Demographic, neurological and neuroanatomical predictors of functional outcomes in stroke: A longitudinal assessment using machine learning

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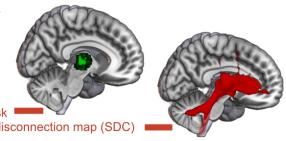
Introduction. Stroke is a major cause of disability worldwide, yet the prediction of functional outcomes remains challenging (Salvalaggio et al., 2020). Lesion neuroanatomy could help in this endeavor, yet a systematic comparison with established prognostic factors, like the neurological exam is missing. This study evaluated the added prognostic value of lesion masks and Structural Disconnection (SDC) Maps, which estimate the disruption of white matter pathways caused by the lesion, in predicting the functional outcome in the first year after stroke.

Method. The sample comprised 199 first-ever stroke patients who were assessed longitudinally at 2 weeks, 3 months and 1-year post-stroke in eight functional outcomes including cognitive and motor functions (Corbetta et al., 2015). The added prognostic value of lesions and SDC compared to neurological and demographic information was evaluated across all time points and outcomes. Cross validation was exploited to estimate generalizability of the fitted models.



Sample

Selection criteria:
– First ever stroke
– No comorbid neurological or psychiatric conditions
– less than two lacunae

Final enrolled sample:
– N = 199
– mean age = 55 years
– N females = 90
– N right hemisphere strokes = 95
– Mean admission NIHSS = 7.4
– Attrition rate at 3 months and 1 year = 70% - 54%

Predictors

Demographic
– Age
– Sex
– Education
– Ethnic Minority
– Handedness

Maps
– Lesion mask
– Structural disconnection map (SDC)

Neurological
– Stroke type (hemorrhagic vs. ischemic)
– Lesion side
– NIHSS total score
– NIHSS language, neglect and arm subitems

Admission — 2 weeks — 3 months — 1 year

Outcomes
– Language
– Verbal memory
– Spatial memory
– Attention (visual field bias)
– Attention (general)
– Motor left
– Motor right
– Functional Independence Measure (FIM)

Lesion/disconnection do not improve prediction above demographic and NIHSS variables

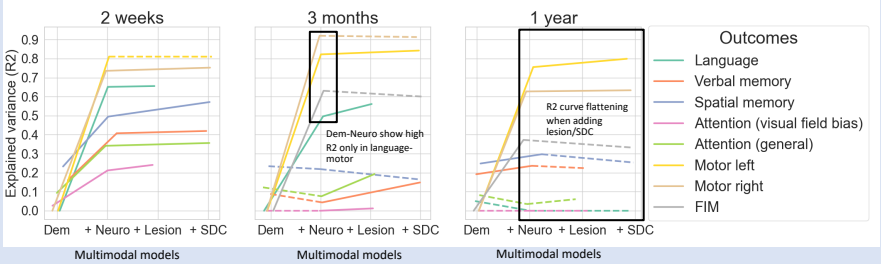


Fig. 1 Each panel shows the prediction of a specific time point, while each line represent one outcome. Y axis shows the explained variance (R2). On the x axis are described the multimodal models, starting from the simplest demographic model (first model on the left), to the most complex, including demographic, sub-acute neurological information and lesion/SDC. Solid lines indicate a statistically significant increase in R2 compared to the simpler model. Black boxes hint at the main results.

Acute NIHSS is strongly associated with recovery of language and motor outcomes, while age and education predict chronic memory functions

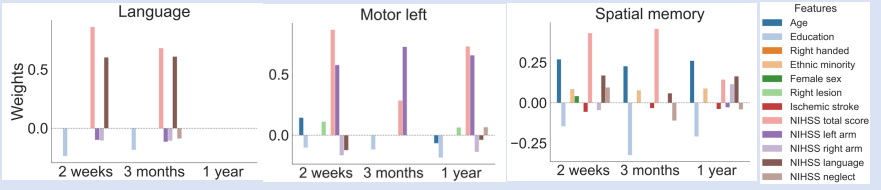


Fig. 2 The weights of the demographic-neurological model for language, left motor and spatial memory outcome. Each panel shows one outcome and all statistically significant weights of the given model for each time point. Predictors with positive weights are associated with a worse outcome.

Results.

The **model containing demographic and neurological information was the best across all domains** (Fig. 1), **with prognosis largely driven by the NIH Stroke Scale** (Fig. 2).

Predictions of memory and attention were generally poor, likely due to the lower sensitivity of the NIHSS to these functions and the small number of impaired patients.

When adding lesion or SDC to the neurological and demographic information, minor improvements in the sub-acute phase were observed across most domains, however such gains were not maintained in the chronic stages (Fig. 1).

Why does lesion neuroanatomy not increase prognostic accuracy?

- The relation between neuroanatomy and function may be strong right after stroke and then weakens due to the interaction with demographic/comorbidities
- The NIHSS is a good proxy of lesion topography, thus lesion/SDC largely provide redundant information resulting in absent/negligible gains in R2
- High dimensional maps, like lesion/SDC, suffer from overfitting, causing the model to generalize poorly to new patients.

Corbetta, M., Ramsey, L., Callejas, A., Baldassarre, A., Hacker, C. D., Siegel, J. S., ... & Shulman, G. L. (2015). Common behavioral clusters and subcortical anatomy in stroke. *Neuron*, *85*(5), 927-941.
Salvalaggio, A., De Filippo De Grazia, M., Zorzi, M., Thiebaut de Schotten, M., & Corbetta, M. (2020). Post-stroke deficit prediction from lesion and indirect structural and functional disconnection. *Brain*, *143*(7), 2173-2188.