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Could Oxidative Stress From Psychosocial Stress Affect Neurodevelopment in Autism?

Woody R. McGinnis

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Dear Editor:

A recent study reported greater gestational psychosocial stress in autism (Beversdorf et al., 2005). Potential confounders render the results highly preliminary, and further research is needed to validate any association, let alone causality. The study does offer an interesting platform for hypothetical discussion.

Oxidative damage to biomolecules apparently results from emotional stress, as well as strictly “physical” factors such as toxins, nutritional deficiencies and genetic variations. Oxidized nucleic acids in blood correlated with Tension-Anxiety scores in workers (Irie, Asami, Nagata, Miyata & Kasai, 2002), and meditation lowered blood lipid peroxides (Schneider et al., 1998).

In animals, experimental approximations of emotional stress increased oxidative injury to brain. Immobilization stress lowered energy production and increased free-radicals (Madrigal et al., 2001), lipid peroxides, oxidized protein, and oxidized DNA in brain (Liu et al., 1996).

Retina, a virtual extension of brain, underwent peroxidation after “emotional-pain stress” (Shvedova, Kagan, Kuliev, Dobrina & Prilipko, 1982). Peroxidation of brain induced by the water-platform method was prevented by antioxidants (Silva et al., 2004).

Catecholamines and cortisol tend to rise during emotional stress, and in doing so may mediate greater oxidative stress. Inherently, catecholamine metabolism generates free-radicals and other reactive species (Baez, Segua-Aguilar, Widersten, Johansson, & Mannervik, 1997).

Glucocorticoid administration during gestation produced persistent post-natal depression of catalase and mitochondrial function in granule cells and increased susceptibility to cell death from exposure to environmental oxidants (Ahlbom, Gogvadze, Chen, Cels, & Ceccatelli, 2000).

The relationship of catecholamines and cortisol to oxidative stress is admittedly complex. Under certain circumstances, greater catecholamines and cortisol are known to lessen net oxidative stress, as by increasing glucose or decreasing inflammation. An oxidative mechanism is but one of many biological effects these messengers may have on the development, differentiation and function of neurons (Kreider et al., 2005; Pifl, Kattinger, Reither, & Hornykiewicz, 2002).

Recent observations are not inconsistent with a possible oxidative mechanism in the neuropathogenesis of autism. One investigator reports an increased oxidative marker—carboxyethyl pyrrole—in brains of autistic children (Perry et al., 2005). Another is finding increased frequency of polymorphisms in genes for glutathione sulphotransferase and catechol-O-methyltransferase which associate with reduced glutathione redox ratios (James et al., 2006). An important function of these latter enzymes is metabolism of catecholamines and their reactive metabolites.

Maternal stress modulates the effects of oxidative neurotoxicants (Corey-Slechta, Virgolini, Thiruchelvam, West, & Bauter, 2004), sensitivity to which is greatest during rapid growth (Kaindl et al., 2005) from the sixth month of pregnancy (Felderhoff-Mueser et al., 2004). At 21–32 weeks, greater psychosocial stress in the Beversdorf study is again suggestive, not probative.

The preliminary reports of increased maternal stress and of increased oxidative species in autism, taken together

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71 with the animal studies of stress and oxidative damage,
 72 prompt the hypothesis that at least some of the purported
 73 effects of maternal stress in autism might be mediated
 74 through oxidative mechanisms. Studies in this area might
 75 benefit from a coordinated consideration of maternal stress
 76 and reactive oxidative species.
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