Children with autism have elevated levels of steroid hormones in the womb

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Quinn, an autistic boy, and the line of toys he made before falling asleep. Repeatedly stacking or lining up objects is a behavior commonly associated with autism. Credit: Wikipedia.

Scientists from the University of Cambridge and the Statens Serum Institute in Copenhagen, Denmark have discovered that children who later develop autism are exposed to elevated levels of steroid hormones (for example testosterone, progesterone and cortisol) in the womb. The

finding may help explain why autism is more common in males than females, but should not be used to screen for the condition.

Funded by the Medical Research Council (MRC), the results are published today in the journal *Molecular Psychiatry*.

The team, led by Professor Simon Baron-Cohen and Dr Michael Lombardo in Cambridge and Professor Bent Nørgaard-Pedersen in Denmark, utilized approximately 19,500 amniotic fluid samples stored in a Danish biobank from individuals born between 1993-1999. Amniotic fluid surrounds the baby in the womb during pregnancy and is collected when some women choose to have an amniocentesis around 15-16 weeks of pregnancy. This coincides with a critical period for early brain development and sexual differentiation, and thus allows scientists access into this important window in fetal development. The researchers identified amniotic fluid samples from 128 males later diagnosed with an autism spectrum condition and matched these up with information from a central register of all psychiatric diagnoses in Denmark.

Within the amniotic fluid the researchers looked at 4 key 'sex steroid' hormones that are each synthesized, step-by-step from the preceding one, in the 'Δ4 sex steroid' pathway: progesterone, 17α-hydroxy-progesterone, androstenedione and testosterone. They also tested the steroid hormone cortisol that lies outside this pathway. The researchers found that levels of all steroid hormones were highly associated with each other and most importantly, that the autism group on average had higher levels of all steroid hormones, compared to a typically developing male comparison group.

Professor Baron-Cohen said: "This is one of the earliest non-genetic biomarkers that has been identified in children who go on to develop autism. We previously knew that elevated prenatal testosterone is associated with slower social and language development, better attention

to detail, and more autistic traits. Now, for the first time, we have also shown that these steroid hormones are elevated in children clinically diagnosed with autism. Because some of these hormones are produced in much higher quantities in males than in females, this may help us explain why autism is more common in males."

He added: "These new results are particularly striking because they are found across all the subgroups on the autism spectrum, for the first time uniting those with Asperger Syndrome, classic autism, or Pervasive Developmental Disorder Not-Otherwise-Specified. We now want to test if the same finding is found in females with autism."

Dr Michael Lombardo said: "This result potentially has very important implications about the early biological mechanisms that alter brain development in autism and also pinpoints an important window in fetal development when such mechanisms exert their effects."

Steroid hormones are particularly important because they exert influence on the process of how instructions in the genetic code are translated into building proteins. The researchers believe that altering this process during periods when the building blocks for the brain are being laid down may be particularly important in explaining how genetic risk factors for autism get expressed.

Dr Lombardo adds: "Our discovery here meshes nicely with other recent findings that highlight the prenatal period around 15 weeks gestation as a key period when important genetic risk mechanisms for autism are working together to be expressed in the developing brain."

Professor Baron-Cohen said: "These results should not be taken as a reason to jump to steroid hormone blockers as a treatment as this could have unwanted side effects and may have little to no effect in changing the potentially permanent effects that fetal steroid hormones exert

during the early foundational stages of brain development."

He cautioned further: "Nor should these results be taken as a promising prenatal screening test. There is considerable overlap between the groups and our findings showed differences found at an average group level, rather than at the level of accurately predicting diagnosis for individuals. The value of the new results lies in identifying key biological mechanisms during fetal development that could play important roles in atypical brain development in autism."

Provided by University of Cambridge