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SCIENCE'S COMPASS

in ADHD. PDDs are characterized by impairments in several areas of development that include social interaction, communication skills, or the presence of stereotyped activities, interests, or behaviors (4). Some of the disorders under this heading include autistic, Rett's, childhood disintegrative, and Asperger's disorders, as well as PDD not otherwise specified. These disorders are often recognized during the first years of life and are associated with some degree of mental retardation. We feel that the DAT-KO mice do not display these phenotypes because they socially interact with their littermates, appear to be coordinated in their movements, and show no loss of skills over time, and both males and females are affected. Additionally, although the DAT-KO mice show impaired performance in the radial-arm maze, they are not debilitated. Occasionally, individual mutant mice could solve the maze. Importantly, psychostimulants served to attenuate the hyperlocomotion of the DAT-KO mice. As Sarkis notes, children diagnosed with PDD respond poorly to these drugs.

Another issue that Sarkis mentions is that the neurochemistries of the DAT-KO mice and human ADHD patients may not be congruent. He says that "repeated studies have indicated that ADHD patients have low extracellular dopamine"; however, comparisons between ADHD patients and normal control individuals in terms of urine, plasma, cerebrospinal fluid, or platelet levels of monoamines and their metabolites have yielded inconsistent results (5). None of these approaches can assess extracellular dopamine levels directly in humans. In our initial studies with the DAT-KO mice (6, 7), we reported that although extracellular levels of dopamine were high, striatal tissue stores were low. Additionally, levels of the dopamine D1 and D2 receptors were significantly reduced in striata from these animals. More recent evidence from our lab confirms that dopamine autoreceptor function is down-regulated or may be completely lost in these mutants (8). In this context, the attenuation or loss of dopamine receptor function and the low tissue stores of dopamine in the DAT-KO mice could be interpreted as a presumed dopaminergic hypofunctioning that Sarkis attributes to ADHD patients.

Another point is that psychostimulants do not exert their actions only through the dopamine transporter. Dextroamphetamine and methylphenidate can bind not only to the dopamine transporter, but also to the norepinephrine and serotonin transporters, as discussed in our report. Because ADHD patients may display a range of behaviors

associated with this condition, and because at least 25% of these patients do not respond to psychostimulants, it is likely that more than one neurotransmitter system may contribute to the disorder.

In conclusion, despite our reservations that the phenotype of DAT-KO mice may not precisely recapitulate all symptomologies of ADHD patients, we do think that these mice may help us to better understand the basic mechanisms that contribute to the etiology and manifestation of the disorder (9).

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CORRECTIONS AND CLARIFICATIONS

News Focus: "On the hunt for a wolf in sheep's clothing" by Michael Balter (17 Mar., p. 1906). In the table in the sidebar (p. 1907), the sheep polymorphism VRQ should have been labeled "most vulnerable," and ARR "least vulnerable."

Special Issue News article: "Can old cells learn new tricks?" by Gretchen Vogel, (25 Feb., p. 1418). The credit for the image on p. 1418 should have read as follows: G. C. Kopen *et al.*, *Proc. Natl. Acad. Sci. U.S.A.* **96**, 10711 (1999).

ScienceScope: "Still connected" by Jeffrey Mervis (18 Feb., p. 1181). The employment status of Luther Williams, former Assistant Director for Education and Human Resources at the National Science Foundation, was incorrect. He retired from NSF at the end of 1999.

News of the Week: "Shadow and shine offer glimpses of otherworldly Jupiters" by Mark Sincell (3 Dec., p. 1822). The description of Jupiter's density in the second paragraph was incorrect. It should have read "one-third greater than the density of water."