Study confirms mitochondrial deficits in children with autism

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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.

Children with autism experience deficits in a type of immune cell that protects the body from infection. Called granulocytes, the cells exhibit one-third the capacity to fight infection and protect the body from invasion compared with the same cells in children who are developing

normally.

The cells, which circulate in the bloodstream, are less able to deliver crucial infection-fighting oxidative responses to combat invading pathogens because of dysfunction in their tiny energy-generating organelles, the mitochondria.

The study is published online in the journal *Pediatrics*.

"Granulocytes fight cellular invaders like bacteria and viruses by producing highly reactive oxidants, toxic chemicals that kill microorganisms. Our findings show that in children with severe autism the level of that response was both lower and slower," said Eleonora Napoli, lead study author and project scientist in the Department of Molecular Biosciences in the UC Davis School of Veterinary Medicine. "The granulocytes generated less highly reactive oxidants and took longer to produce them."

The researchers also found that the mitochondria in the granulocytes of children with autism consumed far less oxygen than those of the typically developing children—another sign of decreased mitochondrial function.

Mitochondria are the main intracellular source of oxygen free radicals, which are very reactive and can harm cellular structures and DNA. Cells can repair typical levels of oxidative damage. However, in the children with autism the cells produced more free radicals and were less able to repair the damage, and as a result experienced more oxidative stress. The free radical levels in the blood cells of children with autism were 1 ½ times greater than those without the disorder.

The study was conducted using blood samples of children enrolled in the Childhood Risk of Autism and the Environment (CHARGE) Study and

included 10 children with severe autism age 2 to 5 and 10 age-, race- and sex-matched children who were developing typically.

In an earlier study the research team found decreased mitochondrial fortitude in another type of immune cell, the lymphocytes. Together, the findings suggest that deficiencies in the cells' ability to fuel brain neurons might lead to some of the cognitive impairments associated with autism. Higher levels of free radicals also might contribute to autism severity.

"The response found among granulocytes mirrors earlier results obtained with lymphocytes from children with severe autism, underscoring the cross-talk between energy metabolism and response to oxidative damage," said Cecilia Giulivi, professor in the Department of Molecular Biosciences in the UC Davis School of Veterinary Medicine and the study's senior author.

"It also suggests that the immune response seems to be modulated by a nuclear factor named NRF2," that controls antioxidant response to environmental factors and may hold clues to the gene-environment interaction in autism, Giulivi said.

Provided by UC Davis