New insight into fragile gene

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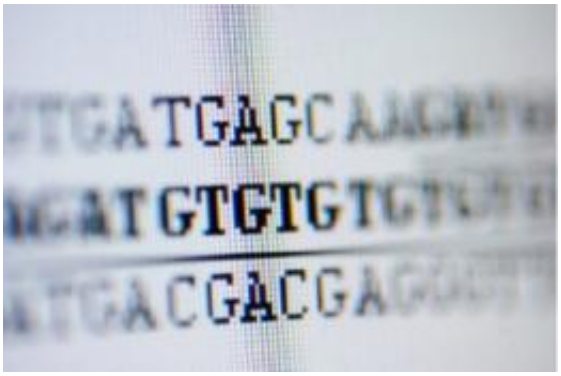

DNA sequence

(Medical Xpress) -- New research could change the way health professionals identify and treat late-onset dementia.

Monash researcher Professor Kim Cornish and colleagues at the University of London examined impulsivity, attention and working memory skills of men aged 18 to 69 years, who were "carriers" of the FMR1 (Fragile X Mental Retardation 1) gene. Their findings will be published in the August edition of the prestigious journal *Neurology*.

Fragile X Syndrome (FXS) is a leading cause of inherited intellectual disability worldwide and one of the few known single-gene causes of autism. It occurs when the FMR1 gene, found on the X chromosome, mutates.

Approximately 70,000 Australian men and women will be carriers, and for many years it was assumed that carriers were unaffected by any of the challenges faced by those with FXS. The Monash research showed that, despite having none of the obvious symptoms of the syndrome earlier in life, carriers may be at high risk of developing severe dementia as they age.

The FMR1 gene contains a DNA sequence which is prone to excessive repetition. In these cases, the gene is said to undergo "expansion". Individuals whose FMR1 gene is affected by this excessive repetition are usually considered to be in one of two categories: small-medium expansion and large expansion.

Those with small-medium expansions are known as carriers. They have the gene in a premutation (PM) state and do not have Fragile X Syndrome, but can pass it on to successive generations. Those with large expansions are considered to have the "full mutation" of the gene. These individuals will have Fragile X syndrome.

The men were tested for their ability to phase out irrelevant information as well as actively store short-term information. These core brain functions decline with late-stage dementia.

The research found that carriers of the gene who were at the upper end of the medium expansion range were more likely to have problems with inhibition and remembering materials, demonstrating cognitive dementia symptoms, whereas those who had expansions just within the medium range appeared risk-free.

The findings will make it easier to accurately identify men who may go on to develop Fragile X-associated dementia and influence current approaches to diagnosing, preventing and treating the disorder.

Professor Cornish, who conceptualised and designed the study, said that it provided the first clear evidence that being a male carrier with a larger expansion may infer some risk.

"Until 10 years ago, it was assumed that carriers of FXS would remain free of symptoms as they grew older," Professor Cornish said.

"It is now well-documented that approximately 30 to 40 per cent of PM males will develop FXS-related late-stage dementia."

Recognising the need to identify risk factors in Australian carriers of the FXS gene, a new study funded by the Australian Research Council and led by Professor Cornish will for the first time chart the history of strengths and challenges facing carriers across their lifespan.

More information: Professor Cornish will be featured in the August issue of Neurology. Her team is based in the School of Psychology and Psychiatry and also in the newly established Monash Institute for Brain Development and Repair (MIBDR).

Provided by Monash University