

## Authors and Disclosures

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**Caroline Helwick**

## From Medscape Medical News > Psychiatry Dendritic Spines Respond to Stress



Caroline Helwick

June 24, 2011 (New Orleans, Louisiana) — Neuroplastic or neurodegenerative changes in dendritic branching and spines may affect brain circuitry and behavior, a presentation delivered here at the 16th Annual International "Stress and Behavior" Neuroscience and Biopsychiatry Conference suggests.

Ronald F. Mervis, PhD, from the Center of Excellence for Aging and Brain Repair at the University of South Florida College of Medicine in Tampa, told delegates that the dendritic arbor of a typical neuron makes up over 95% of the volume of the neuron.

Most synapses are directly located on dendritic spines. Therefore, morphologic changes in dendritic branching and spines will sensitively reflect the earliest changes associated with alterations or disruptions of neural circuitry.

Golgi impregnation can evaluate neurons from cortex, hippocampus, cerebellum, striatum and other regions. It yields a picture of dendritic branching (estimated total dendritic length, amount and distribution of dendritic arbor, and complexity of dendritic tree), determines dendritic spine density and configuration, and defines the total branching and spine microcircuitry network for a given cell population and brain region.

Dysmorphic alterations in various dendritic measures include both atrophic and neuroplastic changes that can influence the transfer of information. Disruption of this process will ultimately be reflected by changes in learning, memory, or behavior, Dr. Mervis explained.

### Indicator of Early Damage?

"These changes may be associated with early neuronal damage, often when intervention strategies would be most beneficial," said Dr. Mervis, who is also president and chief scientific officer for NeuroStructural Research Laboratories, a nonprofit contract laboratory that specializes in Golgi staining and quantitative morphologic assessment of dendritic branching and spines.

"Our studies can show neurodegenerative changes (branching atrophy and spine loss) as well as neuroplasticity reflecting neuroprotection and/or recovery from damage."

"With this method we are getting a snapshot of a neuron in time," he added. "It is a very effective way of determining the health of the neuron and the integrity of the circuitry of the brain in that region."

In a model of post-traumatic stress disorder that involved a predator stress approach in rats (a lurking cat), Dr. Mervis and colleagues found a relationship between the rat's innate anxiety level and the spine density on granule cells of the dentate gyrus, an indicator of hippocampal brain circuitry.

Extrapolating to humans, he said the experiment was a way of "looking for factors that may predispose some

individuals while not others to develop this severe anxiety disorder."

The hypothesis was that response to predator stress would differ according to whether the subject's innate level of anxiety was low (well-adapted) or high (maladapted).

Baseline anxiety was determined by the rat's response in an elevated plus maze, a validated screening instrument that is based on a rat's aversion to open spaces.

Among nonstressed rats, those that were more anxious had significantly fewer spines than the less anxious rats ( $P = .0404$ ). Similarly, in the predator-stressed cohort, more anxious rats had significantly fewer spines than less anxious ones ( $P = .02$ ).

### **Genetic Vulnerability**

For both nonstressed and stressed rats, therefore, baseline (innate) anxiety was associated with a reduction in dendritic spines of 10% to 14%, and exposure to the predator did not result in greater loss of granule cell dendritic spines.

"These results suggest that altered hippocampal circuitry (partially a function of dendritic spine density) in the maladapted, highly anxious rats may represent the basis for a possible genetic vulnerability to [post-traumatic stress disorder]-related stress anxiety," he said. "It is the innate propensity to anxiety that contributes to dendritic spine density. It's not stress per se."

In another study, chronic stress was associated with a loss of spine density in the hippocampus. The stress paradigm involved exposing adult mice to multiple stresses over a 21-day period.

Using Golgi staining of the dendritic spines of the hippocampal CA3 pyramids, the investigators observed a highly significant 21% loss of dendritic spine density in the stressed animals vs controls ( $P = .0001$ ).

"This showed the extent of what chronic stress is doing to CA3," Dr. Mervis said.

In yet another experiment, male rats were isolated after weaning for 12 weeks, with as little handling as possible, then sacrificed at 15 weeks of age. Dendritic branching in granule cells of the dentate gyrus was significantly reduced compared with branching in controls ( $P = .0001$ ).

"During a critical period of brain development, isolation, which is equivalent to a form of stress, has a widespread impact on the disruption of normal patterns of dendritic maturation," Dr. Mervis noted.

### **Positive Effect of Blueberries**

On the other hand, positive effects were observed on dendrite spines among aging animals fed a diet high in blueberries. Aging rats (18 to 21 months of age) were fed a diet enriched with 2% blueberries (equivalent to 1 cup of blueberries per day in humans) for 3 months, then compared with old and young (5 months of age) controls who consumed no blueberries.

Whereas the young controls still displayed the most dendritic interactions among the 3 groups, the aged rats receiving the blueberry diet had significantly more dendrite branching than the aged controls that did not receive the dietary intervention ( $P < .01$ ).

Commenting on the presentation for *Medscape Medical News*, Douglas Guarnieria, PhD, associate research scientist in the Department of Psychiatry at Yale University Medical School, New Haven, Connecticut, said the

research "offers an incredible chance, in a high-throughput way, to study samples and get a snapshot of what is happening to dendrites. It's a great first pass in which we are asking whether we should look further. But there are big questions."

"The main unanswered question is the relationship between these spines and function. There are 16,000 spines on one neuron, so you wonder which ones matter? Many spines don't function. Some are silent. We are interested in the observation that they are changed by stressors, but what does this really mean?"

*Dr. Mervis is president and chief scientific officer for NeuroStructural Research Labs, which performs Golgi staining. Dr. Guarnieria has disclosed no relevant financial relationships.*

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