Editorial

Transient Ischemic Attack and Minor Stroke
Definitively Not So Harmless for the Brain and Cognitive Functions

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During the past 10 years, there were major changes in the management of transient ischemic attack (TIA) and minor stroke, including urgent management in specialized units, implementation of immediate investigations, and rapid treatment with appropriate prevention strategies.[1,2] In this context, data from the TIAregistry.org project which included ≈5000 patients from 61 TIA clinics revealed a lower risk of cardiovascular events after TIA than previously reported.[3] Indeed, when patients benefited from a fast-track evaluation, the 1-year cardiovascular rate was 6.2% while the 1-year stroke rate was only 5.1%. The use of ABCD2 score, findings on brain imaging, and status with respect to large-artery atherosclerosis also helped stratify the risk of recurrent stroke. More precisely, the 1-year risk of stroke after a TIA or minor stroke is twice higher when patients have multiple infarctions on brain imaging, large-artery atherosclerosis, and an ABCD2 score of 6 or 7.[3]

In this issue of *Stroke*, these reassuring data are counterbalanced by the study of Bivard et al[4] that explored whether a TIA would be able to induce global or remote atrophy, as well as cognitive or mood changes. Patients with a hemispheric perfusion abnormality on brain imaging consistent with their clinical presentation of TIA were enrolled in a prospective study while those with symptoms typical of TIA/stroke mimics, previous history of TIA or stroke, and those with a diffusion-weighted imaging lesion were excluded. On 90-day brain imaging, all patients experienced a decrease in global cortical gray matter. Patients with anterior circulation TIA also had a significant reduction in the volume of the pons, ipsilateral parietal lobe, occipital lobe, frontal lobe, temporal lobe, and thalamus. These patients also had a significant decrease in the Montreal Cognitive Assessment that was correlated to thalamic atrophy.[4]

These findings strengthen the results from a study previously published in *Stroke* journal where early cognitive impairments were found after TIA or minor stroke.[5] In this study, Montreal Cognitive Assessment but not Mini-Mental State Examination detected cognitive impairments while magnetic resonance imaging found white matter damages. The pathophysiology of such modifications remains unknown, but the evidence of a perfusion lesion and the focal nature of the observed atrophy in the study of Bivard et al[4] suggest that the underlying mechanism may be a focal phenomena triggered by the initial hypoperfusion. Using diffusion tensor imaging, Ferris et al[6] showed that individuals with TIA presenting with sensorimotor symptoms have decreased fractional anisotropy in frontal white matter tracts, including anterior thalamic radiations. Despite normalization at 90 days, all these abnormalities suggest a more profound type of brain damage associated with TIA than has been previously described. Diffusion tensor imaging may then have use as a marker of early TIA-associated changes to white matter pathways.[6]

Other markers may also be used to discriminate early brain changes and possibly long-term cognitive impairments. Through a translational approach using data from both an animal model and patients with minor stroke, we found that hippocampal deformations and entorhinal cortex atrophy would be an anatomic signature of long-term cognitive impairment.[7] In male wistar rats subjected to transient middle cerebral artery occlusion, significant impairments in hippocampus-dependent memories were observed 6 months later without significant atrophy of the hippocampus volume but with a significant deformation and thinner entorhinal cortex in magnetic resonance imaging studies. In parallel, in 90 initially dementia-free patients having experienced a first-ever minor stroke, more than half displayed cognitive impairments at 6-month post-stroke with a decrease in both Montreal Cognitive Assessment and Mini-Mental State Examination. Shape analysis revealed marked deformations of their left hippocampus and a significantly lower entorhinal cortex surface without any hippocampal atrophy.[7] Similarly, changes in hippocampal mean diffusivity and hippocampal connectivity predict cognitive state at 6 and 12 months after a mild stroke.[8] Structural and functional changes, including these subtle changes to hippocampal shape and texture, atrophy in areas outside of hippocampus, and disruption to functional networks are also seen in the course of Alzheimer disease,[9] suggesting that TIA or minor stroke possibly induce a long-term neurodegenerative process.

To date, TIA was mainly considered as an alarm bell that urges stroke community to rapidly act to prevent the risk of a subsequent stroke or deleterious cardiovascular outcome. Clinical data from large registry seem reassuring[3] when other clinical data also emphasize the fact that TIA may contribute to protect the brain against a future stroke.[10,11] The short duration of clinical symptoms and the absence of apparent brain imaging abnormalities blinded us to the deleterious consequences of TIA or minor stroke in terms of cognitive functions. All taken together, recent literature underlines that TIA or minor stroke is definitively not so harmless. Various brain imaging markers and simple clinical testing, such as Montreal Cognitive Assessment, could help us to discriminate patients

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at risk of long-term cognitive impairments. As recently stated by Pantoni et al,[12] it is time for stroke clinicians to give consideration to the long-term cognitive consequences of stroke. We must develop new strategies in both diagnostic tools and therapeutic approaches to avoid the burgeoning epidemic of poststroke cognitive impairments.[13]

Disclosures

None.

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