

## **Novel non-verbal learning tasks for the assessment of cognitive change in Fragile X Syndrome**

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Our understanding of the effect of the lack of the production of the Fragile X Mental Retardation protein (FMRP) on brain structure and function has grown substantially over the past decade. This new knowledge has provided a clearer picture of the mechanisms in nerve cells that are disrupted when FMRP is not produced in the brain. In turn, promising drug interventions are being developed or tested that may compensate for the characteristic thinking deficits that occur in Fragile X Syndrome. If we anticipate improvements in thinking abilities that result from these drug interventions, it stands to reason that we should be able to measure these changes objectively. Unfortunately, the current technology available for measuring thinking skills (i.e., IQ testing) falls short of what is needed to accomplish this important task. The proposed research project will evaluate a set of new tests that have several distinct advantages over traditional tests of thinking abilities. First, these tests do not require verbal responses from the test participant, allowing the majority of individuals with Fragile X to be tested. Second, the tests are presented as a fun game that is intrinsically rewarding thereby maximizing motivation, allowing individuals to demonstrate their 'best' performance. Third, the tests are derived from well-established tasks of problem solving commonly used with animals. As such, the effects of promising drugs tested in laboratory animals can be easily compared with human performance. Fourth, for some of the tests, researchers have already identified which brain areas are involved in successful performance allowing important inferences to be drawn about the brain areas that are most affected by Fragile X Syndrome. Furthermore, changes in thinking abilities may only occur on some of the tasks, these new tests will be sensitive to such subtle changes. We will be comparing the performance of individuals affected by Fragile X Syndrome on these tasks with that of individuals affected by Down Syndrome. This will allow us to extract the specific pattern of strengths and weaknesses in thinking abilities that is related to Fragile X Syndrome excluding the effect of mental retardation. We will also be comparing performance of these same individuals affected by Fragile X Syndrome at several time points to ensure that results are independent of previous experience with the tests. This research will therefore allow us both to better understand the thinking abilities in Fragile X Syndrome and provide us with a validation of much needed technology to measure change in thinking abilities to be used in drug trials.