

# Diuretic drug improves symptoms of autism

Small-scale trial provides hope for treatment of autistic behaviour in children.

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A drug normally used to increase the rate at which people urinate improves some of the symptoms of autism in children, according to a small clinical trial published today in *Translational Psychiatry*<sup>1</sup>.

Autism is a neurodevelopmental disorder characterized by impaired communication and social interactions, and also by repetitive behaviours in those affected. Research has shown that signalling by a molecule called GABA, a neurotransmitter which normally dampens down neuronal activity, is altered in autism. And that this disruption of GABA is due to increased levels of chloride ions in the brain cells.

Reducing these chloride ion levels might help to treat the condition, hypothesized Yehezkel Ben-Ari, a neuroscientist at the Mediterranean Institute of Neurobiology (part of INSERM, France's national biomedical research agency) in Marseilles, and his colleagues .

In 2010, Ben-Ari and his co-author reported that a three-month course of bumetanide — a diuretic that lowers the concentration of chloride ions by blocking the entry of ions into the cell — decreased autistic behaviour in five infants without causing side effects<sup>2</sup>.

Now, the researchers have conducted a randomized, controlled clinical trial to confirm their earlier findings and to evaluate the safety of the drug.

They recruited 60 children for the study, aged between 3 and 11 years, who had been diagnosed with either autism or Asperger's syndrome, and randomly assigned them to receive either 1 milligram of bumetanide daily for three months, or a placebo daily for the same period. The researchers used a standard scale to assess the children's behaviour at the start and end of the three-month dosing period, and then assessed them again a month later.

## Take notice

Video footage of the children was also taken at the start and end of the study, so that their behaviour could be examined by independent evaluators. And their parents were asked to report any change in the severity of symptoms that they saw in their children.

In children taking bumetanide who were less severely affected by autism, the researchers saw small but significant improvements in behaviour. The drug also



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Children with autism show impaired communication and social interactions, but a small clinical trial suggests that symptoms can be reduced using a diuretic drug.

seemed to be safe and well tolerated with few side effects, they say.

"This study is based on a randomized, controlled design and that makes me take notice," says cognitive neuroscientist Uta Frith, who studies autism at University College London, UK.

She adds, however, that the effects of the drug were small, and that one-third of the placebo group also showed some amelioration of symptoms.

"The effects were only noticeable on some gross behavioural measures, [but the findings are] consistent with my view that there is a lot of spontaneous fluctuation in symptoms and a general tendency to improve over time," she adds.

### Neurons and networks

The authors suggest that bumetanide could be a new type of treatment for autism, and that their findings warrant larger trials. Earlier this year, Ben-Ari co-founded a company called Neurochlore, based in Marseilles, which is now aiming to develop and commercialize bumetanide as a treatment.

But Frith remains sceptical. "I have seen a number of treatments for autism come and go, and this leaves many questions open, such as what is the [drug's] mechanism, and will the effect be replicated?"

Ben-Ari says: "We do not claim that we are curing autism ... but want to determine how neurons and networks operate in animal models and humans." He adds that understanding this is more important than identifying genetic mutations in autism, as mutations do not "really tell us what is happening".

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### References

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1. Lemonnier, E. *et al.* *Transl. Psychiatry* **2**, e202 (2012).
2. Lemonnier, E. & Ben-Ari, Y. *Acta Paediatr.* **99**, 1885–1888 (2010).