12 monkeys minus one: What to make of shrinking monkey brains?

By David N. Brown

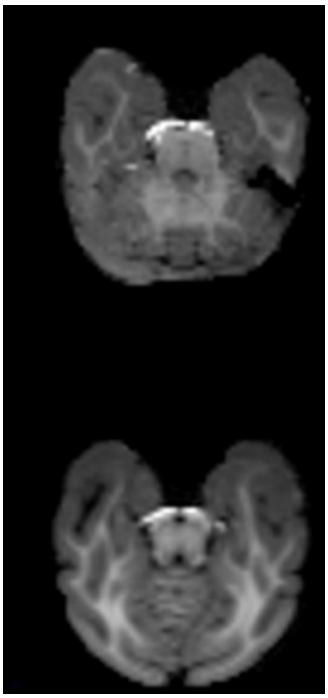
Earlier this year, Andrew Wakefield received a further blow to his ego when *Neurotoxicology* withdrew his last paper from press a few weeks before it was to see print. (See "Return of Wakefield", "Spanking a Dead Monkey".) Now, Wakefield's crew is back, with another "study" supposed to show that vaccines cause autism. This time around, Wakefield's name is absent, but his influence is still obvious. Perhaps more importantly, the current effort is clearly led by Laura Hewitson, who by all indications was the one most responsible for carrying out the Neurotoxicology study, and as a qualified primatologist had the least excuse for its numerous flaws. (In an error I have been meaning to correct, it was my initial impression that Hewitson had no such qualifications.) In a sign of the declining fortunes of Wakefield et al, the new study, titled "Influence of pediatric vaccines on amygdala growth and opioid ligand binding in rhesus macaque infants: A pilot study", has been published in not just a minor journal, but a minor eastern European journal, *Acta Neurobiologiae Experimentalis*. Even worse, they appear in a "special" issue along with Mark Geier, a strong candidate for the most despicable and dangerous member of the "autism biomed" movement. (See "Even Worse".)

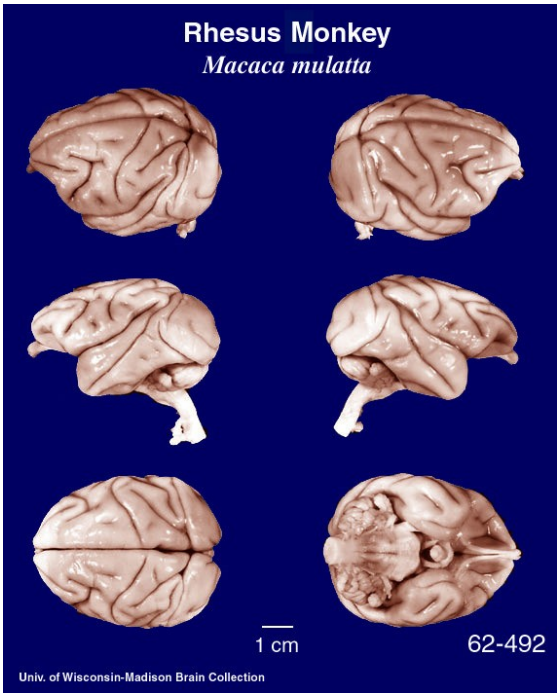
Critics more or less instantly pounced on the major flaws of the study, for the most part strikingly similar to those of the withdrawn *Neurotoxicology* paper:

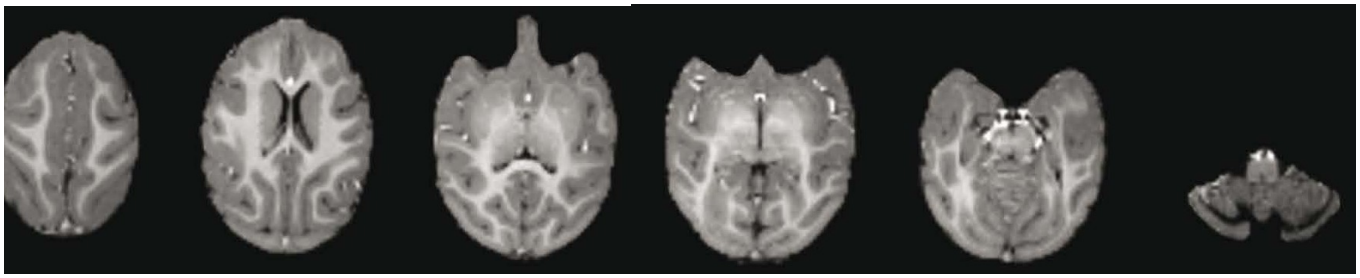
i. The paper appears to be a development of a 2008 abstract.
ii. Said abstract appears to have reached the opposite conclusion from the current paper, describing "attenuated" growth of the brain in the vaccinated where the paper reports "hypertrophy".
iii. The sample size was small, and the control group disproportionately so, with only 9 vaccinated monkeys and two "control" animals used.
iv. The abstract indicates that 16 animals, including four control animals, were used originally. Little or no explanation is offered for the apparent removal of more than a quarter of the animals, including *half the controls*.

But, what has drawn most attention is a very curious report: According to Hewitson, in the control animals a part of the brain called the amygdala shrank on average. Even more curiously, Hewitson concluded that this did not mean that one or both "controls" had abnormal brain development, but that it was in fact the brains of the vaccinated that were "hypertrophied", as many neurologists believe happens in the brains of autistic children. Unsurprisingly, both the phenomenon and its interpretation are ubiquitously being challenged. As Sullivan of LBRB put it, "A feature of most animals is that their brains grow during infancy. Brains shrinking during infancy (as with the unvaccinated monkeys) is generally not considered a good sign." Even AoA commenters were critical whether the results could be both accurate and representative of healthy development: "It is very unlikely, given what we know about neurodevelopment (although it is impossible to tell without a larger sample size,) that macaques lose almost 40% of their amygdala volume during normal development. This indicates that the control group was of questionable validity, as it doesn't look like what we'd expect from truly normal animals." In discussions at Respectful Insolence, comments (including my own) raised the possibility that at least one "control" specimen in fact had a serious pathology, or even man-made damage such as a craniotomy. If true, this would represent serious negligence or outright misconduct in the study.

In the interests of discussion, here are a published figure of the MRIs of "exposed" and "unexposed" specimens at T2, a figure from online of a "normal" rhesus macaque brain from several angles, and a sequence from the paper of MRI sections of a control animal. It can be seen from the first image that the "exposed" (bottom) and "unexposed" (top) brains do appear very differently developed. Ironically, it is the "control", with its striking asymmetry, shrunken ventricle (a storage body for cerebrospinal fluid, dark space in left front), and thinner nerve bundles, that suggests some kind of defect, illness or injury. But the other images offer a possible, different perspective.







Something that warrants special attention at the start is that the MRI images are, essentially, two-dimensional representations of a three-dimensional object. As such, they have a strong potential to mislead. This can be seen through the use of conic sections in geometry. Cutting the same cone at different levels and angles can produce shapes of widely varying size and form. Apter still is the allegory of Flatland: To the two-dimensional Flatlanders, a finger pressing on a piece of paper would seem to change shape and size, appear, disappear or multiply inexplicably, all simply as a result of limited perspective.

Considered in these terms, much of the oddity disappears. First, the cross-section sequence does not show the degree of apparent abnormality in the one cross-section used for comparison. If this is the same "control" animal, the apparent anomalies are limited to a very specific part of the brain. Second,quite a few of the differences between exposed and unexposed brain cross-sections can be

accounted for by sectioning at different "levels": Most likely, the "unexposed" specimen's cross-section was made closer to the base of the brain; compare to the bottom right specimen photo. Third, the most curious features of the unexposed brain can be accounted for by "tapering". Take the "notch" toward the rear of the right side. This readily suggests a possible pathology, such as a subdural hematoma. But the simplest explanation is that it is a space between the lower hind brain and the overhanging mass of the frontal lobes, corresponding to a visible "shadow" in about the same place on the bottom right photo.

This leaves unresolved the asymmetry of the control brain. But this is not nearly as significant as it might seem. It is typical for the hemispheres to have a certain amount of asymmetry, and while such asymmetry is widely thought to have a qualitative influence on personality and ability (hence the colloquial phrases "left brain" and "right brain"), it is not associated with gross handicaps in cognition. The appearance of abnormality is further diminished by close examination of the "exposed" brain, which has a similar if much less pronounced left/right asymmetry. It can be added that asymmetry could easily be exaggerated through a cross-section at an angle- which, on careful consideration, is likely to be true of any cross-section of a living, potentially uncooperative animal!

That will bring us to what I judge a subtle but altogether the most troublesome problem with Hewitson's conclusions:

> "The exposed animals had a significantly greater total brain volume independent of time... no significant differences in total brain volume in the exposed vs. unexposed animals at either T1 or T2... for the unexposed group there was a significant decrease in total amygdala volume over time... However, there were no significant main effects on total amygdala volume of either exposure (Wald χ_2=0.75; P = 0.39) or time... As in the amygdala as a whole, after controlling for total brain volume and using time and exposure as factors, there was a statistically significant interaction between time and exposure such that the pattern of change over time in right amygdala volume differed according to exposure status... For the exposed group there was a nonstatistically significant increase in right amygdala volume over time... For the unexposed group there was a significant drop in right amygdala volume over time...mean volume in the exposed animals at T1 was slightly lower than in the unexposed animals and the difference between the groups at T2 had increased, with volume in the exposed animals being higher, but it was not significant... For the exposed animals there was an increase in left amygdala volume over time, although this was not statistically significant... In contrast, for the unexposed animals there was a significant decrease in left amygdala volume from T1 to T2...Overall, these data indicate that there was a statistically significant interaction between time and exposure on left amygdala volume, such that the pattern of change over time differed according to exposure..."

What all this appears to mean is that, while Hewitson found measurable differences in total brain volume, total amygdala volume, and left and right amygdala volumes, these differences were unequivocally "statistically significant" *only for the left amygdala*. Given what has already been noted about the brain, this finding, even if true, has no biological/ cognitive significance: For all we might tell, both could have been of "normal" cognitive ability, and even approximate equals. An inference that an environmental cause is involved is even more tenuous: Where asymmetry is not necessarily accounted for as pure biology, the next most likely cause is individual behavior. On this note, it is all the more troubling that so many animals were simply removed from consideration. It would appear nearly certain that with more animals, even the finding of "statistical significance" would have disappeared, and all too convenient that such a large proportion were removed.

In summary, this study easily meets the description of "fraudulent". But its rotten core is not the doubtful methodology and downright suspicious sample, but a temptation to rush to judgment, and to use one ambiguous anomaly to explain another. There is a long pattern that, when a biological

abnormality is reported in a criminal or other misfit, a certain number of people propose it as the cause of deviancy. Such “explanations” have notably failed under scrutiny, even for the individual in question: Either the anomaly is dismissed as coincidental, like a tumor found in the brain of “Texas Tower” shooter Charles Whitman, or found to be entirely nonexistent, like Richard Speck's alleged “double Y” chromosomal anomaly. In the present case, Hewitson has compounded the usual mistakes by using an abnormality of uncertain significance to redefine healthy growth as abnormal, all for the transparent purpose of sustaining the belief that vaccines could cause autism.

In closing, let's see if we can extract a sensible conclusion from Hewitson's report. Brains develop in different ways. Some developmental paths lead to substantially cognitive handicaps, while others produce basically harmless differences, or have no clear effect at all. These differences can occur with or without vaccination, and if anything are proportionately more likely to occur in the unvaccinated, due to possible direct and indirect effects of vaccine-preventable disease. In the meantime, claiming such a poorly understood and doubtfully documented anomaly as Hewitson's “shrinking amygdalas” as related to autism does not do any useful service for science or society. If it has any effect at all, it will be in creating confusion, panic and, at worst, outright prejudice, as seen with “double Y” pseudoscience. Scientists- and parents- have enough problems trying to understand the many forms of biological and psychological development without the “static” of junk studies like this one.

David N. Brown is a semipro author, diagnosed with Asperger's Syndrome as an adult. Previous works include the novels *Walking Dead, The Rookie* and *Zombie Vegas*, and the nonfiction ebook *The Urban Legend of Vaccine-Caused Autism*. This and other articles related to autism are available free of charge at evilpossum.weebly.com.