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BRAIN AND MIND ARTICLES

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Cover Art: Han Yan, Meds 2017

Description: A technique developed in 2007 and adapted here in chalk, "Brainbow" maps individual neurons simultaneously with fluorescent proteins. This method randomly expresses different ratios of red, green and blue derivatives, allowing for more than 100 different neurons and their connections to be illuminated.

Mysteries of the brain and mind

> If it seems to neurologists that our present understanding of the brain and the mind of man is hardly more than a beginning of science it may be reassuring to recall that our task is the ultimate one. The problem of neurology is to understand man himself.
>
> **— Dr. Wilder Penfield, 1965[1]**

The human brain, at approximately three pounds with an estimated 86 billion neurons,[2] is the most complex organ in the human body and arguably, the most complex structure in the known universe. It controls all processes in the body, from autonomic functions that maintain life, such as heart rate and respiratory rate, to the ability to perceive and act on our environment. The brain is responsible for our emotions and thoughts, and enables us to learn, innovate, and create. It shapes our awareness of time and space, and of others and ourselves, and ultimately makes us human. Unsurprisingly, disorders of the brain can be deadly or severely debilitating for patients, their families, and society.

Although our current understanding of the human brain and mind is indeed "hardly more than a beginning of science," technological developments over the past fifty years have enabled many problems in neuroscience to be approached. For example, advances in functional genomics and the ability to sequence the entire human genome have enabled scientists to characterize neuronal diversity at the molecular level, identify genes that contribute to disease, and examine fundamental principles of neurobiology.[3] Optogenetics has provided neuroscientists with a tool for manipulating specific neuronal activity to study the neural circuits that underlie behavior.[4] With regard to investigating human brain function and dysfunction, functional magnetic resonance imaging (fMRI) has undoubtedly become the method of choice due to its noninvasive nature, relatively high spatial resolution, and ability to image the whole brain.[5]

Supported by basic science, clinical neuroscience seeks to improve our understanding of disease processes and guide prevention, diagnosis, and treatment. Notably, insights into the neural basis of cognition, emotion, and social behaviour have the potential to transform how psychiatric disorders are diagnosed and treated. Accordingly, the U.S. National Institute of Mental Health launched the Research Domain Criteria project five years ago to help reframe mental disorders as brain disorders based on genetics, neural circuits, behaviour, and symptoms.[6] Knowledge of brain function can also be translated into effective interventions. As an example, deep brain stimulation has become an established therapy for the management of Parkinson's disease, tremor, and dystonia, and is being investigated for the treatment of psychiatric disorders such as obsessive-compulsive disorder and treatment-resistant depression.[7]

Beyond the scientific and medical community, brain research has received considerable attention from politicians, governments, and the general public. In 2013, two major brain research projects — the European Commission's Human Brain Project and U.S. President Barack Obama's Brain Research Through Advancing Innovative Neurotechnologies (BRAIN) Initiative — were independently announced with the goal of ultimately understanding how the brain works.[8] Overall, the influence of neuroscience on society can readily be seen in mass media, literature, and film.[9] Last year, the discovery of neurons that encode spatial location and enable spatial navigation (ie the "brain's GPS") was celebrated with the Nobel Prize in Physiology and Medicine.[10]

In this issue, the UWOMJ would like to celebrate the brain and mind, and provide a glimpse at the current state of neuroscience in science, medicine, and society. A lot has changed since the time of Wilder Penfield, and although neuroscience is still in its infancy, current research and discoveries bring us closer to understanding the mysteries of the brain and mind, and human nature itself.

Jason L. Chan
Editor in Chief

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Care and curriculum

Does clinical empathy decline during medical education?

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ABSTRACT

Background: Clinical empathy has been repeatedly shown to increase patient satisfaction and improve clinical outcomes; therefore it forms an important cornerstone of the physician-patient therapeutic relationship. While some studies have shown that empathy in medical students decreases over the course of their education, other studies have contested these findings.

Purpose: This paper reviews studies and relevant literature in order to explore the relationship between medical education and clinical empathy, and in particular, the difference in results between those studies that demonstrated a decline in clinical empathy and those studies that did not.

Conclusion: Study design and methodology, differences in clinical culture, and differences in curriculum were identified as three possible influences that explain the lack of consensus in the literature. This paper recommends a twofold approach to further research in the field of clinical empathy development. First, future studies examining this phenomenon should focus on longitudinal designs that incorporate objective measures and patient factors rather than relying exclusively on cross-sectional studies utilising self-assessment. Second, medical schools should be encouraged to adopt or develop techniques to assess the clinical empathy of their students and implement solutions to mitigate a decline in empathy if required.

INTRODUCTION

Clinical empathy, or "the ability of the physician to understand a patient's experience, to communicate and confirm the understanding with the patient and then to act in a helpful and/or therapeutic manner",[1] is central to fostering therapeutic relationships with patients and their support network.[2] Literature reviews indicate that empathy positively impacts patient satisfaction,[3–5] decreases perceived distress and ultimately leads to improved clinical outcomes.[5,6] Moreover, empathetic physicians encourage patient disclosure of symptoms leading to enhanced diagnostics[4,7] as well as improved adherence.[3–5] Conversely, a lack of empathy has been shown to have negative effects on patient care.[8]

Unfortunately, several cross-sectional and longitudinal studies following medical students through their years of study demonstrate that medical students show a decline in self-reported empathy, most noticeably after their clerkship year and continuing through residency.[6,7,9–11] On the other hand, studies confirming an empathy decline during medical education seem to be localised to the Americas, as cross-sectional studies conducted in Iran[12] and Pakistan[4] find no variation in empathy based on student year, and studies in Japan,[13] Korea[14] and Portugal[5] find an increase between early and later year students. These studies may cast doubt on the notion that empathy declines over the course of medical education, but they also point to cultural or curriculum-based factors that may explain the difference in results.

Given the importance of empathy in physician-patient encounters, and given the uncertainty in the literature concerning the nature and severity of the alleged decline of empathy in medical students, this paper will evaluate the research to assess whether or not clinical empathy is at risk of decline in medical students.

EVALUATION OF THE RESEARCH

Analysis of the available literature revealed three main themes which may be contributing to the lack of consensus regarding empathy decline in medical students: study design and methodology, differences in clinical culture, and differences in curriculum. Lessons learned from these areas may strengthen study methodology and may be used to enhance medical curriculum where necessary.

Study Design and Methodology

Any discussion regarding empathy is complicated by the ambiguity of the term; this has made the relevant research difficult to navigate[15] and created challenges when designing psychometric tools to measure it. In developing such measures, one must consider the threats to construct validity that can arise due to variations in how cultural communities define empathy.[12–14,16]

For example, it has been suggested that Japanese social cues rely less on gestures and facial expressions when compared to their American counterparts,[13] and as such, some standards of empathic communication may not be perfectly translatable cross-culturally. Great care must be taken in developing tools so that they account for such differences.

It is worth noting that the studies that did not demonstrate a decline were cross-sectional in nature, and could be subject to cohort effects; longitudinal studies following a class of medical students throughout their education would provide a more robust data set from which to draw further conclusions.[4,5,13]

Finally, all of the studies in question utilised self-report questionnaires and many used a version of the Jefferson Scale of Physician Empathy (JSPE) to construct those questionnaires. Even though the JSPE was designed specifically to measure clinical empathy, and has been reported to correlate with patient/observer scores, one must consider the role of social desirability bias when interpreting self-reported results.[4,14,17]

Differences in Clinical Culture

Both physician and patient expectations play an important role when measuring clinical empathy. For example, there is much in

the literature to suggest that patients acclimatized to an East Asian clinical context are more comfortable sharing a vertical relationship with their physician than their American counterparts, who may view such an arrangement as showing a lack of empathy.[14,18] Behaviour in one cultural context may be seen as lacking empathy while the same behaviour in another may be considered satisfactory or laudable. More work needs to be done understanding the cultural differences in patient expectations before interventions can be designed; interventions that may increase a patient's feeling of physician empathy in a traditional American context might instead create the appearance of "uncertainty, lack of competence, and weakness"[18] in a traditional Japanese or Korean context. This is of particular note when patients carry their expectations across borders, and physicians must be aware of their own cultural expectations, as well as those of their patient.

Interestingly, baseline empathy scores for medical students were lower in the Japanese and Korean studies, compared with American and Italian medical students.[18] While the Japanese and Korean students showed an increase in clinical empathy throughout medical education, physicians from these populations scored lower on empathy measures overall than physicians from the American and Italian populations. Though outside the scope of this paper, it would be worth investigating the shift of both groups compared to their respective general populations to better understand the relationship between cultural factors and clinical empathy.

The clinical culture of subspecialties can also influence empathy decline. In the studies where a decline was noted, students that indicated a preference for people-oriented specialties (eg family medicine, internal medicine and psychiatry) had higher levels of empathy at admission and experienced less decline in empathy than those who gravitated towards technology-based specialties (eg radiology and surgery).[10,17,19] This difference may be related to the emphasis that people-oriented specialties place on interpersonal communication, which may reduce patient objectification.[20] Another related factor may be the increased reliance on technology in certain fields, which shifts the focus from patients to test results.[18,21]

Differences in Curriculum

Each of the aforementioned studies focused on a single school, and thus the results may not be generalisable to all schools of that country or region. It has also been suggested that the academic culture of a school itself may play a role in the results obtained. For example, a highly competitive school with an emphasis on research may attract certain types of students, thus skewing the baseline results. This may have been the case in the study conducted at Seoul-National University College of Medicine (SNUCM), which is one of the top-ranking medical schools in Korea.[14]

Curriculum itself may play a role in fostering clinical empathy. The second year students evaluated during the study conducted in Pakistan received more patient interaction, history-taking training and examinations designed to evaluate professionalism than their American counterparts,[4] and professionalism has been shown to be positively correlated with clinical empathy.[22] This is not an isolated effect: of the four studies that do not show a decline, all have similar curriculum profiles in regard to patient-centred and humanistic training. For example, third year students at SNUCM are required to take psychiatric courses and higher empathy scores in the following year may be a result of techniques learned during these courses.[14] The first and second year students surveyed at Okayama University in Japan spent only one day a week studying medical science while the rest of the curriculum was focused on other subjects from the arts and humanities; this early academic diversification may contribute to the eventual rise of their empathy scores later in their academic careers.[13] Lastly, students surveyed in the Portuguese study were exposed to a curriculum emphasising patient-centred healthcare, humanities training, interpersonal communication skills, clerkships in urban, sub-urban and rural communities, and frequent assessments of professionalism.[5]

Based on their study of medical students at the University of the West Indies, Youssef et al (2014) theorised that a decline in empathy during later years may be attributable to an increase in stress caused by novel challenges that typically arise during this period of study.[23] This theory correlates well with a study by Brazeau et al (2010) that demonstrated a link between medical student burnout and lower empathy scores.[22] This indicates a potential point of curricular intervention for schools noting a decline in the empathy of their students over time.

PRESCRIPTIONS AND CONCLUSIONS

Based on the evidence that we have presented here, whether or not a study demonstrates a decline in empathy appears to be influenced by the sampling/study methodology used as well as the clinical culture and curriculum to which students are exposed.

The first way to approach these findings is to focus on improving the tools and methodology underlying clinical empathy research. Some improvements could include using controlled or randomised controlled studies, utilising longitudinal designs, measuring patient factors or skills-based outcomes rather than relying solely on self-assessment, and incorporating objective measures from the patient perspective to assess whether results are reflective of future performance (eg 10-item Consultation and Relational Empathy questionnaire).[3,6,24] Critically, psychometric tools such as the JSPE must continue to be validated cross-culturally and against other established measures to ensure the data collected is reliable and predictive.

The second way to approach these results is from an institutional perspective. Since few contest the value of clinical empathy, the goal should be using robust tools to: measure empathy at the institutional level, analyse potential weaknesses in the curriculum, and validate interventions designed to increase empathy. It is likely that curriculum and the wider clinical culture influence whether or not empathy declines, remains unchanged, or increases; therefore medical schools experiencing a decline should look to schools where such a decline is not present for methods to manage and enhance the clinical empathy of their students.

While the data on empathy change in medical students does not currently allow for definitive conclusions, further research will not only provide greater insight into this phenomenon, but also raise awareness of the importance of clinical empathy for future physicians.

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Tick tock

Thrombolysis & acute management of ischemic stroke

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ABSTRACT

Ischemic stroke causes morbidity and death in 55 000 Canadians each year. While acute supportive therapy is essential for stabilizing ischemic stroke patients, resolution of cerebrovascular occlusion can only be accomplished by injection of thrombolytic agents. However, older guidelines restrict thrombolysis to within the first 3 hours of symptom onset. This short window of opportunity for thrombolytic treatment is complicated by its inherent adverse reactions, making it necessary to readily identify potential stroke cases, but also to diagnose accurately to avoid inappropriate treatment. In light of statistics that identify late presentation as the most common reason for stroke patients not to receive thrombolytic treatment, and meta-analyses that now show benefits of thrombolytic treatment up to 6 hours after stroke onset, guidelines are undergoing revision to allow larger treatment windows. This, along with continuing improvements in stroke treatment access and infrastructure, will hopefully lead to better outlooks for Canadians who suffer ischemic stroke.

It is not just a cliché: every minute really does count. On average, 1.9 million neurons, 14 billion synapses, and 12 kilometers of myelinated fibres are destroyed every 60 seconds following a large vessel ischemic stroke. Reminiscent of Christopher Nolan's *Interstellar*, the ischemic brain can age 3.6 years for every hour that a cerebral artery is left occluded.[1] Unfortunately, this is not just fiction. Ischemic stroke is a leading cause of death and disability, a crippling reality for 55 000 patients across Canada every year.[2] While prevention is crucial, therapeutic options are especially effective when prompt thrombolytic intervention is possible. Given the time-sensitive nature of stroke management, it is important to be familiar with the general approach to acute stroke. We will focus on thrombolytic therapy for ischemic stroke but first, we will review the key points of stroke diagnosis.

DIAGNOSIS

History and physical examination offer vital information when an ischemic stroke is suspected. Usually, presentation will include a history of sudden onset focal neurological symptoms (Table), though symptoms may fluctuate in severity or worsen gradually. Headaches will occur in approximately 1 in 4 cases of stroke. For determining treatment options, the time of symptom onset is a critical feature of the history and should be detailed whenever possible. Ischemic stroke often occurs without pain, so many patients may not be woken by a stroke that occurs during sleep. In this case, it is assumed that the stroke began at the last time the patient was known to be symptom-free. Most presenting patients are alert, though infarction of the brainstem can cause a decreased level of consciousness. Nausea and vomiting may also occur if the brain stem is affected.[3]

As many as 1 out of 8 initial diagnoses of stroke may be incorrect, so it is important to consider all of the possible mimics.[4,5] Many of these mimics will tend to have more global presentations than most strokes, although the opposite is sometimes true.[3] For example, vertigo can often present with nausea and ataxia, mimicking the presentation of a stroke, particularly vertebrobasilar ischemia.[4] However, vertebrobasilar ischemia is more likely to present with cranial nerve deficits, such as loss of corneal sting sensation and loss of nasal tickle, and other focal symptoms (eg diplopia, dysarthria, hemianopsia, transient global amnesia). One of the most common non-stroke referrals to stroke teams is syncope due to suspicion of brain stem ischemia, for which assessment for arrhythmias and excessive parasympathetic stimulation can rule out more common causes of syncope. Of all stroke mimics, unrecognized seizures followed by post-ictal paralysis or confusion may be the most common.[4,5] Vigilance for a history of epilepsy and signs of seizure activity would direct appropriate investigations including electroencephalography. Other mimics include metabolic abnormalities (eg hypoglycemia, hepatic encephalopathy), drug overdose, neoplasia, and infection, which can be evaluated for with routine laboratory tests.[3,4]

Clinical evaluation can help differentiate hemorrhagic and ischemic strokes. Intracranial hemorrhage is more likely with the presence of coma on arrival, vomiting, severe headache, current anticoagulation therapy, hypertension, or non-diabetic hyperglycemia. However, imaging studies are still necessary to confidently rule out a hemorrhagic stroke or other vascular brain lesions.[4] The current standard of imaging is noncontrast-enhanced CT, owing to the scan's speed, availability, and relatively low cost. The target timeframe for diagnosis of stroke patients is to complete CT examination within 25 minutes of arrival, with interpretation complete by the 45 minute mark from arrival.[6] Laboratory tests should also be complete by this time and to ensure this kind of efficiency, stroke centres have to implement appropriate infrastructure.

GENERAL SUPPORT & THROMBOLYTIC THERAPY

Acute ischemic stroke can lead to rapid patient destabilization, even without initial overt failure of vital function, so protective measures are imperative for the recovery of stroke patients. This includes monitoring oxygen saturation with a pulse oximeter and

Table: Common patterns of focal neurological impairments correlated to region of infarct[a]

Dominant (left) hemisphere	• Aphasia • Contralateral hemiparesis, sensory loss, spatial neglect, homonymous hemianopia, impaired conjugate gaze
Nondominant hemisphere	• Contralateral hemiparesis, sensory loss, spatial neglect, homonymous hemianopia, impaired conjugate gaze
Subcortical & brain stem	• Unilateral hemiparesis, sensory loss • Dysarthria • Absent abnormalities of cognition, language or vision
Brain stem	• Motor or sensory loss in all four limbs • Crossed signs (ipsilateral cranial nerve & contralateral spinal deficits) • Dysconjugate gaze • Nystagmus • Ataxia • Dysarthria, dysphagia
Cerebellum	• Ipsilateral limb ataxia • Gait ataxia

[a] Adapted from Adams et al.[3]

providing oxygen supplementation as needed to maintain ≥95% O_2 saturation. Endotracheal intubation and careful monitoring of respiratory function may also be indicated if there is suspicion of brainstem ischemia or compression.[7] Myocardial infarction and cardiac arrhythmias may develop secondary to stroke, and a 12-lead ECG should be monitored for all stroke patients.[3] Fever development after stroke onset is a poor prognostic factor, and studies indicate that this should be treated with antipyretics and cooling devices.[8] Induced hypothermia has been theorized to be neuroprotective, but evidence to support this approach is still indefinite.[9,10,11]

The specific goal for thrombolysis and subsequent brain tissue reperfusion is to salvage tissue in the ischemic penumbra—tissue surrounding the ischemic core that has not been yet been infarcted.[3] This is accomplished with rapid intravenous administration of recombinant tissue plasminogen activator (rtPA), powerful thrombolytic agents that accelerate the breakdown of the fibrin meshwork of offending thromboemboli. Several drugs belong to the serine protease class of rtPA (alteplase, reteplase, tenecteplase), and all cleave endogenous plasminogen to its active form, plasmin, which degrades fibrin. With intravenous administration of thrombolytics, 37% of patients in Canadian hospitals achieve excellent clinical outcomes (n = 1135).[12] In comparison, only 27% of ischemic stroke patients would be expected to achieve this level of recovery on standard therapy without thrombolysis.[12,13] Excellent outcome was defined as a return to the level of function prior to stroke, as assessed by the modified Rankin Scale. Since these drugs are so effective at dissolving blood clots, they come with very serious risks of hemorrhage, including intracranial hemorrhage. This is especially of concern with hemorrhagic stroke, but it is also a consideration in the treatment of ischemic stroke due to danger of conversion to intracranial hemorrhage. Understandably, active or recent bleeding are contraindications for thrombolytic therapy. Aspirin or other anticoagulants should not be given at the same time as thrombolytic therapy, as they increase the risk of bleeding.[14]

LOOKING FORWARD

Ongoing trials are investigating refinements to thrombolytic therapy, and the literature is very extensive and sometimes polarized. Many thrombolytics have been developed in an attempt to improve therapeutic benefit, to expand the window of opportunity for drug administration, and to reduce the rate of adverse events, namely hemorrhage. New drug candidates are often theorized to improve thrombolytic therapy because of increased biological half-life or improved target specificity. However, a Cochrane meta-analysis did not find adequate evidence to indicate any superior alternative to alteplase (0.9 mg/kg), the only FDA approved agent that is indicated for acute ischemic stroke.[15] Similarly, intraarterial thrombolytic administration was theorized to reduce adverse events because of more localized delivery and lower therapeutic doses, but this was also found to be unsupported.[15] The potential advantage of intraarterial over intravenous administration may be offset by the delay in drug delivery because of relative procedural difficulty.

Although initial clinical trials on thrombolytic therapy found unfavourable outcomes in patients greater than 80 years of age and patients that have had symptoms for longer than 3 hours, more recent studies have had success with expanded inclusion criteria. The most recent Cochrane review suggests patients older than 80 years equally benefited from thrombolysis, and while treatment within 3 hours is still far more optimal in all age groups (OR 0.66, 95% CI [0.56 – 0.79], n = 2187), treatment within 6 hours still significantly reduced death or dependency (OR 0.84, 95% CI [0.77 – 0.93], n = 6729).[14] Unchanged since 2001, The Canadian Asssociation of Emergency Physicians still recommends rtPA treatment within 3 hours only, while the 2010 Canadian Best Practice Recommendations for Stroke Care indicate that rtPA can be given within 4.5 hours of symptom onset.[16,17] Centres involved in thrombolysis protocol research may expand the window for treatment, so differences should be expected. London Health Sciences Centre currently offers rtPA treatment within 4.5 hours of symptom onset to patients of any age.

Despite the advances in patient outcomes, only 6.1% of ischemic stroke patients received thrombolysis throughout Canada's provinces in 2008-2009 (n = 9588). The territories were excluded in this study, leaving us only to speculate on the challenges for stroke management in these regions. Rates for utilization of thrombolytic agents were variable: comprehensive stroke centres treated 11% of ischemic stroke cases with thrombolysis, compared to 5.7% in primary stroke centres, and just 1.0% in other centres. In this same study, the reasons documented for not treating with thrombolysis included patients presenting too late in 42% of cases, neurological deficit too mild in 24%, clear medical contraindication in 5%, and no reason was documented in 25%.[18] While refining the eligibility criteria for rtPA treatment is important, these variable utilization

rates indicate that serious infrastructure improvements will also have to be made in our ability to identify and respond to ischemic stroke events. With prompt identification and management, further improvements in thrombolysis, and national coordination of stroke care, we can look forward to better prognoses for acute ischemic stroke.

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A brief review of neuroimaging using functional magnetic resonance imaging (fMRI)

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INTRODUCTION

Since the turn of 21st century, improvements in medical imaging have been considered one the greatest triumphs in the history of modern medicine. Advancements in magnetic resonance imaging (MRI) have allowed physicians to peer into human anatomy with ever greater resolution. MRI works through the magnetization of hydrogen protons in the body followed by short bursts of radio waves which are reemitted and subsequently detected for noninvasive neuroimaging. However, this technique was limited to forming static structural images without providing real-time information on brain activity or function.

Blood-oxygen-level-dependent (BOLD) MRI, also known as functional MRI (fMRI), overcomes these limitations and enables physicians to visualize the activity of the brain.[1] Changes in blood flow act as a marker for metabolic activity and thus neuronal firing, as blood flow increases to more active regions. BOLD was first developed in 1989 and demonstrated that deoxyhemoglobin (a natural paramagnetic substance) could act as contrast agent.[2] In this article, we will review the advantages and limitations of fMRI, while introducing some developments in the field.

INDICATIONS

Currently, fMRI is mainly used for research purposes but there are a growing number of specialized clinical indications. For example, prior to neurosurgery fMRI may be used to map critical areas of the brain such as the language centres.[3] It can also be used to assess brain function of patients with seizures.[4] Some studies indicate that fMRI remains promising for use as a detection tool for the diagnosis of early Alzheimer's disease.[5,6] This technology may also have wide-ranging applications for common psychiatric disorders. Patients with major depressive disorder, schizophrenia, attention-deficit hyperactivity disorder and autism were distinguished from the resting state of controls using BOLD imaging.[7-10]

However, brain activity is often variable, so clinical interpretation given the patient's context is essential. Clinicians should also consider the effect of sedation, medications and anxiety on the hemodynamic response and subsequent signal. fMRI can also be dangerous for people with pacemakers and metal valves. Nevertheless, as a fairly young technology, fMRI and its variants have the potential to become a gold standard imaging tool in neuro-medicine.[1]

ADVANTAGES

When compared to other non-invasive functional imaging techniques, the central advantage of fMRI is its high spatial resolution in the millimeter and potentially submillimeter range.[11,12] Its ability to distinguish between smaller regions of activity is superior to positrom emission tomography (PET) and much greater than magnetoencephalography (MEG) or electroencephalography (EEG), which have spatial resolution on the order of centimeters.[13] Although seemingly insignificant, such a difference in resolution is vast considering that a few square millimeters of grey matter may contain millions of neurons, constituting billions of synaptic connections.

fMRI can also detect activity deep inside the brain in three dimensional space, while EEGs generally reflect global neural activity on the cortical surface. Compared to PET, BOLD imaging does not require radioactive contrast agents or metabolites and provides higher temporal resolution.[14] Thus, it is a relatively safe imaging tool, even for children and pregnant women. Along with advancements in computational software, multivariate analysis in fMRI allows many small units of the brain to be tracked in unison, without simply averaging the activity of whole brain regions together.[1] Instead of having large areas of average brain activity, the use of these three-dimensional pixels (voxels) allows for greater spatial resolution and reduced noise.

The critical assumption that hemodynamic response indicates neuronal activity has been questioned, yet there is a great deal of evidence that supports the validity of blood-oxygen-dependent imaging. Electrode implants have confirmed that neuronal activation correlates with BOLD MRI recordings.[15] Similarly, recent advances in optogenetics have allowed the activation of specific neuronal circuits that have also been found to match the fMRI signal.[16,17] Although the scanners themselves are costly, they are common and the same platform can be used for both functional and anatomic imaging.[14]

LIMITATIONS

Despite being correlated with the electrical activity of neurons, fMRI is an indirect imaging method. Often studies are able to demonstrate correlation of a brain region with a given task or condition but cannot establish causation. Subtle small-scale changes in neuronal activity likely go undetected as they do not induce a significant change in blood flow, while routine hemodynamic variations may generate noise.[14] fMRI cannot distinguish the number of neurons firing. A hypothetical circuit may have excitatory and inhibitory signals that cancel out, but this would only be detected as generalized neuronal activity.

Hemodynamic responses are inherently slower than electrochemical ones, which can be detected by MEG/EEG in the millisecond range.[13] The temporal resolution of fMRI being on the order of

2-3 seconds means that the technique is not truly real-time.[18] Moreover, there is generally a trade-off between spatial and temporal resolution since it takes more time to acquire images with smaller voxels.[14]

In addition, the interpretation of fMRI is statistically demanding. The use of different statistical techniques can lead to subjective interpretations. Correction for multiple comparisons is absolutely necessary to reduce false positives. One humorous study demonstrated false-positive brain activity in a dead salmon when multiple comparison corrections were not made.[19]

Finally, there are currently few studies for practical clinical use, although research is actively being conducted in this area. To obtain higher resolution, MRIs with stronger magnetic fields are being developed. Although the genotoxic effects of a static magnetic field have been demonstrated at the cellular level, they are thought to be negligible.[20]

NEW DEVELOPMENTS

The basis of fMRI is to track brain function using a surrogate marker that can be detected by MRI. Thus, one avenue being explored has been to develop newer and safer intravenous contrast agents that allow sharper resolution and faster image acquisition compared to the oxygenation state of hemoglobin used by BOLD MRI. However, the benefit of these agents has not been firmly established in humans yet.

From a clinical perspective, clinician-scientists are also employing fMRI in new ways to help patients. For example, researchers at the Robarts Institute (Schulich School of Medicine & Dentistry, Western University) are using fMRI to communicate with patients in vegetative states.[21] Moreover, fMRI has the potential to become a diagnostic test to assess patients with hypoxic-ischemic brain injury, perhaps even providing a new method to determine brain death.

Another development is to use multiple modalities simultaneously to map activity in the brain. One of these combinatorial approaches is the EEG-fMRI.[22] Researchers have been able to use fMRI to guide EEG signal acquisition to map the electrical activity of neurons in three-dimensional space. The challenge with multimodal imaging techniques arises when trying to find a suitable method to synthesize and interpret information from the two very different imaging tools.

CONCLUSION

Since it was first described by Ogawa et al, fMRI technology has rapidly developed as a noninvasive method to map brain activity. While it remains for the most part a research tool, fMRI has great potential to become widely adopted in clinical medicine. Already, practical applications such as localizing key brain regions prior to surgery exist. With advancements in MRI technology and increases in computational power, fMRI will be an important player in the field of neuroimaging in the future.

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Cognitive liberty

Protecting the right to neuroenhancement

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INTRODUCTION

Advances in neuroscience and biotechnology in recent decades have opened up unprecedented possibilities for altering and modifying the human brain to enhance cognitive and mental functions. Although one gets the impression that much of the current neuroscience research in "mind enhancement" is still only nascent, in the case of certain studies it is already possible to see clearly their implications for—and consequently their challenges to—some of our current medical, legal and cultural conventions. Take, for instance, the example of recent research in a neuroscience field called optogenetics. In 2013, a group of neuroscientists developed a way of inducing a "false memory" in experimental mice. These researchers had identified a specific population of neurons in the dentate gyrus of an animal subject's hippocampus, known to be involved in memory formation and storage, that was naturally activated whenever the animal was exposed to painful stimulus (eg electric shock). These neurons would be reactivated in the future in response to the same or similar context, even in absence of the painful stimulus, producing a fear response—that is, because a "fear memory" had been formed. By reactivating these same cells artificially (using light energy—hence the name, optogenetics) in a different context than the one used to condition the original fear memory, the fear response could again be elicited in the animal subject, this time to an entirely new context—thus forming a "false memory."[1] If extrapolated to the human brain, these and similar discoveries in nanotechnology, biotechnology, information technology, and cognitive science (NBIC), open up exciting and in some cases potentially alarming new possibilities. The imaginable applications of such techniques span a spectrum, from medical therapies that could cure individuals traumatized by abuse to the ominous spectre of a government reprogramming the minds of criminals and perhaps political dissidents.

COGNITIVE LIBERTY

Recently, an attempt has been made to confront the issue of NBIC technology as a moral-philosophical problem by articulating the novel ethical concept of "cognitive liberty." According to Sententia, a leading neuroethicist on this subject, cognitive liberty is the idea that every person has a fundamental right not only to think independently (a right already contained in liberalism's commitment to 'freedom of thought,' as defended by J. S. Mill), but also "to have autonomy over his or her own brain chemistry." It would seem to follow that, as a fundamental right, cognitive liberty would require strong legal protections for the private use of neuroenhancement (NE) technologies.[2] This view of cognitive liberty as a fundamental right directly challenges a number of contemporary norms. For instance, it seems to imply the need to protect the recreational use of psychotropic drugs, a practice that is currently illegal in many places.

From a philosophical standpoint, there are opposing stances on how NE shapes the definition of being a self: the essentialist viewpoint that NE compromises what it means to be a person, and the existentialist opinion that NE is a choice people can make as the agents of their own development. According to theologian Alan Watts, there is a longstanding view within Western culture of the person as an "individual, self-determining, responsible ego."[3] Essentialists would argue that NE jeopardizes this definition of personhood and compromises the "authenticity of persons" by interfering with individuals' natural journey of self-discovery and personal growth.[4] Individuals might confuse their understanding of themselves as they are with that of their neuroenhanced selves. Conversely, existentialists would support NE, as they believe that acting as the responsible agent of one's development is a fundamental part of being a person. It follows that actively shaping who one wants to be includes how one wants to think, under the influence of NE or not. So long as these NE interventions pose low risk to health, should individuals not have the right to benefit from their enhancing effects?[3]

Ethical issues of cognitive liberty also concern the social impact of NE. On one hand, society as a whole might benefit from NBIC-related medical innovation; thus, one could argue that there is an obligation to pursue research into NBIC-related technologies such as optogenetics. Yet one might also have reason to fear that unequal access to memory- and attention-improving tools could increase social inequality within our society. In an era of competitive job markets and information overload, those who can access and afford NE may be perceived as having an unfair advantage over those who cannot. Ethicists have raised concerns over how increasing the standard of cognitive fitness within such a competitive environment might actually impede rather than enhance cognitive liberty, as non-users will feel pressured to use NE in order to keep up with their cognitively advantaged peers.[4]

LEGAL AND SOCIAL DIMENSIONS

Cognitive liberty is implicit in the freedoms of thought and action.[3,4] However, proponents of NE argue that cognitive liberty and its boundaries must be explicitly defined within positive law in order for individuals to be protected in their elective use of NE and protected from government imposition of NE.[3] Proponents of

elective NE use would argue that the value society places on bodily integrity (the autonomy of persons over their own bodies) supports the legal right to cognitive liberty.[5] Our legal system allows individuals to engage in behaviours that put the physical body at risk, such as extreme sports. Instead of prohibiting these activities, regulations are put in place to ensure safety and informed consent, and the onus is placed on the individual to determine whether the behaviour is appropriate.[4] Given that individuals are allowed to make informed decisions regarding behaviours with potential physical harms, how can behaviours with neurologic effects be criminalized? After all, the nervous system is part of the physical body. This question is especially relevant to NE with low risk-profiles, as the harm principle, which states that power cannot be exercised against a civilized community's will unless it is to prevent harm, is a precursor to criminalization.[3,6] The counterargument to this notion is that mind and body are distinct, as are our understandings of these entities. Injury to the body is well researched, whereas the definition of "illegitimate mental harm" remains unclear.[4] Critics of NE would argue that it is counterintuitive to draft policies in support of NE while our understanding of the mind remains limited and fully informed decisions about its use cannot be made. Nevertheless, as our knowledge of brain function is expanding, policy-makers must consider explicitly defining cognitive liberty within positive law in order to lay the foundations for safe and regulated use of NE in the future.[2]

Although no court has yet ruled on a cognitive liberty case, there are precedents in other areas of constitutional case law that help us predict how courts might decide on the question of cognitive liberty in the future. Constitutional guarantees of individual rights in Canada and the United States strongly reflect the harm principle, yet the courts have not applied this principle in a consistent or unqualified way. Rather, the courts have restricted individual liberty in a wide range of areas of private life, such as prohibiting the recreational use of some drugs (methamphetamines) and not others (nicotine and alcohol); allowing the sex industry to exist, but banning prostitution; and allowing self-harm, but only up to a point—namely, not to the point of suicide. The reason for this is that the courts have recognized other principles enshrined in the law that are distinct from the harm principle. Section 1 of the Charter of Rights and Freedoms accepts that "reasonable limits" to fundamental individual freedoms may be prescribed by law in order to uphold a "free and democratic society," and in accordance with this constitutional provision the Supreme Court of Canada (in *R. v Oakes*) has established precedents for limiting individual freedoms as a way of defending "collective goals of fundamental importance."[7] Thus, for example, in 1993 the Canadian Supreme Court ruled in *R. v. Tremblay*, a case involving sex trade workers in Quebec, that the law may restrict individual liberty in accordance with a "community standard of tolerance"—in this case, for acts of "anti-social" indecency. The court considered this community standard to be a legitimate imposition on individual liberty that was consistent with a liberal constitution.[8]

In these and other such cases, the courts have recognized the need to balance the common good against individual autonomy, following a long tradition of democratic thought, from Aristotle up to the intellectual founders of the Anglo-American republic, that has understood a functioning political order as deriving at least some of its stability from a certain moral consensus or majority opinion—whether that opinion is more enlightened, or less.[9,10] The question, then, is whether it is likely that the majority moral opinion can now or will in the future be able to tolerate such practices—psychotropic drugs, optogenetic memory alteration, cognitive enhancement—as are defended by advocates of cognitive liberty. For now, it can only be said that it will likely be able to tolerate some (eg certain medical therapies), but not others (eg hallucinatory recreational drugs, or their NE equivalents). This is complicated by the possibility that the majority moral opinion of a community may change over time. Democratic regulation of NE will continue to be a challenge within our ever-evolving society.

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Physician compensation structures and how they incentivize specific patient care behaviour

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INTRODUCTION

The word "altruism" is commonly ascribed to those who pursue a career in healthcare. However, looking at medicine through the lens of altruism shuts our eyes to the inherent humanity of physicians and limits our ability to provide optimal care. It is unreasonable to expect that physicians will (whether consciously or unconsciously) always prioritize ideal health outcomes in the face of varying incentives. This is especially true given that there is no single universally accepted definition of what "ideal health outcomes" would be. Unsurprisingly, a recent Cochrane review of the subject found that physician compensation models do in fact influence behavior.[1] How then can we align physician incentives with quality care?

There are four discrete compensation structures in use, with a blend of these commonly employed. Fee-for-service (FFS) models compensate doctors a set amount for each service they perform. Capitation models offer compensation based on the total number of patients under a doctor's care, regardless of how frequently each patient seeks care. Salary models offer physicians fixed remuneration that does not vary based on the services they perform nor patient demographics and are commonly employed by hospitals and community health centers. Pay for performance (P4P) models provide direct financial incentives for meeting certain specific treatment goals.[2,3]

In Canada, 40% of physicians primarily receive FFS payments (>90% of their income), 10% primarily receive salaried payments, and 1% primarily receive capitation compensation. 33% of physicians receive a blend and about 16% receive the majority of their compensation through other forms, including P4P/incentives, short term contracts, and per diems.[4]

HEALTH OUTCOMES

There are several key health outcomes which are affected directly by physician remuneration schemes. The most significant include quantity of patient visits, quality of patient care, efficiency of resource use, and physician acceptance of complex patients.[2,3]

The effect that a given compensation scheme has on health outcomes is closely correlated with the "variability" in remuneration received, which is a representation of a physician's control over their own income. FFS and P4P schemes are considered widely variable, while salaried systems are considered fixed. Capitation models fall somewhere in between, but generally produce outcomes more in line with salary models.[4] This establishes a spectrum by which we can compare the different models.

FFS models give physicians considerable control over their earning potential but in so doing create a mixed bag of externalities. It creates an incentive for physicians to provide a higher quantity of treatment to patients, as payment is dependent on the quantity delivered. FFS also incentivizes physicians to perform a high volume of procedures and tests that have greater fees attached to their provision. By extension, FFS unfortunately encourages the provision of unneeded investigations and treatments, undermining the principles of resource management, and potentially biasing physicians in favor of carrying out more expensive actions when a simpler option may suffice.[5-7]

Capitation models are perhaps the best at reinforcing the importance of preventative medicine and resource management. However, this model does not offer additional remuneration for seeing the same patient multiple times, so a physician is unintentionally rewarded for seeing a patient as little as possible. The result is an emphasis on prevention, the conservation of resources and the use of treatment plans that require little management and have fewer side effects and complications. Potential negative consequences include an adverse impact on meaningful doctor-patient relationships, and a decreased incentive to see the same patient multiple times (even when warranted) or accept complex cases.[7-13]

Salary models reimburse physicians independent of the number of patients they see, the amount of time spent with patients, and the type of services provided. Monetary incentives are significantly limited, so there is no financial motivation for a physician to work harder than the minimum or to conserve resources; however, on the positive side this also means there is no financial deterrent to spending more time with patients, taking on difficult patients, or utilizing more intensive and involved treatment regimes.[5,14]

P4P models seek to correct many of the problems inherent to FFS, capitation, and salary systems. Since 2002, Ontario has gradually introduced more P4P measures, particularly within the realm of family medicine. Such measures include incentives for providing monitoring tests to diabetics (HbA1c levels, cholesterol levels, and eye tests), administering flu shots to vulnerable populations, and many others. A recent Cochrane review showed that 6 of 7 published studies on the effectiveness of P4P showed clear positive impacts on patient outcomes.[15] The actual magnitude of these impacts however were somewhat modest, and some research has pointed out that some specific types of P4P (for example those associated with mental health and drug abuse) are in need of optimization before they become cost-effective.[16] Despite this, the effects when these incentives are fine-tuned and implemented on a broader scale are certainly worth investigating.

LITERATURE REVIEW

There are several studies that seek to quantifiably contrast physician compensation models. An analysis of family physician behavior showed that primarily-FFS physicians spent a mean 37 hours seeing approximately 134 patients every week. In comparison, salaried physicians spent only 30 hours seeing 72 patients per week. Physicians compensated through capitation fell between these figures spending 33 hours seeing 96 patients. Thus, the less variable the payment scheme, the fewer hours worked and number of patients seen.[18]

A study by Dumont (2008) showed that although the number of services provided was found to decrease with the rigidity of the payment scheme, the actual amount of time spent performing each service increased, supporting the notion that there may be an inherent balancing of quantity versus quality across payment schemes.[17] Interestingly, salaried and mixed compensation physicians appeared to use this extra time to pursue teaching or research interests, with a twofold propensity to engage in these activities compared to FFS physicians.[14]

It was found that doctors operating under less variable payment schemes (eg salary) accepted more complex patients, including Aboriginals, low income patients, and those suffering from substance abuse, mental health problems, and/or homelessness.[5-11] Salaried physicians saw 2–3 times more complex patients on average than FFS physicians, while mixed compensation physicians saw approximately 1.5–2 times more than FFS physicians.[17]

In a general sense, the literature supports the theory that more fixed models of compensation emphasize preventative care, following the logic that healthier patients are seen less often, minimizing work for healthcare providers. Resource efficiency is also significantly improved in more fixed models with fewer unnecessary consults, procedures, and testing. However, more fixed models see a conspicuous decrease in number of patients seen and hours worked as a whole, as the financial incentive to be productive by that measure is no longer present.[4]

CONCLUSION

With some overlap, each system creates a host of beneficial and deleterious incentives for physician behaviour. The ideal compensation structure would strike a fine balance between these behaviours in optimizing key health outcomes. This ideal model would motivate physicians to see a large enough number of patients to reduce barriers to access, but small enough to ensure each patient receives adequate time and attention. It would ensure doctors do not discriminate against patients for being too complex, and ensure the feasibility of spending lengthy amounts of time with patients who require it. It would also create strong incentives for efficient resource use, limiting the provision of unneeded services.

Since the practice of any two doctors within the same specialty can vary widely, a rigid salary model is not a practical nor equitable choice for the majority of physicians. A salary model is likely only appropriate as a niche form of compensation for certain practice types like emergency physicians, rural doctors with a small patient base, and some academic physicians.

Capitation, although forward-thinking in terms of prioritizing preventative care, encourages a potentially hazardous mindset—undermining the doctor-patient relationship and decreasing the frequency of contact points with the healthcare system. Current data supports the notion that capitation may be better suited playing a role as part of a blended arrangement than as a sole method of remuneration.

In the short period of time P4P has been in use, it has been utilized largely as an experiment of limited scope, but the results of this experiment are quite promising.[18-23] More research should be done to determine what services are in need of incentivizing, and what magnitude of incentive motivates behavioral shifts. A harmonized FFS-P4P blend represents a tremendous opportunity to revolutionize medical care.[10,24,25] Change is always difficult, but such a change would likely be popular for both physicians who would gain increased autonomy and patients who would benefit from improved outcomes. If Ontario could garner enough political capital to embrace such a change in policy, it has the opportunity to become a leader in applying economic principles to the provision of medical services and quality care for patients and families.

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What kills us and what costs us

An examination of the ALS Ice Bucket Challenge

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DISEASE BURDEN: A CHANGING LANDSCAPE

Over the 85 years this journal has been publishing, medicine has adapted to the changing landscape that is disease burden. In 1930, the majority of diseases that medicine fought were infectious in nature. Influenza, pneumonia, tuberculosis, and gastrointestinal infections were the top killers. After 85 years of scientific advancement, infectious diseases have become well controlled in the developed world, and the population no longer fears these ailments. In 2015, different beasts threaten our lives—heart disease, cancers, and chronic airway diseases comprise the majority of our disease burden.[1] *Valar morghulis*—all men must die. As medicine saved patients from acute conditions, they began living long enough to die from chronic diseases. As the disease burden shifted, so too did the attention and anxiety of the population, which in turn shifted one of the most important drivers of medical progress: funding.

A FUNDING DISPARITY

According to Jones and colleagues, the "goal [of medicine] should be an integrated policy under which health care and public health programs together fully address the disease burden,"[1] This implies that funds should be allocated in proportion to the disease burden they represent; for example, since heart disease is the major contributor to disease burden in North America, it should receive the greatest amount of funding. However, this is not the case. According to the NIH, while heart disease causes more deaths than any other disease, in 2006 it received only 3.3% of NIH funding ($398 million), while HIV/AIDS, with a prevalence ten times lower, received seven times more (~$2.9 billion). The funding disparity is pervasive: together, HIV/AIDS, diabetes mellitus, perinatal conditions, dementia, and alcohol abuse account for 49% of NIH research funds, but none of these conditions are listed in the top ten causes of mortality.[2]

ALS ICE BUCKET CHALLENGE – A CASE IN POINT

This funding disparity extends beyond government funding to publicly raised charity funding. The most recent example of a disconnect between disease burden and funding raised through charitable donation is the viral phenomenon of the ALS Ice Bucket Challenge. Amyotrophic lateral sclerosis (ALS), also known as Lou Gehrig's Disease for the baseball player who made it famous, is a progressive, incurable, neurodegenerative disorder causing muscle weakness and eventual death. It is the most common form of motor neuron disease and upon diagnosis, it has a median survival of 3-5 years. Prevalence rates range between 2.7 and 7.4 per 100 000 across North America and Europe, with the disease being slightly more common in men (M:F ratio of 1.3-1.5:1).[3]

ALS recently made waves in the media through a viral fundraising campaign involving filming the dumping of a bucket of ice water on someone's head in an effort to promote awareness of ALS and subsequently raise money for research. Most videos end with a challenge to others to follow suit.

The phenomenon began in Florida in July 2014 when a local golfer, Chris Kennedy, was nominated to do the Ice Bucket Challenge or donate money to a charity that benefitted a local child with cancer. When Kennedy passed the challenge along, he chose a charity benefitting ALS because he had an afflicted relative. A video posted to YouTube on July 15, 2014 appears to be the first incidence of the Ice Bucket Challenge being connected to ALS. Through social media, the trend exploded and spread across countries and organizations.[4]

According to CBC, more than 260 000 Canadians took part in the Ice Bucket Challenge and raised over $16.2 million for ALS, ~$10 million of which will go directly to research, and ~$6 million of which will go to supporting those living with ALS. The Canadian government also contributed $10 million to ALS.[5] This is undoubtedly an impactful contribution but the Ice Bucket Challenge is wrought with issues.

Paradoxically, the usual challenge is to perform the Ice Bucket Challenge within 24 hours or make a charitable contribution to ALS, in other words allowing people to forego donation if they complete the challenge. Many people throughout the campaign raised concerns, especially since every video showing the challenge being completed seemed to imply that dumping cold water on your head is preferable to donating to ALS. Several individuals suffering from ALS have also spoken out that the campaign reduces a debilitating and lethal disease to a social bandwagon onto which people eagerly jump without any real regard for its purpose.[6] However, there is a more worrisome issue at the heart of the ALS Ice Bucket Challenge.

According to Statistics Canada, the number of Canadians reporting charitable contributions on their income tax is decreasing (down 0.6% from 2010 to 2011), suggesting that fewer people are donating money to charity. However, the rise in charitable contributions suggests that fewer people are donating more. Further, only 15% of Canadian donations are to healthcare organizations, amounting to $1.59 billion. Charitable donations are affected by economic conditions such as the recent economic downturn, suggesting that the surge in funding for ALS may represent an equal decrease in contributions to all other healthcare charities.[7,8] This opportunity cost is the most troubling aspect of the Ice Bucket Challenge.

In 2011 (most recent data), 47 627 Canadians died of heart disease, accounting for 19.7% of deaths, yet the Canadian Heart and Stroke Foundation received only $114.5 million in fundraising donations, equivalent to approximately $2404 per individual death.[9,10] By comparison, between 700 and 1100 Canadians die of ALS each year, while the Ice Bucket Challenge alone (not counting donations outside of the challenge) raised $16.2 million in Canada; equivalent to between ~$16 200 and ~$23 150 per individual who died.[5,11] Moreover, economic costs due to cardiovascular disease in Canada in 2000 totaled $22.2 billion, representing 17% of all hospitalizations (2005-2006) and 10% of all visits to community physicians (2007).[12] Contrast this with ALS, with an economic burden amounting to approximately $182 million.[13] The discrepancy between what kills us and what costs us, and where we donate is a costly one, in terms of both dollars and lives.

Of course, the question must be raised: if we divert funding to the most lethal and burdensome diseases, what becomes of the rare diseases like ALS? Research and treatment for rare diseases remains incredibly important, and funding is scarce by comparison to the major destinations of Canada's health research funds. The top disease groups funded by Canada's health research funding agency, the Canadian Institutes of Health Research, are cancer, diabetes, cardiovascular disease, and respiratory health, representing the major disease burden in Canada.[14] This means that rare diseases like ALS need to be funded almost exclusively by charitable contributions. In fact, ALS Canada has successfully raised substantial amounts of money towards research. In 2013, over $3.8 million was raised to support ALS research—a modest sum compared to the ~$16.2 million raised by the Ice Bucket Challenge alone—however, one that is more in keeping with the proportional impact of ALS on the population.[15]

CONCLUSIONS

If we, as a society in Canada, wish to maximize the utility of our charitable donations, we might aim to be better informed as to what health problems are most pervasive and costly. The greater good of society should factor into decisions about where to direct charitable donations instead of relying solely on emotional or social motivations. Addressing this requires appropriate and balanced education. The recent ALS Ice Bucket Challenge phenomenon served as a great success for the fight against ALS, raising both money and awareness of the disease. However, it may represent a setback in the fight of society at large against the modern, chronic burden of disease. The goal is not to eliminate all funding for ALS, but rather to fund all diseases in proportion to their prevalence, economic cost, and mortality. A broad-minded society would attempt to erase the discrepancy between the diseases that kill us and cost us, and those which garner our attention. The final decision however, rests firmly in the hands of the donors.

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Separation and reunion

A short history of mind-body dualism

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> In a hospital, the body is divided into departments. One department for the ear, nose and throat, one for the eyes, one for the stomach and the intestines, one for the sexual organs, one for heart and blood vessels, and one for the soul, which is treated in the psychiatric wards.
>
> **— Karl Ove Knausgaård, *The Other Side of the Face***

As medical students trained with a mind for science, it is sometimes difficult to consider the human body as anything other than a series of anatomical parts. It is as if the human body is a great, complex machine that begins ticking early in the life of the embryo, and continues its autonomous functioning until the end, when system by system, the machine will slowly dissemble and finally lay itself to rest. The comparison of the human body to machine is called mechanization, and it is something that people have been doing since the 17th century, the mechanical century. Thinking of this kind is closely linked to materialism—a philosophy that attributes all phenomena, including mental phenomena and consciousness, to be the result of material interactions—and largely informs the way we understand the brain and mind today. When materialism influenced the understanding of the brain and mind during the 17th century however, it posed a problem for Descartes, who was trying to accord the presence of a consciousness with the theological principles of the time. Cartesian mind-body dualism considered thought processes to be distinct from the body-machine, and it ascribed the thinking properties of the mind to an immortal and immaterial soul. The brain, specifically the pineal gland, was the seat of the soul. The soul was an individual's connection to the heavens, and therefore not reduced to the materiality of the body.[1]

While the consideration of the soul with respect to the brain and mind may seem strange to the scientific-minded medical student, it is not an alien concept in medicine. Consider the two specialties that deal primarily in the brain and mind, neurology and psychiatry. Materialism is recognizable in neurology: a neurologist locates aberrant anatomical lesions throughout the nervous system and is generally able to explain neurological disease on the basis of objective findings and sound physiological reasoning. Mental illnesses, on the other hand, are quite unique in that they are almost exclusively characterized by subjective symptomatology and rarely on discrete or objective findings. At the same time, we recognize today that mental disorders can manifest with bodily symptoms. Not unlike Cartesian dualism then, mental illnesses have required the framework of a conceptual separation of mind and body. Descartes' "soul" may not have disappeared from our mode of thinking after all, but instead, as Francis Azouvi suggests in an essay titled "Physique and Moral," the concept of the soul may have simply been replaced by the psychological.[1]

The division between brain and mind had not always been so apparent in medicine. It was not until the 19th century that medicine of the brain and mind truly diverged into the two separate specialties of neurology and psychiatry. As neuroanatomists were able to locate lesions related to specific diseases, the explanation for neurological illnesses became increasingly anatomical; likewise, the understanding of germ theory and use of microscopy enabled infectious disorders of the mind, such as neurosyphilis, to be understood and treated definitively. Yet, psychiatric illness that could not be placed in the anatomical or physiological realm remained, and the understanding of the etiology of those mental illnesses was still heavily influenced by the tremendous optimism for materialism at the time.[2] It is not surprising then, that the various treatments offered at asylums were somatic in nature—aimed at correcting a flawed nervous system using methods such as hydrotherapy, electrical stimulation, and rest.[3] But in the late 19th century to early 20th century, the understanding and treatment of mental disorders would begin to look to the soul, or as it would come to be known, the psychological.

Psychoanalysis has probably been most famed and subsequently defamed by the work of Sigmund Freud, although several other prominent neurologists, psychologists, and psychiatrists have made major contributions to the psychoanalytic movement and its resultant schools of thought. In the absence of disease-specific brain abnormalities, proponents of psychoanalysis recognized that some illnesses appeared to have no discernable organic basis, and theorized that psychological causes originating in childhood experiences and the unconscious were the root of mental disease. Treatment was thus focused on techniques such as dream interpretation, free association, or transference, which did not aim to alter a physical aberration related to mental disease, but rather to subjectively explore the mind. The immaterial nature of a patient's "psychology", therefore, was investigated and manipulated in order to diagnose, treat, and sometimes cure mental disorders.

At the turn of the 20th century, the connection between the body and mind in the history of medicine was not well defined. Both brain and mind had been implicated as the cause for mental and somatic disorders, and manipulating both the body and the mind had been considered as treatment regimens. Today, it is clear that a more modern understanding of the brain and mind incorporates a

unity between the two; thus over the course of the 20th century, we would come to see the divergent relationship of the brain and mind converging once again in medicine.

The union of the structural and abstract theories of the brain and mind began in the late 19th century, but did not come to popular attention until the 1930s.[4] In 1935, the first frontal lobotomy was performed in Lisbon, Portugal by Egas Moniz, a professor of neurology, and Almeida Lima, a surgeon. The principle of the surgery was based on research that showed the association of the frontal lobes of the brain with temperament and behavioural control. Proponents of lobotomy surgery believed that dysfunctional behaviour was caused by pathological material located in the frontal lobes. Ablating the pathological tracts of the frontal lobe was the goal of the therapy. The side effects from the procedures performed were numerous: while some patients became more docile after the operation, others experienced an increase in impulsive behaviour, lack of initiative, and reduced ability to think or plan clearly. Effectiveness of the procedure was strongly debated, and it was popularized by the media as one of the greatest medical blunders of the time; however, though infamous, frontal lobotomy has contributed greatly to the study of mind and behaviour, particularly by demonstrating the role of neuroanatomy in human psychology.[5]

Three years after the first lobotomy surgery was performed in Portugal, two Italian physicians, Lucio Bini and Ugo Cerletti, completed the first session of electroconvulsive therapy (ECT) on a catatonic patient. This initial use of ECT relied on the understanding that electrical stimuli could be used to induce seizures in order to treat psychiatric abnormalities. The 1938 treatment was a success, and even though the exact mechanism remains elusive, ECT is used today for treatment of major depressive disorders in select patients.[6] The use of ECT was closely followed by treatments established in psychopharmacology. The introduction of psychopharmacology began in the early 1950s, with the first wave of psychotropic medications providing a treatment option for previously untreatable psychiatric conditions.[7] The therapies were based on an understanding that neurochemical imbalances in the brain can precipitate psychological disorders, and offered yet another physiological mode of viewing the interaction between brain function and mental phenomena.

Today, it is recognized that a combination of psychotherapy, medical therapy, and even surgical therapy can be effective in treating mental illnesses.[8] But unlike a pathogen being eradicated by an antibiotic, or a structural defect being corrected, individual patient responses to psychiatric treatments are unique; that is, those that respond to some therapies may not respond to others, and the response cannot always reliably be predicted. In light of these enduring limitations of modern medicine, it causes one to question how far we have come from the lobotomy surgeons of the past.

The scientific investigation of the brain and mind has made great strides over the past century in order to advance the study of mental disorders. Improvements in surgical techniques and imaging modalities will only act to further advance the understanding of the brain and mind. The trouble of course is that there is still much to understand before we can arrive at a complete understanding of mental disorders. The Diagnostic and Statistical Manual of Mental Disorders (DSM) is just one example of how psychiatric medicine is still largely reliant on subjective symptomatology. Despite the impressive research in functional neuroanatomy and neurobiology being undertaken, there still does not exist a laboratory test, or diagnostic imaging that can reliably identify psychiatric illness. This may be because the brain and mind is one of the most complicated areas of medicine that humans have attempted to understand. No other anatomical structure contains such a vast amount of information transmission to decode. If one considers that the knowledge we currently have may represent only the tip of the iceberg, the fact that many of the treatment regimens we use today work for patients can seem miraculous. So if the discovery of how the mind works is still ahead of us, we must somehow create a model of the brain and mind that does not rely on the purely physical or the purely psychological. It seems that despite our vast increase in knowledge since the time of Descartes, not much has changed in the fundamental theory of body and soul.

In *A Scandalously Short Introduction to the History of Medicine*, Jaclyn Duffin warns us that the over-mechanization of the 19th century risked the loss of insight into the mind-body connection.[2] But increasingly the culture of medicine has been reaching back to incorporate the subjective patient experience to include a spiritual, cultural, and psychological understanding of illness. In the 21st century, perhaps a rigorous pursuit of knowledge will not cause us to lose sight of the mind-body connection, but instead, enlighten us with a greater appreciation for the body and the soul. This happy marriage of objective science and subjective patient experiences may be the aspect of modern medicine that allows for a deeper understanding of the mind-body connection, and ultimately, creates a culture of medicine that reserves a space for the soul.

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A day with an orthoptist

Jeffrey Law (Meds 2016), Charles Yin (MD/PhD 2021)
Reviewer: Charla Snow, BSc, OC(C)

CASE PRESENTATION

The patient was only 6 years old but he had already been to the hospital almost a dozen times. Today, as he was led to the examination room, he clung tightly to his mother's side. When asked to take a seat in the examination chair, he began to cry. Although he had been to the hospital more often than most kids his age, he clearly didn't find the setting enjoyable and he didn't want to be separated from his mother.

The patient had mild exotropia (outward deviation of the eyes) from an early age. While he had never explicitly complained of vision problems, he had a history of squinting frequently and turning his head in an attempt to see more clearly. His mother, on several occasions, had further suspected him of "seeing double". On examination, the patient was diagnosed with amblyopia and strabismus, and placed under the care of Charla, an orthoptist at St. Joseph's Hospital, London.

On this occasion, the patient was very distraught by being in the examination room. Charla was reluctant to have him take a seat because he obviously wanted to be with his mother. Luckily, Charla had a number of toys she kept in the office that she was able to take out and have the patient play with to distract him.

The clinical exam comprised of a cover test for type of ocular deviation, horizontal and vertical prism bars to measure the size of strabismus, Worth's four light test for assessing degree of binocular vision and suppression and having the patient go through an image book and choose the image that looked "3D" in order to assess binocular vision.

Over the course of the 30-minute appointment, a drastic change overcame the demeanor of the patient. He had transformed from being quite distressed to more comfortable and actually seemed to enjoy the various "games" that made up his exam. The patient and his parents left the office with instructions to patch the unaffected eye in order to strengthen the muscles in the weaker eye and restore proper vision and alignment.

DISCUSSION

The 6-year-old boy with amblyopia and strabismus was one of many patients I saw with an orthoptist during an observership in the ophthalmology clinic at St. Joseph's Hospital. Prior to my observership, I had never even heard of the profession. Luckily, I got to spend the day with Charla Snow, a practicing orthoptist at St. Joseph's.

Orthoptists are allied health professionals who specialize in the study of eye movements, eye alignment and binocular vision.[1] Orthoptists work closely with ophthalmologists in managing disorders such as amblyopia and strabismus. While ophthalmologists formulate and implement surgical interventions, orthoptists provide primary care in the assessment, diagnosis and non-surgical treatment of optical complaints.[1]

Strabismus is a condition in which the eyes are not properly aligned. It is caused by an inherently misaligned eye or by a lack of coordination between the extraocular muscles, preventing the eyes from being able to focus on the same point in space.[2] Symptoms include diplopia, eyestrain and loss of depth perception.[2] In young patients such as the 6-year-old from the case presentation, strabismus is particularly worrisome because of the risk of developing amblyopia, a condition in which the brain compensates for the lack of ocular alignment by suppressing vision in one eye.[3] The result is a form of cortical blindness where connections between the eye and the brain do not develop properly and the brain consequently ignores the images coming from that eye.[3] In the management of strabismus and amblyopia, orthoptists use a combination of glasses, occlusion (patching) and prism therapy.[1] Orthoptists also monitor and reinforce the treatment plan by meeting with the patients on a regular basis and offer support and guidance to the patient and his or her family.[1]

Orthoptists work with a patient population that ranges from infants just a few months old to seniors, but the majority of their practice deals with children. As such, orthoptists have special skills that facilitate working with this age range.[1] In general, children have shorter attention spans and are more difficult to examine than adults.[4] As such, orthoptists use a variety of tests designed to work within the brief window of a child's attention span. For example, in order to check extraocular eye movements, Charla would have the children track a toy with their eyes. The tests are also customized for various age groups: the younger children were given the simpler task of naming shapes, while the older children were given the more complex task of naming letters.

During my day at the clinic, I learned that orthoptics training is at least two years in length following an undergraduate degree, and often includes a third thesis year for the completion of a master's degree.[5] The curriculum involves learning the unique anatomy, physiology and clinical skills required to excel in such a specialized career. Just like medical schools, orthoptics programs in Canada are accredited by the Canadian Medical Association and all trainees must write a 3-part national examination set by the Canadian Orthoptic Council.[5]

When we had a break between patients, I asked Charla where orthoptists fit into the larger scheme amongst optometrists, ophthalmologists and general practitioners. I was told that her practice has a very specialized scope of practice and orthoptists are able to specialize in studying ocular motility and visual development.[1] Although orthoptists cannot perform surgeries and require an ophthalmologist to work with them, having an orthoptist involved in patient care means the management and treatment can be monitored more closely, enhancing the quality of patient care and overall sense of patient satisfaction.[6,7]

CONCLUSION

Towards the end of the day, I asked whether Charla ever ran into conflicts with other members of the ophthalmology team. She told me that having the ophthalmology clinic centralized at one hospital makes them a tight-knit group and contributes towards a high level of interprofessional collegiality. Although there are occasionally differing opinions on the final diagnosis or different thoughts about how a patient should be managed, Charla emphasized the importance of trusting the skills that each specialty brings to the table. Spending the day in clinic with Charla really brought home to me that, regardless of what medical specialty I end up choosing, developing a trusting and respectful relationship with allied health professionals and working together effectively would be critical to providing the best patient care possible.

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Optogenetics

Illuminating the brain

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ABSTRACT

The nature of the brain presents many challenges to its study, from the intricacy of its structure to the minute timescale at which it functions. Traditional research techniques, such as electrophysiological manipulation and pharmacologic intervention, are limited by their inability to operate with both high temporal and spatial resolution. Optogenetics is a novel technology that provides unparalleled specificity in this regard. It allows for control of neural activity with high temporospatial resolution in a manner that does not disrupt the normal physiology of the system. It is an elegant research tool that uses light to control the electrical activity of genetically defined neuron populations with millisecond precision in systems as complex as freely moving live animals. First demonstrated in 2005, it was identified by *Nature* as the Scientific Method of the Year in 2010 and is currently used by thousands of labs across the world. It has already yielded new discoveries in a variety of neuroscience subfields and will undoubtedly continue to do so. The technology currently exists in a basic science capacity, but has potential for therapeutic application. It is not without its own limitations, but has advantages over more crude alternatives and has proven to be a powerful tool in the hand of the neuroscientist.

INTRODUCTION

The human brain is the most intricate organ in the body and has been referred to as "the most complex object in the known universe."[1] A recent estimate put the number of neurons in the human brain at 86 billion[2] with each neuron forming hundreds, if not thousands, of individual connections through which they communicate on the millisecond scale. The complexity of its structure and function is astounding. For neuroscientists, this makes the brain both irresistibly fascinating and prohibitively difficult to study. In order to overcome the challenges that result from the inherent complexity of the brain, investigators must be creative and innovative in their approach to its examination. The recent development of a research tool known as optogenetics provides an ideal example of such innovation.

BACKGROUND

Traditional methods of study, such as with electrophysiological devices or pharmacologic intervention, have provided countless insights into how the brain operates. However, each technique has limitations. Direct electrical stimulation of tissue has high temporal resolution, but indiscriminately affects all cells around the microelectrode and thus has poor spatial resolution.[3–5] Given that specifically targeted neurons are often sparsely embedded within tissue, this is a significant drawback. Pharmacologic intervention on the other hand has high spatial resolution, as drugs can be designed to act on only certain neuron populations, but because the drug can stay in the system for anywhere from minutes to hours such an approach lacks temporal resolution.[4,5] Given the minute timescale at which the brain operates, this is also a significant hindrance.

The idea of using light as a medium to control the activity of neurons is not novel. It was speculated on by Francis Crick as far back as 1979,[6] however it was only first demonstrated in 2005.[7,8] Since then, the lab of Karl Deisseroth at Stanford University has published extensively on the topic[9–17] and optogenetics has spread to thousands of labs across the world.[18] It is an elegant technique that uses light to control the activity of genetically engineered neurons and has significant advantages over its more crude alternatives. Its significance has been recognized throughout the scientific world, notably with *Nature* naming it Scientific Method of the Year in 2010 and its early developers being honored as recipients of The Brain Prize by the Grete Lundbeck European Brain Research Foundation in 2013.

DETAILS

Optogenetics, quite literally, refers to the convergence of optics and genetics. When applied to neuroscience, it is a technology that uses light to control the electrical activity of neurons with both high temporal and spatial resolution in a manner that minimally disrupts the normal physiology of the system. Thus, it overcomes some of the limitations associated with traditional research techniques as described above.

In order to achieve this, single-component, microbial-derived, light-activated ion channel proteins called opsins are artificially expressed in the membranes of neurons. This is predominantly accomplished through the use of viral vectors carrying specially designed genetic constructs, but can also be achieved using transgenic animals.[19] Regional specificity when using viral vectors can be ensured via the use of specific promoters, by localized viral injection, and by restriction of opsin activity via targeted light delivery.[4,20] The family of proteins in play, opsins, was first discovered as a component of bacterial cell membranes over 40 years ago.[21] Since then, further research has enlarged the family and proteins have even been altered in the laboratory to be more suitable for optogenetics research purposes.[22] There currently exist dozens of opsin types with unique characteristics, thus allowing for a variety of experimental configurations.[22]

The genetic engineering techniques employed ensure that the opsins are expressed exclusively in genetically defined target population(s) of neurons and thus provide spatial resolution to the cell-type level.[23] Light is delivered via surgically implanted fiber optics[9–11] or other means.[7,20,24] Upon exposure, the opsins alter their conformation such that the flow of ions in or out of the neuron of which they are a part is altered.[22] Depending on both the type of opsin involved and the wavelength of light used, the target cell(s) are either depolarized (excited) or hyperpolarized (inhibited).[22] This use of light as the metaphorical on/off switch for neuron activity provides the high temporal resolution. The light source can be pulsed with enough speed and precision so as to reliably elicit single spikes in neuron electrical activity.[8] Furthermore, light is an ideal medium to use for this purpose as it does not affect unaltered neurons (neurons without opsins) and thus minimally disrupts normal brain physiology.[8]

RECENT RESEARCH

Before discussing relevant current research, it is important to note that optogenetics currently plays a role in basic science research exclusively. That is, its goal is not directly therapeutic, but to give neuroscientists the ability to more closely examine the brain and thus better understand how it functions. It is used in models of both health and disease with the hope that the knowledge gained will lead to the development of future therapies.

Optogenetics has been applied to nearly every area of neuroscience research[18] and in models ranging from ex vivo cell lines[8] to nonhuman primates.[20] A sample of notable work using murine models includes controlling behavior in freely moving animals,[15] increasing functional recovery after stroke,[10] mapping of Parkinsonian neural circuitry,[12] inhibiting symptoms in a model of Parkinson's,[11] eliminating cocaine seeking behavior after addiction,[16,25] and inducing REM sleep.[26] Last year researchers used optogenetics to control in vivo transcription of endogenous genes in the brain, as opposed to electrical neural activity.[27]

These represent some of the most dramatic recent advances in optogenetics, but there are countless examples of labs applying this technology to less complex in vitro systems. In vitro application of optogenetics, such as in vitro slice electrophysiology, benefits from the same principles that allow for exciting research in in vivo models, but is significantly less expensive (a few thousand dollars will provide for a good start).[28]

FUTURE DIRECTIONS

Although optogenetics has come a long way since its debut a decade ago, it remains in its infancy. There is enormous ongoing research into its refinement and further development with exciting papers being published almost monthly.[29] One intriguing topic is the development of optical systems capable of the simultaneous control and recording of neural activity. This is not possible to perform with electrophysiological devices and is just beginning to be performed using optogenetic systems. It would provide unprecedented information about the organization and function of intact neural networks.[18,20,23]

The use of optogenetics as therapy for human disease is a natural direction to look in when considering the future of this technology. This, for reasons discussed below, is a distant, but not impossible, prospect. Based on current research, it could be applied in various forms to assist in treating disease states including Parkinson's,[11,12] addiction,[16,25] stroke recovery,[10] epilepsy,[17,30] and a variety of neuropsychiatric diseases.[4,31,32]

LIMITATIONS

As with any new technology, the limitations of optogenetics are slowly appearing. Relating to basic science use, the pattern of ion concentration changes induced by opsins does not perfectly replicate the actions potentials observed in normal physiology.[29] The conductance tends to be smaller[33] and the magnitude of the ion concentration changes risks exceeding physiologic ranges.[18] Exposure of multiple opsin-containing neurons to light means their resulting activity is synchronized and, given the precise timing of neural networks, potentially results in nonphysiologic patterns of activity.[18] Furthermore, although light has desirable properties the heat created by its use poses a significant risk of damaging delicate tissue and is something researchers must be cognizant of.[28] These limitations, among many others, threaten the validity of conclusions drawn solely from the interpretation of optogenetic results.

Besides the onerous task of compiling the knowledge of neural function and dysfunction required to even hypothesize about the use of optogenetics in the treatment of human disease, a major limitation to this application is the dependence on genetic manipulation. Proving the long-term safety of gene therapy in humans to the satisfaction of regulatory bodies is an immense undertaking.[18,34] Combined with additional objectives, such as refining the methods of light delivery in intact living tissue and demonstrating therapeutic effects beyond the scope of other methods, an enormous deal of work needs to be completed before therapeutic application of optogenetics can be considered.[5]

SUMMARY

Optogenetics is a novel and sophisticated research tool. Through the convergence of genetics, optics, and neurobiology it allows for the control of neural activity with unparalleled temporospatial resolution in systems as complex as freely moving live animals. It is an elegant technique with significant advantages over more crude alternatives and has provided us with new insights into how the brain functions. With continued application and refinement it will continue to do so. It is currently applied only in terms of basic science research, but has potential for a therapeutic role in a variety of diseases.

Given its intriguing core principle (controlling the brain with light), optogenetics is a topic prone to sensationalization and one needs to keep in mind that significant limitations exist at both the basic science and potential therapeutic levels.

In closing, I paraphrase the cautious champion of optogenetics, Karl Deisseroth, who said that optogenetics, although exciting, should be viewed as only one tool among the many available to a neuroscientist.[32] Nevertheless, considering the task at hand, it is one that I would want in my kit.

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Conversations with a pediatric psychiatrist

Interview with Dr Javeed Sukhera

Han Yan (Meds 2017), Ramona Neferu (Meds 2018)
Faculty Reviewer: Dr Javeed Sukhera, MD, FRCPC (Department of Psychiatry)

In the first of three interviews in this issue, we speak to Dr Javeed Sukhera. Dr Sukhera is an Assistant Professor in the Department of Psychiatry and Senior Designate Physician Lead for Child and Adolescent Psychiatry at London Health Sciences Centre/Victoria Hospital. He is also the Academic Director of the Global Health Curriculum at Schulich. Dr Sukhera has previously served for two years on the board of directors of the Association of American Medical Colleges.

UWOMJ: Tell us about yourself, specifically your education and career.

Javeed Sukhera: I am originally from Toronto and did my undergraduate training there. I took the opportunity to study medicine in Israel, which is where I was able to further explore my interests in global health. I studied at the Medical School for International Health, an innovative collaboration between Columbia University and Ben-Gurion University in Israel. During my fourth year, I returned to Canada for an elective in adolescent psychiatry and that is what sparked my interest in psychiatry. Prior to the elective, I was was close to pursuing family medicine, but inevitably chose psychiatry. I then completed my residency in Rochester, New York, as well as my fellowship. Two years ago, I decided to return to Canada, and I came to London, Ontario.

What made you interested in pediatric psychiatry? What makes this field unique?

I think that psychiatry is very unique because it is so different from every other field in medicine. All throughout medical school, you are taught to think a certain way. In psychiatry, you have to unlearn the need to always try to find a solution or a cure. There is not always a medication or a quick fix within psychiatry, and often, there is the opportunity for different methods of patient management. Pediatric psychiatry is especially interesting because you are working with a population during a developmentally sensitive period that can have a long-lasting impact on the patient's life.

Tell us about your other academic or personal interests and how you balance that.

Between clinic, research and academic teaching responsibilities, I would roughly estimate that 40 percent of my time is clinical, 40 academic and 20 research. I was recently awarded a grant to conduct research on unconscious biases within medicine and how they affect patient outcomes. Due to my appointment, I also have several academic responsibilities. For example, I am the Academic Director of Global Health Curriculum at Schulich. At the Office of Global Health, we have worked hard to integrate global health and public health topics into all four years of the undergraduate curriculum. Specific examples include the cultural competence workshop in your Population Health course and a Health Equity Panel in the Healthcare Systems course.

Global health is something that is very important to me and is an important part of my career. The old version of global health involved going abroad and providing healthcare in countries outside of Canada. Over time, we have recognized the problem of medical tourism, but also recognize that there is a benefit to learning medicine in different cultural environments. More recently, global health is more about the patients sitting in front of us, especially in Canada, and how understanding local and global contexts helps us understand the social and cultural determinants affecting this specific patient's care. Many students struggle with the idea of global health in a local setting, but the same principles relating to cultural competency apply both locally and globally.

How would you compare psychiatry to neurology or neurosurgery? What are the similarities or differences that you see? Do you often work in interdisciplinary teams?

I would say that neurology is somewhere between psychiatry and neurosurgery. We definitely work with neurology on certain cases. The problems that we see are often biosocial in nature, and there are referrals that flow in both directions. I would think of neurology as a field that deals with the brain whereas psychiatry is a field that deals with the mind. It is on rare occasions that we might work with the neurosurgeons. More often than not, we might be consulted by neurosurgery. The main difference for psychiatry that makes it unique from other specialties is that psychiatric complaints are multifaceted and very complex. Just this morning, I saw a boy with attention deficit hyperactivity disorder (ADHD)—a very bright boy. Early on, he had acknowledged how he might have been different and he has done well working with me. Our conversation was not limited to his medication, but also the social aspects of his illness. When someone has ADHD, it affects many parts of his life, such as his education and friends, just as some examples. My treatment extended beyond offering medication and included providing the opportunity to openly speak about the challenges of being a teenager who may need to rely on medication while trying to fit in with his peers.

Tell us about your family, or hobbies you have outside of work.

I am very lucky to have two beautiful children with my wife. We all enjoy travelling, but my favourite hobby would probably be just doing nothing on a Sunday afternoon.

Do you have a memorable case to share?

There are just so many cases that are memorable. This one case that I remember is actually from when I was a fourth-year medical student. The patient was an adolescent male who adhered to Orthodox Jewish practices. He had very specific requests for his psychiatric care. For example, he refused to be touched by the female nurse. At the time, my supervisor was actually also a rabbi, and he was able to communicate genuinely with the patient. His approach showed a lot of patience and understanding. In the end, the solution that was finally agreed upon was for the patient to receive care from the nurse, who would be able to touch him with gloves on.

What do you see as the challenges/innovations within psychiatry in the next 20 years?

I think a current challenge is the bias within medicine that a lot of my patients face. You would be surprised at some of the comments that I hear from other physicians that stigmatize patients with psychiatric illness. The treatment that a lot of psychiatric patients receive is simply unfair and stems from ignorance. Especially in emergency rooms, these patients often face a lot of discrimination.

With psychiatry, there is also a great need to advocate for my patients. There are essential and vital medications or treatments that are not available everywhere. For example, some of my patients from more rural locations do not have access to a psychiatrist near them. Can you imagine that for other illnesses? For a diabetic not to have access to insulin or a heart failure patient to not be able to be pay for ACE inhibitors? It would be unheard of! Within psychiatry, there is a lot more for us to advocate for. This is a real challenge that I unfortunately see in my practice. Moving forward, there is a lot of room for improvement.

I see a lot of changes upcoming in psychiatry, especially with new psychotherapies, and psychopharmacological treatments that are being researched. So, there are some positive things to look forward to as well.

What are your thoughts about the new Diagnostic and Statistical Manual of Mental Disorders (DSM) V?

I am not a huge fan of the DSMs because I find that their categorizations oversimplify the problems that we are presented with. The DSM is helpful for providing guidelines for diagnosis, but most of our patients do not fit neatly into the categories that the DSM provides. I prefer to address the person in front of me instead of treating a formulaic diagnosis provided by the DSM.

If a medical student is interested in psychiatry, do you have any advice for them?

I would just say that there are many different facets to psychiatry. Pediatric psychiatry, for example, is very different. There is a lot to experience and see in psychiatry. Use the clerkship psychiatry rotation to explore and be open minded. You may be surprised at what interests you and what field you can imagine yourself practicing in.

Conversations with a neurologist

Interview with Dr Christen Shoesmith

Han Yan (Meds 2017), Ramona Neferu (Meds 2018)
Faculty Reviewer: Dr Christen Shoesmith, MD, FRCPC (Department of Clinical Neurological Sciences)

In the second of three interviews in this issue, we speak to Dr Christen Shoesmith. Dr Shoesmith is a neurologist and the director of the Motor Neuron Diseases Clinic at the London Health Sciences Centre (LHSC). She runs the local clinical research trials in amyotrophic lateral sclerosis (ALS) and also sits on the ALS Canada Scientific Medical Advisory Panel. She is also heavily involved in medical education at the undergraduate, residency, and fellowship levels. She is an Assistant Professor of Neurology at Western University.

UWOMJ: Tell us a bit about yourself, specifically your education, career, and personal interests.

Christen Shoesmith: After studying medicine at the University of Manitoba, I completed my neurology residency and fellowship here in London. I was fortunate enough to stay on staff after fellowship and have been a staff neurologist at LHSC since 2007.

I subspecialize in ALS and am the clinical director at the Motor Neuron Diseases clinic at University Hospital. I also have a particular interest in patients who have neurological symptoms during pregnancy.

Aside from my career, I love spending time with my husband and my two beautiful daughters who are 7 and 5 years old, and I enjoy jogging and yoga.

Why did you choose neurology?

I came into medical school with an interest in neurology, but was open to other potential specialties, which I explored through observerships. My undergraduate degree was in chemistry and mathematics, so the analytical and algorithmic approaches to neurological problems were very stimulating for me. I also loved the diverse patient population and the thrill of the diagnosis. In neurology, we see patients in their 20s through their 90s with a variety of neurological disorders. In my first two years of medical school, I attended weekly neurology teaching rounds at the adjoining hospital, and had great mentors who helped me grow in my knowledge and exposure to neurology in medical school.

When I started my neurology residency here at Western, I loved everything about the field, but it became clear early on that I had an interest in palliative care. Initially I explored neuro-oncology but I didn't feel it involved sufficient intellectual challenge for me, since the diagnosis is already there when the patient comes into your care. In contrast, working in the field of neuromuscular disease and ALS gave me the thrill of localization and diagnosis, so it was a natural fit. I also had the complete fortune of having Dr Michael Strong as my mentor in my residency and fellowship. He was instrumental in guiding me through my early career opportunities.

Thoughts on ALS ice bucket challenge?

In the ALS community, everyone is absolutely thrilled that the ice bucket challenge happened. Patients spread awareness about the disease they're living with, and the community has a much broader understanding of how ALS can affect individuals and families.

Some people in the lay media have spoken out against the ice bucket challenge saying that the funds should have been divided more equitably amongst other diseases initiatives. However, ALS rarely has its face in the spotlight or gets large sums of funding, unlike cancer or heart and stroke.

The other negative publicity issue is that people have looked at the financial statements of ALS Canada and assumed that the distribution of the new funds would be made in the same percentages as previously. However the cost of running the organization won't change substantially, so this one-time donation can be diverted directly to patient support services and research.

Is there a memorable case you would like to share?

The cases that I remember most are the ones where I have made the right diagnosis that other clinicians may have missed. It is rewarding to know that you've spent the time and energy to make a correct diagnosis. The cases where I have made mistakes or where I did not use the best clinical judgment are also memorable, as well as those cases with complex ethical issues. Some patients have displaced their anger on me about their diagnosis of ALS. I've learned to appreciate that patients have different reactions to diagnoses, and a negative reaction doesn't necessarily mean that you've provided bad care to the patient.

What can you do as a neurologist to make sure that you catch the diagnoses others have missed?

It is very important in neurology to take a great history: let the patient tell their story and not put words into their mouth. Listening to all facets of the story is really important so you can hear about the progression of their symptoms over time. Next, unlike a lot of other areas of medicine, a meticulous physical examination in neurology is still extremely important and it is vital to arriving at a correct diagnosis. To put together a diagnosis, it's important to take the time to think about what all the findings mean. You also can't be afraid to revisit a diagnosis, whether it is your own or someone else's.

The field of neurology is still perceived by many to be a field of diagnosis rather than curing. What are your thoughts on this issue?

From an outsider's perspective, there is the perception that neurology is a "diagnose and adios" profession. But neurology has

absolutely changed—it's a very different field than when I was a medical student. When I started as a medical student, there were very few treatments available for multiple sclerosis (MS). Now, we've got multiple drugs that have substantially improved the course of MS. Inflammatory conditions, stroke, epilepsy, and seizures have also seen tremendous improvements in management.

There are, of course, neurologic disorders that we can't treat yet, but there are huge amounts of research being done and I certainly think that in my lifetime, diseases like ALS will have better treatments. I never tell my patients we can't do anything about their diagnosis. I explain that we can help manage symptoms with pharmacological management and we also direct people to appropriate allied health professionals. For example, getting an ankle foot orthotic for someone that has foot drop, or getting the appropriate therapist to help with dysphagia can make a huge difference in a patient's quality of life.

How much do you interact with neurosurgeons or psychiatrists?

In London we have a Clinical Neurological Sciences department, so neurosurgeons and neurologists are part of the same faculty, sharing the same resources and physical space. At our site, there is likely more academic interaction between neurology and neurosurgery than at centres where the two specialties are under separate departments (medicine and surgery). This model allows for a shared type of care where we can learn from each other.

Where do you see neurology going in the next 20 years or so?

There will be more treatments for genetic conditions in neurology. A lot of research is being done but right now there aren't specific treatments for most genetic disorders in neurology. As well, we'll be moving more towards more personalized medicine where different genetic factors will predict different treatments for neurological disorders.

From a career perspective, what are the job options and opportunities for neurologists when they finish residency?

Unlike neurosurgery where underemployment is an issue, neurology doesn't have that problem. There are certainly many urban centres and smaller centres like Thunder Bay and Sudbury that are looking for more neurologists. The majority of the positions are not in academic institutions at the moment, but soon many neurologists will be retiring. As well, because the baby boomer population is getting older and neurological disorders are more prevalent with increasing age, there will be an increased need for neurologists over time.

If students are interested in neurology, what should they do to further explore the field?

For students who are interested in neurology, it's worth getting perspectives from different types of practices and many neurologists through observerships and electives. Medical students can also attend Clinical Neurological Sciences grand rounds, as well as neurology lunchtime rounds. The schedule for weekly rounds is available online on the Clinical Neurological Sciences website. Research is sometimes a bonus when applying for neurology residencies, but not necessary. From a preceptor's point of view, the students that are eager to learn in a clinical setting and have a basic knowledge of neurology/neuroanatomy are the ones that are teachable and a good fit for the program.

Conversations with a neurosurgeon

Interview with Dr Fawaz Siddiqi

Han Yan (Meds 2017), Ramona Neferu (Meds 2018)
Faculty Reviewer: Dr Fawaz Siddiqi, MD, MBA, FRCSC, FACS (Department of Clinical Neurological Sciences)

In the third of three interviews in this issue, we speak to Dr Fawaz Siddiqi. Dr Siddiqi is an Assistant Professor of Neurosurgery and Orthopaedics at Western University. He is the president of the Professional Service Organization and sits on the Medical Advisory Committee as well as the London Health Sciences Centre Board of Directors. He is also the course chair for the Healthcare Systems course at the Schulich School of Medicine and Dentistry.

UWOMJ: Tell us a bit about yourself, your career path and your education path.

Fawaz Siddiqi: I did my undergraduate degree in biochemistry at the University of Ottawa and came to Western for medical school. I did my neurosurgery residency training and an orthopaedic spine fellowship here, after which I came on as faculty. Clinically, I'm one of four spine surgeons in our combined neurosurgery and orthopaedic spine program at Victoria Hospital in London. My practice encompasses degenerative spinal conditions, oncology, and trauma.

What made you interested in neurosurgery? What makes it unique?

My attraction to neurosurgery happened relatively early in my career. I spent my summers after first and second year of medical school with the neurosurgical service at a hospital back home in Ottawa. Spending time with the neurosurgical team helped me determine whether it was something I wanted to do.

Neurosurgery is a challenging field to work in and it attracts people who really crave that sort of challenge. The procedures and patient population are very diverse. Neurosurgeons perform many procedures to help people with a variety of conditions. Neurosurgeons help with chronic pain through spinal cord stimulation, with movement disorders such as Parkinsonism through the use of deep brain stimulation, and curing epilepsy with surgical resections. In addition, we deal with oncological conditions of the brain and spine as well as vascular conditions, such as cerebral aneurysms and vascular malformations.

Spinal surgery itself is very rewarding. Patients come in who have a lot of difficulty walking and they can walk again after the operation. That's not something that a lot of specialties can lay claim to.

How would you compare neurology, psychiatry, and neurosurgery?

While the pathologies may overlap, the objectives and practice patterns of the practitioners are very different. That said, there is a huge amount of crossover between neurosurgery and neurology in terms of pain management, treatment for movement disorders, and epilepsy. Surgeons who work in those fields usually work in interdisciplinary teams. Epilepsy is a perfect example. You can't be an effective epilepsy surgeon if you don't have an effective epilepsy neurology partner. The same is true with movement disorder work. The bulk of my collaboration with other physicians is with oncologists and neurologists. As for psychiatry, there are more and more data suggesting that stimulation of certain areas of the brain, namely the areas of the limbic system and the cingulate gyrus, can actually help with depression as well.

Can you tell us a little bit about your Master of Business Administration (MBA) or other academic or personal interests you have?

During training, neurosurgical residents usually get a research/elective period of about 9 months. Most people will use that to do a master's degree of some sort or a research project or an elective. When I looked at the breadth of options available to me, the MBA seemed to be the most effective degree in looking at healthcare systems operationally and being able to work through some of the problems that we have such as delivery of care to our patients.

For a physician who is involved in management, it can be a very powerful tool to have in your back pocket. I encourage people to look into it as a professional career option as the healthcare system evolves and encounters new difficulties, whether it be a funding perspective or from a structural perspective. We are going to need more and more physician voices involved in these issues.

One of the current projects that I am involved with at an institutional level is collaborating on working towards achieving better physician participation in healthcare management. Since the bulk of healthcare costs actually are driven by the physician's pen, physicians need to be more engaged in healthcare institution management in order to achieve efficient healthcare delivery. Traditionally, physicians worked as islands in most hospitals and clinics with very little oversight or participation in attempting to make the system better. This archaic model has to change.

What do you think the challenges are in neurosurgery in the next twenty years?

The outcomes from primary brain tumour treatment haven't changed much in the last number of years, and the prognosis remains pretty dismal for some types of brain tumours (12-14 months median survival with maximal therapy for primary high-grade glioma). So, from a research and innovation perspective, the causative factors of primary brain tumours still remains elusive.

The other challenge is really delivery of care. The wait list for a spinal surgery can often times reach two years for consultation, and an additional year for surgery. The way we deliver consultative services to patients has to change. We can't rely on the traditional model where you have a physiotherapist, chiropractor, or family physician refer to a surgeon in isolation. We really need an interdisciplinary model of care for this specific patient population that will shorten wait times and improve evidence-based care.

What's new and exciting in your field of neurosurgery?

We are achieving a much better understanding of spinal biomechanics and becoming better at treating spinal diseases, whether minimally invasively or with open surgery. There is increasing awareness of the role of neurosurgery for epilepsy surgery, as well as for Parkinsonism, movement disorders, and chronic pain conditions.

Do you have any comments about future job prospects in neurosurgery in Canada and elsewhere?

We have not had enough jobs in Canada to sustain the number graduating from neurosurgery, so many neurosurgeons found jobs in the United States after training. Most centres in the US are still hiring Canadian-trained neurosurgeons and recognizing the Canadian training. In my year, we had three of us stay in Canada and everyone else went to the US, and as far as I know, everyone is employed and has fantastic jobs.

Are there opportunities for working abroad for medical relief purposes?

Organizations tend to recruit pediatric neurosurgeons due to the high burden spina bifida and hydrocephalus in these nations. There is a role for surgeons in medical education abroad through entities such as the American College of Surgeons.

How is the balance between family time, call-time, and day-to-day work?

All twelve members in our faculty are married, and most of us have children. I think achieving a work-life balance is very manageable. The Victoria Hospital neurosurgeons have a call frequency of 1 in 4 and we do call a week at a time, but I usually go home around 6:30 PM, and am back for meetings around 7:00 AM. In general, I'm not up every single night operating, and we have a good vacation roster. Gone are the days where people are living in the hospitals and not seeing their families.

If a medical student is interested in neurosurgery, what advice would you have for them?

The best thing to do is really explore the specialty through clinical electives and spend time with the neurosurgical service. That will give you the best perspective as to what the practice looks like and the pathology that you will be dealing with on a regular basis. It's harder if you haven't had that experience to look at it as a viable specialty option because you really haven't experienced what it's like and you have only an abstract concept of what a neurosurgeon might do. But that's really advice that I give for anybody who is looking at any specialty.

When the beat clots

Ischemic stroke in atrial fibrillation

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An emergency room physician is asked to see a 68-year-old male complaining of mild chest discomfort, intermittent palpitations, and worsening shortness of breath. The patient presented to the emergency room with an acute onset of palpitations and states a 3-month history of fatigue. At triage, blood pressure is 135/90 mmHg, respiratory rate is 16 breaths per minute, and an irregular heart rate at 125 bpm at rest is identified. Additionally, his history is notable for a 30-pack-year smoking history and longstanding, reasonably controlled hypertension. On further evaluation, the patient develops increasing confusion and light-headedness.

A 12-lead electrocardiogram (ECG) demonstrates the absence of discrete P waves and an irregularly irregular ventricular rate, diagnostic of atrial fibrillation. However, immediately following the identification of atrial fibrillation on ECG, the patient begins describing a weakness in his left hand. His symptoms progress over the next ten minutes until he can no longer lift his arm and has trouble speaking. Concerned, the emergency physician immediately begins assessment of ischemic stroke.

THROMBOGENEISIS IN ATRIAL FIBRILLATION

Atrial fibrillation (AF) is a supraventricular tachyarrhythmia characterized by uncoordinated atrial activation and subsequent diminution of mechanical function.[1] Rapid, ectopic firing of multiple atrial foci, resulting in the asynchronous depolarization of the atria, produces the characteristic cardiac arrhythmia. Due to the rapid and chaotic atrial activity, AF leads to disorganized mechanical atrial function, irregular ventricular rate, and hemodynamic irregularities, ultimately generating a prothrombotic environment.[2]

The most serious complication of atrial fibrillation is a thromboembolic event, such as an ischemic stroke, which can lead to permanent neurological damage. An ischemic stroke may occur in patients with AF either as the primary presenting manifestation of AF or in patients with previously diagnosed AF despite appropriate medical management. In such patients, a cardiac embolus most frequently originating from the left atrium is thought to be a main source of ischemic strokes in patients with AF.[3]

INITIAL ASSESSMENT OF ISCHEMIC STROKE IN ATRIAL FIBRILLATION

Atrial fibrillation is the most common cardiac arrhythmia seen in clinical practice and is an important contributor to increased morbidity and mortality, largely due to thromboembolic events such as ischemic stroke.[4,5] As a result of an acute embolic obstruction to cerebral circulation, an ischemic stroke manifests with the abrupt onset of focal neurologic deficits, with symptoms of stroke remaining indefinitely if irreversible neurological damage occurs as a result of the cerebral ischemia. As such, prompt assessment and management is key when stroke is strongly suspected. Following the assessment of vital signs and ensuring the stabilization of airway, breathing, and circulation, a focused history and physical examination should be promptly obtained.[6]

The single most influential item with regards to patient history in stroke evaluation is the time of symptom onset, defined as the last known time when the patient was at their previous baseline or symptom-free state.[1] Determining the time of ischemic stroke symptom onset is of crucial importance, and acts a main determinant of eligibility for acute intravenous thrombolysis treatment. For patients unable to provide this information at the time of presentation, consulting patient family members, bystanders, or emergency medical service personnel may be required. After identifying time of symptom onset, a thorough history and physical exam should follow, focusing on identifying the progression of symptoms, possible embolic sources, and any concomitant patient comorbidities that may impact management of an ischemic stroke. Any contraindications to thrombolytic treatment should also be assessed at this time.[6]

An initial neurological examination should be promptly performed following physical examination. Formal stroke evaluations, as guided by documents such as the National Institutes of Health Stroke Scale (NIHSS), have demonstrated clinical utility as a form of rapid neurological assessment, and may be administered successfully by a broad spectrum of healthcare providers.[7,8] The three most predictive examination findings for the diagnosis of acute stroke are facial paresis, abnormal speech, and arm drift/weakness.[9,10] Blood should be drawn to evaluate complete blood count, platelet count, blood glucose, electrolytes, cardiac markers, and coagulation studies. Furthermore, timely brain imaging remains critical to the rapid evaluation and diagnosis of patients with potential ischemic strokes. Imaging may be used to exclude the presence of intracranial hemorrhage, assess the degree of brain injury, and identify the vascular lesion responsible for the ischemic deficit. Either computed tomography or magnetic resonance imaging may be used as the initial imaging modality for the emergent assessment of patients with suspected stroke.[6]

The emergency physician, quickly recognizing the signs of stroke and noting the onset of stroke symptoms, immediately begins the clinical stroke evaluation using the NIHSS. Blood is drawn, immediately sent to the laboratory, and imaging studies are arranged. An urgent consult to the stroke service is made and decisions for early management are considered.

ACUTE MANAGEMENT OF ISCHEMIC STROKE

Following the diagnosis of ischemic stroke, timely restoration of cerebral blood flow using fibrinolytic therapy is the most effective pharmacological maneuver for salvaging viable ischemic brain tissue.[11] As previously mentioned, the single most influential item with regards to patient history is the time of symptom onset, in order to aid in determining the eligibility for acute intravenous fibrinolytic treatment. Additionally, any contraindications to intravenous thrombolysis must also be strictly evaluated.[6]

For eligible patients with acute ischemic stroke, intravenous fibrinolytic therapy in the form of intravenous recombinant tissue-type plasminogen activator (rtPA) alteplase is currently the widely accepted approach.[12,13] Timely thrombolytic therapy administered within the therapeutic window, recognized as within 4.5 hours from symptom onset, has demonstrated significant reductions of long-term disability with no increase in long-term mortality.[14,15] Most importantly, earlier treatment is more likely to result in favorable outcomes, further emphasizing the importance of timely emergency department evaluation and diagnosis of ischemic stroke.[16]

Intracranial hemorrhage remains the major risk of intravenous rtPA treatment, with early neurological symptoms associated with intracranial hemorrhage occurring in 6.4% of patients treated with intravenous rtPA.[17] Thus, strong emphasis must be placed on initial assessment and patient history to ensure appropriate selection of patients for intravenous fibrinolysis.

For patients ineligible for intravenous rtPA, a number of endovascular treatment options have become available including intra-arterial fibrinolysis, mechanical clot aspiration or retrieval, and acute angioplasty with stenting. Although these therapies may offer favourable outcomes, these alternative therapies should be pursued only in a highly selected patient population ineligible for intravenous rtPA and in centres well equipped for these modalities.[1]

Returning to the case, the initial investigations and imaging results return and demonstrate early signs of cerebral infarction and identify the site of thromboembolism. Additionally, the imaging results exclude any signs of intracranial hemorrhage. Without any contraindications to fibrinolytic therapy, and presenting within the narrow therapeutic window, the patient is started on intravenous rtPA and monitored closely for the next 24 hours.

LONG-TERM PREVENTION OF THROMBOEMBOLISM IN ATRIAL FIBRILLATION

Long-term management of patients with AF often involves three considerations: rate control, rhythm control, and prevention of thromboembolism. Initially, the AF management decision involves the determination between either a rate or rhythm control strategy; however, regardless of which strategy is pursued, attention must also be directed to antithrombotic therapy for prevention of thromboembolism.[18]

Multiple clinical strategies have been proposed to stratify the risk of ischemic stroke in patients with AF to determine which patients might benefit from antithrombotic therapy. A currently accepted stratification scheme, the $CHADS_2$, integrates elements from several strategies and identifies patients which will benefit from antithrombotic therapy. The $CHADS_2$ scoring system is a point-based system in which 2 points are assigned for a history of stroke or transient ischemic attack, and 1 point each is assigned for the presence of cardiac failure, hypertension, diabetes, and age over 75 years.[19] In patients with AF and a $CHADS_2$ score ≥1, long-term oral anticoagulation with warfarin or a new anticoagulant, such as apixaban, dabigatran, or rivaroxaban, unless contraindicated, is recommended. Patients with a $CHADS_2$ score of 0, if over 65 years, still benefit from long-term oral anticoagulation, while patients with AF and no additional risk factors need no therapy.[18] Antithrombotic therapy has been shown to successfully lower the risk of embolization in all patients with AF, however its use is associated with an increased risk of bleeding and requires monitoring for risk of bleeding complications.[20,21]

Due to the rapid response and recognition of the signs of ischemic stroke by the emergency physician, the patient suffered only minimal neurological sequelae. During the recovery from his ischemic stroke, the patient is educated on his arrhythmia and metoprolol is initiated to achieve rate control. Anticoagulation is also initiated to reduce the risk of further stroke—his $CHADS_2$ score is 3. He is followed up by a cardiologist to review the management of his atrial fibrillation and risk for recurrent stroke. Further discussions are made to ensure proper maintenance of his hypertension and discuss future considerations for smoking cessation.

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Maggots on the brain (and in it)

A case of cerebral myiasis

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INTRODUCTION

In the aftermath of a traffic collision, it can be common for emergency responders to find the victims disoriented, confused, or even aggravated. Often, this is the result of the psychological or physical trauma sustained during the collision.[1] On occasion, any number of prior medical conditions may be contributing to a victim's altered mental status. These may even be the primary cause for their presentation, complicating the situation for both the initial responders and emergency room medical staff.[2] Our case begins in just such a fashion. After a low-velocity collision, a 75-year-old Californian man was found behaving erratically and aggressively by emergency responders. Responders diligently removed the patient's hat to check for injuries. Under the hat was not an injury related to blunt trauma sustained during the collision, as one might expect, but rather a lesion with exposed cerebral matter which contained a clear infestation by maggots. The patient was subsequently brought to the emergency room for further investigation.[3]

While simple lesions of the scalp are often benign, resulting from minor trauma or common dermatological conditions, lesions which perforate the skin, bone, and meninges such as the one seen in our case are quite rare.[4] Penetrating head injuries, neoplastic conditions and severe cranial infections are the most likely suspects.[3,5,6] In the case of penetrating head injuries, gunshot wounds, stabbings, and motor vehicle collisions are the most prevalent.[5] Possible neoplastic conditions include osteoma or osteosarcoma of the cranial bones, hemangioma, and angiosarcoma.[3,6,7] Potential cranial infections include brain abscesses due to bacterial or fungal infections.[8]

CASE PRESENTATION & DIAGNOSIS

Investigation continued at the hospital with a patient history provided by family members. The lesion had started as a reddish-purple nodule on the frontal scalp. Over the course of a year, it had expanded, ulcerated, and ultimately become infested with maggots. Although various family members had advised treatment for the nodule, the patient had refused, citing religious reasons. The patient resided with his wife, who had been diagnosed with advanced Alzheimer's, and his contact with the rest of his family was infrequent. Additionally, later investigations revealed extremely poor living conditions, exemplified by garbage accumulation, animal fecal matter, and the presence of rodents. These factors allowed the lesion erosion and subsequent infestation to develop undetected until the collision.[3]

On physical examination, the patient displayed obvious poor hygiene and presented with a strong putrid odour. The patient's vital signs and temperature were unremarkable. The cranial lesion was examined in detail. It presented with substantial erosion, measuring 15 cm x 17 cm, and extended bilaterally over the frontal cranial region from the orbital rim to the parietal scalp. Within the lesion the dura was absent, exposing cerebral brain tissue. Two cortical defects were found around the midline of the lesion, each of which contained dense clusters of live maggots embedded within the brain tissue. A count of the number of live maggots was deemed impractical and not performed. The maggots engaged in active movement in all regions of the defect, including the surface of the exposed cerebral tissue.[3]

The patient remained conscious but torpid, and responded to simple commands. Further neurological examination was normal. A complete blood count and white blood cell differential was performed, revealing a WBC count of 20 100/mm^3, 91% neutrophils and no bands. Blood culture in the emergency room indicated the presence of penicillin-sensitive group G *Streptococcus*.[3]

Finally, a computerized tomography scan identified multiple skeletal and abdominal lesions, including a destructive soft tissue mass in the left posterior chest wall. This mass was centered at the T9 vertebral body and extended into the spinal canal. Needle biopsies of the lesion sites revealed poorly differentiated spindle-shaped CD31-, CD34-positive cells. Additionally, the patient had swollen parotid glands, which also tested positive for the same cell types. These finding supported a diagnosis of metastatic angiosarcoma.[3]

MANAGEMENT

The patient was admitted to intensive care. Broad-spectrum antibiotics were started, specifically a regimen of intravenous vancomycin, ceftriaxone, and metronidazole. Maggot extraction was moderately successful, and was performed via gentle suction. The remaining maggots were covered with sterile surgical dressings soaked in a mild bleach solution. No living maggots remained after 3 days.[3]

Psychiatric evaluation determined the patient competent to make his own medical decisions. The patient declined any surgery and any treatments for his metastatic angiosarcoma. The family as well as the ethics committee upheld his decision. Because he declined surgery, the cortex remained exposed following treatment, until his death 3 months later following his transfer to a nursing facility.[3]

DISCUSSION

Cerebral myiasis is an exceedingly rare condition, with only a handful of described cases worldwide. The vast majority of these cases have been identified postoperatively. All reported cases which state an outcome have unfortunately resulted in death of the patient, although the cerebral myiasis may not have been a main con-

tributor to their deaths. In this case, the more immediate threat was likely the presence of group G β-hemolytic *Streptococcus*, which can present indistinguishably from a group A streptococcal infection, while the ultimate cause of death was presumably due to the untreated metastatic angiosarcoma.[3,9] Indeed, without the open cranial lesion caused by the angiosarcoma, the maggot infestation would have likely been self-limiting; the short lifecycle of the fly species discovered (*Phaenicia sericata*, commonly called the green bottle fly) would have resulted in the elimination of live maggots within a week or so without continuous deposition of new eggs by adult flies.[3,10]

With the exception of the case presented here, all have occurred outside North America. Reported cases of cerebral myiasis indicated lesions which were less extensive than the one seen in this case. The presence of angiosarcoma as the primary cranial lesion could have contributed to the extent of the infestation. Maggots of the common green bottle fly preferentially feed on dead tissue, and have been used in maggot therapy to debride away dead tissue. In this case, tumor growth may have continuously provided necrotic material to sustain the maggots.[3,10,11]

As there have been so few cases of cerebral myiasis, no standard treatment exists. Removal of the maggot infestation, as was conducted in this case, would seem to be an appropriate course of action. Broad spectrum antibiotics to treat concurrent bacterial infections and ward off secondary infection would also appear to be prudent, particularly as the presence of *Phaenicia sericata* larvae may help protect against bacterial infections, a protection that may be removed with the elimination of the infesting maggots.[3,11] Evaluation of mental status should be undertaken to determine the extent of cognitive impairment, if any, and to establish competence to direct care.[3]

CONCLUSION

This is an extremely unlikely case of cerebral myiasis that has invaded through the meninges. That this case was identified only after evaluation after a low-speed collision, and that cognitive function was still largely intact is truly remarkable given the extent of the infestation. In medicine, we are told that when we hear hoof beats, we should think horses, not zebras, and certainly not fictional unicorns. This first reported case of cerebral myiasis in North America with its highly improbable presentation is about as close to a unicorn as we come in modern medicine.

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