NIDCD Supports Collaborative Efforts in Translational Research

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It all started on a racquetball court around 1990. Stephen Camarata and Keith Nelson had come to Pennsylvania State University from two different worlds: Nelson a developmental psychologist, and Camarata a speech pathologist. They would get together to play racquetball. Occasionally, conversation would break out. “Conversation,” Nelson said, “that led to a very rich collaboration.”

With funding from the National Institute on Deafness and Other Communication Disorders, their collaboration led to translational research that is now benefiting children worldwide, even while the treatments they developed are still being tested and refined.

“I had never done a study with language-late kids until I met Steve,” said Nelson, an APS Fellow and Charter Member. “As far as I know, he had never done a study with language-typical children.” They thought it might be interesting to see if interventions that worked with normally developing children could help children with Specific Language Impairment, those whose ability to use language correctly develops late.

It wasn’t long before they found a huge gap in the literature. “It was a classic circumstance,” he said. “Kids were being seen in the lab and in the clinic, but nobody was systematically collecting data about how they talked to their parents or their peers outside the clinic.”

They started swapping videotapes of their treatments, and soon discovered that “even though we had different theoretical underpinnings, the actual therapies being delivered were highly similar,” said Camarata, now at Vanderbilt University. A 1992 meeting to discuss those similarities led to NIDCD funding to compare “language-typical” and “language-late” children. That research produced “two nice surprises.”

First, when children were taught using highly focused, socially and emotionally appropriate conversation instead of imitation and modeling techniques, “those with substantial language delays were able to make considerable gains that did meet the gold standard,” Nelson explained. “They were talking outside the treatment setting to other people with a newly advanced level of language.”

The second surprise was that, when 6-year-olds who were talking like 3-year-olds were compared to normal 3-year-olds under the same learning conditions, the SLI-affected children were able to learn as rapidly as the 3-year-olds.

Nelson’s Language Intervention Clinic at Penn State is built upon those surprises. It uses a technique he calls “recasting” to extend children’s vocabularies and grammatical structuring. It’s what many parents do: a child says, “Big dog,” and the clinician (or parent) says, “Yes, that big dog is jumping.”

“It turns out that children like having what they say extended,” Nelson said. “The surprise to many people was that we could put this technique into an experimental format and produce changes in particular structures that children were not using before.”

To verify that the communication improvements are sticking, they videotape children at home and in the playroom. “Parents and teachers are the real translational consumers,” Nelson said. “Generally, they are not going to care about our standardized test scores. They are going to want to see a difference that they recognize.”

Nelson’s clinic is part of the Child Language Intervention Project started in 1997, also with NIDCD funds. It applies the “transactional model” described in the early 1970s by psychologist Arnold Sameroff – that a child’s development is driven by interactions with the parents.

“We wanted to do the translational research,” Camarata said, “applying this cognitive model to children that had speech and language disorders and other kinds of challenges. It’s very powerful. We see it in autism, in mental retardation, in language disorders, in speech intelligibility disorders, and in Down’s Syndrome. When the child initiates communication, it is very effective in terms of the child learning language structures. Those are teachable moments.”

CLIP is now treating nearly 1,000 children from ages two and a half to seven. More than 300 live in the Nashville area and are treated at the clinic, and another 625 come from across the United States and worldwide. Camarata’s team makes a diagnosis, either in person or by viewing videotapes or other records, then recommends a treatment.

“We’re rigorous in our assessment,” Camarata said. “When a child is late talking, there are lots of different things it could be, but it could also be normal variation.” Some children are kept out of treatment for six months to establish a baseline trajectory of their normal progress so researchers can tell how well the treatment works. They even have a placebo in one study, putting a randomly selected group of children in the clinic without instruction.

To “increase our odds of being effective,” CLIP has sought NIDCD funding to test the diagnostic power of event-related potentials, neuroimaging that can tell how rapidly a child processes speech. With ERP, the child sits under a net connected with electrodes and listens to nonsense syllables. ERP picks up brain activity that tells how fast it is processing the differences among sounds. “If the brain is not processing very quickly, that can predict how they will react to a particular intervention,” Camarata said.

They’d like to do something similar with genetics. According to Camarata, certain DNA replications are implicated in autism, but not full-blown autism. If the DNA testing passes the test of a clinical trial and carries over into real-world diagnoses, they will have both genetics and brain-wave imaging to help predict which children will do well under which treatment.

“Right now,” he said, “all we have is clinical experience, impressions, but they aren’t consistent. You might get a great clinician who is very accurate, but then again you may not.”

SLI, which has no known cause, is more common than autism: 7.6 percent of all kindergarten children are affected (compared to less than 1 percent for autism), yet by the end of kindergarten only about 27

percent of these will be identified to receive any special services. Untreated, they'll probably never catch up and problems will persist into adulthood; 40 percent to 75 percent will have difficulty learning to read.

Understanding Autism

Helen Tager-Flusberg, Boston University School of Medicine, has also been using NIDCD funding to investigate how best to diagnose children with speech and cognition problems, but her target condition is autism.

"Because autism is a very variable syndrome, trying to understand some of that variability has been a major effort in recent years," Tager-Flusberg said. "It's not enough to see the children, evaluate them and say they have autism. You have to go beyond that to see what particular features they may or may not have, because that's going to influence their ability to learn things."

In recent work she and her colleagues found that autistic indicators are not limited to linguistic deficits-some children have normal linguistic skills but significant social impairment, such as restricted interests, repetitive behaviors and poor communication skills. The core cognitive problem in autism is "theory of mind impairment," Tager-Flusberg said. Many autistic children are unable to interpret others' mental states. The benchmark test for that is to determine whether the child understands that another person can hold a false belief.

But until age four, even normal preschoolers tend to fail such theory-of-mind tasks. In a study with normally developed preschoolers, Tager-Flusberg demonstrated that "if you train these preschoolers on grammatical constructions, like 'John said Mary was sleeping,' they'd be able to pass theory-of-mind tasks."

Autistic kids who can do the task seem to do it via language, not because they intuitively understand that people have mental states. To Tager-Flusberg, this suggests a possible way of training children with autism: "If we taught them this construction in language," she explains, "they would not only acquire the language piece, they also would also do better on theory-of-mind tasks."

She is considering a collaboration with a software company to develop the training program. "I have spent 25 years doing research in autism, and to my shame I have never gone that final step to translational research. In my mind, and to most psychologists working in the field, we think that's our job-to identify the deficits and the problems. Then it's up to educators and clinicians and other therapists to take our work and develop it into treatments. But it will not happen unless I get involved at that level."

Standing between Tager-Flusberg and this lofty goal are the same obstacles faced by Nelson, Camarata, and other inspired translational researchers. To evaluate different behavioral or psycho-educational treatments objectively is "extremely expensive and very hard to do," Tager-Flusberg said. "That's just a fact of life."

But Nelson, who faces the same financial demon, said "finding collaborators and funding isn't as bad as it once was. There's a lot of work yet to be done, but we have an excellent base now that wasn't in place 15 or 20 years ago."