

Lay Summary

BRAIN UK Ref: 15/002

Investigating cortical development in Trisomy 21

Dr. Rick Livesey (contact: Dr. Peter Kirwan), University of Cambridge

Down syndrome is the most common form of intellectual disability, with a worldwide prevalence of 1 in 750 live births. In the majority of cases, Down syndrome is caused by the presence of an extra copy of chromosome 21, so that people have three copies of that chromosome, instead of two – referred to as trisomy 21. To date, little is known about how the brains of individuals with Down syndrome develop and how this may lead to intellectual disability. Using human stem cells, we developed technologies to replay how nerve cells of the part of the brain that is affected in learning disability, the cerebral cortex, are formed during development. When we compare stem cells with trisomy 21 with those the normal number of chromosomes, we have found a major difference in how many cerebral cortex neurons are produced during development, and also a lack of specific types in trisomy 21. Our observations using stem cells in the lab predict that there are changes in the numbers and types caused in the developing cerebral cortex in trisomy 21, and those changes will contribute to learning disability. In order to confirm this, we would like to analyse the numbers and types of neurons in the developing cerebral cortex in Down syndrome/trisomy 21, compared with the cerebral cortex with the normal number of chromosomes. This work could lead to a significant advance in our understanding of brain development in people with Down syndrome, and how this contributes to learning disability.

Down syndrome is the most common form of learning disability, occurring in 1 out of every 750 live births world wide. In the majority of cases, Down syndrome is caused by the having an extra copy of chromosome 21, so that people have three copies of that chromosome, instead of two. This is called trisomy 21. We don't know much about how the brains of individuals with Down syndrome develop and how this may lead to learning disability. Using human stem cells, we developed technologies to replay how nerve cells of the part of the brain that is affected in learning disability, the cerebral cortex, are formed during development. When we compare stem cells with trisomy 21 with those the normal number of chromosomes, we have found a major difference in how many cerebral cortex neurons are produced during development, and also a lack of specific types in trisomy 21. We have seen using stem cells in the lab predict that there are changes in the numbers and types made in the developing cerebral cortex in trisomy 21. These changes will contribute to learning disability. In order to confirm this, we would like to analyse the numbers and types of neurons in the developing cerebral cortex in Down syndrome/trisomy 21, compared with the cerebral cortex with the normal number of chromosomes. This work could lead to a significant advance in our understanding of brain development in people with Down syndrome, and how this contributes to learning disability.