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XXXVII Cycle

Longitudinal monitoring of stroke recovery biomarkers: A pilot study

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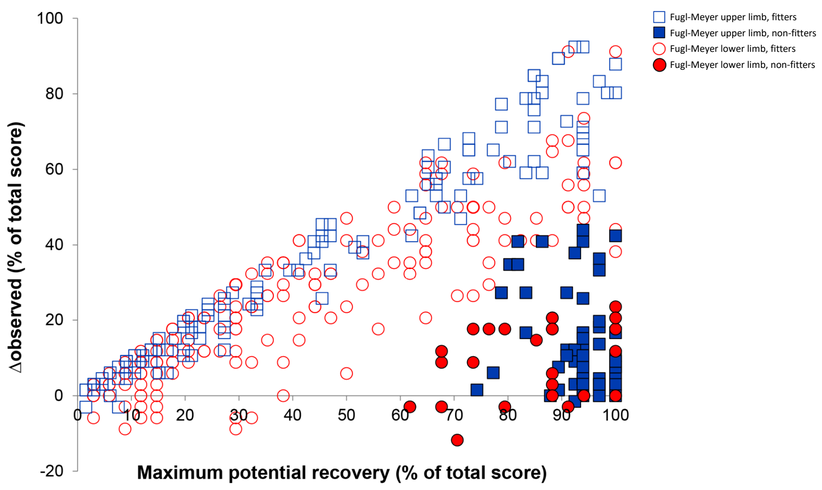
Research context and motivation

- 15 million people worldwide suffer a stroke every year, 5 million of which are left with permanent disabilities placing a burden on family and community. The estimated global cost of stroke is over US$721 billion. There are two main causes of stroke associated with its etiology: ischemia and hemorrhage. Ischemic stroke may develop from various origins, including embolism, decreased perfusion and thrombosis. It leads to irreversible injury in a brain core region and partially reversible damage in the surrounding penumbra zone. In contrast, hemorrhagic stroke is associated with the leakage or rupture of the artery and accounts for 13% of the cases.
- Acute damage of neural matter results in the inflammatory reaction (release of IL-6, CRP, IL-α, TNG- α, sICAM-1), loss of function and neurodegeneration, but functional recovery and structural rebuilding processes are stimulated concomitantly (e.g., BDNF, Irisin, VEGF).
- Spontaneous recovery, however, is often incomplete and the recovery rates of neurological function vary. Thus, rehabilitation directed at the affected functioning domains has a key role in fostering the recovery. Functional outcome prediction, based on lesion size and location, stroke mechanism, age, initial severity of deficits, and previous medical comorbidities, is routinely performed to designed effective treatment.
- The acute (0-7 days) and subacute (7 days - 6 months) disease phases are the critical period in which most motor function gains is achieved thanks to a combination of the underlying processes of angiogenesis and neuroplasticity, and rehabilitation directed at the affected functioning domains.
- Clinical assessment scales (e.g., Fugle-Meyer score) are used to quantify the patient functional recovery over time. The percentage of motor function gained out of the predicted achievable recovery is referred to as proportional recovery. The proportional recovery observed over the first 6 months after the stroke onset ranges 59–69%. However, 13% of patients do not fit the proportional recovery rule. The use of prognostic biomarkers could help to early identify the non-fitters, flag potential needs of treatment changes, and develop tailored treatment.



Consistency of proportional recovery between FMA-LE and FMA-UE expressed in percentages (%).

Veerbeek JM, Winters C, van Wegen EEH, Kwakkel G. Is the proportional recovery rule applicable to the lower limb after a first-ever ischemic stroke? PLoS One. 2018 Jan 12;13(1):e0189279. doi: 10.1371/journal.pone.0189279. PMID: 29329286; PMCID: PMC5766096

Novel contributions

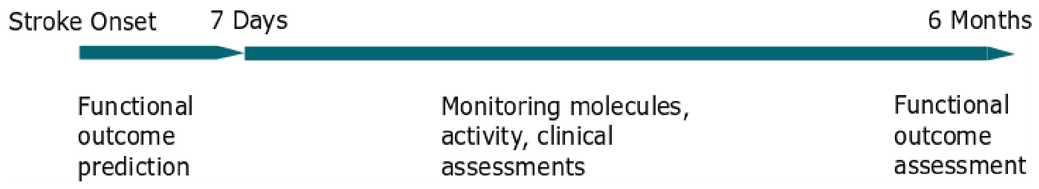
- Research and development of a multisensing POCT device, hardware and software, to monitor stroke recovery blood biomarkers
- Using a POCT device to monitor longitudinally biomarkers related to stroke recovery to better understand and characterize the motor function gain described by the proportional recovery rule. Development of algorithms to explain the correlation between biology and motor functions.

Adopted methodologies

1. Identification of sensing technologies available:
- Literature and web review of technologies to sample the selected blood molecules.

Molecule	Typology
BDNF	Neuroplasticity
Irisin	Neuroplasticity
VEGF	Angiogenesis
IL-6	Inflammation
CRP	Inflammation
IL-α	Inflammation
TNG-α	Inflammation
sICAM-1	Inflammation

2. Study design:
- Participants: sample of convenience of 10 patients will be monitored over the course of the 6 months after the stroke event.
- Exclusion criteria: patients with previous comorbidities; spinal cord injured.
- Study procedure:
  - At baseline, individual factors influencing the functional outcome prediction at 6 months are collected;
  - Over the 6 months rehabilitation period, the selected technologies will be used to collect molecules of interest. The patient's affected limb activity will be monitored continuously with a wearable accelerometer band.
  - At 6 months, the functional outcome will be assessed.



- Ethical committee: the study will be submitted for ethical approval to the Institutional Review Board (IRB).
- Data collection site: Spaulding Rehabilitation Hospital, Boston, Massachusetts, USA.

Addressed research questions/problems

- Definition of project aims:

1) Develop a point of care technology device (POCT) to monitor stroke recovery prognostic blood biomarkers;
2) Longitudinal monitoring of stroke recovery biomarkers to develop tailor treatments.

The project has been conceptualized by:

- developing transversal knowledge: stroke disease (typologies, mechanisms), recovery and prevention.
- Identification of gap of knowledge: longitudinal monitoring of stroke recovery prognostic biomarkers and necessity of new technologies to easily monitor them.
- Literature review: identification of potential clinical biomarkers of stroke.
- Definition of study design

Future work

- Identify sensitivities and ranges requirements for the selected molecules.
- Identify sensing technologies available commercially or developed by other academic groups.
- Gather available devices to measure the selected molecules; available sensors to be used to build a POCT device; ELISA lab kit for not available sensors.
- Submit the designed study to the IRB.
- Enroll subjects at Spaulding Rehabilitation Hospital, Boston, US.
- Start data collections.

Submitted and published works

- Parisi, F. , Bromet, J., Pugliese, B. L., Angelucci, A., Fabara, E., Sapienza, S., Mura, M., Demarchi, D., and Bonato, P., "A deep learning-based algorithm to estimate the knee flexion-extension angle using a sleeve with optical sensors ", 2022 IEEE-EMBS International Conference on Wearable and Implantable Body Sensor Networks (BSN), Ioannina, Greece, 2022
- Parisi, F., Duroyon, E., Adans-Dester, C., Pugliese, B. L., Fabara, E. and Bonato, E., "A deep learning-based algorithm to track the recovery of motor function in stroke survivors undergoing rehabilitation interventions", 2022 IEEE-EMBS International Conference on Wearable and Implantable Body Sensor Networks (BSN), Ioannina, Greece, 2022

List of attended classes

- 01UJUIU – Human-Ai Interaction (8/2/2022, 4)
- 01DUCRV – Principles of digital image processing and technologies (didattica di eccellenza) (21/7/2022, 5)
- 02SFURV – Programmazione scientifica avanzata in matlab (25/5/2022, 6)
- 01DOCRV – The Hitchhiker's Guide to the Academic Galaxy.That is:Basic knowledge about writing,presenting, publ [...] (15/6/2022, 4)

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