

# EFFECTS OF COMBINED THERAPIES OF EXERCISE, MINDFULNESS AND COGNITIVE STIMULATION IN COGNITION AND NEUROPLASTICITY IN PATIENTS WITH CHRONIC ISCHAEMIC ICTUS

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#### **1. Project summary**

Stroke is one of the leading causes of disability worldwide. Post-stroke cognitive and emotional disturbances are common consequences in the chronic stages of stroke and have important clinical implications for the functionality and quality of life of affected individuals and their caregivers. In addition, patients who have suffered a stroke are at higher risk of having a new stroke, accelerated cognitive impairment, and dementia. Strategies such as mindfulness, exercise, or computerized cognitive training can benefit stroke patients by affecting neuroplasticity and brain health and preventing neurodegeneration.

The MindFit project is a prospective randomized clinical trial designed to examine the effects of mindfulness and exercise interventions combined with cognitive training on the cognitive and emotional recovery of patients with chronic stroke and to elucidate the underlying neurophysiological and neuroplasticity mechanisms.

A total of 141 patients with chronic ischemic or hemorrhagic stroke were randomly assigned to receive a stress-reduction intervention based on mindfulness + cognitive training (n = 47), a multicomponent exercise program + cognitive training (n = 47) or cognitive training alone (n = 47). The interventions consisted of 12-week programs, five days a week. Before and after the interventions, data from cognitive, psychological, and physical tests, blood and stool samples, and structural and functional brain scans were collected. Clinical, neuropsychological, and physical assessments (excluding blood extraction and MRI) were conducted online using video-conferencing technology, as well as the physical exercise, the mindfulness, and the cognitive training interventions, following international recommendations for adapting assessments and interventions to the virtual context.

The effects of the interventions on the cognitive and emotional outcomes will be described both in the analysis of the sample by intention to treat and in the sample by protocol, i.e. both with the subjects who were originally assigned to the different groups regardless of their adherence to treatment, and only with subjects who complied with more than 80% of the established protocol. Possible moderators and mediators such as genetic, molecular, brain, demographic and clinical factors, will also be explored in our protocol sample.

The MindFit project design adopts a multimodal biopsychosocial approach that will generate new knowledge at multiple levels of evidence, from molecular bases to behavioral changes.

### 2. Results obtained

The MindFit project was originally intended to be done in person. The COVID-19 pandemic forced us to stop the project, leaving evaluations and intervention groups unfinished and participants on a waiting list, and we had to redesign the study, adapt it to a virtual format, and restart it. Although the non-attendance allowed us to include participants from outside Barcelona province, and even from outside Catalonia, and thus to have a high rate of inclusion enabling us to complete the desired sample (141 participants) in a very short time (10 months), it has delayed the analysis and publication of the results. The study protocol is currently being submitted for review in an international journal and the first two articles are being analyzed and drafted. The results of the randomized clinical trial, ranging from molecular examinations to neuroimaging and behavioral data, will allow us to obtain maximum evidence of the impact and effectiveness of these interventions and have an in-depth view of the mechanisms underlying neuroplasticity.

Preliminary analyses with baseline data from MindFit Project participants suggest a more efficient use of the brain-derived neurotrophic factor (BDNF), one of the key molecules in brain plasticity, in the brains of those patients with healthier lifestyles. It also confirms the importance of physical activity for better physical condition and cognition in patients in the chronic phase after a stroke.

On the other hand, in the intent-to-treat sample, the 12-week mindfulness program improved the dynamic balance and agility compared to the control group. The exercise program improved aerobic capacity, strength and flexibility. Both interventions are valuable in reducing post-stroke motor difficulties. This is the first evidence of the effect of mindfulness on fitness in a chronic stroke population.

#### 3. Relevance with possible future implications

The results of the clinical trial may be crucial in providing evidence to guide rehabilitation programs after stroke in the clinical setting and to drive the development of new preventive strategies in the field of neurorehabilitation.

## 4. Generated scientific bibliography

Effects and Mechanisms of Mindfulness Training and Physical Exercise on Cognition, Emotional Wellbeing, and Brain Outcomes in Chronic Stroke Patients. Study Protocol of the MindFit Project Randomized Controlled Trial. Adrià Bermudo-Gallaguet, Mar Ariza, Rosalia Dacosta-Aguayo, Daniela Agudelo, Neus Camins-Vila, Maria Boldó, Òscar Carrera, Sandra Vidal, Blai Ferrer-Uris, Albert Busquets, Marc Via, Guillem Pera, Cynthia Cáceres, Meritxell Gomis, Alberto García-Molina, José María Tormos, Ana Arrabé, Gustavo Diez, Maria José Durà Mata, Pere Torán-Montserrat, Juan José Soriano-Raya, Sira Domènech, Alexandre Perera-Lluna, Kirk I. Erickson, Maria Mataró. Under review.

Effects of Mindfulness, Exercise and Cognitive Training on Cognition in Chronic Stroke Patients. The MindFit Project, a Randomized Controlled Trial. In process of analysis and review.

Effects of Mindfulness, Exercise and Cognitive Training on cardiovascular risk factors and Physical Fitness in Chronic Stroke Patients. The MindFit Project, a Randomized Controlled Trial. In process of analysis and review.