WORK IN PROGRESS

Richard Shrubb reports on the development of drugs that could treat fragile X syndrome

Computer simulation of a human x chromosome. A mutation in a gene on this chromosome can cause fragile X syndrome

A group of drugs in the early stages of development could help some people with fragile X syndrome.

The drugs have passed the first hurdle in the approval process and will now be tested in patients.

Fragile X syndrome is a genetic abnormality on the X chromosome that causes learning disabilities and, in a third of people affected, autistic spectrum disorders.

Fragile X inhibits the production in the brain of protein FMRP, which is responsible for keeping levels of other synaptic proteins in check. Too much of some proteins impairs brain development.

Research has shown that blocking the production of glutamate, using drugs such as mGluR5 antagonists, can help counterbalance the effects of reduced FMRP levels. Keeping protein levels in check may prevent damage and reverse symptoms such as learning problems, anxiety and autistic behaviours that are found in people with the syndrome.

SUMMARY

New drugs are being developed for people with fragile X syndrome, a condition that causes learning disabilities and autism spectrum disorders.

Keywords

Autism spectrum disorders • Drug trials • Fragile X syndrome • Learning disability

For people with fragile X, the problem is not that too little information is being processed by the brain, but too much. According to the Fragile X Research Foundation in the United States, there is 'too much of a certain kind of learning'. By reducing that excess learning, researchers hope this drug will help patients to understand the world better.

Neil Summers, senior lecturer in the health and social care school at the University of England, Bristol, is cautious. 'We need to be realistic about the likelihood of success of any drug attempting to control or treat the many conditions associated with fragile X,' he says. 'However, these drugs may be useful when used with other therapeutic and social approaches that strive to support and enhance the social value of individuals with learning disabilities.'

Luca Santarelli, head of early development for central nervous system drugs at the pharmaceutical company Roche, says: 'We have completed safety and tolerability testing on mGluR5 antagonists, and are recruiting for phase II trials now.'

Phase II of a trial assesses how well the drug works in a group of volunteers and patients, while phase I safety assessments continue.

If a drug fails in development, it usually occurs during phase II trials because it does not work as planned or has toxic effects.

Phase III is the large-scale, final stage. This looks at the drug's efficacy, although serious side effects may be identified. Phase II trials may involve up to 1,000 patients, but phase III recruits 20 times that number.

The drug, which could benefit people with anxiety or other mental health problems, has a long way to go even if it survives phase III. It may win a licence for use in the UK, but the National Institute for Health and Clinical Excellence may not find it suitable for general use in the NHS.

Dr Santarelli is realistic about the timescale: 'The business plan is for a 2017 release' **NS**

Richard Shrubb is a freelance journalist