PANDORA'S BOX

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Living in harmony with our gut bacteria

Symbiosis, the positive coexistence of diverse organisms in the same body, is a common phenomenon in the world of plants and animals. In recent years, we finally caught up with the existence of this relationship in humans and started examining the value, or lack of, of the presence and quality of our gut microbe population, referred to as the gut microbiome or microbiota. Although still a controversial area of research, the link between gut fauna and brain health continues to attract increasing interest.

A recent study provided population-scale evidence for a gut microbiome link with mental health. Surveying a large microbiome population cohort ($n = 1054$), the Flemish Gut Flora Project, with validation in independent data-sets ($n = 1070$), researchers studied how microbiome features correlate with host quality of life and depression. They found that butyrate-producing *Faecalibacterium* and *Coprococcus* bacteria were associated with higher quality of life indicators. By contrast, the depletion of *Coprococcus* and *Dialister* bacteria was associated with depression, and this association persisted when correcting for the effects of antidepressant drugs.

In order to study further the gut microbiota–brain interaction, the authors developed a module-based analytical framework, which describes the microbial pathways that metabolise molecules with the potential to interact with the human nervous system. In a review of the literature, they annotated 56 gut–brain modules, each of which corresponded to production or metabolism of a single neuroactive compound. They were able to show that several microbiome pathways, including γ-aminobutyric acid and tryptophan metabolism, are enriched in human gut-associated microorganisms, which indicates a potential role in host–microbe symbiosis.

Valles-Colomer M., Falony G., Darzi Y., *et al* (2019) The neuroactive potential of the human gut microbiota in quality of life and depression. *Nature Microbiology*, 4, 623–632.

Sleeping ourselves to brain health

We spend one-third of our life asleep, and sleep disturbances are associated with changes in cognitive performance and mental disorders. Sleep is part of life for all organisms, even those with a very primitive nervous system, and is not an atavistic evolutionary function; sleep deprivation can be lethal. The cellular basis for the role of sleep has until now been a mystery.

A recent study has shed some light on the importance of sleep in keeping our brains healthy. The brain's DNA is damaged by various noxious agents, including oxidative stress, but also by its own neuronal activity during wakefulness. For this reason, there exist DNA repair systems in each cell to manage this damage.

This study was carried out in living zebrafish, as they are highly and literally transparent and have a brain very similar to that of humans! These properties make them a perfect subject in which to access and examine a single cell under physiological living conditions. The researchers used three-dimensional time-lapse imaging to define sleep at single-chromosome resolution in the zebrafish. They observed that during wakefulness chromosome dynamics are low and DNA accumulates, reaching unsafe levels. By contrast, sleep increases the activity of chromosomes, altering their structure and hence reducing DNA double-strand breaks.

The conclusion is that sleep protects our brains!

Zada D., Bronshtein I., Lerer-Goldshtein T., *et al* (2019) Sleep increases chromosome dynamics to enable reduction of accumulating DNA damage in single neurons. *Nature Communications*, **10**(1), 895.

What accelerates brain ageing?

Thanks to modern lifestyles and medical advances, we are able to live longer lives and hopefully slow down the process of ageing in our bodies and brains. However, people with chronic, enduring psychiatric disorders such as schizophrenia and bipolar disorder have higher levels of physical morbidity and shortened lifespan. Are their brains similarly affected?

In the largest ever collaborative study of brain imaging, researchers sought to identify the main factors involved in premature brain ageing. They studied brain scans of more than 30 000 people aged from 9 months to 105 years seen in various psychiatric clinics using single photon emission computed tomography. They evaluated 62 454 brain scans examining cerebral blood flow in 128 brain regions to predict chronological age. Accelerated brain ageing was considered to be present when the age predicted by the scan was older than the actual chronological age.

Some psychiatric conditions were found to be particularly associated with accelerated brain ageing. The main culprits were (in descending order of magnitude of effect) schizophrenia, cannabis misuse, bipolar disorder, attention-deficit hyperactivity disorder and alcohol misuse. It is of note that depression was not found to have an effect.

The authors will take this work further with the aim of examining how healthy patterns of cerebral blood flow are affected by psychiatric conditions.

Amen D. G., Egan S., Meysami S., *et al* (2018) Patterns of regional cerebral blood flow as a function of age throughout the lifespan. *Journal of Alzheimer's Disease*, **65**(4), 1087–1092. doi:10.3233/JAD-180598.

Of women and men

Women are still striving for parity with men in all spheres of life. However, Mother Nature has given us some advantages, one of them being that women retain their cognitive ability for longer than men, whose brains tend to shrink faster.

Understanding gender-related factors in brain ageing and brain metabolism may help us to understand and hopefully prevent vulnerability to neurodegenerative disorders. Brain development and brain maturation use glucose via the process of aerobic glycolysis. Day-to-day brain activities use the rest of the glucose supplies for fuel. Over the years, the glucose fraction used for aerobic glycolysis decreases and levels off by the time we get to our 60s.

In a recent study, researchers carried out positron emission tomography scans measuring oxygen and glucose utilisation in the brains of 121 women and 84 men, aged from 20 to 82 years. They determined the fraction of glucose used for aerobic glycolysis in various parts of the brain as a measure of brain metabolism. Using a machine-learning algorithm, they determined the relationship between age and brain metabolism and compared their findings between men and women.

Women's brain appeared 3 years younger than those of their male counterparts, and this difference was present regardless of age, including in younger subjects (in their 20s). The researchers aim to carry out further studies to examine whether women's younger brains can explain why they experience less cognitive decline than men.

Goyal M. S., Blazey T. M., Su Y., *et al* (2019) Persistent metabolic youth in the aging female brain. *Proceedings of the National Academy of Sciences*, **116**, 3251–3255.

'Extremism means extremism'

Extremists with violent behaviour towards the 'other' exist in various forms. Western extremists attack Muslim minorities or others who disagree with them, and Muslim extremists carry out terrorist activities against the West or others. Both groups claim the moral right to do so.

In a series of studies, social psychologists demonstrated that perceived inter-group threat is a common driving force in the psychology of out-group hostility. They studied a total of 705 Muslims and 522 non-Muslim Westerners in three groups and seven cultural contexts: non-Muslim Westerners, Muslims in Western societies and Muslims in the Middle East.

They found that the more individuals in each group felt that the other group was a threat to their culture, traditions, norms, values and way of life, the higher their hostility. This attitude was the same in all subjects, irrespective of whether they were Westerners or Muslims, living in the West or the Middle East.

Symbolic and realistic threats had the same effects. A meta-analysis of all the studies showed that symbolic threat was most strongly associated with inter-group hostility, and that individuals with high religious group identification experienced higher levels of threat.

These findings go some way towards explaining such extremist inter-group hostility, but the issues surrounding violent inter-group actions are far more complex.

Obaidi M., Kunst J. R., Kteily N. S., *et al* (2018) Living under threat: mutual threat perception drives anti-Muslim and anti-Western hostility in the age of terrorism. *European Journal of Social Psychology*, **49**, 670–670.

To act or not to act?

Being treated unfairly causes anger and a wish to take revenge. Some of us act on our anger and punish the culprit, and some don't. Are these differences in our actions reflected in our brain activity and, if so, what are the areas involved?

Researchers in Geneva, Switzerland, examined the relationship between feelings of anger and revenge and brain activity. They devised an economic inequality game aimed at triggering a sense of injustice and anger and offering the possibility of revenge. Twenty-five subjects were recruited to play with two other players, who were pre-programmed (the participants were unaware of this). One of the players was friendly, offering the participant financial interactions and sending nice messages, while the other player made sure to multiply only his own profits, going against the participant's interests and sending annoying messages.

All subjects underwent magnetic resonance imaging (MRI) of the brain throughout the three phases of the test to identify the areas activated in the process of playing the economic game.

In phase 1, the participant was in control and able to choose which profits he shared with the other two, and it was observed that in general participants were fair with the other players.

In phase 2, the participant was in the passive position of receiving the decisions of the other two players, one of whom was acting in a provocative and unfair way; the participant was asked to rate his anger in response to this, on a scale from 0 to 10. During this phase, MRI activity was observed in the superior temporal lobe and the amygdala (the latter is generally associated with feelings of fear); the higher the level of anger as rated by the subject, the stronger the activity in these areas.

In phase 3, the participant was back in control and was given the choice to penalise the other two players. Most of the participants remained nice to the fair player but took revenge on the unfair player. However, 11 of them also remained fair to the unfair player. This allowed the researchers to look at differences in brain activity between those who took revenge and those who did not. They found that that the greater the activity in the dorsolateral prefrontal cortex (DLPFC) during the provocation phase, the less the participants punished the unfair player. By contrast, lower activity in the DLPFC was associated with more pronounced revenge on the unfair player.

The DLPFC is the executive power of our brains, the area that regulates our actions in response to our emotions. The more our DLPFC is engaged, the more control we can exert on our actions, at least according to this paradigm.

Klimecki O. M., Sander D. & Vuilleumier P. (2018) Distinct brain areas involved in anger versus punishment during social interactions. *Scientific Reports*, **8**, 10556. doi:10.1038/s41598-018-28863-3.