NIH Meeting on COVID-19 Neurologic and Psychiatric Effects

Website | Speaker Biographies | July 15, 2021

Key Findings

- Evidence pertaining to Post-Acute COVID-19 (PASC, or long-COVID) was considered by a multi-expert panel. Experts discussed evidence surrounding the neurological and psychiatric effects of long-COVID experienced by patients, such as fatigue, brain fog, headache, and numbness, and, in some cases, cognitive issues. Some evidence reveals that individuals who were infected with COVID-19 display visible changes in the brain.
- Discussion covered disparities in COVID-19 infection rates between individuals from underrepresented ethnic minority groups and their White counterparts, disparities in long-COVID symptom severity, and disparities in access to treatments.
- The expert panel emphasized the need for ongoing scientific collaboration, data analysis, and research of the neurological and psychiatric effects of long-COVID.

Introduction

Dr. Avindra Nath, Clinical Director, Division of Intramural Research, National Institute of Neurological Disorders and Stroke, NIH

- Discussed past viral infections and their effects on the long-term neurological effects of infected patients.
  - o Post-Ebola Syndrome.
  - o Myalgia Encephalomyelitis/Chronic Fatigue Syndrome.
- Long-COVID can be divided into three categories including fatigue, neurological, and dysautonomia.
- The more we understand about other viral infections and how they cause long-term neurological effects, the better we can understand, diagnose, and treat the neurological symptoms associated with long-COVID.

Session I: Post-Acute Sequelae of SARS-CoV-2

Kiran Thakur, Columbia University, New York, NY

- It is important to address the unheard voices when talking about long-COVID.
  - o Hispanics, Blacks, and uninsured individuals have inequitable access to the new COVID-19 clinics, and these disparities must be addressed.

- There is a complex interplay among long-COVID symptoms.
  - There are major cognitive symptoms that have hindered individuals' ability to return to work.
  - Further, there are major psychiatric symptoms among 90% of responders reporting a change in mood and emotion.
- Pediatric and adolescent populations have been impacted directly and indirectly because of social isolation, high stress levels, and acute COVID-19 infections.

Igor Koralnik, Northwestern University, Chicago, IL

- At the beginning of the COVID-19 outbreak there was no "gold standard" test for discovering long-COVID.
- About 80% of patients reported 4 or more symptoms with the most common being brain fog, headache, numbness, and fatigue. Many of the patients also experienced cognitive issues.
- Based on past data, long-COVID is an issue that will become extremely prevalent. Therefore, additional research and funding must be poured into it.

Serena Spudich, Yale University, New Haven, CT

- There is evidence of visible changes in the brain among individuals who experienced COVID-19 when compared to those who did not.
- A loss of regional grey matter in the frontal areas of the brain and elevated cerebrospinal fluid markers of neuroinflammation and neuronal injury have been observed.
- Physical changes in the brain help explain the neurological effects that long-COVID patients are experiencing, but we are still in the early stages of understanding what exactly is happening.

Session II: Patient-Led Research

Athena Akrami, University College London, London, UK

- Conducted a survey in 9 languages, with 250 questions with over 7,000 respondents from 85 countries.
- Results found that individuals who recovered from COVID-19 disease were sick for an average of 91 days and many of their symptoms peaked during week two.

Hannah Davis, New York, NY

- Davis is a long-COVID patient with extreme symptoms. She had over 10 symptoms in the post-acute phase of long-COVID.
- She discussed how debilitating the disease was, and how she was unable to do anything on her own. Brain fog, intense fatigue, migraines, and pain made it impossible for her to live her life in the same manner as she did before she contracted COVID-19.
- Research objectives and bias in long-COVID research can lead to inaccurate perspectives or conclusions. To improve long-COVID research, we must comprehensively select the patients we study. We must also ask the correct questions; otherwise, we will misrepresent long-COVID symptoms.

Session III: Personal and Journalistic Perspectives

Chimere Smith, Baltimore, MD

- Smith described her long-COVID symptoms of memory loss, delusions, cerebral pain, and body tremors. She described social, emotional, and financial barriers that arose in her life as a result of her long-COVID sickness and her race. She called for further research.
- Stated that doctors must accurately tell the story of patients in their medical notes.

Pam Belluck, New York, NY

- Belluck described symptoms of delirium, cognitive decline, concentration and memory issues, psychosis, and poor mental health that many long-COVID patients experienced.
- Authored several articles related to Neuro-COVID in *The New York Times.*

Session IV: Special Issues related to Neuro-COVID

Nicte Mejia, Massachusetts General Hospital, Boston, MA

- Black, Latino, and Indigenous patients remain 3-4 times more likely to receive hospitalized care for COVID-19. Disparities also exist in vaccine distribution.
- Mejia presented a framework for action to reduce disparities caused by systemic inequities and racism to produce long-lasting, improved health outcomes.
- She noted the importance of fostering access to neurological clinicians, specialists, and therapeutics for individuals from underrepresented communities who are experiencing long-COVID.

Ameet Dravid, Noble Hospitals and Research Center, Pune, India

- Dravid presented neurological issues of long-COVID for Noble Hospital patients and reported that 25% of India's population has been vaccinated with at least one dose.
- Ongoing data collection of Noble patients who experienced neurological issues during or after COVID-19 infection.
- He stated that pre-existing neurological comorbidities are associated with higher mortality in patients, and neurological complications are seen in almost 50% of patients with severe COVID-19.
- Secondary neurological complications, like encephalopathy, developed in 9% of patients.

Session V: Resources for Neuro-COVID Research

Joseph Mankowski, Johns Hopkins University, Baltimore, MD

- Data from COVID-19-infected animal models was presented. The central nervous system after SARS-Cov-v2 infection was examined in mice, golden Syrian hamsters, and primates.

Lara Jehi, Cleveland Clinic, Cleveland, OH

- The Cleveland Clinic COVID-19 registry includes neurological-COVID-19 data measuring headache, loss of taste, loss of smell, epilepsy, confusions/memory loss, and stroke. The registry data has been used in predictive modeling and big data science research publications.
- The data can help inform new experimental designs and clinical trials. The registry data set includes:

- o 80k COVID-19 patients with 240k COVID-19 patients matched for age, gender, race, and testing period.
- o Blood on 1,000 COVID-19 positive and 1,500 COVID-19 negative patients.
- o Identified 6,000-50,000 patients with different neurological complications.
- o >300 data points/patient.

Eliezer Masliah, National Institute on Aging (NIH), Bethesda, MD

- Data on COVID-19-infected patients with existing neurological conditions was discussed.
- The NIA Alzheimer's Diseases Centers have 15,000 participants.
- The NIA Alzheimer's Disease Sequencing Project plans to better understand relationships between genetic makeup and ancestry with COVID-19 infection.
- Funding opportunities were announced for research on COVID-19 and neurodegeneration.

Sharon Meropol, NYU Langone Medical Center, New York, NY

- Discussed COVID-19 Neuro Databank/Biobank data. Data on neurological conditions, clinical courses, vulnerable patient populations, pregnant individuals, and post-acute sequalae characteristics are being collected.
- A Global Unique Identifier (GUID) is utilized for individual patients at clinical sites.

Tarun Dua, Unit Head, Brain Health, WHO

- The WHO Global Forum on Neurology & COVID-19 was discussed. The forum promotes research collaboration across 27 countries.
- Four working groups exist within the Global Forum on clinical care, essential services, surveillance, and long-term impacts.
- Most recent studies examine long-COVID conditions.

Elizabeth Oelsner, Columbia University, New York, NY

- C4R, the Collaborative Cohort of Cohorts for COVID-19 Research was designed to minimize biases inherent in observational studies of COVID-19. Utilizes fourteen NIH-funded studies.
- Key research questions included the major determinants of incidence and clinical severity of COVID-19, long-term complications, and social determinants of health on infection rates.

Panel Discussion

- What are the gaps and challenges that low- and middle-income countries face in catalyzing research for COVID-19 neurological conditions?
  - o Health systems in these countries that are underperforming lack sufficient workforce to gather research. Funding for local entities is a priority.
- How do we design and implement studies of long-COVID? Who are the comparison groups, and how long should individuals be studied?
  - o The baseline will likely be two years. As many people as possible should be studied before studies begin to restrict populations to positive test subjects only.
  - o Respiratory symptoms appear to decline in long-COVID. Neurological studies need to be the focus.
- How do we harmonize studies and data?
  - o Multi-tiered studies where large amounts of data are gathered on big populations could incorporate smaller subset test population groups.
- What would you say about creating comparison groups for studies?

- o More in-depth studies about COVID-19 can be conducted after we understand what COVID-19 is and why certain people develop symptoms.
  - o We need to start with large studies and slowly work our way into more specific studies, but we need to know what we are dealing with to get the right perspective on what studies come next.
- Should we only be studying people who have had COVID-19 proven by PCR (polymerase chain reaction) testing, or should we study patients who have symptoms but no proof of Acute COVID-19?
  - o Rather than only focusing on one group, it could be better to study both and see if we can find any differences or similarities between the two groups.

Special Session: Roundtable with NIH Leadership

Joshua Gordon, Director, National Institute of Mental Health, NIH

- There have been differences in how members of diverse groups respond to COVID-19 and are impacted by it.
  - o Black Americans are more likely to commit suicide because of COVID-19.
  - o Individuals with preexisting mental disorders are more likely to get COVID, and more likely to face severe symptoms or death.

Walter Korshetz, Director, National Institute of Neurological Disorders and Stroke, NIH

- We need to look at how the body responds to and recovers from COVID-19 disease.
- We also must look to the horizon to predict how COVID-19 may have an impact on other ailments in the future, such as dementia.
- Autopsy studies will be one of the next types we take advantage of.
- It's time for neurologists and psychiatrists to advance our knowledge of COVID-19.

Nora Volkow, Director, National Institute on Drug Abuse, NIH

- Research should be pointed toward determining long-term effects of COVID-19 on children and their developing brain.

George Koob, Director, National Institute on Alcohol Abuse and Alcoholism, NIH

- Discussed alcohol and its connection to COVID-19.
- Alcohol is a major contributor to various types of deaths (driving, overdose, liver disease, violence).
- Social isolation leads to stress, and stress can lead to alcoholism; thus, it is important to look at the social determinants that COVID-19 may have affected, which could have fueled alcohol abuse.

Helene Langevin, Director, National Center for Complementary and Integrative Health, NIH

- Effects of chronic stress on brain microglia activation (the resident immune cells of the central nervous system).
- The brain has extreme stress because of the social effects associated with the pandemic, as well as the inflammation caused by Acute COVID-19.
- Stress management has been studied for years, and that is the first place to get perspectives on how to treat some of the neurological symptoms that long-COVID patients face.

Eliezer Masliah, Director, Division of Neuroscience, National Institute on Aging, NIH

- We must find the connections between long-COVID and Alzheimer's.
- Both have a reduced expression of antiviral genes.
- More research must be done to find a connection between the diseases.

Alison Cernich, Deputy Director, Eunice Kennedy Shriver National Institute of Child Health and Human Development, NIH

- COVID-19 maternal and child subgroup facilitated funding of supplemental studies include the studies on:
  o Long-term impacts on adolescent mental health.
  o Protective contributions of a parenting model.
  o Effects on COVID-19 on pregnant and nursing women.
- Further research is needed to discover the best way to return underserved children to school.

Andrea Lerner, Medical Officer, Immediate Office of the Director, National Institute of Allergy and Infectious Diseases, NIH

- The focus is on understanding the variability of recovery and neurological effects on recovery.
- Longitudinal studies that observe people with prior COVID-19 monitor complications and whether the disease had any significant impacts on their health.

Susan Sullivan, Program Director, National Institute on Deafness and Other Communication Disorders, NIH

- The sudden loss of smell has been one of the most common symptoms of COVID-19 disease.
- About 80 percent of patients lose their sense of smell. 5-10 percent of those who lose their smell never get their sense of smell back (to date).

Lillian Shum, Director, Division of Extramural Research, National Institute of Dental and Craniofacial Research, NIH

- Dental, oral, and craniofacial tissue are affected by COVID-19.
- Saliva is the primary transmitter of COVID-19 in dental settings.
- Studies were presented on how dental health and hygiene can impact COVID-19 transmission.

Yolanda F. Vallejo, Program Director, National Center for Advancing Translational Sciences, NIH

- National Center for Advancing Translational Sciences (NCATS) gathers data on new technologies and medical devices used for identifying and treating COVID-19.
- NCATS integrates data from multiple sites and uses machine learning to identify factors that predict their patient outcomes.
- NCATS allows researchers to start teams where they can analyze different subject areas, work with different subject matter experts, and create publications.

Sean Coady, Deputy Branch Chief, National Heart, Lung, and Blood Institute, NIH

- Creates collaborative cohort studies of COVID-19. He maintains a grant portfolio consisting of research project grants.