# Researchers join forces to improve life for children with genetic disorder

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Stephanie DeLuca (center), director of the Virginia Tech Carilion Research Institute Neuromotor Research Clinic, and therapist Dory Wallace (right) work with a toddler in an intensive therapy session in this February 2017 file photo. Credit: David Hungate/VTCRI

Audrey Alves had just turned 2 when she first visited the Virginia Tech Carilion Research Institute Neuromotor Research Clinic a year ago. Unlike most toddlers her age, she struggled to sit, crawl, and

communicate.

Audrey has a medical condition known as microcephaly, which causes her head, brain, and body to be smaller compared with other children. Genetic testing traced her problems to a flaw in a gene called CASK.

But after three weeks of intensive therapy at the Virginia Tech Carilion Research Institute Neuromotor Research Clinic, Audrey played with toys, was gleeful at the sound of Elmo's voice, and was intent on getting her hands on "magic beads"—which she asked for with her newfound baby sign language abilities.

Now, Audrey's accomplishments and those of two additional girls who received intensive therapy at the VTCRI Neuromotor Research Clinic based on innovative pediatric neurorehabilitation research at the VTCRI have been documented in a report published in *BMC Research Notes*.

An analysis led by Stephanie C. DeLuca and Konark Mukherjee, assistant professors at the Virginia Tech Carilion Research Institute, showed the three girls advanced an average of 24 developmental months during their therapeutic interventions.

Audrey was the youngest of the children and made the most gains.

"Intensive therapy produces improvements in skills and abilities in children that sometimes takes years to obtain in a more traditional setting," said DeLuca, the director of the VTCRI Neuromotor Research Clinic. "Gaining years of development in such a brief time might greatly alter each child's long-term developmental trajectory."

DeLuca, a developmental psychologist devoted to advancing adult and pediatric neurorehabilitation techniques, works closely with Mukherjee, who studies the fundamental biological mechanisms of

neurodevelopment and who also leads one of the only research teams in the world devoted to understanding the CASK gene's role in neurological disorders. Both also hold research faculty appointments in Virginia Tech's College of Science.

Together, their bench-to-bedside work may help scientifically validate intensive therapy techniques and, in turn, influence the way therapy is delivered to help more people.

Mukherjee studies mice that have the same CASK genetic mutation that affects the children with microcephaly. By testing how mice respond to therapy, the researchers can better understand effects of the intervention on neural activity and communications between nerve cells in the brain.

"One would rarely find two scientists as diverse in expertise as Dr. Mukherjee and Dr. DeLuca in such collaborative partnerships in medical centers with traditional organizational structures," said Michael J. Friedlander, the executive director of the Virginia Tech Carilion Research Institute and Virginia Tech's vice president for health sciences and technology. "We are fortunate to have researchers of their caliber with the openness to explore possibilities beyond the boundaries of their own areas of expertise and take bold steps to bring leading edge science to the improvement of human health at the research institute."

In the intensive therapy as described in BMC Research Notes, children each received four hours of attention during weekdays for 10 treatment days total. Normally, the same therapy would be delivered in hour-long sessions over 40 days.

DeLuca, who has extensively used the accelerated form of therapy to help children born with cerebral palsy, said she expected families facing the developmental challenges caused by a flaw in the CASK gene to have similar success.

Prior to arriving at the VTCRI Neuromotor Research Clinic, Audrey received an hour of therapy five days a week. Each day, the therapy was focused on a different task, such as speech, movement, and eating.

Even this daily, hour-long therapy paled in comparison to the accelerated therapy, according to Audrey's mother, Rachel Alves, of Sacramento, California.

"We've heard so many 'may nevers,'" Alves said. "She may never walk, she may never talk. I was just thrilled to see her communicating and playing with toys."

Therapist Dory Wallace of the VTCRI Neuromotor Research Clinic spent four hours per session with Audrey, helping her sit, crawl, grasp toys, and eat from a fork. She also helped her learn to use "signs" to communicate with her hands.

"You see growth within four weeks because kids literally change," Wallace said. "They become new little people because they have so many more abilities, and it lights up their personalities and increases their confidence. And you see that impact the parent's lives."

Mary Rebekah Trucks, a senior occupational therapist at the VTCRI Neuromotor Research Clinic, also contributed to the design and implementation of the treatment protocol and the authorship of the article in BMC Research Notes.

The team approach allows Mukherjee to apply strategies such as DeLuca's intensive therapy techniques on mice, monitor their neural changes, and pass information back to DeLuca about methods that seem to be most effective.

Since CASK was discovered, it has been found in all animals and people,

Mukherjee said. But health problems caused by the CASK mutation have been mysterious. Likewise, the brain mechanisms underlying the improvements that the children experienced are unknown.

Animal studies indicate intensive training may stimulate generation of new brain cells and facilitate strengthened communication between existing nerve cells , Mukherjee said. The researchers believe it is possible intensive neurorehabilitation in children with microcephaly may trigger the growth of new brain cells—a process called neurogenesis—and strengthen neuronal communications —a process called synaptic plasticity.

DeLuca believes early, intensive intervention will make a difference for families facing the challenges of microcephaly, and it will also be more cost-effective for families and society in the long-term. Finding a therapy for microcephaly has become more urgent with the emergence of the Zika virus, which can infect expectant mothers and affect developing fetuses.

"I want to take what we learn from each child and put it out there in a way that has a chance of helping every child that needs it," DeLuca said.

**More information:** Stephanie C. DeLuca et al, A clinical series using intensive neurorehabilitation to promote functional motor and cognitive skills in three girls with CASK mutation, *BMC Research Notes* (2017). DOI: 10.1186/s13104-017-3065-z

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