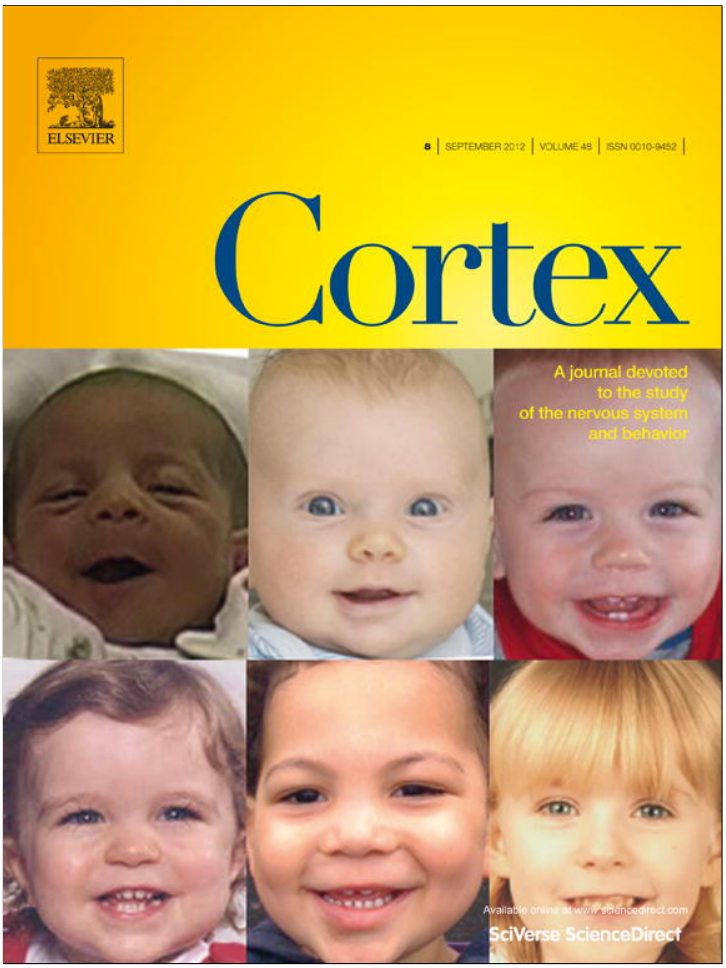

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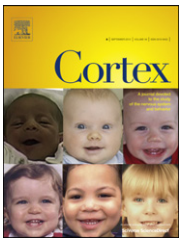

Historical paper

Ubi irritatio, ibi affluxus: a 19th century perspective on haemodynamic brain activity

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ABSTRACT

The impact of cognitive operations on haemodynamic activity in the human brain is a cornerstone of modern cognitive neuroscience. This essay presents an early speculation about why there is increased blood flow following cognitive operations: Emil Harleß, a 19th century German physiologist, proposed that this blood flow responds to irritations caused by "the will" in order to restore homeostasis. Peculiar from a modern perspective, this speculation shows how neuroscientific concepts – and corresponding perspectives on cognitive function – have changed over the centuries.

Cognitive processes lead to increased cerebral blood flow in the brain areas that mediate these cognitive operations. This effect lies in the very heart of modern brain imaging techniques such as positron emission tomography (PET) or functional magnetic resonance imaging (fMRI) – techniques that target the interplay of cognitive processes and metabolic brain function. Already in the late 19th century, about 100 years before these techniques should become the backbone of cognitive neuroscience, Angelo Mosso (1881) described first experimental results that suggested increased cerebral blood flow as a consequence of mental activity (see also Zago et al., 2009). However, across the 19th and 20th century, researchers struggled to demonstrate a clear relation between these events (cf. Raichle, 1998). For instance, several pioneers of (cognitive) neuroscience predicted that increases in cerebral blood flow might in turn increase the scalp temperature, and this prediction was indeed supported by empirical investigations (Berger, 1901; Broca, 1879; Mosso, 1894). Still, the study of cerebral blood flow as a window on cognitive operations fell into discredit during the first decades of the 20th century and was treated cautiously until the advent of PET and fMRI imaging techniques (see Raichle, 1987, 1998, for a more detailed overview).

Despite this long debate on *whether* cognitive processes lead to increased blood flow, the question of *why* blood flow increases seems to be trivial from a modern point of view. The metabolic function of cerebral blood flow is well documented and the same is true for the relation between metabolic function and its indirect quantifications with functional imaging techniques (Logothetis et al., 2001; Magistretti et al., 1999). However these insights were far from trivial in the second half of the 19th century, when the scientific

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investigation of cerebral blood flow began. This becomes apparent when James (1890) writes: "Blood very likely may rush to each region of the cortex according as it is most active, but of this we know nothing." (p. 98).

An interesting, but almost forgotten hypothesis about why cerebral blood flow increases as a result of cognitive processes was formulated more than 150 years ago by Emil Harleß (1861). Harleß had studied medicine, physics, and chemistry and had thus been trained in a number of fields relevant for the study of brain physiology and haemodynamics (cf. Hintzenstern et al., 2001; Pfister and Janczyk, in press). His empirical work also spanned a number of disciplines, ranging from now classic chemical studies on anaesthesia (Hintzenstern et al., 2001; Bibra and Harleß, 1847) to the physiological and psychological foundations of human action control (Harleß, 1861; cf. Pfister and Janczyk, in press). Furthermore, he included an extended discussion of cardiovascular mechanisms in his published lectures (Harleß, 1851).

Of particular interest for the present essay, speculations about the relation of cerebral blood flow to cognitive operations are explicitly included in Harleß (1861) *Der Apparat des Willens* [The Apparatus of Will; for an English translation, see Pfister and Janczyk, in press, supplement]. Here, he assumes cognitive operations – "the will" – to disturb an equilibrium state of the brain. More precisely, he refers to the classic medical maxim "ubi irritatio, ibi affluxus" to describe the impact of cognitive operations (Harleß, 1861, p. 66). Translating to "where the irritation is, there is increased blood flow", this law was originally used to describe physical perturbations of homeostasis such as a physical wound in the skin (Allison, 1844). This wound – the "irritatio" – will inevitably lead to increased blood flow – the "affluxus". Eventually, this increased blood flow will restore homeostasis.

Typically expressed as "ubi stimulus, ibi fluxus", references to this maxim were prevalent in 19th century medicine and were applied to diverse phenomena (e.g., Allison, 1844; Johnson, 1866), ranging from wounds (Gamgee, 1881) and inflammation (Chalvet, 1869) to overt mental pathology (Blandford, 1871). Crucially, Harleß assumed the same process to occur for cognitive operations. Accordingly, he claimed that "each act of the will is an irritatio", while simultaneously highlighting "the importance of this affluxus of blood for our nutrition and thus the functionality of the organism" (Harleß, 1861, p. 66; cited after Pfister and Janczyk, in press; supplement).

Interestingly, Harleß (1861) focuses on voluntary movements when describing the functions of "the will". This view departs from earlier concepts of irritation, most noteably from those of Albrecht von Haller (1753; cf. Neuburger, 1897). Haller concluded that only pure reflexes are driven by perturbations of an equilibrium state and, in fact, he defined the concept of irritability only with regard to muscular fibres. Accordingly, he did not believe that voluntary actions could be described in (mechanical) physiological terms (Steinke, 2005). Harleß, by contrast, offered a mechanistic physiological explanation for voluntary action (Pfister and Janczyk, in press) that included precise physiological and especially haemodynamic mechanisms.

Thus, in Harleß' days, cognitive processes were interpreted as a state of disequilibrium and 'irritation' that had to be counter-acted by haemodynamic activity. Over the centuries, this perspective has changed tremendously to the present-day view in which cerebral blood flow provides necessary resources to perform ubiquitous mental operations, rather than to alleviate the 'irritation' caused by them. The development of this idea is an excellent example of how scientific concepts change over time, from first theoretical drafts to empirically supported frameworks. However, despite the long way in between, the first ideas and insights formulated by pioneers like Harleß, James, or Mosso still form the fundament of our own modern understanding of cognitive neuroscience and should therefore not fall into oblivion.

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