Summary

Dystonia is a neurological syndrome characterized by the involuntary contraction of opposing muscles, causing twisting movements or abnormal postures (modified by Fahn, 1987). Writer's cramp is the most common form of task-specific focal dystonia.

In the first study, patients with writer's cramp were evaluated for differences in cortical activation during movements likely to induce cramps (complex movements) and movements which rarely lead to dystonia (simple movements). Although complex patient movements during fMRI were never associated with dystonic cramps, they exhibited abnormally decreased cortical activity. This was not observed in simple movements and was unrelated to the character of handwriting or the presence/absence of visual feedback. Our results support the theory of dualistic sensorimotor system behavior in writer's cramp.

As the somatosensory system is believed to be affected in focal dystonia, we focused on modulation of the primary somatosensory cortex (SI) induced by repetitive transcranial magnetic stimulation (rTMS) in the second study, in order to improve writer's cramp. In conclusion, 1 Hz rTMS of the SI cortex can improve manifestations of writer's cramp while increasing cortical activity in both hemispheres. Handwriting as well as subjective assessment improved in most patients, and lasted for two to three weeks. The beneficial effects of rTMS paralleled the functional reorganization in the SI cortex and connected areas, reflecting the impact of the somatosensory system on active motion control.

In the third study we presented a case involving deep brain stimulation (DBS) of the globus pallidus interna (GPi) and its positive clinical effects in a 30 year old male with dystonia-deafness phenotype, with severe cervical dystonia and swallowing and breathing difficulties. GPi-DBS resulted in dramatic improvement of dystonia documented by a 75% m

DYT6 is an early-onset dystonia caused by variable mutations of the gene encoding the thanatos-associated protein (THAP1). In the fourth study **w**e described a novel mutation of the THAP1 gene in two siblings (male and female) with rapid generalization to life threatening status dystonicus in the male. In contrast to the seven previously reported patients, we observed excellent response to bilateral Gpi-DBS determined by an 85% decrease in BFMDS.