



A service of the National Library of Medicine  
and the National Institutes of Health

My NCBI   
[Sign In] [Register]

All Databases

PubMed

Nucleotide

Protein

Genome

Structure

OMIM

PMC

Journals

Books

Search PubMed for

Limits  Preview/Index  History  Clipboard  Details

Display AbstractPlus Show 20 Sort by Send to

All: 1 Review: 0 

1: [J Comp Neurol.](#) 1996 Jun 24;370(2):247-61.

[Links](#)

### Embryological origin for autism: developmental anomalies of the cranial nerve motor nuclei.

**Rodier PM, Ingram JL, Tisdale B, Nelson S, Romano J.**

Department of Obstetrics and Gynecology, University of Rochester School of Medicine, New York 14642, USA.

The underlying brain injury that leads to autism has been difficult to identify. The diagnostic criteria of the disease are not readily associated with any brain region or system, nor are they mimicked by vascular accidents, tumors, or degenerative neurological diseases occurring in adults. Fortuitously, a recent report of autism induced by thalidomide exposure provides evidence that the disease originates by an injury at the time of closure of the neural tube. The human data suggest that the initiating lesion includes the motor cranial nerve nuclei. To test this hypothesis, we first examined motor nuclei in the brainstem of a human autistic case. The autopsy brain exhibited near-complete absence of the facial nucleus and superior olive along with shortening of the brainstem between the trapezoid body and the inferior olive. A similar deficit has been reported in Hoxa-1 gene knockout mice in which pattern formation of the hindbrain is disrupted during neurulation. Alternatively, exposure to antimetabolic agents just after neural tube closure could produce the observed pattern of deficits. Thus, the lesions observed in the autopsy case appear to match those predicted by the thalidomide cases in both time of origin and central nervous system (CNS) location. To produce similar brain lesions experimentally, we exposed rat embryos to valproic acid, a second teratogen newly linked to autism. Dams received 350 mg/kg of valproic acid (VPA) on day 11.5 (the day of neural tube closure), day 12, or day 12.5 gestation. Each treatment significantly reduced the number of motor neurons counted in matched sections of the earliest-forming motor nuclei (V, XII), and progressively later exposures affected the Vth and IIIrd cranial nerve nuclei. All treatments spared the facial nucleus, which forms still later. Counts from the mesencephalic nucleus of trigeminal, the dorsal motor nucleus of the vagus, and the locus ceruleus were not affected by exposure to VPA, even though these nuclei form during the period when exposure occurred. Despite its effects on the motor nuclei, valproic acid exposure did not alter the further development of the brain in any obvious way. Treated animals were robust and had no external malformations. The autopsy data and experimental data from rats confirm that CNS injuries occurring during or just after neural tube closure can lead to a selective loss of neurons derived from the basal plate of the rhombencephalon. The results add two new lines of evidence that place the initiating injury for autism around the time of neural tube closure.

PMID: 8808733 [PubMed - indexed for MEDLINE]

Display AbstractPlus Show 20 Sort by Send to

### Related Links

Linking etiologies in humans and animal models: studies of auti [Reprod Toxicol. 1997]

NTP technical report on the toxicity studies of Dibutyl Phthalate (C) [Toxic Rep Ser. 1995]

Formation of the cranial motor neurons in the absence of the f [Int J Dev Neurosci. 1995]

Cranial nerves and anopia are altered after in vitro tr [Brain Res Dev Brain Res. 1996]

A dynamic regulation of GDNF-family receptors correlates wit [Eur J Neurosci. 2000]

[See all Related Articles...](#)

[Write to the Help Desk](#)  
[NCBI](#) | [NLM](#) | [NIH](#)  
[Department of Health & Human Services](#)  
[Privacy Statement](#) | [Freedom of Information Act](#) | [Disclaimer](#)

Apr 4 2007 12:47:27