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## Molecular Imaging Changes with Cognition

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## Molecular Imaging Changes with Cognition

Whatever lies behind aging and its underlying cognitive deterioration, very little is usually observed in the early stages. One popular model is that of chronic ischemia, in which vascular insufficiency of one kind or another and its reduction in blood flow directly affect cognitive functions. Carotid stenosis is a major cause of stroke and thus of cognitive deterioration in the aging population. While the radiologic standards for the exact definition of carotid stenosis are rather well-defined and can be achieved by a variety of invasive or noninvasive methods,<sup>1,2</sup> the impact on the target organ, the brain, is occasionally not very clearly visualized. Besides those using standard anatomic imaging, a few studies have been performed that convincingly demonstrate associated neuropsychological changes. In one, the authors themselves state that the study was done at high field, in a large series of patients, and in a very systematic manner. Thus, in the article entitled "Postoperative Changes in Cerebral Metabolites Associated with Cognitive Improvement and Impairment after Carotid Endarterectomy: A 3T Proton MR Spectroscopy Study," the authors demonstrate the impact on the brain of carotid stenosis by means of high-field MR spectroscopy.<sup>3</sup> They found a correlation between changes in brain metabolites and changes in cognitive function. Anyone involved in the field of diagnosing and treating carotid stenosis for years has been confronted with this most elusive form of chronic cognitive dysfunction related to chronic ischemia. While everyone has observed this in single patients, it has proved elusive both radiologically and clinically. Although treating mildly significant stenoses can, in selected cases, improve the quality of life and cognitive function, this result is not yet supported by evidence. This raises the question of when a clinical sign is a relevant one. Indeed, must a significant neurologic deficit be present to discuss treatment? This is one of the questions this article raises.

The authors found that differences in post- and preoperative ratios of NAA/Cr correlate with postoperative evolution. This is an extraordinary finding, with metabolic alterations varying according to the neuropsychological status and thus complicating a successful intervention. Both the hard science of spectroscopy and the softer data of neuropsychology are thus validated in this well-constructed study. The metabolites are selected simply and wisely: NAA represents neuronal integrity and should thus be related to function, and Cr is stable as a reference.

Although carotid surgery has recently been reinstated in its principal role as a treatment of choice for carotid stenosis, in

many patients the impact of the disease may not be visible and severely debilitating neuropsychological changes may occur. This certainly indicates that the management of cerebrovascular disease is a multidisciplinary field in which one has to rely on not just images provided by 1 technique but on the evaluations by many experts. However, it is sometimes difficult to really assert the causes of brain malfunction. It is evident that the revascularization is supposed to reintroduce normal perfusion values, but its impact on brain function and metabolism have to be demonstrated.

This is one area in which "modern" neuroimaging techniques that go beyond the merely visible may provide insights and hopefully lead to improved treatment and outcome. While it is still unclear what could be affected in the early stages of cognitive dysfunction in carotid stenosis, possibilities include the accumulation of small acute ischemic lesions and the slow erosion of neurons and axons due to diminished blood flow and metabolism. Most important, the continued development of high-field scanners and more advanced techniques may allow us to further study these patients. Tools such as MR spectroscopy, DTI,<sup>4</sup> perfusion, and others may help to increase our knowledge of brain changes in these patients at a molecular level and thus initiate early preventive therapy before irreversible lesions occur. In summary, while the present findings are promising, there will remain additional questions to be answered by methods including perfusion, diffusion, or even newer techniques.

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