Dutch multicentre, prospective follow-up cohort study comparing the neurological and neuropsychological sequelae of hospitalized non-ICU- and ICU-treated COVID-19 survivors

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Introduction COVID-19 has become known for its damage to the respiratory system. However, as the number of infected individuals grew, so did the concern about a potential impact on the brain.[1,2] This has been affirmed by imaging studies that report brain abnormalities.[3] These brain abnormalities may cause neuropsychological dysfunction (i.e., cognitive dysfunction and/or emotional distress). Dysfunction can then result in cognitive complaints and reduced well-being.[4] This large-scale prospective follow-up cohort study investigates COVID-19-associated brain damage, neuropsychological dysfunction, and long-term impact on the well-being of patients and their close ones. It is hypothesised that structural brain damage and cognitive dysfunction primarily occur in severely ill patients, as compared to moderately ill patients.

Cognitive complaints, emotional distress and impact on well-being are hypothesised to independent on illness severity.

Methods and analysis For this multicentre study, 200 patients with COVID-19 (100 intensive care unit (ICU) patients and 100 non-ICU patients) formerly hospitalised in one of the six recruiting hospitals during the first European infection wave (ie, March to June 2020) and their close ones will be recruited. At minimally 6 months posthospital discharge, patients will perform a set of neuropsychological tests and are subjected to a 3T MRI scan. Patients and close ones will fill out a set of questionnaires, also at minimally 6 months posthospital discharge and again another 6 months thereafter. Data related to COVID-19 hospitalisation will be extracted from the patients' medical records. MRI abnormalities will ultimately be related to neuropsychological test performance and questionnaire outcomes.

- 1. Leonardi M, Padovani A, McArthur JC. Neurological manifestations associated with COVID-19: a review and a call for action. J Neurol 2020;267:1573–6.
- 2. Correia AO, Feitosa PWG, Moreira JLdeS, et al. Neurological manifestations of COVID-19 and other coronaviruses: a systematic review. Neurology, Psychiatry and Brain Research 2020;37:27–32.
- 3. Egbert AR, Cankurtaran S, Karpiak S. Brain abnormalities in COVID-19 acute/subacute phase: a rapid systematic review. Brain Behav Immun 2020;89:543–54.
- 4. Gulko E, Oleksk ML, Gomes W, et al. Mri brain findings in 126 patients with COVID-19: initial observations from a descriptive literature review. AJNR Am J Neuroradiol 2020;41:2199–203.