ECT-induced connectivity mechanisms in treatment resistant depression

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Primary objectives:1.) Investigate changes in functional connectivity between different resting state networks as a function of ECT treatment and therapeutic response.2.) Investigate changes in VTA-related BOLD-signals coding for Temporal Difference...

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Mood disorders and disturbances NEC
Study type	Observational non invasive

Summary

ID

NL-OMON52975

Source
ToetsingOnline

Brief title
ECT-induced connectivity

Condition

- Mood disorders and disturbances NEC

Synonym
Depression, Major Depressive Disorder

Research involving
Human

Sponsors and support

Primary sponsor: Radboud Universitair Medisch Centrum
Source(s) of monetary or material Support: Ministerie van OC&W,ZonMw

Intervention

Keyword: Connectivity, Depression, ECT, GABA

Outcome measures

Primary outcome

- changes in functional connectivity in resting state networks as a function of treatment (response)

- changes in VTA-related BOLD-signals and habenula-VTA connectivity coding for Temporal Difference Errors in reward/punishment-related learning as a function of treatment (response)

Secondary outcome

- changes in structural brain characteristics (cortical thickness, subcortical volumes) as a function of treatment (response)

Study description

Background summary

Depression is one of the most prevalent psychiatric disorders with a highly recurrent course leading to a large socioeconomic burden not only for the patients but also for those who care for them. Despite 50 years of intensive research into treatment options, 1/3 of the patients will not respond to psychotherapy and pharmacotherapy. For these treatment resistant depression (TRD) patients electroconvulsive therapy (ECT) is the last resort. However, the neurobiological effects of ECT at the human system level remain unclear, possibly because animal guided research has mainly focused on specific neurotrophic effects such as for example adult neurogenesis. Here, we propose an exploratory two staged model investigating the effects of ECT on a cortico-limbic network related to the pathophysiology of depression. In a first step we will identify depression related changes in the default mode network, the emotional salience network and the cognitive control network. We will longitudinally assess the changes in the connectivity as a function of ECT treatment and therapeutic response. In the next stage we want to augment these dynamic changes in brain function with changes in structural brain measures

that were identified in previous studies (cortical thickness and hippocampus and amygdala volumes). By these means we aim generating a coherent network-based mechanistic explanations for the treatment effects, which can be used for future approaches that are less invasive and have less side effects.

Dopaminergic dysfunction - Amendment 28-4-2021
Another potential mechanisms of action of ECT will be additionally investigated. It has been suggested that dopaminergic dysfunction plays an important role in the pathophysiology of TRD, the main indication of ECT. We will investigate changes of dopamine dysfunction via dopamine neuron activity in the habenula-Ventral Tegmental Area (VTA) network during a reward/punishment-related learning task before and after ECT treatment. Moreover, we will also investigate the association between change in dopamine dysfunction and treatment response.

Study objective

Primary objectives:
1.) Investigate changes in functional connectivity between different resting state networks as a function of ECT treatment and therapeutic response.
2.) Investigate changes in VTA-related BOLD-signals coding for Temporal Difference Errors in reward/punishment-related learning, as a function of ECT treatment and therapeutic response

Secondary objectives:
1.) Correlate changes in functional connectivity and GABA with changes in structural brain measures (cortical thickness, amygdala and hippocampal volume).
2.) Investigate potential neural markers that will discriminate between patients who relapse and patients who don*t after successful ECT treatment during a follow-up period of one year.

Study design

A longitudinal study with 50 patients suffering from TRD and eligible for ECT treatment will be concluded. Patients will receive care as usual and undergo fMRI at four time points during and after treatment (before start or ECT, after 6 sessions, after treatment is discontinued and at 3 months after treatment). A control group of 50 healthy controls matched for sex and age will undergo fMRI during a similar timecourse as the ECT-treated patients to distinguish changes specific to MDD.

Study burden and risks

All psychiatric measurements are administered routinely at our out- and inpatient depression unit. The (f)MRI measurements will require a maximum of

75-90 minutes of the patients time at four time points during and after treatment. Risks associated with the measurements used in this study are negligible.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

• Males and females between 18-70 years of age
• First or recurrent episode of unipolar major depressive disorder, with and without psychotic features (as defined by DSM-IV-TR)
• Treatment resistance for at least two antidepressants

Exclusion criteria

• ECT within one year prior to the current course
• Use of benzodiazepines within 24 hours before ECT
• Presence of a current or past relevant somatic disorder
• Presence of comorbid bipolar disorder, schizophrenia or substance abuse disorder
• MRI-related exclusion criteria (i.e. claustrophobia, pregnancy, internal metal objects, etc.)
• ECT-related exclusion criteria (recent cerebrovascular disease or brain surgery, recent cardiac arrest, unstable angina pectoris (NYHA IV), pheochromocytoma)

Study design

Design

Study type:	Observational non invasive
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)

Primary purpose: Basic science

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	28-01-2015
Enrollment:	100
Type:	Actual

Ethics review

Approved WMO

Date:	06-08-2014
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

Approved WMO Date:	02-03-2016
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	17-06-2021
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	17-01-2023
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
CCMO	NL48067.091.14