

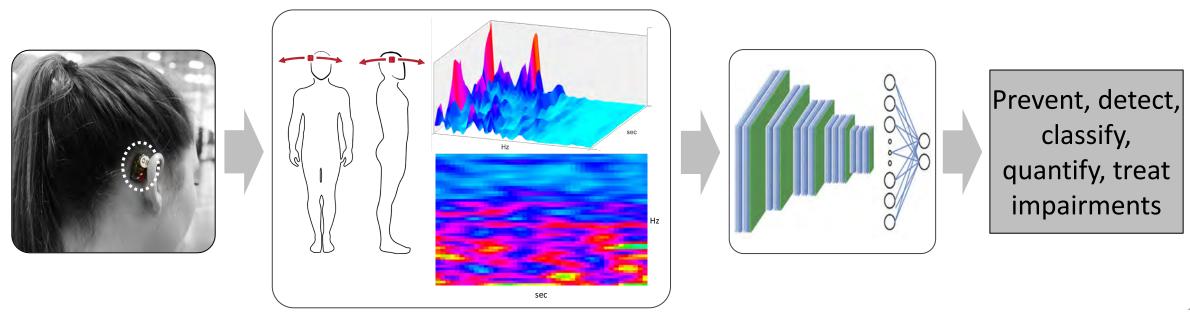
PROT Mission: Accessible Precision Healthcare Solutions

Technology Innovations

- wearable sensors
- machine learning
- remote patient monitoring

Go-to-Market Focus

- "phybrata" sensing
- enormous under-realized potential to quantify and treat neurodegenerative medical conditions



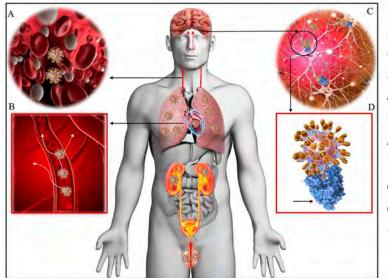
PROT and COVID-19

- 1. <u>Challenge:</u> Patients and healthcare workers with potential COVID-19 neurological infections need to be identified earlier in order to receive appropriate treatment and rehabilitation.
 - Neurological infection is the most common extra-respiratory complication in COVID-19 patients.
 - COVID-19 neurological infections lead to impairments of multiple physiological systems, including the central nervous system, peripheral nervous system, and musculo-skeletal system.
 - Neurological symptoms are significantly more prevalent in severe COVID-19 cases, and carry poorer prognoses, higher mortality rates, and shorter times to death.
- 2. <u>PROTXX Solution</u>. The PROTXX physiological tremor sensor (PTS) enables rapid, non-invasive, and highly sensitive identification and quantification of potential neurological impairments in COVID-19 patients and healthcare workers, providing a *comprehensive picture of each patient's unique impairment signature* and each patient's unique recovery trajectory.

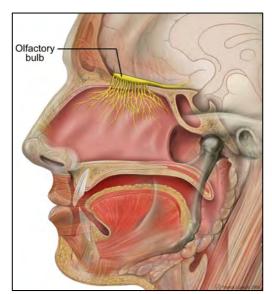
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Background: COVID-19 and Neurological Impairments

- > COVID-19 patients with neurological infection have worse outcomes and higher mortality rates.
 - Widely documented studies of the pathology of human influenza reveal that central nervous system (CNS) infection is the most common extra-respiratory complication [1], and evidence exists for influenza virus CNS invasion along the olfactory route, especially in immuno-compromised individuals [2,3].
 - Neurological and respiratory tract infections in Coronavirus patients have been observed to show distinct features [4], and influenza viruses have been linked to neurodegenerative sequelae including stroke, Parkinson's symptoms, postencephalitis Parkinson's disease [5].
 - Published evidence now exists for COVID-19 targeting the CNS [6], and CNS infection may be the major cause of death even when low levels of the virus are detected in the lungs [3]. Published studies of infected patients in China also reveal how the neuro-invasive potential of the SARS-CoV2 virus that causes COVID-19 may accelerate respiratory failure [7].
 - COVID-19 neurological symptoms fall into three categories [8,9]: central nervous system (CNS) symptoms or diseases (headache, dizziness, impaired consciousness, ataxia, acute cerebrovascular disease, including ischemic stroke and cerebral hemorrhage, and epilepsy), peripheral nervous system (PNS) symptoms (hypogeusia, hyposmia, hypopsia, and neuralgia), and skeletal muscular symptoms.
 - Neurological symptoms were significantly more common in severe COVID-19 cases as compared with non-severe cases, and carried poorer prognoses, higher mortality rates, and shorter times to death [8,9].



Dissemination of COVID-19 virus throughout the body via the blood stream. The lungs, heart, kidneys, intestines, brain, and testicles are well-known to express ACE2 receptors and are possible targets of COVID-19 [6].



CNS infection may occur via circulation and/or an upper nasal trancribrial route that enables the COVID-19 to reach the brain via neurons in the nose (olfactory bulb) [2]. The virus can then rapidly spread to connecting nerve cells and bind and engage with ACE2 receptors, resulting in extensive nerve damage.

CNS infection can be the major cause of death even when low levels of the virus are detected in the lungs [3].

Background: COVID-19 and Neurological Impairments

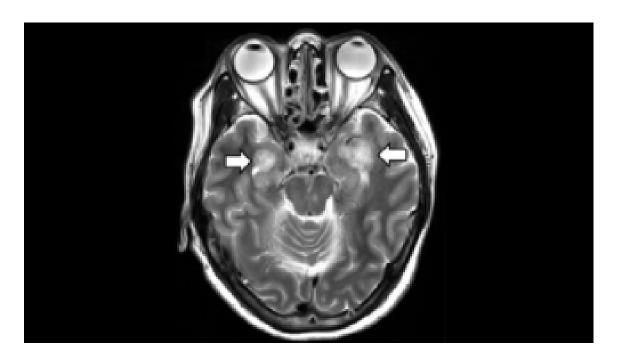
References:

- [1] "Pathology of Human Influenza Revisited." Kuikena T et al. Vaccine. 2008; 26(Suppl 4): D59–D66.
- [2] "Evidence for Influenza Virus CNS Invasion along the Olfactory Route." van Riel D et al. Journal of Infectious Diseases. 2014; 210: 419–423.
- [3] "Severe Acute Respiratory Syndrome Coronavirus Infection Causes Neuronal Death in the Absence of Encephalitis in Mice Transgenic for Human ACE2." Netland J et al. Journal of Virology. 2008; 82(15): 7264–7275.
- [4] "Coronavirus Infections in the Central Nervous System and Respiratory Tract Show Distinct Features." Li Y et al. Intervirology. 2016; 59: 163–169.
- [5] "Parkinson's disease or Parkinson symptoms following seasonal influenza." Toovey S et al. Influenza and Other Respiratory Viruses. 2011; 5(5): 328–333.
- [6] "Evidence of the COVID-19 Virus Targeting the CNS: Tissue Distribution, Host–Virus Interaction, and Proposed Neurotropic Mechanisms." Baig AM et al. https://pubs.acs.org/doi/10.1021/acschemneuro.0c00122
- [7] "The Neuroinvasive Potential of SARS-CoV2 May Play a Role in the Respiratory Failure of COVID-19 Patients." J Med Virol. 2020; 1–4. doi: 10.1002/jmv.25728
- [8] "Neurological Manifestations of Hospitalized Patients with COVID-19 in Wuhan, China: a Retrospective Case Series Study." Mao L eta al, medRxiv 2020. doi: https://doi.org/10.1101/2020.02.22.20026500.
- [9] "COVID-19 in neurology and neurosurgery: A scoping review of the early literature." Wilson MP, Jack AS. Clinical Neurology and Neurosurgery (2020). doi: https://doi.org/10.1016/j.clineuro.2020.105866

COVID-19 Neurological Impairments in the News

"Some Coronavirus Patients Show Signs of Brain Ailments"

New York Times - 4/1/2020: https://www.nytimes.com/2020/04/01/health/coronavirus-stroke-seizures-confusion.html



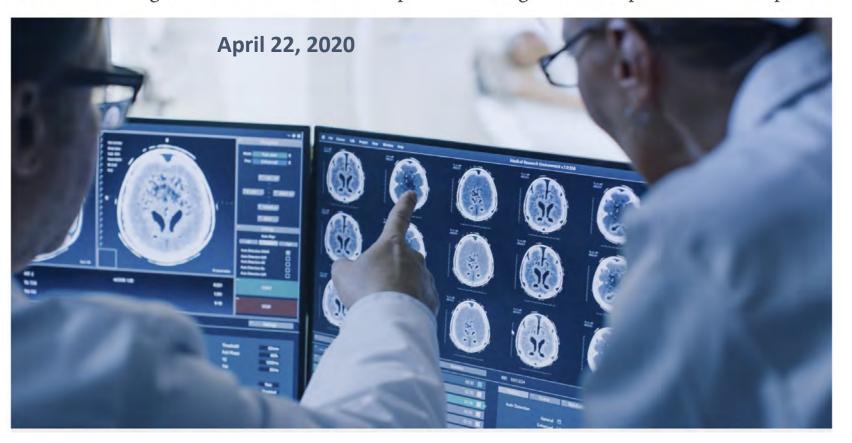
"In Some Cases, COVID-19 May Harm the Brain"

WebMD - 4/2/2020: https://www.webmd.com/lung/news/20200402/in-some-cases-covid-19-may-harm-the-brain#1

COVID-19 Neurological Impairments in the Canadian News

University of Alberta neurologists watch for signs that COVID-19 can attack the brain

Understanding the effect now could help in directing effort for potential therapies.



https://www.folio.ca/university-of-alberta-neurologists-watch-for-signs-that-covid-19-can-attack-the-brain/

Healthcare Workers at Risk as Well

"Covid-19 hits doctors, nurses and EMTs, threatening health system"

Washington Post – 3/17/2020: https://www.washingtonpost.com/health/covid-19-hits-doctors-nurses-emts-threatening-health-system/2020/03/17/f21147e8-67aa-11ea-b313-df458622c2cc story.html

"COVID-19: protecting health-care workers"

The Lancet - 3/21/2020: https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(20)30644-9/fulltext

A Call to Action from the American Academy of Neurology

American Academy of Neurology call for papers on neurologic aspects of COVID-19 infection:
https://www.neurology.org/covid

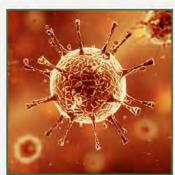
Neurology[®] Journals



COVID-19 and neurologic disease

Call for Papers!

Expedited Peer Review and Online Publication



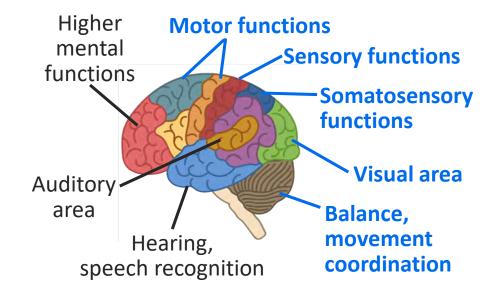
Neurology is interested in papers that address the neurologic aspects of COVID-19 infection and challenges to the management of patients with chronic neurologic conditions who have, or are at risk for, the infection. Papers that pass internal review will undergo expedited peer review and online publication. We will consider papers posted in preprint servers. Submit observational studies and clinical trials as Articles, and case series and case reports as Clinical/Scientific Notes.



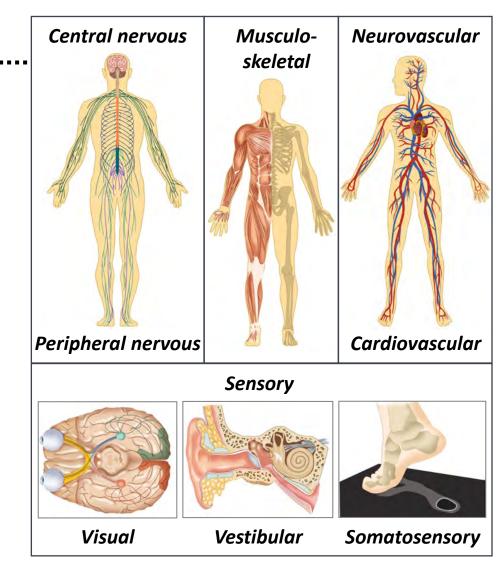


Problem: Neurodegenerative Medical Conditions

- Disruptions widespread throughout brain
- Impairments to multiple physiological systems
 - Highly individual impairment profiles, fluctuating symptoms



 Current solutions: (i) multiple time-consuming tests, multiple clinical specialists, expensive equipment;
 (ii) subjective observations, patient self-reporting.



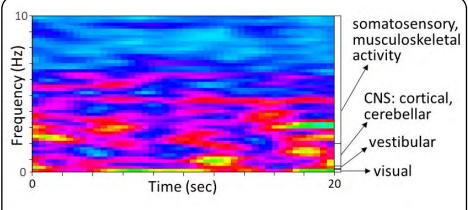
Solution: **Phy**siological Vi**brat**ion **A**nalysis (**Phybrata**) Sensor



Unobtrusive, non-invasive, head-mounted wearable sensor











Identifies, quantifies, tracks physiological impairments thru entire patient lifecycle: intake, treatment, rehabilitation

- Guides adjustments to treatment and rehabilitation therapies, quantifies corresponding patient responses.
- Accelerates recovery, improves patient outcomes, reduces healthcare lifecycle costs.

Ease of use of simple vital sign monitors

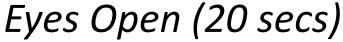


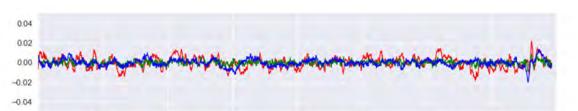
Diagnostic power of clinical test systems



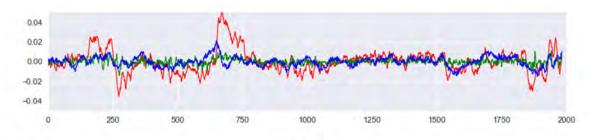
Phybrata Demo

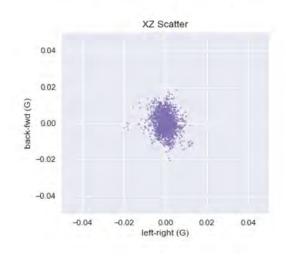


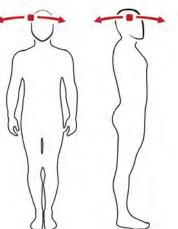


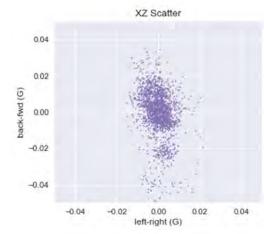












- Involuntary movements (normal and pathological)
- Interaction of multiple physiological systems



- Neurological / central nervous system
- Peripheral nervous system (afferents, efferents)
- Sensory systems (visual, vestibular, somatosensory)
- Musculoskeletal system
- Cardio/neuro-vascular systems

Phybrata and COVID-19



- There will not be a one-size-fits-all solution for COVID-19. Patients with potential neurological infections need to be identified earlier and will require specialized therapeutic treatments and longer rehabilitation times.
 - The Phybrata sensor can be utilized for rapid, non-invasive, and highly sensitive identification and quantification of neurological impairments in *COVID-19 patients and healthcare workers*.
 - Phybrata sensor data provide a comprehensive picture of each patient's unique neurological impairment signature at the time of presentation and each patient's unique recovery trajectory throughout treatment.
 - The Phybrata sensor is already utilized to identify and quantify neurological impairments resulting from age-related disorders (e.g. stroke), disease (e.g. Parkinson's), injuries (e.g. concussions and sub-concussive head impact exposure), and medical treatment (e.g. invasive neurosurgeries) based upon their *unique underlying physiological impairment signatures*.



Thank You

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