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Is electroconvulsive therapy for depression more effective than placebo? A systematic review of studies since 2009.

### **ABSTRACT**

Background: A 2010 review of studies and previous reviews and meta-analyses found minimal evidence that ECT for depression was more effective than placebo during the treatment period and no evidence at all of efficacy beyond the end of treatment. The current review explored whether any contradictory evidence has since been generated. Method: MEDLINE and PsycINFO were searched to identify all post 2009 studies that had compared ECT and simulated ECT for depression, or had in any other way generated valid depression data for ECT recipients at two or more points in time. Results: Ninety-one studies met inclusion criteria. There were no new placebo-controlled trials. There have now been no such studies since 1985. Only four placebo-controlled studies have ever produced data beyond the end of treatment, none of which had found any advantage for ECT over placebo. Of the 91 studies only two aimed to evaluate the efficacy of ECT. Both were severely flawed. None of the other 89 produced robust evidence that ECT is effective for depression, primarily because at least 60% maintained ECT participants on medication and 89% produced no meaningful follow up data beyond the end of treatment. No studies investigated whether ECT prevents suicide. Conclusions: There is still no evidence that ECT is more effective than placebo for depression reduction or suicide prevention. Given the

well-documented high risk of persistent memory dysfunction, the cost-benefit analysis for ECT remains so poor that its use cannot be scientifically, or ethically, justified.

**Key words**: electroconvulsive therapy; depression; suicide; efficacy; placebo; literature review

### INTRODUCTION

The administration of electricity to the human brain to cause a seizure, in the hope of ameliorating depression and other problems, remains the most controversial of psychiatric treatments. While much of this controversy focuses on whether or not it causes brain dysfunction and increases risk of mortality (Breggin, 2008; Read & Bentall, 2010; Read, Bentall, Johnstone, Fosse, & Bracken, 2013; Ross, 2006; Sackeim et al., 2007) there is also debate about what benefits there are which might outweigh the risks.

In 2010 the first author of the current paper, and the renowned British clinical psychologist Professor Richard Bentall, published a peer-reviewed systematic review of seventy years of research on the effectiveness of ECT on depression (its primary target today) and 'schizophrenia'. The review found only ten depression studies comparing ECT to the appropriate placebo (simulated ECT [SECT] - in which the general anesthetic is applied but the electricity is withheld). Six of the ten studies reported some short-term benefit during the course of treatment for a minority of the ECT recipients, sometimes perceived only by psychiatrists but not by other raters. The other four studies reported no differences at all. None of the ten studies reported any difference between ECT and SECT beyond the end of treatment. In fact, only four studies had followed participants beyond the end of treatment. None of these four found any difference between ECT and SECT (Read & Bentall, 2010).

As revealing as the findings themselves are, it is equally concerning that in 70 years since the introduction of ECT there had only ever been four placebo controlled studies examining whether ECT has any benefits for depressed people after the treatment has finished. The last of these had been in 1985 (Gregory, Shawcross, & Gill, 1985) (finding no difference between the ECT and SECT groups at either one month or three months after the last electroshock). So, despite the absence of any evidence up until 1985 that ECT has any lasting effect on depression, there had, in 2010, been no further attempts to produce any evidence for 25 years.

Similarly, the review identified no evidence that ECT has any benefit beyond the end of treatment for people diagnosed with 'schizophrenia'. The two most recent studies comparing ECT and SECT for people diagnosed with 'schizophrenia' had found no differences at all, either during or after treatment (Sarita, Janakiramiaiah, Gangadhar, Subbakrishna, & Rao, 1998; Ukpong, Makanjuola, & Morakinyo, 2002).

The 2010 review noted, moreover, that there had been eight meta-analyses on ECT for depression (Gabor & Laszlo, 2005; Greenhalgh, Knight, Hind, Beverley, & Walters, 2005; Janicak et al., 1985: Kho, van Vreewijk, Simpson, & Zwinderman, 2003; Pagnin, de Queiroz, Pini, & Cassano, 2004; Tharyan & Adams, 2005; UK ECT Review Group, 2003; van der Wurff, Stek, Hoognendijk, & Beekman, 2003), and three on ECT for 'schizophrenia' (Greenhalgh, et al., 2005; Painuly & Chakrabarti, 2006; Tharyan & Adams, 2005). None of these meta-analyses had identified any studies showing that ECT had any benefit beyond the day of the final treatment. There has been one subsequent depression meta-analysis (Dierckx, Heijnen, van den Broek, & Birkenhäger, 2012). It cited no studies providing any data beyond the end of treatment (or even any studies comparing ECT to placebo *during* treatment).

The 2010 review also reported that there was no evidence, of any kind, in support

of the hypothesis that ECT prevents suicide (Read & Bentall, 2010, pp. 339-340).

In the four years preceding 2010, two peer-reviewed reviews (Rasmussen, 2009; Ross, 2006), and two books - based on scientific studies (Breggin, 2008) and personal evidence (Andre, 2008) - had reached similar conclusions to the 2010 review; e.g.: 'Rigorously defined endogenously depressed patients did exceptionally well with sham ECT, as well as with real ECT (Rasmussen, 2009, p. 59).

The current review sought, first, to update the 2010 review, by determining if there was any new evidence that ECT recipients experience more reduction of their depression than recipients of SECT at any point in time after the final shock has been administered. Secondly a systematic review was conducted to identify any new evidence (since 2010), of any kind, that ECT is an effective treatment for depression.

### **METHOD**

An electronic search was conducted to identify all studies published since December 2009 comparing ECT and SECT, or in any other way generating meaningful depression data for ECT recipients. MEDLINE and PsycINFO were searched using the following terms: ("ECT" OR "electroconvulsive therapy" or "electroshock therapy" or "electroconvulsive treatment" OR "electroshock treatment") in combination with ("depression" OR "depressive" or "mood disorder") OR ("placebo" OR "sham" or "simulated"). Inclusion criteria were: original research studies that reported depression scores at two or more points in time of adult (>18 years old) ECT recipients, regardless of the research question; and use of any empirically validated measure of depression. Case reports, review articles, letters to the editor (with no empirical research), animal studies and papers written in languages other than English were excluded. Data from study samples identified as overlapping were excluded.

The abstracts of all retrieved articles were assessed for relevance using the above inclusion and exclusion criteria. The full text was accessed if relevance could not be determined from the abstract. The reference lists of relevant reviews were also manually screened to identify any additional studies. As our search yielded only two studies explicitly aiming to investigate the efficacy of ECT, data were extracted from studies with other aims. Studies were included for data extraction if depression scores were available for all participants receiving ECT (without adjunct treatments).

Studies meeting the inclusion criteria are summarized in Table 1, listed according to study design, inclusion of a follow-up period, reporting of suicide rates or suicidality, whether concomitant use of drug therapy was allowed, and the diagnoses of the samples. Most of the data was extracted from studies not directly investigating the efficacy of ECT, so not all studies reported on the statistical significance of change in depression over time. As such, we also ranked the format of reported results in the following hierarchical manner (from strongest to lowest level of evidentiary support): reporting statistical significance of change in depression; reporting pre-post ECT scores without indicating statistical significance; graphical representation of change only; and reporting only the proportion of responders or remitters to ECT treatment course.

# Table 1 and Figure 1 about here

### **RESULTS**

# Focus and design of the 91 studies

Details of the search process are presented in Figure 1. Of the 2513 studies yielded by the search process, 91 met the inclusion criteria. Table 1 outlines the methodological

components of the studies that produced data that directly (2) or indirectly (89) addressed the efficacy of ECT for depression. Randomized Controlled Trials (RCTs) were defined as studies with active control arms (including other treatments) and were not limited to studies with a placebo/non-active control component. All prospective cohort or non-comparative studies were defined as 'Observational Studies'.

(Prospective cohort studies follow a group of individuals over time to see whether factors on which people in the group differ affect certain outcomes).

Between 2010 and 2015 there were zero placebo-controlled studies comparing ECT and SECT for depression.

Since 2010, only two studies have explicitly attempted to investigate the efficacy of ECT. One attempted to examine the efficacy of ECT through comparison with another treatment. Schoeyen et al. (2015) conducted an RCT comparing the effectiveness of ECT to pharmacological treatment for individuals with a diagnosis of bipolar disorder. Magid, Truong, Trevino, and Husain (2013) also conducted a retrospective review for the purpose of performing a "preliminary evaluation of the efficacy and efficiency" (p. 258) of ultra-brief right unilateral ECT, a newer form of ECT.

All other data in this review were extracted from 89 studies that did not aim to examine the efficacy of ECT but nevertheless included either pre-post ECT depression measures, or the proportion of responders/remitters after a course of ECT. Of these 89 studies, 24 were RCTs (Abdallah, Fasula, Kelmendi, Sanacora, & Ostroff, 2012; Abdollahi et al., 2012; Bailine et al., 2010; Bjølseth et al., 2015; Brakemeier et al., 2014; Ghasemi et al., 2014; Hansen et al., 2011; Kayser et al., 2011; Kellner et al., 2010; Keshtkar, Ghanizadeh, & Firoozabadi, 2011; Kumar, Sharma, & Mani, 2012; Loo et al., 2012; Loo et al., 2015; Masoudzadeh, Yahyavi,

Rashidi, Mohammadpour, & Kiani, 2013; Matthews et al., 2013; Mayur, Bray, Fernandes, Bythe, & Gilbett, 2010; Mayur, Byth, & Harris, 2013; Purtuloglu et al., 2013; Quante et al., 2011; Roepke et al., 2011; Spaans et al., 2013; Wang et al., 2012; Yildiz et al., 2010; Yoosefi et al., 2014); and five were non-randomized trials (Allen et al., 2015; Aten, Oudega, van Exel, Stek, & van Waarde, 2015; Gedge et al., 2012; Lin et al., 2014; Okamoto et al., 2010).

Forty seven of the 89 were observational studies (Azuma et al., 2011; Bär et al., 2010; Bayless et al., 2010; Beall et al., 2012; Bersani et al., 2014; Bilgen et al., 2014; Burgese & Bassitt, 2015; Casarotto et al., 2013; Chiaie et al., 2013; Dannlowski et al., 2013; Dukart et al., 2014; Ebert et al., 2010; Galletly, Paterson, & Burton, 2012; Goto et al., 2012; Guloksuz et al., 2015; Hu et al., 2010; Johansson, Ehnvall, Friberg, & Myredal, 2010; Joshi et al., 2015; Kalogerakou et al., 2015; Kautto et al., 2015; Lin et al., 2013; Loo, Mahon, Katalinic, Lyndon, & Hadzi-Pavlovic, 2011; Lucca et al., 2010; Lyden et al., 2014; McCall et al., 2013; Medda et al., 2014; Meeter, Murre, Janssen, Birkenhager, & van den Broek, 2011; Minelli et al., 2014; Nickl-Jockschat et al., 2015; Nordanskog, Larsson, Larsson, & Johanson, 2014; Ota et al., 2015; Oudega et al., 2011; Perrin et al., 2012; Piccinni et al., 2013; Rapinesi et al., 2015; Rapinesi et al., 2013; Royster et al., 2012; Saijo et al., 2010; Samuelsson, Gerdin, Öllinger, & Vrethem, 2012; Tendolkar et al., 2013; Valevski, Pickholtz, Roz, Weizman, & Rehavi, 2010; van Waarde et al., 2013; Virit et al., 2010; Vukadin, Birkenhager, Wierdsma, Groenland, & van den Broek, 2011; Warnell, Swartz, & Thomson, 2011; Weeks et al., 2013; Wei et al., 2014).

Thirteen of the 89 were other retrospective reviews (Birkenhäger, Pluijms, Ju, Mulder, & van den Broek, 2010; Fernandez, Philpot, Marsh, Hartney, & Kozel, 2014; Galvez et al., 2013; Graveland, Wierdsma, van den Broek, & Birkenhäger, 2013;

Järventausta et al., 2013; Lapidus et al., 2013; Loo, Garfield, Katalinic, Schweitzer, & Hadzi-Pavlovic, 2013; Martinez-Amoros et al., 2014; Niemantsverdriet, Birkenhäger, & van den Broek, 2011; Pulia, Vaidya, Jayaram, Hayat, & Reti, 2013; Ueda, Koyama, & Okubo, 2010; Vaidya et al., 2012; Watts & Groft, 2010).

The aims of these 89 studies varied. About half (n = 45) investigated potential mechanisms of action in ECT and/or predictors of response to ECT. Five compared ECT with other treatments; 12 examined the effects of differing parameters of ECT delivery; 12 compared the effects of different anesthetic agents; seven examined the effects of various adjuncts to ECT; three examined cognitive deficits after ECT and three naturalistic studies described the use of ECT over a period of time. Additionally, there was one study examining the effects of ECT on Parkinson-disease induced psychosis, and one examining response to treatment after one session of ECT.

The majority of studies involved individuals with unipolar depression (52%) or included samples with mixed diagnoses (42%). Of the 91 studies meeting inclusion criteria, 50 (55%) reported on the statistical significance of the differences in depression scores over time. The remainder of the studies indicated some changes but did not report the statistical significance. Seventeen studies (19%) had some form of follow up period (>1 week) after the end of the treatment period, seven of which were randomized controlled trials (RCTs).

Concomitant psychopharmacological medication was continued in 55 of the 91 studies (60%), with a further 14 (15%) not stating whether this was the case. So in only 22 (24%) were the ECT recipients definitely not receiving medication. Only one study reported on suicidality, but none reported on whether ECT prevented suicide.

## Changes in depression during the treatment period

There have been no placebo-controlled ECT studies on depression in the last six years, during (or beyond) the treatment period.

There has been only one study that aimed to directly investigate the efficacy of ECT in depression through comparison with another treatment modality. It had no placebo control group and no data beyond the end of the treatment period. Schoeyen et al. (2015) performed a prospective randomized study with 73 individuals with treatment resistant bipolar disorder. Participants were randomly assigned to receive a 6-week course of ECT, or algorithm based pharmacological treatment. The primary outcome measure was the longitudinal profile on the Montgomery-Asberg Depression Rating Scale (MADRS) (R). Secondary outcome measures included longitudinal profiles on the Inventory of Depressive Symptomatology-Clinician Rated, times to response and remission, and proportion of responders/remitters at the end of the 6 week treatment period. Response was defined as a decrease in MADRS score of at least 50% from baseline. Remission was defined as a MADRS score of 12 or lower. Linear mixed-effects modeling analysis indicated that the mean MADRS and Inventory of Depressive Symptomatology-Clinician Rated scores were significantly lower in the ECT group than the pharmacology group at the end of the 6 week treatment period. However, due to differences in the handling of missing values, t-test comparison indicated that the mean MADRS score (the primary outcome measure) did not differ between the pharmacological treatment group and the ECT group at the end of the 6-week treatment period. Among treatment completers (n = 43), the response rate was higher in the ECT group than in the pharmacological treatment group, but there was no difference in the remission rates.

Schoeyen et al. (2015) conclude that their "results show that ECT is more effective than pharmacological treatment in the acute phase of treatment-resistant bipolar

depression, which supports ECT as a treatment option" (p. 49). However, several major limitations need to be considered. First, to be included in this study, participants were required to be 'treatment resistant' – defined as having no response to two or more trials with antidepressants and/or mood stabilizers with documented efficacy in bipolar disorder. A history of non-response to ECT was conversely an exclusion criterion. Thus, the study sample comprised only individuals for whom pharmacological treatment had already demonstrated inefficacy, and excluded all individuals for whom ECT had demonstrated inefficacy. Given that pharmacological treatment was already ineffective for these individuals, the superiority of ECT over pharmacological treatment is neither unexpected nor generalizable. Second, although blind raters co-rated some assessments, neither the patients nor the treating psychiatrists (who rated the outcome assessments) were blinded to treatment modality. Lack of blinding can bias both treatment outcomes and assessment thereof. Third, if individuals in the ECT group reached remission before the end of the 6-week treatment period, they were switched to an algorithm-based pharmacological maintenance treatment (in accordance with the same treatment protocol as the pharmacological treatment group). However, the authors did not report on the number of participants in the ECT group that switched treatment groups and what maintenance treatment these individuals received. Thus, it is unclear how many individuals in the 'ECT' group received ECT only, and how many received the same pharmacological treatment as the comparison group, or for how long. In other words an early responder to ECT may have not relapsed because they were now on medication rather than because they had received ECT.

Besides Schoeyen et al. (2015), there was only one other study that directly aimed to investigate the efficacy of ECT. It has no data beyond the end of the treatment

period and no control group, placebo or otherwise. Magid et al. (2013) retrospectively reviewed the preliminary efficacy and efficiency of ultrabrief right unilateral ECT after the adoption of a new ECT protocol at the University of Texas Southwestern Department of ECT. Response to ECT was defined as >5 point decrease on the Patient Health Questionnaire 9 (PHQ-9) (Spitzer, Kroenke, Williams, & Patient Health Questionnaire Primary Care Study, 1999) and a final PHQ-9 score of less than 10. Remission was defined as a final PHQ-9 score of 5 or less. The review demonstrated that 68% of the 62 participants (including diagnoses of unipolar and bipolar depression) responded to ECT and 44% reached remission criteria. Although this study directly aimed to investigate efficacy, PHQ-9 scores before and after ECT were not reported. Further, the study is limited by its retrospective design and, most importantly, again, by the lack of any sort of control group.

Of the other 89 studies included in this review, 46 reported on whether or not their findings were statistically significant during the treatment period (three additional studies reported on statistical significance but only at follow up). Only one of these 46 did not find a statistically significant reduction in depression during the ECT treatment course. Ueda et al. (2010) examined whether ECT could alleviate psychosis related to Parkinsons disease and antiparkinsonian medication. The mean of the 17-item Hamilton Depression Rating Scale (HDRS-17) decreased but did not reach statistical significance in this sample of five individuals. All other studies that reported level of significance found a statistically significant reduction on a depression measure during the course of ECT treatment. This included 31 observational studies, 10 RCTs including an ECT only group, two non-randomized trials, and two retrospective reviews. In none of these studies was ECT compared to any kind of control group and, therefore, reductions in depression cannot be attributed

to ECT. Reductions could, for instance, have been spontaneous remission and/or the result of placebo effects such as the hope and expectation created by any treatment and particularly by a major procedure such as ECT (Ramussen, 2009; Read & Bentall, 2010).

## Changes in depression beyond the treatment period

Even if there was strong evidence that ECT reduces depression in the period during which it is being administered, without evidence that reduction lasts beyond the end of the treatment period it cannot be claimed that the treatment is effective for the condition in question. It is well established that ECT recipients have very high relase rates after the end of the treatment period (Kellner et al., 2006; Read & Bentall, 2010; Sackheim et al., 2001).

Only 17 of the 91 studies (19%) included a follow up period (defined as >1 week after the final treatment). Four of these were uninformative about the long term effects on ECT recipients in general, because data beyond the treatment period were selectively reported only for those individuals who responded, or remitted, during treatment (Brakemeier et al., 2014; Lucca et al., 2010; McCall et al., 2013; Yildiz et al., 2010), Two other studies did not report whether the level of difference at follow up was statistically significant and one study did not analyze the follow up data due to small numbers (Loo et al., 2012; Loo et al., 2015; Rapinesi et al., 2013).

The remaining ten studies that included a follow up period all reported reduced depression. Five of these studies reported a significant decrease in depression at the one-month follow up time point, in comparison to baseline severity (Hansen et al., 2011; Kayser et al., 2011; Minelli et al., 2014; Weeks et al., 2013; Yoosefi et al., 2014). Two observational studies (Johansson et al., 2010; Kalogerakou et al., 2015)

both reported a significant decrease in depression compared to baseline, at 8-9 weeks follow up and 6 months since the beginning of treatment respectively. Three studies compared levels of depression at follow up with depression at the end of the treatment period (Dukart et al., 2014; Meeter et al., 2011; Nordanskog et al., 2014). All three of these studies reported a significant improvement in depression during the treatment period. There were no further improvements in any of these studies during the follow up period, but the level of depression appeared to remain stable during the follow up periods of three and six months.

Overall, although only 10 studies (11%) provided useable follow up data, reduction in depression scores appeared to be maintained during the follow up period. However, as with the studies demonstrating change during the treatment period, none of these studies included a placebo control group. Many were observational studies and/or had no group comparisons at all.

## Suicide

Of the 91 included studies, none aimed to investigate whether ECT prevented suicide. Only one study examined suicidality in relation to ECT. Yildiz et al. (2010) conducted a pilot controlled study investigating early continuation pharmacotherapy as an adjunct to ECT. In addition to receiving ECT, participants were randomized to additionally receive early continuation pharmacotherapy, late continuation pharmacotherapy or placebo after the fourth session of ECT. The study considered the change in expressed suicidal thoughts, as recorded on item 10 on the MADRS at baseline and after completion of ECT treatment course. However, data were only reported for all participants combined. As a result of this reporting, the change in suicidal thoughts in the placebo group, who only received ECT, was not determined.

#### DISCUSSION

In the decades since the introduction of ECT most medical practitioners have come to subscribe to the principles of evidence-based medicine, which have been defined as "the conscientious, explicit and judicious use of current best evidence in making decisions about the care of individual patients" (Sackett, Rosenberg, Gray, Haynes, & Richardson, 1996). Subscribers to these principles tend to accept that although clinical decision-making can be informed by a range of types of knowledge, the most robust of these is data from placebo-controlled randomized trials (Cipriani, Girlanda, & Barbui, 2009). By 2010 there had only been 10 such studies for ECT and depression, and none since 1985. Those ten had produced minimal evidence of some temporary benefits, for a minority, during the treatment period, and no evidence at all of benefits beyond the end of the treatment period.

In other medical disciplines this state of affairs might have led either to a phasing out of the procedure or at least to a plethora of studies seeking to determine whether the treatment in question does actually work. This is not the case for psychiatry and ECT. There has now not been a single placebo-controlled trial (randomized or otherwise) of whether ECT reduces depression for over 30 years.

It is not the case, however, that there is no ECT research being conducted. Our review reported a multitude of studies, many seeking to establish whether one type of ECT is more effective, or produces less cognitive dysfunction, than another; but all simply assuming that it does work. Only two studies in the last six years have made an explicit attempt to determine whether ECT works (Magid et al., 2013; Schoeyen et al., 2015). Both were so methodologically flawed as to be unable to answer the question in a scientifically meaningful way. Of all the studies that inadvertently

generated data that might have provided some support for the hypothesis that ECT is an effective treatment for depression 45% did not report statistical significance, 60% continued the ECT recipients on psychiatric drugs (with this being undetermined for a further 15%), 89% had no meaningful follow up data beyond the end of treatment (and 81% no follow up data at all), and 100% had no placebo control group. Despite the best, most inclusive, efforts of the reviewers no new robust evidence has emerged in the past six years to support the hypothesis that ECT is any more effective in reducing depression than placebo. There has also been no new evidence to support the hypothesis that ECT prevents suicide.

Such continued failure to produce any evidence would be of less concern if there were not robust evidence that ECT causes long lasting memory loss for a significant proportion of recipients (Breggin, 2008; Read et al., 2013; Rose, Wykes, Leese, Bindmann, & Fleischmann, 2003; Ross, 2006; Sackeim et al., 2007).

# Memory loss

A 2003 review of studies of memory loss at least six months post-ECT found a range of 51% to 79%), and a range for "persistent or permanent memory loss" of 29% to 55% (Rose et al., 2003). In 2007 ECT proponent Professor Harold Sackeim and his colleagues conducted the largest prospective study and found that autobiographical memory was significantly (p < .0001) worse than pre-ECT levels both shortly after ECT and six months later (Sackeim et al., 2007). Furthermore, the degree of impairment was related to the number of administrations of ECT. Even using the very conservative cut off of two standard deviations worse than pre-ECT scores, 12% met the criterion for 'marked and persistent retrograde amnesia', with higher rates for the two demographic groups who receive ECT disproportionately - women and older

people. The impairment was also greater among those who received bi-lateral ECT rather than unilateral ECT. (Bilateral remains the most common form of ECT). Significant memory loss is also consistently reported by many participants in qualitative studies of the subjective experience of ECT recipients (Fisher, 2012; Johnstone, 1999; Rose et al., 2003, 2004). Although ECT proponents often seek to dismiss these findings as 'subjective memory loss' (Read & Bentall, 2010, p. 343), i.e. either imagined or caused by depression rather than ECT, a 2006 review concluded that "There is no evidence of a correlation between impaired memory/cognition after ECT and impaired mood, much less a causal relationship" (Robertson & Pryor, 2006, p. 230).

The most recent statement by the UK's Royal College of Psychiatry (RCP) is:

"Memory problems can be a longer-term side effect. Surveys conducted by doctors and clinical staff usually find a low level of severe side-effects, maybe around 1 in 10. Patient-led surveys have found much more, maybe in half of those having ECT. .....

Some people do complain that their memory has been permanently affected, that their memories never come back" (RCP, 2016). A New Zealand Government report concurs, stating that "ECT may permanently affect memory and sometimes this can be of major personal significance" and bemoaning the "slowness in acceptance by some professional groups that such outcomes are real and significant in people's lives" (Ministry of Health, 2004, p. 16). A review of studies of the effects of ECT suggests that "ECT affects the brain in a similar manner as severe stress or brain trauma which activates the HPA axis and the dopamine system and may compromise frontotemporal functions" (Fosse & Read, 2013, p.1).

#### Conclusion

We conclude that the continued use of ECT is not consistent with an evidence-based approach to the practice of medicine. There is no new evidence in the last six years to challenge the conclusion, in the 2010 review, that "the cost-benefit analysis for ECT is so poor that its use cannot be scientifically justified" (Read & Bentall, 2010, p.333).

The use of ECT has been steadily declining in many countries. In England for example, individual administrations have fallen from 159,600 in 1980 to 27,128 in 2006 (Singhai, 2011), and to less than 15,000 in 2013 (Cresswell & Hodge, 2013). Nevertheless it was estimated that at the turn of the century about one million people worldwide were still receiving this procedure annually (Prudic, Olfson, & Sackeim, 2001). A more recent review, of seventy studies, found 'large variation between continent, countries and regions in utilization, rates and clinical practice' (Leiknes, Jarosh-von Schweder, & Hoie, 2012, p. 296). High users include Australia, Belgium, Norway, Sweden and the U.S.A. In Australia (Oakley-Brown, 2015) and Texas (Swanson, 2014) the use of ECT has actually been increasing in recent years. An evidence-based approach to clinical care would, however, see a rapid *decline* in the use of this procedure. It seems appropriate to suggest, again, that:

The continued use of ECT therefore represents a failure to introduce the ideals of evidence-based medicine into psychiatry. This failure has occurred not only in the design and execution of research, but also in the translation of research findings into clinical practice. It seems there is resistance to the research data in the ECT community, and perhaps in psychiatry in general (Read & Bentall, 2010, p. 344).

We should, meanwhile, remain cognizant of the fact that the archetypal ECT recipient remains, as it has for decades, a distressed woman over the age of 50 (Leiknes et al., 2012; Read et al., 2013).

At the beginning of 2016 the U.S.A.'s Food and Drug Administration was taking submissions on their proposal to reclassify ECT devices from class III (high risk) to class II (low risk). On January 29, 2016, the president of the American Psychiatric Association, Dr. Renée Binder, urged members to support the proposal and drafted a letter for members to submit to the FDA, which included: "The APA considers ECT a safe and effective evidence-based medical treatment" (Binder, 2016). She did not recommend any research, old or recent, that they might submit in support of this claim. It seems there is none.

## Limitations

The primary limitation of this review is that there were insufficient properly designed studies (none) to permit any conclusions about whether ECT is effective for depression. The review could have been improved by searching more than two databases, having a second person check the selection of relevant articles, and attempting to retrieve unpublished and ongoing studies. It should also be acknowledged that a review protocol was not pre-registered.

# **REFERENCES**

- Abdallah, C., Fasula, M., Kelmendi, B., Sanacora, G., & Ostroff, R. (2012). Rapid antidepressant effect of ketamine in the electroconvulsive therapy setting. *Journal of ECT*, 28(3), 157-161.
- Abdollahi, M. H., Izadi, A., Hajiesmaeili, M., Ghanizadeh, A., Dastjerdi, G., Hosseini, H., . . . Abbasi, H. (2012). Effect of etomidate versus thiopental on major depressive disorder in electroconvulsive therapy, randomized double-blind controlled clinical trial. *Journal of ECT*, 28(1), 10-13.
- Allen, A., Naughton, M., Dowling, J., Walsh, A., Ismail, F., Shorten, G., . . . Clarke, G. (2015). Serum BDNF as a peripheral biomarker of treatment-resistant depression and the rapid antidepressant response: A comparison of ketamine and ECT. *Journal of Affective Disorders*, 186, 306-311.
- Andre, L. (2008). Doctors of Deception: What They Don't Want You to Know About Shock Treatment. New Brunswick, NJ: Rutgers University Press.
- Aten, J., Oudega, M., van Exel, E., Stek, M., & van Waarde, J. (2015). Repeated dose titration versus age-based method in electroconvulsive therapy: A pilot study. European Archives of Psychiatry and Clinical Neuroscience, 265(4), 351-356.
- Azuma, H., Yamada, A., Shinagawa, Y., Nakano, Y., Watanabe, N., Akechi, T., & Furukawa, T. (2011). Ictal physiological characteristics of remitters during bilateral electroconvulsive therapy. *Psychiatry Research*, *185*(3), 462-464.
- Bailine, S., Fink, M., Knapp, R., Petrides, G., Husain, M., Rasmussen, K., . . . Kellner, C. (2010). Electroconvulsive therapy is equally effective in unipolar and bipolar depression. *Acta Psychiatrica Scandinavica*, *121*(6), 431-436.
- Bär, K.-J., Ebert, A., Boettger, M., Merz, S., Kiehntopf, M., Jochum, T., . . . Agelink, M. W. (2010). Is successful electroconvulsive therapy related to stimulation of the vagal system? *Journal of Affective Disorders*, 125(1-3), 323-329.
- Bayless, J., McCormick, L., Brumm, M., Espe-Pfeifer, P., Long, J., & Lewis, J. (2010). Preand post-electroconvulsive therapy multidomain cognitive assessment in psychotic depression: Relationship to premorbid abilities and symptom improvement. *Journal of ECT*, 26(1), 47-52.
- Beall, E., Malone, D. Dale, R., Muzina, D., Koenig, K., Bhattacharrya, P., . . . Lowe, M. (2012). Effects of electroconvulsive therapy on brain functional activation and connectivity in depression. *Journal of ECT*, 28(4), 234-241.

- Bersani, G., Iannitell, A., Caredda, M., Bersani, F., Orsi, P., & Pacitti, F. (2014). Seizure threshold variations in ECT-treated chronic patients with schizophrenia: A brief report. *Rivista di Psichiatria*, 49(2), 84-88.
- Bilgen, A., Bozkurt Zincir, S., Zincir, S., Özdemir, B., Ak, M., Aydemir, E., & Şener, İ. (2014). Effects of electroconvulsive therapy on serum levels of brain-derived neurotrophic factor and nerve growth factor in treatment resistant major depression. *Brain Research Bulletin*, 104, 82-87.
- Binder, R. (2016). *Time is now to support the ECT reclassification effort*. Retrieved February 12th, 2016, from <a href="http://www.psychiatry.org/news-room/apa-blogs/apa-blog/2016/01/time-is-now-to-support-the-ect-reclassification-effort">http://www.psychiatry.org/news-room/apa-blogs/apa-blog/2016/01/time-is-now-to-support-the-ect-reclassification-effort</a>
- Birkenhäger, T., Pluijms, E., Ju, M., Mulder, P., & van den Broek, W. (2010). Influence of age on the efficacy of electroconvulsive therapy in major depression: A retrospective study. *Journal of Affective Disorders*, 126(1-2), 257-261.
- Bjølseth, T., Engedal, K., Benth, J., Dybedal, G., Gaarden, T., & Tanum, L. (2015). Clinical efficacy of formula-based bifrontal versus right unilateral electroconvulsive therapy (ECT) in the treatment of major depression among elderly patients: A pragmatic, randomized, assessor-blinded, controlled trial. *Journal of Affective Disorders*, 175, 8-17.
- Brakemeier, E., Merkl, A., Wilbertz, G., Quante, A., Regen, F., Buhrsch, N., . . . Bajbouj, M. (2014). Cognitive-behavioral therapy as continuation treatment to sustain response after electroconvulsive therapy in depression: a randomized controlled trial. *Biological Psychiatry*, 76(3), 194-202.
- Breggin, P. (2008). Brain-disabling treatments in psychiatry. New York: Springer.
- Burgese, D., & Bassitt, D. (2015). Variation of plasma cortisol levels in patients with depression after treatment with bilateral electroconvulsive therapy. *Trends in Psychiatry and Psychotherapy*, *37*(1), 27-36.
- Casarotto, S., Canali, P., Rosanova, M., Pigorini, A., Fecchio, M., Mariotti, M., . . . Massimini, M. (2013). Assessing the effects of electroconvulsive therapy on cortical excitability by means of transcranial magnetic stimulation and electroencephalography. *Brain Topography*, 26(2), 326-337.
- Chiaie, R., Capra, E., Salviati, M., Trabucchi, G., Pancheri, C., Corrado, A., & Biondi, M. (2013). Persistence of subsyndromal residual symptoms after remission of major depression in patients without cardiovascular disease may condition maintenance of

- elevated platelet factor 4 and β-thromboglobulin plasma levels. *Journal of Affective Disorders*, 150(2), 664-667. doi:10.1016/j.jad.2013.03.017
- Cipriani, A., Girlanda, F., & Barbui, C. (2009). Superiority, equivalence or non-inferiority. *Epidemiology and Psichiatric Sciences*, *18*(311-313).
- Cresswell, C., & Hodge, S. (2013). *ECT Minimum Dataset: Activity Data Report England & Wales*. London.
- Dannlowski, U., Domschke, K., Birosova, E., Lawford, B., Young, R., Voisey, J., . . . Zwanzger, P. (2013). Dopamine D3 receptor gene variation: Impact on electroconvulsive therapy response and ventral striatum responsiveness in depression. *International Journal of Neuropsychopharmacology, 16*(7), 1443-1459.
- Dierckx, B., Heijnen, W., van den Broek, W., & Birkenhäger, T. (2012). Efficacy of electroconvulsive therapy in bipolar versus unipolar major depression: A meta-analysis. *Bipolar Disorders*, *14*(2), 146-150.
- Dukart, J., Regen, F., Kherif, F., Colla, M., Bajbouj, M., Heuser, I., . . . Draganski, B. (2014). Electroconvulsive therapy-induced brain plasticity determines therapeutic outcome in mood disorders. *PNAS Proceedings of the National Academy of Sciences of the United States of America*, 111(3), 1156-1161.
- Ebert, A., Jochum, T., Ritter, J., Boettger, M., Schulz, S., Voss, A., & Bär, K.-J. (2010). Does parasympathetic modulation prior to ECT treatment influence therapeutic outcome? *Progress in Neuro-Psychopharmacology & Biological Psychiatry*, 34(7), 1174-1180.
- Fernandez, J. W., Philpot, R., Marsh, P., Hartney, R., & Kozel, F. (2014). The need to expand access to electroconvulsive therapy: A retrospective analysis of a new academic service. *Journal of Psychiatric Practice*, 20(4), 308-315.
- Fisher, P. (2012). Psychological factors related to the expereince of and reaction to electroconvulsive therapy. *Journal of Mental Health*, *21*(6), 589-599.
- Fosse, R., & Read, J. (2013). Electroconvulsive treatment: Hypotheses about mechanisms of action. *Frontiers in Psychiatry*, *4*, 94-103.
- Gabor, G., & Laszio, T. (2005). The efficacy of ECT treatment in depression: A metanalysis. *Psychiatria Hungarica*, *20*, 195-200.
- Galletly, C., Paterson, T., & Burton, C. (2012). A report on the introduction of ultra brief pulse width ECT in a private psychiatric hospital. *Journal of ECT*, 28(1), 59.
- Galvez, V., Loo, C., Alonzo, A., Cerrillo, E., Menchon, J., Crespo, J., & Urretavizcaya, M. (2013). Do benzodiazepines moderate the effectiveness of bitemporal

- electroconvulsive therapy in major depression? *Journal of Affective Disorders*, 150(2), 686-690.
- Gedge, L., Beaudoin, A., Lazowski, L., du Toit, R., Jokic, R., & Milev, R. (2012). Effects of electroconvulsive therapy and repetitive transcranial magnetic stimulation on serum brain-derived neurotrophic factor levels in patients with depression. *Frontiers in Psychiatry*, 3, 12.
- Ghasemi, M., Kazemi, M. H., Yoosefi, A., Ghasemi, A., Paragomi, P., Amini, H., & Afzali, M. H. (2014). Rapid antidepressant effects of repeated doses of ketamine compared with electroconvulsive therapy in hospitalized patients with major depressive disorder. *Psychiatry Research*, *215*(2), 355-361.
- Goto, S., Terao, T., Hoaki, N., Wang, Y., Tsuchiyama, K., Araki, Y., & Kohno, K. (2012). Is serotonergic function associated with the antidepressant effects of modified-electroconvulsive therapy? *Journal of Affective Disorders*, *136*(3), 1062-1066.
- Graveland, P., Wierdsma, A., van den Broek, W., & Birkenhäger, T. (2013). A retrospective comparison of the effects of propofol and etomidate on stimulus variables and efficacy of electroconvulsive therapy in depressed inpatients. *Progress in Neuro-Psychopharmacology & Biological Psychiatry*, 45, 230-235.
- Greenhalgh, J., Knight, C., Hind, D., Beverley, C., & Walters, S. (2005). Clinical and cost-effectiveness of electroconvulsive therapy for depressive illness, schizophrenia, catatonia and mania: Systematic reviews and economic modelling studies. *Health Technology Assessment*, *9*, 1-170.
- Gregory, S., Shawcross, C., & Gill, D. (1985). The Nottingham ECT study. *British Journal of Psychiatry*, 146, 520-524.
- Guloksuz, S., Arts, B., Walter, S., Drukker, M., Rodriguez, L., Myint, A.-M., . . . Rutten, B. P. F. (2015). The impact of electroconvulsive therapy on the tryptophan–kynurenine metabolic pathway. *Brain, Behavior, and Immunity, 48*, 48-52.
- Hansen, P., Ravnkilde, B., Videbech, P., Clemmensen, K., Sturlason, R., Reiner, M., . . . Vestergaard, P. (2011). Low-frequency repetitive transcranial magnetic stimulation inferior to electroconvulsive therapy in treating depression. *Journal of ECT*, 27(1), 26-32.
- Hu, Y., Yu, X., Yang, F., Si, T., Wang, W., Tan, Y., . . . Chen, D. (2010). The level of serum brain-derived neurotrophic factor is associated with the therapeutic efficacy of modified electroconvulsive therapy in Chinese patients with depression. *Journal of ECT*, 26(2), 121-125.

- Janicak, P., Davis, J., Gibbons, R., Eriksen, S., Chang, S., & Gallagher P. (1985). Efficacy of ECT: A meta-analysis. *American Journal of Psychiatry*, *142*, 297-302.
- Järventausta, K., Chrapek, W., Kampman, O., Tuohimaa, K., Björkqvist, M., Häkkinen, H., . . . Leinonen, E. (2013). Effects of S-ketamine as an anesthetic adjuvant to propofol on treatment response to electroconvulsive therapy in treatment-resistant depression: A randomized pilot study. *Journal of ECT*, 29(3), 158-161.
- Johansson, M., Ehnvall, A., Friberg, P., & Myredal, A. (2010). Arterial baroreflex dysfunction in major depressive disorder. *Clinical Autonomic Research*, 20(4), 235-240.
- Johnstone, L. (1999). Adverse psychological effects of ECT. *Journal of Mental Health*, 8(1), 69-85.
- Joshi, S., Espinoza, R., Pirnia, T., Shi, J., Wang, Y., Ayers, B., . . . Narr, K. (2015). Structural Plasticity of the Hippocampus and Amygdala Induced by Electroconvulsive Therapy in Major Depression. *Biological Psychiatry*, 79(4), 282-292.
- Kalogerakou, S., Oulis, P., Anyfandi, E., Konstantakopoulos, G., Papakosta, V. M., Kontis, D., . . . Tsaltas, E. (2015). Episodic Visual Learning/Memory and Attentional Flexibility in Patients With Major Depressive Disorder After Clinically Effective Electroconvulsive Therapy. *Journal of ECT*, 31(4), 246-252.
- Kautto, M., Kampman, O., Mononen, N., Lehtimaki, T., Haraldsson, S., Koivisto, P., & Leinonen, E. (2015). Serotonin transporter (5-HTTLPR) and norepinephrine transporter (NET) gene polymorphisms: susceptibility and treatment response of electroconvulsive therapy in treatment resistant depression. *Neuroscience Letters*, 590, 116-120.
- Kayser, S., Bewernick, B., Grubert, C., Hadrysiewicz, B., Axmacher, N., & Schlaepfer, T. E. (2011). Antidepressant effects, of magnetic seizure therapy and electroconvulsive therapy, in treatment-resistant depression. *Journal of Psychiatric Research*, 45(5), 569-576.
- Kellner, C., Knapp, R., Husain, M., Rasmussen, K., Sampson, S., Cullum, M., . . . Petrides, G. (2010). Bifrontal, bitemporal and right unilateral electrode placement in ECT: Randomised trial. *The British Journal of Psychiatry*, *196*(3), 226-234.
- Kellner C., Knapp R., Petrides G., Rummans T., Hussain M., & Rasmussen K. (2006).
  Continuation ECT versus pharmacotherapy for relapse prevention in major depression: A multi-site study from CORE. Archives of General Psychiatry, 63, 1337-1344.

- Keshtkar, M., Ghanizadeh, A., & Firoozabadi, A. (2011). Repetitive transcranial magnetic stimulation versus electroconvulsive therapy for the treatment of major depressive disorder, a randomized controlled clinical trial. *Journal of ECT*, 27(4), 310-314.
- Kho, K., van Vreewijk, M., Simpson, S., & Zwinderman A. (2003). A meta-analysis of electroconvulsive therapy in depression. *Journal of ECT*, 19, 139-147.
- Kumar, A., Sharma, D. K., & Mani, R. (2012). A comparison of propofol and thiopentone for electroconvulsive therapy. *Journal of Anaesthesiology Clinical Pharmacology*, 28(3), 353-357.
- Lapidus, K., Shin, J. W., Pasculli, R., Briggs, M., Popeo, D., & Kellner, C. (2013). Low-dose right unilateral electroconvulsive therapy (ECT): Effectiveness of the first treatment. *Journal of ECT*, 29(2), 83-85.
- Leiknes, K. A., Jarosh-von Schweder, L., & Hoie, B. (2012). Contemporary use and practice of electroconvulsive therapy worldwide. *Brain and Behaviour*, *2*(3), 283-344.
- Lin, C.-H., Chen, M.-C., Lee, W.-K., Chen, C.-C., Huang, C.-H., & Lane, H.-Y. (2013). Electroconvulsive therapy improves clinical manifestation with plasma BDNF levels unchanged in treatment-resistant depression patients. *Neuropsychobiology*, 68(2), 110-115.
- Lin, Z., He, H., Zhang, C., Wang, Z., Jiang, M., Li, Q., . . . Huang, X. (2014). Influence of Val108/158Met COMT Gene Polymorphism on the Efficacy of Modified Electroconvulsive Therapy in Patients with Treatment Resistant Depression. *Cell Biochemistry and Biophysics*, 1387-1393.
- Loo, C., Garfield, J., Katalinic, N., Schweitzer, I., & Hadzi-Pavlovic, D. (2013). Speed of response in ultrabrief and brief pulse width right unilateral ECT. *International Journal of Neuropsychopharmacology*, *16*(4), 755-761.
- Loo, C., Katalinic, N., Garfield, J., Sainsbury, K., Hadzi-Pavlovic, D., & MacPherson, R. (2012). Neuropsychological and mood effects of ketamine in electroconvulsive therapy: A randomised controlled trial. *Journal of Affective Disorders*, *142*(1-3), 233-240.
- Loo, C., Katalinic, N., Smith, D. J., Ingram, A., Dowling, N., Martin, D., . . . Schweitzer, I. (2015). A randomized controlled trial of brief and ultrabrief pulse right unilateral electroconvulsive therapy. *International Journal of Neuropsychopharmacology*, 18(1), 1-8.

- Loo, C., Mahon, M., Katalinic, N., Lyndon, B., & Hadzi-Pavlovic, D. (2011). Predictors of response to ultrabrief right unilateral electroconvulsive therapy. *Journal of Affective Disorders*, *130*(1-2), 192-197.
- Lucca, A., Rossini, D., Malaguti, A., Zanardi, R., Magri, L., & Smeraldi, E. (2010). Use of electroconvulsive therapy in the city of Milan: A naturalistic study. *Journal of ECT*, 26(2), 148.
- Lyden, H., Espinoza, R. T., Pirnia, T., Clark, K., Joshi, S., Leaver, A., . . . Narr, K. (2014). Electroconvulsive therapy mediates neuroplasticity of white matter microstructure in major depression. *Translational Psychiatry*, *4*, e380.
- Magid, M., Truong, L., Trevino, K., & Husain, M. (2013). Efficacy of right unilateral ultrabrief pulse width ECT: A preliminary report. *Journal of ECT*, 29(4), 258-264.
- Martinez-Amoros, E., Galvez Ortiz, V., Porter Moli, M., Llorens Capdevila, M., Cerrillo Albaiges, E., Garcia-Pares, G., . . . Urretavizcaya Sarachaga, M. (2014). Propofol and thiopental as anesthetic agents in electroconvulsive therapy: a retrospective study in major depression. *Revista de Psiquiatría y Salud Mental*, 7(1), 42-47.
- Masoudzadeh, A., Yahyavi, S., Rashidi, H., Mohammadpour, R., & Kiani, R. (2013). Use of liothyronine in preventing electroconvulsive therapy-induced memory impairment: Evaluation. *The Psychiatrist*, *37*(2), 49-53.
- Matthews, J., Siefert, C., Blais, M., Park, L., Welch, C., DuBois, C., . . . Fava, M. (2013). A double-blind, placebo-controlled study of the impact of galantamine on anterograde memory impairment during electroconvulsive therapy. *Journal of ECT*, *29*(3), 170-178.
- Mayur, P., Bray, A., Fernandes, J., Bythe, K., & Gilbett, D. (2010). Impact of hyperventilation on stimulus efficiency during the early phase of an electroconvulsive therapy course: A randomized double-blind study. *Journal of ECT*, *26*(2), 91-94.
- Mayur, P., Byth, K., & Harris, A. (2013). Acute antidepressant effects of right unilateral ultra-brief ECT: A double-blind randomised controlled trial. *Journal of Affective Disorders*, *149*(1-3), 426-429.
- McCall, W., Reboussin, D., Prudic, J., Haskett, R., Isenberg, K., Olfson, M., . . . Sackeim, H. A. (2013). Poor health-related quality of life prior to ECT in depressed patients normalizes with sustained remission after ECT. *Journal of Affective Disorders*, 147(1-3), 107-111.

- Medda, P., Mauri, M., Toni, C., Mariani, M. G., Rizzato, S., Miniati, M., . . . Perugi, G. (2014). Predictors of remission in 208 drug-resistant depressive patients treated with electroconvulsive therapy. *Journal of ECT*, *30*(4), 292-297.
- Meeter, M., Murre, J., Janssen, S., Birkenhager, T., & van den Broek, W. (2011). Retrograde amnesia after electroconvulsive therapy: A temporary effect? *Journal of Affective Disorders*, 132(1-2), 216-222.
- Minelli, A., Maffioletti, E., Bortolomasi, M., Conca, A., Zanardini, R., Rillosi, L., . . . Bocchio- Chiavetto, L. (2014). Association between baseline serum vascular endothelial growth factor levels and response to electroconvulsive therapy. *Acta Psychiatrica Scandinavica*, 129(6), 461-466.
- Ministry of Health (2004). *Use of ECT in New Zealand: A review of efficacy, safety and regulatory controls.* Ministry of Health: Wellington, New Zealand.
- Nickl-Jockschat, T., Palomero Gallagher, N., Kumar, V., Hoffstaedter, F., Brügmann, E., Habel, U., . . . Grözinger, M. (2015). Are morphological changes necessary to mediate the therapeutic effects of electroconvulsive therapy? *European Archives of Psychiatry and Clinical Neuroscience*, 1-7.
- Niemantsverdriet, L., Birkenhäger, T., & van den Broek, W. (2011). The efficacy of ultrabrief-pulse (0.25 millisecond) versus brief-pulse (0.50 millisecond) bilateral electroconvulsive therapy in major depression. *Journal of ECT*, *27*(1), 55-58.
- Nordanskog, P., Larsson, M., Larsson, E., & Johanson, A. (2014). Hippocampal volume in relation to clinical and cognitive outcome after electroconvulsive therapy in depression. *Acta Psychiatrica Scandinavica*, 129(4), 303-311.
- Oakley-Brown, M. (2015). *Chief Psychiatrist's annual report 2012-13 and 2013-14*. Melbourne Department of Health and Social Services.
- Okamoto, N., Nakai, T., Sakamoto, K., Nagafusa, Y., Higuchi, T., & Nishikawa, T. (2010). Rapid antidepressant effect of ketamine anesthesia during electroconvulsive therapy of treatment-resistant depression: Comparing ketamine and propofol anesthesia. *Journal of ECT*, 26(3), 223-227.
- Ota, M., Noda, T., Sato, N., Okazaki, M., Ishikawa, M., Hattori, K., . . . Kunugi, H. (2015). Effect of electroconvulsive therapy on gray matter volume in major depressive disorder. *Journal of Affective Disorders*, 186, 186-191.
- Oudega, M., van Exel, E., Wattjes, M., Comijs, H., Scheltens, P., Barkhof, F., . . . Stek, M. (2011). White matter hyperintensities, medical temporal lobe atrophy, cortical

- atrophy, and response to electroconvulsive therapy in severely depressed elderly patients. *Journal of Clinical Psychiatry*, 72(1), 104-112.
- Pagnin, D., de Queiroz, V., Pini, S., & Cassano G. (2004). Efficacy of ECT in depression: A meta-analytic review. *Journal of ECT*, 20, 13-20.
- Painuly, L., & Chakrabati S. (2006). Combined use of electroconvulsive therapy and antipsychotics in schizophrenia: The Indian evidence. *Journal of ECT*, 22, 59-66.
- Perrin, J., Merz, S., Bennett, D., Currie, J., Steele, D., Reid, I., & Schwarzbauer, C. (2012). Electroconvulsive therapy reduces frontal cortical connectivity in severe depressive disorder. *PNAS Proceedings of the National Academy of Sciences of the United States of America*, 109(14), 5464-5468.
- Piccinni, A., Veltri, A., Vizzaccaro, C., Dell'Osso, M. C., Medda, P., Domenici, L., . . . Dell'Osso, L. (2013). Plasma amyloid-β levels in drug-resistant bipolar depressed patients receiving electroconvulsive therapy. *Neuropsychobiology*, *67*(4), 185-191.
- Prudic, J., Olfson, M., & Sackeim, H. (2001). Electro-convulsive therapy practices in the community. *Psychological Medicine*, *31*, 929-934.
- Pulia, K., Vaidya, P., Jayaram, G., Hayat, M., & Reti, I. (2013). ECT treatment outcomes following performance improvement changes. *Journal of Psychosocial Nursing and Mental Health Services*, *51*(11), 20-25.
- Purtuloglu, T., Ozdemir, B., Erdem, M., Deniz, S., Balkc, A., Unlu, G., & Oznur, T. (2013). Effect of propofol versus sodium thiopental on electroconvulsive therapy in major depressive disorder: a randomized double-blind controlled clinical trial. *Journal of ECT*, 29(1), 37-40.
- Quante, A., Luborzewski, A., Brakemeier, E. L., Merkl, A., Danker-Hopfe, H., & Bajbouj, M. (2011). Effects of 3 different stimulus intensities of ultrabrief stimuli in right unilateral electroconvulsive therapy in major depression: a randomized, double-blind pilot study. *Journal of Psychiatric Research*, 45(2), 174-178.
- Rapinesi, C., Kotzalidis, G. D., Curto, M., Serata, D., Ferri, V. Scatena, P., . . . Girardi, P. (2015). Electroconvulsive therapy improves clinical manifestations of treatment-resistant depression without changing serum BDNF levels. *Psychiatry Research*, 227(2-3), 171-178.
- Rapinesi, C., Kotzalidis, G. D., Serata, D., Del Casale, A., Scatena, P., Mazzarini, L., . . . Girardi, P. (2013). Prevention of relapse with maintenance electroconvulsive therapy in elderly patients with major depressive episode. *Journal of ECT*, 29(1), 61-64.

- Rasmussen, K. (2009). Sham electroconvulsive therapy studies in depressive illness: A review of the literature and consideration of the placebo phenomenon in electroconvulsive therapy practice. *Journal of ECT.*, 25, 54-59.
- Read, J., & Bentall, R. (2010). The effectiveness of electroconvulsive therapy: a literature review. *Epidemiologia e psichiatria sociale*, 19(4), 333-347.
- Read, J., Bentall, R., Johnstone, L., Fosse, R., & Bracken, P. (2013). Electroconvulsive Therapy. In J. Read & J. Dillon (Eds.), *Models of madness: Psychological, social and biological approaches to psychosis* (pp. 90-104). Hove: Routledge.
- Robertson H. & Pryror R. (2006). Memory and cognitive effects of ECT: Informing and assessing patients. *Advances in Psychiatric Treatment*, 12, 228-238.
- Roepke, S., Luborzewski, A., Schindler, F., Quante, A., Anghelescu, I., Heuser, I., & Bajbouj, M. (2011). Stimulus pulse-frequency-dependent efficacy and cognitive adverse effects of ultrabrief-pulse electroconvulsive therapy in patients with major depression. *Journal of ECT*, 27(2), 109-113. doi:10.1097/YCT.0b013e3181e63302
- Rose, D., Wykes, T., Leese, J., Bindmann, J., & Fleischmann, P. (2003). Patients' perspectives of electroconvulsive therapy: Systematic review. *British Medical Journal*, 326, 1363-1366.
- Rose, D., Fleischmann, P., & Wykes, T. (2004). Consumers' views of electroconvulsive therapy: A qualitative analysis. *Journal of Mental Health*, *13*(3), 285-292.
- Ross, C. (2006). The sham ECT literature: Implications for consent to ECT. *Ethical Human Psychology and Psychiatry*, *8*, 17-28.
- Royal College of Psychiatrists. (2016). *Information about ECT*. Retrieved October 3, 2016, fromhttp://www.rcpsych.ac.uk/mentalhealthinformation/therapies/electroconvulsivetherapy.ect.aspx.
- Royster, E., Trimble, L., Cotsonis, G., Schmotzer, B., Manatunga, A., Rushing, N., . . . Musselman, D. (2012). Changes in heart rate variability of depressed patients after electroconvulsive therapy. *Cardiovascular Psychiatry and Neurology*, 2012, 794043.
- Sackeim H., Haskett R., Mulsant B., Thase M., Mann J., Pettinati, H., ... Prudic J. (2001).

  Continuation pharmacotherapy in the prevention of relapse following ECT: A randomized controlled trial. *Journal of the American Medical Association*, 285, 1299-1307.
- Sackeim, H., Prudic, J., Fuller, R., Keilp, J., Lavori, P., & Olfson, M. (2007). The cognitive effects of ECT in community settings. *Neuropsychopharmocolgy*, *32*, 244-254.

- Sackett, D., Rosenberg, W., Gray, J., Haynes, R., & Richardson, S. (1996). Evidence based medicine: What it is and what it isn't. *British Medical Journal*, *312*, 71-72.
- Saijo, T., Takano, A., Suhara, T., Arakawa, R., Okumura, M., Ichimiya, T., . . . Okubo, Y. (2010). Electroconvulsive therapy decreases dopamine D2 receptor binding in the anterior cingulate in patients with depression: A controlled study using positron emission tomography with radioligand [11C]FLB 457. *Journal of Clinical Psychiatry*, 71(6), 793-799.
- Samuelsson, M., Gerdin, G., Öllinger, K., & Vrethem, M. (2012). Taurine and glutathione levels in plasma before and after ECT treatment. *Psychiatry Research*, *198*(1), 53-57.
- Sarita, E., Janakiramiaiah, N., Gangadhar, B., Subbakrishna, D., & Rao, K. (1998). Efficacy of combined ECT after two weeks of neuroleptics in schizophrenia. *NIMHANS Journal*, *16*, 243-251.
- Schoeyen, H., Kessler, U., Andreassen, O., Auestad, B., Bergsholm, P., Malt, U., . . . Vaaler, A. (2015). Treatment-resistant bipolar depression: A randomized controlled trial of electroconvulsive therapy versus algorithm-based pharmacological treatment. *The American Journal of Psychiatry*, 172(1), 41-51.
- Singhai, A. (2011). ECT and its place in the management of depression. *Progress in Neuroogy and Psychiatry*, 15, 19-26.
- Spaans, H., Verwijk, E., Comijs, H., Kok, R., Sienaert, P., Bouckaert, F., . . . Kho, K. (2013). Efficacy and cognitive side effects after brief pulse and ultrabrief pulse right unilateral electroconvulsive therapy for major depression: a randomized, doubleblind, controlled study. *Journal of Clinical Psychiatry*, 74(11), e1029-1036.
- Spitzer, R. L., Kroenke, K., & Williams, J. (1999). Validation and utility of a self-report version of PRIME-MD: the PHQ primary care study. *Journal of the American Medical Association*, 282(18), 1737-1744.
- Swanson, D. (2014). *Texas sees resurgence in use of electroconvulsive-therapy*. Retrieved January 25th 2016, from <a href="http://www.dallasnews.com/news/state/headlines/20141213-texas-sees-resurgence-in-use-of-electroconvulsive-therapy.ece">http://www.dallasnews.com/news/state/headlines/20141213-texas-sees-resurgence-in-use-of-electroconvulsive-therapy.ece</a>.
- Tendolkar, I., van Beek, M., van Oostrom, I., Mulder, M., Janzing, J., Voshaar, R., & van Eijndhoven, P. (2013). Electroconvulsive therapy increases hippocampal and amygdala volume in therapy refractory depression: A longitudinal pilot study. *Psychiatry Research: Neuroimaging, 214*(3), 197-203.
- Tharyan, P., & Adams C. (2005). Electroconvulsive therapy for schizophrenia. *Cochrane Database of Systematic Reviews* Issue 2, CD000076.

- Ueda, S., Koyama, K., & Okubo, Y. (2010). Marked improvement of psychotic symptoms after electroconvulsive therapy in Parkinson disease. *Journal of ECT*, 26(2), 111-115.
- UK ECT Review Group. (2003). Efficacy and safety of ECT in depressive disorders. *Lancet*, *361*, 799-808.
- Ukpong, D., Makanjuola, R., & Morakinyo, O. (2002). A controlled trial of modified electroconvulsive therapy in schizophrenia in a Nigerian teaching hospital. *West African Journal of Medicine*, *21*, 237-240.
- Vaidya, P., Anderson, E., Bobb, A., Pulia, K., Jayaram, G., & Reti, I. (2012). A within-subject comparison of propofol and methohexital anesthesia for electroconvulsive therapy. *Journal of ECT*, 28(1), 14-19.
- Valevski, A., Pickholtz, E., Roz, N., Weizman, A., & Rehavi, M. (2010). Lack of modulatory effect of short-term repeated electroconvulsive therapy on platelet vesicular monoamine transporter 2 (VMAT2) in depressed patients. *Journal of Neural Transmission*, 117(7), 881-885.
- van der Wurff, F., Stek, M., Hooogendijk, W., & Beekman, A. (2003). Electroconvulsive therapy for the depressed elderly. *Cochrane Database of Systematic Reviews Issue* 2, CD003593.
- van Waarde, J., van Oudheusden, L., Heslinga, O., Verwey, B., van der Mast, R., & Giltay, E. (2013). Patient, treatment, and anatomical predictors of outcome in electroconvulsive therapy: A prospective study. *Journal of ECT*, *29*(2), 113-121.
- Vırıt, O., Dalkiliç, A., Bulut, M., Bülbül, F., Altindağ, A., Armutçu, F., . . . Savaş, H. A. (2010). Decreased superoxide dismutase activity after ECT and correlation between higher oxidant levels and poor response to ECT in depression. *Archives of Neuropsychiatry*, 47(3), 247-251.
- Vukadin, M., Birkenhager, T., Wierdsma, A., Groenland, T., & van den Broek, W. (2011). Post-dexamethasone cortisol as a predictor for the efficacy of electroconvulsive therapy in depressed inpatients. *Journal of Psychiatric Research*, 45(9), 1165-1169.
- Wang, X., Chen, Y., Zhou, X., Liu, F., Zhang, T., & Zhang, C. (2012). Effects of propofol and ketamine as combined anesthesia for electroconvulsive therapy in patients with depressive disorder. *Journal of ECT*, 28(2), 128-132.
- Warnell, R., Swartz, C., & Thomson, A. (2011). Cognitive side effects of bitemporal electroconvulsive therapy at .05 msec pulse width. *Annals of Clinical Psychiatry*, 23(4), 257-262.

- Watts, B., & Groft, A. (2010). Retrospective evaluation of the dexamethasone suppression test as a predictor of response to electroconvulsive therapy in patients with comorbid major depressive disorder and posttraumatic stress disorder. *Journal of ECT*, 26(3), 213-217.
- Weeks, H., Tadler, S. C., Smith, K. W., Iacob, E., Saccoman, M., White, A. T., . . . Light, K. C. (2013). Antidepressant and neurocognitive effects of isoflurane anesthesia versus electroconvulsive therapy in refractory depression. *PLoS One*, *8*(7), e69809.
- Wei, Q., Tian, Y., Yu, Y., Zhang, F., Hu, X., Dong, Y., . . . Wang, K. (2014). Modulation of interhemispheric functional coordination in electroconvulsive therapy for depression. *Translational Psychiatry*, 4, e453.
- Yildiz, A., Mantar, A., Simsek, S., Onur, E., Gökmen, N., & Fidaner, H. (2010).Combination of pharmacotherapy with electroconvulsive therapy in prevention of depressive relapse: A pilot controlled trial. *Journal of ECT*, 26(2), 104-110.
- Yoosefi, A., Sepehri, A. S., Kargar, M., Akhondzadeh, S., Sadeghi, M., Rafei, A., . . . Ghaeli, P. (2014). Comparing effects of ketamine and thiopental administration during electroconvulsive therapy in patients with major depressive disorder: A randomized, double-blind study. *Journal of ECT*, 30(1), 15-21.

 Table 1. Methodological qualities of the 91 ECT studies

	Sham- controlled studies	Efficacy RCTs	Data extracted from RCTs	Data extracted from non- randomized trials	Data extracted from observational studies	Data extracted from retrospective reviews	Total N
Total N	0	1	24	5	47	14	91
Efficacy Reports statistical significance	0	1	11	2	33	3	50
Reports pre-post ECT change	0	0	10	1	9	8	28
Graphical representation only	0	0	2	2	2	0	6
Reports % of responders/remitt ers	0	0	1	0	3	3	7
Follow up	0	0	7	0	10	0	17
Suicide	0	0	1	0	0	0	1
<b>Medication</b> Continued	0	0	17	3	29	6	55
Discontinued	0	1	4	1	13	3	22
Not reported	0	0	3	1	5	5	14
<b>Sample</b> Unipolar Depression	0	0	10	5	27	5	47
Bipolar Depression	0	1	0	0	0	0	1
Schizophrenia	0	0	0	0	1	0	1
Other substance- induced psychosis	0	0	0	0	0	1	1
Mixed Diagnoses Not reported	0	0 0	14 0	0	18 1	6 2	38 3

<sup>\*</sup>RCT = Randomized Controlled Trials.

Figure 1. Flow chart of search process

