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COVID-19 (GCS-NeuroCOVID) established a formal collaboration, thus forming the largest global network to date. An important research priority is to develop consensus and harmonisation of data elements with uniform definitions, which was emphasised in a recent Editorial in *The Lancet Neurology*.⁴

The design and principals of the GCS-NeuroCOVID consortium studies were previously reported.⁵ The GCS-NeuroCOVID group, in close partnership with the Pediatrics Neurocritical Care Research Group, formed and rapidly developed a paediatrics arm of the consortium to investigate the effects of COVID-19 in children and adolescents. Currently, the GCS-NeuroCOVID consortium includes 123 sites registered for adults and 96 sites registered for paediatrics across all continents (appendix).

In parallel, the EAN created a prospective registry (The EAN NeuroCOVID Registry Consortium [ENERGY]) to evaluate the prevalence of neurological manifestations in confirmed COVID-19 cases and their outcomes at 6 months and 12 months. So far, over 254 sites have registered to ENERGY from 69 countries and three continents. This initiative was preceded by a survey of 2343 clinicians on neurological manifestations, completed on April 27, 2020, by the EAN-core COVID-19 task force.¹

Together, this new global collaborative effort has extensive global outreach, with 473 sites representing all continents (appendix). In addition to global data elements and the harmonisation of definitions, this collaborative brings together complementary neurological expertise from acute resuscitation and critical care to outpatient clinic and rehabilitation settings, encompassing all ages of the population. This strong global collaborative infrastructure will serve as a crucial framework for current and future pandemics that threaten global neurological health.

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- 1 Moro E, Priori A, Beghi E, et al. The international EAN survey on neurological symptoms in patients with COVID-19 infection. *Eur J Neurol* 2020; published online June 17. <https://doi.org/10.1111/ene.14407>.
- 2 Mao L, Jin H, Wang M, et al. Neurologic manifestations of hospitalized patients with coronavirus disease 2019 in Wuhan, China. *JAMA Neurol* 2020; **77**: 1–9.
- 3 Helms J, Kremer S, Merdji H, et al. Neurologic features in severe SARS-CoV-2 infection. *N Engl J Med* 2020; **382**: 2268–70.
- 4 The Lancet. The neurological impact of COVID-19. *Lancet Neurol* 2020; **19**: 471.
- 5 Frontera J, Mainali S, Fink EL, et al. Global Consortium Study of neurological dysfunction in COVID-19 (GCS-NeuroCOVID): study design and rationale. *Neurocrit Care* 2020; **33**: 25–34.

Lessons from a neurology consult service for patients with COVID-19

In March, 2020, the USA watched anxiously as the number of COVID-19 cases rose throughout the country. Yale New Haven Hospital, a tertiary care centre in Connecticut that is less than 80 miles east of New York city, swiftly planned for a large surge in patient numbers. Preliminary reports described frequent and varied neurological complications of COVID-19 (appendix p 1).^{1,2} In anticipation, the Yale New Haven Hospital neurology department created a subspecialty consult service led by a neuroinfectious disease specialist, to diagnose and treat an expected wave of patients with novel neurological issues. Although neurologists worldwide have participated in the care of patients with COVID-19 on medical wards and in intensive care units, to our knowledge very few health systems have created services solely to manage the neurological complications of COVID-19.

From April 6 to May 29, 2020, the Yale NeuroCOVID team reviewed 100 cases, unburdening the primary neurology consult service, identified trends in disease presentations and demographics, and provided diagnostic and treatment recommendations based on emerging scientific literature (appendix p 2). In reviewing our NeuroCOVID patients, it was striking to observe that 25 (25%) were Hispanic and 25 (25%) were Black, while Connecticut is demographically 17% Hispanic and 12% Black.³ This disproportionate representation of non-white patients requiring NeuroCOVID consultation parallels racial and ethnic disparities in COVID-19 disease presentations noted in the USA and Europe.⁴ Hispanic NeuroCOVID patients were younger (median age 55 years, IQR 45–68) and had lower in-hospital mortality (16%) compared with white or Black patients (median ages 72 years, IQR 64–81 and

On the **Global Consortium Study of Neurological Dysfunction in COVID-19** see <https://www.neurocriticalcare.org/research/covid-19-research-opportunities>

See Online for appendix

See Online for appendix

On the **EAN Neuro-COVID Registry Consortium** see <https://forms.gle/hS6zFCV3e6vXkCj8>

64 years, 58–74, respectively, with 40% mortality). Long-term morbidity related to the neurological effects of acute COVID-19 in surviving patients is unknown.

In *The Lancet Neurology*, Mark Ellul and colleagues⁵ report neurological complications of 901 patients that might be linked to COVID-19 and outline criteria for categorising the likelihood of association of severe acute respiratory syndrome coronavirus 2 infection with a patient's clinical neurological disease.⁵ In addition to their diagnostic criteria, we propose that a dedicated NeuroCOVID consult team has the unique potential to develop expertise, supplement clinical care, and identify the particular needs of local communities. The underlying cause of racial and ethnic disparities observed in patients with COVID-19 deserves critical investigation from pathogenetic and public health perspectives. Our experience suggests that identifying the populations hit the hardest by COVID-19 and creating policies that address fundamental barriers to disease prevention has the potential to avert neurological disease in at-risk communities.

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- 1 Mao L, Jin H, Wang M, et al. Neurologic manifestations of hospitalized patients with coronavirus disease 2019 in Wuhan, China. *JAMA Neurol* 2020; **77**: 683–90.
- 2 Zubair AS, McAlpine LS, Gardin T, Farhadian S, Kuruvilla DE, Spudich S. Neuropathogenesis and neurologic manifestations of the coronaviruses in the age of coronavirus disease 2019: a review. *JAMA Neurol* 2020; published online May 29. <http://dx.doi.org/10.1001/jamaneurol.2020.2065>.
- 3 United States Census Bureau, QuickFacts Connecticut. <https://www.census.gov/quickfacts/CT> (accessed June 16, 2020).

- 4 Kirby T. Evidence mounts on the disproportionate effect of COVID-19 on ethnic minorities. *Lancet Respir Med* 2020; **8**: 547–48.
- 5 Ellul MA, Benjamin L, Singh B, et al. Neurological associations of COVID-19. *Lancet Neurol* 2020; **19**: 767–83.

Studies of deep brain stimulation in Parkinson's disease

We read with interest the Comment by Günther Deuschl and Paul Krack¹ in *The Lancet Neurology* on our Article reporting the results of the INTREPID study.² We appreciate their thoughtful comments on the rigorous study design. However, we would like to point out some of the differences in study design between INTREPID and the studies with which it was compared in their commentary, which are important for the interpretation and comparison of the findings.

Their Comment noted that our primary outcome results (3.03 h [95% CI 1.3–4.7] improvement in ON time in the group receiving active therapeutic stimulation compared with the control group receiving subtherapeutic stimulation)² were similar to those of other studies (4.4 h and 3.0 h improvement^{3,4}). However, these studies were either open label or single blinded versus our double-blinded study, they used baseline scores obtained before implantation, and the 3.03 h improvement score in our study included patients whose reported ON time was set to zero if they had increased antiparkinsonian medication during the 3-month blinded phase.

We also reported a 5.6 h improvement in ON time in the active group at 3 months compared with screening (pre-implant). Okun and colleagues³ reported a 4.27 h improvement at 3 months compared with baseline (pre-implant). Weaver and colleagues⁴ reported a 4.6 h improvement at 6 months compared with baseline (pre-implant), but this study included patients having deep brain stimulation

(DBS) of the subthalamic nucleus and those having DBS of the globus pallidus interna, without discerning between them. A subsequent study by Follett and colleagues⁵ found a 4 h improvement in ON time for DBS of the subthalamic nucleus at 24 months.

In INTREPID, the average 42% improvement in Unified Parkinson's Disease Rating Scale part 3 (UPDRS III) scores (stimulation ON and medication OFF) at 3 months compared with screening was recorded during the blinded phase of the study. The other trials used for comparison by Deuschl and Krack¹ were open label, except for the single-blinded study by Weaver and colleagues.⁴ A more appropriate comparison would be the study by Follett and colleagues,⁵ in which an improvement of 24.9% in UPDRS III scores was reported for subthalamic nucleus stimulation.

Regarding the larger lesion effect reported in INTREPID compared with in previous studies, differences in the time of assessment after implantation could account for this finding given that assessment in INTREPID was within 2–4 weeks after implantation, whereas Okun and colleagues³ assessed UPDRS III scores (medication OFF and stimulation OFF) 3 months after implantation.

Deuschl and Krack suggest that our trial provides evidence “corroborating the choice of subthalamic nucleus as the preferred target”³ for DBS in the treatment of patients with advanced Parkinson's disease. INTREPID focused only on the subthalamic nucleus, and as such was not designed to address target comparison, as was the case in several previous randomised controlled trials.

JLV is a consultant for Medtronic, Boston Scientific, Adamas, LivaNova, and Abbott, and serves on the scientific advisory board for Surgical Information Systems, during the time of the conduct of the study; he also has stock options as a scientific advisor for Surgical Information Sciences. PAS has received non-financial support from Boston Scientific, during the conduct of the study, and non-financial support and funding for fellowship training from Medtronic, outside of the submitted work; he also has a patent (US patent number 9 295 838) relevant to deep brain stimulation.