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The excitable cerebral cortex
Fritsch G, Hitzig E. Über die elektrische Erregbarkeit des Grosshirns. Arch Anat Physiol Wissen 1870;37:300–32.

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Clinical medicine today, regardless of the chosen discipline, relies on the judicious interpretation and application of a series of "known facts." Based on the patient's clinical signs and symptoms, combined with diagnostic test results, the physician generates a hypothesis as to the underlying disease process. On the basis of the underlying pathophysiology of the illness and the mechanisms by which various treatment options modify the disease process, a treatment regimen is chosen. No matter how skilled a physician may be, if the underlying facts on which a diagnosis or treatment is based are incorrect, the entire process is fundamentally flawed and is doomed to failure. In *The Descent of Man*, Charles Darwin aptly discussed the danger of "facts":

> False facts are highly injurious to the progress of science, for they often endure long; but false views, if supported by some evidence, do little harm, for everyone takes a salutary pleasure in proving their falseness; and when this is done, one path towards error is often closed and the road to truth is often at the same time opened [1].

In the neurosciences today, the excitability of the cerebral hemispheres is accepted as fact. However, in the 19th century, it was an established fact that the cerebral hemispheres were nonexcitable. "[S]ince the beginning of the century the conviction has very generally spread that the cerebral hemispheres are absolutely unexcitable by all the common physiologic stimuli" [2]. This was so firmly established that Gustav Fritsch (1837–1927) and Eduard Hitzig (1839–1907) were relegated to performing the experiments that demonstrated the excitability of the cerebral hemispheres on a dressing table at home [3,4].

Prior to their experiments, numerous renowned scientists had established the nonexcitability of the cerebral hemispheres. Fritsch and Hitzig reviewed the studies of major contributors to this established doctrine. Julius Ludwig Budge (1811–1884), in his 1842 article, summarized the observations of cerebral hemispheric stimulation in mammals with the statement "not one single observer saw movement of such muscles after excitation of the named central parts" [2]. A detailed discussion of Jean Pierre Marie Flourens' (1794–1867) experimental evidence leading to the conclusion that the cerebral hemispheres "are not the site of the direct principle of the muscle movements, but must be the only site of the will and sensations" is provided in their article. These studies were performed primarily in birds, although there were also some experiments in mammals. Following "numerous resections of the cerebrum," external stimulation was noted to produce "very mechanical movements in all muscles of the body." Birds with only one hemisphere were "blind in the eye of the opposite side, but retained their complete will power over all voluntary muscles, and after overcoming a weakness of the opposite half of the body, they in no way differed from animals that were not mutilated" [2].

These experiments and those of others led to the concept of two forms of excitation: "the pathway of the reflex," which "runs from the periphery outward," and "the pathway of the will, of the mental impulses," which "radiates from the center"; this center was felt to lie within the "ganglionic substance of the |%1e[OK]cerebral hemispheres" in a diffuse, nonlocalized fashion [2]. The experimental evidence was further supported by the observation of congenital or acquired brain defects in which no clear disorder was observed; this provided evidence as to "how insignificant the brain is to life."

Based on direct observation of voluntary muscle movements following stimulation in a human, Hitzig and Fritsch challenged the established dogma, albeit without the direct support of the Physiological Institute in Berlin. In their landmark article, they studied cortical hyperexcitability in dogs via systematic stimulation across the hemispheres. In so doing, they identified regions in which direct stimulation results in contralateral limb movement and began to describe the organization of the hemispheres with respect to motor function, observing that "Generally expressed, the motor part lies more forward, the non-motor part toward the back" [2].

These experimental observations established evidence for the excitability of the cerebral cortex and supported the hypothesis that functions were localized within the brain. This hypothesis was considered "disproven" after Flourens' experiments on pigeons. And even after the clinical–pathological cases of aphasia and others after 1861, many neurologists and psychiatrists considered it incorrect to localize a function. Even those, such as Broca, who argued for localized functions, argued that motor functions were in the basal

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ganglia, not the cortex. Furthermore, Fritsch and Hitzig's studies provided evidence for a functional role for the cortex in initiating movement. In observing the sharp departure of their findings from those of other experts, they noted "[T]he method creates the result" [2] and speculated that others had failed to truly stimulate the entire cortex systematically.

Because they challenged the "false facts" of the time, their results were sharply attacked and criticized [3], but ultimately inspired further investigation by other physicians and scientists, many trying to disprove these "false views." Ultimately this led to further evidence of functional localization within the cerebral cortices by Sir David Ferrier (1843–1928), John Hughlings Jackson (1835–1911), and many others [4,5]. Although our understanding of the functional organization of the brain has evolved substantially from these initial observations, continued investigation into brain function remains an active area of investigation throughout the world; the path to our current understanding and future discoveries, however, took a lengthy diversion in the wrong direction until Fritsch and Hitzig's work was published in 1870.

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