Cognitive deterioration following stroke: Intervention trials for prevention and treatment

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Previous randomized trials aiming at improving recovery after stroke such as with levodopa, natural biologicals, or SSRI’s have been shown to enhance motor recovery. In contrast, no established treatment exists for the preservation or restoration of cognitive status following stroke. In spite of the frequent delay in onset of cognitive deterioration following stroke which offers a large therapeutic window for intervention, it is surprising that large studies have yet to be performed.

Single or combined drug interventions tested up to now were based only on secondary outcome analyses. These included antihypertensive drugs which showed only a modest effect on cognition. No consistent effect was shown for lipid lowering drugs. Combination of antiplatelet drugs have been tested in the SPS3 trial but showed no effect on cognitive outcomes. Life-style interventions including nutritional studies included a trial of Mediterranean diet with extra virgin olive oil and nuts that had a powerful effect on the reduction of stroke occurrence, but no further data on post-stroke cognition exist. The same applies for physical exercise programs which show good effects on physical fitness but no large studies were performed on cognitive status following stroke.

Ongoing registered stroke testing either drug and/or lifestyle interventions all are planned either for small sample sizes and/or a complex endpoint or combination of endpoints that are not likely to produce practice-changing results.

Multi-domain intervention studies are much more likely to be effective on cognition because they perform multiple risk factor management with lifestyle adaptation including diet changes with increase of drug compliance and adherence. Intensifying these interventions and to monitor them is crucial. The first comprehensive multi-domain intervention trial (ASPIS) in stroke patients has recently been terminated. The primary endpoint was a significant change of the z-score of 5 neuropsychologically assessed cognitive domains. While the overall result was neutral, a signal for change of dysexecutive function was seen and follow-up studies might have to consider this finding.

In the future, there is a need to include cognitive outcome measurements in all trials targeting the brain, to consider larger sample sizes, to harmonize assessment strategies, to focus on a high risk population, and to include biomarkers and imaging data for confirmatory analyses. Overall, it is crucial to aim for intervention intensities that create significant group differences.