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Androgen Exposure May Put the Finger on ALS Risk

By Kristina Fiore, Staff Writer, MedPage Today
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MedPage Today Action Points

- Note that prenatal levels of testosterone are thought to play a role in motor neuron function, and that the ratio of index-to-ring-finger length is at least in part dependent upon prenatal testosterone levels.

- Point out that this study found a decreased ratio of index-to-ring-finger length possibly consistent with higher levels of prenatal testosterone in patients with ALS later in life.

Review

A patient's risk of amyotrophic lateral sclerosis (ALS) may actually be foretold by palm reading -- as long as you're looking at the right lines, researchers said.

When measured from the defined crease at the base of the digits, ALS patients have a smaller index-to-ring-finger ratio, according to Ammar Al-Chalabi, MD, of King's College London in England, and colleagues.

Longer ring fingers are a marker of higher prenatal exposure to testosterone, which has been associated with motor neuron disease later in life, they reported online in the *Journal of Neurology, Neurosurgery, and Psychiatry*.

"Our results are therefore consistent with the hypothesis that testosterone levels during development modify the subsequent risk of ALS," they wrote.

Studies have shown that in adults, low testosterone levels are associated with motor neuron degeneration. It's hypothesized that in utero exposure to the hormone could diminish a patient's sensitivity to it later in life.

One way to measure that exposure is to look at the index-to-ring-finger ratio, which, according to established findings, is lower for patients who had greater testosterone exposure in the womb.

Though the disease is more common in men (who generally have a higher exposure to testosterone in utero), the researchers hypothesized that prenatal testosterone exposure, rather than male sex alone, is tied to ALS.

To explore this, they assessed ALS patients and controls, and based their findings on the 110 patients with usable results.

They found that index-to-ring-finger ratio was significantly lower among ALS patients than it was among controls (*P*=0.007).

In linear regression models that controlled for sex, the difference in ring finger length persisted, they found, suggesting that the finding wasn't explained solely by the higher proportion of men in the patient group.

"This finding suggests that the reason [for developing ALS] is not something to do with maleness necessarily, but more to do with the balance of hormones in the womb," Al-Chalabi said in an email.

The ratio could also predict case versus control status with a sensitivity of 72%, a specificity of 65%, a positive predictive value of 61%, and a negative predictive value of 71%.

Al-Chalabi and colleagues wrote that the ratio says nothing about adult circulating testosterone levels, "making it compatible with the observation that people with ALS have low levels of free testosterone."

It may simply suggest that the patient's sensitivity to testosterone may have been diminished by that early exposure, they explained.

Al-Chalabi emphasized that the relationship shouldn't be used as a screening tool for ALS risk.

"Everyone is exposed to male and female hormones during their development, and those with a slightly more masculine mix are more likely to be male, sporty, and to have relatively longer ring fingers," he wrote. "Hardly any of them will go on to develop ALS, so this is not a predictor of ALS any more than it is of being male."

The study was limited because it excluded patients with contractures, but the researchers still concluded that the association between index-to-ring-finger ratio and ALS "supports the possibility that very early factors in embryonic development might influence adult-onset motor neuronal degeneration."

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The researchers reported no conflicts of interest.

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Vivekananda U, et al "Low index-to-ring finger length ratio in sporadic ALS supports prenatally defined motor neuronal vulnerability" *J Neurol Neurosurg Psych* 2011; DOI: 10.1136/jnnp.2010.237412.

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