



Brain donation in the era of COVID 19: challenges to the harvest in the face of a pandemic

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Abstract We have experienced numerous new challenges during the process of brain harvesting in the period of COVID-19. Although brain harvests have continued successfully during this time period, the numerous uncertainties and challenges described in this paper have nearly derailed the process several times. While the interface of the medical profession with patients in the context of a pandemic has been well-documented on several fronts, and particularly for those health care workers on the front lines, we are not aware of any documentary accounts of the challenges facing research and tissue donation programs. With this paper, we contribute an additional perspective and describe the lessons we have learned in addressing these novel issues.

Keywords Brain banking · COVID-19 · Brain donation · PPE · Autopsy

Introduction

On January 21st, 2020 the first case of COVID-19 in the United States was confirmed by the Center for Disease Control and Prevention (CDC) (aCDC 2020). Almost one month after initial reports were made in Wuhan, the world was beginning to comprehend the full extent of the virus and its possible repercussions (World Health Organization 2020). Many countries began to use social distancing interventions as the most effective tool to prevent the rise of cases and slow the pandemic's vertiginous advance (Matrajt and Leung 2020); some nations such as Spain and Italy made it mandatory for citizens to abide by the quarantine orders (Oksanen et al. 2020). However, it was not until March 11th, 2020 that the World Health Organization declared the outbreak a global pandemic (Cucinotta and Vanelli 2020). By this date, New York City confirmed its first fatality associated with the virus (Gross et al. 2020), and shortly after, this metropolis became the new epicenter of the pandemic (Gross et al. 2020). The health care system and funeral services industry inevitably became overwhelmed by a significant rise in the number of deaths (Vieira et al. 2020).

Since then, the virus has caused numerous changes in the world's economy and the dynamics of social interactions and mental health showing that the consequences of the pandemic extend beyond the loss of human lives (Bondi and Lannitelli 2020). Harvesting brains in the midst of the COVID era has raised

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new challenges for those involved in the *Essential Tremor Centralized Brain Repository* (ETCBR), which is situated in the New York Brain Bank (NYBB) at Columbia University. The act of brain donation is a generous and selfless act, and is a crucial component for research to understand human neurologic diseases. Brain donors and their families work with ETCBR personnel for many years to obtain clinical evaluations and establish a detailed brain donation plan (Trujillo Diaz et al. 2018). For more than 15 years, the ETCBR has collected brains from donors all over the United States (Gillman et al. 2014) and the current circumstances have not been cause for exception.

The following reflection describes the issues encountered during ten donations in the states of New York, New Jersey, Arizona, Michigan, Illinois, and Washington from April to June 2020. It gives special mention to how families faced grief during a world crisis.

Will you accept the donation? Uncertainty faced by brain donor's families during the COVID-19 crisis

When my father passed away, one of my priorities was to make sure his last wish of donating his brain came true. After years of planning I couldn't help but wonder if it was feasible in the current world crisis. - Anonymous next of kin.

For those involved in the world of brain harvest, the intricate steps involved in tissue banking are well known. The final process begins with the family notifying the program of their loved ones passing and giving consent for the donation to take place. Shortly after, a pathologist, technician or diener is informed and the organ is removed. Finally, the body remains in the custody of the funeral home chosen by the participant according to their previous arrangements (Trujillo Diaz et al. 2018). The tissue is later processed and stored at the NYBB.

Between April and June 1st 2020, ten ETCBR participants from New York, New Jersey, Washington, Arizona, Michigan, and Illinois passed away and the brain bank coordinators were contacted to initiate the plan for the harvest. In each case, the next of kin asked the same opening question: *will the study be*

able to accept the brain? Beneath the surface of this inquiry lay another: how would the uncertainty of COVID-19 impact the carefully crafted donation plans?

In the United States more than 800,000 Americans live in assisted living facilities (ALF), 52% are older than 85 years and 30% are between 75 and 84 years of age (Jeng et al. 2020). Since the elderly are more susceptible to complications caused by the coronavirus, such as pneumonia, respiratory failure and death, the potential fatal consequences are a matter of concern in ALFs (Armitage and Nellums 2020; Jeng et al. 2020). At the same time, the design of these residences, with common areas and staff tending to many elders at a time, make them even more prone to the transmission of the virus (Yen et al. 2020). By April 2020, more than 20 states reported cases in such facilities. Of these institutions, several were under investigation due to the high number of cases among residents (Jeng et al. 2020).

The CDC recognized the potential threat for high rate of transmission in ALFs and recommended early in the pandemic they should institute social isolation measures despite the psychological repercussions of social distancing in the elderly (Armitage and Nellums 2020; Yen et al. 2020).

The ETCBR's inclusion criteria require the potential brain donors to be older than 75 years; thus a high percentage of our participants are under the care of ALFs. The study was placed in a delicate situation upon the passing of these residents in ALFs: the cause of death could be related to COVID-19 or the participant could have been asymptomatic at the time of death (Mizumoto et al. 2020). Furthermore, the NYBB had decided to refuse tissue with a positive COVID-19 polymerase chain reaction (PCR) result, given the risk to autopsy personnel in working with fresh unfixed specimens.

To be able to reassure the family members and design a system to determine which donations could be accepted, the donors had to be evaluated individually. First, a nurse or health care personnel who tended to each participant answered a set of questions screening for COVID-19 related symptoms (Etkind et al. 2020). Afterwards, the study inquired about the number of cases reported in such facilities since the coronavirus outbreak. The medical history of the patient was one of the last things to be discussed: chronic diseases, recent hospitalizations and events

leading to death. Performing a post-mortem PCR was possible for only one participant.

Based on the information collected, the study was able to collect data on possible exposure to COVID-19, consider the likelihood of transmission, and then classify the donations based on risk. The participants grouped as low risk had no signs of coronavirus infection, no cases had been reported in their ALFs, and during their last weeks they had been in hospice care with limited contact with family members and other residents. High risk cases did not present COVID-19 related symptoms, but there were several coronavirus cases reported in their living facilities. However, terminal diseases and chronic cardiovascular problems offered plausible cause of death and helped reduce the possibility of the participants being labeled as definite COVID19 cases.

Funeral arrangements: overwhelmed funeral service providers in the city of New York struggle to cover the demand for funeral arrangements

I flew from Europe to LaGuardia to be with my mother in her last hours... I never imagined what I would find in New York City. After she passed, I rapidly learned that funeral homes were completely booked. I spent 48 hours trying to find a place for my mother while her body was stored in a container outside of the hospital. The prospect of a common grave loomed over my head as perhaps the only available option. - Anonymous next of kin.

The health system in the United States has been overwhelmed since the pandemic started. First responders, nurses, and doctors have in many instances worked around the clock to be able to attend to and save the lives of thousands of patients seeking medical care. Countless acts of kindness have supported this workforce, from personal protective equipment (PPE) donations to food drives for clinical staff. However, as much as the living were being cared for, the dead also posed a challenge to the public administration, particularly in the state of New York.

Never before have funerals become such a complicated and uncertain social ritual. At the beginning of the pandemic, the public health recommendations in many countries prohibited washing bodies for funeral arrangements and mandated cremation or burial

within 24 hours of the time of death (Crubezy and Telmon 2020; Gonzalez et al. 2020). It was later determined that the transmission of the virus from corpses was low, allowing governments around the world to ameliorate the established measures and extend the timeframe for inhumation. However, vigils and family gatherings to honor the dead were forbidden since they violated social distancing measures (Gonzalez et al. 2020). The change in recommendations encouraged the creation of temporary morgues in the form of refrigerated trucks, which became prevalent worldwide due to the unprecedented number of decedents (Gonzalez et al. 2020). Furthermore, if family members did not claim the bodies or the next of kin failed to cover funeral arrangements, common graves were used to dispose of them.

New York City confronted the same challenges faced by previous epicenters between March and July 2020. With Bronx and Queens leading the list of United States counties with the most COVID-19 cases and deaths in May 2020, morgues were at their maximum capacity (John Hopkins Coronavirus Resource Center 2020). Suddenly the containers for storing bodies, or so-called “Mobile Morgues,” were parked on the streets as if it was a normal occurrence (Feuer and Salcedo2020).

Funeral homes, unable to respond, were forced to create waiting lists for families requiring their services. Cremation or burial could take from weeks to months since crematories and cemeteries were also saturated. Meanwhile, many other families that could not afford funeral arrangements had to turn to common graves as the final resting place for their loved ones.

In this spiral of events, a brain donation seemed almost impossible. Funeral homes are the link between the donor and the pathologist performing the procurement (Trujillo Diaz et al. 2018). These institutions will lend their facilities for the brain removal to take place. Between April and June 2020 the space available for such activities had been scarce due to the piling up of corpses. The unknown COVID-19 status of most of the bodies stored increased the risk of exposure for the pathologists collaborating with the study.

One particular ETCBR donation in New York City stood out among the others. A family spokesperson faced the decision of using a common grave since no funeral home could accept the body. That night, the research team and the participant’s family made call after call only to receive the same answer every time, -

“we don’t have the capacity to help you, we are really sorry.” Most funeral homes did not have enough storage, some had already committed to several families, and others were charging higher rates for their services. A clear picture of an overwhelmed funeral industry emerged as described by the *US News and World Report* (Schulte 2020).

In the end, after hours of searching, a funeral home accepted the family’s request. Nonetheless, the taste of reality lingered in the air. That day the unfortunate reality of the coronavirus crisis was made clear to the study team. The fact that a next of kin had no choice but to forgo a funeral in order to clear space for future decedents was heartbreaking.

Pathology services: concerns about potential exposure to coronavirus and challenges to safe brain procurement

I understand that some pathologists might refuse brain donations but if I have the protective equipment needed to keep doing procurements then I’ll do it. To stop working is not an option for me. – Anonymous morgue technician.

Coordinating a brain bank with potential donors all over the United States is a challenging endeavor even under ordinary circumstances. A successful donation relies on pathologists or medical examiners performing the procurement on our behalf. However, during the COVID era, many health professionals abstained from collaborating with the study. Since the outbreak of the virus in the United States, pathology services have been taking precautions nationwide to protect their personnel from infection.

In the United States 315,531 COVID-19 cases were reported between February 12th and April 9th and 9282 patients were health care personnel (HCP) (Center for Disease Control and Prevention b). Out of this number, 1423 HCPs reported contact with a laboratory-confirmed COVID-19 patient. Nonetheless the CDC reports that the number of affected personnel has been underestimated due to asymptomatic infections (New York City Department of Health and Mental Hygiene 2020). As of July 14th 2020, documented COVID-19 infections in HCP were 98,851 with 531 deaths. (Center for Disease Control and Prevention 2020a, b, c)

In April, at the height of the pandemic in NYC, the problem was enhanced by the shortage of PPE on the front lines (Boskosi et al. 2020). Furthermore, having the supplies was not enough; frequent replacement of N95 respirators, face masks, gowns and gloves is also necessary for the safety measures to work (Zhang et al. 2020). The ETCBR faced all of these issues and numerous restrictions on brain removals. Finding technicians and pathologists who would agree to fulfill our participants’ will was not an easy task. The majority of the professionals reached were not in a capacity to assist for several reasons: the unknown COVID-19 status of the decedent, the shortage of PPE, and the risk of potential exposure at the funeral homes where COVID-19 cases were stored (Kampf et al. 2020).

A COVID-19 PCR test was requested by many of the pathology services initially contacted for the harvest in the states previously mentioned. Furthermore, the vulnerability of morgue technicians with lack of adequate protective equipment made these harvests particularly challenging. Due to the previously limited testing capabilities, acquiring a PCR test was not possible for most of the cases located outside of New York. Many autopsy centers were not able to provide the swab and the logistics involved were overwhelming for the parties involved. To overcome these problems, we applied a clinical approach to determine whether risk of COVID-19 infection was low. Most of the donations were included in this category since several participants were either in hospice care with known illnesses and limited exposure to family members, or lived at ALFs where visitations and communal interactions were significantly restricted. The technicians and pathologists were provided with this clinical information so they could make an informed decision. Only professionals with the proper PPE and saws that would reduce exposure to bone dust were approached with the request for brain procurement. Despite the difficulties, for each of our donors during this period, a pathologist willing to perform the harvest was located and the donations were completed.

Lastly, additional safety measures had to be taken in order to transport the tissue to the NYBB. Formalin, commonly used for organ preservation, is known to inactivate the virus without significantly altering its structure (Capsid and RNA) allowing for further identification of the virus in the specimens (Guerini-

Rocco et al. 2020; Kampf et al. 2020; Zhang et al. 2020). The brains considered at high risk of exposure were fixed and stored for two weeks before they were shipped to NYBB. The low risk tissues, however, were sent fresh for extensive analyses.

The need for new guidelines and modified protocols to ensure the safety of personnel

New guidelines were drafted in reaction to the novel situation. Modifications to the current ETCBR protocol were made to ensure the safety of laboratory personnel: participants who tested positive for COVID-19 were not eligible for brain donation, and a negative PCR was required prior to the autopsy of participants performed at the New York Presbyterian Hospital autopsy service. If the donor had a previous negative PCR result, the laboratory test would be repeated to minimize false negatives. However, this additional testing did not cause a significant delay in the sensitive timeline for brain procurement. The results were available within three hours, and provided important reassurance to the technicians that they could safely proceed. Extensive banking of the tissue was possible in the New York cases since the 24-hour mark was not exceeded.

These precautions were taken to diminish the potential transmission of COVID-19 due to the bone dust generated by the saw used to open the skull. Furthermore, the safety measures were similar to guidelines for Creutzfeldt-Jakob disease (CJD) autopsies. A vacuum unit is attached to reduce the dust and the technician is required to wear a powered air-purifying respirator (PAPRs) (Zhang et al. 2020).

Whole body autopsies have similar safety requirements. Negative pressure isolation rooms are mandatory, tissue is sampled in portions instead of total en bloc organ removal, and the use of the saw is avoided, especially for opening the chest where clippers are preferred. Whole body suits with individual respirators seem to provide almost complete protection; valved fold flat and molded protection masks are considered 95% effective and are suitable for use in anticipated COVID-19 cases (Hanley et al. 2020; Perkins et al. 2020).

Between March 11 and May 2, 2020, 13,831 laboratory confirmed COVID-19 associated deaths were reported in New York City. In a matter of weeks, the morgues of the five boroughs were filled with

dozens of bodies and the workload increased exponentially. The New York Presbyterian Hospital autopsy service was no exception. Additionally, the large nationwide interest to obtain autopsies on COVID-19 infected cases, limited staff and facility resources often complicated the dynamic of the service. In response to these conditions, autopsies had to be restricted considerably and brain procurements for research purposes were not accepted.

The donors in the vicinity of the NYBB, who relied on the New York Presbyterian Hospital technicians to perform the brain donation, were suddenly left in a difficult predicament and alternative arrangements had to be made. The challenging issue was not only finding a pathologist, but also a place where the bodies could be taken for the procurement.

Under these circumstances, keeping research initiatives active became a real challenge. Even if the efforts are not entirely visible to the public, research workers are counted among the task force fighting the battle against coronavirus. Each team strives to ensure the continuity of studies in a situation where collecting data is anything but simple.

Challenges to the grieving experience:
an additional feature of brain donation during these times

My husband dedicated his adult life to Essential Tremor Research. He was so proud of being a brain donor that even during the quarantine, when I witnessed his mind decline every day, he refused to forget his final wish.- Anonymous next of kin.

It pains me to think that I couldn't spend much time with my mother before her passing. I saw her last on Mother's Day and I could tell that the absence of my visits had a negative effect on her.- Anonymous next of kin.

The feeling of completing a brain donation is, without a doubt, bittersweet. It is a difficult conversation to inform the next of kin of the successful harvest while reaffirming that their loved ones are no longer among them.

In their grief, family members always manage to express gratitude and pride in their loved one's choice,

a solace in the midst of a tragedy that will linger for years to come. During this pandemic, their words and stories resonate even more loudly and, in their generosity, they have allowed us to share their experiences through this publication.

Out of the ten brains we have harvested since the beginning of the COVID-19 era, six came from participants in ALFs and of these, four had been placed in hospice care days prior to their passing. Restrictions on visits from family members suggest that these participants spent at least a month isolated from their loved ones, unable to participate in family interactions. Many next of kin mentioned that the declining in the brain donor was more evident during this time and they felt hopeless due to the reduced amount of time they could spend together.

The heightened anxiety and depression experienced by families of donors during these uncertain times likely contributed negatively to the grieving experience leading to complicated grief (Wallace et al. 2020).

Disenfranchised grief might also be present due to the lack of public mourning or acknowledgment by the community. The limited numbers of options for expressing grief are aggravated by social gathering prohibitions in funeral homes (Wallace et al. 2020). In the context of COVID-19 with its delayed cremations, postponed funeral ceremonies and vigils conducted through video calls, the burden of loss has assumed a different meaning.

A sense of normalcy is found at the end of this winding road. The outcome remains as usual, the tissue is banked and processed to keep feeding our data bases. However, within a mass of continuing brain pathology analyses, the testimonies shared give special meaning to the generous and selfless act of brain donation and the dedication of research personnel to complete this final wish.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical Approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later

amendments or comparable ethical standards. The study was approved by the Bioethics Committee of the Medical University of Texas Southwestern Medical Center (No. STU-2020-0565).

Informed Consent Informed consent was obtained from all individual participants included in the study and at the time of death the Next of Kin authorized the ETCBR to proceed with the brain donation.

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