

Moderating effects of diagnosis and gender on the influence of age on electroconvulsive therapy outcome

Research Letter

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Dear Editor,

Electroconvulsive therapy (ECT) continues to be a valuable treatment option for refractory cases across diagnostic categories. In elderly patients, the presence of clinical comorbidities and pharmacological interactions have traditionally suggested the consideration of ECT even in non-refractory cases. As such, older age may influence the risk-benefit balance, offering better efficacy with less risk compared to medication (Luccarelli *et al.*, 2022). Some studies have indicated that age does indeed impact the efficacy of ECT, with older patients having better results. However, other studies have suggested that the effect of age on outcome may be confounded by variables such as illness and episode duration, body mass index, and specific diagnoses (Nakajima *et al.*, 2022). Here, we report the influence of age on remission across diagnostic categories in a naturalistic sample of inpatients undergoing ECT for acute mental illness.

We included in a retrospective cohort study all adult inpatients who underwent ECT for acute indications at Hospital de Clínicas de Porto Alegre between January 2009 and December 2015 (see (Tedeschi *et al.*, 2021) for more detailed descriptions). High-potency right unilateral electrode placement was employed, and the stimulus dose for the first session was determined using the titration method. The primary ICD-10 episode diagnosis for which the ECT procedure was indicated was obtained from the medical records. In our analysis, we grouped the diagnoses into indication categories, including depression (unipolar or bipolar), mania, psychotic disorders (schizophrenia, schizoaffective disorder, and delusional disorder), and other diagnoses (anxiety disorders, substance use disorders, organic disorders, and movement disorders), which served as a residual category. A Clinical Global Impression (CGI) was assigned based on the best information available by an investigator blinded to all other study data; a score of 1 (remission) was the primary outcome of the study. Models were estimated with binary Poisson regression with robust estimation of variances. We restricted the main analyses to only those patients who had at least six sessions. We constructed a statistical model testing first the sole effect of age and then added gender and diagnoses, along with their interactions with age to check if they modified the effect of age on remission.

Four hundred and twenty-seven patients fulfilled the inclusion criteria, and 292 patients underwent at least 6 sessions and had sufficient clinical data. The median age for the sample was 46 (IQR 33–60) and the median CGI was 6 before ECT and 1 after; a complete improvement was recorded for 56.2% of patients. In bivariate regression, age was not a significant predictor of remission (IRR = 0.998, 95% CI 0.990–1.006, $p = 0.662$). However, this effect becomes significant with diagnoses and gender added in the model, with older ages predicting a higher likelihood of nonremission (IRR = 1.025, 95%CI 1.009–1.042, $p = 0.002$; Fig. 1). An interaction indicating a significantly different effect of age according to gender was also found, with the effect of age on nonremission being stronger in men (IRR = 0.983, 95%CI 0.968–0.997, $p = 0.021$). A model controlling for other covariates such as medications used, number of previous episodes, and initial CGI revealed largely similar effects (not shown).

Meta-analytic data from observational studies have suggested age is associated with a better ECT response (Pinna *et al.*, 2018). More recent studies, however, have suggested age may be confounded by other clinical variables, such as psychosis and motor retardation and overall illness characteristics (Socci *et al.*, 2018). Here, we demonstrate diagnosis and gender could be further variables of interest in the relation of age and ECT. Specifically, since age was associated with remission when these factors were adjusted for, these factors may be effect suppressors, that is, analysing all diagnoses in both genders may obscure specific age effects. Previous studies were primarily based on samples of people with major depressive disorder and we include here psychosis and mania, where age effects are even less clear. The picture that emerges is one where nonremission is influenced by age in depression and mania but not so in psychosis. Men also had a significantly greater impact of age on the chance of nonremission than women.



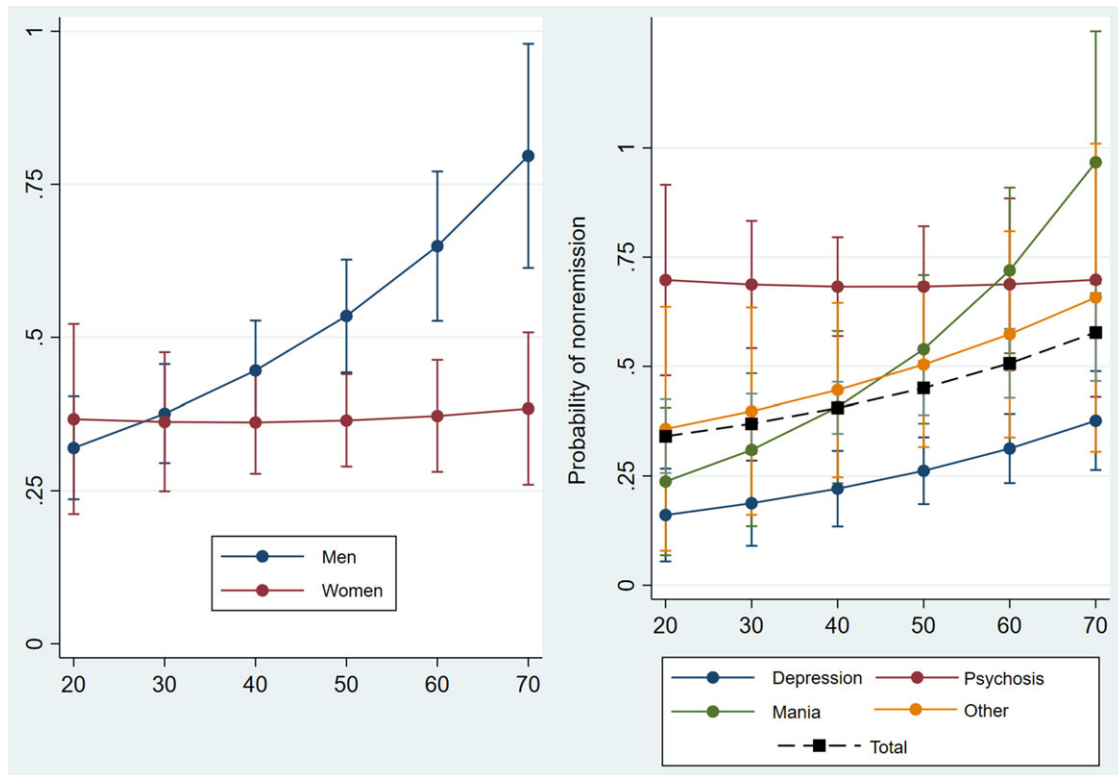


Figure 1. Age-related probability of nonremission according to gender (a) and diagnosis (b).

This is not a controlled experiment and causal explanations for the associations found are not warranted; retrospective studies are inherently limited by having their data collected for purposes other than research. The absence of a control group of patients treated without ECT means we do not know whether the poorer response seen in depression and mania with older ages would not still be higher than similar inpatients treated with medication. This is also a report from a single site with consistent and stable use of electroconvulsive therapy, mostly right unilateral ECT, and generalising to other centres using different clinical strategies is unwarranted. Notwithstanding such limitations, the data presented here suggest one further mechanism for understanding the association between age and ECT outcome. Future cross-diagnostic studies should be able to be better able to probe this association by testing interactions with patient diagnosis and gender.

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