Cortical spreading depression- better understanding and more questions

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This issue of the Journal contains a provocative, carefully conducted series of studies that challenge a very tightly held belief about cortical spreading depression (CSD) showing propagation of the dilation of cortical surface arterioles at a greater velocity than the wave changes in cellular activity (Brennan et al., 2007). How could this be? Do not changes in blood flow follow neuronal changes passively with flow-metabolism coupling? It seems the issue is not that simple.

Cortical spreading depression (CSD) was first described by Leao (1944a; 1944b) who observed a depression of EEG activity that moved across the cortex at a rate of 3-6 mm/minute. It has been observed in clinical practice that the migraine aura, a transient neurological disturbance (Headache Classification Committee of The International Headache Society, 2004) that moves slowly across the visual field or over the limbs, has the same rate of progression, at least for visual changes (Lashley, 1941). The observation by Olesen and colleagues (1981) of a spreading reduction in cerebral blood flow, spreading oligemia, in patients with migraine aura triggered a revolution in thinking about migraine aura. For much of the twentieth century aura was considered a vascular process, ie primarily vasoconstriction as the initial event, with head pain as a consequence of a reactive vasodilation (Wolff, 1948). The CSD hypothesis completely reversed this concept with the primary event being neural and brain blood flow changes being secondary to changes in neuronal activity (Lauritzen, 1994). Indeed cerebral blood flow changes seen with SPECT (Olesen et al., 1990) and perfusion-weighted MRI (Cutrer et al., 1998) lent support to this notion as a spreading oligemia was observed during aura, considered to be due to changes in neuronal activity, with different imaging modalities. Most recently fMRI changes again consistent with CSD have been seen in migraine aura (Hadjikhani et al., 2001), so it is generally accepted that CSD is the animal experimental equivalent of migraine aura- thus its importance to human neurobiology.

It has been shown with single modality blood flow, such as autoradiographic methods (Duckrow, 1991; Duckrow, 1993) or laser Doppler flowmetry (Piper et al., 1991), that triggering CSD results in a wave of reduced cortical blood flow. Moreover, using dual modality methods, such as laser Doppler flowmetry and extracellular electrophysiology (Akerman and Goadsby, 2005; Goadsby et al., 1992), changes in neuronal firing and cerebral blood flow could be seen to occur together. However, these methods have lacked the combination of parcellspatial and temporal resolution. Brennan and colleagues (Brennan et al., 2007) have overcome this by combining electrophysiological measurements with optic intrinsic signal imaging. They show vasomotor changes in cortex travelling at significantly greater velocity than the neuronal changes, a circuitous pathway and crucially dissociation of vasomotor and neuronal changes. Their data suggest a mechanism that requires the vasculature and not the neuronal component.
These data demand a complete re-evaluation of flow-metabolism coupling, blood flow changes that accompanying changes in demand for energy substrates in the brain (Edvinsson and Krause, 2002), as the single explanation for brain blood flow changes in migraine. Moreover, the authors challenge the cerebrovascular physiology community to consider this remarkable new mechanism. As is typical for more interesting studies, the work by Brennan and colleagues raises more questions than it answers.

References

Lashley KS. Patterns of cerebral integration indicated by the scotomas of migraine. Archives of Neurology and Psychiatry 46: 331-339, 1941.