Fehr S, Bebbington A, Ellaway C, Rowe P, Leonard H and Downs J 2011, Altered attainment of developmental milestones influences the age of diagnosis of Rett syndrome, *Journal of Child Neurology*, vol. 26, issue 8, pp. 980-987.

Background

Regression, including the loss of previously learned skills, such as hand function and communication skills, is one of the most suggestive features of Rett syndrome. These symptoms often first appear when the child is about 18 months of age. However early development of the girls prior to this age can be variable.

What we did

We examined the patterns of achieving motor and communication milestones in 293 girls whose parents provided information to the Australian Rett Syndrome Database and the International Phenotype Database, InterRett. We then examined how this pattern related to other factors such as the age at regression, age at diagnosis and *MECP2* mutation.

What we found

We found that most girls learned to sit by 10 months of age, were able to either babble or use words, and approximately half learned to walk. About half the girls began to regress at about 18 months and many parents expressed concerns about unusual behaviours or development during infancy. Parents often commented that their daughter was “floppy”, excessively quiet or placid or had delayed crawling.

Girls with the p.R133C, p.R306C or p.R294X mutations were more likely to achieve developmental milestones with the majority learning to sit, walk and either babble or use words. Girls who had the p.R133C mutation or C-terminal deletions also tended to regress at a later age than those with other mutations.

Girls who were able to walk unassisted and able use words were diagnosed at a later age. Those who had achieved fewer milestones tended to be diagnosed earlier. Girls with C-terminal deletions, large deletions, p.R133C, p.R294X or p.R306C mutations were diagnosed later then those with the p.R255X mutation.

What does it mean

Our findings suggest that early development in girls with Rett syndrome was often atypical. Many parents felt that their child had displayed unusual behaviours or development during infancy and was often described as overly calm, placid and/or ‘‘floppy”. As they became older, some parents were also concerned about their child’s difficulties in rolling, crawling, or pulling to stand.

Our findings also suggest that these patterns of early development often precede the appearance of other symptoms more characteristic of Rett syndrome. Even though these patterns are not specific to Rett syndrome, their presence should not delay confirmation by *MECP2* testing if other criteria for Rett syndrome are met.

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