

Cases of Unconventional Information Flow Across the Mind-Body Interface

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Abstract

Neuroscience, and behavioral science more broadly, seek to characterize the relationship between functional cognition and the underlying processes operating in living tissue. The current paradigm focuses heavily on the brain, and specific mechanisms thought to underlie mental content and capabilities. One of the most interesting approaches to any field, which often leads to progress, is to highlight data which do not comfortably fit a specific dominant framework. Here, we review clinical and laboratory data in several unconventional systems which are not predicted by the current models in the field. Reduced brain mass or absent brain tissue without the expected loss of function (e.g. hydrocephalus, hemi-hydranencephaly), discrepancies between cognitive state and brain function (e.g. accidental awareness during anesthesia, terminal lucidity), and cases of cognitive abilities exceeding the apparent skill of the individual, all highlight interesting features of the immense plasticity of the mapping between cognition and its living substrate. These cases suggest new avenues for research that at the very least stretch existing frameworks, and parallels to discoveries being made in the emergent form and behavior of synthetic constructs. We speculate on a roadmap for the study of interesting and still poorly-understood features of embodied minds that could be impactful for biomedicine and engineering, as well as foundational philosophical issues.

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Treasure your exceptions!
 Keep them always uncovered and in sight.
Exceptions are like the rough brickwork of a growing building
Which tells that there is more to come
And shows where the next construction is to be.

William Bateson (1908)

1. Introduction

It is well known that paradigms in science can function as self-maintaining attractors, exerting influence with respect to the amount of attention and funding that is available for various research directions, especially ones that threaten to disrupt them. Thus, one of the most interesting and sometimes rewarding approaches is to specifically look for data which does not comfortably fit a given paradigm. It is also important to ask what the world would look like if a specific paradigm was importantly incomplete – what would we see, and what kind of experiments would then be emphasized?

Specifically, this approach does not simply look for data that cannot *post hoc* be explained by a paradigm. Most frameworks today are sufficiently ingenious that they can be stretched to accommodate quite a lot. In our view, the most exciting aspect of conceptual frameworks is the degree to which they facilitate new discoveries – experiments and research programs with surprising new outcomes that could stretch our understanding and lead to practical applications (Doerig *et al.* 2023). Rather than look backwards, after data appear, and try to fit them into an existing set of ideas, it is interesting to look forward and ask: Did our framework suggest a given experiment and its result? And if not, what else could it be missing?

In that spirit, we offer a discussion of laboratory and clinical data bearing on the relationship of mind to brain. Neuroscience has progressed immensely in the last century. However, a number of large problems remain wide open (Bayne *et al.* 2020a, 2020b, Carter *et al.* 2018, de Haan *et al.* 2020, Haun and Tononi 2019, Juel *et al.* 2019, Livaditis and Tsatalmpasidou 2007, Seth 2021, Tononi and Koch 2015), numerous biomedical needs are unmet, and the impending advances of bioengineering technologies race ahead of conceptual understanding and ability to predict their impact (Clawson and Levin 2022, Gillett 2006, Pio-Lopez 2021, Rouleau and Levin 2023).

Our goal here is not to suggest specific revisions to the brain-mind identity thesis, but to highlight experimental and observational data that – together with recent advances in diverse intelligence and non-neural cognition – point to new research directions and the possibility of a greater

unification across disciplines than possible with current ways of thinking about embodied minds.

The context for our discussion is the emerging field at the intersection of basal cognition, bioengineering of synthetic morphology, artificial intelligence, exobiology, and autonomous robotics (Levin *et al.* 2021, Lyon 2006, 2015, 2020, Lyon *et al.* 2021, Rouleau and Levin 2023), which seek fundamental invariants across cognitive systems of very different origins, composition, and capabilities. Frameworks are needed which go beyond the stale and increasingly non-functional binary categories of “human”, “machine”, etc. to enable a functional understanding of what is essential about cognition and agency regardless of its specific implementation or origin story (evolved vs. engineered) (Bongard and Levin 2021, McShea 2013, 2016). Continued progress, in terms of positive impact on human flourishing and the ethics of relationships to unconventional beings (such as forthcoming enhanced humans, cyborgs, new brain-machine interfaces, etc.) require us to have a better understanding of the natural biological substrate of mind, and the space of the possible minds that can exist.

Developmental biology reveals that all of us make the journey from the “just physics and chemistry” of an unfertilized oocyte to the advanced metacognition of an adult human. It also, like evolution, reveals that this is a slow, gradual process offering no sharp line at which a “human mind” snaps into being. The progressive awakening of an emergent self from a collection of cells requires an actionable, principled story about how we are simultaneously a collective intelligence and a singular, coherent, emergent being, and how those properties map onto the details of the biological substrate.

More specifically, our bodies self-construct as a multiscale competency architecture, in which different levels of organization solve problems in and navigate upon the landscapes of physiological, metabolic, transcriptional, and anatomical spaces (Fields and Levin 2022). For example, the tools of neuroscience have been extended far beyond neurons to the study of how the collective intelligence of cells during development and regeneration results in a robust navigation of anatomical morphospace (Levin 2023a, McMillen and Levin 2024). Specifically, it turns out that bioelectric networks – first deployed for this purpose in bacterial biofilms (Liu *et al.* 2017, Martinez-Corral *et al.* 2019, Prindle *et al.* 2015, Yang *et al.* 2020) – are a widely used mechanism to integrate competent subunits and scale up the setpoints of homeostatic processes (Fields *et al.* 2020, Pezzulo and Levin 2015).

Consistent with the ancient origins of electrophysiological and neurotransmitter mechanisms, the advances of the diverse intelligence field have revealed a rich plethora of behavioral and proto-cognitive skills across many kinds of minimal media, including learning in: molecular networks (Biswas *et al.* 2022, Biswas *et al.* 2021, Csermely *et al.* 2020), cells (Baluška

and Levin 2016, Gershman *et al.* 2021, Saigusa *et al.* 2008, Vallverdu *et al.* 2018), and primitive organisms such as slime molds (Boisseau *et al.* 2016, Vogel and Dussutour 2016). Thus, the questions to be answered by any paradigm in this arena include:

- What is the cognitive glue (connection as well as interaction policies among the parts) that binds competencies of individual cells into a centralized, unified functionality and experience we enjoy as a cohesive self? (Levin 2019)
- How to make sense of an emergent, temporary dynamical system known as a self that is the owner of memories, preferences, and other features that belong to none of its parts in a way that will allow us to detect its presence in unfamiliar embodiments and address its disorders via definitive therapeutics?
- Why do some minute brain defects (mini-strokes or small aneurisms) result in life-changing effects but other massive deficiencies (such as a missing hemisphere) show little to no impairment? More broadly, how to predict the consequences of damage or the appearance of ultra-learners such as child prodigies?
- How and where are memories encoded into physical substrates, stored despite molecular and cellular turnover, and decoded? (Gallistel 2020, Gershman 2023, Langille and Gallistel 2020, Levin 2024b, Queenan *et al.* 2017)
- How are memories moved and remapped – both spatially across tissue and across diverse architectures? (Blackiston *et al.* 2015, Westerman 1963)
- What underlies temporal robustness or degradation of memory across the noise and constant replacement of cellular material?
- How do cognitive competencies relate to the structure of the brain – what is necessary and sufficient to implement the various kinds and degrees of mental function?
- How many selves can exist within a single human body? How does this number change during normal life, embryonic maturation, and adaptation to trauma? What is the computational density of the cognitive medium (maximum selves that can be accommodated per unit of tissue)?
- How do bioelectric and other mechanisms transduce across scales, to enable high-level executive and social goals to eventually regulate the movement of ions across cell membranes during voluntary motion in the daily execution toward those goals?

This last question reminds us that mind-body medicine such as changes of gene expression by meditation (Saatcioglu 2013, Venditti *et al.* 2020), placebo and nocebo effects (Benedetti *et al.* 2007, Evers *et al.* 2018, Lui *et al.* 2010, Piedimonte and Benedetti 2016), voodoo death (Cannon 1957, Lester 2009, Samuels 2007, Sternberg 2002), etc.) is not some rare and unusual phenomenon but a simple consequence of our modular information and control structure – an inevitable consequence of the fact that minds and bodies both self-construct out of components which were once individual organisms themselves. Thus, numerous areas of biomedicine – including not only the connection between mind and body but emerging attempts to control *the mind of the body* for regenerative therapeutics (Lagasse and Levin 2023, Mathews *et al.* 2023) – both depend on and inform fundamental philosophical conceptions of embodied minds.

2. How Do Minds Map onto Bodies?

The process of metamorphosis in the caterpillar lifecycle provides a unique case study of the transfer and remapping (Levin 2024b) of information across bodies. During the pupal stage of metamorphosis, caterpillar brains and nervous systems are largely broken down, and subsequently rebuilt into those of the butterfly. Memories formed during caterpillar life survive such a drastic remodeling into the butterfly stage, in a way that maintains the salience of the memory but re-interpreted to apply to a new body which lives in a higher-dimensional world (via flight) and requires different controller policies to move via hard elements unlike the soft larval stage.

For example, caterpillars trained via associative learning give rise to butterflies that display a trophic response to stimuli, but now in the context of a different food type (nectar, not leaves) (Blackiston *et al.* 2008, 2015). We currently lack theories that would explain how the memories survive drastic refactoring of the brain and, more importantly, how specific engrams are remapped onto a different architecture and generalized to new instances of categories (such as “food”) more appropriate to a new and very different embodiment.

This and other examples of memory persisting through metamorphosis (Goldsmith *et al.* 1978, Punzo and Malatesta 1988, Sheiman and Tiras 1996) raise the broader issue of how memories relate to the material substrate of cognition, and what implications their portability may have. Memories have been reported to be transferred through transplants of tissue, cells, and even extracted (purified) chemical species (Bisping *et al.* 1971, Byrne *et al.* 1966, Carrier 1979, Corson 1970, Frank *et al.* 1970, Golub *et al.* 1970, Hartry *et al.* 1964a, 1964b, Jacobson 1966, Maldonado and Tablante 1976, Martin *et al.* 1978, McConnell 1962, McConnell 1964, McConnell and Shelby 1970, Miller and Holt 1977, Morange 2006, Peretti

and Wakeley 1969, Pietsch 1981, Pietsch and Schneider 1969, Ray 1999, Reinis 1968, 1970, Reinis and Kolousek 1968, Rosenblatt, Farrow, and Herblin 1966, Rosenblatt, Farrow, and Rhine 1966, Setlow 1997, Stein *et al.* 1969, Ungar 1966, 1974, Ungar *et al.* 1972, Ungar and Irwin 1967, 1968, Westerman 1963, Whiddon *et al.* 1976, Wilson and Arch 1972, Wilson and Collins 1967, Zippel and Domagk 1969).

In trained and decapitated planaria, memories are regenerated along with brain tissue from tail fragments (Blackiston *et al.* 2015, Shomrat and Levin 2013), suggesting a fascinating research program: How do memories get imprinted on new brain tissue? What do non-brain tissues do with stored memories, and do they interpret them or store them as passive data until the brain re-forms? How can this be used therapeutically, for disorders of memory? On-going work on the mechanistic basis of innate behaviors, in unitary animals as well as swarms, is likely well-poised to contribute to this field (Anholt 2020, Avalos *et al.* 2020, Jiang and Pan 2022, Tinbergen 2020, Walsh *et al.* 2021). Likewise, these questions will surely be impacted by improvements in the understanding of the information dynamically available to subcellular networks, cells, organ systems, the entire organism, and swarms as these layers of organization process genetic, cytoplasmic, and environmental information as cues and prompts for a generative, creative process of sense-making (Levin 2023b, 2024b, Mitchell and Cheney 2024).

The reality with biological substrates, in contrast to most of our information technology, is that they are inherently unstable, and their components are prone to noise and degradation over time. Not only are they exposed to ever-changing environmental perturbations that are often unpredictable, but they are also faced with their own instabilities, such as aging and cell death, cancer, biohacking by other organisms, hijacking by viruses, and genetic mutations – the latter are now known to be plentiful in the normal human brain (Lodato *et al.* 2015).

All of the above implies that living material has to be tolerant and even somewhat creative in interpreting the highly compressed engrams of prior experience stored in an unreliable medium, and that robust biological cognitive architectures should be willing to acquire and utilize cross-modal information present in a variety of sources in their microenvironment (Bongard and Levin 2023, Levin 2024b). This unconventional perspective has several implications which have been supported by findings but are not predicted by the standard picture of neuroscience, beyond the memory persistence and transfer examples cited above. For example, that adult behavior can be specifically informed by the analysis of novel molecules by embryonic cells (Hepper and Waldman 1992), and that the reimposition of transplanted memories by chemical substrates can occur without having to target those chemical engrams to any specific anatomical location in the recipient (Bédécarrats *et al.* 2018, Chen *et al.* 2014).

Questions about the relationship of memories to a neuronal substrate (Abraham *et al.* 2019, Biderman *et al.* 2023, Dasgupta and Gershman 2021, Gallistel 2017a, 2017b, 2020, Gershman 2017, 2023, Langille and Gallistel 2020, Queenan *et al.* 2017) are likely to be informed by a consideration of basal cognition – the scaling of memory capacity and learning behavior from its most humble unicellular origins, both on an evolutionary and developmental timeframe (Crisp *et al.* 2016, Gershman *et al.* 2021, Keijzer *et al.* 2013, Levin *et al.* 2021, Lyon 2006, 2015, 2020).

Examples of learning and intelligent behavior in a wide range of non-neural systems (reviewed by (Baluška and Levin 2016) suggest a much tighter relationship than currently appreciated between these information-processing systems (thought to be the province of neuroscience) and cell biology more generally. The dynamics of behavioral memory and morphogenetic memory (regeneration of lost complex body parts) are especially fused in species like *Physarum polycephalum*, in which memory-driven behavioral motility in space is accomplished via morphogenetic change (Boisseau *et al.* 2016, Boussard *et al.* 2019, Vogel and Dussutour 2016). Moreover, there are also clinical implications of the evolutionary conservation of both molecular mechanisms and algorithms across neurally-driven behavior in the 3D world and the morphogenetic behavior of cell groups in anatomical space (Fields *et al.* 2020, Fields and Levin 2022, Friston *et al.* 2015, Levin 2023a, Pezzulo *et al.* 2021, Pezzulo and Levin 2015).

Many of the most striking laboratory data, suggestive of a broader unification of conceptual and mechanistic knowledge, exist in so-called “lower” animal models. This has made it tempting to ignore them as irrelevant to the big questions of biomedicine and cognitive science. Importantly, however, the human clinical literature provides a crucial complement that hints at exciting opportunities to extend our understanding of the capabilities and dynamics of the cognitive architecture.

3. Clinical Cases: Beyond “Simple” Model Systems

We now turn to consider some clinical cases which shed light on the limitations or possible extensions of the current paradigm. As suits one’s level of appetite for disruption, these can be taken as: serious challenges requiring major re-thinking, disparate facts to be accommodated with the paradigm by minor extension, or even just as hypothetical thinking aids for stretching our theoretical skills to consider “what would it mean if it were true”.

3.1 How Much Neural Substrate is Required for Normal Function?

In humans, the brain is regarded as the basis of all mental attributes, arising from the function of neural architectures which were strongly

shaped by evolutionary selection for the most adaptive functionality under constraints of energy demand and pregnancy risk for head size (Hofman 2014). Many aspects of consciousness and cognition are regarded as an emergent property of collective interaction of neuronal networks with a basis in the brain. It is widely accepted that many of the higher neurological functions, including somatosensory processing, motor processing, conscious experience, memory, and emotion, are all based in the brain and are the result of cerebral function. Neuroscientists such as Brodmann who pioneered brain mapping (Zilles 2018), have attributed functionality to particular brain regions, such as associating Broca's area with speech production and associating the postcentral gyrus with the primary somatosensory cortex.

In search of a seat of consciousness, modern neuroscience approaches attribute conscious experience and cognitive processing in large part to the central nervous system (CNS), especially in the cerebral cortex, where most of the thinking and processing is posited to take place. Conventional cognitive neuroscience assumes that consciousness, memory and cognition are generated by the brain and operate within the brain and CNS. This is strongly supported by many lines of argument, as seen in the event of traumatic brain injuries, neurodegenerative conditions, tumors, strokes, brain hemorrhage and the brain mass effect in contusions or focal lesions. These can dramatically impact cognition, intelligence, communication, and sensorimotor function and be life-threatening.

However, there have been numerous clinical cases recorded in medical literature, in which patients have some kind of brain dysplasia (either congenital or acquired), reduced brain size, or some kind of massive lesioning, or a drastic absence of a brain matter, but exhibit normal cognitive development and function (Fig. 1). These cases in human clinical literature demonstrate important challenges to our understanding of the relationship of functional cognition to a specific substrate (Wahbeh *et al.* 2022).

3.2 Reduced Brain Mass or Absent Brain Tissue Unaccompanied by Loss of Function

We first dive into well-documented examples of patients with microcephalus, hydrocephalus, hemihydrencephaly, and hemispherectomy, or absence of cortical material, who are missing a large amount of brain matter but tend to lead ordinary lives with average, or above average, intelligence. Such cases demonstrate that brain size, amount of cortical tissue and neuron quantity, even within a single species, do not directly predict intelligence.

3.2.1 Hydrocephalus

Hydrocephalus is an accumulation of cerebrospinal fluid (CSF) in the ventricles of the brain which presses towards the skull, thus reducing the

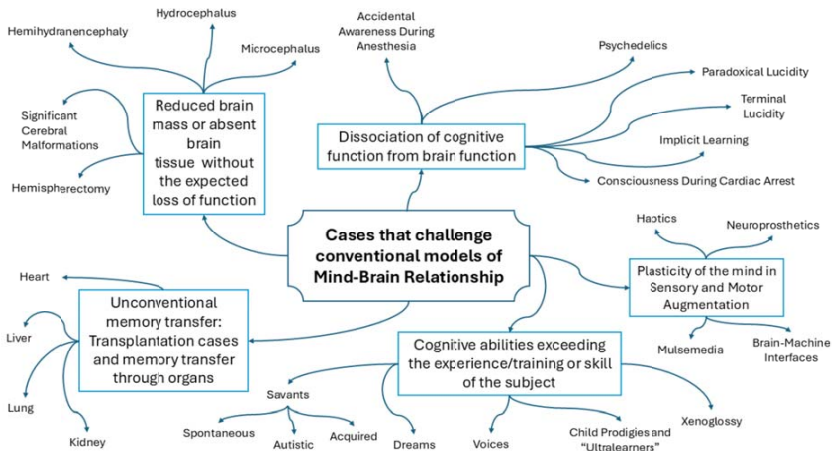


Figure 1: Mind map of the variety of clinical cases in humans reviewed. Cases fall under five distinct categories: Reduced brain mass or absent brain tissue, dissociation of cognitive function from brain function, unconventional memory transfer, the plasticity of the mind in sensory and motor augmentation, and cognitive abilities exceeding the training of an individual subject. The degree and quality of data in each case varies significantly.

amount of cortex. This is typically caused by some blockage in the system, stenosis of the transporting valves or aqueducts, or an inability to drain circulated CSF (McMullen *et al.* 2012). Standard neurosurgical approaches to treat hydrocephalus, especially in newborns, include installing ventriculoatrial and ventriculoperitoneal shunts. These surgically inserted plastic tubes drain fluid away from the brain and may alleviate symptoms to encourage normal neurological development in hydrocephalic infants.

Magnetic resonance imaging can identify the extent of CSF accumulation in the ventricles. Hydrocephalus accompanied by normal brain function has been documented in animals (Lipp and Wolfer 2022, McMullen *et al.* 2012, Qin *et al.* 2021), including the 2019 case of Rat R222 (Ferris *et al.* 2019) who survived a life-time of extreme hydrocephalus, hippocampus malformation and compression of most brain areas, and substantial cortical thinning. Despite this, Rat R222 performed decently in a wide range of behavioral tasks, retained normal motor function, somatosensation, and memory even with the “bare minimum” brain material.

The neurologist John Lorber identified numerous patients in his medical practice who had severe hydrocephalus as evidenced by their brain imaging results (Lewin 1980). The ventriculomegaly went practically unnoticed and the patients led otherwise normal lives with very little brain tissue. For example, Lorber described a university honors mathematics student who had so much CSF that there was almost no white matter; the

ventricular enlargement took up so much space and the actual brain was a thin mantle lining the inner skull. In contrast to the normal thickness of brain tissue between ventricles and outer cortex as being 4.5 cm, this student's brain mantle measured a mere millimeter or so. Yet, this patient was socially normal, with an IQ of 126 and great academic achievement in math. Lorber's patients had an utter lack of brain tissue which went totally unnoticed until imaging was taken.

Another hallmark case report of a hydrocephalus patient with no cognitive deficits was reported in 2007 by Feuillet *et al.* (2007). Feuillet describes a 44-year-old "white collared worker" who presented with leg weakness. He had a history of receiving a ventriculoatrial shunt for post-natal hydrocephalus. After a revision of the shunt at 14 years, the patient did not experience any further neurological development issues or notable medical conditions. He led a normal life as a civil servant, married with two kids and an average IQ of 75. Yet, during his neurological assessment at age 44, his CT and MRI scans showed extreme ventricular enlargement of the 1st and 2nd lateral ventricles, and the 3rd and 4th ventricles due to hydrocephalus and a very thin cortical mantle (Fig. 2A). He nearly had no brain matter as the ventricular enlargement compressed his cerebrum. The drastic lack of brain material did not bring about any cognitive issues for the patient, the hydrocephalus went unnoticed, and he led a normal life.

Alders *et al.* (2018) presented the case report of a 60 year old male who presented to the clinic with low mood and behavioral changes. An MRI scan exposed extreme ventriculomegaly, a significant expansion in the ventricle size bilaterally, with a severe dilation of both lateral ventricles and the third ventricle (Fig. 2B). They noted the CSF volume in the patients ventricles were 46 times the norm for patients in the same age group, and due to the excess volume, his cortex and corpus callosum were extremely thin with a very small amount of gray and white matter. Despite this, he possessed an average IQ, and enjoyed playing guitar. His chief medical complaints were not neurological at all, these included central obesity, short stature, and psychiatric and cognitive complaints, such as rumination, anxiety, and excessive guilt.

In 2021, physicians from Canada (Persad *et al.* 2021) reported the case of a 72-year-old woman who presented with a tonic-clonic seizure, her CT showed massive ventriculomegaly, and hydrocephalus was diagnosed (Fig. 2C). She led a normal life working retail jobs and living independently; her neurological examination was normal.

In 2022, a case in France was presented of extreme hydrocephalus in a 67-year-old man. Macrocephaly (large head diameter) was diagnosed in childhood; however, the patient defied his poor prognosis and any symptoms such as falls, or stunted development resolved themselves "against all odds". The patient completed his education and vocational training

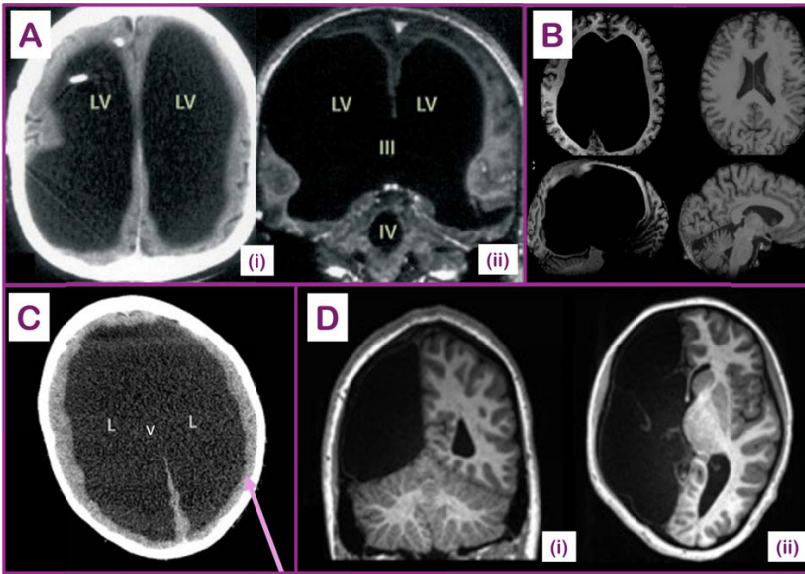


Figure 2: Select cases of reductions in brain matter with normal function. (A) Image from Feuillet *et al.* (2007) showing a white collared worker case of extreme hydrocephalus; he led a normal life as a civil servant with an average IQ of 75. During his neurological assessment at age 44, his (i) CT scan and (ii) T1 weighted MRI scans with contrast showed extreme ventricular enlargement. LV indicates lateral ventricle, III and IV indicate the third and fourth ventricles, respectively. (B) Image from Alders *et al.* (2018), showing the case of a 60-year-old with a bad mood with massive ventriculomegaly and severely reduced cerebral mantle and corpus callosum, that went largely unnoticed. The left column is T1 weighted MRI images taken in the transverse, coronal, and sagittal planes of the patient. The right column represents T1 weighted MRI scans of a healthy control. (C) Image from Persad *et al.* (2021) of a Canadian living a normal, independent life with massive hydrocephaly. MRI scan taken from the axial view (plane parallel to the ground) at the level of the lateral ventricles (arrow points to extremely thin layer of cortical mantle, LV stands for lateral ventricle). (D) Image from Asari-dou *et al.* (2020), showing the T1 weighted MRI scans of a child born without left hemisphere taken (i) in the coronal plane and (ii) in the axial plane. The child had normal cognitive development and language skills despite hemihydrencephaly of the left hemisphere and near-absence of the corpus callosum. All images re-used with permission.

without any striking difficulties and maintained a career in insurance for just over 40 years. His brothers reported that he had a great memory, an apt for history and unremitting commitment to his profession without interruption. Yet brain scans revealed he was working with very little brain tissue in his skull. This is yet another modern rare case of extreme ven-

tricular dilatation and cortical thinning with normal intellectual ability and cognition.

3.2.2 *Hemihydranencephaly*

Hemihydranencephaly refers to the complete or almost-complete unilateral absence of the cerebral cortex, where one cerebral hemisphere is entirely missing and replaced with CSF, reviewed by Pavone *et al.* (2013). In this congenital condition, the cerebellum, pons, medulla, thalamus, and basal meninges remain intact. Hemihydranencephaly tends to be much more pathological than hydrocephaly. In hydrocephaly, a thin layer of cerebral cortex is preserved, while in hemihydranencephaly no cerebral cortex is preserved in the affected hemisphere.

Hemihydranencephaly is a very rare, debilitating and often fatal congenital condition. A handful of cases have been reported in the literature to date. Patients with hemihydranencephaly have been reported to experience severe neurological symptoms, such as contralateral hemiparesis and motor dysfunction. Certain patients with hemihydranencephaly had their cognitive and language functions preserved, and these patients attended middle school and high school as average or above average students.

A case of a 14-year-old girl with hemihydranencephaly but no intellectual disability was reported by Asaridou *et al.* (2020). The girl was examined from 14 months to 14 years, after being born without a left hemisphere and diagnosed with hemihydranencephaly (Fig. 2D), showing a nearly absent corpus callosum. The condition was congenital and is assumed to have arisen during early gestational period. The girl's overall development and language development reached age-appropriate levels during her schooling years. She had normal cognitive function. Furthermore, she showed mixed performance in phonic activities, number sense, and spatial reasoning, ranging from average to exceptional, even though she was completely missing a brain hemisphere.

Additional patient cases of hemihydranencephaly without intellectual disability are covered by Balpande *et al.* (2009a,b), Becker *et al.* (2016), Greco *et al.* (2001), Moser and Seljeskog (1981), Pavone *et al.* (2013), Ulmer *et al.* (2005), Vandoornik and Hennekam (1992).

3.2.3 *Hemispherectomy*

Hemispherectomy is the surgical removal of an entire brain hemisphere. The procedure is used for drug-resistant severe epilepsy and seizure mitigation. In modern day, hemispherectomy has become a routine, low risk and effective in the pediatric population that has been effective treatment in alleviating seizures with minimal complications (Lew 2014, Shurtleff *et al.* 2021). Hemispherectomies are performed in patients experiencing conditions such as severe epilepsy, hemimegalencephaly, and are a mainstay

for Rasmussen's encephalitis, which is marked by one-sided hemisphere dysfunction and severe inflammation of unknown etiology (Liu *et al.* 2022, Nava *et al.* 2023).

Hemispherectomies generally have few complications and are commonly performed at epilepsy centers around the world, successfully reducing or eliminating seizures post-surgically (Alotaibi *et al.* 2021). Cognitive function (including language, intelligence, memory, learning, etc.) typically remains stable or is improved after hemispherectomy (Shurtleff *et al.* 2021). Hemispherectomy can be performed effectively in children as well as adults and adolescents with similar outcomes (McGovern *et al.* 2019).

It can be difficult to explain how memories remain unperturbed and the ability to form new memories remains consistent with pre-operative abilities. Furthermore, it is puzzling to understand the immense and instantaneous re-organization that would need to take place to relocate the known language center of the brain upon removal of the hemisphere which it is normally mapped to, given that language comprehension and production is not lost post-operatively.

3.2.4 Microcephaly

It is widely accepted that throughout human evolution an increase in brain size has been a result of natural selection favoring a rise in general intelligence (Lee *et al.* 2019). Even then, the relationship between brain size and cognition cannot be scaled that easily. For example, microcephaly is a congenital condition which is often associated with intellectual disability due to a very small head and brain size. Head circumference measures 2-3 standard deviations below the mean in microcephalic patients (Hanzlik and Gigante 2017).

However, there have been cases of microcephaly reported where patients had normal intelligence (Abdel-Salam and Czeizel 2000, Seemanova *et al.* 1985). Patients with Nijmegen breakage syndrome, a condition common in Slavic populations marked by severe microcephaly, tend to experience decline in intelligence as they age. Yet there have been reports of patients successfully reaching developmental milestones and showing normal intelligence and motor function, such as that of a 15-month-old girl with profound microcephaly: a head circumference of 36 cm (Green *et al.* 1995). Interestingly, she had normal intellectual development and brain function which was surprising to clinicians given her severe brain condition and lack of brain growth.

3.2.5 Large Cerebral Malformations

In some cases, patients with multiple cerebral malformations still have normal function. One study in particular presented a case report of a 34-

month-old girl with very complex cerebral malformations with normal cognitive function (Distelmaier *et al.* 2007). She had Dandy-Walker malformations (abnormal cerebellum developments), hydrocephalus which was treated by shunting when she was a newborn, bilateral schizencephaly (fluid filled slits in both cerebral hemispheres), and a dysgenesis in her corpus callosum. Despite her severe cerebral malformations, by month 34, the girl showed interest in toys matching her age, and interacted socially. Even though she did have motor developmental delays upon neuropsychological assessment, she had a surprisingly good clinical course given her severe congenital malformation. Past works note that half the patients with Dandy-Walker syndrome have normal intellectual development (Bodaert *et al.* 2003).

These extraordinary cases demonstrate that physical amount of grey and white matter, size of brain, or number of neurons in the CNS is not a reliable predictor of observed phenotype: The cognitive capacity and mind are not always dependent on the form of the brain. Altogether, patients with damaged or strongly reduced brain tissue can still have their higher cognitive processes remain intact. Under the purported mind-brain relationship, we would expect higher-order thinking and cognitive abilities to be the first ones to decline upon such gross reductions in brain material. But these cases show that a large removal or damage to brain tissue sees cognition (and phenomenal consciousness) largely unaltered.

More generally, one can attempt to explain these cases with concepts of plasticity and redundancy – remaining tissues taking over the work of missing ones. This is especially tricky with rapid reduction of brain tissue (such as hemispherectomy), as compared to developmental phenotypes in which functional roles of neural assemblies can adapt over months. And no doubt plasticity and redundancy play a role (Bennett *et al.* 2020, Mizusaki and O'Donnell 2021, Silva *et al.* 2018). However, the bigger point is that brain tissue is incredibly expensive – both in terms of the total percentage of body metabolism it consumes (Faria-Pereira and Morais 2022, Pellerin and Magistretti 2003) and in terms of the risk to the mother during births of babies with large heads (Hofman 2014, Lipschuetz *et al.* 2015).

If it were possible to simply have the necessary cognitive skills in a smaller amount of computational medium, selection would exert significant pressure to reduce brain size. Important directions for future work include addressing hypotheses for cryptic functions of brain tissue volume, and possible factors of evolvability on longer timescales than is apparent within the fitness of cognitive performance of a single human (Levin 2023b, Liard *et al.* 2020, Nehaniv 2003, Raff 1994). Interesting model systems in which to address those questions include the tiny parasitic wasp *Megaphragma mymaripenne*, which is smaller than a unicellular organism such as a *Paramecium* and evolved numerous accommodations (such as neurons without nuclei) to accomplish the necessary processing in an

extremely minimal nervous system (Diakova *et al.* 2018, Polilov 2017, Polilov *et al.* 2023).

3.3 Dissociation of Cognitive Function from Brain Electrophysiology

Brain activity can be monitored via electrophysiological recordings, with the current paradigm driving the expectation that when electrical activity ceases, so does cognition. Next, we review cases suggesting mental activity despite documented significant diminution or collapse of brain activity (with or without pathophysiology of the brain). This was, in some cases, paradoxically associated with periods of greater cognitive capacities, mental clarity, implicit learning, and vivid experiences.

Normally, EEG research suggests that delta waves are present when consciousness is absent, as seen in sleep stages, anesthesia, epileptic seizure, coma and vegetative states; consciousness does not disappear during the lowest frequency delta waves in a wide variety of case studies (Frohlich *et al.* 2021). We also discuss cases of awareness during interoperative general anesthesia, terminal and paradoxical lucidity and psychedelic experiences. They all serve as interesting test cases for current models of the mind-brain relationship and the role of brain activity, as measured by conventional electrical recordings does not tell the full story of the richness of conscious experiences and cognitive performance.

3.3.1 *Accidental Awareness During General Anesthesia*

The mainstream model of the mind-brain relationship implies two things: (1) it should be straightforward to detect brain activity because the cognition-relevant events are electrical signals which are easily measured, and (2) a lack of brain activity means the absence of consciousness and awareness. With respect to the first, it turns out that the situation is far from simple.

Anesthesiologists commonly monitor patient brain activity to ensure patients are unaware during a procedure. Brain function monitors are recorders based on electroencephalography measure and record cortical and sub-cortical activity (American Society of Anesthesiologists 2006). After induction of anesthesia, the EEG pattern resembles that seen during unconsciousness, with low to no frequency electrical waves read on the monitor, as well the patient is unresponsive to pain stimuli.

There have been many technological tools developed to track depth of anesthesia more precisely using EEG tools such as Bi-Spectral Index (BIS) encephalography, as well as isolated forearm technique that tracks responses to commands (Chang *et al.* 2019, Mashour and Avidan 2015). Ideally, patients at greater risk of awareness during general anesthesia (elderly, emergency trauma patients, etc.) are monitored. If the BIS

signal is low enough, this would indicate a low likelihood of awareness and/or explicit recall.

No method of monitoring is perfectly reliable though, and there have been cases reported in which the anesthesiologist does not see any signs of brain activity resembling the conscious state, yet the patient is still conscious and aware during their procedure (Cascella 2016, 2020a). With this consideration, anesthesiologists routinely administer benzodiazepines to produce anterograde amnesia, in the event of accidental awareness during anesthesia.

For quite some time, BIS monitoring was considered the best solution to the anesthesia awareness problem, yet after a lot of controversy and investigation there appears to be no accepted definitive way to establish neural correlates of awareness. Studies found that BIS monitoring did not provide a perfectly reliable way of reducing incidence of anesthesia awareness, thus there is no totally reliable way to ascertain no awareness, especially in risk groups (Avidan *et al.* 2008). Thus, anesthesiologists tend to rely on signs like rapid hypertension and breathing rate as a cue that something might be awry intraoperatively.

With regards to the efficacy of modern depth of awareness monitoring methods, anesthesiologist Cascella (2020b) states:

Probably, the main gap of [depth of awareness] technologies lies in their impossibility of discriminating with precision between consciousness and unconsciousness. Indeed, their functioning is based on EEG signal analysis rather than consider the corticocortical connectivity and communication processes. This is a complex topic encompassing (1) consciousness/unconsciousness transition and mechanisms, and (2) the operating mechanism of general anesthetics. Neuronal and functional mechanisms that regulate the switch from consciousness to unconsciousness still require investigation.

With respect to the expected cessation of cognition upon quieting of brain electrical signaling, there has been a consistent incidence of cases reported for many decades (Andrade *et al.* 2008, Bischoff and Rundshagen 2011, Breckenridge and Aitkenhead 1983, Errando *et al.* 2008, Ghoneim and Block 1992, Jones 1994, Liu *et al.* 1991, Ranta *et al.* 1998, Sandin *et al.* 2000, Sebel *et al.* 2004) of accidental awareness during anesthesia (Bischoff *et al.* 2015). Incidences are estimated to be ranging from 0.017% to 4% (Chang *et al.* 2019, Hachenberg and Scheller 2023) and higher in risk groups such as obstetric surgeries (Odor *et al.* 2021, Srivastava *et al.* 2021).

In addition, incidents of implicit learning and memory during anesthesia have been extensively reviewed over the past decades (Andrade 1995, Ghoneim and Block 1997). There are two kinds of general anesthesia awareness – anesthesia awareness with recall and anesthesia awareness

without recall, as not all patients are able to consolidate memories after their awareness experience (Cascella 2020a). “Recall” is the ability of a patient to retrieve memories and remember what went on while they were under general anesthesia. This is a subset of patients who are aware during their surgeries and can encode, store and later retrieve these memories (Chung 2014).

Explicit and implicit memories can form during a surgery under general anesthesia. Intraoperative awareness with recall takes place when a patient is cognizant during their surgery, is aware of and memorizes sounds and discussions and feeling severe pain. While being unable to move, breathe, speak, the feeling is often devastating (Bombardieri *et al.* 2019). Most patients report feeling hearing voices in the operating room, some recall entire conversations. Other patients have described how medical procedures felt, such as endotracheal tube insertion, or discomfort at the incision site (Cascella 2020a).

Uncomfortable sensations are reported but pain is not commonly reported. In the relatively rare cases where pain is reported, it is often described as severe and distressing. Sometimes patients report feeling buried alive, paralyzed, or suffocated (Cascella 2020a). This is especially distressing if muscle relaxants and neuromuscular blocking agents were administered. Often patients who go through intraoperative awareness and recall it after the surgery experience psychological consequences and acquire post-traumatic stress disorder, nightmares, an aversion to future surgeries, and other life-altering emotional sequelae.

There is still a very incomplete understanding of the neural correlates of consciousness and awareness (Mashour *et al.* 2011, Tasbihgou *et al.* 2018), and a very active field of research that seeks to specify precisely what features of neurons (or other physico-chemical media) are necessary or sufficient for inner experience (Hudetz *et al.* 2016, Sanders *et al.* 2015, Tononi *et al.* 2016). A specific research program suggested by these data, paralleling the search for the medium of memory beyond synaptic tuning (Abraham *et al.* 2019, Dasgupta and Gershman 2021, Gallistel 2017b, 2020, Gershman 2023, Gershman *et al.* 2021, Langille and Gallistel 2020, Queenan *et al.* 2017), is the investigation of other biophysical events in tissue, such as cytoskeletal dynamics (Craddock *et al.* 2012, Dent 2017, Fields and Levin 2017, Lamprecht 2016, Priel *et al.* 2010, Smythies 2015) and biochemical networks (Biswas *et al.* 2021, 2022, Katz and Fontana 2022, Katz *et al.* 2018), which could underlie aspects of cognition in human and other life forms that are normally attributed to neurons (Baluska, Miller, *et al.* 2022, Baluska and Reber 2021, Baluska, Reber, *et al.* 2022, Reber and Baluska 2021).

3.3.2 Implicit Learning and Consciousness during Cardiac Arrest

The most all-encompassing work on consciousness and awareness near-death is Parnia's AWARE studies (Parnia *et al.* 2014, 2023). These investigate the transition to death by interviewing patients who have transitioned into death but then survive by resuscitation (Parnia and Fenwick 2002, Parnia *et al.* 2014, Shlobin *et al.* 2023). Electrical activity of the brain was monitored throughout the resuscitation effort by way of EEG. In the original 2014 study, 46% of cardiac arrest survivors are reported to have formed memories during this time. While the near-death experience is associated with absent cerebral activity as monitored through EEG, patients experience heightened consciousness and a paradoxical level of awareness.

In the most recent AWARE study, Parnia and his team studied consciousness, awareness and anesthesia during cardiac arrest and cardiopulmonary resuscitation in a hospital setting, and some patients recalled their heightened conscious experience, even though they were clearly unconscious by all other measurements during the cardiac arrest (Parnia *et al.* 2023). The study concluded that even if consciousness is clinically not detectable, consciousness might still be there. Cardiac arrest patients went through phenomenological experiences while they were being resuscitated and as they approached brain death but not reached it – as no one has been brought back to life past brain death (Shlobin *et al.* 2023).

Survivors of the resuscitation efforts were offered to be interviewed and shared their cognitive experience and memories while they were experiencing cardiac arrest. A proportion of consenting patients after resuscitation had recalled experiences of death and/or transcendental experiences – a form of paradoxical lucidity where patients go through a meaningful review of their life at a drastically increased level of consciousness, they re-evaluated moral highs and lows in their own life (Parnia *et al.* 2023).

3.3.3 Terminal Lucidity and Paradoxical Lucidity

Unlike salamanders and planaria (Agata and Umesono 2008, Endo *et al.* 2007, Pietsch 1981), human brains are not thought to regenerate. The standard picture of advanced age and degenerative disease is that of consistent monotonic decline in cognitive capacities. However, this prediction is challenged by frequent reported cases of terminal lucidity, a phenomenon that has been reported in patients since the 18th century in many different retrospective case studies, as reviewed in (Macleod 2009, Nahm and Greyson 2009, Nahm *et al.* 2012).

Terminal lucidity occurs in patients with terminal conditions, including neurodegenerative conditions, minutes, hours, or days before death. Patients experience a sudden mental clarity, the return of memories and normal cognitive function shortly before dying, which seems impossible given the extent of their past state, and history of brain degeneration and

damage. These coherent interactions can have a duration ranging from minutes to days, and most patients pass away within the next few days (Lim *et al.* 2020).

This phenomenon has been observed in most enigmatic cases including Alzheimer's patients, dementia patients, chronic schizophrenia patients, comatose patients, as well as those patients with brain abscess, brain tumors (Mutis *et al.* 2019), strokes, and meningitis (Nahm *et al.* 2012). For example, a case was reported of a young man with metastatic lung cancer, who was unable to speak or to move because the tumor had replaced his brain matter. However, in the hours before his death, he woke up and conversed with his family, said goodbye, then died shortly after (Nahm *et al.* 2012).

In another case, a 91-year-old patient was paralyzed and had a totally frozen countenance after two consecutive strokes, yet right before death she sat up in bed, raised her arms and exclaimed the name of her husband (Nahm *et al.* 2012). Another case study involved Anna Katharina Ehmer, a 26-year-old patient with severe mental disabilities. She reportedly never uttered a word in her life, yet spontaneously sang songs for half an hour right before her death (Nahm and Greyson 2013).

Terminal lucidity has been recorded in the pediatric population as well, lately including unresponsive children suddenly regaining communication ability, physical activity, and reduced mental impairment through elation, energy, and calmness just prior to their passing. A common theme was that the dying children reassured their parents they would "be alright" (Roehrs *et al.* 2023).

These cases are not one-offs: cases of terminal lucidity and other end-of-life phenomena (Claxton-Oldfield and Dunnett 2018) are typically reported by hospital staff, families and friends of the bereaved, and palliative care hospice workers. It can be a profoundly emotional but also confusing experience for loved ones of the ill patient, that has been compared to being granted one last dance on a cold November night with a loved one as a last farewell, after seeing them drained of life (Zieneldien 2023). These cases offer examples of completely unexpected cognitive and motor function despite months of coma, severe brain damage or dysfunction.

A similar, yet distinct term has been defined by the National Institute of Aging workshop in recent years: paradoxical lucidity (Peterson, Clapp, Harkins, *et al.* 2022, Peterson, Clapp, Largent, *et al.* 2022). Paradoxical lucidity is the remission and return of cognitive capacities and communication ability in those with dementia or some other severe neurodegenerative conditions, not necessarily at the time of death (Mashour *et al.* 2019, Nahm 2022).

Not all paradoxical lucidity is terminal lucidity, and not all terminal lucidity is paradoxical lucidity, but there can be overlap when a case is both terminal and paradoxical. A 2021 study highlighted 124 cases

of patients with dementia experiencing paradoxical lucidity in a survey (Batthyany and Greyson 2021). In this study, while 90% of their sample size had extreme cognitive impairments brought on by dementia, 80% of their sample regained seemingly normal communication skills and attitudes during their lucid episode, although the majority of the sample passed away shortly after the experience.

3.3.4 *Psychedelics*

Psychedelic drugs, including mescaline, psilocybin (from magic mushrooms), and LSD, give rise to a mind-expanding intensive hallucinogenic trip reported by those who consume the drugs. Another implication of a straightforward mind-brain mapping is that the strength of conscious experience should roughly correlate with the strength of brain signaling. However, despite the stimulatory and out-of-this-world nature of their psychedelic trips, there are several examples in modern literature where these are accompanied by a paradoxical reduction in brain activity.

BOLD-fMRI tracks neural correlates of brain activity by using oxygen as a proxy for an activation of brain regions. If conscious experiences are determined by the activity state of the brain, we would expect the high intensity of the psychedelic trip to proportionally correlate with neural activity, thus hypothesizing to see increased hemodynamic activity through BOLD-fMRI. Research studies such as that by Carhart-Harris *et al.* (2012) demonstrated a contradictory result, as did other studies with other hallucinogens such as LSD and Ayahuasca reviewed by Masi (2023). Brain activity under the influence of psilocybin was measured and compared to the awake state. BOLD-fMRI reports demonstrated a paradoxical decrease in blood flow and oxygenation.

The psychedelic state, a very rich sensory experience which patients report, is associated consistently with reduced brain activity, despite which users reported changes to their surroundings, altered sights and sensations, wandering thoughts, and an uninhibited rich sensory experience. The regions that showed the strongest reduction in activity are typically the most interconnected regions of the brain. Hallucinogens are thought to cause fragmentation or dissociation in the brain which results in uninhibited cognition. Kastrup (2016) summarizes that psychedelic experiences have been reported to incorporate voyages to parallel universes:

death- and birth-like experiences; conversations with what is often described as alien entities or deities; unfathomable and countless insights into the underlying nature of reality and self; the witnessing of indescribably complex structures and motion; synesthetic traversals of the entire gamut of human emotions and beyond.

The presence of richer and more intense conscious experiences, in the context of suppressed brain function, is a phenomenon that is not clearly

predicted by traditional theories of brain-mind mapping (Kastrup 2016, 2017) – although it may be compatible with integrated information theory (Tononi *et al.* 2016).

4. Expanding Model Systems for Mind-Brain Research

4.1 Unconventional Memory Transfer during Organ Transplantation

The mind is traditionally thought of as being centered in the brain, and familiar thought experiments in philosophy of mind and personal identity usually revolve around “brain transplant” scenarios. However, with the rise of transplantation surgery in modern surgical practice there have been cases in which the recipient of a transplant into the upper/lower abdominal or thoracic cavity, not the cranium, experiences a remarkable change in psychology, preferences and behavior, including a personality change which closely parallels the donor’s personality (Liester 2020). Improved international success of heart transplantations and increased longevity and survival have given rise to an increase in reported cases of changing personality/emotional state/identity following heart transplantation (Bunzel *et al.* 1992, Liester 2020).

Especially in heart transplantation, there have been observed clinical cases where the recipient experienced an abrupt change in food preferences, sexual preferences, emotions, personality, and identity, as outlined by Liester (2020). Importantly, recipients of the heart transplants in some instances were strictly barred from accessing information about the identity of their organ donors. In one example, a former McDonalds and meat foodie developed a strong aversion to meat after receiving a heart from a donor with vegetarian tendencies. A different heart transplant recipient case experienced a sudden interest in art museums. Other recipients who formerly had no proclivity towards music developed an extremely strong interest in music after their heart transplants from music-lovers. Cases involving a change in sexuality include a lesbian recipient of a heterosexual donor’s heart become inexplicably but strongly attracted to men. Critically, upon separate interview of the deceased donor’s next of kin, investigators found that the new personality trait or acquired tendencies had profoundly resembled the traits of the donor while the donor was alive (Liester 2020, Pearsall *et al.* 2000). Cases of heart memory transfer have also been reported recently (Lakota *et al.* 2021, Liester 2020).

There is also discussion in the literature about other organ transplants besides heart, including lung, liver, and kidney transplantations. Changes to emotions and personality attributes were observed in the respondents. In one recent study, 91.3% of heart transplantation patients reported having any personality changes, while 87.5% of other organ transplant recipients reported experiencing any personality changes (Carter *et al.* 2024).

Thus, the study suggests that personality changes may not be exclusive to heart transplantations. Personality changes reported refer to changes in temperament, emotions, food, sport spectating, physical activity, religious/spiritual beliefs, among others. All in all, reaching a strong conclusion in these transplantation cases will require much more data, especially to correlate the new personality traits with those of the donor. But as with other types of clinical observations presented above, such transfer via non-neural tissue is not a prediction of any conventional theory of the brain-mind relationship.

4.2 Plasticity: Adaptation to Novel Embodiments during Organ Transplantation

Behavior, and thus brain structure and function, are key to evolutionary success and have been under very strong selection. A baseline assumption might be that the details of behavior, cognition, and the inner experience of self and world should be closely tied to the default nervous system architecture that has evolved in our species – specifically, highly dependent on the normally reliable and consistent human form.

However, a fascinating plasticity to the brain-mind relationship is revealed when prosthetics are used to extend the standard complement or connectivity of brain and sensory-motor affordances: the mind is apparently ready, with no further rounds of mutation and selection, for quite diverse embodiments. Whereas the previous sections focused on informative cases of damage, loss, and suppressed function, we now consider the effects of augmentation (Kasten and Eilers 2023).

In the rubber hand illusion (Castro *et al.* 2023), an experimenter simultaneously brushes a visible dummy hand and the hidden real hand in synchrony. A sudden strike of the rubber hand with a hammer elicits a strong fear response in the patient, revealing that a healthy subject embodies the dummy hand, perceiving it to be part of their own body. Is it not remarkable that millions of years of history as a tetrapod – an extremely reliable dataset in terms of knowing exactly how many hands one has – is over-ridden in minutes by simple visual experience? The mind’s ability to model the body is extensive and not tightly bounded by the past (Iani 2022).

In a similar vein, neuroscience studies in astronauts (Clément and Reschke 2010) have noted how the body’s self-perception changes when subject to microgravity in space (weightlessness). The body adjusts its proprioception and vestibular system under changing sensory inputs and conflicting sensory information with what the space-travelers (and all of their land-dwelling evolutionary ancestors) were accustomed to back on Earth. Thus, both the rubber hand illusion and space studies demonstrate conditions or instances where the relationship between the subjective perception of self and physical body is challenged and demonstrates

the brain's potential for recalibration of very fundamental and ancient lifestyle assumptions.

With rising investigation into neuroprosthetics in biomedical engineering, it is becoming clear that the standard complement of sensors and effectors is not the only one which our CNS can control. Brains can expand their commands and interact with effectors and sensors outside our fixed set, beyond the integrated sensory-motor homunculus that we were born with, as demonstrated through recent success with expanding our sensory perception and motor control: brain-machine interfaces (Ifft *et al.* 2013, Lebedev and Nicolelis 2011, Rothschild 2010), neuroprosthetics, and haptic devices.

Motor prosthetics such as brain machine interfaces (BMI) and neuroprosthetic limbs in specific help restore motor function in patients with paralysis or amputated limbs. These interfaces directly interact with the brain. Control strategies used in neuroprosthetic systems are discussed by Wright *et al.* (2016), including neuromodulation implants, neuroprosthetics, neurorobotic devices, and control strategies of BMIs and feedback approaches in such systems (Adewole *et al.* 2016, Lebedev and Nicolelis 2017, Armstrong *et al.* 2021, Fiani *et al.* 2021, Luckiewicz 2021).

In addition to existing work on BMIs, there has been progress into designing haptic wearables. Haptic devices are devices worn on the body that are attached directly to the skin ungrounded for daily life outside of the lab. Depending on the extent of the sensory impairment in the patients, haptics can act as sensory replacers (such as for use in totally impaired blind or deaf individuals), sensory augmenters in those with partial impairment, and can even be used as a trainer in patients without any impairment. For instance, Eagleman's studies are among those researchers in the field of sensory substitution, sensory augmentation and haptics attempting to innovate ways in which those that are deaf can acquire the ability to hear (receive auditory input) through their skin. An in-depth overview of Eagleman's and others' efforts in the field is discussed by Eagleman and Perrotta (2022).

As discussed in the context of near-death and out-of-body experience cases, the way that the brain maps the human body and our representations of the brain are labile in some instances. Likewise, the augmentation and instrumentation of the human brain demonstrates that the current state is not the upper boundary for human cognition (Clawson and Levin 2022). The rise of bioengineered devices and the exploration of expanding the BMI has shown adaptation of our nervous systems to sensory augmentation and motor augmentation (Levin 2023b, Raisamo *et al.* 2019).

Given that brain regions are very good at taking over un-used computational real-estate, as in cases where the loss of one kind of sensory organ leads to brain regions being taken over for processing by others (Bedny *et al.* 2011, Loiotile *et al.* 2019, Sabourin *et al.* 2022, Scott *et al.* 2014), it

is interesting to consider what other kinds of biological and technological media could be integrated into the human mind.

4.3 Cognitive Abilities Exceeding Apparent Experience, Training or Skill: Savants, Prodigies, and Voices

A standard prediction of a strong mind-brain dependency would be that the capacities for cognition and behavior should be limited to those afforded by the brain and its history of educational experiences. However, this prediction does not match a number of cases in which knowledge or skill set are revealed in the absence of conventional routes to these capabilities.

In one bizarre case, there was a report of a cancer diagnosis made by a woman's hallucinatory voices (Azuonye 1997). Hallucinatory voices could occur in healthy patients, such as those grieving the death of a loved one, or psychiatric patients, such as schizophrenics. In this case, a woman in her thirties from London experienced voices in her mind which spoke and pressured her to go get diagnostic scans for her brain tumor. She had no prior neurological signs or symptoms so there was no clear justification to request diagnostic imaging. Yet, once the doctor conceded to the voices' instruction and ordered a head CT scan, a brain tumor was indeed identified. After the tumor was removed, the voices said goodbye and never returned to the woman again (Azuonye 1997, Bobrow 2003).

It is unknown whether this is evidence of previously-unknown modules in the human mind which have access to normally unconscious physiological body states and can occasionally report them via the linguistic interface, or something else. Such cases of conscious perception of low-level physiological events in the body are complemented by the ability, in the context of hypnotic, meditative, and yoga/biofeedback practices (Black *et al.* 2019, Dossett *et al.* 2020, Mason 1952, Shenefelt 2000, 2010, Venditti *et al.* 2020), to control autonomic and other cellular- or even molecular-level properties normally not under conscious control. Together, they may hint at biomedically-untapped abilities of biological subsystems to communicate across scales of organization.

Many other cases exist in which information is presented to the main personality in a way that feels as though it was coming from another being. One example is the mathematician Srinivasa Ramanujan (1887-1920), who attributed his astounding mathematical discoveries to communication with the Hindu Goddess Namagiri (Lu 2019, Rajendran 2012). While the perceived phenomenology of such experiences is not a reliable guide to underlying processes, data on multiple personalities interacting within one person, such as dissociative identity disorders (Braude 1995, Kelly and Kelly 2007) and split-brain cases (de Haan *et al.* 2020, Rosen 2018), underscore the importance of understanding both the inner perspective and

the objective behavioral coherence of distinct cognitive selves operating within a conventional embodiment.

An exciting frontier for future research is the investigation of the mechanisms that establish and maintain a border between self and outside world (Kirchhoff *et al.* 2018, Levin 2019). Fascinating questions include how those functional borders relate to their first-person perspective and awareness of each other's informational content, and the understanding of how a specific volume of neural tissue can support multiple perspectives (whether verbal or not) and under what circumstances they can communicate with each other.

One aspect of this field concerns the ability to estimate the cognitive performance of a given embodiment from relevant parameters of anatomy, physiology, and history of experiences. Savant syndrome is a condition including individuals with severe cognitive disabilities, such as autism spectrum disorder or intellectual disability, who suddenly exhibit extraordinary ability in specific domains, such as exceptional mathematical or musical ability (Treffert 2009).

For example, the patient Kim Peek who inspired the movie *Rain Man* had considerable dysplasia in his brain and cerebellum, including encephalocele (malformed cerebrum), hollow CSF-filled areas in his brain, and a missing corpus callosum (Nahm *et al.* 2017, Treffert and Christensen 2005). Among many other incredible capabilities, Peek memorized thousands of books and had extraordinary geographic erudition and photographic memory despite drastic damage to his brain and an absent corpus callosum (Treffert 2009, Treffert and Christensen 2005).

Skills seen in savants can be categorized as impressive talent in music / piano (Young and Nettelbeck 1995), art (Hou *et al.* 2000), mathematics, and exceptional mechanical and spatial sense such as gauging distances and lengths without any tools or navigation (Treffert 2009, Treffert and Christensen 2005). For example, some savants possess the ability to compute prime numbers, yet were weak in their overall arithmetic ability (Welling 1994). Other skills reported in savants include synesthesia (e.g. involuntary association of numbers to colors or sounds to letters), excellence in a specific academic field, calendar calculations, and readiness to learn new languages (as polyglots).

Savants can be classified as talented or prodigious. Talented savants show special abilities in stark contrast with their cognitive disability. Prodigious savants, while very rare, demonstrate outputs that would be outstanding even for a comparable unimpaired neurotypical individual. Nahm *et al.* (2017) reviews the cases of blind pianists Thomas Berthune and Leslie Lemke, who were visually blind, yet musically gifted savants. They never participated in any piano classes yet could play incredibly complex and lengthy pieces after hearing them once and memorize every chord and note.

Savant syndrome can be associated with a pre-existing neurodevelopmental condition or can be acquired after brain injury. The syndrome can arise in individuals following a brain injury such as a lightning strike, hemorrhage (Lythgoe *et al.* 2005), dementia (Miller *et al.* 1998), injury, trauma. These cases are known as “acquired savant syndrome”. It has been suggested that damage in one lobe enhances the function in its counterpart (Hou *et al.* 2000).

Furthermore, savant syndrome can arise spontaneously. Treffert and Treffert (2021) describe eleven cases of acquired savant syndrome that were not preceded by any notable cause, injury, or disability. These reported cases involve a 43-year-old woman, with no former interest in art, who woke up in the middle of the night with a sudden compulsion to draw and dedicates 8 hours per day to beautiful, original works.

Another case was of a 28-year-old attorney, who could only play simple popular memorized melodies on the piano, sat down at a mall piano and suddenly gained a deep knowledge of musical theory and composition. When he searched for music theory on Google later, he was surprised to learn that he already understood it all. Treffert hypothesizes that these cases support the possibility that many (or all) humans have a latent potential for these extraordinary skills buried deep within them, remaining obscured behind normal cognitive processes. A similar line of thought was suggested by Snyder (2009).

Another instance where people demonstrate skills without prior training include xenoglossy, which is when an individual becomes fluent in a language that they have had no apparent knowledge or training in, reviewed by Wahbeh *et al.* (2022). For example, Stevenson in 1976 described the case of a woman whose husband hypnotized her to relieve a backache. In her trance, she started to respond to her husband in German, a language which she had no known prior background nor childhood exposure in (Bobrow 2003, Stevenson 1976). The conventional process of learning foreign languages requires significant and obvious effort. Cases of language facility without the traditionally required amount of practice and exposure to large quantities of training data suggest the presence of faster routes to this skill than is predicted by current theories of memory and language acquisition by human brains.

Finally, we consider the very intriguing occurrence of child prodigies. These children show exceptional mastery in specific domains at a striking early age, without necessarily having a disability like the autistic savants. Prodigies in various domains such as chess and piano rapidly acquire skills at a pace unseen in most people, excelling in the domain prior to adolescence. Ericsson’s theory of deliberate practice is challenged in the cases of child prodigies because child prodigies reach a high proficiency level in a compressed period, therefore practice time is not always the main distinguishing factor that explains child prodigies (Chang 2016).

It is unclear whether the immense variation in human talent and expertise can be explained by practice and genetics (Hambrick *et al.* 2016). A recent study closely examined musical prodigies and compared them relative to non-prodigy musicians to understand what differentiates a prodigy from a regular child, by assessing associations with intelligence, personality, practice level, motivation, and many other factors (Marion-St-Onge *et al.* 2020). The study's main conclusion was that deliberate practice is insufficient to make a prodigy and it is the combination of early deliberate practice with a natural brain predisposition for musical ability that determines their incredible success in early childhood. In other words, child music prodigies are at the high end of the huge variation in the human continuum of expertise.

Other works on musical talent have also found no causal effect between practice and musical ability, suspecting that human variability affects both skill potential and willingness to practice (Mosing *et al.* 2014). Another study by Chang (2016) followed a young child chess prodigy and found that spending time studying chess alone and participating in chess activity is not sufficient to reach a prodigy-level of chess performance. It took the child much under 10,000 hours and under 10 years to reach mastery.

Altogether, studies of child prodigies support innate ability and the “nature” in nature-versus-nurture as the strongest driver of talent (Ruthsatz *et al.* 2014). The phenomenon of young virtuosos does not accord with standard developmental timelines and learning processes and challenges the field to develop models that predict what features of the brain would confer such remarkably rapid gains in skill – and why they can sometimes be induced in adults by unusual circumstances, such as head injury, in acquired savant syndrome (Treffert and Treffert 2021).

It is common to all the above cases that standard theories do not predict the surprising amount and type of cognitive performance sometimes found in normal or even impaired brains. Despite much neuroscience research on normal and exceptional abilities we still do not really understand the “carrying capacity” of brain tissue. Unlike with standard computing devices, we simply do not know how much and what kind of brain tissue is necessary for a specific degree of performance (despite a plethora of data on how various competencies can be rendered non-operable by a myriad of injuries and disorders).

Taken together, savant and multiple-personality type cases remind us that unlike in computer science, where we know the precise computational capacity of a given amount of medium, we simply do not know how many personalities, memories, and skills can “fit” in a given amount of brain tissue. Much more research is needed on this topic, including the tradeoffs that have prevented evolution from making these skills available widely in populations.

4.4 Endless Forms Most Beautiful 2.0

An emerging field that will revolutionize the study of the mind-brain relation is that of synthetic organisms. Cyborgs, hybrot, biobots, and chimeras between biological and technological components are currently being made – a natural extension of prosthetics and repair technology (Clawson and Levin 2022). These beings reveal the astronomically large space of the possible – bodies (and minds) far beyond the $N = 1$ example of natural evolutionary history here on Earth.

These technologies enable many fascinating lines of inquiry. First, what kinds of cognitive performance is possible – without restriction on brain size or architecture, what depth and breadth of IQ is achievable? Second, where do “kinds of minds” (Dennett 1996) come from, in addition to evolution? Recent discoveries of proto-organisms made from wild-type frog or human cells (Blackiston *et al.* 2021, 2023, Gumuskaya *et al.* 2022, 2023, Kriegman *et al.* 2020, 2021, Levin 2020) reveal novel form and function that have no evolutionary history of selection in their configurations. If not eons of selection, where do their behavioral properties come from? This question will stand increasingly sharper as the memory and problem-solving capacities of such novel constructs (Ebrahimkhani and Levin 2021, Kamm *et al.* 2018, Sample *et al.* 2019) are explored.

Novel embodiments of mind will be increasingly merged with research on mental content that moves throughout the body. Memories can move naturally, such as when tails of trained planaria imprint the memories on the newly-regenerated brain (McConnell *et al.* 1959, Shomrat and Levin 2013), or be moved experimentally during transplant experiments with cells or mRNA/protein extract (Bédécarrats *et al.* 2018, Chen *et al.* 2014). Thus, the normal dynamics of memory in minds must be widened to include additional substrates and processes for its distribution and transformation (Blackiston *et al.* 2015).

More broadly, developments in diverse intelligence research are now finding strong parallels between familiar (neural-based) minds traversing familiar 3D space of behavior and unconventional intelligences in our bodies that navigate and solve problems in spaces such as physiological, transcriptional, and anatomical morphospace (Fields and Levin 2022).

Recent work on developmental bioelectricity (Levin 2023a) suggests it to be a precursor to neural computation, and also the cognitive glue that holds together the morphogenetic collective intelligence (just as bioelectricity in the brain binds neurons into a collective intelligence of the familiar human personality). The expansion of neuroscience techniques beyond neurons hints at a fascinating vista of research into the mind-body relationship of beings of very unconventional composition, which surely will shed light on our understanding of conventional brains and minds.

One possibility is that the remarkable diversity of cognitive outcomes for various normal and abnormal configurations of brain tissue is a result of plasticity that is fundamental in living matter. It has been argued that evolution operates on a fundamentally unreliable biochemical medium. Physiological noise at all scales, unpredictable changes of environment, and inevitable mutations all mean that the most adaptive, successful strategies are not stable, fixed solutions to specific niches but instead problem-solving agents. Molecular networks, cells, and tissues deploy on-the-fly problem-solving capacities at several scales of organization and time (Levin 2023b, 2024b).

Evolution, and embryogenesis, cannot take the lessons of the past too seriously, but must accommodate novel circumstances and pull together coherent form and function each time (Levin 2023b, 2024b). For this reason, while embryogenesis under normal circumstances reliably produces the same outcome, wild-type cells can be readily hacked (by parasites or human bioengineers) and adopt novel configurations with ease (Ebrahimkhani and Levin 2021, Gumuskaya *et al.* 2023, Kamm *et al.* 2018).

This need to improvise, and continuously re-interpret information in current context, has been suggested to form an intelligence ratchet, first deployed in metabolic, transcriptional, and physiological spaces, but eventually pivoted to anatomical morphospace and then the neurally-guided space of conventional behavior (Fields *et al.* 2020, Fields and Levin 2022). The regenerative capacity of cells, which includes problem solving at the beginning of embryogenesis (how to re-grow an entire body from 1 cell) and throughout lifespan (how to regenerate organs damaged by injury, and continuously maintain tissue despite cellular senescence and replacement), is likely to be a foundational basis of the plasticity described above. It may be that the ability to organize a mind, despite brain damage, is a consequence of the ubiquitous need for living material to persist and thrive under challenging and rapidly changing circumstances.

How many human minds can be formed from one human fertilized egg? The answer is not fixed by genetics, as splitting early embryos gives rise to monozygotic twins, triplets, etc. – whether individual or conjoined (multiple brains and personalities in the same body; Savulescu and Persson 2016). The biological substrate is a pool of potentiality for some number of individual selves, and the mapping between cognitive being and the physical substrate offers many questions. The intelligence ratchets (Levin 2023b) formed by cycles of evolution over increasingly competent living material offer rich possibilities for computational modeling and experiments in tractable model systems that may address evolutionary dynamics governing exceptional human performance (including that which manifests despite reduction in brain capacity).

5. Discussion

The questions raised by these unusual clinical cases and laboratory data in diverse intelligence research are especially important as society prepares for the impending plethora of not just non-neurotypical humans, but ones that are modified and augmented by chimerization with technology, trans-individual connections with other humans and AIs, and by changes to genetics and physiology (Camargo 2023, Cozza *et al.* 2022, del Valle Quintana 2024, Harzheim 2024). As novel kinds of bodies, brains, and other cognitive media are invented and modified, a full picture of the relationship between minds and their substrate becomes critical.

In order to understand the practical and moral status of the plethora of forthcoming unconventional beings, it is essential to gain a better understanding of the one example of mind in the physical universe that we have – the members of the web of life on Earth (Levin 2024a). More immediately, the needs and opportunities of regenerative medicine of the brain and body likewise require a solid foundation for understanding what happens to the minds of patients whose brain is partially replaced by the new progeny of therapeutic stem cells or assisted by corrective or augmenting technology.

5.1 Limitations of the Study

Many of the exceptional clinical cases described above are either individual instances or involve very small sample sizes. Single- or small case studies must be interpreted especially carefully, as minor details can significantly alter interpretations and lead to incorrect conclusions. Conversely, it is entirely possible that a significant “file drawer problem” exists in this field, with numerous relevant cases being under-reported because the current paradigm does not facilitate study or reporting of drastically divergent examples.

In addition, regarding some of the anesthesia awareness data, we acknowledge that EEG signals are highly noisy and despite their excellent use in modern-day clinical medicine, they provide only correlates of consciousness. Therefore, one cannot assume that the absence of measurable signals directly equates to a total lack of neural activity. We acknowledge the limitations of tools such as EEG, (f)MRI, and single-cell ablation in studying brain function.

5.2 Conclusion and Outlook

The relationship between mind and brain (or more accurately, mind and body; Pfeifer *et al.* 2007) is among the most fundamental questions that science and philosophy can address. Here, we make no firm conclusions nor push a specific theory. However, we hold that the issue isn’t

whether a model can have epicycles attached to it to save it from uncomfortable observations – almost always, it can (for a while, anyway). The better question is, do we have models that actively predict the existence of the kind of phenomena we describe above – that entail them as a primary consequence, embrace them comfortably, and most crucially, suggest ways to use them for new biomedicine and for driving new discoveries on the nature and possible futures for humankind.

The data discussed above have implications along two main lines. The first concerns the fundamental understanding of evolution, cognition, and neuroscience, not to mention philosophy of mind (Ameriks 1976). The second comprises a set of practical applications impacted by aspects of mind-brain mapping, including cryogenics, hibernation in space exploration, biomedicine of brain regenerative therapies (memory persistence), the transplants of memories (via organs, RNA, or other means), neural decoding, memory prostheses and brain-computer interfaces, virtual reality, etc. So, what conceptual roadmap could help update existing models and facilitate advancements in these areas? The following is one attempt at an unconventional direction for research.

All living beings exploit mathematical affordances and embody in-hierencies that are no direct result of selection (Belousov 2008, Belousov and Grabovsky 2007, Newman 2017, 2019a, 2019b) but strongly contribute to the course of evolution. For example, having discovered a voltage-gated ion channel protein, evolution has made a transistor (a voltage-gated current conductance) which immediately (and for free) brings with it the historicity of feedback loops (memory), the truth tables of logic functions that exist for transistors in specific configurations, the special status of the NAND gate, Turing and Gödel limits, and much more. Having discovered proteins with two different levels of adhesion, evolution automatically unlocked the self-organization of multi-layered spheres (Foty and Steinberg 2005).

There are numerous other examples, from the curious behavior of cellular automata, Fibonacci series, and fractal forms to theorems of calculus, logical paradoxes, cybernetics, Gödelian results, etc. (Belousov 1976, Isalan 2009, Losa 2009, Peitgen *et al.* 1992, Thompson and Whyte 1942, Vogel 1988, West 1990, Winfree 1980). Given the likely parallels between the self-construction of bodies and of minds (Bateson 1972, Grossberg 1978, Pezzulo and Levin 2015, Piaget 1976), these examples are instructive for asking how specific cognitive capacities relate to their material substrate.

Questions about living form – “where does the pattern come from?” can be tracked backwards through the chain of biophysical mechanisms studied in developmental biology but always bottom out in a mix of three features: genetics, environment, and wherever the truths of mathematics come from (Panza and Sereni 2013, Penrose 2004, Tegmark 2015). The

first two alone are not sufficient as a guide to explaining existing forms, and repairing (and making) new ones (Davies and Levin 2023).

In a sense, our physical capacity for self-assembly during embryogenesis, and self-repair during maintenance and regeneration, is the result of genetically specified hardware acting as boundary conditions on the “free lunches” provided by the results discovered by mechanics, geometry, computation, calculus, information theory, and many others. In this sense, body structures may be considered as “receivers”, tuned by evolution to exploit affordances that are not tangible in the physical world but nevertheless are instructive and causally potent – along with virtual governors (Dewan 1976, Pezzulo and Levin 2016), constraints and absences (Deacon 2012), etc.

How might this be relevant for the understanding of the mind-brain relationship? Consistent with the above framing is the “filter theory” of mind (Dossey 2012, Hawkins 2011, Marshall and Marshall 2005), which emphasizes the importance of screening out a massive amount of incoming perceptions to maintain adaptive cognition. It is interesting to note that the classical notion of the brain as a reducing valve or filter (Huxley 2010) has a parallel in machine learning. Variational autoencoders function via a narrow bottleneck which stands between a rich input and the novel output.

Learning, generalization, and the creativity of the output layers (which must interpret an impoverished signal given to them) depend on the squelching of the details in the bottleneck layer that allows focus on general patterns abstracted from raw experience (learning and insight). It is also possible that this work impacts on research in AI. Is it possible that artificial minds are likewise not entirely constructed, but to some extent reflect universal patterns seen through the filter of, and embodied via the interface of, a given connectionist architecture (whether that be silicon-based or proteinaceous)?

Overall, perhaps the mind-brain relationship (whether biological or synthetic) is similar to the relationship between mathematical laws (forms) and bodies. With respect to the ancient question of whether mathematics is discovered or invented, current neurobiologists and AI coders often assume their work product is invented. We propose that it may be interesting to explore hybrid views. Just as body structures determine which specific universal patterns are embodied at any given time, some of the above-discussed phenomena may become better integrated into frameworks that seek to characterize the space of universal cognitive competencies that can be manifested by specific neuro-physiological dynamics. While it is too early to say anything definitive about how kinds of minds (Dennett 1996) relate to the partially mapped-out space of mathematical forms, we believe it to be essential to explore this direction.

One practical way to do so is by paralleling the work done to un-



Figure 3: Structures (galls) made by leaves in response to signals from a parasite (e.g., a wasp).

derstand the morphospace of body anatomies and functions, by producing minimal synthetic agents that exhibit coherent patterns of form and behavior without the benefit of eons of evolutionary selection (Abramson and Levin 2021, Atmanspacher 2024, Atmanspacher and Fach 2005, Atmanspacher and Fuchs 2017, Atmanspacher and Rickles 2022, Blackiston *et al.* 2023, Braitenberg 1984, Doursat and Sanchez 2014, Doursat *et al.* 2013, Fach *et al.* 2013, Gumuskaya *et al.* 2023, Kamm and Bashir 2014). Such biobots, hybrot, and cyborgs (Clawson and Levin 2022, Ding *et al.* 2018, Li and Zhang 2016, Li *et al.* 2019, Aaser *et al.* 2017) serve as exploration vehicles for the latent space of possibilities – outcomes that are discovered, not constructed by micromanagement (Davies and Levin 2023, Lagasse and Levin 2023).

There are also natural examples of this, such as the fantastic and surprising shape of plant galls coaxed from normal plant leaf cells (Fig. 3). Without the work of a non-human bioengineer (a wasp), we would have had no idea that such shapes exist within the latent space belonging to an oak genome. Discussions of whether these patterns “really” exist are less important than the practical question of what axes, distance metrics, and other properties may be used to organize the contents of the option space of these patterns, and how we may systematically investigate its contents via biophysical systems that we find, modify, and engineer. To what extent the space of patterns is real (vs. familiar 3D space of physical objects) will be revealed by the degree of progress made by the research agenda of systematically mapping it and making use of its contents in bioengineering and biomedical settings.

To the extent that physical structures, such as brains, serve as indices (pointers) into that space of patterns, the external capabilities and inner perspective of these structures will be difficult to predict. The discovery of novel competencies and behaviors in much-studied simple algorithms (Zhang *et al.* 2024), and the surprising behavior of minimal matter (Cejkova *et al.* 2017, Hanczyc 2014, Strong *et al.* 2024), implies the need for caution. If we do not yet understand the capabilities of very simple

systems that we built ourselves, and do not yet have tools for readily envisioning intelligence in high-dimensional, unfamiliar problem spaces, very little can be said confidently about the status of a paramecium, AI, cyborg, or human in an exceptional state.

This impacts current debates around AI, because we simply do not yet know how materials, properties, and causal architectures index into the space of possible morphological and behavioral patterns. Some of the same arguments that warrant caution about assuming limitations on human cognition from the biochemical facts about brain tissue should likewise temper the common belief (held by many mechanist and organicist thinkers alike) that “machines” cannot access these patterns (Bongard and Levin 2021).

Discussions about what percentage of the brain people use, or how big a computer needs to be to rival performance of a specific organism based on the size of their brain or the number of synapses, are premature given the data reviewed above. This parallels discussion in the field of developmental genetics, in terms of unexpected amounts of DNA found in various species that does not seem to correlate well with their perceived complexity (Eddy 2012, Elliott and Gregory 2015, Lakhotia 2023). The discrepancy in genetics arises for exactly the same reason that it does in cognitive science: because the mapping between genes and morphology, as with neural components and cognition, is not direct (Levin 2023b, Lobo *et al.* 2014, Mitchell and Cheney 2024).

Much more progress needs to be made in this field before confidently talking about what kind of mind a constructed artificial system (whether biological, silicon-based, or hybrid) does or does not have. This is true for the same reason that we do not sufficiently understand the mapping of cognition onto the biological wetware (cognitive capability per cubic centimeter of brain tissue).

What is the cognitive analog of the discovery of surprising, complex, large-scale outcomes that can be summoned by simple signals sent to a competent living medium (Rouleau and Levin 2023)? Such discoveries can be made by probing the intelligence of engineered and modified beings – all manner of combinations of evolved and designed material (Clawson and Levin 2022, Ding *et al.* 2018, Li and Zhang 2016, Li *et al.* 2019, Mehrali *et al.* 2018, Orive *et al.* 2020, Aaser *et al.* 2017, Pio-Lopez 2021, Saha *et al.* 2020), in various scales of collective intelligence (Sole *et al.* 2016), to learn to predict and ethically relate to their emergent cognition. This is now entirely within reach of existing technology. While it is not being facilitated by existing conceptual models, the work will continue and is likely to feed back to eventually shape those models to better fit the emerging empirical data.

We propose a research agenda aiming at a synthesis of behavioral sciences applied to unconventional agents of entirely novel embodiments,

with the study of exceptional examples in human clinical medicine that rock the familiar picture of mind-body mapping. This is likely to uncover new vistas in numerous aspects of science and philosophy that will positively impact human flourishing by shedding much needed light on our true nature and capabilities.

*If the doors of perception were cleansed
everything would appear to man as it is, infinite.*

William Blake (1979)

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