A Burst of Speed for Neurological Research

NEURONEXT STREAMLINES RESEARCH PROCESSES TO ENCOURAGE COLLABORATION AND MAKE RAPID ADVANCES

Through a cooperative venture between the National Institute of Neurological Disorders and Stroke (NINDS) and 27 research institutions nationwide, a new clinical trials network has been established. The goal of the Network for Excellence in Neuroscience Clinical Trials (NeuroNEXT) encourages collaboration among academia, industry, and foundations while accelerating drug development for neurological disorders.

“It has been observed that current research processes are not as streamlined as they could be,” says Petra Kaufmann, MD, MSc, Director of the Office of Clinical Research at NINDS and an early proponent of the concept. “For even small trials, the infrastructure had to be built, people had to enter into multiple subcontracts, and each center had its own Institutional Review Board (IRB). We thought it would be great if some of these efforts, as well as the time and money spent on them, could be redirected toward scientific and clinical uses.”

Centralized IRBs
To address these issues, NINDS assembled representatives from 27 research institutions. The result was establishment of an overall Clinical Coordination Center (CCC) at Massachusetts General Hospital in Boston. The CCC then entered into multiyear, multi-study master contracts for research services with other sites. The Boston hospital is also responsible for a centralized IRB to cover all of the network’s studies.

“Having the individual sites cede IRB responsibility to the CCC makes that step much shorter,” says Elizabeth McNeil, MD, Scientific Program Director for NeuroNEXT in the NINDS office. “In addition, since all of the other sites have already subcontracted with the CCC, trying to get contracts approved by 25 different institutions for each study is no longer necessary. This takes away two of the most time-consuming parts of getting trials ready to go.”

McNeil notes that getting IRB approval for their first study on spinal muscular atrophy (SMA) biomarkers (see sidebar) took just 51 days. This is in contrast to the literature indicating an average time of six to nine months. She noted that the SMA study is being conducted in infants and uses an investigational device, making rapid IRB approval even more impressive.

In order to similarly streamline the statistical and data-gathering aspects of a study, a centralized Data Coordinating Center (DCC) was established at the University of Iowa in Iowa City.

In addition to these two coordinating centers, each site has its own lead investigator and coordinator funded through NIDNS grants.

Diversity in Participants
The NeuroNEXT network also opens opportunities for important studies to be undertaken by more diverse sets of investigators. Younger researchers, the private sector, and even disease-specific advocacy groups are invited to submit proposals.

“Previously to get a grant, you had to be a well-established trialist,” says Merit Cudkowicz, MD, Chief of Neurology at Massachusetts General Hospital and principal investigator for the NeuroNEXT Clinical Coordination Center. “That was a barrier to many who had good ideas but not the skills to design trials. The network provides this kind of expertise to help people with their ideas.”

This means junior researchers get experience in running trials earlier than possible otherwise. The result could be increases in the number of people qualified to do trials for neurologic disorders and effectively elongating these researchers’ productive careers by starting them earlier. It also means that the best ideas for therapies can be brought forward faster.

SMA Biomarkers First Study
Stephen J. Kolb, MD, PhD, Associate Professor of Neurology at The Ohio State Univer-
The Protocol Principle Investigator running NeuroNEXT’s SMA infant biomarker study. “The existence of the CCC and the DCC has been very helpful to me as a first-time investigator,” he says. “I have benefited from the expertise embedded in the Network during the entire process and don’t think that I would be in this position for a couple more years without it.”

Private Sector Partnering
Another goal is to coordinate research efforts with the private sector through public–private partnerships. This makes available all of the expertise in NeuroNEXT while the private partners provide trial funding and novel therapeutics to be tested. The streamlining brought about by NeuroNEXT may change the risk/reward ratio and make research into neurological disorders more feasible.

“NINDS would also like to see more applications from advocacy groups,” says McNeil. “NeuroNEXT gives small patient groups an avenue to try and get a trial done using sites that are very experienced and well distributed geographically around the United States.”

Phase II Focus
Currently, NeuroNEXT plans to focus mostly on finding biomarkers for various diseases and on phase II treatment trials, because phase III trials tend to be large, expensive, require many patients, and have a very long time span.

“We realized early that we couldn’t possibly answer all of the important questions in later phase studies given current funding and other considerations,” notes Kaufmann. “We shifted to phase II trials because they can help us prioritize the projects that we can take into later phase trials. Finding viable biomarkers may allow us to shave years off of a phase III trial by seeing changes in markers before clinical changes become noticeable.”

Those interested in NeuroNEXT can get background information and access to the submission forms by going to www.neuronext.org. There are tabs for researchers and industry, outlining what is needed for consideration.

“I am very excited about how far we have gone so far,” said Kaufmann. “NeuroNEXT provides such a great opportunity for early phase neurology trials and I hope that leads to advances more quickly.”

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NeuroNEXT SMA Biomarkers Study

The first project undertaken by the NeuroNEXT group is a trial looking for biomarkers to spinal muscular atrophy (SMA) in infants. It is currently enrolling infants newborn to six months old that have SMA, as well as a cohort of healthy controls.

“Animal models for the most severe form of SMA indicate that there may be a short window of opportunity to effectively treat an infant and hopefully help cure the disease,” says Stephen J. Kolb, MD, PhD, Assistant Professor of Neurology at The Ohio State University/Wexner Medical Center in Columbus and NeuroNEXT’s Protocol Principal Investigator for the study. “What we want to do is identify the critical things to measure during a treatment clinical trial in infants that will help us make efficient decisions about efficacy in the future. One of the novel aspects of our study is that nobody has looked at large numbers of infants in this population in a well-controlled way.”

Infant motor function tests studied and associated with potential physiologic biomarkers include electrical impedance myography and compound muscle action potential. At the molecular level, they are evaluating tests for messenger RNA, protein levels of the SMN gene, and various serum protein levels.

“This is not as glamorous as a treatment study,” says Kolb. “What we hope to do, however, is give future interventional researchers the tools they need to quickly and confidently evaluate possible therapy candidates. This study could tell those of us planning future trials which tests are useful, and provide solid baseline data that may be useful in studies involving infants with other diseases.”

Kolb says the biggest positives in his experience are NeuroNEXT’s Central Coordinating Center and the Data Coordination Center. The former saves time and money by consolidating Internal Review Board and contracting functions. The latter provides a centralized data acquisition and analysis center and robust biostatistical support, addressing a weakness of some clinicians.

“The SMA Infant Biomarker Study would not be possible without the clinical study infrastructure and large network of excellent academic neurology departments distributed across the country that NeuroNEXT provides,” he says, “I highly recommend the network to investigators with phase II and biomarker projects targeting neurological disease in academia and industry.”

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