

Seeking biomarkers for electroconvulsive therapy in depression

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NACT May 2024

AHUS

ECT clinic located at the emergency psychiatric unit

ECT capacity: 25 patients a week.

n= 100 patients/year

Part of PRECISE-study. First patients enrolled.



Consortium for Precision Treatment with ECT in Severe Depression: (PRECISE)

The goal of this project is to map central phenotypic and biological factors that predict long-term treatment response to electroconvulsive therapy (ECT), using a naturalistic approach to enable clinically transferable discovery in a large dataset

PRECISE

Inclusion criteria:

- Age \geq 18 years
- Diagnosis of unipolar major depressive episode
 - According to the Mini International Neuropsychiatric Interview (MINI), with or without psychotic symptoms
 - ICD-10 codes F32.2, F32.3, F33.2, F33.3
- Ability to
 - co-operate in testing

Exclusion criteria:

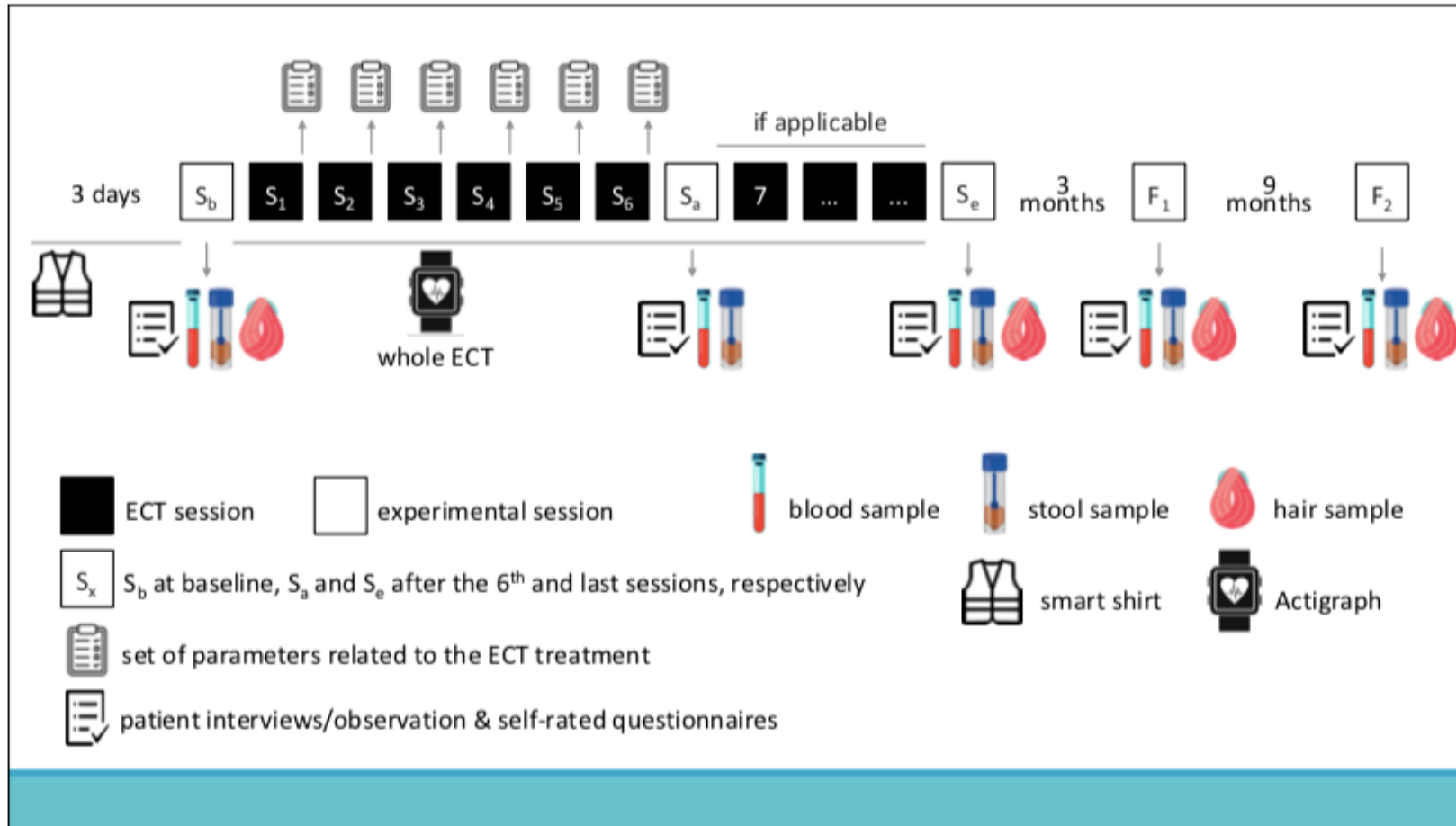
- Pregnancy

AHUS study nurses



PRECISE

Summary of study procedures



Overview of the presentation

- What are biomarkers?
- Understanding the significance of biomarkers for ECT in depression
- Overview of widely studied circulating biomarkers
- Meta-analysis NSE and S100

Biomarkers

- “A defined characteristic that is measured as an indicator of normal biological processes, pathogenic processes or responses to an exposure or intervention.”

FDA-NIH Biomarker Working Group. BEST (Biomarkers, EndpointS, and other Tools)2016

Biomarkers and ECT: Paving the way for tailored depression treatment?

- Predict ECT response
- Differentiate between likely responders and non-responders
- Minimize trial and error in treating depression
- Objective measure beyond traditional symptom-based assessments

Biomarkers for ECT in depression

- Monoaminergic
- Endocrine
- Neurotrophic
- Inflammatory and immune biomarkers
- Genetic/Epigenetic biomarkers
- mRNA
- Neuroimaging
- Clinical predictors

Monoaminergic biomarkers

Monoamine metabolite: Homovanillic Acid (HVA) (*Okamoto et al. 2008*)

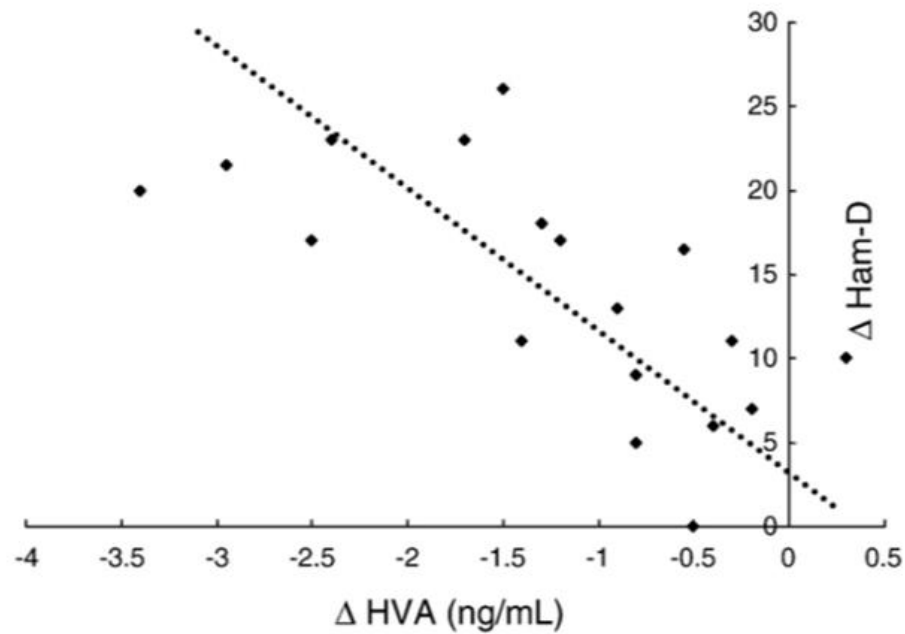


Fig. 2. Negative association between the changes in Ham-D and the changes in plasma HVA levels before and five weeks after start of ECT ($n=18$). $\rho=-0.620$, $p=0.0052$.

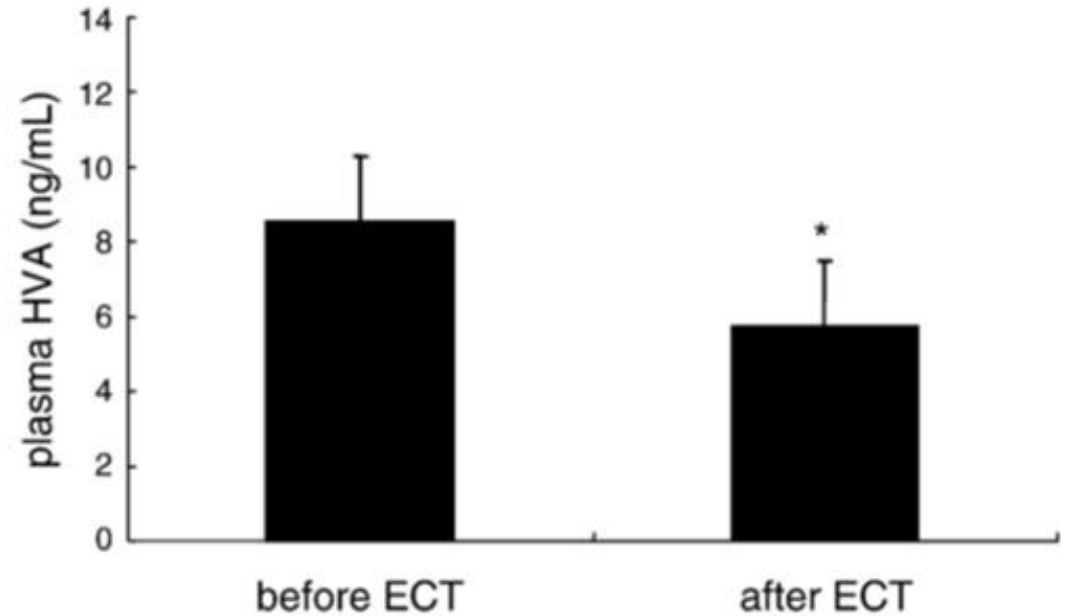
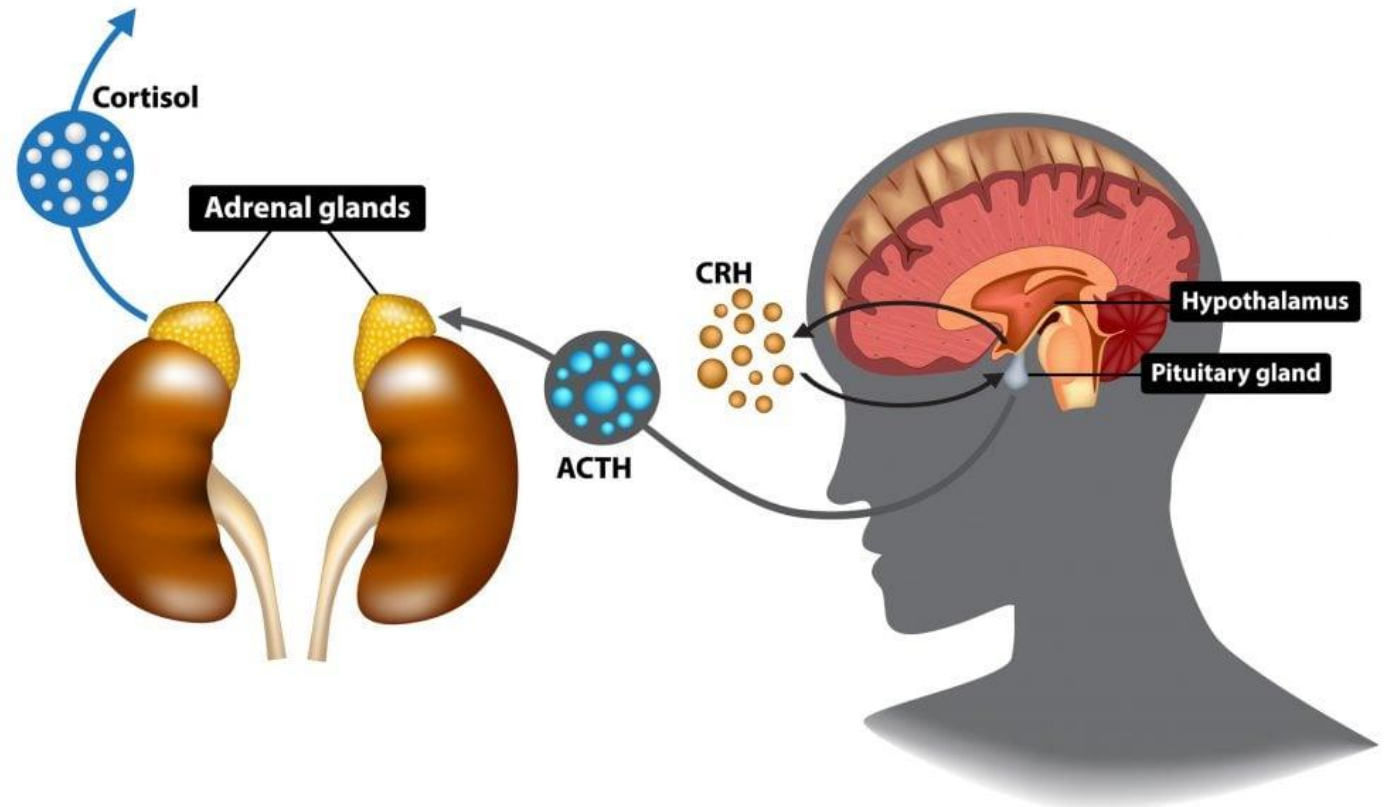


Fig. 1. Changes in plasma HVA levels before and after (i.e., five weeks after starting) ECT treatment ($n=18$). $*p=0.008$, compared with before ECT.

Endocrine biomarkers

- HPA-axis



Endocrine biomarkers

Brain Stimulation 11 (2018) 29–51

Contents lists available at [ScienceDirect](#)



ELSEVIER

Brain Stimulation

journal homepage: <http://www.journals.elsevier.com/brain-stimulation>

Corticotropic axis:
22 studies included
6-62 patients

Electroconvulsive therapy, depression, the immune system and inflammation: A systematic review

Antoine Yrondi ^{a, b, *}, Marie Sporer ^a, Patrice Péran ^b, Laurent Schmitt ^a,
Christophe Arbus ^{a, b}, Anne Sauvaget ^c

^a Psychiatric Department, CHU Toulouse-Purpan, 330 Avenue de Grande Bretagne, 31059 Toulouse, France

^b Toulouse NeuroImaging Center, ToNIC, University of Toulouse, Inserm, UPS, France

^c CHU Nantes, Addictology and Liaison Psychiatry Department, Neuromodulation Unit in Psychiatry, Nantes, France

Neurotrophic biomarkers

- Brain derived neurotrophic factor (BDNF)
- 28 studies n=778
- Mean age 50 (SD 12)

THE WORLD JOURNAL OF BIOLOGICAL PSYCHIATRY
2023, VOL. 24, NO. 1, 24-33
<https://doi.org/10.1080/15622975.2022.2058083>



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ORIGINAL INVESTIGATION



BDNF blood levels after electroconvulsive therapy in patients with mood disorders: An updated systematic review and meta-analysis

Rebeca Pelosof^{a*} , Leonardo A. dos Santos^{a*} , Luis C. Farhat^a , Wagner F. Gattaz^{a,b} , Leda Talib^{a,b}  and André R. Brunoni^{a,b,c} 

^aDepartment of Psychiatry, Faculdade de Medicina FMUSP, Universidade de São Paulo, São Paulo, Brazil; ^bService of Interdisciplinary Neuromodulation, Department of Psychiatry, Laboratory of Neurosciences (LIM-27), Faculdade de Medicina FMUSP, Universidade de São Paulo, São Paulo, Brazil; ^cInterdisciplinary Center for Applied Neuromodulation University Hospital, Universidade de São Paulo, São Paulo, Brazil

BDNF change pre and post-ECT in blood

All studies*

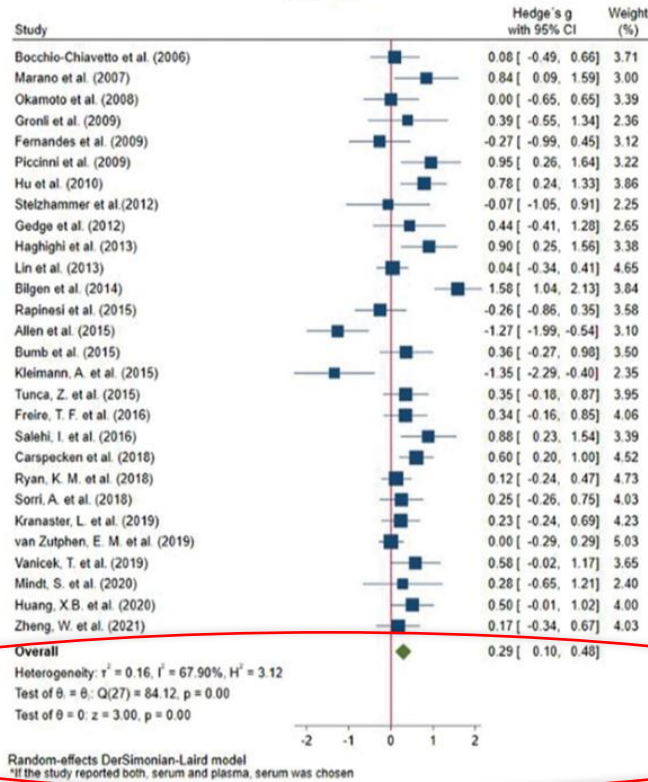


Figure 2. Forest plot for the BDNF meta-analysis.

Depressive scales change pre and post-ECT

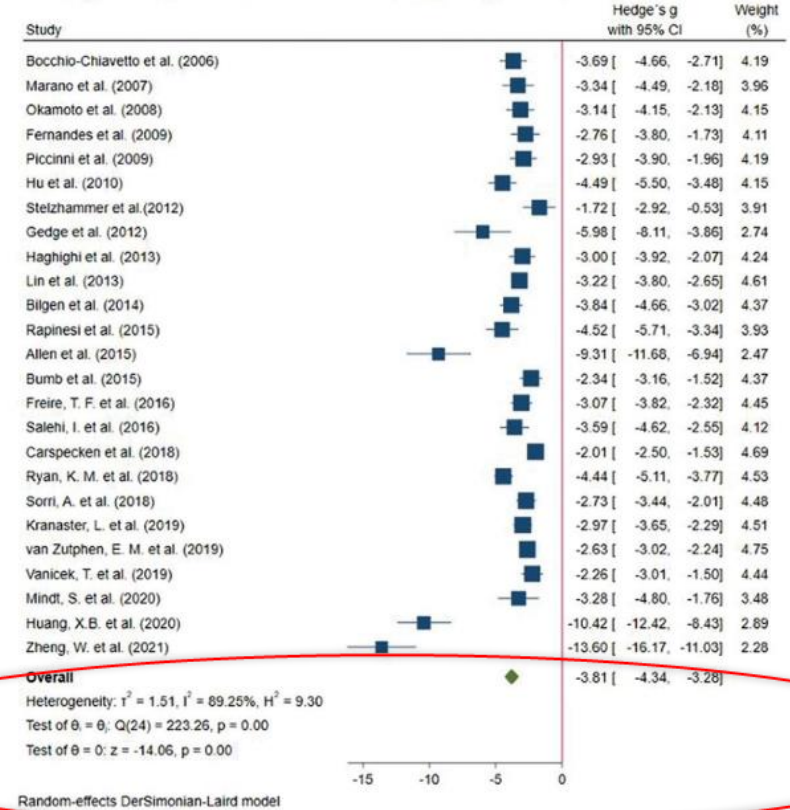


Figure 4. Forest plot for the depressive symptoms meta-analysis.

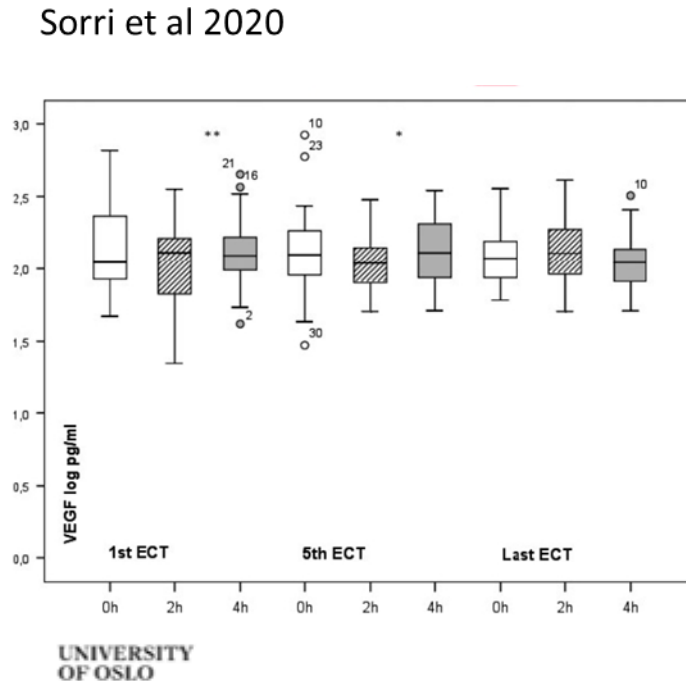
BDNF as a
biomarker for
predicting ECT
treatment
outcomes in
depression



Neurotrophic biomarkers

- Vascular endothelial growth factor (VEGF) (Minelli et al. 2011, Minelli et al. 2014, Clark-Raymond et al. 2017, Ryan & McLoughlin 2018, Kranaster et al. 2019, Maffioletti et al. 2020, Sorri et al. 2020, Maffioletti et al. 2021(review))

FIGURE 1 Plasma VEGF log levels of the first, the fifth and the last ECT sessions



Minelli et al 2014

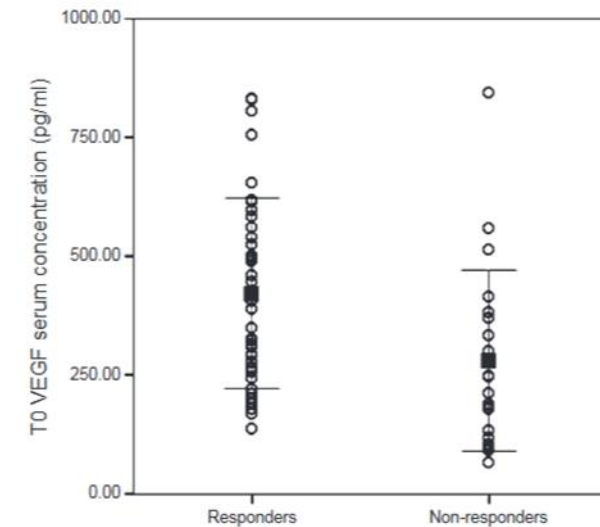
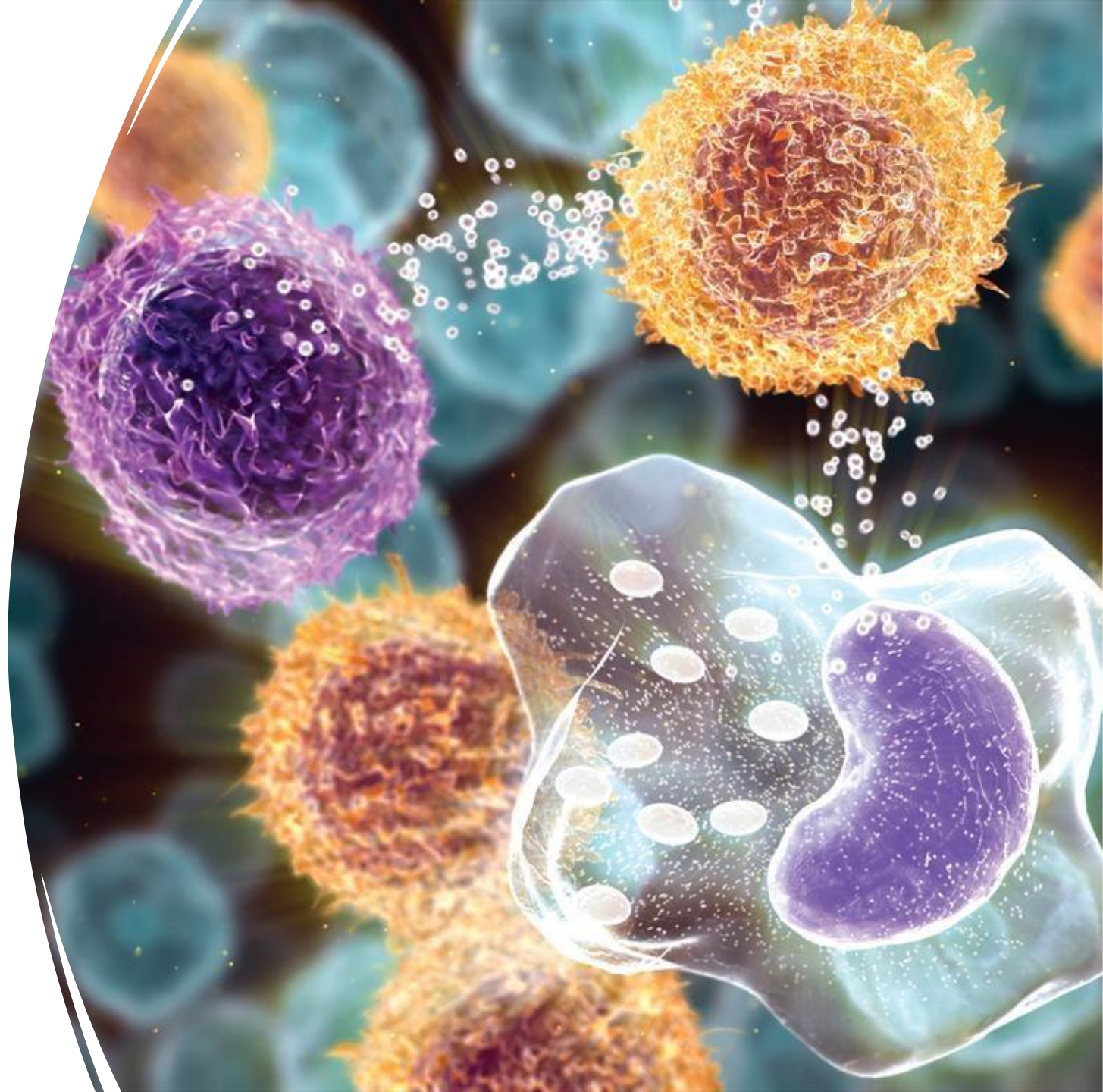


Fig. 1. Difference of the VEGF serum levels at baseline between patients that did or did not respond to ECT treatment by the time of follow-up. Error bars show mean \pm 1.0 SD.

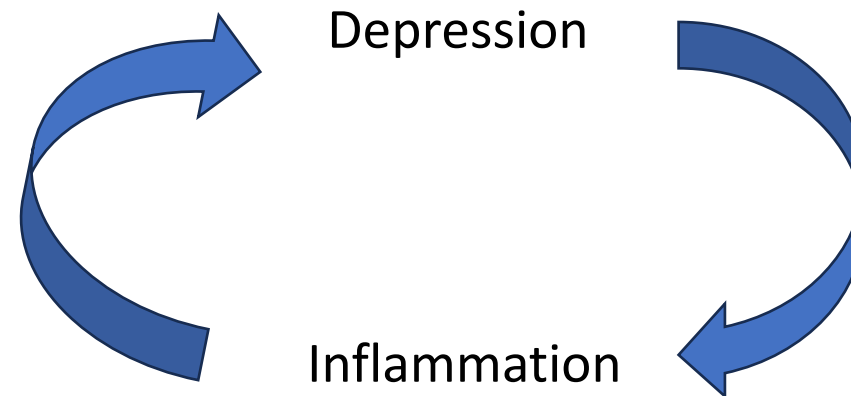
VEGF as a
biomarker for
predicting ECT
treatment
outcome in
depression



Inflammatory and Immune biomarkers



Inflammatory and immune biomarkers



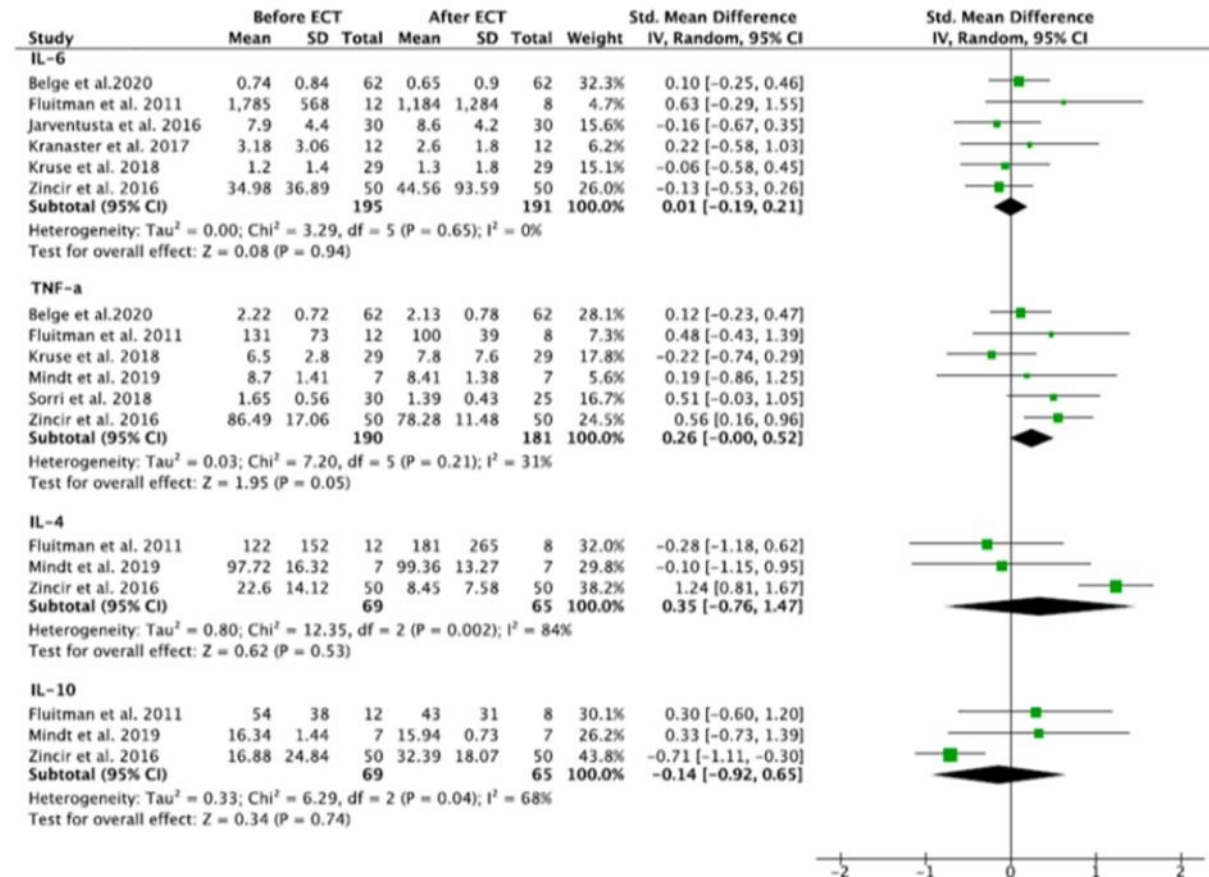
Kiecolt-Glaser et al Am J Psychiatry 2015

Inflammatory and immune biomarkers

- **Cytokines ; Gay et al 2021 :** Cytokines changes associated with electroconvulsive therapy in patients with treatment-resistant depression: a Meta-analysis

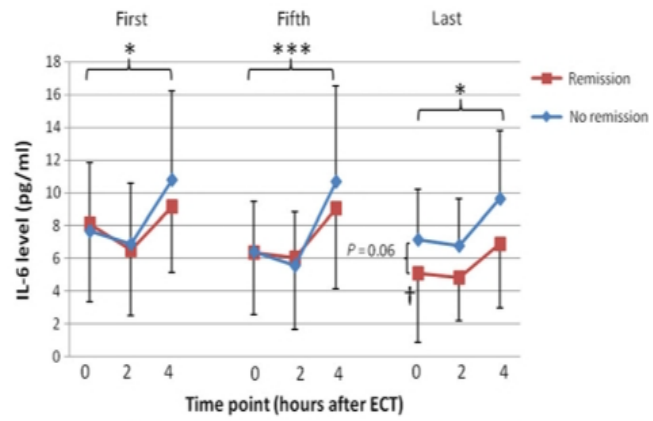
n= 198 patients

Mean age : 48,87 years [33-59 years]

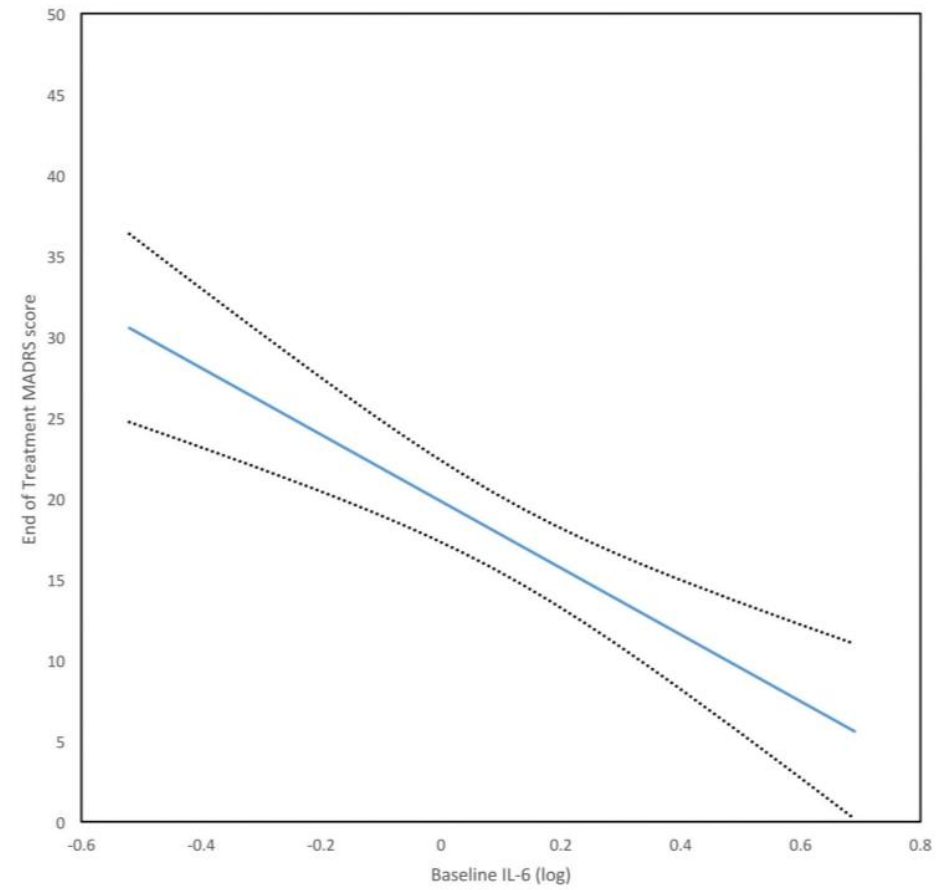


IL-6

Järventausta et al. 2017



Kruse et al. 2018

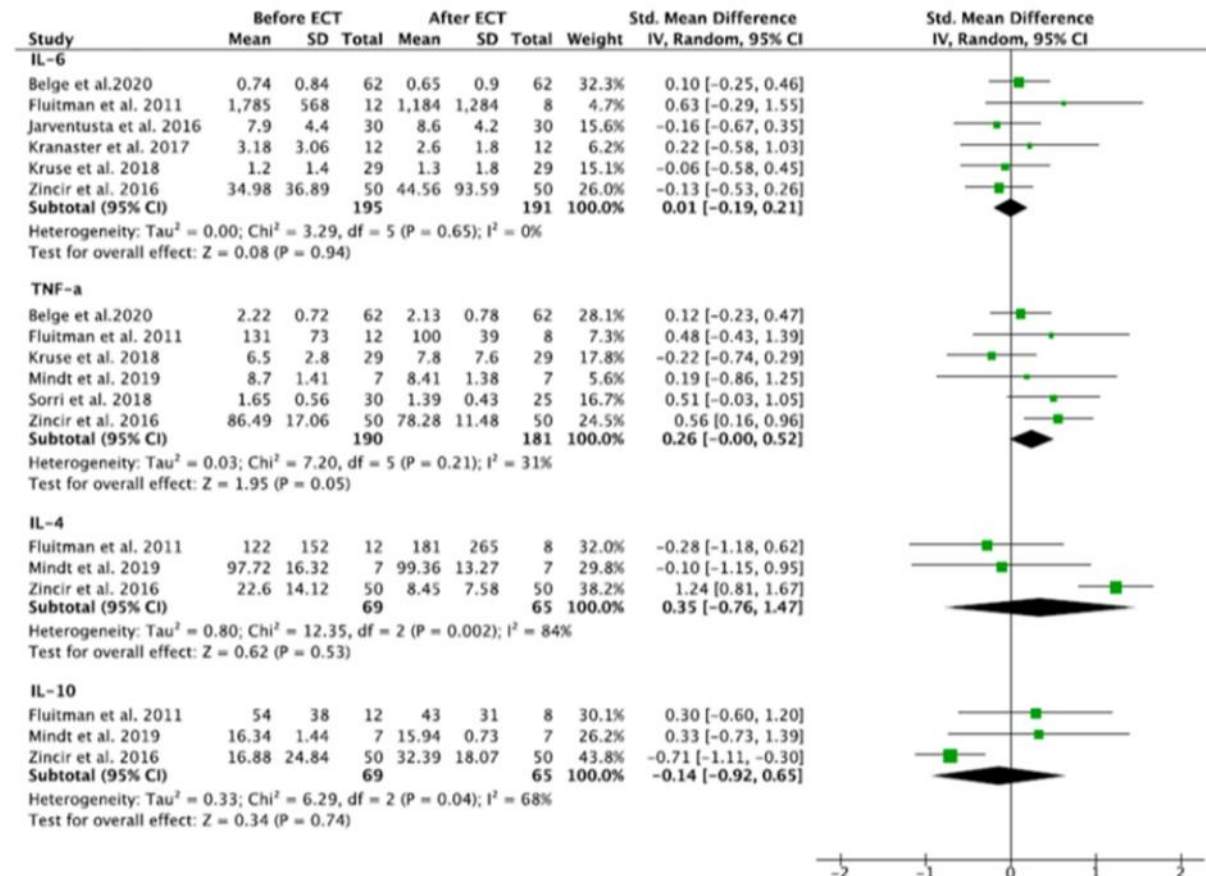


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TNF- α

Hestad et al. 2003

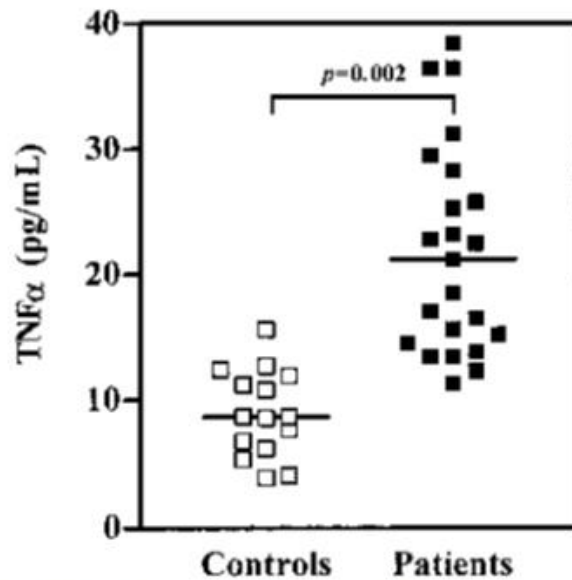
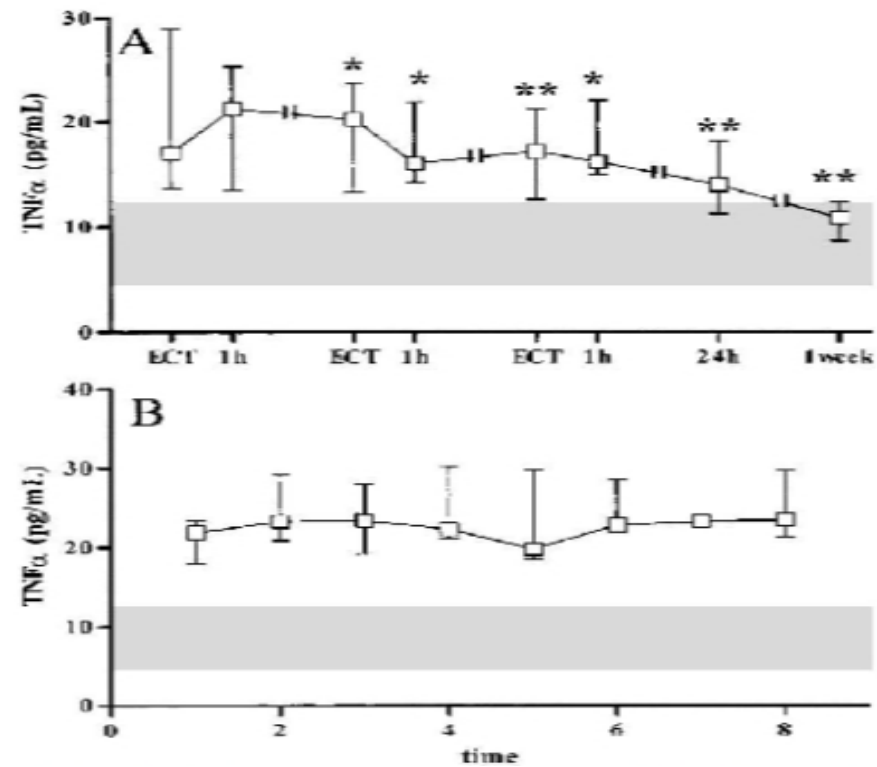


FIGURE 1. Plasma levels of TNF α in 23 patients with depression and 15 sex- and age-matched healthy controls. Horizontal lines represent median values.

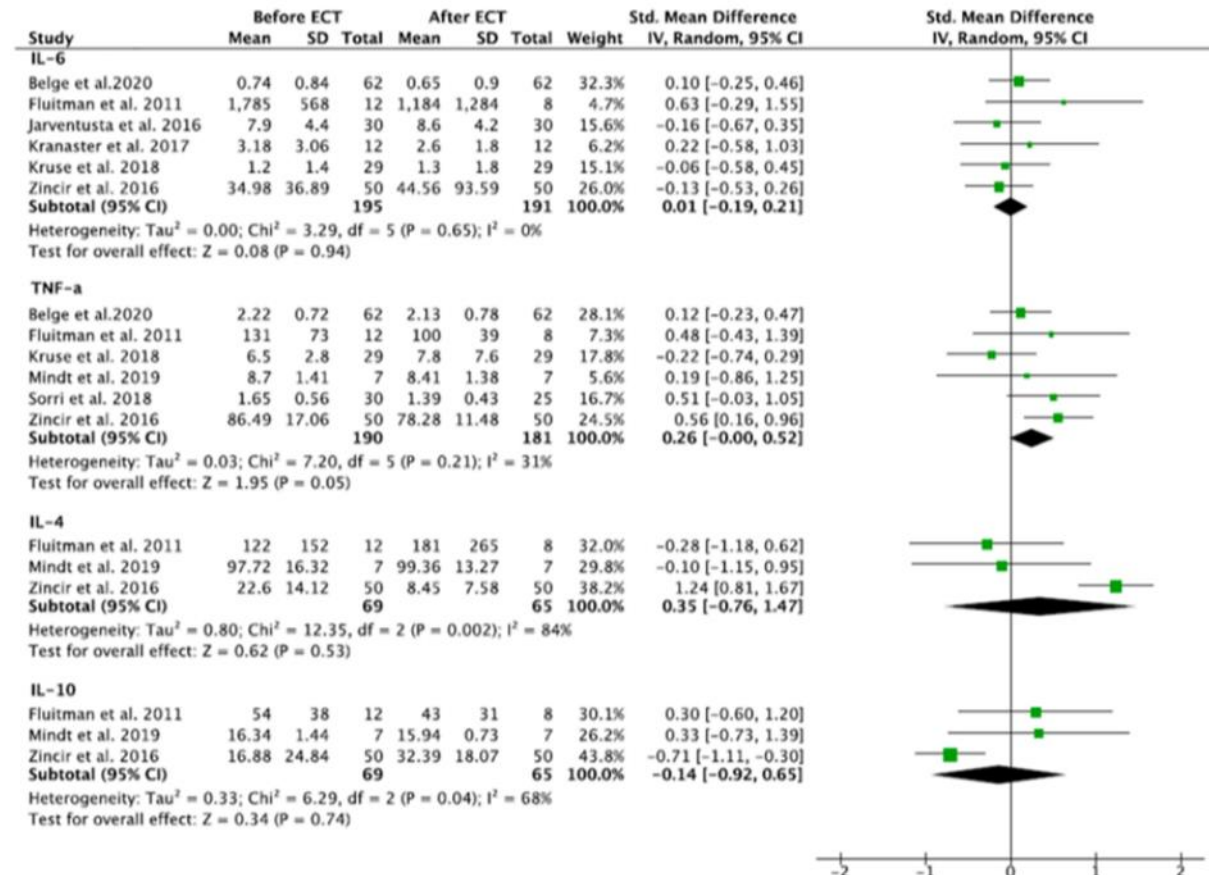


Inflammatory and immune biomarkers

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Inflammatory and immune biomarkers

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ACTA PSYCHIATRICA SCANDINAVICA

Meta-analysis

Interleukin-1 β -targeted treatment strategies in inflammatory depression: toward personalized care

Ellul P, Boyer L, Groc L, Leboyer M, Fond G. Interleukin-1 β -targeted treatment strategies in inflammatory depression: toward personalized care.

**P. Ellul¹, L. Boyer², L. Groc³,
M. Leboyer^{1,4}, G. Fond^{1,4}**

1MINDERMEDIC, 2ACTE, 3Translational Biobioinformatics

Inflammatory and Immune biomarkers

- C-reactive protein (CRP)
Kruse et al. 2018, Carlier et al. 2019, Ryan&McLoughlin 2022

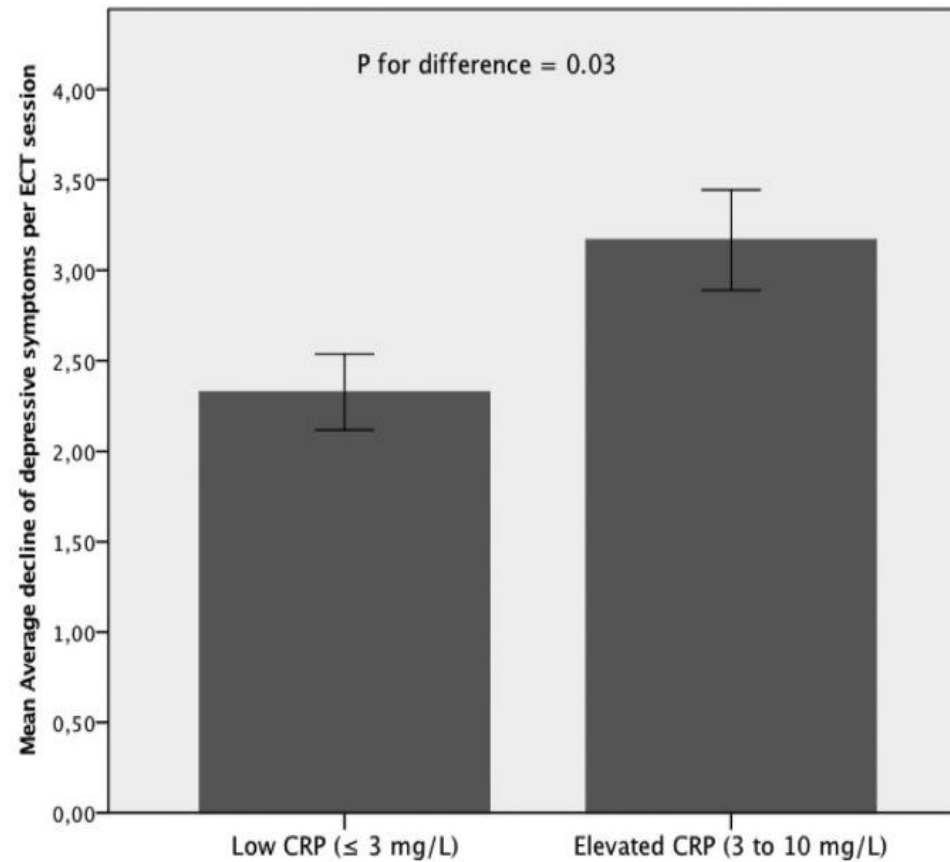


Fig. 1. Contribution of low and elevated CRP levels to the speed of decline in MADRS points, per ECT administration in depressed patients
Using linear regression, we examined the association between elevated CRP and the speed of decline of depressive symptoms per ECT administration, adjusting for age, gender, and MADRS score at baseline.

Can inflammatory and immune markers be used as biomarker(s) for predicting ECT treatment outcome in depression

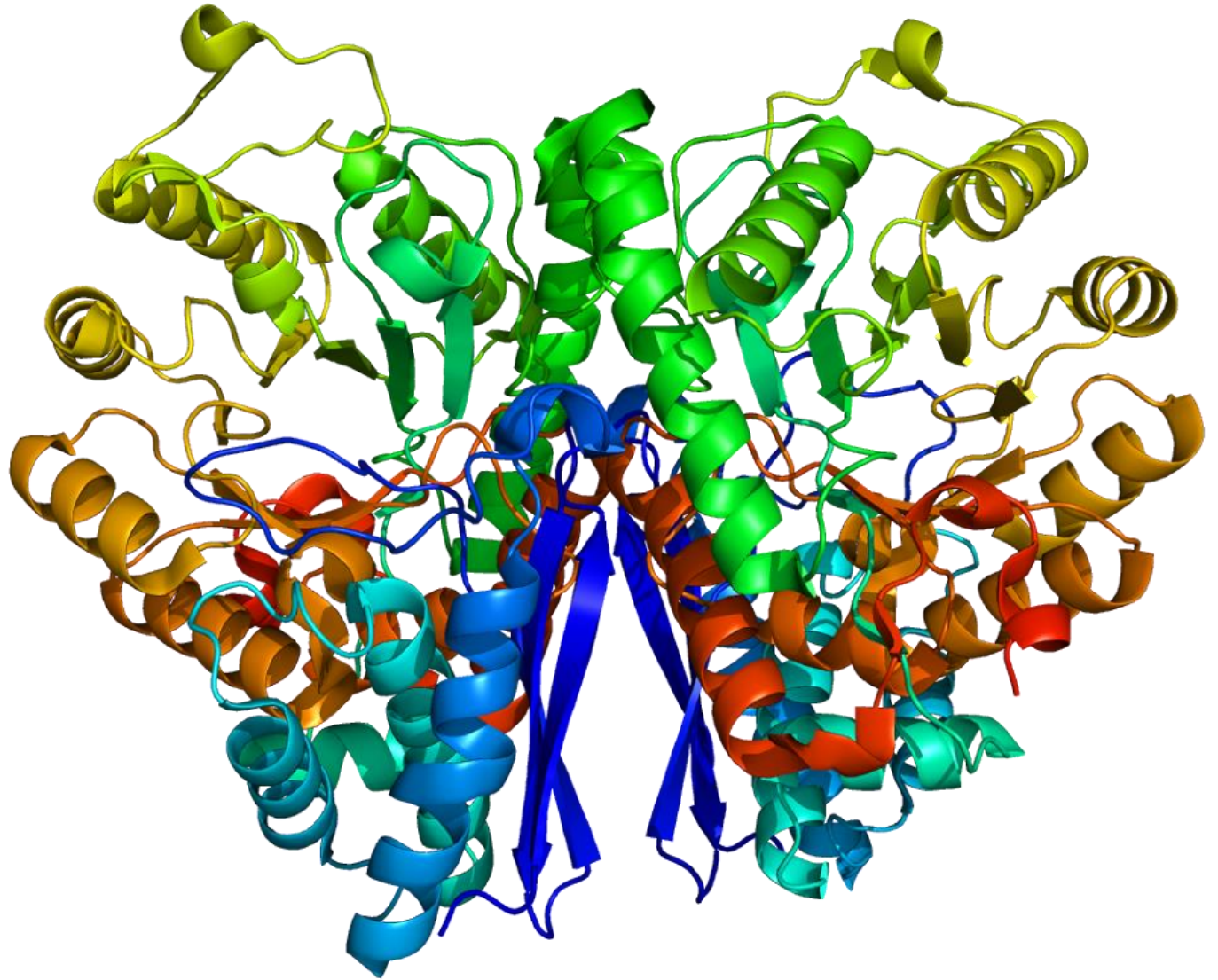


Meta-analysis NSE and S100 protein

- **Systematic review and meta-analysis of the levels of neuron-specific enolase and S100, markers of cellular damage in brain tissue, before versus after electroconvulsive therapy in patients experiencing psychiatric illness.**

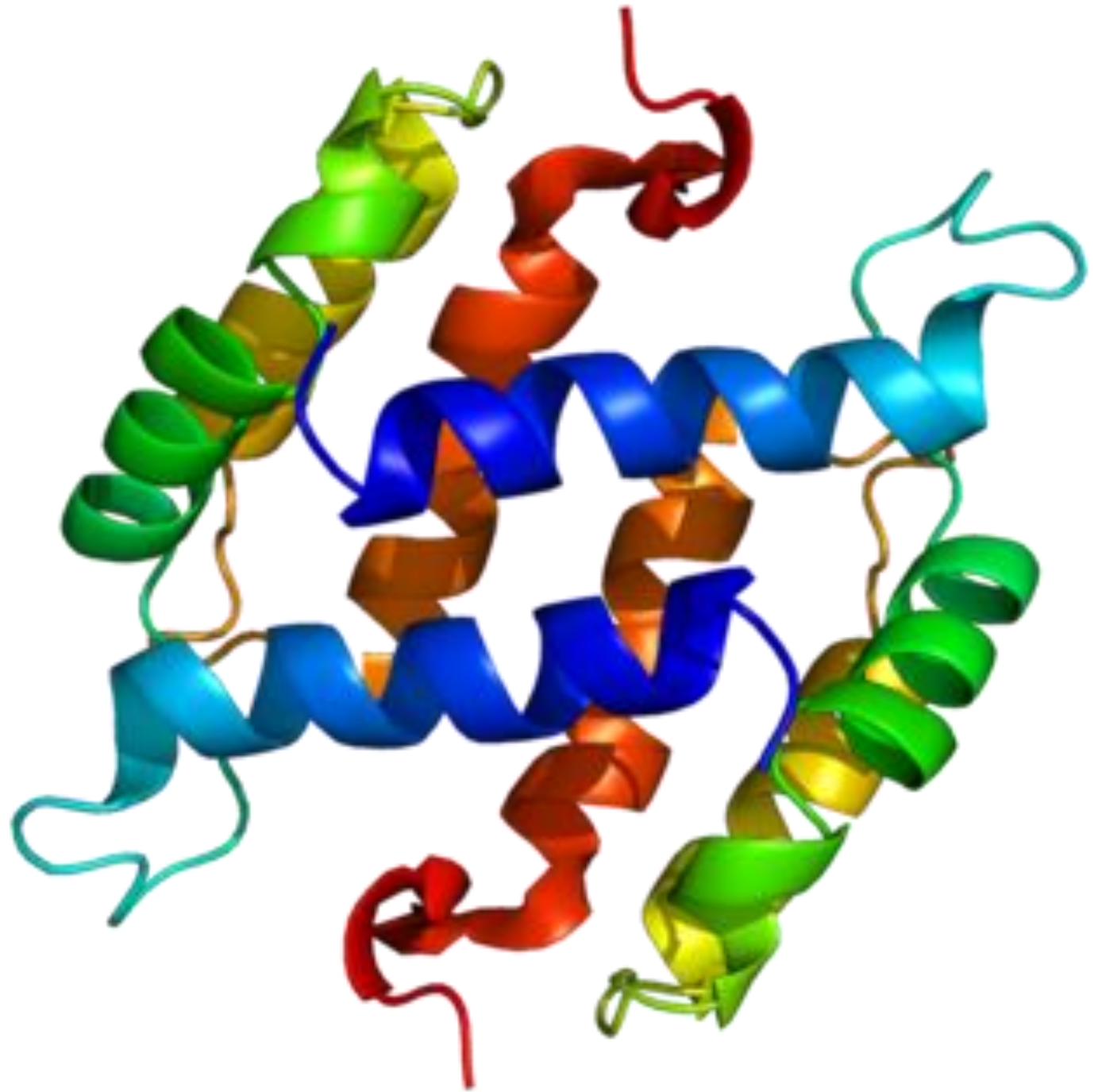
NSE

- Dimeric glycolytic enzyme
- Found in the cytosol of many cells in the CNS



S100 protein

- Protein family with 21 members
- S100B



The journey ahead





THANKS FOR THE ATTENTION



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