Completed analyses in GEMRIC

Site - boardmember	Proposer	Title	Aim&Hypotheses	Method	Status	Last progress reports	Monpoly rule
Leif Oltedal Bergen, Norway	**Leif Oltedal**	ECT-induced structural brain changes; a collaboration using data from multiple centers.	ECT induces structural brain changes occur both in cortical and subcortical regions. The changes are largest in, but not restricted to the hippocampus and medial temporal lobe cortical regions. The dentate gyrus (stem cells, neurogenesis) is expected to show the largest changes. The structural changes are hypothesized to depend on; a)Age; relative change negatively correlated to age b) Stimulus time and number of sessions; relative change positively correlated to "dose" c) Clinical response parameters; remission rate correlates with relative change	Structural FreeSurfer, Quarc, R	3 papers published: Oltedal et al 2017, Oltedal et al 2018, Ousdal et al 2019.		
Miklos Argyelan New York, USA	**Miklos Argyelan**	Electrical field modelling of ECT therapy to predict response and side effects	Structural differences leading to greater electrical fields influencing the SCC will predict enhanced treatment response and above threshold electrical fields reaching hippocampus will cause memory side effects.	Structural analyses (Freesurfer) + Electric Field modeling	1 paper published: Argyelan et al 2019	apr.2021 second manuscript in preparation	
Katherine Narr Los Angeles, USA	**Benjamin Wade**	Factor analysis of ECT-related change in clinical response scales and relationships with brain features	i) At pre-treatment, sub-items of the HDRS and (separately) the MADRS will cluster to form lower-dimensional latent variables reflecting key aspects of depression subtypes such as anxiety and somatoform disturbances. ii) Over ECT index, we will observe more pronounced reductions in specific aspects of depression as captured by the HDRS and MADRS scales.	Clinical + Structural	1 paper published: Wade et al 2019		
Indira Tendolkar Nijmegen, Netherlands	**Indira Tendolkar & Philip van Eijndhoven**	Prediction of response to ECT by support vector classification	Is it possible to reliably categorise ect patients in reponders vs non-responders on the basis of structural changes after ect treatment	Structural FreeSurfer, Quarc, R	1 papers published: Mulders et al. 2019		

Ronny Redlich Department of Psychiatry, Münster, Germany	**Nils Opel**	Influence of pre-treatment BMI on clinical and brain structural changes during ECT	Assess if pre-treatment BMI might influence clinical and brain structural effects of ECT in MDD.	Structural Statistical analyses using Freesurfer estimates	1 paper published: Opel et al. 2021		
Akihiro Takamiya Tokyo, Japan	**Akihiro Takamiya**	Brain structure and ECT response in psychotic depression.	i) To investigate brain structural differences between PD and NPD ii) To investigate the relationship between brain structural differences and ECT response iii) To investigate whether PD showed different longitudinal structural changes with ECT.	Structural. Freesurfer & SPM-VBM approach Supervised machine learning analysis	1 paper published: Takamiya et al. 2021		

Ongoing analyses in GEMRIC

Site - boardmember	Proposer	Title	Aim&Hypotheses	Method	Status	Last progress reports	Monopoly rule valid through
Leif Oltedal University of Bergen, Norway/Louise Emsell, Leuven	**Olga Therese Ousdal (and Maarten Laroy)**	Effects of ECT on amygdala and hippocampus subfield volumes. Amendment 27.04.2021: + cognitive side effects	Assess ECT-related volumetric increases in different hippocampal and amygdala subfields. We predict that the volumetric changes of hippocampal subfields essential for memory encoding and retrieval (i.e. dentate gyrus, cornu ammonis 1-4 and subiculum) will be specifically related to memory impairments pre-post ECT. We predict that subfield volumetric changes associated with side effects will also be associated with electric field strength.	Structural Freesurfer	Analyses ongoing	nov.20 apr.21 (incl. amendment of proposal) nov.21 apr. 2022	nov.21

Louise Emsell KU Leuven, Belgium/ Leif Oltedal, Norway	Maarten Laroy (and Olga Therese Ousdal)	Characterization of gray matter volume normalization following termination of electroconvulsive therapy in depressed patients. (Project replaces earlier proposal lead by Ousdal)	This study aims to explore the characteristics of the volume normalization following termination of ECT by leveraging the statistical power afforded by the larger sample of the GEMRIC consortium dataset. Variables that are known to be related to volume increase following ECT such as age will be investigated, as well as the classic cognitive and clinical correlates.	Structural, FreeSurfer	Approved	Previous proposal (Ousdal) nov. 20 apr.21 nov.21 apr. 2022	nov.21
Annemieke Dols Amsterdan, Netherlands	**Anemieke Dols & Guido van Wingen**	Does a neuroimaging marker predict the outcome of electroconvulsive therapy in severe depression? A replication study applying multivariate pattern analysis.	Electroconvulsive therapy is the most effective intervention for severe depression. Initial studies have identified neuroimaging biomarkers that may enable personalized treatment. However, sample sizes were small and replication across larger multicenter datasets is required. Therefore, we aimed to develop robust maging markers based on multicenter data from the Global ECT-MRI Research Collaboration (GEMRIC).	We used multimodal data (i.e., clinical, sMRI and resting-state fMRI) and evaluated which data modalities or combinations thereof could provide the best predictions for treatment response (≥50% symptom reduction) or remission (minimal symptoms) using a support vector machine classifier.	rsFMRI collected from sites, prepocessing and analyses finished. Currently undergoing submission process.	nov.20 apr.21 nov.21 apr. 2022	nov.21
Annemieke Dols Amsterdan, Netherlands	**Mardien Oudega**	Gender differences in symptoms of severe depression and response to ECT	Is there a difference in presentation of severe depression and response to ECT in females and males?	Clinical (no imaging) Classical statistics	Submitted	nov.20 apr.21 apr. 2022	nov.21

Annemieke Dols Amsterdam UMC & Bergen, Norway	**Machteld A.J.T. Blanken, Alexander Lundervold**	BrainAGE as compared to chronological age as predictor of response to electroconvulsive therapy in patients with major depression.	Does BrainAGE predict response, remission and relapse? Does BrainAgeGap predict response, remission and relapse? Does BrainAGEGap decrease after successful ECT? Is there a difference in response prediction between chronological age and biological age? Our main objective is to assess whether there is a decrease of mean diffusivity in the hippocampus and amygdala in MDD populations during ECT. Our secondary objectives are i) to compare MD between MDD population and control at baseline; ii) to evaluate whether this decrease is associated with an increase of volume (hippocampi and amygdala) and iii) to evaluate whether this decrease is associated with a clinical improvement. Is there a difference in prediction outcome and utility between FreeSurfer-based brain age calculation (method adopted from ENIGMA or the Kaufman et.al. 2019 method) versus the deep learning-based approach (Bergen: L.Oltedal, A. Lundervold – state-of-the-art deep learning approach based on raw DICOMs)	Structural T1 data, Freesurfer measurements and measurements from a deep learning algorithm	Ongoing	nov.20 apr.21	nov.21
Jeroen van Waarde Rijnstate, Amsterdam, Netherlands	**Freek ten Doesschate**	Dynamic causal modelling in depression and its treatment with ECT	Study the effective intra- and internetwork connectivity of the SN, DMN, DAN and FPN in depression and how it is affected by ECT.	Functional (resting-state) Independent Component Analysis (ICA) and Dynamic Causal Modeling (DCM)	Under review	nov.20 apr.21 apr. 2022	nov.21
Jeroen van Waarde Rijnstate, Amsterdam, Netherlands	**Freek ten Doesschate**	The effect of electroconvulsive therapy on resting-state networks using longitudinal independent component analysis (L-ICA)	Leaver et al. (2016) found effects of ECT in several resting-state networks. We aim to replicate and extend these findings using a larger sample and more sensitive methods. Regarding the effects of electrode placement, we expect a bilateral treatment to have a more widespread effect on resting-state connectivity, whereas unilateral treatment is also expected to show more lateralized effects.	Resting-state fMRI. Longitudinal ICA.	Ongoing	nov. 2021 apr. 2022	nov.21

Miklos Argyelan New York, USA	**Miklos Argyelan**	The relationship between the changes in resting state dynamics and the local electrical field induced by ECT therapy	Assess the correlation of electrical field and charge with changes in slow frequency fluctuations and functional connectivity of the BOLD signal.	Functional (resting-state) Electrical Field Modeling and multivariate methods for multimodal fusion of brain imaging data	Approved	apr.21	nov.21
Miklos Argyelan New York, USA	**Miklos Argyelan**	**Detection of state-dependent connectivity changes in ECT**	Here, we present a longitudinal rsfMRI method, where we proactively removed the trait dependent variance in a data-driven multivariate analysis to determine the effect of a full treatment course of ECT on the state-dependent changes in functional connectivity. We hypothesized that removing the trait-dependent variance of unique connectivity fingerprints could help uncover the effect of ECT and can cluster sessions in a data driven way.	Resting state	Approved	apr.21	nov.21
Amit Anand Cleveland Clinic, OH, USA	**Amit Anand**	ECT Effects on the Brain's Structural Functional Connectome	1. ECT effects will be associated with changes in the organization of the functional and structural networks as measured by graph theory measures	Functional (Resting-state) + Structural (DWI)	Approved	nov.2020 apr.2022 update by mail	nov.21
Katherine Narr University of California, Los Angeles, USA	**Benjamin Wade**	Multimodal feature fusion with deep learning to predict clinical outcome	i)To predict response along latent symptom dimensions of HDRS and/or MADRS scales using multimodal feature fusion of imaging, clinical, and demographic data with deep learning. ii)To use multimodal feature fusion developed in (i) to predict cognitive impairment captured by the MMSE.	Structural (T1+T2) and RSFC images, e-field maps, and tensor-based morphometry. Outcomes are latent symptom dimensions of the HDRS and/or MADRS derived from exploratory factor analysis and the MMSE. Clinical & demographic variables include age, sex, site, pre-treatment symptom levels, BMI, electrode placement, and medication status.	Approved	apr.2021 apr. 2022	nov.21

Katherine Narr Los Angeles, USA	**Evangelia Tsolaki**	The role of structural connectivity of Subcallosal cingulate Area as a potential biomarker for ECT response	To investigate the relationship between baseline structural connectivity of SCC to cortico-limbic-striatal circuitry with depression scores and symptom dimensions, ii.) To explore the impact of ECT to SCC structural connectivity in a large group of MDD patients.	Structural (DTI) FSL, Matlab, SPSS	Approved	apr.2021 apr. 2022	nov.21
Carles Soriano-Mas, Barcelona, Spain	**Carles Soriano-Mas**	Modulation of voxel-wise multiband amplitude of low frequency fluctuations after ECT	Analyze fALFF changes after a complete ECT course. for the different oscillation bands, from slow-5 to slow-2.	Functional (resting-state) Analysis of the fractional Amplitude of Low Frequency Fluctuations-fALFF	Approved		nov.21
Carles Soriano-Mas, Barcelona, Spain	**Carles Soriano-Mas**	Structural covariance of the hippocampus and hippocampal volume changes after ECT	Assess the pre-ECT pattern of structural covariance of the hippocampus and to investigate the correlations between volume changes in the hippocampus with those observed in other brain areas after ECT.	Structural SPM-VBM approach	Writing manuscript	nov.20 apr.21 nov. 21	nov.21
Bogdan Draganski Lausanne, Switzerland	**Bogdan Draganski**	Interaction between ECT-induced grey matter volume changes and antidepressant medication	Assess the spatial and temporal pattern of ECT induced changes on brain volumes and structural connectivity. Assess differences between MDD and Bipolar Disorder. Assess interactions with pharmacological treatment and disease duration.	Structural SPM-VBM approach for volumetry and deterministic diffusion tractography from DWI data.	Approved		nov.21
Akihiro Takamiya Tokyo, Japan	**Akihiro Takamiya**	The relationships between brain asymmetry, electrode placement, and ECT response	(1) Baseline structural (and functional) asymmetry could be a useful marker for predicting patients who needed bilateral stimulation (i.e., patients who switched from RUL to BL) or RUL nonresponders. We hypothesized that patients who had prominent left-sided abnormalities needed bilateral stimulation. (2) Changes in asymmetry index following ECT would relate to changes in mood scores	Structural T1 (Freesurfer outputs to calculate asymmetry index). In the future, also resting-state functional data.	Approved	nov.20	nov.21

Indira Tendolkar Nijmegen, Netherlands	**Peter Mulders**	Predicting Treatment Response to ECT using Spatial Patterns for Discriminative Estimation	i.) To assess whether Discriminative patterns based on resting-state data separating responders from non-response are similar to those based on structural changes, ii.) To assess whether discriminative patterns at baseline are predictive of treatment response to ECT.	Functional (resting-state) Spatial Patterns for Discriminative Estimation (SPADE)	Approved under the assumption that it will be attuned with older project from Amsterdam	nov.2020 apr.2021 apr. 2022	nov.21
Maximilian Kiebs, Bonn, Germany	**Maximilian Kiebs**	The role of brain plasticity and functional connectivity in altered memory performance after a course of electroconvulsive therapy	1. Female sex, increased age and number of ECT sessions predict the undesired effects on cognition, esp. verbal and autobiographical memory 2. In patients, other cognitive domains show either no change or improvement compared to pre-ECT performance 3. In patients, several structural and functional modulations induced by ECT19–21 positively correlate with the undesired effects in the domains mentioned above 4. At baseline, multimodal functional neuroimaging may be used to predict the occurrence of undesired effects 5. Exploratory analysis of structural (e.g. low pre-existing gray matter volume) and functional correlates of undesired effects 6. Moderating effects of treatment efficacy and number of ECT sessions are explored	Anatomical 3D-T1 VBM approach), resting state fMRI	Approved	nov.20 apr.21	nov.21
Antoine Yrondi Toulouse, France	**Antoine Yrondi**	Decrease in hippocampus and amygdala mean diffusivity in major depressive disorder during electroconvulsive therapy	Our main objective is to assess whether there is a decrease of mean diffusivity in the hippocampus and amygdala in MDD populations during ECT. Our secondary objectives are i) to compare MD between MDD population and control at baseline; ii) to evaluate whether this decrease is associated with an increase of volume (hippocampi and amygdala) and iii) to evaluate whether this decrease is associated with a clinical improvement.	Structural (Diffusion data)	Work in progress	nov.2020 apr. 2022 update by mail	nov.21

Joan C. Camprodon Massachusetts USA	**Joan C. Camprodon**	Predictors and mechanisms of ECT antisuicidal properties	FC of the ACC to nodes of the dorsal attention and executive control network will predict and explain the reduction in suicide risk as well as associated changes in positive and negative affect. 2. Diffusion properties in WM tracts connecting the ACC with the dorsal attention and executive control networks will predict and explain the reduction in suicide risk, as well as associated changes in positive and negative affect. 3. Volumetric changes in affective and default network nodes willl predict and explain the reduction in suicide risk as well as associated changes in positive and negative affect.	T1, DWI and resting-state data	nov.21		nov.21
Joan C. Camprodon Massachusetts USA	**Joan C. Camprodon**	Investigating white matter fibre density and morphology changes following ECT using fixelbased analysis.	We hypothesize that ECT will not affect whole-brain white matter but that its effects are localized in specific pathways following the laterality of the stimulation. We expect an increase in right uncinate fasciculus fibre density for RUL patients following ECT. We hypothesize that this increase will be correlated with changes in HDRS-17 and its subscores of reward and suicide.	DWI data	Approved		nov.21
Guido van Wingen AMC, Amsterdam Netherlands	**L.A. van de Mortel**	Relation between ECT-induced structural and functional brain changes	Brain regions displaying significant structural changes after ECT contribute to changes in its local function and functional connectivity with other brain regions.	**Structural**: FreeSurfer, VBM; **Functional**: ALFF, ReHo, Graph approaches	Finalized analysis, drafting manuscript	apr2021 nov 21 apr. 2022	nov.21
Joan Prudic Columbia University, New York, USA	**Joan Prudic**	Resting state functional connectivity predictors of treatment response to electroconvulsive therapy in depression	To test whether a model of brain functional connectivity patterns determined by fMRI, and trained on a previous published pilot sample of depressed patients undergoing ECT can predict response to ECT within the larger GEMRIC sample. Both the degree to which RSFC (fMRI) can predict ECT response and the degree to which changes in RSFC correlates with symptom change will be explored.	Resting-state fMRI	Approved	apr.2021 nov. 21	nov.21

Louise Emsell, KU Leuven, Belgium	Maarten Laroy	Functional connectivity changes in the hippocampus and their association with cognitive functioning following electroconvulsive therapy	1. The increase in hippocampal gray matter volume following ECT is negatively correlated with changes in cognitive performance after a course of ECT. 2. Changes in hippocampal based functional connectivity networks following ECT are negatively correlated with changes in in cognitive performance after a course of ECT. 3. Functional changes following ECT are more pronounced in patients treated with bilateral (bilateral or bifrontal) electrode position compared to patients who received right unilateral stimulation, which in turn results in stronger negative effects on cognitive performance following ECT.	Structural, Functional, FreeSurfer, SPM	Approved	nov.21	apr.21
Maximilian Kiebs, Bonn, Germany	Maximilian Kiebs	Neurocognitive data of The Global ECT-MRI Research Collaboration (GEMRIC): Rationale and Multi-site investigation	1. In patients, cognitive performance shows either no change, improvement or decrease compared to pre-ECT performance 2. Matched controls show no change in cognitive performance 3.Exploratory analysis of moderating effects ECT-parameters (stimulation protocol, sessions per week and number of sessions), age and sex have a significant effect on the cognitive performance after ECT compared to baseline 4.Descriptive statistics of each cognitive task (clinical, sociodemographic, n MRI, ECT-parameters, n blood draw)	Descriptive statistics of each cognitive task (clinical, sociodemographic, n MRI, ECT-parameters, n blood draw). Pre-Post AN(C)OVA of each instrument. Moderation analysis of HAM & MADRS Score. Regression analysis of ECT-parameters (stimulation protocol, sessions per week and number of sessions), age.	Approved	apr.22	nov.22

Joan Camprodon, Boston, MA, USA	Lipeng Ning, Joan A. Camprodon	Joint structural-functional connectivity and electric field-based analysis for ECT treatment response	**Aim 1:** Longitudinal effects of ECT on structurally constrained effective connectivity, and its relationship to clinical response **Hyp 1**:ECT affects the dMRI-based microstructural and rsfMRI-based EC measures of specific pathways following the laterality of the stimulation **Aim 2**: The relationship between the properties of the electric field induced by ECT and the longitudinal effects of ECT on structurally constrained effective connectivity **Hyp 2**: Changes of microstructural and EC measures of a subset of brain connections are correlated with the difference of electric potential induced by ECT between the underlying brain regions. **Aim 3**: The predictive value of structurally constrained effective connectivity and E-field properties combined on ECT clinical response **Hyp 3**:dMRI and fMRI measures at the baseline and the electric field measures of specific pathways will be correlated with changes in clinical depression severity.	Autoregressive model with structual contraints, minimum-entropy-based causality measure	Proposal 04.2022		apr.23