that motor neuron instability results from increasing firing rates and decreasing ATP production for its compensation. Additionally, the energetic imbalance is aggravated with rising Calcium concentrations due to mitochondrial overload, emerging again in reduced ATP synthesis. Finally, with an ATP deficit imposed upon the axonal end, local influx of high-concentration ions appears to spill the metabolic deficit into neighbouring sections. The local energy crisis thereby propagates to neighbouring compartments, eventually spreading from the distal axon to the soma[34] . These processes illustrate how even small local energy dysfunction may grow to cell-wide critical proportions in neurons with a vulnerable relationship between neuronal morphology, neuronal firing, and metabolic load.

Interestingly, an involvement of voltage–gated calcium channels and ATP-sensitive potassium channels have been discussed to be present in neurodegenerative disorders like PD; here especially dopaminergic midbrain neurons of the substantia nigra seem to be specifically vulnerable yielding to a selective degeneration[35]. But also in other regions of the BG, like the GPi, parvalbumin (PV) concentrations, a $Ca^{2+}$-binding protein, are markedly reduced in PD[36,37]. Although the mean estimates for GPi volume and the numbers of GPi neurons in PD were not significantly different from those for the controls in an earlier study, sub-population of neurons (PV positive neurons) that project from the GPi to the thalamus were selectively and significantly decreased[38]. Past studies suggest, that PV plays an important role for repetitive fast-firing[39]; herewith it appears, that subpopulations of GPi have altered firing capacity in advanced PD patients. This has been expressed by an excessive synchronicity of neurons in the GPi found during microelectrode recordings with an impairment of motor processing reflected by a bradykinesia[40]. Here, on a cellular level, pallidal gap junctions, that are strongly involved in the ion exchange between the extra- and intracellular space could play a major role modifying this synchrony, because they show functional plasticity under the influence of dopamine and after neuronal injury[41].

## Discussion

Intentional movements rely on a closely interrelated brain network including several regions. In essence, movements initiate in the cerebral motor cortex projecting directly – but also indirectly via local premotor circuits – to the brain stem or spinal motor neurons that again convey movement information to the muscles. Before a motor signal descends from the motor cortex to the brain stem and spinal cord, however, several cortical and subcortical centers, including the basal ganglia and the cerebellum, pose their influence upon the motor cortex 'shaping' the final, descending signal. Whereas the prevalent functional role of the basal ganglia lies in the learning and selection appropriate motor or behavioural programs [42], specifically via reinforcement learning; the cerebellum mainly takes the supervised learning of motor control into account[43] . In addition to integrating already learned information into motor control, both systems show involvement in the integration of non-motor behaviour such as e.g., limbic and/or associative loops[44,45]. This illustrates the complex information processing within ancient subcortical structures taking place next to cortical processing. With the appearance of neocortex in mammals, BG outputs to motor cortex via thalamus became of greater significance, especially in primates, in which a parallel expansion of cerebral cortex and BG occurred[46]. Despite the general evolutionary trend for neocortex and cerebellum to change in tandem, humans and other apes have a significantly larger cerebellum in relation to neocortex size than other anthropoid primates[47]. Thus, it illustrates the need for careful analyses of the interaction of the cerebellum, the BG and the cortex despite the massive development of the neocortex.

In this review we tried to expand the actual view of BG-cerebellar interaction with the thalamus to a complex integration system, in which we have overlapping regions next to a pure segregated informational processing. Together with the cerebral cortex these regions regulate complex motor paradigms and might even be part of a compensatory function in movement disorders like PD. We hypothesize that a change in frequency bands in oscillatory activity might be a product of underlying axonal degeneration and that axonal degeneration can also be worsened by pathological oscillatory activity resulting in a vicious circle. The thalamus, as main relay station between the basal ganglia and the cerebellum seems to be involved in this disease pathology in Parkinson's disease. In future, the combination of *in vivo* tractography and electrophysiological mapping might help to solve the question of the development of degenerative movement disorders like PD.

## Conflicts of interest

LT received payments as a consultant for Medtronic Inc, Boston Scientific, SAPIENS, St. Jude Medical, Bayer Healthcare, UCB Schwarz Pharma, Archimedes Pharma. L.T. received honoraria as a speaker on symposia sponsored by TEVA Pharma, Lundbeck Pharma, Bracco, Gianni PR, Medas Pharma, UCB Schwarz Pharma, Desitin Pharma, Boehringer Ingelheim, GlaxoSmithKline, Eumecom, Orion Pharma, Medtronic, Boston Scientific, Cephalon, Abott, GE Medical, Archimedes, Bayer, TAD Pharma.

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