PET scan studies and diffusion tensor imaging (DTI) studies in DYT1 dystonia

- Fluorodeoxyglucose (FDG) PET scan studies of individuals with a TOR1A pathogenic variant with and without dystonia show an abnormal network with relative increased metabolism in the lentiform nucleus, cerebellum, and supplementary motor cortex.

- Individuals with a TOR1A pathogenic variant with dystonia have been found to have a distinct metabolic pattern characterized by relative metabolic increases in the pre-supplementary motor area (SMA) and parietal association cortices and decreases in the inferior cerebellum, brain stem, and ventral thalamus [Carbon & Eidelberg 2009].

- Other imaging abnormalities (using [11C] raclopride and PET imaging) detected in individuals with a TOR1A pathogenic variant include decreased striatal D2 receptor binding [Asanuma et al 2005].

- Studies combining PET scanning and psychomotor testing in individuals with a TOR1A pathogenic variant without dystonia show subtle sequence-learning abnormalities in motor performance and recruitment of brain networks [Carbon et al 2002, Ghilardi et al 2003, Carbon et al 2008]. This PET evidence suggests the presence of abnormal brain processing in individuals with a TOR1A pathogenic variant regardless of the presence or absence of dystonia [Carbon et al 2011].

- Diffusion tensor imaging (DTI) studies have shown microstructural changes involving the subgyral white matter of the sensorimotor cortex and the dorsal pons in manifesting and non-manifesting individuals with a pathogenic variant in TOR1A [Carbon et al 2004a, Carbon et al 2004b, Carbon et al 2008], with a greater degree of abnormality in the dorsal pons (in the region of the superior cerebellar peduncle) in the manifesting individuals [Carbon et al 2008], implicating abnormalities in the cerebello-thalamo-cortical pathways in the pathogenesis of dystonia.

- Subsequent studies using DTI in conjunction with probabilistic tractography showed that the presence or absence of clinical manifestations in individuals with a TOR1A pathogenic variant is determined by tract changes occurring along the course of the cerebello-thalamo-cortical pathways. Reductions in structural connectivity involving cerebellothalamic projections (the “proximal” pathway segment) are observed in individuals with a TOR1A pathogenic variant, whether or not they manifest signs and symptoms of dystonia. A second fiber tract abnormality involving thalamocortical projections (the “distal” pathway segment)
are also identified, but only in asymptomatic individuals with a TOR1A pathogenic variant [Argyelan et al 2009]. These findings suggest that the distal pathway segment regulates penetrance by controlling the transmission of aberrant cerebellothalamic signals to the cerebral cortex [Niethammer et al 2011].

References


