, USA).

3. Results

3.1. Participant characteristics: 83 service users, who completed or withdrew from a course of ECT, were assessed for their eligibility, and 76 (91.6%) of them fulfilled the eligibility criteria. As none refused consent, 76 participants were recruited. Seven service users, who were excluded, did not differ significantly from the participants on their gender ($z=-0.03$; $p=0.98$), age ($t=-0.10$; $p=0.92$), and the number of years of education ($t=0.28$; $p=0.78$). Table-1 presents the sociodemographic and clinical characteristics of the participants. Majority of the participants were single ($n=41$; 54.0%), unemployed ($n=45$; 59.2%), and from rural areas ($n=40$; 52.6%). Median number of ECTs during the ECT course was 10 (range 6-13). Co-mediations included antidepressants ($n=10$; 13.2%), first ($n=20$; 26.3%) or second generation ($n=68$; 89.5%) antipsychotics, benzodiazepines ($n=43$; 56.6%), and anticholinergics ($n=46$; 60.5%). Numbers of participants, who had dyslipidaemia, microcytic hypochromic anaemia, and hypothyroidism, were 20 (26.3%), 13 (17.1%), and 5 (6.6%), respectively. Mean serum levels of morning cortisol, creatinine, and thyroid stimulating hormone of the participants were 16.35 (SD=5.30) $\mu\text{g/dL}$, 0.92 (SD=0.21; $n=73$) mg/dL , and 3.67 (SD=11.66; $n=65$) mg/dL , respectively. Mean serum cortisol levels of participants with schizophrenia (16.65 $\mu\text{g/dL}$; 95%CI 14.94-18.36 $\mu\text{g/dL}$), mania (14.69 $\mu\text{g/dL}$; 95%CI 12.48-16.90 $\mu\text{g/dL}$), depression (17.96 $\mu\text{g/dL}$; 95%CI 12.47-23.46 $\mu\text{g/dL}$), and other diagnoses (15.73 $\mu\text{g/dL}$; 95%CI 12.36-19.11 $\mu\text{g/dL}$) did not differ significantly ($F=0.74$; $df=3$; $p=0.53$).

3.2. Presence of memory deficits: 21 participants (27.6%; 95% CI 17.6-37.7%) reported memory deficits. Numbers of participants reporting moderate, severe, and extremely severe memory deficits were 15 (19.7%), 4 (5.3%), and 2 (2.6%), respectively. 29 (38.2%) participants did not report any memory deficits, while ten (13.2%) reported minimal deficits. MMSE-defined memory deficits were present in 42.1% (95% CI 31.0-53.2%) of the participants. Pre-ECT cognitive assessment had been documented in 72 ECT records, and 27 (37.5%; 95% CI 26.3-48.7%) of them showed seven or more points decline in their post-ECT MMSE scores. Median AMS total score in this cohort was 40 (range 24-50; IQR=21), and 28 (36.8%; 95% CI 26.0-47.7%) participants scored below 40. 52 participants (68.4%; 95% CI 58.0-78.9%) had at least one of these memory deficits (Supplementary table-1).

3.3. Agreement between memory deficits: Table-2 presents the agreement between self-reported, MMSE-defined, and autobiographical memory deficits. Self-reported memory deficits showed poor agreement with MMSE-defined and autobiographical memory deficits (Figure-1). However, agreement between MMSE-defined memory deficits and autobiographical memory deficits was fair (Viera and Garrett, 2005).

3.4. Correlates of memory deficits: Table-3 and Table-4 present the associations of the memory deficits with various individual, illness, and treatment-related variables. Age, less years of education, duration of illness more than two years (median value), hypothyroidism, and having received more than one course of ECT were significantly associated with MMSE-defined memory deficits. Autobiographical memory deficits were significantly associated with age, urbanicity, anaemia, having received more than one course of ECT, and higher pre-ECT BP. Moreover, self-reported memory deficits were significantly associated with residual psychopathology and serum cortisol levels. Mean total BPRS scores, and serum cortisol levels in those, who reported moderate to extremely severe memory deficits, were 34.0 (SD=8.0), and 19.51 (SD=5.23) µg/dL, respectively, while mean total BPRS scores, and

serum cortisol levels in those, who did not report such memory deficits, were 25.7 (SD=8.9), and 14.95 (SD=4.79) $\mu\text{g/dL}$, respectively. After Benjamini-Hochberg correction, only the associations between self-reported memory deficits and serum cortisol levels, as well as between autobiographical memory deficits and mean pre-ECT diastolic BP were statistically significant ($p=0.0375$). Marital status, unemployment, clinical diagnosis of schizophrenia, bipolar disorder, or depression, family history of psychosis, age of onset of illness, duration of current episode of illness, duration of untreated psychosis, axis-II comorbidity, antipsychotic or antidepressant co-medications, pre-ECT MMSE scores, and post-ECT BP were not significantly associated with self-reported, MMSE-defined, or autobiographical memory deficits in this cohort.

4. Discussion

This is the largest naturalistic study conducted to date in Asia that has investigated the agreement, and correlates of self-reported, MMSE-defined, and autobiographical memory deficits in a cohort that received ECT. It has demonstrated the poor agreement between self-reported and objective memory deficits. It has found specific correlates of self-reported, MMSE-defined, and autobiographical memory deficits.

Previous studies have established the associations of MMSE-defined memory deficits with electrode placements, treatment schedules, electrical stimulus dosing, wave pattern, and anaesthetic parameters (McCall et al., 2000; McClintock et al., 2014; Shapira et al., 2000; Sobin et al., 1995; UK-ECT-Review-Group, 2003). Naturalistic study design and the institutional practice of ECT ensured that these risk factors were uniform among the study participants. Unlike the studies from Europe and USA, the participants of this study were predominantly young men with schizophrenia. However, the estimates of self-reported, MMSE-defined, and autobiographical memory deficits following ECT course were comparable to the estimates, reported by the Western studies (Fraser et al., 2008; Rose et al.,

2003; Sackeim et al., 2007). Only six participants were diagnosed to have depression, and the residual depressive symptoms were not significantly associated with the memory deficits. Hence, our findings indicate that service users receiving ECT may have memory deficits regardless of their diagnosis and severity of depression (Fernie et al., 2014).

Several western studies have reported that the agreement between self-reported and MMSE-defined memory deficits is poor (Berman et al., 2008; Brakemeier et al., 2011). Our findings have confirmed the poor agreement between self-reported and objective memory deficits following ECT in Asian settings. Besides, individual-related factors such as age and female gender have been associated with memory deficits (Sackeim et al., 2007; Sobin et al., 1995). Our results have confirmed the associations with age, but not with gender. A recent review has reported that the relationship between the years of education, and the neurocognitive effects of ECT had not been investigated (McClintock et al., 2014), and our study has added relevant evidence. Liothyronine has been reported to reduce the memory deficits following ECT in people with depression, but the relationship between hypothyroidism and the memory deficits has not been studied (Mohagheghi et al., 2015). Findings of this study added evidence for the association between hypothyroidism and MMSE-defined memory deficits. Our results have confirmed that clinical psychiatric diagnoses (Ikeji et al., 1999), and anti-cholinergic medication (Calev et al., 1991) are not associated with the memory deficits. However, previously reported associations of the MMSE-defined memory deficits with pre-ECT global cognitive impairment, and the time to post-ECT recovery were not observed in this cohort (Sobin et al., 1995).

A small study (N=16) has reported that higher salivary cortisol levels were associated with deficits in executive function, visuospatial processing speed, and verbal memory following ECT (Neylan et al., 2001). Higher post-peak salivary cortisol levels have been associated with subjective memory complaints of older people, who had not shown any

deficits on objective neuropsychological testing (Peavy et al., 2013). Higher urinary cortisol levels have been associated with subjective memory complaints of middle aged and older people without any objective cognitive deficits (Wolf et al., 2005). Moreover, a glucocorticoid receptor antagonist, mifepristone, has been reported attenuating ECT-induced retrograde amnesia in rats (Nagaraja et al., 2007). This is the first study to report the association between serum cortisol levels and self-reported memory deficits following ECT. This finding indicates the possibility that the service users reporting post-ECT subjective memory deficits have underlying neurobiological changes that often go unnoticed. Self-reported memory complaints following ECT cannot be readily attributed to health anxiety or artefacts due to direct questioning (Berman et al., 2008). They should be documented, discussed empathetically, and followed up periodically. Self-reported memory deficits were significantly associated with residual psychopathology in this cohort, and there can be a bidirectional relationship between serum cortisol levels and psychopathology in schizophrenia (Zhang et al., 2005). Service users, who have high levels of psychopathology at the end of their ECT course, often need complex treatment regimens after ECT. Failing to address their self-reported memory complaints empathetically may impact their engagement with the services, and their treatment adherence.

Neurobiology underlying various memory and non-memory cognitive deficits following ECT remains uncertain (McClintock et al., 2014). Age, less years of education, and longer duration of illness have been hypothesised to increase the risk for memory deficits following ECT (McClintock et al., 2014), and our findings have confirmed this. Iron deficiency anaemia may lead to cognitive deficits because of altered expression of brain-derived neurotrophic factor and insulin-like growth factor (Estrada et al., 2014), and microcytic hypochromic anaemia was significantly associated with autobiographical memory deficits in this cohort. Hence, prior literature and our findings indicate that the service users,

who are older, lack formal education, have been chronically ill, have already received another course of ECT, or have anaemia or hypothyroidism, are likely to be at risk of developing memory deficits following ECT. Besides, the interest in the hypothesis of intra-ictal hypertensive surge leading to transient blood-brain barrier breach and post-ECT memory deficits (Andrade and Bolwig, 2014) has been rekindled by the association of autobiographical memory deficits with pre-ECT systolic and diastolic BP in this cohort.

4.1. Strengths and limitations: Selection bias was minimised by recruiting all consecutive eligible service users, and by the null refusal rate. Availability of reliable collateral information from the families of all participants, and access to well-documented medical records reduced the possibility of recall bias. Observer bias was minimised by the two independent investigators, blind to each other's findings, assessing the memory deficits and their correlates. However, this study has employed relatively brief cognitive assessment that can be incorporated into routine clinical practice, and it has not employed comprehensive neuropsychological assessments. It has assessed the memory deficits within a week after the ECT, and it did not follow their course longitudinally. Although MMSE is widely used in Asian settings, its scores can be affected by age, education, and cultural background (Tombaugh and McIntyre, 1992). The AMS has been specifically designed for the people in south India, but its psychometric properties needs further evaluation (Mohan et al., 2009). Information regarding baseline self-reported and autobiographical memory deficits were not recorded in medical records of any participants. Moreover, several electrophysiological parameters have been associated with cognitive deficits following ECT (Azuma et al., 2007; Sackeim et al., 2000), but routine electroencephalographic monitoring was not feasible in our setting.

4.2. Future directives: The American Psychiatric Association task force report on ECT recommended weekly objective cognitive assessments, and documenting service users'

reports in 2001 (APA, 2001). Many European professional organisations have suggested periodic cognitive assessments before, during, and after a course of ECT (Porter et al., 2008). However, these recommendations are not routinely implemented in most of the Asian clinical settings (Leiknes et al., 2012; Rajkumar et al., 2006, 2007). High numbers of service users receiving ECT, resource limitations, cross-cultural issues in cognitive assessment, unequal physician-patient relationships, and difficulties in generalising Western research findings to Asian settings contribute to this shortcoming. Findings of this research highlight the need for periodic cognitive assessments evaluating multiple cognitive domains of all service users before, during, and after a course of ECT, and the need to formulate specific guidelines for Asian settings. Although short culturally-modified cognitive assessment batteries often have suboptimal sensitivity, they may help overcoming the hurdles in improving the quality of care in many clinical settings practising ECT. A short assessment battery for ECT related cognitive deficits has been developed, and used in a small sample of service users (N=30) in south India (Viswanath et al., 2013). This research has confirmed the feasibility of employing another short cognitive assessment battery in a relatively larger south Indian cohort that received ECT. Identified correlates of memory deficits following ECT indicate the need for more frequent follow-up of specific subgroups of service users, and may help prioritisation and resource allocation. There is a need for further research developing and validating culturally-appropriate cognitive assessment instruments for Asian settings. Longitudinal Asian studies investigating the course of ECT related cognitive deficits, and further investigations of underlying neurobiology are warranted.

Authors' contributions:

APR and KSJ conceived the idea, and APR designed this study. CPP, AR, and GS collected the data. APR, AR, and PT analysed the data. All authors were involved in interpretation of the results. AR, and FD wrote the initial draft. All authors were involved in further critical revisions, and all authors have approved the final version of the manuscript.

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Ethical standards:

The protocol of this study was approved by the institutional review board of CMC, Vellore, India.

Conflict of interest disclosure statement:

Apart from employing ECT in their clinical practice, all authors declare that they do not have any competing interests.

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Figure legends:

Figure-1: Overlap between self-reported, MMSE-defined, and autobiographical memory deficits following ECT (N=76)

Self-reported: Participants self-reportedly reporting moderate to extremely severe memory deficits in a six point Likert scale; AMS: Autobiographical memory scale total score less than 40; MMSE: MMSE-defined memory deficits, defined by participants failing seven or more items of Mini Mental Status Examination.

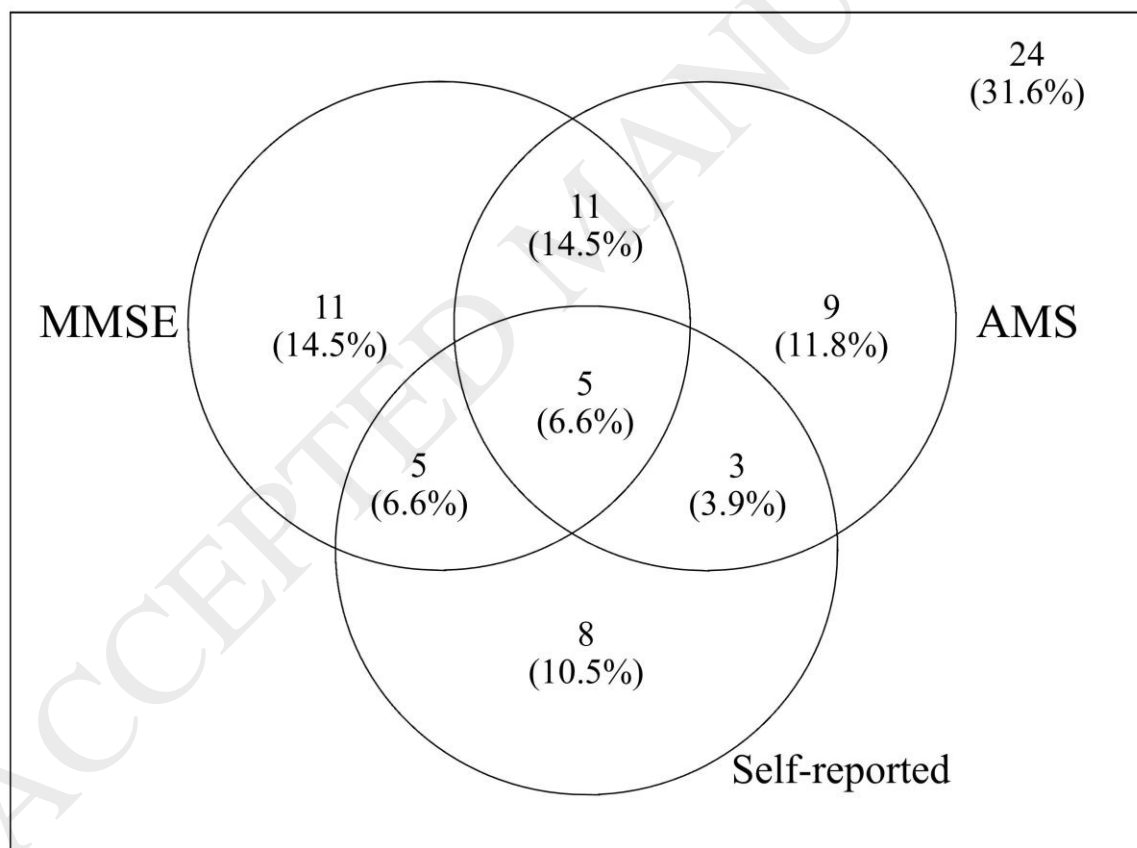


Table-1: Sociodemographic and clinical characteristics of the participants (N=76)

Characteristics		N (%) / Mean (SD)
Men		43 (56.6)
Age (years)		29.1 (8.7)
Number of years of formal education		11.6 (4.1)
Clinical Diagnosis	Schizophrenia	47 (61.8)
	Mania	15 (19.7)
	Depression	6 (7.9)
	Others ^a	8 (10.5)
High risk of suicide before Electroconvulsive therapy (ECT)		20 (26.3)
Pre-ECT Mini Mental Status Examination total score (n=72)		28.7 (1.8)
Post-ECT Mini Mental Status Examination total score		23.6 (4.6)
Post-ECT Brief Psychiatric Rating Scale total score		28.3 (9.4)
Number of ECT in this course		9.5 (1.8)
Has received one more course of ECT in the past		12 (17.6)
Mean ECT energy level (millicoulombs)		124.0 (46.3)
Mean duration of motor seizures (seconds)		37.9 (8.0)
Mean dose of Sodium thiopental (mg)		172.2 (32.7)
Mean dose of Suxamethonium chloride (mg)		30.2 (8.4)

^a Other diagnoses include schizoaffective disorder (ICD-10 F25; n=4), acute psychoses (ICD-10 F23; n=3), and persistent delusional disorder (ICD-10 F22; n=1).

Table-2: Agreement between self-reported, MMSE-defined, and autobiographical memory deficits following ECT

Memory deficit	Self-reported	Autobiographical	Post-ECT MMSE failed items ≥ 7	Pre-ECT - post-ECT MMSE total scores $\geq 7^a$
Self-reported	1			
Autobiographical	0.02 (0.11; 0.89)	1		
Post-ECT MMSE failed items ≥ 7	0.07 (0.11; 0.55)	0.23 (0.11; 0.04)	1	
Pre-ECT - post-ECT MMSE total scores $\geq 7^a$	0.12 (0.12; 0.30)	0.32 (0.11; 0.006)	0.91 (0.05; <0.001)	1

Each cell presents the kappa statistic with its standard error and p value in parentheses; Self-reported: Participants reported moderate to extremely severe memory deficits in a six point Likert scale, following Electro Convulsive Therapy (ECT) (N=76); Autobiographical: Autobiographical memory scale total score less than 40 (median value) following ECT (N=76); MMSE: Mini Mental Status Examination; ^a Pre-ECT MMSE total scores were available only for 72 participants; Statistically significant ($p < 0.05$) findings have been presented in bold.

Table-3: Participant and illness related factors associated with memory deficits following ECT (N=76)

Explanatory variable	Self-reported ^a		MMSE-defined ^b		Autobiographical ^c	
	ARR (95% CI)	p	ARR (95% CI)	p	ARR (95% CI)	p
Age (in years) ^d	1.03 (0.99-1.06)	0.11	1.03 (1.00-1.05)	0.03	1.02 (1.00-1.04)	0.02
Male gender	0.87(0.42-1.81)	0.71	1.42 (0.63-3.18)	0.39	1.11 (0.63-1.97)	0.72
Rural residence	0.99 (0.48-2.03)	0.98	1.19 (0.64-2.20)	0.58	0.54 (0.29-0.99)	0.04
Number of years of education	1.06 (0.98-1.16)	0.14	0.92 (0.84-0.99)	0.04	0.97 (0.91-1.05)	0.48
Presence of suicidal risk	0.85 (0.37-1.99)	0.72	1.09 (0.54-2.18)	0.81	1.45 (0.81-2.60)	0.22
History of catatonia	1.10 (0.38-3.16)	0.86	1.40 (0.75-2.61)	0.29	0.63 (0.18-2.20)	0.47
Duration of illness more than two years	1.43 (0.58-3.51)	0.44	2.27 (1.02-5.05)	0.04	1.50 (0.75-3.02)	0.25
Presence of anaemia ^e	1.65 (0.68-3.98)	0.27	0.92 (0.44-1.90)	0.81	2.31 (1.18-4.54)	0.02
Presence of dyslipidaemia	0.70 (0.24-2.03)	0.51	0.65 (0.31-	0.25	1.23 (0.63-2.41)	0.55

			1.35)			
Presence of hypothyroidism	1.50 (0.44-5.07)	0.51	1.88 (1.11-3.15)	0.02	1.48 (0.69-3.19)	0.32
Serum cortisol level (µg/dL) following ECT	1.14 (1.05-1.24)	0.001	1.04 (0.99-1.08)	0.14	1.00 (0.94-1.06)	0.95
Residual psychopathology ^f	1.02 (1.00-1.04)	0.02	0.99 (0.97-1.01)	0.50	1.04 (0.95-1.15)	0.37
Residual depressive symptoms ^g	1.38 (0.82-2.33)	0.22	0.82 (0.66-1.03)	0.09	0.86 (0.60-1.23)	0.40

Each cell presents a multivariate generalised linear model with binomial distribution and log-link function. Each model included hypothesised explanatory variable, defined memory deficit (dependent variable), and age (in years) as well as the number of ECTs as covariates; ARR: Adjusted risk ratio; ^a participant reported moderate to extremely severe cognitive deficits in a six point Likert scale, following ECT; ^b Participant failed seven or more items of Mini Mental Status Examination (MMSE), following ECT; ^c Autobiographical memory scale total score less than 40 (median value); ^d This row included age (in years) as explanatory variable, defined memory deficit as dependent variable, and the number of ECTs as covariate; ^e Microcytic hypochromic anaemia was documented in the medical records by the treating psychiatrists; ^f Total score of Brief Psychiatric Rating Scale (BPRS), 18 items version; ^g Score on BPRS “Depressive mood” item (Item 9); Statistically significant (p<0.05) findings have been presented in bold.

Table-4: Treatment related factors associated with memory deficits following ECT (N=76)

Explanatory variable	Self-reported ^a		MMSE-defined ^b		Autobiographical ^c	
	ARR (95% CI)	p	ARR (95% CI)	p	ARR (95% CI)	p
Past history of another course of ECT	0.29 (0.03-1.56)	0.13	2.07 (1.19-3.58)	0.01	1.92 (1.01-3.64)	0.04
Number of ECTs in this course	0.97 (0.80-1.18)	0.75	1.06 (0.91-1.22)	0.46	1.18 (0.98-1.41)	0.07
Anticholinergic co-medication during ECT ^d	0.53 (0.24-1.17)	0.12	0.88 (0.51-1.52)	0.66	1.56 (0.82-2.96)	0.18
Benzodiazepine co-medication during ECT	1.31 (0.60-2.88)	0.50	1.18 (0.65-2.12)	0.59	1.49 (0.75-2.98)	0.26
Mean pre-ECT systolic BP (mm Hg)	0.99 (0.96-1.01)	0.31	1.02 (1.00-1.04)	0.07	1.03 (1.01-1.06)	0.009
Mean pre-ECT diastolic BP (mm Hg)	0.99 (0.94-1.04)	0.70	1.02 (1.00-1.05)	0.09	1.05 (1.02-1.09)	0.001

Mean dose of Sodium thiopental (mg)	1.00 (0.99-1.01)	0.65	1.00 (0.99-1.01)	0.84	1.00 (0.98-1.01)	0.82
Mean dose of Suxamethonium chloride (mg)	0.97 (0.93-1.01)	0.20	0.97 (0.93-1.02)	0.26	1.03 (0.94-1.13)	0.56
Mean ECT energy level (millicoulombs)	1.00 (0.99-1.01)	0.76	1.00 (1.00-1.01)	0.20	1.00 (0.99-1.01)	0.78
Mean duration of motor seizures (seconds)	1.01 (0.96-1.05)	0.80	1.00 (0.95-1.05)	0.94	0.98 (0.94-1.01)	0.14
Mean post-ECT oxygen saturation (%)	0.98 (0.86-1.11)	0.77	0.73 (0.47-1.15)	0.18	1.10 (0.15-8.16)	0.92
Mean time to post-ECT recovery (minutes)	1.02 (0.97-1.08)	0.35	1.00 (0.95-1.05)	0.93	0.98 (0.93-1.04)	0.58

Each cell presents a multivariate generalised linear model with binomial distribution and log-link function. Each model included hypothesised explanatory variable, defined memory deficit (dependent variable), and age (in years) as well as number of ECTs as covariates; ARR: Adjusted risk ratio; ^a participant reported moderate to extremely severe cognitive deficits in a six point Likert scale, following ECT; ^b Participant failed seven or more items of Mini Mental Status Examination (MMSE), following ECT; ^c Autobiographical memory scale total score less than 40 (median value); Statistically significant ($p < 0.05$) findings have been presented in bold; ^d Presence of regular prescription of anticholinergic medication during the course of ECT.