Discrepancy Between Cerebral Structure and Cognitive Functioning

A Review

Michael Nahm, PhD, David Rousseau, PhD,†‡ and Bruce Greyson, MD**

Abstract: Neuroscientists typically assume that human mental functions are generated by the brain and that its structural elements, including the different cell layers and tissues that form the neocortex, play specific roles in this complex process. Different functional units are thought to complement one another to create an integrated self-awareness or episodic memory. Still, findings that pertain to brain dysplasia and brain lesions indicate that in some individuals there is a considerable discrepancy between the cerebral structures and cognitive functioning. This seems to question the seemingly well-defined role of these brain structures. This article provides a review of such remarkable cases. It contains overviews of noteworthy aspects of hydrocephalus, hemihydranencephaly, hemispherectomy, and certain abilities of "savants." We add considerations on memory processing, comment on the assumed role of neural plasticity in these contexts, and highlight the importance of taking such anomalies into account when formulating encompassing models of brain functioning.

Key Words: Hydrocephalus, hemihydranencephaly, hemispherectomy, savant syndrome, neural plasticity

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Although it is generally acknowledged that current neuroscientific models are not sufficiently developed to explain every detail of brain functioning, neuroscientists usually suppose that human mental functions are created by the brain and its various macro- and microstructures, including the different cell layers of the neocortex. These cerebral components form neuronal networks and circuits and are thought to possess and to exert specific functions that complement one another to generate an integrated self-awareness (Hart, 2016).

Nevertheless, several cases involving brain dysplasias (abnormal cell development) and brain lesions (cell damage) indicate that large amounts of brain mass and its organic structures, even entire hemispheres, can be drastically altered, damaged, or even absent without causing a substantial impairment of the mental capacities of the affected persons. These exceptional individuals display a notable discrepancy between the condition of their cerebral structures and the quality of their cognitive functioning (*e.g.*, Bell and Karnosh, 1949; Lorber, 1983; Muckli et al., 2009; Treffert, 2010). In the following, we provide a review of noteworthy cases that highlight this curiosity. We present overviews of remarkable aspects of hydrocephalus (enlarged cranium due to excess cerebrospinal fluid pressure), hemihydranencephaly (HHE) (complete or near-complete unilateral absence of the cerebral cortex), and hemispherectomy (surgical removal of one cerebral hemisphere), as well as of notable skills of some savants (persons with profound brilliance in certain areas of cognition, often accompanied by significant cognitive disability in other areas). Finally, we will discuss the questions these findings pose for the commonly assumed models of brain and memory functioning and for the assumed role of neural plasticity in these circumstances.

*Division of Perceptual Studies, Department of Psychiatry and Neurobehavioral Sciences, University of Virginia Health System, Charlottesville, Virginia; †Centre for Systems Philosophy, Surrey; and ‡Centre for Systems Studies, University of Hull, Hull, East Yorkshire, UK.

Send reprint requests to Bruce Greyson, MD, Division of Perceptual Studies, Department of Psychiatry and Neurobehavioral Sciences, University of Virginia Health System, 210 10th Street, NE, Suite 100, Charlottesville, VA 22902–4754. E-mail: cbg4d@virginia.edu.

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REMARKABLE DISCREPANCIES BETWEEN CEREBRAL STRUCTURE AND COGNITIVE FUNCTIONING

Remarkable Aspects of Hydrocephalus

In this first section, we will present a short overview of remarkable hydrocephalus cases, in which the mental faculties and, sometimes, the motor faculties of the individuals are prima facie surprising given the degree of their hydrocephalus. In one of the earliest reports of such a case, Martel (1823) described a boy who died at the age of 10. During the first years of his life, he seemed healthy, but eventually, his health deteriorated considerably. He had severe headaches, gradually lost all his senses except hearing, developed fits, and became confined to his bed, but he nevertheless seemed mentally unimpaired until his death. His head appeared enlarged, and upon autopsy, apart from "residues of meninges," "no trace of a brain" was found inside the skull (Martel, 1823, p. 20).

More recent cases were uncovered and documented by Lorber, who specialized in treating children with hydrocephalus and/or spina bifida. When assessing the IQ of his patients, he used the Wechsler Intelligence Scale for Children, and with adults who agreed to retesting, he used the Wechsler Adult Intelligence Scale. The most remarkable and well-known case concerns a highly intelligent student of mathematics (Lorber, 1978; Lonton, 1979) who received worldwide attention due to an article published in *Science* (Lewin, 1980) that drew attention to some of the most remarkable cases that Lorber studied.

The aforementioned student of mathematics had a global IQ of 130 and a verbal IQ of 140 at the age of 25 (Lorber, 1983), but had "virtually no brain" (Lewin 1980, p. 1232). Still, the student apparently developed normally throughout his childhood. Judging from photographs in his family album, he did have hydrocephalus from early in life, but it was not diagnosed and thus not treated. At the age of 20, he sought medical advice because of problems of endocrine maturation. Up to that time, he had not had seizures and he had no motor handicap. Similarly, his vision was perfect apart from a refraction error. Nevertheless, later studies showed the apparent absence of a visual cortex, and from the age of 23, he became subject to occasional grand mal seizures. He was featured in a documentary film about Lorber's work in 1982, in which he appeared behaviorally normal (Lawson, 1982). This student belonged to the group of patients that Lorber classified as having "extreme hydrocephalus," meaning that more than 90% of their cranium appeared to be filled with cerebrospinal fluid (Lorber, 1983).

Of the 687 patients whose brains Lorber scanned, 16 persons belonged to this group, and half of them were regarded as cognitively

normal—that is, they had an IQ of 100 or more (Lewin, 1980; Lorber, 1983). He classified patients whose cranium appeared to be filled with cerebrospinal fluid to a degree of 50% to 90% as having "gross hydrocephalus" and included details regarding the most remarkable cases in an article (Lorber, 1983). Apart from the above-mentioned student of mathematics, he described a woman with an extreme degree of hydrocephalus showing "virtually no cerebral mantle" who had an IQ of 118, a girl aged 5 who had an IQ of 123 despite extreme hydrocephalus, a 7-year-old boy with gross hydrocephalus and an IQ of 128, another young adult with gross hydrocephalus and a verbal IQ of 144, and a nurse and an English teacher who both led normal lives despite gross hydrocephalus.

Lorber stressed that the heads of the patients with hydrocephalus, including those who had a high IQ, usually had an enlarged circumference and that in these cases, the brain volume would probably be greater than the thinness of the cerebral mantle would suggest. Consequently, Lorber attempted to determine the brain volume of the patients with hydrocephalus using a method that seemed to provide realistic estimations (Jackson and Lorber, 1984). Regarding cases of extreme hydrocephalus, the brain volume of the mathematics student was determined to be 56% of the normal value. For the girl with an IQ of 123 (case 4(a) in Lorber, 1983), it was rated about 61% of normal. Regarding six cases with gross hydrocephalus, the calculated brain volumes were between 70% and 90% of the median. The authors concluded that although their data "indicated that there is more brain mass even in very severe hydrocephalus than the ventricular enlargement suggests, it is worth considering that the measurements include supratentorial structures other than the hemispheres," suggesting that the volume of the hemispheres alone was reduced to a greater extent (Jackson and Lorber, 1984, p. 93).

Lorber (1983) also drew attention to two other groups of patients with hydrocephalus he considered remarkable. The first of these two groups group consisted of 54 patients who showed an extreme congenital hydrocephalus in infancy (showing a cerebral mantle of 10 mm or less). The brains of 21 of these children regenerated completely after being shunted, showing no sign of hydrocephalus subsequently. For example, a boy whose cerebral mantle measured 3 mm at the age of 7 weeks developed normally and had a global and verbal IQ of 135 at the age of 10. The boy was doing exceptionally well in school and attended a class with children who were 3 years his senior. Remarkable cases in which the extreme hydrocephalus did not resolve completely include a baby whose cerebral mantle measured less than 5 mm at 3 weeks of age. At the age of 18, he still showed moderate hydrocephalus, but his global IQ was 121. However, the extreme congenital hydrocephalus of an otherwise physically normal girl barely changed over time. At the age of 18, she still had gross hydrocephalus but had an IQ of 115. In the two latter cases, it was established that the blood supply of the existing brain tissue was substantially reduced compared with what would be expected in normal circumstances. Such a reduced blood supply, and thus correspondingly reduced oxygen supply, was also reported for the student of mathematics.

The second group comprised patients with grossly asymmetrical hydrocephalus. In some of these cases, one ventricle was normal and the other grossly dilated. Nevertheless, some of these patients did not show the typical signs of paralysis or spasticity on the contralateral side of the body. In this context, it is also of interest that Lorber (1965) reported a seemingly inexplicable case of supposed hydranencephaly (HE). In contrast to hydrocephalus, in which the brain hemispheres are pressed toward the cranium and can become extremely thin, HE is characterized by the absence of hemispheres (see also below). However, it later turned out that the boy concerned must have had very extreme hydrocephalus during his early years rather than HE (case 2(c) in Lorber, 1983; see also Shewmon et al., 1999, p. 372, who seemed unaware that this case was followed up by Lorber). After a shunt treatment, the boy's right hemisphere regenerated fully, whereas the left hemisphere still showed gross hydrocephalus. He showed no hemiplegia (paralysis of one side of the body), but he had a global IQ of only 66.

After these publications, Lorber co-authored an article describing three children with gross hydrocephalus who, respectively, had verbal IQs of 77, 82, and 92 (Berker et al., 1992). More recently, other remarkable hydrocephalus cases were reported. A well-known case was described by Feuillet et al. (2007). The degree of this man's hydrocephalus would most likely be classified as extreme or very gross in Lorber's system. His neurological development and medical history were otherwise normal. He married, had two children, and worked as a civil servant. He had a global IQ of 70, a verbal IQ of 84, and a performance IQ of 70. However, no further details on his brain structure and cognitive abilities were provided.

Another interesting case is that of a 44-year-old woman with very gross hydrocephalus described by Masdeu (2008) and Masdeu et al. (2009). She had a global IQ of 98, worked as an administrator for a government agency, and spoke seven languages. In Leipzig, Germany, staff members of the Max Planck Institute for Human Cognitive and Brain Sciences recorded a similar case. A man was examined because of his headache, and to his physicians' surprise, he had an "incredibly large" hydrocephalus. Villinger, the director of the Cognitive Neurology Department, stated that this man had "almost no brain," only "a very thin layer of cortical tissue." This man led an unremarkable life, and his hydrocephalus was only discovered by chance (Hasler, 2016, p. 18).

An alleged additional case of severe hydrocephalus with normal intelligence was published by de Oliveira et al. (2012). This case was cited in at least four sources as a second recent example of this phenomenon, in addition to the case reported by Feuillet et al. (2007) (see Forsdyke, 2014, 2015a, 2016; Rudrauf, 2014). However, the publication by de Oliveira et al. (2012) has been retracted, as it seemed to have described the same individual previously reported by Feuillet et al. (2007).

Remarkable Aspects of HHE

A class of brain anomalies related to hydrocephalus is HE, which differs from extreme hydrocephalus cases by the absence, rather than the compression, of the hemispheres. Nevertheless, in these cases, rudimentary bits of cortical tissue can be present. In HE, consciousness is severely impaired and often barely recognizable. Nevertheless, there are cases in which a surprising amount of discriminative awareness can be detected in subjects with HE. It is assumed that the remaining brain structures, such as cortical remnants and the brainstem, are responsible for their consciousness (Merker, 2007; Shewmon et al., 1999). Hemihydranencephaly is a related, but much rarer, condition in which only one hemisphere is almost or completely lacking, whereas the meninges, basal ganglia, pons, medulla, cerebellum, and falx are preserved (Pavone et al., 2013). The cause of HHE is generally thought to be a unilateral vascular disruption in early developmental stages of the brain. In the following, we will briefly introduce examples of published HHE cases in which this drastic brain dysplasia, resulting in the loss of one entire brain hemisphere, was not accompanied by a corresponding impairment in the patients' mental or motor functions.

Greco et al. (2001) described a boy who had both HHE and hydrocephalus. He showed right-sided hemiparesis and other signs of neuronal dysfunction, including a low cognitive potential. Nevertheless, by the age of 12 he attended a junior high school and did well with the support of a teacher (Pavone et al., 2013). Ulmer et al. (2005) presented a case of a 36-year-old man who was examined because of left-sided headache. It was found that his left hemisphere was almost completely lacking. The patient reported some disabilities in his right hand concerning fine motor tasks, but his intellect and language abilities were unimpaired, and he was working in a security department. Balpande et al. (2009) described a 13-year-old boy whose brain scans showed a nearly complete absence of the right cerebral hemisphere, including

its basal ganglion. Nevertheless, the boy's sensorimotor and language development during childhood was not restricted, and he attended a regular school as an average student. Similarly, Muckli et al. (2009) described a 10-year-old girl who lacked the entire right cortical hemisphere. The loss of this hemisphere was discovered when she was 3½years old and underwent an magnetic resonance imaging scan because of brief, involuntary twitching on her left side. Nevertheless, she successfully attended a regular school and mastered activities that require bilateral coordination, such as roller skating and bicycle riding.

In general, it is assumed that the remarkable capacity of the human brain to compensate for the loss of an entire cerebral hemisphere is mediated via neural plasticity and that this compensation begins at early stages of fetal development (Balpande et al., 2009; Pavone et al., 2013). This view is supported by the fact that apart from HHE, there are also other pathological conditions in which large parts of one hemisphere are missing or severely damaged from childhood, but which do not seem to have a notable effect on the intellectual capacities of the subjects. For example, Baudoin (1996) described the case of a 30-year-old woman who had a large lesion on her right cerebral hemisphere. The right occipital and parietal lobes were entirely missing, as well as the inferior part of the right temporal lobe. The brain lesion was discovered only because of the patient's first seizures at the age of 30. Similarly, Duyff et al. (1996) presented the case of a 32-year-old lawyer whose brain showed a large arachnoid cyst in the right frontotemporal region that had displaced (or replaced) the temporal lobe and parts of the frontal and parietal lobes. His development had been completely normal, and no abnormalities were discovered upon neurological examination. His condition was discovered only because he had a persistent headache after a skiing accident in which he had fallen on his head.

Remarkable Aspects of Hemispherectomy

In the cases described in the previous section, people who grew up with only one hemisphere developed all the neuronal foundations needed for ordinary cognitive and most motor skills. Even so, it seems additionally surprising that one hemisphere can accomplish this after the other has been removed or was isolated anatomically and functionally from the rest of the brain, as it is the case of surgical hemispherectomy. The first series of hemispherectomies was described by Dandy (1928) for malignant glioma. Since then, the technique has evolved, and it is still applied, especially for treating forms of epilepsy in which epileptic discharges disrupt the damaged hemisphere and interfere with the function of the normal hemisphere to a very severe degree (*e.g.*, van Schooneveld et al., 2016). Although most hemispherectomies are performed on young children, adults are also operated on with remarkable success (*e.g.*, Bates and Zadai, 2003; Bell and Karnosh, 1949; McClelland and Maxwell, 2007; Schramm et al., 2012).

It is astonishing that many patients can lead an ordinary life after this drastic procedure, having only minor motor disabilities that result from mild hemiplegia. Physicians have long wondered about the surprising finding that one can lead a normal life with only one hemisphere. For example, McFie (1961) was astonished that "not only does it perform motor and sensory functions for both sides of the body, it performs the associative and intellectual functions normally allocated to two hemispheres" (p. 248). Moreover, physicians noted decades ago a greater improvement of the patient's condition when the entire hemisphere was removed rather than only parts of the damaged area, even if the remaining cortex appeared normal (McFie, 1961).

The discrepancy between cerebral and cognitive functioning in these cases is strikingly highlighted by the fact that most patients, even adults, do not seem to lose their long-term memory such as episodic (autobiographic) memories. Even so, this puzzle, and possible explanatory models for this retention of long-term memory, is only rarely discussed in the medical literature dealing with hemispherectomy. Although memory features are sometimes assessed by using the Wechsler Memory Scale (*e.g.*, Loddenkemper et al., 2004), we were unable to find a single peer-reviewed publication in which the peculiar retention of the patient's autobiographic memory was explicitly addressed. That said, this remarkable phenomenon was at least casually mentioned by authors such as Dandy (1933) and Bell and Karnosh (1949), who stated that their patient's memory seemed unimpaired after hemispherectomy. Similarly, Vining et al. (1997) were surprised by the apparent retention of memory after the removal of the left or the right hemisphere of their patients. Dorman (1991) described the extraordinary case of a subject who was able to perform brilliant calendar calculations, although his left hemisphere had been removed several years before. Dorman related this case to those of other savants who, in comparison, usually perform their tasks with two hemispheres.

Although there is no established explanatory model for the retained memory after hemispherectomy, a suggestion was sketched in an interview with Freeman, available on the Internet, which proposed that memory is stored in both hemispheres, so that it is retained when one hemisphere is removed (Zuger, 1997). It seems, however, that this proposition is not an accepted hypothesis for explaining the storage and recall of autobiographic memory. Numerous studies suggest that encoding memories involves diverse areas of the brain, forming functional neuronal circuits especially between the hippocampus and the different cortical regions (for a review and further references, see Tonegawa et al., 2015). In particular, certain kinds of memory seem to depend on regions specific to one of the two hemispheres. For example, the right temporofrontal cortex seems crucial for recalling episodic memories (Calabrese et al., 1996), whereas the prefrontal and temporal regions of the left hemisphere seem to mediate retrieval of (context-free) "world" knowledge (Markowitsch et al., 1999). It is noteworthy that up to the present, no such specific memory deficits have been reported after hemispherectomies.

It might be possible that memories cease to be stored in the hemisphere that is affected by severe diseases like tumors or encephalitis such as Rasmussen's disease and that previously encoded memories are transferred from the affected hemisphere to the healthy hemisphere. As a result, the memories would be retained after the removal of the damaged hemisphere. However, apart from the lack of evidence for such processes, patients who underwent a hemispherectomy state that only memories from the time immediately before the operation are missing (if any are missing) (Traufetter, 2003). This evidence appears incompatible with the transfer of memories from a diseased hemisphere to a healthy one.

Moreover, both of these explanatory models fail to account for individuals who had a sudden unilateral brain lesion that resulted in very severe amnesia. A well-known case of this sort concerns the Russian soldier Lyova Zazetsky, who sustained a considerable brain lesion in the left parieto-occipital area in combat (Luria, 1972). At first, Zazetsky had no memories at all. During a consistent, 25-year-long struggle to regain his identity, he managed to retrieve several memories, but they predominantly concerned his childhood. A logical question that arises as a consequence from the earlier observations is whether Zazetsky could have had better access to his memories if his left hemisphere had been completely removed.

Remarkable Aspects of the Savant Syndrome and Memory Processing

Finally, we will present additional considerations about memory processing, especially in savants. In this respect, Kim Peek (1951–2009) was most remarkable in that he seemed to possess a perfect memory: he forgot nothing he ever read and remembered complete melodies, even if he heard them only once. Most remarkably, his brain showed considerable malformations that included a deformed cerebellum, abnormalities of the left hemisphere, and the complete lack of the corpus callosum, as well as the anterior and posterior

commissures. In addition, much of the skull interior comprised empty areas that were filled with cerebrospinal fluid, as in hydrocephalic subjects (Treffert and Christensen, 2005). Nevertheless, he memorized more than 12,000 books, apparently verbatim, the contents of which amounted to an encyclopedic knowledge in multiple areas of interest. Typically, he would read a page in eight to ten seconds, and then turn to the next page. He even read two pages of smaller books such as paperbacks simultaneously, using one eye each for each page. Moreover, he had impressive calendar calculating abilities (Treffert, 2010).

One may wonder about a plausible neural mechanism to explain Peek's ability to remember practically everything. For example, it is known that brain cells and neuronal circuits undergo characteristic activities during memory encoding (*e.g.*, Tonegawa et al., 2015) and that the transfer of the contents of short-term memory (sometimes also termed "working memory") into long-term memory is accompanied by the synthesis of new proteins (*e.g.*, Buffington et al., 2014). Many of these findings are derived from conditioning studies performed with animals. Nevertheless, it remains uncertain whether such studies can satisfactorily explain long-term memory storing and processing in humans, especially in savants such as Peek. In his case, everything he ever read was immediately encoded in a long-term memory reservoir, seemingly bypassing selection mechanisms of short-time memory processing.

Certain musically gifted savants display similarly perplexing abilities. For example, blind pianist Thomas Berthune (1849–1908) was able to repeat even complex and long piano pieces without mistake after a single hearing, just as was blind Leslie Lemke (born in 1952) 100 years later. Every chord and note of every piece they heard were indelibly imprinted in their minds. Neither had had a single piano lesson in his life (Treffert, 2010). At present, there does not seem to be a convincing hypothesis that could explain how all these linguistic and musical phrases were permanently and instantly stored in the long-term memory of Peek, Berthune, or Lemke—to name only a few such savants. For example, the synthesis of new proteins takes seconds to minutes, and it can thus not account for the prompt and perfect reproduction of previously unknown piano pieces. Regarding the molecular processes involved in short-term memory or working memory encoding, not much is known at present. It seems that the release of calcium at synapses plays a crucial role (Mongillo et al., 2008). On a more general level, Snyder (2009) suggested that savant skills are latent in us all but that they typically stay inaccessible during the normal functioning of cognitive brain processes. Nevertheless, as indicated above, it remains unknown how the barrier to savant skills can be overcome, especially on a neurophysiological level, and Snyder regard his proposition only as a hypothesis that needs yet to be proven. How activated circuits of neurons, being under constant input stimuli, can mediate the perfect memorizing of every single piano note heard is still essentially unknown.

This is an important issue because, as Treffert noted, no model of brain function, in particular with regard to memory, will be complete until it can account for these remarkable feats (Treffert, 2006, p. 3). This appraisal is, of course, also valid for memory processing with only one hemisphere. Moreover, it is important to recall that the fundamental question of how biochemical reactions of molecules and electrical activities of neurons are translated into self-conscious experience, including autobiographical memory, intentionality, and volition, is still unsolved (*e.g.*, Bennett and Hacker, 2003; Gauld, 2007; Majorek, 2012).

DISCUSSION

In the previous sections, we presented summaries of peculiar medical findings that exemplify remarkable discrepancies between cerebral and cognitive conditions of patients with hydrocephalus, HHE, hemispherectomy, and savant syndrome. In the following, we will present reflections by clinicians on the potential relationship between the developmental status of the brain and cognitive abilities.

Regarding hydrocephalus, Lorber stressed that the brain of a baby can sometimes regenerate from almost nothing to normal, provided the increased intracranial pressure can be reduced to almost normal in early infancy (Lorber, 1983). It might indeed be the case that most neurons of the brain are still present even in severe hydrocephalus, despite being stretched or damaged by the pathological cranial conditions and the diminished blood flow in these tissues (del Bigio, 2010). This might facilitate the remarkable regeneration of the hemispheres and their functioning after shunt treatment. Indeed, in a sample of children with hydrocephalus, the degree of global cortical thinning during the first months of life before a shunt treatment was not related to the children's subsequent intelligence (Dennis et al., 1981).

Similarly, in patients with grossly asymmetrical hydrocephalus, a reorganization of the better-developed brain parts might take over the functions of the damaged or absent structures. Lorber invoked findings pertaining to hemispherectomy to support this view, stressing that an infant rat's behavior would, several weeks after hemispherectomy, be indistinguishable from that of normal rats (Lorber, 1983). Indeed, humans can also recover to an almost normal condition after hemispherectomy, especially with regard to their mental faculties, and even redevelop their language center if it was removed or disconnected during the surgical operation. In general, these processes of reorganization work better and faster the younger the patient is, and they are attributed to the formation of new synaptic circuits due to the brain's neural plasticity (Huttenlocher, 2002), even though the specific mechanisms involved remain obscure.

Lorber stressed that the imbalance between the brain size and structure of several of his patients with hydrocephalus and their performance should be regarded as the first step in the rethinking of some aspects of neuroanatomy and neurology, and he recommended future in-depth investigations (Lorber, 1983, p. 12). As of today, however, we have only a few narrowly focused studies (Masdeu, 2008; Masdeu et al., 2009), and no in-depth investigations along the lines suggested by Lorber have been undertaken. Clearly, the macro- and microanatomy of the brain and its tissue layers differ drastically in people with severe hydrocephalus compared with people with normally developed brains. For example, brain structures such as the thalamus, the amygdala, and the corpus callosum were not visible at their usual positions in the scans obtained from the patient described by Feuillet et al. (2007), but were most likely pressed toward the cranium together with the layers of the cortical mantle (Pelletier, 2008). Often, these malformations result in impaired mental and motor skills, as should be expected, but this is not always the case.

This raises interesting questions about how important the usual anatomy of the brain and its cellular layers really is. It still needs to be determined according to which principles the involved synapses, cells, and tissues of the brain successfully organize their fine-tuned neural circuits under such abnormal anatomical and physiological conditions. This problem is even more apparent after hemispherectomies in which, for example, the language center was removed along with the malfunctioning hemisphere. Assuming that a given brain structure dictates the mental capacities of the individual, it remains difficult to explain how the remaining brain structures and their neural activities can "know" that a "language center" is missing now, and how these neurons induce and guide its duplication in their own hemisphere. Majorek (2012) argued that this activity requires the existence of a higher control center that would be able to detect this gap in function and to initiate steps that lead to its mending. He stressed that so far, the existence of such a control center in the brain has not been reported and that, given the decentralized organization of the brain, it would be difficult to imagine where such a control center could be located.

Indeed, one might wonder whether such processes of reorganization are purely self-organizing processes of neuronal tissue in response to external stimuli, or whether the mind or "the self" actively participates in these processes. Several studies suggest that the brain can

indeed be altered by mental stimuli and processes on the molecular, cellular, and neural circuit levels. In a review focusing on neuroimaging studies, Beauregard (2007) summarized examples of mental influence on brain structure from research into emotional self-regulation, psychotherapy, and placebo experiments. He concluded that these studies strongly support the view that thoughts, feelings, beliefs, and volition do exert a causal influence on brain plasticity, and he pointed to the obvious fact that mental causation is an essential ingredient for successful therapies. This is, of course, also valid for patients who train to regain lost faculties after strokes, hemispherectomy, or brain injuries. The degree of success in rewiring the brain is clearly dependent on the patients' volition and purposeful training. According to Beauregard (2007), such findings call into question positions in which all mental processes are thought to be entirely reducible to biochemical processes.

In sum, the relation between the brain's structure and its functional capacities, and the principles that govern neural rewiring processes after or during developmental damage are still poorly understood. The cases presented in this article highlight that there is still much to learn about "the brain and its self" (Knoll, 2005) from a neurobiological perspective. On the basis of the different cases of discrepancy between cerebral and cognitive functioning discussed in the present article, some authors doubt that the brain serves as a comprehensive memory store, arguing that its function more closely resembles a receptor or transmitter of memory and allied cognitive processes (*e.g.*, Forsdyke, 2009, 2015a, 2015b; Kelly et al., 2007, 2015).

CONCLUSION

Remarkable discrepancies between cerebral and cognitive conditions of some patients with hydrocephalus, HHE, hemispherectomy, and savant syndrome illustrate complexities of the neurobiological underpinnings of cognition. We hope that this article will stimulate further research into extraordinary cases of discrepancy between cerebral conditions and mental functioning. It is research into such extraordinary phenomena that may push scientific exploration into as yet underresearched topics, as well as raising important questions related to research concerned with the function of normal brains.

DISCLOSURE

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