Could you begin by providing an insight into the impetus that led to the creation of the Laboratory of Nutrition and Integrative Neurobiology (NutriNeuro)?

SL & VP: We were both conducting research separately in Bordeaux initially, but soon our groups were collaborating thanks to our common interest in neuroscience and nutrition and the ability to combine the two disciplines. It was easy to understand each other and to bring new ideas into this interesting area of research. We therefore decided to build a structure composed of people with knowledge in nutrition and brain function, as we believed it was the right time to develop such an area of research in France. The elongation of life expectancy and the development of the agri-food industry – which arise as a result of the economic development of societies, sociocultural evolution and progress in the field of health – have promoted the emergence of nutritional problems completely distinct from those that existed in France less than half a century ago. These changes have been coeval with the rise of a number of cognitive and neuropsychiatric disorders. The development of research into human nutrition is therefore fundamental to establishing new scientific data essential to improving our understanding of the relationship between diet and brain health in modern society.

What is your academic background?

SL: My scientific background is in psychoneuroimmunology. In 2003, I joined the National Institute for Agronomic Research (INRA) at the University of Bordeaux to develop a research programme on the effect of lipids on brain function and wellbeing. I built a research team around my goals of understanding the influence of obesity on mood disorders, focusing on the role on neuroinflammatory pathways, and elucidating the effect of n-3 polyunsaturated fatty acids (PUFAs) on neuroinflammation and synaptic plasticity.

VP: My scientific background is quite different and lies in biochemistry and nutrition. The work I have done since my PhD, first as an Assistant Professor then as a Professor at the University of Bordeaux, has concerned the action of vitamin A and the interaction of its signalling with hormones and other nutrients. In the last decade, my team has demonstrated that vitamin A contributes to neurobiological processes that underlie memory performance via its active metabolite retinoic acid. This is of particular significance in ageing, as over time vitamin A metabolism decreases and the production of retinoic acid in the brain is altered, contributing to memory decline. In 2011, we demonstrated in a clinical study that dietary vitamin A supplements can prevent these trends. I have been expanding my research programme since I joined NutriNeuro.

How do you ensure that NutriNeuro research has translational impact?

SL & VP: This is a priority in our laboratory so, when it is relevant, we develop clinical components to our research. This ensures that we have the expertise needed to achieve this endeavour. Some researchers in the lab are specialists in nutrition, capable of carrying out a nutritional evaluation or characterising the nutritional status of subjects; other researchers are neuropsychologists, competent in addressing the evaluation of mood disorders or human cognition. Furthermore, to ensure the logistics of clinical studies, subject recruitment and medical follow-up, we collaborate with several structures, including the Clinical Investigation Centre of the University Hospital of Bordeaux, clinical services (such as services dealing with bariatric surgery) and a contract research organisation specialising in nutrition.

With a large, diverse staff, are there difficulties fostering a fruitful, collaborative working environment?

SL & VP: Actually, the diverse competencies brought to the project by neurobiologists and nutritionists working together in concert eradicate most difficulties. Furthermore, by developing specific teaching in this new area of research (both through our master’s degree in Bordeaux and the International NutriBrain Summer School), we have safeguarded our ability to attract promising students to the lab. The main difficulty that we face is securing funding – but this is the same everywhere!
ACCORDING TO THE World Health Organization (WHO), depression affects more than 350 million people globally each year. This figure is on the rise, and by 2030 WHO predicts that depression will be the leading cause of mortality and morbidity out of all health conditions. Despite this, healthcare professionals still lack efficient pharmacological therapeutics for the disease, patients are often resistant to treatments and full remission is rare. An alternative approach might therefore be to prevent the condition from occurring in the first place – but unfortunately the causes of depression are not entirely clear and are likely to consist of a mixture of genetic and environmental factors. However, the scientific community has noted that the rising incidence of depression has coincided with a shift in diet and lifestyle and, as the condition is also linked with obesity, scientists are increasingly interested in the link between food and mental health.

The Laboratory of Nutrition and Integrative Neurobiology (NutriNeuro) in Bordeaux, France, is dedicated to investigating this connection between nutrition, brain function, mood and the development of cognitive disorders. Based at Bordeaux Segalen University, NutriNeuro was established as a collaboration between the National Institute of Agronomy Research (INRA), Bordeaux University and Bordeaux Polytechnic Institute in 2011. The lab addresses a complex subject and is comprised of two research teams staffed by 54 scientists with diverse academic backgrounds. However, the research conducted under the NutriNeuro banner is united by one general hypothesis: imbalances in lipid nutrition disrupt mood and cognition, and play a role in the pathophysiological progression of mood disorders and cognitive deficit.

PROBLEMATIC PUFAs

One of the most important changes to general lipid nutrition in developed countries is the replacement of n-3 polyunsaturated fatty acids (PUFAs) with saturated fats and n-6 PUFAs, and omega-3 with omega-6. In a typical Western diet, the ratio of n-6 to n-3 PUFAs is 20:1 – a far cry from the optimal ratio of 1:4 – and this imbalance has already been associated with an increased risk of depression by NutriNeuro scientists; an association that has been supported by research conducted in other labs. On a cellular level, however, the mechanisms of this interaction are still not well understood, and this is why Dr Sophie Layé, NutriNeuro Director and Principal Investigator of its Psychoneuroimmunology and Nutrition group, has been working alongside her collaborators to investigate them.

The NutriNeuro researchers believe that examining neuroinflammation is the key to understanding the cellular impacts of PUFAs. Dietary PUFAs are able to modify synaptic activity in the neuronal circuits involved in emotional behaviour and high cognitive function, including those of the prefrontal cortex, hippocampus and nucleus accumbens. Neuroinflammatory pathways in the brain could enable these effects, while also explaining the close link between depression and obesity (a condition characterised by low-level chronic inflammation). It is possible that both of these effects are found together because imbalance in dietary PUFAs leads to increased inflammation and also denies the brain the nourishment it needs.

MOODFOOD

Layé’s team has already demonstrated that dietary PUFA imbalance decreases brain n-3 PUFA levels, leading to the impairment of certain receptors and resulting in the same prefrontal cortex plasticity associated with behavioural despair. This discovery supports the idea that nutrition can control behaviour by modifying specific neuromodulator systems and their associated synaptic functions. Based on this concept, the NutriNeuro researchers’ current work is focused on determining whether an n-3 PUFA unbalanced diet impairs synaptic circuits linked to depression vulnerability, and the work they produce to this effect will be shared through the recently established MoodFood project consortium.
FOOD AND MEMORY

In a second branch of study coordinated by Professor Véronique Pallet, NutriNeuro’s Associate Director, scientists are also investigating the potential effects of diet on memory. The first project (NutriMemo) started in 2010. It aims to test the efficacy of a cocktail of lipid vitamins and omega-3 on memory loss in the elderly. The lab’s second project was launched in 2011 as part of the international Neurophenols initiative, which brings together French and Canadian researchers with industrial partners to address age-related cognitive decline. In a number of papers, NutriNeuro scientists have implicated neuronal plasticity impairment and neuroinflammation in memory loss and even neurodegenerative disorders such as Alzheimer’s disease; in collaboration with the Neurophenols consortium, the NutriMemo group is now pushing that work even further.

Nutrophens’s first role within the consortium was to conduct a preclinical trial of a polyphenols dietary supplement designed to preserve memory of mice. Having completed this process, the French researchers will now conduct half of a bi-central clinical trial, the other half being undertaken by researchers in Quebec, Canada at Laval University.

In this trial, the Neurophenols dietary supplement will be given to a population of patients aged between 60 and 70 years over a one-year period. During this time, they will take a number of memory tests. “The design stages of the study, the approval by the ethical committees and the formulation and manufacture of clinical batches have already been carried out,” Pallet reveals. “Furthermore, we already have more than one quarter of our participants signed up.”

FUTURE INNOVATION

The research programme being undertaken by NutriNeuro has expanded consistently and rapidly since the unit’s formation less than five years ago. Making use of state-of-the-art molecular, optical, biological and behavioural methods, as well as a diverse team with a vast skillset and an enhanced capacity for translational work in rodent and human populations, the future looks promising for NutriNeuro, and for the field of nutritional neurology in general – a ray of hope for individuals suffering from mental disorders.

SOPHIE LAYÉ is the founding Director of NutriNeuro, a research institute devoted to studying the influence of nutrition on brain functions, based at Bordeaux University, France. She received her PhD in Neurobiology from Bordeaux University in 1995. After being a postdoctoral recipient of the European community at Stockholm University, Sweden, for two years, Layé became Associate Professor at Bordeaux University, before moving to INRA to develop research on lipid nutrition, brain and mood and cognitive disorders.

VÉRONIQUE PALLET is Associate Director of NutriNeuro and Professor of Nutrition at the Bordeaux Polytechnic Institute. She received her PhD in Biochemistry from Bordeaux University, France, in 1990. She then obtained a position of Assistant Professor at Bordeaux University and began to research the role of vitamin A in the adult brain. She was the co-founding Director of NutriNeuro.