

## Parent Neurodevelopmental Prescreening Questionnaire (NPQ)

*Primary Investigator: Glen P. Aylward, Ph.D., ABPP*

*Funding Agencies: National Institutes of Health Small Business Initiative Research; National Institutes of Child Health & Human Development*

Low birth weight has been shown to predict major disabilities (mental retardation, cerebral palsy, epilepsy, vision/hearing impairment) and low severity dysfunctions (learning disabilities, low IQ, Attention Deficit Hyperactivity Disorder, neuropsychological dysfunctions, behavioral problems). Early detection of problems enables earlier intervention to improve outcomes.

This project involves the longitudinal follow-up of at-risk babies at 6, 12, and 24 months corrected age (chronological age minus weeks of prematurity), and at 36 months in the SIU/St. John's Hospital Developmental Continuity Clinic, aimed at testing a Neurodevelopmental Prescreening Questionnaire (NPQ).

The Bayley Infant Neurodevelopmental Screener (BINS; Aylward, 1995) is a national screening test administered at the first three evaluation sessions, and an IQ test is used at 3 years. Parent-completed prescreening questionnaires identify children in need of a more focused evaluation such as the BINS. Dr. Aylward and his team have studied prescreening at six ages: 3-4, 5-6, 7-10, 11-15, 16-20, and 21-24 months to see if such a technique may be applicable to infants at increased risk for neurodevelopmental problems.

In this study, caretakers are first shown a brief video of a child of comparable age to their own baby completing various BINS tasks. Caretakers then rank how their infant would perform the same tasks. Finally, an examiner administers the BINS. Based on data from 1,400 infants, Dr. Aylward has found an average 75 percent agreement in high risk/low risk status between the NPQ and the BINS. He is investigating which items are problematic and what background variables affect agreement.

Dr. Aylward hopes to implement the NPQ as a prescreener in general

practice. Then, the BINS can be administered to high-risk children. These questionnaires also indirectly teach parents what types of developmental activities are reasonable for their child's age.



## Recombinant human lactoferrin and necrotizing enterocolitis

*Primary Investigator: Michael Sherman, M.D.*

*Funding Agency: National Institutes of Health*

Necrotizing enterocolitis is the most common and serious gastrointestinal disorder among hospitalized preterm infants. Each year in the United States, one to three prematurely-born infants per 1000 births develop this intestinal infection, and 2,600 infants in the United States annually die from the disease.

Studies show that preterm infants who receive their mother's milk rather than formula have a five-fold lower incidence of necrotizing enterocolitis. Human milk contains a major protein called lactoferrin, which has intestinal growth-promoting and natural antibiotic properties. Unfortunately, mothers cannot produce sufficient milk to feed their premature infants shortly after birth. Preterm infants also cannot drink their mother's milk for days to weeks after birth.

This valuable human milk protein can be produced by biotechnology. In pre-clinical studies, newborns fed human lactoferrin were subsequently protected from intestinal infections caused by *Escherichia coli*. *Escherichia coli* is a frequent cause of serious infection in newborns. Children and adults also develop food poisoning and other infections caused by *Escherichia coli*.

Dr. Sherman is planning a clinical trial where premature infants will be nourished with lactoferrin from the day of birth. Pre-clinical studies suggest early nutrition with this protein will reduce necrotizing enterocolitis and its devastating effects in premature infants who cannot take human milk.

## Facilitated recovery from traumatic brain injury: Z-bisdehydrodoisynolic acid

*Primary Investigator: Richard Clough, Ph.D.*

*Funding Agency: SIU Central Research Committee*

Traumatic Brain Injury (TBI) is a frequent, devastating and both clinically and socially expensive phenomenon in humans. Experimental models of TBI show prolonged deficits in motor performance, including balance and dexterity, as well as deficits in memory acquisition tasks.

The ovarian steroid estradiol has been shown to be neuroprotective in brain injury and ischemia models but appears have negative side effects. Estrogenic-like compounds are being studied as alternatives to acute estrogen therapy for brain injury.

Dr. Clough's team is exploring a non-steroidal compound, Z-bis-dehydrodoisynolic acid [(±)-Z-BDDA], that has potent estrogenic and antioxidant effects, ameliorates metabolic syndrome and obesity and is cardioprotective. His preliminary studies suggest that (±)-Z-BDDA also enhances recovery of behavioral function following experimental TBI.

Initial results suggest that three-day treatment with (±)-Z-BDDA after TBI improves beam walk, water-maze performance, foot fault score on an open grid and pellet retrieval in a forelimb-reaching paradigm in male and/or female rats. Present experiments are aimed at finding the optimal dose, isoform and therapeutic schedule that affords the best recovery from acute brain injury.

This project will determine whether specific enantiomers (plus or minus isoforms) are more, less, or equally effective as (±)-Z-BDDA in TBI function recovery.

Dr. Clough also will address the time lag between TBI injury and treatment, studying the temporal window of effectiveness of the compound on recovery of cognitive and motor behaviors. A third aim is to study TBI's neuropathology profile as it relates to (±)-Z-BDDA enhanced recovery of function.

Follow-up studies will look at mechanisms of action of (±)-Z-BDDA in "neuroprotection" associated with functional recovery from TBI.