



TECHNOLOGY

Non-invasive medical device for the study of syndromes of altered state of consciousness

COMMERCIAL TECHNOLOGY NAME

Neurowave™

PRODUCER / SUPPLIER

Khymeia Group, Padua, Italy

USE

- therapeutic
- diagnostic
- other

CATEGORY

Medical device

THERAPEUTIC OR DIAGNOSTIC FIELD OF APPLICATION

Neurologic

PATIENTS / CLINICAL CONDITION

Syndromes of altered state of consciousness: Coma, Vegetative State (VS), Minimally Conscious State (MCS).

TECHNOLOGY DESCRIPTION

Diagnostic level

The system consists of an integrated and portable device for uni- and unconventional multi-modal sensory stimulation (audio, video, tactile) of the patient and the synchronised acquisition of correlated physiological signals (EEG, EMG, ECG, EOG, pulseoximetry, respiratory rate, video-monitoring, cognitive event-related potentials). Other biophysiological phenomena, such as the change in heart rate or the activation of muscle regions, can be related to audio/video stimulation, with or without emotional value. The system enables the planning of sensory stimulation protocols to be performed within a single day or several days and also to populate a centralised database on the course of the patient's recovery of consciousness. The data collected may help to define more reliable prognostic models than those currently available.

Diagnostic level

The system allows to apply planned stimulations for therapeutic purposes. In this context the possible applications appear to be the following ones:

- to limit the status of sensory deprivation, which is known to compromise, also in

THE REPORT

A brief presentation of a technology, providing sufficient information to decide whether to undertake a comprehensive assessment process.

The reported information derives from:

- › the consultation of web materials supplied by the producer and of current national and/or regional registries
- › the search of secondary studies on HTA databases and of primary studies, indexed on Medline.

! The report does not represent a definitive assessment of the technology.

UPDATED

January 2010

ISSUED BY

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- healthy subjects, the functions of the Central Nervous System (1)
- to repeatedly stimulate the patients whose index of consciousness recovery appears to be correlated with specific patterns of stimulation.

TARGET PATIENTS

Data from the international literature on incidence and prevalence of vegetative state (VS) indicate a high variability, due to the different inclusion criteria employed. The estimated incidence of VS at six months after the event - acute brain injury from any cause - varies from 0.5 to 4/100 000 inhabitants, while its prevalence ranges from 0.6 to 10/100 000 inhabitants (2).

For the year 2008, in the Emilia Romagna Region, the estimated prevalence of the condition of minimal consciousness (MCS) is around 5.2/100 000 inhabitants, while the prevalence of VS is around 5.9/100 000 inhabitants (GRAD and GRACER regional flows). The incidence of VS after severe acquired brain injury (severe-ABI) is estimated to be 3.3/100 000 inhabitants.

Based on this information, the number of prevalent VS and MCS cases in the RER is estimated to be around 500 per year, while number of incident VS cases (severe-ABI only) is around 150 per year.

The facilities that treat VS or MCS patients in the regional area are:

- 20 rehabilitation wards operating within hospital units for acute patients
- 13 rehabilitation wards providing intensive care
- 25 territorial rehabilitation units
- 15 socio-sanitary structures (RSA) with dedicated wards.

STANDARD TREATMENT / METHOD

- Activities aimed at supporting the patient's life.
- Intermittent monitoring of clinical and instrumental signs for the recovery of consciousness and the degree of awareness of the subject. Possible processes of sensory stimulation, short-term and not based on proven effective protocols.
- Multiple drug treatments.

MAIN EXPECTED BENEFITS

- Definition of reliable prognostic methods for patients with syndromes of altered state of consciousness deriving from diseases of the Central Nervous System (e.g. of hypoxic, haemorrhagic, viral, bacterial and traumatic nature).
- Possibility of continuous monitoring of such patients.

AVAILABLE EVIDENCE AND RESULTS

N° and type of studies

Currently no studies have described the use of the Neurowave™ system.

The technology is still experimental and any results on its technical performance, safety and clinical efficacy are not available.

Therefore only results of studies on the therapeutic efficacy of sensory stimulation in patients with syndromes of altered state of consciousness are reported. Most of these studies are of low methodological quality.

Key studies published up to 2009:

- Systematic Review (2001) (3) on physiotherapy following severe brain injury, containing a paragraph on the efficacy of programs of sensory stimulation.
- Cochrane Systematic Review (2002) (4) of studies comparing programs of sensory stimulation with standard methods of rehabilitation on comatose or VS patients. Three included studies: 1 RCT (5) (N=14) and 2 controlled case series (6; 7) (N=30 and N=24). The RS concluded that the methodological quality of such studies is poor (statistical analysis of the data is not appropriate and sample size is low). The two studies employing controlled case series use the GCS scale only, without any further indicators of functional status. Only one study presents a functional assessment during a reasonably long follow-up period (3 months).
- Systematic Review (2008) (8) on the appropriateness of physiotherapy following traumatic brain injury. One chapter is dedicated to sensory stimulation, where data refer to the two above mentioned Systematic Reviews.

A Medline search did not produce any further major conclusive studies.

Outcomes

- EFFICACY
Sensory stimulation: none of the above studies provides convincing evidence on outcomes



of clinical relevance to draw conclusions about the effect of sensory stimulation in comatose patients.

- SAFETY

Sensory stimulation: none of the studies reports data on safety/adverse events/improper use of sensory stimulation.

Notes

The few and low quality data available from the literature suggest the need to carry out studies that use rigorous methods, with reproducible schemes and protocols, to determine the stimulus-response correlations capable of inducing/accelerating the awakening of the patients. Complexity and multiplicity of syndromes of altered state of consciousness, which are due to heterogeneous etiological causes, should be addressed.

COSTS

The product list price is € 195 000 + VAT, including the centralised database. The cost of consumables (conductive gel and electrodes, both of common availability) should be added to this figure.

The Neurowave™ system is an international patent by Khymeia and it has no national or international competitors, so it is accompanied by a statement of exclusivity that allows the purchase through direct assignment without any bid for tender.

PRESUMED IMPACT

Clinical issues

Clinical and research activities for which the Neurowave™ technology may have an important role are:

- testing of the correlations between sensory stimulation and changes of the patient's status, measured through the monitoring of physiological and neurophysiological (especially EEG, ECG) and electrophysiological (ERP, ERD and ERS) parameters;
- development of standardised protocols for evaluating the rehabilitative efficacy of multisensory stimulation;
- assessment of possible synergies between different modes of stimulation.

Economic issues

The economic investment required for the technology is not negligible, compared to current state. The technology could lead to an early domiciliation.

Organisational issues

It can be envisaged that the Neurowave™ technology can have a significant impact on the organisation of intensive care and rehabilitation units, both for the training of dedicated staff, and for the organisation of hospital wards, especially concerning the bed spaces dedicated to the patients. In fact, from the literature it is evident the importance of adapting the environment by reducing background noise, to avoid phenomena of *habituation* to excessive sensory stimulation, even if unintentional (1; 9; 10). In an ideal situation, patients should be allowed to stay in single rooms.

Ethical-social issues

Use of the technology could lead to benefits measurable in terms of compliance and satisfaction of family members and health professionals. In fact, the Neurowave system is capable of allowing family members to communicate remotely (e.g. from home) with the hospitalised patient through an external multimedia station (with authenticated and authorised access) and, conversely, could enable rehabilitators to follow the patient once domiciled.

Even the possibility of early domiciliation may contribute to a beneficial social impact.

ONGOING STUDIES

Ongoing studies do not appear to be registered.

AUTHORISATIONS

CE marking: available (for non-implantable device).

FDA authorisation: currently unavailable.

DIFFUSION / DIFFUSION PREDICTION

Currently there are 8 systems operating in Italy in three different locations (1 in the Lombardy, 2



in the Veneto Region). The diffusion of other equipment could be done initially in highly specialised centres, possibly engaged in research activities.

Notes

The producer has also contacted the Tuscany Region that would be available to test the technology and to initiate a collaboration with the Emilia-Romagna Region for the conduct of a multicentre study, involving facilities of both regions.

BRIEF SUMMARY

The technology is still experimental and results on its technical performance, safety and clinical efficacy are not yet available. The clinical and research activities in which the Neurowave™ technology can have a relevant role can involve the continuous monitoring of patients and/or testing of correlations between sensory stimulation and any change in the patient's status.

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This document should be cited as:

L. Ballini, T. Giovannini, A. Negro, G. Pirini, L. Vignatelli *Non-invasive medical device for the study of syndromes of altered state of consciousness - Short Report n.3* Agenzia sanitaria e sociale regionale - Regione Emilia-Romagna. Bologna, January 2010