INJURY MORTALITY IN AUTISM

Guan and Li[1] recently examined epidemiological patterns of injury mortality among those diagnosed with an autism spectrum disorder (ASD). The authors screened the causes of death using the multiple cause-of-death data files in the National Vital Statistics System among individuals with a diagnosis of ASD (*International Classification of Diseases, 10th Revision* [Geneva, Switzerland: World Health Organization; 1992] code F84.0) who died between 1999 and 2014. Individuals with ASD died earlier than did the referent US population, and the calculated proportionate mortality ratios indicated that nearly a third of the deaths in individuals with ASD were attributed to injury, with suffocation, asphyxiation, and drowning being the most common cause of injury mortality. These findings on injury mortality confirm the increased risk of injury among neurodevelopmental disorders, including attention-deficit/hyperactivity disorder.[2]

Consistent with evidence purporting a link between air pollution and neurodevelopmental risk, previous investigations have suggested that environmental exposure to the agricultural and combustion pollutant nitrous oxide (N_2O) may contribute to the increasing prevalence of neurodevelopmental impairment.[3] A review of this novel hypothesis highlighted long-standing toxicological mechanisms of N_2O exposure. These include NMDA (N-methyl-D-aspartate) receptor antagonism, dynorphinergic release, and activation of the κ opioid receptor (an opioidergic class strongly implicated in behavioral stereotypy and sociability deficits in animals); inhibition of certain cholinergic receptors implicated in attention-related processes; and suppression of acetylcholine synthesis as well as clinically relevant effects on ophthalmic, auditory, and gastrointestinal functioning. The review integrated these known physiological effects with reported biological signatures in neurodevelopmental disorders.[4]

A discussion of the prevalence and risks associated with recreational N_2O use has highlighted myriad neurologic effects, including disorientation, loss of balance, impaired memory and cognition, and leg weakness. These lead to an increased risk of injury, with some fatal incidents being attributed to asphyxiation (hypoxia).[5] Animal studies assessing chronic N_2O toxicity (one month) have shown altered behavior, including lethargy and hind limb weakness.[6] Kindregan et al.[7] reviewed the evidence in support of altered gait abnormality and abnormal lower leg functioning in those diagnosed with ASD. These studies suggest that the injury risk profile in neurodevelopmental disorders may resemble the risks found with chronic N_2O exposure. Future work on injury risk and ASD should seek to explore this link further, including trying to understand whether the increased risk of drowning in ASD is related to underestimated, indirect emissions of N_2O from bodies of water.[4] It is also important to clarify whether psychotropic medications used to manage disorder symptoms affect these injury profiles.[2,4] AJPH

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REFERENCES

1. Guan J, Li G. Injury mortality in individuals with autism. *Am J Public Health*. 2017;107(5):791–793.

2. Mikolajczyk R, Horn J, Schmedt N, Langner I, Lindemann C, Garbe E. Injury prevention by medication among children with attention-deficit/hyperactivity disorder: a case-only study. *JAMA Pediatr*. 2015;169(4):391–395.

3. Fluegge K, Fluegge K. Exposure to ambient PM10 and nitrogen dioxide and ADHD risk: a reply to Min & Min (2017). *Environ Int*. 2017;Epub ahead of print.

4. Fluegge K. Does environmental exposure to the greenhouse gas, N_2O, contribute to etiological factors in neurodevelopmental disorders? A mini-review of the evidence. *Environ Toxicol Pharmacol*. 2016;47:6–18.

5. van Amsterdam J, Nabben T, van den Brink W. Recreational nitrous oxide use: prevalence and risks. *Regul Toxicol Pharmacol*. 2015;73(3):790–796.

6. Singh SK, Misra UK, Kalita J, Bora HK, Murthy RC. Nitrous oxide related behavioral and histopathological changes may be related to oxidative stress. *Neurotoxicology*. 2015;48:44–49.

7. Kindregan D, Gallagher L, Gormley J. Gait deviations in children with autism spectrum disorders: a review. *Autism Res Treat*. 2015;2015:741480.

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GUAN AND LI RESPOND

We thank Fluegge for his interest in our article about autism and injury mortality, and for his comment about the implications of our findings for etiological studies of autism. We agree with him that if there is a causal relationship between environmental exposure to nitrous oxide (N_2O) and the risk of autism, the effects of N_2O on cognitive, physical, and behavioral functions may help illuminate the biological mechanisms linking autism to heighted injury risk.