

MOTOR FUNCTION REGAINED, COGNITIVE RESERVE LOST: HOW THE BRAIN FAILS TO PRESERVE COGNITIVE FUNCTION FOLLOWING STROKE

Michael Brainin

Department of Clinical Neurosciences and Preventive Medicine, Danube University Krems, Austria

Prevalence of post-stroke cognitive impairment (PSCI) has been estimated to occur in up to 30% of patients. Thus, it is 3-4 times more frequent than recurrent stroke and ranges from mild impairment of executive functions to clear-cut vascular dementia.

More recently, PSCI has been described in DSM 5 as a (mild) neurocognitive disorder syndrome: "This mild NCD syndrome is new to DSM-5, its presence is consistent with its use in other fields of medicine, where a significant focus of care and research, notably in individuals with Alzheimer's disease, cerebrovascular disorders, HIV, and traumatic brain injury."

Post-stroke cognitive changes occur in a dynamic fashion and their onset is quite time-dependent. There are at least three different groups. In a minority of patients the onset of cognitive deterioration is immediate and massive following a stroke. This is called strategic infarct dementia, caused by direct ischemic destruction of the nuclei and pathways involved in cognitive networks. In such patients, especially those showing involvement of the thalamus, there is no reasonable hope for recovery. In a second group, prestroke cognition was already on a lower level but becomes manifest with the occurrence of an infarct. Also in this group, the deterioration of cognition becomes visible almost immediately following a stroke. The corresponding preclinical changes have not yet been clearly identified but involve amyloid deposits, microvascular disease and microbleeds as well as other genetically determined factors including the apolipoprotein E status. In others still – and this is the most frequent and therapeutically important group - the appearance of cognitive deficits is seen only after a weeks or months following the stroke. Clinical experience shows that many of these patients have physically recovered from their stroke and have resumed many of their previous activities but gradually tend to show some mental and cognitive changes that had not been apparent during the acute phase or early recovery. These changes may even become the major hindrance for restoring their life at their pre-stroke level. It is in this latter group that a time window of treatment opportunity after stroke exists.

We must recognize that in such patients post-stroke changes occur in the brain in a delayed fashion and these changes are not directly dependent on the infarct itself but are triggered and mediated by the peri-infarct healing processes. These delayed-onset changes in the brain often are remote from the site of the infarct and involve the hippocampal region which usually is spared by infarcts (with the exception of posterior-medial infarcts and anterior choroidal infarcts). Thus, in such patients involvement of memory function must be assumed to relate to these remote changes. Further changes that involve the forebrain and relate to executive functions must also be acknowledged. This leads to important assumptions about such post-stroke processes. The most important one is that these changes occur in a dynamic and time-dependent fashion. A number of imaging studies confirm the dynamics of such a mechanism.

An overview of published as well as ongoing studies is given. Testing of combined interventions are the most promising area for development of therapeutics. Multimodal intervention studies are pragmatic studies that aim at target modification at multiple levels. They have been shown to be effective in several disease prevention domains such as in prediabetes and early Alzheimer states. Mostly, they consist of multimodal approaches that combine supervised, motivated behavioural modifications, lifestyle changes, dietary modifications and risk factor modification and compliance with drug prescriptions. They can be combined with drugs that carry stem cell-like regenerative effects when applied in the early recovery phase of stroke. The ongoing trials are described, such as the ASPIS trial that offers a new design by which multiple interventions are tested for their ability to preserve cognition after stroke.