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**Background:** Metabolic abnormalities and targeted treatment trials have been reported for several neurobehavioral disorders but are relatively understudied in autism.

**Objective:** The objective of this study was to determine whether or not treatment with the metabolic precursors, methylcobalamin and folinic acid, would improve plasma concentrations of transmethylation/transsulfuration metabolites and glutathione redox status in autistic children.

**Design:** In an open-label trial, 40 autistic children were treated with 75 µg/kg methylcobalamin (2 times/wk) and 400 µg folinic acid (2 times/d) for 3 mo. Metabolites in the transmethylation/transsulfuration pathway were measured before and after treatment and compared with values measured in age-matched control children.

**Results:** The results indicated that pretreatment metabolite concentrations in autistic children were significantly different from values in the control children. The 3-mo intervention resulted in

significant increases in cysteine, cysteinylglycine, and glutathione concentrations ( $P < 0.001$ ). The oxidized disulfide form of glutathione was decreased and the glutathione redox ratio increased after treatment ( $P < 0.008$ ). Although mean metabolite concentrations were improved significantly after intervention, they remained below those in unaffected control children.

Conclusion: The significant improvements observed in transmethylation metabolites and glutathione redox status after treatment suggest that targeted nutritional intervention with methylcobalamin and folic acid may be of clinical benefit in some children who have autism. This trial was registered at [clinicaltrials.gov](https://clinicaltrials.gov) as NCT00692315.