Patterns of late-life depression: On the nature of depressive subtypes and the role of aging

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CHAPTER 6

Differences in speed of response of depressive symptom dimensions in older persons during Electro Convulsive Therapy

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Introduction: Electro Convulsive Therapy (ECT) is an important and effective treatment for depression. However, research on course trajectories of depressive symptoms during ECT is limited. Insight into putative differences in speed of response of depressive symptom dimensions may enable clinicians to optimally inform patients and their relatives. Therefore, we aim to examine course trajectories of depressive symptom dimensions in depressed older persons during ECT.

Methods: Data were derived from the Mood Disorders in Elderly treated with Electro Convulsive Therapy (MODECT) study, including 110 persons, aged 55 years or older, with a current diagnosis of major depressive disorder and referred for ECT. Exploratory factor analysis was used to identify symptom dimensions, using the ten depression items of the Montgomery-Asberg Depression Rating Scale (MADRS). Differences in course trajectories of symptom dimension during two weeks were examined by multilevel analyses.

Results: Three symptom dimensions were identified: a 'mood', 'melancholic' and 'suicidal' dimension. 'Mood' showed a significantly greater severity decline as compared to 'melancholic' and 'suicidal' at one-week follow-up. At two–week follow-up, both 'mood' and 'melancholic' demonstrated a significantly greater decline as compared to 'suicidal'. However, since scores on the suicidality item of the MADRS were already lower at baseline compared to the other items, a floor effect cannot be ruled out.

Discussion: All symptom dimensions of depression showed a rapid response to ECT. Our findings did not support the general assumption that suicidal symptoms may be the first to improve. However, a floor effect on the suicidality item cannot be ruled out.

Key words: course trajectories; factor analysis; major depressive disorder; late-life depression

Abstract

Introduction

Depressive disorders among older persons are highly common and frequently of a chronic nature. They cause a high burden for both patients [1] and their caregivers [2], with high societal costs [3,4]. Considering this great personal and societal impact, adequate treatment is of paramount importance. In addition to pharmacotherapy, electroconvulsive therapy (ECT) is an important treatment option for severe depressive disorders in older persons. It was demonstrated that older age is a positive predictor for ECT outcome [5,6], with remission rates from 73-90% in patients over 65 years of age [7,8]. In addition, the speed of remission is high [9,10], and significantly higher for ECT compared to pharmacotherapy [11].

When treating depression, not all symptoms resolve at the same pace or to the same magnitude [12-14]. Both pharmacotherapy and psychotherapy are known to ameliorate not all symptoms to the same extent [15,16], and, on average, remission occurs after several weeks to months. On the other hand, studies on ECT in both depressed older and younger adults have found that depressive symptoms show a very rapid response to ECT [9,10], and within younger adults response has been found especially rapid for psychomotor symptoms, such as inhibition, agitation, or inner tension [17-19]. In a recent study on early remission in ECT, the early remitters [requiring four or less ECT sessions, accounting for 14% of the study population] had a significantly higher age than the other subjects [20]. However, insight into response trajectories of different symptom dimension within depressed older persons is lacking.

In order to gain a better insight into dimensions of depressive symptoms and their course trajectories during ECT in depressed older persons, we explored the speed of response of different depressive symptom dimensions in an elderly cohort receiving ECT.

Materials and Methods

Study population

Data were derived from the Mood Disorders in Elderly treated with Electro Convulsive Therapy (MODECT) study, a two-site longitudinal study including older in-patients (55 years or older) with severe unipolar depression according to criteria of the Diagnostic and Statistical Manual of Mental Disorders-Fourth Edition, Text Revision (DSM-IV-TR) [21], referred for ECT. Patients were recruited from tertiary psychiatric hospitals (GGZ inGeest, Amsterdam, the Netherlands and University Psychiatric Center, KU Leuven, Belgium). Patients with another major DSM-IV diagnosis or major neurological illness (including Parkinson's disease, stroke and dementia) were excluded, thus retaining a data set of 110 persons. Diagnosis was made at admittance to the ward by a psychiatrist and confirmed by the Mini International Neuropsychiatric **Interview** (MINI) 5.0.0, Dutch version [22]. The study protocol of MODECT has been approved centrally by the Ethical Review Board of the VU University Medical Center, Amsterdam, the Netherlands and subsequently by the ethical review board of the Leuven University, Leuven, Belgium. Before participating

in the study, all patients were provided with oral and written information. Written informed consent was obtained from all patients or - in case of inability consent- a legal representative. For a detailed description of the MODECT-study, we refer to Dols et al. [23].

Depressive symptoms

Depressive symptoms were measured by the Dutch version of the 10-item MADRS (Montgomery Åsberg Depression Rating Scale [24,25], a validated questionnaire for investigating ten symptoms of major depressive disorder (MDD), including apparent sadness, reported sadness, inner tension, reduced sleep, reduced appetite, concentration difficulties, lassitude, anhedonia, pessimistic thoughts and suicidal thoughts. For each item, a minimum of 0 points and a maximum of 6 points can be scored, according to symptom intensity. The cumulative score of the MADRS can be used as an indicator for the severity of a depression. In MODECT, MADRS was assessed at baseline (prior to ECT), and weekly during ECT by raters trained to administer the MADRS. For the current study baseline measurements and MADRS-scores during the first two weeks were used, since significant improvement to complete remission is often seen within two weeks already [11,20]. Patients were excluded if baseline MADRS, one-week follow-up, or two-week follow-up MADRS were missing (n=21).

Attrition analysis showed that persons with missing MADRS-scores did not differ with respect to total MADRS score for baseline, week 1 and week 2, sex, age, and education from persons included in the study.

Characteristics

To characterize the study population and to enable comparison to other, similar studies, socio-demographics and clinical variables were examined. For a detailed description of measurement of characteristics and clinical variables, we refer to Dols et al. [23]. In short, socio-demographics included sex, age, and years of education. Clinical variables included early-onset of depression (<55 years) versus late-onset, assessed by interview. Number of prior depressive episodes and prevalence of psychotic features was assessed at baseline by the MINI and clinical interview. Current medication use was assessed by interview and double-checked by chart review. Previous antidepressant treatment and treatment resistance was scored with the Antidepressant Treatment History Form (ATHF) [26,27]. Depression severity was defined as the Montgomery-Åsberg Depression Rating Scale (MADRS) total score [24]. Number of somatic disorders was assessed in a semi-structured interview (see also Dols et al. [23]). Prevalence of cardiovascular disease was being defined as presence of hypertension or a history of myocardial infarct or stroke, and obtained through semi-structured interview. Current smoking was assessed by semi-structured interview. Alcohol use was measured by two questions based on the Alcohol Use Disorders Identification Test (AUDIT) [28] on frequency and amount of alcohol consumption.

ECT-procedures

A course of twice weekly ECT along Dutch standards was given to all patients [29,30]. A course started with right unilateral stimuli. For ECT the Thymatron System IV (Somatics, LLC, Lake Bluff, IL, USA) (maximum energy 200%, 1008 mCoulomb) was used, according to a titration dosing protocol. All patients were treated with brief-pulse ECT (0.5-1.0 ms) twice a week. The stimulus intensity was determined by empirical dose titration at the first treatment, for right unilateral ECT six times the initial seizure threshold, and for bilateral ECT 1.5 times the initial seizure threshold. A motor seizure of less than 20 seconds or a seizure on electro-encephalogram (EEG)-recordings of less than 25 seconds was considered inadequate, upon which the dose was raised according to Dutch guidelines [29,30]. If the clinical condition worsened or if no clinical improvement was seen after six unilateral treatments, a switch to bilateral ECT was applied. ECT was continued until the patient reached a MADRS score of less than 10 at two consecutive ratings with a week interval. Additionally, if no further improvement was seen for two weeks, after a minimum of six unilateral and six bilateral sessions, ECT was stopped. Psychotropics such as benzodiazepines, antidepressants, and mood stabilizers were tapered off within two weeks before starting ECT, if clinically possible. Antipsychotics were allowed if clinically indicated.

Statistical Analyses

Since the MADRS consists of 10 items, examination of course trajectories of all items within depressed persons during 2-week follow-up would entail multiple comparisons, prone to type I error. Therefore, a factor analysis on baseline data incorporating the 10 items of the MADRS was conducted in order to reduce the number of items into a limited number of dimensions. Previously, several studies have addressed factor analysis of the MADRS, with factor structures ranging from two to four dimensions [31]. However, since the number of dimensions across studies differed, and since earlier studies used populations ranging from younger to older persons, we decided to perform an exploratory factor analysis (EFA) instead of a confirmatory factor analysis. Oblique rotation (promax) was used because the final dimensions were expected to be inter-correlated. Dimensions were extracted, based on preferential loading on one dimension, differences between loadings of at least 0.20, and eigenvalues (>1.0) [32], observation of the scree plot, and interpretability of the dimensions. Next, course trajectories of the identified dimensions within depressed persons during one-week follow-up and two-week follow-up were compared using multivariate, multilevel analyses (multivariate with respect to both the different groups, and follow-up in time). For that purpose, depression dimensions were standardized over the entire measurement period, and multilevel analyses were performed on three levels. The dimensions were clustered within time points, and time points were clustered within patients. In multilevel analyses, time, different dimensions (both represented by two dummy variables), and the interaction between time and dimension were added to the model. The EFA was performed with SPSS version 21 (IBM Corp. Released 2012. IBM SPSS Statistics for Windows, Version 21.0. Armonk, NY: IBM Corp) and the multilevel analyses were performed with MLwiN version 2.31 (Multilevel Modelling for Windows, Centre for Multilevel Modelling, University of Bristol).

Results

The total sample consisted of 89 depressed older people, of whom 66.4% were females, with age ranging from 55 to 92 years and a mean age of 73.1 years (SD ± 8.3). Almost half of the sample (46.4%) had psychotic symptoms, and the mean number of prior depressive episodes was 3.7 (SD ± 3.3). MADRS scores at baseline ranged from 20 to 49, with a mean score of 32.6 (SD ± 7.6) and 78.7% had physical comorbidity, with a prevalence of cardiovascular disease of 43.8% (see also **table 1**).

Exploratory factor analysis identified three symptom dimensions (**table 2**), including a dimension consisting of apparent and reported sadness, concentration difficulties and anhedonia (MADRS items 1,2,6,8), henceforth called 'mood' dimension; a second dimension consisting of inner tension, reduced sleep, reduced appetite, lassitude, and pessimistic thoughts (MADRS items 3,4,5,7,9), henceforth called 'melancholic' dimension; and a third, separate dimension consisting of suicidality only (MADRS item 10), henceforth called 'suicidality' dimension. Factor loadings are presented in **table 2**.

Next, the course trajectories of the three symptom dimensions during the first two weeks of ECT were compared. Figure 1 shows the observed development over time in the three depression symptom dimensions. Within depressed persons, all symptom dimensions rapidly declined in severity after the start of ECT. **Table 3** shows the results of the multivariate multilevel analyses. The mood dimension showed a significantly greater decline than the melancholic and suicidal dimension during the first week of ECT (i.e. the mood dimension decreased with 0.31 standard deviation units more than the melancholic dimension between baseline and follow-up). However, during two-week follow-up, the speed of response in the mood dimension did not differ significantly from the melancholic symptom dimension. Notably, although the decline of the suicidality dimension after one week was comparable to the decline of the melancholy dimension, after two weeks the suicidal dimension declined significantly less than the other two dimensions (i.e. the mood dimension decreased with 0.76 standard deviation units more than the suicidal dimension). Post-hoc analyses revealed that the median baseline score on the suicidality item was 2 (IQR=3), which was significantly lower than scores on most other MADRS items, and decreased to 1 (IQR=3) after one week (**table 4**).

Post-hoc, we also performed analyses of the decline over time for each individual MADRS item, to see whether this would generate new insights (supplement 1). All items (apart from lassitude and suicidality) declined significantly each week. In addition, the individual 'mood' items showed greater coefficients of decline in week 1 as compared to week 2, except for reported sadness (coefficient= 0.88 in week 1 versus 0.89 in week 2); and all individual 'melancholic' items showed greater coefficients of decline in week 2 as compared to week 1 (results available upon request).This is in line with findings on speed of response of the aggregated domains, in which the 'mood' dimension shows a significantly higher speed of improvement as compared to 'melancholic' dimension in week 1. Improvement of lassitude seemed to lag behind, since there was only significant improvement in week 2. Suicidality only showed significant improvement in week 1 (as compared to baseline). To conclude, findings are largely in line with findings on aggregated items.

Discussion

The aim of our study was to identify dimensions of depressive symptoms within an older population, and to examine differences in speed of response of symptom dimensions within depressed older persons during the first two weeks of ECT. Three depressive symptom dimensions were identified, including a 'mood', 'melancholic' and 'suicidal' dimension. All dimensions showed rapid and significant improvement during the follow-up, but the mood dimension demonstrated the highest speed of improvement during the first week of ECT, as compared to the 'melancholic' and 'suicidal' dimension. Likewise, both 'mood' and 'melancholic' dimensions improved at a significantly faster speed than the 'suicidal' dimension during two-week follow-up.

Through EFA three dimensions were identified, similar to an earlier study by Parker et al. [33]. This study used MADRS-items in a population of 225 in- and outpatients aged 59 years and older with major depressive disorder. They identified three distinct dimensions: a 'dysphoric apathy/ retardation' dimension, similar to our mood dimension, a 'psychic anxiety' dimension, and a dimension with vegetative symptoms. Our melancholic dimension corresponds to their psychic anxiety and vegetative dimension combined. However, whereas our EFA supports a separate suicidal dimension, Parker et al. [33] included suicidal symptoms in the vegetative dimension. Our finding of a distinct suicidal dimension can be explained by the fact that our study sample contains solely inpatients, while Parker et al. [33] used a mixture of in- and outpatients. Severely suicidal depressed older persons are more likely to be admitted and treated with ECT, which means that suicidality is probably a more prominent symptom in our inpatient sample compared to other studies including outpatients too, even though our population had a moderately high score on suicidality. Unfortunately, the study of Parker et al. [30] does not provide mean MADRS scores on the suicidal item, thereby hampering comparison. Other studies analyzing the factor structure of the MADRS also identified three dimensions, but great differences between theirs and our study population hampers comparisons with our study findings [34].

Our main study aim was to examine differences in course trajectories of the identified dimensions. All dimension improved significantly during the first two weeks, an advantage of ECT over other antidepressant treatments, since the latter usually requires several weeks to reach improvement [11], with studies also finding lagging on different symptoms or symptom dimensions [12-16]. We found that the suicidal dimension significantly lagged behind the mood dimension after the first week of ECT, but a floor effect causing that delay could not be ruled out. In post-hoc analyses, we examined the decline of each individual MADRS item in week 1 compared to baseline, and week 2 to week 1. We found that all items, apart from lassitude and suicidality, decline significantly each week, with a greater improvement of 'mood' items as compared to 'melancholic' items in week 1. To conclude, findings are largely in line with findings on aggregated items. Since the suicidal dimension was comprised of only one item, the responsiveness of this domain may be limited and a floor effect may be present.

Since ECT is known to strongly enhance dopamine [35], the fast improvement of the mood dimension may be caused by the inclusion of anhedonia in this dimension, a symptom linked to disturbances in the dopamine pathways [36-38].

The findings of our study should be interpreted in the context of the following strengths and limitations. The design of this study provided the opportunity to examine course trajectories of depressive symptoms in detail, with weekly assessment of the MADRS. The MADRS however does not fully correspond to the DSM-IV-TR criteria for major depressive disorder [21]. The MADRS only addresses loss of sleep and weight/ appetite, whereas the DSM-IV-TR includes change of sleep and both gain and loss in weight/ appetite. Likewise the DSM-IV-TR criterion of psychomotor changes (both agitation and retardation) is not properly addressed by the MADRS. This may be of particular importance to our study, since psychomotor symptoms are considered to be a predictor of ECT response [19]. Earlier studies found a correlation between the MADRS item 'inner tension' and total CORE score (an instrument to assess psychomotor symptoms in depression), but being a single item measure, this item may not be sufficiently valid to measure the full construct of psychomotor disturbances [39].

Next, our results show that, although suicidality improved rapidly, the speed of response significantly lagged behind the mood dimension in week one, and behind both dimension in week two. Post-hoc analyses revealed that the median baseline score on the suicidality item was 2 (IQR=3), which was significantly lower than scores on most other MADRS items (**table 4**), and decreased to 1 (IQR=3) after one week. These findings suggest that a floor effect probably hampered any further decrease after week one, since the median baseline value was, of all items, closest to zero.

To conclude, our findings show that ECT induces a rapid decline of all symptom dimensions in depressed older persons, with primacy of the mood dimension. Since anhedonia was included in this dimension, these findings suggest that ECT may rapidly restore dopamine-related symptomatology. To what extent the (relatively) lagging behind of suicidal symptoms is related to clinometric properties of the MADRS (e.g. a floor effect) needs to be settled. Above all, since all depressive symptom dimensions already improved during the first week after ECT, this study underlines the potency of ECT to rapidly ameliorate depressive symptoms; a great benefit for clinical practice.

Conflict of interest

No conflict of interest is declared. This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

References

1. Gallo JJ, Bogner HR, Morales KH, et al. The effect of a primary care practice-based depression intervention on mortality in older adults: a randomized trial. *Ann Intern Med*. 2007;146:689-98.
2. Scazufca M, Menezes PR, Almeida OP. Caregiver burden in an elderly population with depression in São Paulo, Brazil. *Soc Psychiatry Psychiatr Epidemiol*. 2002;37:416-22.
3. Hughes D, Morris S, McGuire A. The cost of depression in the elderly. Effects of drug therapy. *Drugs & Aging*. 1997;10:59-68.
4. Unützer J, Schoenbaum M, Katon WJ, et al. Healthcare costs associated with depression in medically Ill fee-for-service medicare participants. *Am J Geriatr Soc*. 2009;57:506-10.
5. Rhebergen D, Huisman A, Bouckaert F, et al. Older age is associated with rapid remission of depression after electroconvulsive therapy: a latent class growth analysis. *Am J Geriatr Psychiatry*. 2015;23:274-82.
6. Geduldig ET, Kellner CH. Electroconvulsive Therapy in the Elderly: New Findings in Geriatric Depression. *Curr Psychiatry Rep*. 2016;8:40.
7. Tew JD Jr, Mulsant BH, Haskett RF, et al. Acute efficacy of ECT in the treatment of major depression in the old-old. *Ann Clin Psychiatr*. 2007;19:1-4.
8. O'Connor MK, Knapp R, Husain M, et al. The influence of age on the response of major depression to electroconvulsive therapy: a CORE report. *Am J Geriatr Psychiatry*. 2001;9:382-90.
9. Kellner CH, Husain MM, Knapp RG, et al. A Novel Strategy for Continuation ECT in Geriatric Depression: Phase 2 of the PRIDE Study. *Am. J. Psychiatry* 2016;173: 1110-8.
10. Kellner CH, Husain MM, Knapp RG, et al. Right Unilateral Ultrabrief Pulse ECT in Geriatric Depression: Phase 1 of the PRIDE Study. *Am. J. Psychiatry* 2016;173:1101-9.
11. Spaans HP, Sienaert P, Bouckaert F, et al. Speed of remission in elderly patients with depression: electroconvulsive therapy versus medication. *British J Psychiatr*. 2015; 206:67-71.
12. Culpepper L, Mathews M, Ghori R, et al. Clinical relevance of vilazodone treatment in patients with major depressive disorder: categorical improvement in symptoms. *Prim Care Companion CNS Disord*. 2014;16:1.
13. Alonzo A, Chan G, Martin D, et al. Transcranial direct current stimulation (tDCS) for depression: analysis of response using a three-factor structure of the Montgomery-Åsberg depression rating scale. *J Affect Disord*. 2013;150:91-5.
14. Brunoni AR, Fragus Junior R, Kemp AH, et al. Differential improvement in depressive symptoms for tDCS alone and combined with pharmacotherapy: an exploratory analysis from The Sertraline Vs. Electrical Current Therapy For Treating Depression Clinical Study. *Int J Neuropsychopharmacol*. 2014;17:53-61.
15. DiMascio A, Weissman MM, Prusoff BA, et al. Differential symptom reduction by drugs and psychotherapy in acute depression. *Arch Gen Psychiatry*. 1979;36:1450-6.
16. Bhar SS, Gelfand LA, Schmid SP, et al. Sequence of improvement in depressive symptoms across cognitive therapy and pharmacotherapy. *J Affect Disord*. 2008;110:161-6.
17. Ziskind E, Somerfeld-Ziskind E, Ziskind L. Metrazol and electric convulsive therapy of the affective psychoses. A controlled series of observations covering a period of five years. *Arch Neurol Psychiatry*. 1945;53:212-7.
18. Buchan H, Johnstone E, McPherson K, et al. Who benefits from electroconvulsive therapy? Combined results of the Leicester and Northwick Park trials. *Br J Psychiatry*. 1992;160:355-9.
19. Parker G, Fink M, Shorter E, et al. Issues for DSM-5: whither melancholia? The case for its classification as a distinct mood disorder. *Am J Psychiatry*. 2010;167:745-7.

20. Spaans HP, Verwijk E, Stek ML, Kho KH, Bouckaert F, Kok RM et al. Early complete remitters after electroconvulsive therapy: profile and prognosis. *J ECT*. 2016;32:82-7.
21. Diagnostic and Statistical Manual of Mental Disorders: Dsm-iv-tr. Washington, DC: American Psychiatric Association, 2000. Print.
22. Lecrubier Y, Sheehan DV, Weiller E, et al. The Mini International Neuropsychiatric Interview (M.I.N.I.): a short diagnostic structured interview: reliability and validity according to the cidi. *Eur Psychiatry*. 1997;12:224-31.
23. Dols A, Bouckaert F, Sienaert P, et al. Early- and Late-Onset Depression in Late Life: A Prospective Study on Clinical and Structural Brain Characteristics and Response to Electroconvulsive Therapy. *Am J Geriatr Psychiatry*. 2017;25:178-89.
24. Montgomery SA, Åsberg M. A new depression scale designed to be sensitive to change. *Br J Psychiatry*. 1979;134:382-9.
25. Hartong EGTM, Goedkoop JG. De Montgomery -Åsberg beoordelingsschaal voor depressie. *Tijdschr Psychiatr*. 1985;27:657-68.
26. Prudic J, Haskett RF, Mulsant B, et al. Resistance to antidepressant medications and short-term clinical response to ECT. *Am J Psychiatry*. 1996;153:985-92.
27. Sackeim HA. The definition and meaning of treatment-resistant depression. *J Clin Psychiatry*. 2001;62 Suppl 16:10-7.
28. Bohn MJ, Babor TF, Kranzler HR. The Alcohol Use Disorders Identification test (AUDIT): validation of a screening instrument for use in medical settings. *J Stud Alcohol Drugs*. 1995;56:423-432.
29. NICE guidance on the use of electroconvulsive therapy. NICE Technology Appraisal Guidance 59. 2003, London.
30. Broek WW van den, Birkenhager TK, de Boer D, et al. Richtlijn elektroconvulsietherapie, Utrecht, The Netherlands, Tijdstroom, 2010.
31. Okazaki M, Tominaga K, Higuchi H, et al. Predictors of response to electroconvulsive therapy obtained using the three-factor structure of the Montgomery and Asberg Depression Rating Scale for treatment-resistant depressed patients. *J ECT*. 2010;26:87-90.
32. Jolliffe IT. Discarding Variables in a Principal Component Analysis. I: Artificial Data. *J Royal Statistical Society. Series C (Applied Statistics)*. 1972;21:160-73.
33. Parker RD, Flint EP, Bosworth HB, et al. A three-factor analytic model of the MADRS in geriatric depression. *Int J Geriatr Psychiatry*. 2003;18:73-7.
34. Suzuki A, Aoshima T, Fukasawa T, et al. A three-factor model of the MADRS in major depressive disorder. *Depress Anxiety*. 2005;21:95-7.
35. Nutt DJ. The role of dopamine and norepinephrine in depression and antidepressant treatment. *J Clin Psychiatry*. 2006;67 Suppl 6:3-8.
36. Pizzagalli DA, Jahn AL, O'Shea JP. Toward an objective characterization of an anhedonic phenotype: a signal-detection approach. *Biol Psychiatry*. 2005;57:319-27.
37. Pizzagalli DA, Holmes AJ, Dillon DG, et al. Reduced caudate and nucleus accumbens response to rewards in unmedicated individuals with major depressive disorder. *Am J Psychiatry*. 2009;166:702-10.
38. Pizzagalli DA. Depression, stress, and anhedonia: toward a synthesis and integrated model. *Ann Rev Clin Psychol.* 2014;10:393-423.
39. Attu SD, Rhebergen D, Comijs HC, et al. Psychomotor symptoms in depressed elderly patients: assessment of the construct validity of the Dutch CORE by accelerometry. *J Affect Disord.* 2012;137:146-50.

Table 1. Characteristics of study population (N=89)

Sociodemographics	
Sex, female, %	66.7
Age, mean (SD)	73.4(9.8)
Education level (in years), mean (SD)	6.4(2.7)
Clinical characteristics	
Age onset, early, %	42.9
# prior depressive episodes, median (IQR)	3(2)
Psychotic features, %	46.4
Current medication use, %	39.8
ATHF (resistance sum score), mean(SD)	6.3(4.9)
MADRS, mean (SD)	32.6(7.6)
Physical health	
Physical comorbidity, present, %	78.7
Cardiovascular disease, %	43.8
Smoking, %	18.2
Alcohol # daily, mean (SD)	2.2(0.7)

Table 2. Factor loadings of MADRS items after oblique rotation (N=89)

	Dimension		
	Mood	**Melancholic**	**Suicidality**
MADRS items			
Apparent sadness	**.275**	-.047	.007
Reported sadness	**.212**	.143	.070
Inner tension	.161	**.197**	-.145
Reduced sleep	-.093	**.497**	-.071
Reduced appetite	.094	**.165**	.147
Concentration difficulties	**.274**	.022	-.208
Lassitude	.030	**.403**	-.213
Anhedonia	**.290**	-.156	.203
Pessimistic thoughts	-.036	**.217**	.198
Suicidality	.008	-.014	**.781**

Grey marked cells indicate highest factor loading

Table 3. Comparison of course of three symptom dimensions

	Mood vs melancholic, Score difference, p (95% CI)	Mood vs suicidal, score difference, p (95% CI)	Melancholic vs suicidal, score difference, p (95%CI)
Baseline – 1 week follow up	**0.31, p=0.03(0.42-0.96)**	**0.35, p=0.01 (0.38-0.92)**	0.05, p=0.73 (0.91-1.24)
Baseline – 2 week follow up	0.18, p=0.23(0.53-1.11)	**0.76, p<0.01 (0.54-0.96)**	**0.55, p<0.01 (0.16-0.74)**

Bold = significant

Table 4. Scores on separate MADRS items (N=89) (mean (SD); median (IQR))

	Baseline	After 1 week	After 2 weeks
1. Apparent sadness	4.2(1.2); 4.0(1)	3.1(1.5); 3.0(2)	2.5(1.4); 3.0(1)
2. Reported sadness	4.4(1.4); 5.0(1)	3.5(1.4); 4.0(1)	2.7(1.5); 3.0(3)
3. Inner tension	3.7(1.2); 4.0(1)	3.0(1.3); 3.0(2)	2.3(1.3); 3.0(2)
4. Reduced sleep	2.7(1.6); 3.0(2)	2.3(1.7); 2.0(3)	1.6(1.5); 2.0(3)
5. Reduced appetite	2.8(1.8); 3.0(3)	2.5(1.8);2.5(3)	1.9(1.6); 2.0(3)
6. Concentration difficulties	3.8(1.3); 4.0(2)	3.2(1.4); 4.0(2)	2.7(1.4); 3.0(2)
7. Lassitude	3.3(1.6); 4.0(3)	3.0(1.6); 3.0(2)	2.3(1.6); 2.0(3)
8. Inability to feel	3.8(1.4); 4.0(2)	2.8(1.3); 3.0(2)	2.3(1.5); 2.0(2)
9. Pessimistic thoughts	3.1(1.7); 3.0(2)	2.8(1.4); 3.0(2)	2.1(1.6); 2.0(2)
10. Suicidal thoughts	1.8(1.6); 2.0(3)	1.4(1.4); 1.0(3)	1.1(1.2); 1.0(2)

Figure 1. Speed of response of symptom dimensions within depressed persons during first 2-weeks of ECT (1=baseline, 2=after one week, 3=after two weeks)

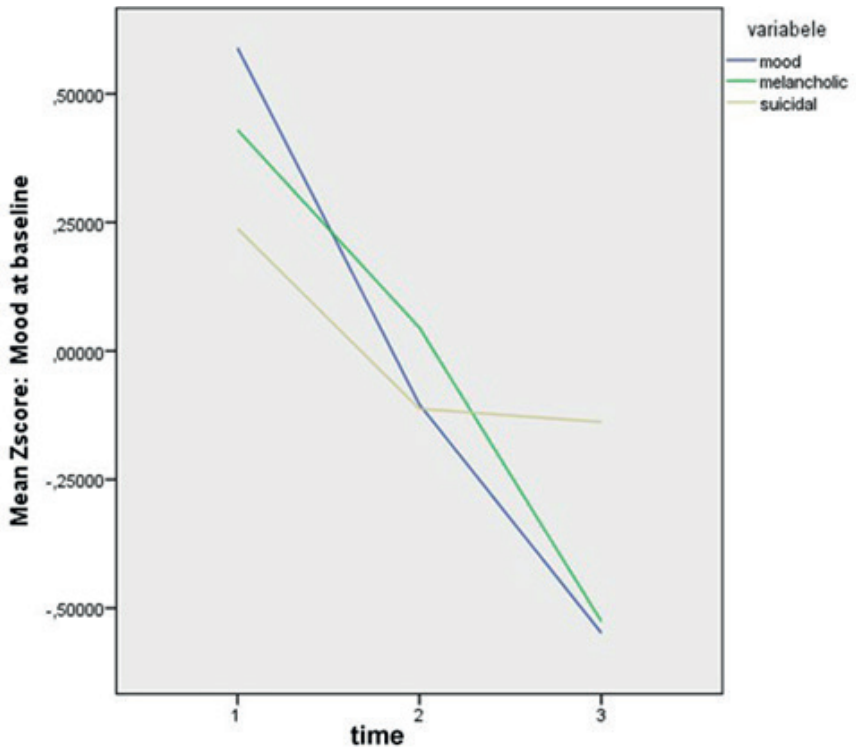

Figure legend: Speed of response of mood (blue line), melancholic (green line), and suicidal (yellow line) cluster, measured at baseline, one, and two weeks. Note that while all symptoms improve rapidly, the decline of the yellow line stalls after one week. This might be due to a floor effect, since baseline scores on the suicidal cluster were lower than both other clusters.

Supplement 1. Coefficients and 95% CIs for separate MADRS items comparing scores at baseline, week 1 and week 2

	Comparison of week 1 and week 2 to baseline (=reference)		Comparison of week 2 to week 1 (=reference)
MADRS items	**Week 1, coef (95%CI)**	**Week 2, coef (95%CI)**	**coef (95%CI)**
1. Apparent sadness	-1.07 (-1.35 – -0.80)	-1.71 (-2.00 – -1.43)	-0.64 (-0.93 – -0.36)
2. Reported sadness	-0.88 (-1.18 – -0.58)	-1.77 (-2.08 – -1.47)	-0.89 (-1.20 – -0.58)
3. Inner tension	-0.59 (-0.87 – -0.31)	-1.32 (-1.61 – -1.04)	-0.73 (-1.02 – -0.45)
4. Reduced sleep	-0.45 (-0.77 – -0.14)	-1.16 (-1.48 – -0.84)	-0.71 (-1.03 – -0.38)
5. Reduced appetite	-0.34 (-0.67 – -0.02)	-0.85 (-1.18 – -0.52)	-0.51 (-0.84 – -0.17)
6. Concentration difficulties	-0.61 (-0.88 – -0.34)	-1.14 (-1.14 – -0.86)	-0.53 (-0.81 – -0.25)
7. Lassitude	-0.30 (-0.61 – 0.01)	-1.09 (-1.40 – -0.77)	-0.78 (-1.10 – -0.46)
8. Anhedonia	-0.94 (-1.21 – -0.66)	-1.50 (-1.78 – -1.22)	-0.56 (-0.85 – -0.27)
9. Pessimistic thoughts	-0.34 (-0.64 – -0.04)	-1.08 (-1.39 – -0.78)	-0.74 (-1.05 – -0.43)
10. Suicidality	-0.46 (-0.72 – -0.20)	-0.71 (-0.97 – -0.45)	-0.25 (-0.51 – 0.02)

Non-significant findings are underlined