

Fetal exposure to antiepileptic drug valproate impairs cognitive development

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The NEAD study is the largest prospective study examining the cognitive effects of fetal antiepileptic drug exposure.

(Medical Xpress)—The effects of antiepileptic drugs during pregnancy have long been a concern of clinicians and women of childbearing age whose seizures can only be controlled by medications. In 1999, a study called the Neurodevelopmental Effects of Antiepileptic Drugs (NEAD) began following the children of women who were taking a single antiepileptic agent during pregnancy. The drugs included carbamazepine, lamotrigine, phenytoin or valproate.

Recently released final data from NEAD shows that at age 6, IQ is 7-10 points lower in children exposed in utero to the anti-epileptic drug valproate (Depakote) than those exposed to the other medications. The children exposed to valproate also did poorly on measures of verbal and memory abilities, and non-verbal and executive functions. The results

were reported in the January 23, 2013, *Lancet Neurology* publication on line.

"Data published at ages 3 and 4.5 showed similar results in cognitive impairment," says lead study author Kimford Meador, MD, professor of neurology at Emory University School of Medicine. "Age 6 IQ was our primary outcome goal because it is standardized and predictive of school performance."

The NEAD study is the largest prospective study examining the [cognitive effects](#) of fetal antiepileptic [drug exposure](#). The researchers monitored women through pregnancy and followed their children, performing cognitive testing at ages 2,3,4.5 and finally at 6. In addition to the effect on cognitive function, earlier data from NEAD showed an increase in the risk of anatomical birth defects.

Valproate is an [anticonvulsant](#) used in the treatment of epilepsy, migraines and bipolar disorder, and is particularly effective in the treatment of primary generalized seizures. Except for a small number of women who only respond to valproate, there are alternative medications.

"These findings consistently show a substantial loss of developmental abilities for these children," says Meador. "Women of childbearing age who have epilepsy should talk with their doctors about their options, and possibly test the safer medications prior to pregnancy to find out if they work."

In order to avoid seizures with potentially serious consequences, Meador emphasizes that women who are already pregnant and taking valproate should not stop without consulting their physicians.

"For a woman who has significant seizures, the risk from the seizure itself is worse than the risk of taking the drugs," he points out. "The

number one reason for miscarriage late in pregnancy for women with epilepsy is trauma resulting from a seizure."

Meador will co-lead a follow-up study with Page Pennell, MD, from Harvard. The new study funded by the National Institutes of Health is called Maternal Outcomes and Neurodevelopmental Effects of [Antiepileptic Drugs](#) (MONEAD), and will investigate the risks of these same drugs to both the mother and the child. The study will be conducted at 19 sites, enrolling 350 women with epilepsy during pregnancy. An additional 100 women with epilepsy who are not pregnant, and 100 healthy pregnant women will serve as controls.

More information: Further information about the MONEAD study can be found at [clinicaltrials.gov/ct2/show/NC ...
0?term=MONEAD&rank=1](https://clinicaltrials.gov/ct2/show/NC_018411?term=MONEAD&rank=1)

Provided by Emory University

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