Imaging seasonal neuroplasticity in Antwerp, Belgium

When Brain and Behaviour "Picture" Together

The plasticity of the brain allows for structural changes that suit individual behaviour and lifestyle. Using MR imaging, Annemie's group has recently discovered that the brain of a songbird gets geared up for the breeding season in more ways than just one. Is there something more to their images?

The clichéd expression "men are from Mars and women from Venus" stems from the notion that behavioural differences exist between the two sexes; while men have an eye for quantity, numbers and logic and are better at performing one task at a time, women think in terms of quality and utility and have an edge over the other gender in efficiently handling multiple tasks all at once. I do not wish to spur a hornet's nest here with a gender debate but I wish to turn your focus to the very many behavioural differences that exist between individuals within any species. Recent research, actuated by the use of powerful imaging techniques has elucidated that such differences in the characteristics of individuals, not limited by gender, in fact, relate to subtle variations in the structural intricacies of the brain. In an interesting study in London, taxi drivers were found to have large hippocampi, the centre for spatial learning, as they sat for hours on end, driving long distances and the size of their hippocampus did actually correlate with the length of their career (*PNAS* vol. 97: 4398-4403)!

Stars of the starling research family (Annemie Van Der Linden 3rd from right)

Gaining a foothold with MRI

On the one hand, the brain orchestrates behaviour and on the other, it is in turn, influenced by behaviour, social status and the immediate environment of an individual. This "interactive process" thus establishes an interdependence of the brain structure and the behaviour of an organism. The 'neuroplasticity' of the brain has acquired great attention with the development of smart imaging tools such as magnetic resonance imaging (MRI) including blood-oxygen level dependent functional MRI (BOLD fMRI) and diffusion tensor imaging (DTI), among others.

Annemie Van der Linden and her Bio-imaging lab at the University of Antwerp, Belgium have been pursuing an exciting study on behaviour-modulated structural changes in the rodent, avian and fish brain with their imaging expertise, for over two decades. Their recent 'Eureka' moment revealed a striking correlation between the ultra-structural features of the auditory forebrain of the songbird (*Sturnus vulgaris*) and its socio-sexual behaviour with the on-coming breeding season.

With their Bio-imaging lab centred on MRI, Annemie and her colleagues have been addressing major questions in neuroplasticity as well as investigating various aspects of neurodegeneration and regeneration, among others in rodents, birds and fish, all of which have a size appropriate for imaging. As a non-invasive *in vivo* technique, MRI has come in handy for their study of structural changes in the brain. "In contrast to conventional histological and electrophysiological methods, MRI does not limit analyses to some sections or regions of the brain, instead it allows for a comprehensive research of the entire brain," elucidates Annemie as she introduces the 'asset' of her lab.

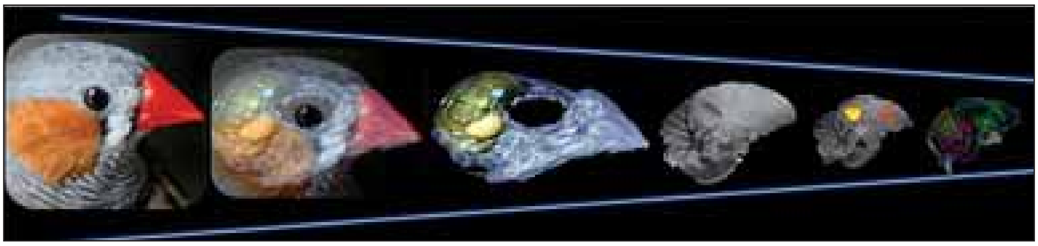
Choice of species is critical

In imaging structural changes in the brain, be it reversible, arising from seasonal changes or irreversible, associated with progression of disease in pathological conditions, MRI out-performs *in vitro* approaches. The latter have the major shortcoming that they produce data collected from several individuals and do not account for inter-animal variations. With MRI, it is possible to perform longitudinal imaging in the *same* subject in order to study periodical changes in the brain structure or to trace back to older images of the healthy animal during the prognosis of a disease. The lab also performs DTI to obtain data on the directionality of water-diffusion movements, which are characteristic of the local 'micro-architecture' of the brain.

"The only limitation with imaging," Annemie prompts, "is that the information you get is a correlate of a set of several features or events in the brain." The molecular mechanism underlying a particular observation is only implied and not lucid. "A change in DTI, for example, could mean anything like axonal loss or demyelination and this speculation requires validation using other approaches," she completes.

Even within the optimum size range of animals of up to 8 cm diameter for sharp imaging, Annemie's group resorts to a variety of species for their experiments. Annemie believes in comparative neuroscience and ascertains that the choice of species is crucial and one must pick the best model to address every specific scientific question. "For example, the rodent brain is a good model for stroke, while the fish brain can cope with anoxia and hypoxia and is well-suited for studies on the response of the brain to changes in oxygen levels. Likewise, the songbird brain serves as a classic model for extreme structural plasticity," she elaborates.

The interdependence of brain and behaviour is best elucidated in the songbird brain. The changes in the structural characteristics of the latter are intertwined with seasonal changes when the bird behaviour is modified and the readout of this behavioural change is that the bird starts to sing. With the onset of the breeding season (spring), neuronal plasticity of the songbird brain becomes more conspicuous. It is then that the song becomes highly sexually-motivated and this change in singing behaviour is exactly encoded by structural changes in the brain, particularly within the song control system (SCS).



Seasonal secrets of a songbird – The neurobiology behind chirping

The latest breakthrough

In a recent study, the Bio-imaging group has identified, for the first time, structural changes in the auditory forebrain of the songbird that complement bird behaviour and seasonal changes. Annemie agrees that bird imaging is challenging though undoubtedly rewarding. Firstly, one is faced with the problem of massive artefacts on the images that arise from air cavities in the skull. Another drawback with birds is the unfavourable surface-volume ratio that is prone to quick body-heat dissipation during imaging. Thirdly, controlling respiration by ventilation of birds could be highly invasive. However, with years of experience in imaging, Annemie and colleagues have their own way out of these difficulties and use additional tools such as DTI and contrast imaging to derive their theories on the plasticity of the bird brain.

In their paper late last year (*J. Neurosci.* vol. 29:13557-65), the Bio-imaging group published a profound characterisation of the structural changes in the songbird brain at the onset of the breeding season. To start off, they obtained a series of brain images of a flock of songbirds in spring (breeding season) and of the same set of birds in summer (non-breeding season). They then arrived at an average spring brain and an average summer brain image, super-imposed the images, chose a number of regions of interest (ROIs) within and outside the SCS and evaluated the differences. They observed an overall decrease in the volume of the telencephalon from spring to summer and, to their surprise, they found statistically significant differences in regions not belonging to the SCS. After careful re-consideration of their images, they made the groundbreaking conclusion that it is, in fact, the secondary auditory region, the caudomedial nidopallium (NCM) and a few other regions of the social behaviour network (SBN) that exhibited a significant seasonal change.

Correlation of imaging and chemistry

This result was the first of its kind since it identified a DTI parameter that correlated with seasonal differences in exactly those regions of the SBN which have been reported to have a high aromatase activity in homologues. Aromatase activity has been shown to peak in the breeding season in canaries and induce neuronal branching and nuclear enlargement, thereby influencing diffusion characteristics of water in these tissues. Thus, the group could show that the DTI parameter actually reported seasonal changes in aromatase activity, a cellular attribute, in the SBN. Their work opens new portals to the application of imaging tools in speculating, with greater precision, cellular properties. It also sheds light on the involvement of multiple senses in the songbird's singing behaviour across seasons.

Manifold implications

Annemie and colleagues are now convinced that neuronal plasticity in the songbird is not exclusive to the SCS and it is essential that further research takes a broadened view on the plasticity of the brain. A study of the seasonal impact on cognition in birds in terms of song learning, song discrimination and recognition memory is on their to-do list. While all this is part of the bird team's agenda, the lab also has a rodent team that will continue to focus on neurodegeneration, to develop early diagnostic readouts using their favourite imaging instrument. With the possibility of relating to cellular attributes with MRI, as the group just discovered, their work now holds major implications in gaining valuable medical insights.

As a full professor of Biology, Annemie has adopted an interdisciplinary approach to address her scientific questions and her team has expertise not only in Biology but also in Physics and Engineering. Their research is supported by the University of Antwerp, European grants and by the National Research Foundation (FWO), Belgium.

The one thing that amuses Annemie and keeps her strongly inclined to Science is "how nature uses evolution to solve problems an organism is confronted with". And as organisms evolve, there's all the more reason to take on comparative research.

Madhuvanthi Kannan