Ageing answers

Professors Osborne Almeida, Barbara Demeneix, Nuno Sousa and Joseph Zihl jointly discuss their research on facilitating healthy ageing, particularly in relation to mental health

Can you introduce your respective areas of academic expertise?

**BD:** I am a molecular comparative endocrinologist interested in evolution and development. My work focuses on brain growth and function, and metabolism and energy balance.

**NS:** I am a neuroradiologist who studies how stress alters neural networks, in particular those that mediate memory and decision-making processes. I am also interested in the physiological determinants of cognition.

**JZ:** I am a neuropsychologist, especially interested in cerebral visual disorders and brain plasticity. I also work on the idea that cognitive reserve may help preserve cognitive functions during ageing.

**OA:** I study how stress and metabolism might initiate age-related mood and neurodegenerative disorders. This work reflects my core interest in how extrinsic factors interact with the genetic blueprint to programme brain function.

How did you come to collaborate?

The basis for our collaboration is shared visions, goals and complementary approaches, built on many years of partnership and a mutual confidence that allows free exchange and joint exploration of ideas. We began working together with institutional and binational grants. Now, thanks to European Union [EU] funding for the Switchbox Project, which also includes partners from Hungary and the Netherlands, we have been able to consolidate and scale up our work over the past four years.

What is the primary objective of the Switchbox Project?

While recognising the need to alleviate suffering, our research aims to delay or prevent age-related deterioration of mental health. In addition to our curiosity regarding the fascinating biological phenomenon of ageing, we have a moral, social and economic responsibility to work towards ‘adding quality to the added years of life’ [to borrow a slogan from the theme of an earlier EU Framework Programme].

How is Switchbox contributing to that? By trying to identify factors and mechanisms that determine healthy ageing of the brain. Our approach is different from other research projects on brain ageing in that we examine reciprocity in brain, hormonal and metabolic signalling.

Could you outline the Switchbox methodology, and describe the outputs you expect from this research?

The rationale underpinning Switchbox research is that mental and physical health are interdependent. Longitudinal studies in humans are extraordinarily expensive and depend on the goodwill of volunteers. Switchbox overcomes these limitations by using carefully designed and controlled studies on women and men from differing age brackets, stratified according to familial longevity or level of education and/or cognitive reserve. Datasets derived from measures of cognitive performance, brain structure, and hormone and metabolic parameters for each participant are then subjected to mathematical analysis and modelling to identify correlates and predictors of healthy brain ageing.

There is also an animal-based arm to Switchbox research that is longitudinal in nature. It focuses on the programming effects of nutritional and stressful experiences, from early life through to old age, on physical health, sleep, mood and cognitive functions. In addition, we study mice with metabolic and endocrine features that appear to contribute to their capacity for healthy ageing.

Taken together, our results should inform on how modifiable factors in the external environment and lifestyle determine an individual’s mental health trajectory. We are confident that we will be able to eventually apply this newly generated knowledge to improve brain health, and therefore quality of life, across age groups.

Which approaches have the greatest potential for better understanding the ageing brain and improving quality of life of older people?

Consolidating clinical and basic science expertise, skills and tools is of critical importance – to this end, Switchbox studies humans and rodents, pooling the expertise of geriatricians, endocrine physiologists, behavioural scientists, neurologists, psychiatrists, neuroimagers, sleep researchers, neuropsychologists and biomathematicians.
Staying healthy in mind and body

The Switchbox Project unites the skills and expertise of a diverse group of researchers from across Europe to answer fundamental questions about how best to ensure healthy ageing.

THE WORLD’S POPULATION is getting older: the World Health Organization (WHO) predicts that people over 60 will comprise 22 per cent of the global population by 2050. This demographic shift introduces many challenges – foremost among them, the promotion of the health and wellbeing of society’s older citizens.

Cognitive decline during ageing seems inevitable; it is estimated that it currently affects 25-30 per cent of people aged 85 or over. Cognitive decline can impact physical and mental health and the capacity for independent living, and adds a significant burden on health systems and caregivers. Therefore, research aimed at preventing and alleviating age-related deterioration of mental health is essential. Indeed, improved understanding of this subject will help guarantee the wellbeing of generations to come.

COLLABORATION ACROSS THE CONTINENT

Funded under the European Union (EU) Seventh Framework Programme, the Switchbox Project brings together researchers from six institutions across Europe. This multidisciplinary endeavour includes expertise that ranges from medicine and physiology to neuropsychology and biomathematics. The project channels a diverse set of approaches towards one common goal: increasing understanding of the factors and mechanisms that contribute to the decline of mental health as people age. In particular, Switchbox researchers are interested in elucidating how hormones that regulate the response to stress and metabolic challenges influence brain ageing.

Switchbox aims to fill this knowledge gap by conducting longitudinal experiments involving both humans and animals. For the former, the researchers are gathering datasets that will help elucidate the interdependence of brain structure, mood and cognitive performance on the one hand, and brain function and physiological responses on the other. The project studies ageing humans stratified according to education, physical health and socioeconomic status. In this way, it expects to identify correlates and predictors of healthy ageing of the brain. Complementary studies in rodents focus on the programming effects of nutrition and stress on physical health, sleep and cognitive functions throughout the life course, as well as metabolic and endocrine profiles that correlate with healthy physical and mental ageing. Together, these efforts should provide clues about how an individual’s mental health span can be extended and overall quality of life maintained.

FUNDAMENTAL QUESTIONS

A large part of Switchbox’s research is dedicated to improving understanding of the neurological and psychiatric challenges associated with ageing. In one set of studies, Switchbox scientists have demonstrated the importance of cognitive reserve as a predictor of healthy brain ageing. “Cognitive reserve can be understood as a buffer against the functional consequences of the ageing brain – it can be activated to cope with the everyday challenges of life, including during older age,” explains Professor Joseph Zihl, a Switchbox researcher and Professor Emeritus of Neuropsychology at Munich University, Germany. “Good memory performance and high cognitive flexibility, as well as varying complex mental activities and positive mood, are key contributors to high cognitive reserve.”

Other members of the Switchbox consortium are working to delineate the different genetic, socioeconomic and lifestyle variables that allow some people to age more healthily than others. Recent Switchbox research suggests that education increases the brain’s ability to age well, and has shown that enhancing brain plasticity by exercising cognitive and social
**SWITCHBOX**

**OBJECTIVES**
- To identify neurostructural, physiological and metabolic correlates and predictors of healthy brain ageing
- To develop strategies to improve the quality of life during ageing, with special emphasis on mood and cognition

**KEY COLLABORATORS**
- Dr Vincent Laudet, Institut de Génomique Fonctionnelle, France
- Dr Akihiko Takashima, National Center for Geriatrics and Gerontology, Japan
- Dr Rysard Przewlocki, Institute of Pharmacology, Polish Academy of Sciences

**PARTNERS**
- Institute of Experimental Medicine, Hungarian Academy of Sciences
- Leiden University Medical Center, Netherlands

**FUNDING**
- EU Seventh Framework Programme (FP7)

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**PROFESSOR OSBORNE ALMEIDA**
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**BARBARA DEMENEIX** is Professor of Physiology and Endocrinology at the CNRS/Natural History Museum in Paris, France. Her work focuses on the evolution of thyroid hormone action, in particular metamorphosis and brain development, as well as neural stem cells.

**PROFESSOR NUNO SOUSA** is a neuroradiologist and currently Dean of Medical Studies and Coordinator of Neuroscience Research at the Institute of Life & Health Sciences at the University of Minho, Portugal.

**PROFESSOR JOSEPH ZIHL** recently retired as Chair of Neuropsychology at Munich University, but continues to research the identification of factors contributing to individual differences in mental performance during ageing.

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**OBJEKTIVES**

**SWITZERBOX**

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**The health, social and economic benefits of research aimed at preventing and alleviating age-related deterioration of mental health cannot be overestimated.**