Improving brain health by identifying structure-function relations in patients with neurosurgical disorders

Use of new technology to map which parts of the brain control different functions is leading to better treatment of patients with neurosurgical disorders, say Liwei Zhang and colleagues

Brain diseases amenable for neurosurgery comprise a group of conditions that are caused by damage to identifiable brain structures. These diseases threaten long term brain health and cause a large burden on both individuals and societies. Tumours originating in the brain, for example, are the most common fatal cancers in children as well as the third most commonly occurring cancers in adolescents and young adults (15–39 years old).1 Epilepsy is another common neurological disorder that is often caused by specific brain structural abnormalities. Around 10 million patients are thought to have epilepsy amenable to surgery, with 1.4 million new cases globally each year.2

Neurosurgery can repair structural problems in the brain that cause dysfunction but may itself affect brain function. A substantial proportion of patients with neurosurgical disorders have some functional impairment. Patients with glioma may experience postoperative impairment of language, emotional, and psychological processing when the tumours are located in areas controlling those functions (eloquent areas), and roughly 46% of long term survivors have a cognitive impairment, especially in memory and executive function.3 Psychiatric or neuropsychological testing would probably show that the current data under-report the extent of impairment caused by neurosurgical disorders.

These neurological deficits are challenging because many patients will live for decades and require supportive care, particularly since young patients are disproportionately affected by neurosurgical disorders. For malignant brain cancers, the global disability adjusted life years (DALYs) were estimated at 7.7 million in 2016, roughly 34 times the number of deaths, which was 227 000.4 Greater use of advanced imaging technology offers the potential to reduce the harms arising from surgery.

Multidisciplinary approach to protect and restore brain function

Maintaining brain function is vital for quality of life, but in practice, insufficient attention is paid to protecting brain functions when developing plans for neurosurgical intervention. Neurosurgical disorders are complex, and interdisciplinary collaboration is advocated when treating patients. For example, the UK National Institute for Health and Care Excellence suggests referring patients with global tumour for neurological rehabilitation assessment, including physical, cognitive, and emotional function after diagnosis and at each follow-up.5

A typical multidisciplinary team includes neurosurgeons, neurologists, neuroradiologists, neuropathologists, intraoperative neuropsychological monitoring professionals, anaesthesiologists, neuropsychologists, psychiatrists, and therapists. A well functioning multidisciplinary team can provide neurosurgeons with proper techniques to assess brain function and its implications for long term brain health.6

Effective strategies to protect and restore brain function depend on a more fundamental understanding of the relation between brain structures and their various functions, as well as advanced neurosurgical and imaging techniques. Advanced multimodality techniques, such as navigation, awake craniotomy, and intraoperative cortical stimulation mapping have decreased the rate of postoperative neurological deficits in patients with gliomas (box 1).7 8 According to a meta-analysis of 90 studies, cortical stimulation mapping decreased the rate of late severe neurological deficits from 8.2% to 3.4% while also enabling a more extensive resection in glioma patients with tumours in eloquent areas.7

Other non-invasive imaging techniques—for example, functional magnetic resonance imaging (fMRI) and diffusion tensor imaging—enhance the detection of eloquent areas. These techniques have shown that vital functions are often distributed across the brain, with many eloquent areas identified outside the brain structures suggested by historical brain atlases. Improved identification has also facilitated serial monitoring.7 Invasive and non-invasive techniques have converged to propel neurosurgery into the modern era of precision medicine, to further improve patients’ brain health.

Multidisciplinary teams have the strength of overcoming the intrinsic limitations of professionals from a single discipline. For example, neurosurgeons often use preoperative fMRI to guide surgery. However, fMRI has a sensitivity of 44% and specificity of 80% and cannot be a substitute for cortical stimulation mapping in patients having awake brain surgery, which requires input from intraoperative neuropsychological

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**Key Messages**

• The incidence of long term brain functional impairment due to damage during surgery for neurological disorders is underestimated
• Such damage can cause significant societal burdens, especially because of the high incidence in younger patients, who require supportive care over their lifespan
• Use of intraoperative imaging can reduce the risk of damage and improve understanding of the structure-function relation in the human brain
• International multidisciplinary research is needed to provide a more accurate brain atlas and high quality evidence on methods to protect brain function
monitoring professionals. In one study of patients with gliomas in areas that were assumed to be unresectable based on functional imaging, most were able to have maximal safe resection guided on functional imaging, most were able to have maximal safe resection guided on functional imaging, most were able to have maximal safe resection guided on functional imaging, most were able to have maximal safe resection guided on functional imaging, most were able to have maximal safe resection guided on functional imaging, most were able to have maximal safe resection guided on functional imaging, most were able to have maximal safe resection guided on functional imaging, most were able to have maximal safe resection guided on functional imaging, most were able to have maximal safe resection guided on functional imaging, most were able to have maximal safe resection guided on functional imaging, most were able to have maximal safe resection guided on functional imaging, most were able to have maximal safe resection 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neurological manifestations and provide a framework for improving plasticity. Of note, recent reports have linked neuronal excitability with growth of gliomas and brain metastases. These and other findings highlight the need for a deeper understanding and clearer visualisation of the relations between abnormal brain structures, lesions, and functions from the neurosurgical perspective, which can create new insights in brain health. Further multidisciplinary research will create an understanding of the pathophysiology of brain function impairments as well as brain plasticity. This will enable greater therapeutic targeting while maintaining function to achieve optimal brain health.

Future directions Neurosurgical disorders directly damage specific brain structures and lead to large individual and societal burdens in the long term. Research that focuses on the patient’s brain functions during and after surgery should be prioritised to reduce these burdens. This represents a major opportunity for neurosurgey to collaborate with other disciplines to advance our knowledge of brain health.

Establishing a multidisciplinary research alliance, using multimodality technologies, and studying more long term functional changes in neurosurgical patients, will improve our understanding of brain functional localisation and mechanisms of damage in brain disorders. By taking part in research approved by ethics committees, neurosurgical patients can help provide unique insight into brain function and health that could in turn benefit the broader clinical, scientific, and patient communities.

International, large, and diverse prospective trials are also needed to assess changes in patients’ brain function attributed to damaged structures in neurosurgical disorders. Initially, the reproducibility and generalisability of brain function observed in patient case series could be validated in a large global population. Such evidence based understanding of brain function and protection techniques could then be used to tailor treatments for a variety of brain disorders.

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