Letter: A Note on Neurosurgical Resection and Why We Need to Rethink Cutting

To the Editor:

This letter reflects the interdisciplinary approach of the Cluster of Excellence, "Matters of Activity. Image Space Material," located at Humboldt University of Berlin, Germany.

PARADIGM SHIFT

In the 1960s, optical magnification and the concept of microsurgery entered the operating room and revolutionized the effectiveness and safety of neurosurgical procedures. By utilizing *natural anatomic pathways* within the brain, the new conceptual foundation, combined with the technological advances in surgical microscopy, allowed *manually invading the brain* with fewer harmful effects. In recent years, the rapidly growing field of computational neuroscience has opened up new perspectives for exploring brain function at the micro and macro scales. Neural network simulations approximate the mechanistic prerequisites of even the highest cognitive functions by modeling their material basis in terms of neural systems.[1] Those systems are characterized by interactive, distributed, dynamic, and adaptable processing within neuron populations interlinked by local and long-distance connectivity within and across functional domains.[2] These models can explain some degree of resilience of large parts of the brain to injury or degeneration and may offer novel perspectives on predicting variable effects of local injuries.[3] We believe that the current decade will witness another paradigm shift: the application of network thinking in clinical neurosurgery through the development of appropriate models and technological means to perform *network-based neurosurgery*.

BRAIN MATTERS

Living matter can move, grow, separate, communicate, and reorganize at any scale. From the cell to brain or from synaptic transmission to large-scale network communication, the underlying structural principles and their functional activity remain unchanged. As the neurosurgeon interacts with the patient, mapping and rerouting neuroanatomic features in real-time, the operation takes on a new dimension, in which the subject *is* the object and the act of cutting is a matter of disconnecting as much as connecting. The embodied cognition of the neurosurgeon and the complex processes of retrieving data from a fundamentally instable matter constitute the very volatility in which lie the infinite possibilities for *a new model of interrelation between sensing, knowing, and operating*. In various artisanal practices, the cut is the central gesture to perfectly separate two boundary layers along planes and hidden interfaces invisible to the human eye. How can learning from implicit expert knowledge complement technological advancements and how can this embodied knowledge augment new models of collaborative robotic tools? We suggest reconsidering the *cutting gesture as a constructive intervention* enabled by a profound understanding of the materiality of the brain and its emergence in dynamic functional networks. *Network-based neurosurgery*, as a variable intervention along multiple axes and across scales, can only be put into practice through an integrated effort of scholars with diverse disciplinary backgrounds, including neuro- and cognitive science, neurocomputation, materials science, engineering, design, and anthropology.

DOWNSCALING AND UPSCALING

Today, clinical planning tools are usually limited to modality-specific cortical mappings[4] and long association fiber visualizations.[5] Yet, every procedure on the brain affects different structural and functional scales, encompassing the microscopic level of neurons, the mesoscopic level of local network interplay, and the macroscopic level of functional interactions between nuclei and areas throughout the brain. Neurocomputational models of perceptual, motor, and cognitive functions need to bridge across these levels[6] and approximate neuroanatomic reality and functional interactions at multiple scales.[7] Only then can network computation become capable of informing the neurosurgical intervention in view of potentially optimizing it. According to this *future vision*, the effects of possible interventions on network dynamics will be simulated and operational strategies modified accordingly based on virtual lesions of neuronal elements and connections within brain-constrained networks. A precondition of this novel strategy is mathematically precise models that can be individualized to the patient's neuroanatomy and used in real-time during surgery for predicting the outcome of any tissue manipulation. Since modeling will entail a probabilistic estimation and, as such, integrate the remaining uncertainty of the final effect, we also need new visualization and interaction methods to engage with these uncertainties. To enable *network-based neurosurgery* that targets multilevel accuracy, model developments must be accompanied by a substantial increase in medical device technology precision, scaling down from the millimeter to micrometer level and from macroscopic to molecular cutting (Figure). These new tools will no longer be operated manually, but require cooperative robotic assistance. Mastering these new cutting tools, which are both predictive and explorative devices, will bring new challenges, as neurosurgery becomes a much more dynamic operation encompassing ever-changing and mind-defying scales.

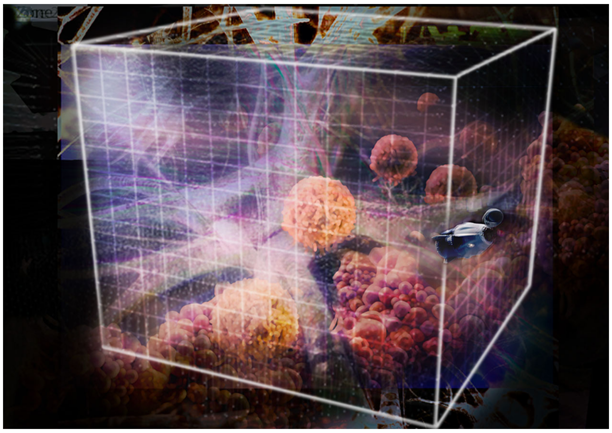

FIGURE. *Fantastic Voyage 2021.*

NETWORK-BASED NEUROSURGERY

Network-based neurosurgery needs to be guided and informed by the unique neuronal network compositions, dynamics, and phenotypes of the individual patient. The process of *informed interface modification*, which includes deleterious and destructive as well as curative and augmentative effects, requires a change in the mindset of the profession. We want to emphasize that *network-based neurosurgery* is about creating new spaces, new functions, and new pathways to knowledge and practice, and likewise about how the neurosurgeon's skillset will be thoroughly enhanced and transformed. Concepts to realize this new notion of *cutting* have already been explored and applied, especially in the field of theranostics, where tools also sense and not only divide. We believe that this approach needs to be further developed. Future adaptively evolving tools will overcome the distinction between modeling and treating, and become radically hybrid: they will be able to autonomously orient themselves (navigate), probe and measure the brain in real-time (diagnose), destroy and create new interfaces (treat), and design neuronal connectivity to restore and enhance cerebral functions (heal), with philosophical and socioethical implications that need to be addressed by all stakeholders.

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