IMproving diagnosis and PRediction of Outcome in patients with seVEre Disorders Of Consciousness (IMPROVE-DOC)

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To provide more objective information regarding the integrity of residual cognitive functions in patients with DOC after severe brain injury, and to relate early-phase behavioural, EEG, and neuroimaging findings to late clinical outcome. This might...

Ethical review	Approved WMO
Status	Will not start
Health condition type	Other condition
Study type	Observational invasive

Summary

ID

NL-OMON49174

Source
ToetsingOnline

Brief title
IMPROVE-DOC

Condition

- Other condition
- Structural brain disorders

Synonym
Coma, minimally conscious state (MCS), vegetative state/unresponsive wakefulness syndrome (VS/UWS)

Health condition

Bewustzijnsstoornissen na ernstig hersenletsel

Research involving
Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: Consciousness, EEG, Functional neuroimaging, Severe brain injury

Outcome measures

Primary outcome

The primary outcome of this study is the change over time in behaviour assessed with the coma-recovery scale * revised (CRS-R), EEG*s, and neuroimaging, and the correlation of these changes with the behavioural state (level of consciousness)/GOSE.

Secondary outcome

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Study description

Background summary

It remains difficult to assess the level of consciousness in patients with severe brain injury and disturbed consciousness. Since signs of behaviour may be minimal or inconsistently present in these patients, standard behavioural assessments remain subject to errors. Therefore, the rate of misdiagnosis of patients with disorders of consciousness (DOC) remains high. This forms a large problem for clinicians, since consciousness is an important parameter for clinical decision-making in both the early as late phase after severe brain injury. Life-or-death decisions are made with the use of fairly limited bedside tests and conventional brain imaging. In addition, there is only limited evidence of outcome in specific subgroups of DOC patients. There is still no standard diagnostic protocol for patients with persistent DOC in the Netherlands. Families are often told that recovery of consciousness is

uncertain, and prognosis remains unknown. However, it has recently been shown that multidimensional testing with the use of electroencephalography (EEG) and additional neuroimaging, such as FDG-PET might provide valuable diagnostic and prognostic information in DOC patients. In this study, a specific diagnostic protocol will be implemented for patients with DOC after severe brain injury in the Amsterdam University Medical Centers, location Academic Medical Center (AMC), in order to complement standard behavioural assessments of consciousness. A multimodal diagnostic approach with specific EEG tests and structural and functional neuroimaging may provide objective information regarding the integrity of residual cognitive functions, and remove the dependency of the patient to move or speak in order to reveal awareness of self or environment. Moreover, more stringent follow-up with repeated behavioral measurements, EEG*s, and neuroimaging will provide valuable data of outcome after DOC and the first opportunity to relate early-phase findings to late clinical outcome. This approach may resolve many of the dilemmas faced by clinicians interpreting solely behavioural indices, and might inform the clinical decision process, lead to more adequate prognostication, and provide families with tailor-made information of the condition of their loved ones.

Study objective

To provide more objective information regarding the integrity of residual cognitive functions in patients with DOC after severe brain injury, and to relate early-phase behavioural, EEG, and neuroimaging findings to late clinical outcome. This might eventually lead to improvements in diagnosis, estimation of prognosis and clinical decision-making in patients with severe brain injury.

Study design

A prospective study.

Study burden and risks

The differential diagnosis between coma, unresponsive wakefulness syndrome (UWS, formerly known as the vegetative state) and minimally conscious state (MCS) is often challenging, as these states occupy a border zone between unconsciousness and awareness. At present, the clinical standard for detecting signs of consciousness is based on bedside behavioural examination. The frequency of misdiagnoses by clinical consensus methods is, however, disturbingly high: around 40%. Motor deficits (paralysis, spasticity), impaired cognition (aphasia, apraxia), sensory impairment (blindness, deafness), pain and fatigability of patients with DOC are some of the factors that account for misdiagnosis. The differential diagnosis between patients in coma, UWS and MCS has important implications regarding prognosis and treatment. Moreover, it is an important factor in clinical decision-making. There is an increasingly body of evidence from EEG techniques and neuroimaging studies that highlights the

necessity for using multimodal and multidimensional diagnostic procedures to measure residual cognitive capacity. However, these techniques have not been implicated in standard clinical care, and there is no standard diagnostic protocol for patients with DOC in the Netherlands. In this study, a multimodal and multidimensional approach with specific EEG tests and structural and functional neuroimaging will be performed in order to obtain objective information regarding the integrity of residual cognitive functions in DOC patients. Moreover, a stringent follow-up protocol with repeated longitudinal behavioural, EEG and neuroimaging measurements will provide valuable data of outcome after DOC and the first opportunity to relate early-phase findings in DOC patients to late clinical outcome. There is only a small risk involved with participation, since EEGs and (functional) neuroimaging are minimal-invasive techniques that are frequently used in normal hospital care. Usually, DOC patients have a long length of hospital stay, since there is a waiting list for rehabilitation and nursing homes. In this time-frame, families often express their need for more objective information on the condition of their beloved-ones. It is therefore expected that there will be willingness for participation. This approach might resolve many of the dilemmas faced by clinicians currently interpreting solely behavioural indices, might inform the clinical decision process, and may lead to more adequate estimation of prognosis. Eventually, it might benefit the whole circle of care after severe brain injury, including the patient, family, and clinicians.

Contacts

Public
Academisch Medisch Centrum

Meibergdreef 9
Amsterdam 1105AZ
NL
Scientific
Academisch Medisch Centrum

Meibergdreef 9
Amsterdam 1105AZ
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

1. Severe brain injury as a result of:
a. Trauma (TBI), or
b. Subarachnoid hemorrhage (SAH), or
c. Intracranial hemorrhage (ICH), or
d. Stroke, or
e. Cardiac arrest
2. Severe disorder of consciousness (coma, UWS, or MCS) that:
- persist three days after the initial injury, or
- three days after discontinuation of sedation
3. Age 18-75
4. Written informed consent from legal representatives

Exclusion criteria

1. Ongoing neurodegenerative disease

Study design

Design

Study type: Observational invasive

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

Recruitment

NL

Recruitment status:	Will not start
Enrollment:	120
Type:	Anticipated

Ethics review

Approved WMO Date:	14-03-2019
Application type:	First submission
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	NL66533.018.18