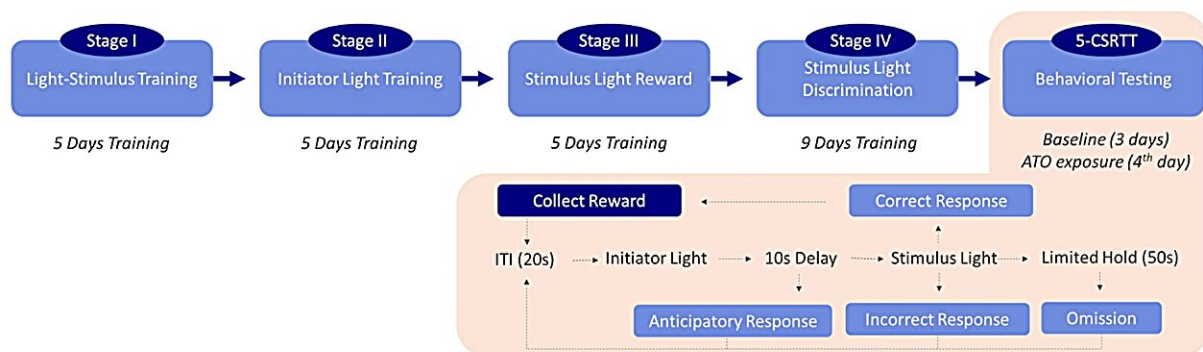


New genes linked to ADHD identified, potentially paving the way for new treatments

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Flow-chart summarizing the 5-CSRTT process. During the 5-CSRTT, fish were required to swim toward one of five spatially distinct LEDs when illuminated. Approaches to the illuminated light were 'correct' and the proportion of correct trials was a measure of attention. Prior to illumination, there was a variable-time (mean 5-s) inter-trial interval, and responses during this interval were punished with subsequent non-reinforcement. Responses during this inter-trial interval (anticipatory or premature responses) were used as a measure of impulse control. Credit: *Translational Psychiatry* (2023). DOI: 10.1038/s41398-023-02601-4

Several new genes associated with conditions such as Attention-deficit hyperactivity disorder (ADHD) have been identified, unearthing a significant connection between these disorders and our immune system that could lead to new treatments. The research from the University of Surrey, now [published](#) in *Translational Psychiatry*, also confirms the role

of gene ADGRL3 in conditions such as ADHD, giving scientists a greater understanding of its workings.

During this innovative study, scientists led by Dr. Matt Parker from Surrey set out to understand more about ADGRL3, a gene closely linked to ADHD and other "externalizing" disorders, in promoting behaviors such as [substance abuse](#), which can be associated with the conditions. Through this work, scientists identified several [new genes](#) related to externalizing disorders, which could lead to the development of new medication to lessen the impact on individuals.

Parker, senior lecturer in neuroscience and sleep science at the University of Surrey, said, "The high degree of heritability of externalizing disorders, such as ADHD, has intensified the search to identify genes which cause such behaviors, which we hope will help develop targeted [treatment options](#) to alleviate their symptoms.

"It is important we do this as not only will it help individuals better manage their condition, but it may also help improve their life chances—for example an estimated 26% of prison inmates have ADHD."

Scientists used zebrafish as they share 70% of genes with humans—84% of these genes are known to be associated with human disease. Using a behavioral task which tracks the ability and willingness of the fish to "wait" for a reward, scientists found zebrafish with the ADGRL3 gene-edited out had higher levels of inattention and demonstrated greater impulsivity when compared to wild-type fish with the normal functioning gene. These characteristics were more prominent in male zebrafish lacking ADGRL3 compared to their female peers.

Treatment with atomoxetine, a medication used to treat ADHD, completely reversed the impulsivity.

Next the team studied [genetic differences](#) in the brains of zebrafish with and without the gene ADGRL3. They did this because ADGRL3 is a gene that is important in the development of the nervous system, so its dysfunction will have knock-on effects elsewhere. Interestingly, they found evidence supporting the idea that the [immune system](#) is crucial in the development of ADHD and similar disorders. They identified several genes and enriched gene clusters that were independent of [drug treatment](#) which may contribute to behaviors of those with externalizing disorders.

Parker added, "The discovery of these genes is very exciting as it demonstrates that there are more genes contributing to externalizing disorders than we previously thought. Identification of such genes is potentially the first step in the development of new targeted medications to help patients better manage their symptoms."

More information: Barbara D. Fontana et al, adgrl3.1-deficient zebrafish show noradrenaline-mediated externalizing behaviors, and altered expression of externalizing disorder-candidate genes, suggesting functional targets for treatment, *Translational Psychiatry* (2023). [DOI: 10.1038/s41398-023-02601-4](#)

Provided by University of Surrey

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