Neurobehavioral Phenotypes in MPS III

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Hypothesis #1: Factor analysis of the revised Sanfilippo Behavior Rating Scale (SBRS) will identify a group of externalizing behaviors and a group of Klüver-Bucy syndrome-like behaviors as two different factors that are at least partially independent.

Hypothesis #2a: Children with MPS III will show more hyperlocomotion, fearlessness, asociality and noncompliance than children of similar cognitive ability with MPS I.

Hypothesis #2b: These behaviors will become more frequent and/or intensify over time, consistent with the Cleary and Wraith (1993) model. Quantifying them will provide a more empirical framework for staging disease progression.

Hypothesis #3: Brain volumetric analysis and diffusion-tensor imaging will reveal abnormalities of frontal and temporal lobe structures that will correlate with externalizing and Klüver-Bucy syndrome-like behaviors, respectively.

Hypothesis #4. Loss of cognitive and language function as measures of neurologic decline will directly precede or co-vary with behavioral decline.

The primary objective of this study is to identify the behavioral phenotype and its neural basis in MPS III (Sanfilippo syndrome). Is the behavioral phenotype similar to that of Klüver-Bucy syndrome, and is there evidence for amygdala abnormality? The secondary objective of this research study is to develop easily administered, sensitive and specific neurobehavioral and neuroimaging markers to characterize the behavioral phenotype(s) of MPS III; to track their progression; and to delineate their neural substrates. Such markers are critical for identifying the stage of disease for each patient, and to measure treatment outcome. Although we know that severe cognitive decline is one essential characteristic of MPS III, the other highly salient characteristic is a range of abnormal and disruptive behaviors that can include, but go well beyond, childhood noncompliance and oppositionality. These behaviors set Sanfilippo syndrome apart from the other MPS disorders. They cause major disruption in the child's familial, school, and community environments. Delineating these behavioral abnormalities will help in better understanding the neurological disease.