**Project title:** Impaired executive functions in chronic hypotension - causation by aberrances in cerebral hemodynamics and autonomic cardiovascular control

Funding: Anniversary Fund of the Austrian National Bank (completed)

**Cooperation partners:** County Hospital of Hall in Tirol, Department of Psychiatry and Psychotherapy (J. Marksteiner); University of Bonn, Germany (U. Ettinger); University of Jaén, Spain (G.A. Reyes del Paso)

In addition to physical complaints, chronic low blood pressure (hypotension) is frequently associated with impaired mood, lack of drive, and concentration and memory problems. Previous studies suggested that aberrances in autonomic cardiovascular control and dysregulation of cerebral blood flow may be implicated in the genesis of these symptoms. As symptoms and psychophysiological peculiarities of hypotension partially overlap with those of depression, they were investigated in both conditions in this project.

The project aimed to quantify executive functions, and to study autonomic cardiovascular control and cerebral hemodynamics in hypotension and depression. Autonomic cardiovascular control was investigated using electrocardiography, impedance cardiography and continuous blood pressure recording. For cerebral blood flow assessment, functional transcranial Doppler sonography was applied, which enables analysis of rapid blood flow modulations with a high time resolution.

Individuals with hypotension and depression exhibited poorer executive function performance than controls. Deficits arose in functional components of shifting (i.e., switching between multiple tasks and mental operations), updating (i.e., monitoring of incoming information, evaluating its relevance to the ongoing task, and replacing old information in working memory with relevant new information) and inhibition (i.e., deliberately inhibiting or overriding dominant or automatic responses). Overall, deficits were more severe in depression than hypotension.

According to psychophysiological assessments, autonomic control in hypotension is mainly characterized by reduced sympathetic influences on cardiac activity; this is associated with lower myocardial contractility and cardiac output, which in turn may lead to reduced organ perfusion and contribute to physical complaints. Moreover, correlations between cardiovascular parameters and cognitive test scores implicated autonomic dysregulation in the cognitive impairments. Reduced heart rate variability was seen in depression, suggesting less parasympathetic influence on heart rate and limited flexibility of autonomic regulation. As expected, individuals with hypotension exhibited more severe depression symptoms than controls. Furthermore, these symptoms correlated negatively with indices of sympathetic cardiac control, which confirmed a role of autonomic control in the genesis of mood impairments in hypotension.

In individuals with hypotension and depression, blunted modulation of cerebral blood flow was seen during preparatory cognitive processes (proactive control). Reduced blood flow adjustment arose during anticipation of both basal and more complex tasks (proactive inhibition and proactive interference control). In both conditions, diminished blood flow dynamics reflect lower activity of the dorsolateral prefrontal cortex and inferior parietal lobe, which are engaged in preparatory cognitive processes. In depression, the time course of the cerebral blood flow response suggested increased neural activity after task onset (reactive control), which may be interpreted in terms of compensation for deficient cognitive preparation. Cognitive models of depression emphasize the importance of executive functions for symptom genesis, which underlines the clinical relevance of our findings.

## **Publications from the project**

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