Preterm progress

Dr Anne Gallagher provides an insight into the novel neuroimaging techniques that her research programme is developing to better serve the needs of babies born prematurely.

Could you outline your overarching research interests?

I currently direct the Laboratory of Optical Imaging in Neurodevelopment (Laboratoire d’Imagerie Optique en Neurodevelopment – LION’s Lab) within the University of Montreal’s Psychology Department and the Sainte-Justine University Hospital Research Center. Imaging the brains of healthy and epileptic infants and children constitutes a significant part of my research programme.

Additionally, a few years ago I began investigating the cerebral development of premature babies. Our research programme on preterm birth aims to identify cerebral markers predictive of neurodevelopmental outcomes. Identification of such predictive markers is crucial in premature children since cognitive and behavioural sequelae are often highlighted when the child starts school, when greater demands are placed on cognitive and psychosocial skills. Late diagnosis and interventions can lead to repeated setbacks in their education, which can have a dramatic impact on psychosocial development. We believe that identification of predictive markers during the pre-school period would enable the provision of earlier interventions, improving neurodevelopmental outcomes.

How have you seen perinatal care develop over recent years, and to what extent has this shaped your work?

For the past several years, tremendous medical progress has been made in the perinatal care of preterm infants. This has significantly raised the survival rate. However, probably due to the paramount importance of the final gestational weeks on brain development, the incidence of sensory deficits (eg visual impairments) and neurodevelopmental disorders (eg. attention deficits with/without hyperactivity disorder (ADHD), learning disabilities, communication deficits) remains unchanged. This growing population of children with special needs drive us to study the sensory and cognitive development of children born prematurely in order to identify early markers of behavioural and cognitive impairments. We hope this will lead to the creation of adapted intervention strategies to improve neurodevelopmental and schooling outcomes.

What is the relationship between visual processing and cognitive development deficits?

We believe that impairments in visual processing may lead to cognitive deficits and learning disabilities such as dyslexia at school age. Our results so far have confirmed that preterm infants show developmental delays in visual processing as early as three months of age, which then persist throughout childhood. In a first set of electroencephalography (EEG) studies, we aimed to characterize early visual processing development in preterm children. Now, we have to better study the relationship between early visual impairments and neuropsychological outcomes.

Could you describe your work on the development of predictive markers for neurodevelopmental deficits?

In addition to early visual processing, we are investigating other predictive markers of neurodevelopmental outcome. One of my PhD students, Natacha Paquette, recently obtained some very interesting results in this area, using electroencephalography (EEG) to identify abnormal auditory and attention processing of verbal stimulation in three-, 12- and 36-month-old preterm infants. She demonstrated that altered neuronal responses in three-month-olds are associated with lower cognitive and language functioning at 36 months, and so might be used as predictive markers for neurodevelopmental impairments. Her EEG paradigm could thus be employed to early identify children at high risk of presenting neuropsychological impairments, such as expressive language problems or attention deficit disorder. We continue following these children who are now almost 10 years old. We are interested in their neuropsychological profile, social abilities and school functioning, and we keep studying their brain development.

In what way do you envision your work will contribute to the care of children born prematurely throughout the rest of their lives?

In the near future, we hope that identification of early predictive markers will have direct impacts on the clinical management of children born prematurely. Specific and early interventions should be developed and eventually offered to those who will be identified at high risk for cognitive and language delay as well as learning disabilities. Indeed, a long-term goal of our research programme is to develop earlier specialised interventions for these children. In collaboration with a multidisciplinary team, we plan to launch a research project to assess the impact on cognition and brain development of an early intervention programme in pre-school children born prematurely who have been identified to be at high-risk of developing cognitive and language delay. Based on my clinical experience as a paediatric neuropsychologist, I believe that implementation of such early strategies can have a major impact on the neurodevelopmental outcome. Later, it should benefit these kids for school functioning, socialisation and quality of life during childhood, adolescence and even adulthood.
In the Sainte-Justine University Hospital Research Center, Canada, a dynamic team of scientists are using their imaging expertise to devise ways to identify indicators of future difficulties in preterm children at the earliest opportunity.

**PRETERM BIRTHS** – those that occur before 37 weeks of gestation – are a common occurrence; in fact, the Centers for Disease Control and Prevention (CDC) calculate that one in every eight infants in the US is born prematurely. At present, the neurodevelopmental trajectory of those that have been born in recent years in the field of perinatal medicine, infants born prematurely more likely to survive than ever before. However, preterm survival does not necessarily equate to preterm health and, despite medical advances, preterm birth remains a leading cause of long-term morbidity worldwide. Studies have consistently shown that infants born prematurely are more likely to be affected by a host of sensory, cognitive and behavioural impairments.

Although some difficulties can be diagnosed early in infancy, many cognitive and behavioural deficits are not recognised until several years later, often when the child is beginning school and when the opportunity for effective early interventions has already passed. It is for this reason that researchers are now searching for early markers predictive of these disabilities, as a means to better screen and help this growing population of prematurely born children. One such scientist is Dr Anne Gallagher.

**THE LION’S LAB**

Gallagher is the Director of the Laboratory of Optical Imaging in Neurodevelopment (Laboratoire d’Imagerie Optique en Neurodéveloppement) – better known as the ‘LION’s lab’ – within the Sainte-Justine University Hospital Research Center in Canada. She is also Assistant Research Professor of Psychology at the University of Montreal. “I have been fascinated by brain research and paediatric neuropsychology ever since my first year as an undergraduate student, when I was introduced to the topic of brain development during a neuroscience class,” Gallagher recalls. She pursued this interest throughout her PhD and postdoctoral training at the University of Montreal and Harvard Medical School, studying healthy brain maturation and paediatric epilepsy before extending her research interests to include neurological development in preterm infants and children.

During her career, Gallagher has used an ever-growing array of child-friendly neuroimaging techniques to assist her investigations, including near-infrared spectroscopy (NIRS), electroencephalography (EEG), magnetoencephalography (MEG) and magnetic resonance imaging (MRI). Along with co-workers, Gallagher hopes to utilise the team’s wealth of experience in paediatric neuroimaging to identify predictive markers for a variety of cognitive and behavioural disorders commonly diagnosed in preterm children once they reach school-age.

To date, the team has made considerable use of evoked potentials – electrical potential records of the nervous system’s response to specific stimuli, which can be obtained using EEG. “Compared to the 19 electrodes typically used for clinical EEG recording, we use at least 128 electrodes. This allows us to perform sophisticated analyses on electrical brain signals,” Gallagher enthuses. “By comparing evoked potentials in preterm and healthy infants and children, we can look for abnormal or delayed brain development associated with prematurity.” There is therefore the possibility that evoked potentials could be used for the identification of early biomarkers of learning disabilities or neurodevelopmental disorders.

The researchers do not rely on evoked potentials alone, however, as Gallagher explains: “Evoked potentials are very good at giving specific information on the timing of the brain response, but they are not very accurate at localising it”. For this reason, Gallagher and her collaborators employ cutting-edge multimodal neuroimaging – the simultaneous utilisation of evoked potentials and near-infrared spectroscopy (NIRS) – in order to obtain both temporal and spatial data.

**THE FUTURE IN THEIR EYES**

As visual impairments in infancy constitute the major sensory sequelae of prematurity, the group has invested considerable time looking at the usefulness of early visual impairments as predictive markers for later cognitive or behavioural disorders or difficulties. The investigators found that developmental delays in visual cerebral pathways in premature infants – that can be identified as early as three-months-old persist and can still be detected as late as seven- or eight-years-old. At school-age, these children also show higher prevalence of attention deficits with/without hyperactivity disorder (ADHD) and learning disabilities than fullterms. These findings add to the body of evidence suggesting that abnormal visual system development in preterm children may be associated with cognitive and learning disabilities later on. Additional research is now required, however, to further delineate the exact neurological relationship between visual brain system development and cognitive deficits and/or learning disabilities.

**PAYING ATTENTION TO ATTENTION**

More recently, the team has turned its attention to establishing how early deficits in attention and language development could be used as predictive markers for later problems, such as language disorders or ADHD. Using EEG, the group has identified abnormal auditory and attention processing development by measuring neurological responses to verbal stimulation in both preterm and fullterm children at the ages of 3-, 12- and 36-months of age. The scientists also confirmed that infants with lower birth weight and younger gestational age are associated with greater visual and cognitive delays.

A number of significant discoveries have been made as a result of this research programme,

![Figure 1](image.png)

Figure 1. The left-panel picture shows a three-month old baby wearing a 128-electode EEG cap. On the right panel, EPs result from visual cortical areas during a visual stimulation comparing fullterm (blue) and preterm (red). Significant differences between both groups (shown by *) reveal brain developmental alterations in the premature brain. Although preterm infants overcome the visual developmental delay over the first year after birth, source analyses (bottom) performed at 12 months of age show different brain activations between the groups, suggesting brain reorganisation in babies born prematurely.
There is the possibility that evoked potentials could be used for the identification of early biomarkers of learning disabilities or neurodevelopmental disorders.