Fundació
La Marató de TV3
XVII SIMPOSIUM
Acquired spinal cord and brain injuries

EARLY NEUROCOGNITIVE STIMULATION IN CRITICALLY ILL PATIENTS WITH ACQUIRED BRAIN INJURY

Lluís Blanch Torra
Hospital de Sabadell

1. Project summary

The objective of the project entitled "Early Neurocognitive Stimulation in Critically Ill Patients with Acquired Brain Injury", funded by Fundació La Marató de TV3 included the development of a platform based on new technologies allowing the application of a neurocognitive stimulation in critically ill patients at risk of long-term neurocognitive impairments. Secondary objective included a safety study of the platform using the on-line monitoring of the physiological variables of each patient, ensuring the maintenance of the vital signs throughout the intervention.

Twenty patients were recruited from adult patients aged 30 to 85 years admitted to the ICU at Parc Taulí Hospital (Sabadell, Spain) who were undergoing invasive mechanical ventilation or had received it for >24 hours prior to inclusion in the study, with an adequate level of consciousness (GCS≥ 8 and SAS≥3) and haemodynamically stable. By contrast, those patients with a history of neurological disease or focal brain injury, patients with severe psychiatric disorders or mental retardation and those with sensory deficits that made it difficult to interact with the platform of neurocognitive stimulation were excluded.

The stimulation sessions were delivered to each patient during ICU stay. The difficulty of each session was increased based on tolerability to the exercises as well as the stability of the monitored physiological signs.
Finally, a neuropsychological and functional assessment was performed on patients at hospital discharge.

2. Results

The proof-of-concept was conducted in 20 patients admitted to the Intensive Care Unit of Parc Taulí Hospital (Sabadell, Spain) between April 2014 and December 2014. Clinical and sociodemographic characteristics of the sample are summarized in table 1. Results are presented as mean and ranges or n/N (%) unless otherwise noted.

Age, years (M, SD)		65.44	10.22
Gender (N, %)	Male	14	63.6
	Female	6	27.3
Diagnosis (N, %)			
	Pneumonia	3	15
	Peritonitis	3	15
	Septic Shock	3	15
	Polytraumatism	2	10
	Intestinal Perforation	2	10
	Haemorrhagic Shock	1	5
	Ingestion Of Toxic Substances	1	5
	Pancreatitis	1	5
	Oesophageal Perforation	1	5
	Acute Respiratory Failure	1	5
	ARDS	1	5
	Pneumoperitoneum	1	5
APACHE-II (M, SD)		24.84	9.04
SOFA (M, SD)		9.58	4.23
RASS (M, SD)		10.33	5.91
MBS Initial		1.72	2.92
Duration of ICU stay, days (M, SD)		25.32	28.88
Duration of intubation (M, SD)		18.74	29.29
Duration of sedation (M, SD)		8.16	8.34
Duration of delirium in ICU (M, SD)		0.8	1.4
Total number of sessions (M, SD)		3.8	2.07
MBS final (M, SD)		0.04	0.14
Septic shock (N, %)		12	60
Cardiorespiratory arrest (N, %)		1	5

APACHE-II: Acute Physiology and Chronic Health Evaluation II; SOFA: Sequential Organ Failure Assessment; RASS; Richmond Agitation-Sedation Scale; MBS: Modified Borg Scale; M: Mean; SD: Standard Deviation; ARDS: Acute Respiratory Distress Syndrome.

Table 1. Clinical and sociodemographic characteristics of the sample

During the proof-of-concept a total of 76 neurocognitive stimulation sessions were delivered. Each patient performed a mean of ~ 4 stimulation sessions of the early neurocognitive intervention. Due to the sample loss (clinical improvement of patients), and in order to provide more conclusive results, we show the results of the first 5 sessions of neurocognitive stimulation.

The analysis of heart rate, blood oxygen saturation and respiratory rate values throughout the 5 intervention sessions are shown in Figures 1-3:

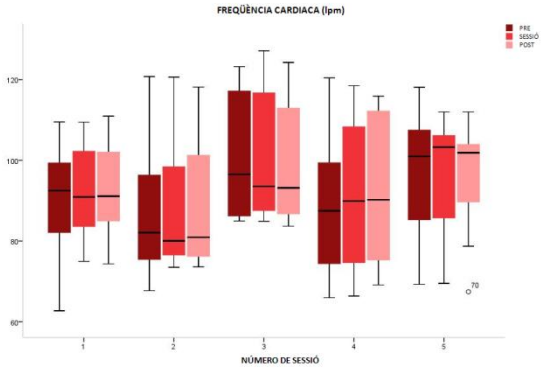

Figure 1. Group values of Heart Rate at baseline, during session and post-session (Heart rate (bpm) Session number)

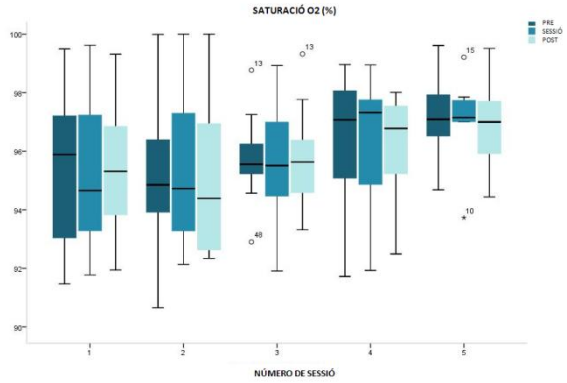

Figure 2. Group values of SpO_2 at baseline, during session and post-session (O_2 Saturation (%) Session number)

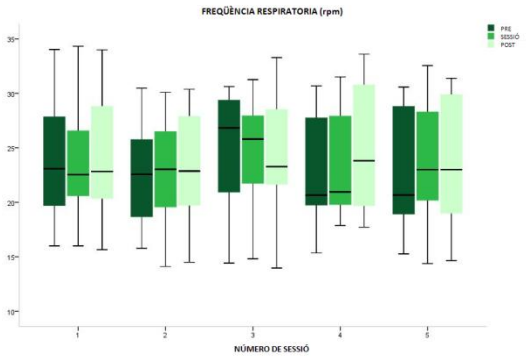

Figure 3. Group values of RR at baseline, during session and post-session (Respiratory rate (bpm) Session number)

For safety analysis, considerations were based on the non-occurrence of the following criteria: (a) absolute values of any physiological variable monitored outside of the safety ranges described in literature consensus and (b) changes >20% from baseline in any physiological parameter were also considered as unsafe events. The safety analysis of the intervention of neurocognitive stimulation throughout the 5 sessions showed the following results:

Heart Rate (HR)

All (100%) of the sample showed HR values within safety limits, by age and sex, at baseline, during and after the 5 sessions of neurocognitive stimulation.
Although the HR values remained within safe limits, a change greater than 20% compared to baseline was observed in 1 patient out of 16 (6.3%) during and after session #1, and after session #4 in 1 patient out of 8 (12.5%).

O_2 Saturation (SpO_2)

All (100%) of the sample showed SpO2 values within safe limits, considering a minimum of 90% SpO2, at baseline, during and after all sessions of stimulation. None of the patients showed changes higher than 20% in SpO2

Respiratory Rate (RR)

Eight patients (50%) showed RR values outside safety limits at baseline (M = 27.36; Min-Max: 21.44-34.03) and during (M = 26.86, 22.12-34.32) session #1, while in post-session 10 patients (62.5%) showed values outside the normal ranges (27.57, 20.82-33.99). During the post session, only 1 out of 10 patients showed a change greater than 20%.

Six patients (42.86%) showed RR values outside the safety limits in the baseline (26.29, 20.75-30.48) at session #2, 4 patients (28.57%) during the session (21.08, 14.11-26.48) and 7 patients (50%) in the post session (25.36, 20.91-30.38).

At post-session, only 1 out of 7 patients showed a change greater than 20%.

In session #3, 6 patients (60%) showed RR values beyond the normal limit at baseline (28.35, 22.56-30.62), 5 patients (50%) during the session (26.79, 21.75-31.26) and 6 (60%) at the post session (26.79; 20.8-33.28).

Results of the analysis of incidents

Incident analysis showed that 12.51% of the sessions had to be interrupted (10 sessions out of 76 sessions). Causes for discontinuation were: fatigue (60%), drowsiness in the patient and difficulty staying awake to perform neurocognitive stimulation (20%), testing and medical procedures requiring mobilization and transfer the patient outside the ICU (10%) and disorientation and confusion.

During the first session of intervention, 35% of the sessions were interrupted before completion: 71.43% by patient fatigue, 14.28% by drowsiness and difficulty in staying awake and 14.28% for tests and medical procedures requiring mobilization and transfer of the patient outside the ICU. The second stimulation session had to be interrupted in 11.76% of cases because of the patient's drowsiness and difficulty in staying awake (100%). The third treatment session was discontinued in 7.70% of cases because of problems of patient fatigue (100%). During the 4th and 5th sessions no incidences were recorded.

Results of neurocognitive assessments at hospital discharge

At hospital discharge, neuropsychological assessments were carried out in 10 patients out of 20. The analysis of the cognitive indices, calculated in standard Z-scores (0 ± 1) based on age and level of education, showed the following results:

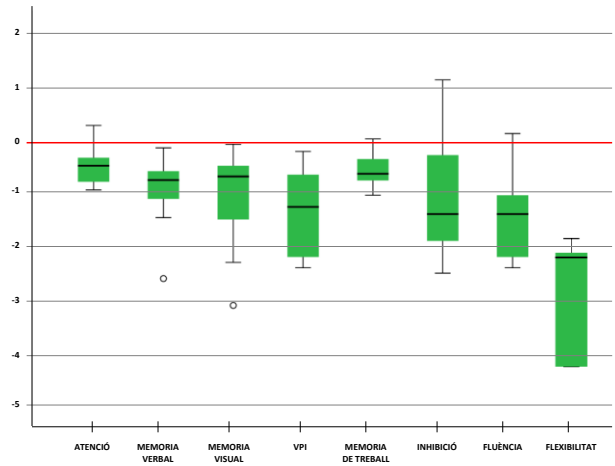

Figure 4. Neurocognitive performance of the simple at hospital discharge (ATTENTION, VERBAL MEMORY, VISUAL MEMORY, IPS, MEMORY OF WORK, INHIBITION, FLUENCY, FLEXIBILITY)

Despite some heterogeneity, most patients showed scores below normality in all cognitive domains assessed, some cases scoring less than 2 standard deviations below the general population.

Executive functions (inhibition, cognitive flexibility and fluency) together with the speed of processing were the most cognitive domains affected in the sample.
A subsequent analysis of correlations between clinical variables of ICU stay and neurocognitive indices was performed. The results showed a relationship between *cognitive flexibility* and *severity of illness* at admission (R = -0.89; p = 0.05) and between *verbal memory* and *days of sedation* (-0.81; p = 0.008) as well as *days of intubation* (R = -0.86; p = 0.003). In addition, a significant trend was found between *working memory* and *days of sedation* (p = 0.07 R = -0.64).

These results suggest a possible relationship between the *level of sedation*, *mechanical ventilation and severity of the disease* with neurocognitive impairments at hospital discharge. In conclusion, the neurocognitive intervention in the ICU patient did not produce any deleterious effect over vital signs.

3. Clinical relevance and implications

There is growing evidence that critical illness often result in significant long-term morbidities (Wolters, et al. 2013; Wilcox et al. 2013). Consequently, patients in Intensive Care Units (ICUs) suffer from neurocognitive impairments that may persist for years after hospital discharge (Rothenhausler et al. 2001; Hopkins et al. 2005; Larson et al. 2007; de Rooij et al. 2008) and adversely impact on functioning and quality of life at long-term (Hopkins et al. 2004; Herridge et al. 2011). Neurocognitive impairments affect at least one third of ICU survivors in a magnitude similar to mild-moderate dementia (Jackson et al. 2003). The results of our study showed that critically ill patients at hospital discharge score 1 to 2 standard deviations below normal in all cognitive domains compared to the general population.

ICU-related neurocognitive impairments are particularly pronounced in regard to memory, executive functioning, attentional functions and speed processing (Hopkins et al. 1999; Jackson et al. 2003; Hopkins et al. 2004; Hopkins et al. 2005; Sukantarat et

al. 2005; Jones et al. 2006; Mikkelsen et al. 2009; Duning et al. 2010; Mikkelsen et al. 2012; Woon et al. 2012; Pandharipande et al. 2013). Consequences of these long-term neurocognitive impairments are far-reaching and impact negatively on patients' lives, contributing to impaired ability to perform activities of daily living, to decreased quality of life of patients and relatives, to increased medical costs, and inability to return to work (Hopkins et al. 2005, Hopkins and Jackson 2006). These neurocognitive impairments generate not only social and health repercussions for ICU survivors, but also economic concerns because of a great resource use after critical illness in order to compensate dependency situations. Although neurocognitive impairments are generally long-lasting and devastating for survivors, rehabilitation rarely occurs after critical illness.

Therefore, given that the prevalence and severity of these neurocognitive impairments and their long-term effect are not negligible, inpatient interventions are needed to prevent or ameliorate this cognitive morbidity.

Critically ill patients present several characteristics and needs of a very heterogeneous variety. A large proportion of patients are necessarily bedridden due to their critical condition. Besides, mechanical ventilation results in an impossibility of verbal communication. ICU patients present low awareness levels, that fluctuate during the day as well as fatigue and muscle weakness that reduces their mobility. These characteristics make that neurocognitive interventions commonly used in post-acute patients might not be feasible in ICU patients. An early neurocognitive stimulation intervention for patients during ICU must consider patients' limitations, such as difficulties in mobility and communication. The hypothesis of our team raised the possibility that an intervention based on new technologies could facilitate the neurocognitive stimulation during ICU stay, solving the difficulties of communication and mobility. The project "Early Neurocognitive Stimulation in Critically ill Patients with Acquired Brain Injury", funded by Fundació La Marató TV3 allowed us to design and develop a platform of neurocognitive stimulation based on new technologies for critically ill patients during their stay in the ICU.

The results achieved in this project have enabled us to confirm that an intervention in neurocognitive stimulation based on new technologies is feasible and safe in critically ill patients. The ability of the platform to detect patient's movement made it easy to

perform cognitive exercises by slight hand movements. The occurrence of myopathy and other difficulties of the fine motor skills in these patients difficult to carry out classic paper-and-pencil cognitive exercises. Because gross motor functions are more preserved in this type of patient, using the movements of the hands and arms was effective in performing cognitive exercise.

Finally, the results showed that none of the sessions had to be interrupted due to clinical instability. The results obtained in this project constitute the first stage in implementing such an intervention on a larger scale addressed to evaluate their efficacy.

4. Literature

2014-2015

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Article. Turon, M., Mercè Jodar, M., Fernandez-Gonzalo, S., López-Aguilar, J., Blanch, Ll. Risk factors and pathophysiological mechanisms of neurocognitive impairment in critically ill patients [*in revision*]

Article. Feasibility and acceptance of an early neurocognitive intervention for critically ill patients based on new technologies [*in preparation*]

Article. Safety of an early neurocognitive intervention for critically ill patients [*in preparation*]

COMMUNICATIONS

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Poster. 28th Annual Congress of the European Society of Intensive Care Medicine. Berlin, 3-7 October 2015. Fernandez-Gonzalo, S., Turon, M., Gomà, G., Martínez-Pérez, M., De Haro, C., Montanyà, J., Jodar, M., López Aguilar, J., Blanch, L. *Early neurocognitive rehabilitation in critically ill patients Turing ICU stay: a safety study.*

Poster. International Neuropsychology Society (INS) Mid-Year Meeting. Jerusalem (Israel) 9-11 julio 2014. Turon, M., Fernandez-Gonzalo, S., Gomez-Simon, V., Sales, B., Montanyà, J., Masdéu, M.J., Palao, D., Blanch, L., Jódar, M. *Early Neurocognitive Rehabilitation in Intensive Care Unit: Proof of Concept*

2013-2014

PUBLICATIONS

Article. Turon, M., Fernandez-Gonzalo, S., Gomez-Simon, V., Blanch, L., Jodar, M. (2013). Cognitive stimulation in ICU patients: should we pay more attention? *Critical Care 17*(3), 158-159

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Oral communication. Turon, M. *Alteraciones cognitivas en el paciente crítico*. VIII Conferència d'Experts: Actualització en sedació i analgèsia del pacient crític. *Societat Catalana de Medicina Intensiva i Crítica. Barcelona,* 15 de enero de 2013

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2012-2013

PUBLICATIONS

Article. Lopez-Aguilar, J., Fernandez-Gonzalo, M.S., Turon, M., Quilez, M.E., Gomez-Simon, V., Jodar, M.M., Blanch, L. GT-IRA de la SEMICYUC (2013). Lung-brain interaction in the mechanically ventilated patient. *Medicina Intensiva 37*(7), 485-92 [doi: 10.1016/j.medin.2012.10.005*]*