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Conclusion: We characterized a cohort of MJD patients. Follow-up analysis showed that early stage disease patients worsen their ability to walk and to perform daily life activities. Recognizing parameters affecting these patients is relevant to identify the needs for therapeutic interventions.

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S8-O3 | WWOX1 and mitochondria crosstalk in diabetic conditions: The beginning of a cell death fait

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Background: Accumulating evidence demonstrates that type 2 diabetes (T2D) increases the risk of cognitive impairment and dementia, particularly Alzheimer's disease (AD). To gain insights into the mechanisms underlying T2D-associated neurodegeneration, we propose to evaluate the contribution of the crosstalk between the putative tumor suppressor WW domain-containing oxidoreductase (WWOX1) and mitochondria in T2D-like neurodegeneration.

Methods: For this purpose, we evaluated WWOX1 activation pattern in the brain cortex of 6- and 14-month-old Goto-Kakizaki (GK) rats, a non-obese, spontaneous model of T2D as well as in 3xTg-AD mice at different ages (3, 6, 9 and 11-month-old), a model of AD. Moreover, studies in differentiated SH-SY5Y human neuroblastoma cells under hyperglycemic conditions were also performed to better understand the relationship between WWOX1 activation and mitochondrial dysfunction.

Results and conclusions: In GK rats, WWOX1 activation, evaluated through Tyr33 phosphorylation, occurs in younger animals while in older animals a significant decrease of WWOX1 activation was observed. Interestingly, a similar pattern of WWOX1 activation is observed in 3xTg-AD, suggesting the involvement of WWOX1 in AD and T2D-associated neurodegeneration. In differentiated SH-SY5Y cells under hyperglycemic conditions, WWOX1 activation occurs after 24 hours of incubation. Interestingly, WWOX1 activation is associated with a loss of mitochondrial membrane potential and increased p53 levels. Moreover, an accumulation of protein particle complex (TPC6A) in mitochondria seems to occur, suggesting its dissociation from WWOX1, with consequent increase in amyloid β (Aβ) production. Curiously, an increase in amyloid precursor protein (APP), β-secretase (BACE) and phosphorylated tau protein levels was also observed. In sum, our results suggest that WWOX1 activation can underlie T2D-associated neurodegeneration.

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S8-O4 | Levels of nitric oxide production in the rats of different age

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Recently, during analyzing the functions of the cardiovascular system, attention is drawn to nitric oxide (NO), which is a free radical with a short life time. In the cardiovascular system, NO controls vascular tone, blood pressure, proliferation of endothelial and smooth muscle cells of the vascular wall. Detailed analysis shows that the different effects of NO donors and NOS blockers may be depended from differences in the experimental conditions. Since in many experiments there are used juvenile animals, the study NO level in heart tissues during ontogenesis is of great interest. Therefore, the aim of investigation was to study the dynamics of NO-containing iron complexes in rat heart tissues during ontogenesis by EPR spectroscopy using the method of spin traps. Rats 14, 21, 70 and 100 days of age were used in the experiment. The records were carried out on EPR spectrometer X-band "Bruker" ER 200E SRC. Three types of paramagnetic complexes of iron ions with NO were recorded in all measured EPR spectra. It is a spin trap based complex of Fe2 + with diethyldithiocarbamate (DETC)2-Fe2 + -NO and two types of iron complexes R- and T-conformers of Hb-NO. It was found that the summer concentration of NO (all three components) produced in rat heart tissues proved to considerably decrease during

ontogeny. However, in 14- day-old rats, the signal from the T-conformer is much greater than in 100-day-old rats. Thus, it can be assumed that the NO system plays an important role in the early stages of postnatal ontogenesis.
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S8-O6 | Type 2 diabetes attenuates brain glycolytic and oxidative glucose metabolism in middle-aged female rats

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