

Electrophysiologic screening for FXTAS using CATSYS 2000

Jorge L. Juncos M.D., Emily Graves-Allen Ph.D., Michelle Rusin Ph.D., Lisa Shubeck, Gloria Novak Ed.S., Richard Letz Ph.D., Stephanie L. Sherman Ph.D.

INTRODUCTION: We examined the sensitivity of the CATSYS 2000 neuromotor testing system to FMR1 premutation-associated FXTAS motor dysfunction in individuals above age 50. We hypothesize that CATSYS quantitative tools will be sensitive to minimal motor dysfunction in evolving FXTAS. We report the CATSYS and neurologic assessment results on the first 15/31 premutation carriers screened so far.

METHODS: Of 124 available subjects, 90 were identified as premutation carriers. Non-carrier siblings served as controls. CATSYS records tremor, hand coordination and postural sway. Abnormal scores consist of values ≥ 2 SD compared to matched controls. CATSYS and psychometric evaluations were conducted by a blinded investigator. Neurologic assessments were performed by a movement disorders specialist using validated scales and video. The diagnosis of FXTAS was made according to Jacquemont et al. (2003). Cognitive status was assessed using a bedside mental status exam and detailed neuropsychologic testing (reported elsewhere).

RESULTS: We studied 14 men and 1 woman mean age of 64 ± 7 years and mean symptom duration of 9 years (range 2-21). Twelve of 15 subjects met Jacquemont's criteria for definite FXTAS. Of the remaining 3, one had a compatible clinical picture but no brainstem changes on MRI; in another, the clinical picture was confounded by an unrelated polyneuropathy; and a third, the woman, presented with atypical features and a normal MRI. Non-carrier siblings tested so far were normal on CATSYS. Three subjects were clinically demented and an additional 9 exhibited abnormalities in word fluency, memory problems or executive dysfunction. There was a weak trend for subjects with high CGG repeats to have an earlier age of onset ($R = 0.14$, $p = 0.16$). There was no correlation between CGG repeat length, dominant phenotype (ataxia vs. tremor) or dementia (3 subjects).

CONCLUSIONS: These early results suggest the CATSYS system is an adequate screening tool for motor abnormalities in FXTAS. A larger cohort of subjects and controls is being examined to corroborate these findings, their specificity, and to properly power further exploration of the possible relationship between CGG repeat length and clinical dysfunction in FXTAS.