Exploring the Neural Basis of Cognitive Processing in the Human Brain: Single Neuron Recordings in Depth-electrode Candidates for Epilepsy Surgery

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Ethical review	Approved WMO
Status	Recruiting
Health condition type	Seizures (incl subtypes)
Study type	Observational invasive

Summary

ID

NL-OMON54764

Source
ToetsingOnline

Brief title
Single Neuron Recordings in Depth-electrode Candidates

Condition

- Seizures (incl subtypes)

Synonym
epilepsy, seizures

Research involving
Human

Sponsors and support

Primary sponsor: Vrije Universiteit Medisch Centrum
Source(s) of monetary or material Support: NWO Onderzoekstalent,ERC grant

Intervention

Keyword: cognitive functioning, epilepsy surgery, memory, single neuron

Outcome measures

Primary outcome

The main study parameters are the macro- and microelectrode recordings of different brain areas during the performance of simple behavioural tasks and during stimulation of macro-electrode contacts. An important goal is to relate performance on the tasks to the neural data.

Secondary outcome

The secondary study parameters are the single- and multi-unit recordings and LFP during stimulation of the macro-contacts (if this is performed as part of the clinical assessment) and a functional MRI scan if an electrode is located in a visual area. We will also use data from two self/report questionnaires which will be administered both pre- and post-implantation. We will use the Beck Anxiety Inventory to assess anxiety and the Beck Depressivity Index to assess depression after the operation. These scores can be used to as co-regressors in our neural analyses. We will administer the questionnaire 3-4 days post-operatively to assess the patient*s state during the experimental phase at which we record the majority of our data.

Study description

Background summary

The present project proposes to investigate the cellular basis of cognitive functions (such as memory and visual information processing) using single-neuron activity recorded via micro-wires implanted in different brain areas of patients undergoing treatment for intractable epilepsy. Significant research at the cellular level in animals, and with fMRI, PET and clinical cases in humans has revealed aspects of cognitive processing. However, studies of the mechanisms underlying various cognitive processes at the single neuron level in awake behaving humans are scarce. The recording of activity from single neurons is the gold standard for neuroscientific research, giving insight into the neural mechanisms underlying cognitive processes ranging from visual perception to memory formation. However, until recently, single-neuron recordings were only possible in animal models. Recent work (e.g. protocol 2009/194) has shown that it is possible to record from single human neurons during treatment for intractable epilepsy. The activity of single neurons and local field potentials will provide unique, direct evidence (contrary to imaging techniques such as PET and fMRI) on the functioning of different brain areas and their interplay during cognitive processing in awake behaving humans. Moreover, it will be possible to study elements of cognition which are impossible to study in animals, such as visual imagery. Therefore, these experiments will not only verify previous findings from the animal literature in the human brain, but will also provide unique data for which there is no alternative method available.

Study objective

The main objective of this study is to investigate the neural basis of cognitive processing in awake behaving patients. The main focus will be on memory processes in the medial temporal lobe (MTL), emotional processing in the insular cortex and visual processing.
The secondary objective of this study is to measure single neuron activity during stimulation of macro-electrode contacts to measure in vivo connectivity between different cortical areas.

Study design

This is a prospective observational study. We will record from both macro- and microelectrodes implanted in the brains of fifty epileptic patients while they perform simple cognitive tasks. The neuronal data will be analyzed according to standard procedures employed in both human and non-human primate electrophysiology.

Study burden and risks

This project uses patients who have been selected to be implanted with depth electrodes as part of their treatment for intractable epilepsy. In a subset of these patients we will select between 4-8 depth electrodes to receive hybrid macro/micro-electrodes. This combination of a depth electrode (macro-electrode) and the micro-wire tetrodes is known as MME depth electrode. This type of electrode has also been used successfully in previous studies in other centers (Despouy et al., 2019; Despouy et al., 2020). The use of a hybrid electrode instead of a standard depth electrode does not impact on the clinical data obtained from the macro-electrode in any way and the volume occupied by the micro-wires is negligible in comparison to the volume occupied by the macro-electrode. As such the only risks that should considered here are any additional risks posed by implanting hybrid electrodes rather than the standard depth electrodes.
Recently, a study was published in the Journal of Neuroscience Methods that specifically looked at the safety of hybrid macro-microelectrodes (Despouy et al., 2020). They reported the characteristics, safety and compatibility of clinical intracranial recordings in 28 patients, implanted with 240 standard clinical macroelectrodes and 102 hybrid electrodes. They concluded that the hybrid electrode is safe, easy to use, and works satisfactorily for conducting multi-scale seizure and physiology analyses. Therefore, to the best of our knowledge, no health risks are involved due to the implementation of microelectrodes. We expect no additional burden and/or risks associated with the use of micro-macro-electrodes (hybrid electrodes) compared to the use of standard macro-electrodes. Moreover, we have no reason to expect any additional burden and/ or risks from recording single neuron activity during macro-contact stimulation.

The burden for patients in this study consists of a short screening session and on average three sessions of simple cognitive tests per day during their stay at the Epilepsy Monitoring Unit. The individual experiments will take on average 10 minutes. Individual sessions will consist of multiple experiments with breaks in-between. We design our tasks so as not to overtire the patients and to maintain their enthusiasm and interest. We have found in a previous study (protocol 2009/194) that most patients are very willing to take part in the study and very enthusiastic about the research and see the tasks as a welcome distraction. Experimental sessions will be scheduled according to the wishes and needs of the patients, hospital staff and visitors.

The burden for a small group of patients who undergo MRI consists of one fMRI session and traveling to the MRI location in Amsterdam.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Inclusion criteria

Epilepsy patients with macro-electrode and micro-wire implants
18 years or older
patients able to perform the experiments at an adequate level
patients need to be mentally competent

Exclusion criteria

IQ<70
serious memory impairment
serious visual impairment
for the fMRI: regular contraindications for MRI

Study design

Design

Study type: Observational invasive

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Other

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	10-06-2016
Enrollment:	50
Type:	Actual

Medical products/devices used

Generic name:	depth-electrode
Registration:	No

Ethics review

Approved WMO Date:	07-04-2016
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	18-05-2017
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	27-03-2018
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO	

Date:	08-07-2020
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	14-04-2023
Application type:	Amendment
Review commission:	METC Amsterdam UMC

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	NL55554.029.15