KINESIS

magazine

ISSUE 11

CONTENTS

BRILLIANT BIOTECHNOLOGY

BIOLOGY AND SOCIETY

BRAIN AND BEHAVIOUR

ECOLOGY AND OUR CHANGING CLIMATE

A LETTER FROM THE EDITOR

As the first term of this year draws to a close, we are excited to present you Kinesis Magazine's 11th issue! The last few months have been busy ones for the society to say the least, with the magazine obtaining record numbers of sign-ups for articles and our blog publishing a plethora of web articles to go alongside.

For this issue, the committee and myself sought to create a holistic reading experience, with article topics ranging from camouflaging cephalopods to the creation of synthetic embryos; there is even a psychoanalysis of the DC supervillain, The Joker! While Kinesis is a magazine rooted in the life sciences, for this issue, we truly have extended our tendrils to the depths of what this category entails.

Kinesis Magazine's purpose is to provide engaging, informative, and accessible science communication. With the rise of social media and the consequent increase in questionable news sources on a variety of topics that affect our world today, the need for direct and engaging forms of science communication have become paramount. This is why being a part of a society like Kinesis, with the opportunity for propelling forward these ideals, is a position I do not take lightly.

This time last year, I was a first-year at UCL who had just joined Kinesis, ready to contribute in whatever way I could, and the path I went down was incredibly fulfilling to say the least. Returning as Managing Editor this year, I definitely felt the pressure to live up to the high standards set by my predecessor, the person who encouraged me to even apply for this position. Now that the issue is complete, I can say that I am wholeheartedly proud of the finished product, the outcome of hours spent communicating with our contributors, maintaining spreadsheets, and managing deadlines!

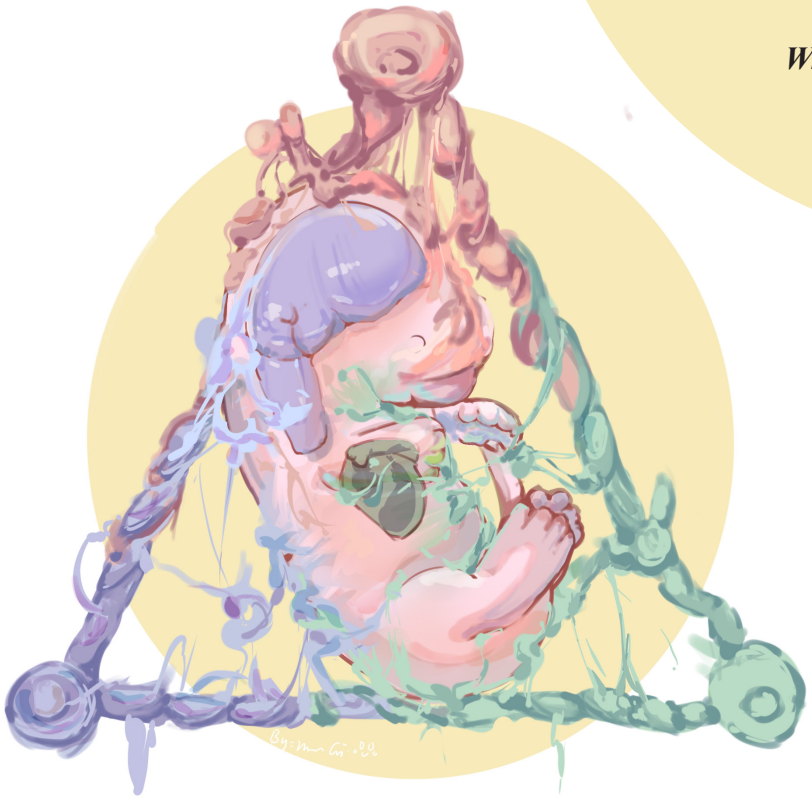
I just want to say a huge thank you to the committee for their tireless work putting this issue together, and also to all our writers, artists and editors!

Nirvan Marathe
Managing Editor

Is it possible to create 'synthetic' embryos with a functioning brain and heart by combining different stem cells?

Cambridge University researchers have generated model embryos from mouse stem cells that form a brain, a beating heart, and the foundations of all the other organs of the body: a new path for replicating the initial stages of life.

Written by Sara Maria Majernikova
Art by Sylvia Tsai



Amadei et al. have built an embryo model without using eggs nor sperm, relying instead on stem cells, which are master cells of the body that can differentiate into virtually any other cell type. In the laboratory, Zernicka-Goetz and colleagues emulated natural processes by taking three types of stem cells widespread in early mammalian development and coaxing them to interact. By stimulating the production of a specific set of genes and providing a unique environment for their interactions, the researchers were able to cause these stem cells to 'speak' to one another.

The stem cells self-organised into structures, which progressed through the developmental stages until they created beating hearts and brain foundations, as well as the rest of the body's components, including the yolk sac from which the embryo receives nutrients during its first few weeks of development. In contrast to other synthetic embryos, the Cambridge-made models produced a whole brain, including the anterior region. This stem cell-derived model has reached a more advanced level of development than any prior model.

According to the researchers, their results, which are the culmination of more than a decade of research that has gradually led to increasingly complex structures resembling embryos, may help them understand why some embryos fail while others develop into healthy pregnancies. Additionally, these discoveries may potentially be applied to the production and repair of synthetic human organs for transplantation.

A healthy human embryo requires a 'conversation' between the tissues that will become the embryo, and the tissues connecting the embryo to the mother. In the first week following fertilisation, three types of stem cells emerge: one will eventually become body tissues, while the other two aid the embryo to expand. One of these extraembryonic stem cell types will grow into the yolk sac, where the embryo develops and obtains nutrients throughout early development; the other will develop into the placenta, which later provides oxygen and nourishment to the foetus.

Numerous pregnancies end when the three types of stem cells begin exchanging mechanical and chemical messages directing the embryo on how to grow properly. This phase is the foundation for everything else that occurs throughout pregnancy: in the event of any complication, the pregnancy will terminate in failure, in other words a miscarriage, even before most women realise they are pregnant. Over the past decade, the Zernicka-group has studied these early moments of pregnancy, notably by investigating into the discussion between the various stem cell types, in order to determine why some pregnancies fail, while others succeed. Because this moment is so mysterious, it is pretty thrilling to be able to observe it in a laboratory, to have access to these particular stem cells, and to learn why so many pregnancies fail—and how we may be able to avoid such failures.

The researchers combined grown stem cells representing each of the three types of tissue in the correct quantities, and the environment needed to promote their development and communication with one another, which resulted in the formation of an embryo via self-assembly. Researchers revealed that extra-embryonic cells communicate with embryonic cells not only chemically, but also mechanically or by touch—thus regulating embryonic development. This is consistent with Zernicka-Goetz's theory, since development of this brain region requires input from extraembryonic tissues. Studies made in 2018 and 2021, in which the researchers used these same component cells to produce embryos at a relatively earlier stage, had already suggested that this exchange was occurring. By extending the development by a single day, the researchers can now confidently assert that their model is the very first to demonstrate the development of the anterior and the entire brain. This ability to fabricate the entire brain, especially the anterior area (which has been a primary goal in the production of synthetic embryos), is a particularly significant advance in the study.

The stem cell embryo model is crucial because it enables us to observe the developing structure at a stage that is normally hidden by the small embryo's implantation into the mother's womb. This accessibility allows us to change different genes in an experimental model in order to better comprehend their developmental roles, opening up new experimental possibilities for the research of neurodevelopmental processes. In fact, they demonstrated this concept in the study by silencing a gene previously believed to be essential for neural tube formation, the precursor to the nervous system, as well as brain and eye development.

Without this gene, synthetic embryos demonstrated the same brain development defects as animals usually found with the corresponding mutation. This suggests that we could apply a similar strategy to the countless genes whose functions in brain development are still unclear. While the current study was conducted on mouse models, the researchers are developing similar human models that have the potential to be directed toward the generation of specific organ types. This would allow them to comprehend the mechanisms underlying critical processes which would be impossible to study in real embryos, since UK law currently permits research on human embryos only up to the fourteenth day of development in the laboratory.

This research is particularly exciting because the knowledge collected may be used to create realistic synthetic human organs, perhaps saving lives that are currently being lost. Indeed, if the Zernicka-Goetz team's project later proves successful with human stem cells, it may be applied to the production of synthetic organs for patients awaiting transplants. Currently, numerous patients throughout the world are on years-long waiting lists for organ transplants. Using the knowledge we now have on mouse organ development, it should be possible to start altering and treating adult organs as well.

Overview/summary

Cambridge University researchers generated model embryos from mouse stem cells that form a brain, a beating heart, and the foundations of all the other organs of the body. They used stem cells instead of eggs or sperm and emulated natural processes by coaxing three types of stem cells to interact. Researchers have developed a stem cell-derived model that resembles an embryo. The model may help explain why some embryos fail to develop while others develop into healthy pregnancies. Three types of stem cells emerge in the first week following fertilisation. One type becomes body tissues, while the other two aid the embryo to expand. Scientists have studied the early moments of pregnancy to determine why some pregnancies fail while others succeed. They have learned how the various types of stem cells exchange mechanical and chemical messages directing the embryo on how to grow properly. The stem cell embryo model is crucial because it allows us to change genes and observe the developing structure. Researchers combined grown stem cells representing each of the three types of tissue to form an embryo via self-assembly. The team has created synthetic embryos that can develop the entire brain, especially the anterior area. This is a significant advance in the study of neurodevelopmental processes, and suggests that we may begin applying this strategy to genes whose functions in brain development are unclear. Researchers are developing mouse models of human organ development to study critical processes that would be impossible to study in real embryos. If the Zernicka-Goetz team proves successful with human stem cells, they may be used to create synthetic human organs, saving lives that are currently being lost.

Treating the Untreatable: Can we edit mtDNA at the base level to cure diseases?

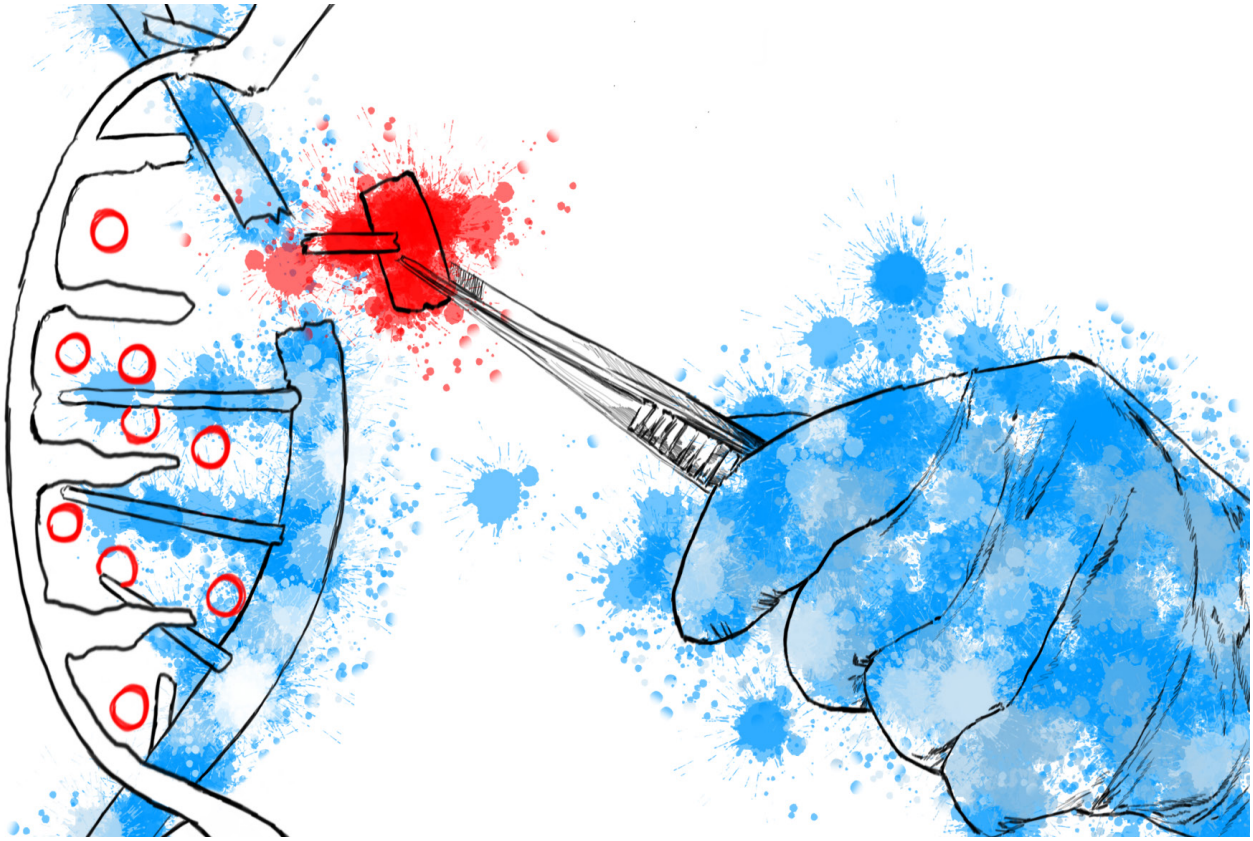
Scientists are now able to edit mtDNA in the hearts of live mice. Could this pave the path for the development of novel therapies to cure mitochondrial diseases?

Written by Ismat Ghuman
Art by Zach Ng

From a young age, we have been repeatedly reminded of the utmost significance a mitochondria houses within a cell, even going so far as to call it the cell's "powerhouse". Each mitochondria is encoded by a minute quantity of mitochondrial DNA (mtDNA) which comprises only 0.1% of the entire human genome and is exclusively transmitted from mother to child. Being the site of vital metabolic processes, necessary for providing energy to the cell, one can only imagine how catastrophic the effects of mutations in mtDNA would be on an individual. mtDNA mutations can impair mitochondrial function, resulting in mitochondrial diseases, affecting approximately 1 in 5,000 individuals and are often fatal. These mutations manifest themselves in the form of organ-specific implications at some point in an individual's life. Despite their detrimental effects, these diseases are considered largely incurable since they lack sufficient research and the available treatments are mostly preventive in nature rather than disease-specific. This was the case until recently, when Silva-Pinheiro and colleagues made an advancement in this field by suggesting a capability to edit mtDNA base pairs in a live animal. They propose using adeno-associated virus (AAV) vectors to deliver a DddA-derived cytosine base editor (DdCBE, which makes a cytosine to thymine base change) into the heart of a mouse. This research lends an insight as to how we might be able to fix mtDNA sequences in humans to treat new symptoms of mitochondrial diseases.

The original issue with manipulating mtDNA arose from difficulties encountered while trying to import nucleic acids into the mitochondria. To counter this, programmable nucleases have been used in the past, but only to a limited extent, since they are incapable of introducing novel mtDNA variants. DdCBE, a cytosine base editor, has been shown to help with C:G to T:A conversions by catalysing cytidine deamination Through the use of adult and neonatal mice's hearts, it was shown that AAV vectors are capable of delivering DdCBE to install mutations in mtDNA that are deemed desirable. This sheds light on the possible use of DdCBE for tissue--specific mtDNA mutagenesis in vivo, in turn opening up a new door to future treatments involving the correction of somatic mitochondrial genes to treat mitochondrial diseases. By "reverse engineering" the genome of mitochondria, this kind of technology could be used to fix mtDNA point mutations and treat the symptoms of primary mitochondrial disease (PMD).

Despite these advantages, the technique could face some shortcomings in-vivo. The process involves the deamination of cytosine to produce uracil (C->U), but in order to do so, mitochondrial base excision repair (BER) would need to be inhibited. Since BER's efficacy in-vivo is not fully understood, further research would be required to establish whether it would have an effect on editing mtDNA with DdCBE. Along with this issue, it is uncertain if the level of mammalian mtDNA replication is high enough to be successfully edited by DdCBEs, although this was the case in neonatal and adult mice, with the latter taking a longer duration. The earlier DdCBE was introduced to neonatal mice, the more efficient the editing. This may be the case because the AAV vector-to-cell ratio was higher when it was given early, which would make it easier for the virus to get into their hearts.



When looking at how DdCBE-mediated editing of mtDNA could be used in future treatments, these issues may make people wonder how effective these therapies would be on adults instead of infants, whose mtDNA replicates at a much higher rate. The scope of this research is also worth taking into consideration since DdCBE is only capable of editing C:G to T:A, and further studies could try incorporating other base editors to manipulate mtDNA in-vivo. Nevertheless, this discovery opens the door to mtDNA editing in a live organism, which could be a potential therapy for treating mitochondrial diseases in humans. DdCBE has been shown to be a tool that can be used to manipulate mtDNA in post-mitotic tissue. It may be capable of changing pathogenic variants back to normal sequences and could potentially help patients recover from mitochondrial diseases completely.

Toggling the epigenetic switches with CRISPR

Written by Kavya Subramanian
Art by Qiwen Liu

***CRISPR** – whether you think it's a bop or flop, you've probably heard of it at some point in the last few years! It could be because you're an absolute academic weapon that read the Nobel-winning 2012 paper published by Jennifer Doudna and Emmanuelle Charpentier; it could be from the Netflix documentaries, the CRISPR patent war, or the designer babies; or it could be from listening to lecturers, or CRISPR enthusiasts like me. The point is that within a decade, CRISPR has become the popular kid on the biotech block.*

'CRISPR' is simply an acronym, since 'Clustered Regularly Interspaced Short Palindromic Repeats' doesn't quite roll off the tongue. In a nutshell, it is a genetic component of some bacteria's antiviral defence, exploited by humans for genetic engineering. To preface the forthcoming subjects, simplifying some key concepts might be useful. DNA is like your aunt's highly confidential and cryptically written soup recipe, while RNA is the working copy of that recipe – decoded and re-written in a way you understand. From this decoded recipe, you prepare the soup which is the protein or the enzyme of interest. However, your aunt's recipe also has directions for her amazing bread to pair with the soup.

The recipe now has two parts or 'domains' – the bread domain and the soup domain. Since you have some bread lying around, you decide not to follow the bread domain. But wouldn't it be amazing if the bread domain could magically disappear and reappear into the recipe as and when you needed it instead of sifting through the recipe every single time? Biology does exactly that through 'gene expression' where selective DNA domains are decoded into RNA to only make necessary proteins, as and when needed.

CRISPR's humble beginnings in genetic engineering was with the discovery of the Cas9 enzyme, which functions as a molecular scissor by binding to the DNA and snipping sections of it. A single stretch of RNA called single guide RNA (sgRNA) guides the Cas9 to scan the genome for regions of sequence complementarity. At these regions, Cas9 generates cuts called double stranded breaks (DSBs), and the cell uses its own DNA repair mechanisms to fix this break, generating a frameshift mutation in the process. The high programmability of the sgRNA to detect almost any genome sequence confers a great advantage to genetic engineering with CRISPR. Simply put, CRISPR-Cas9 is like the backspace key which can erase parts of a cryptically written recipe.

However, this technology is not foolproof. CRISPR can sometimes generate off-target effects – a phenomenon that occurs when the genome is inadvertently cut at an unintended site. When used with Cas9, construction of the sgRNA must be incredibly specific to minimise these off-target effects. Additionally, frameshift mutations can silence genes, but to reactivate them, the reversal or changing of this mutation is far too complex. This limits CRISPR-Cas9 to modifying the DNA sequence and makes it an ineffective tool for modifying gene expression. Given the growing interest in epigenetics – the study of gene expression – and its predominant role in health and disease, the above-mentioned drawbacks majorly limit the therapeutic applications of CRISPR-Cas9. Consequently, members of the biotech community have been focussing on developing a tool for modifying and controlling gene expression, pushing the frontiers of what we now know as epigenome engineering.

CRISPR-based tools with modified or alternative versions of Cas9 are being discovered to overcome CRISPR-Cas9's challenges. In 2021, researchers at the Whitehead Institute-MIT and the University of California, San Francisco jointly published a paper on a CRISPR-based epigenetic editor called CRISPRoff/on. This tool was made by fusing three domains, each coding for a modified dead Cas9 (dCas9), a transcriptional repressor called KRAB and an enzymatic epigenetic modifier.

Transcriptional repressors are enzymes that slow down or stop the decoding of DNA to RNA – like your aunt's newborn who keeps her busy and slows down her decoding the recipe for you. Enzymatic epigenetic modifiers are enzymes that indirectly modify gene expression. CRISPRoff contained an expression silencing methylase domain, and CRISPRon an expression activating demethylase domain. This technology is therefore a highly programmable epigenetic switch as the same tool can both 'switch on' and 'switch off' gene expression based on the epigenetic modifier domain. CRISPRoff/on is among the most exciting breakthroughs in epigenome editing, synergistically combining multiple epigenetic editing approaches from the past to produce heritable, reversible edits in a wide variety of cell types using a technology that is far more efficient and specific than its predecessors.

Increasingly, the therapeutic uses of the CRISPRoff/on system are being explored despite it not allowing for the dialling up or down of the silencing and activation levels. The above-mentioned scientists also discovered that the CRISPRoff/on system significantly, albeit not completely, silenced the tau gene in neurons. Misfolded tau proteins are found in the brain cells of Alzheimer's patients, and the potential for gene silencing of erroneous tau using CRISPRoff could be applied therapeutically. Considering that the team that developed the CRISPRoff/on system comprised two of the co-founders of the U.S. based biotech company Chroma Medicine, it is unsurprising that they are actively further exploring the therapeutic role of epigenome editing. Among various investors in the biotechnology space, Tune Therapeutics has also been keen on exploring epigenome editing technologies. The two companies are now more hopeful than ever in merging epigenome editing with precision medicine.

These biotech companies believe that finding a suitable in vivo delivery mechanism for this technology is crucial in translating its effects therapeutically. Historically, the most commonly used gene delivery vectors (Adeno-Associated Viruses and Lipid Nanoparticles) have been ineffective in delivering CRISPRoff/on due to their own limitations. Active research on overcoming these challenges is directed at bringing an epigenetic angle to precision medicine. With gene therapy and RNA-based vaccines already becoming common therapeutic tools, it won't be long before more researchers and biotechnologists find ways to harness the therapeutic benefits of integrating more genetics into healthcare. But until then, go make yourself some "good soup"!

Turning Back Time: a Technique that Reverses the Age of Skin Cells

Written by Varsha Pramod Rao
Art by Irina Pirvu

As we all undergo the daunting and inevitable process of ageing, we acquire wear and tear on our genomes, associated with gradual decline and the loss of functioning. Ageing is a complex process with several markers that continue to elude our understanding, yet genetics may offer use for predicting an individual's age. Age-related changes consist of measurable epigenetic and transcriptomic alterations which can be exploited to accurately predict the chronological age of cells, offering insight into what natural decline may look like.

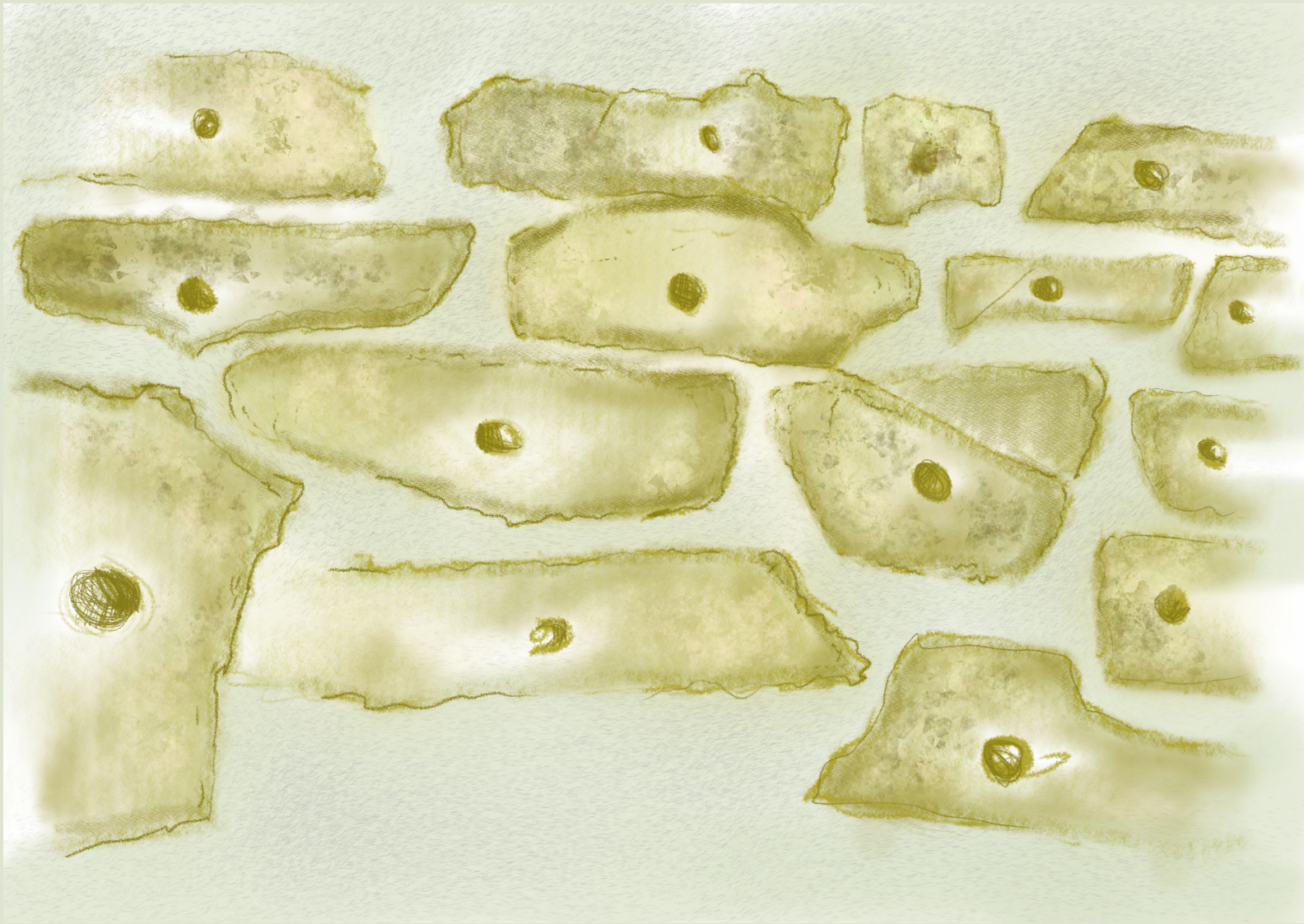
A method of 'de- ageing' cells coined 'maturation phase transient reprogramming' (MTPR) by UK researchers including Dr Diljeet Gill of the Babraham Institute involves reversing the age of fibroblasts, a type of skin cell that provides structure to tissues, by 30 years whilst allowing them to retain their identity. It was administered to fibroblasts of middle-aged donors and the cells of younger donors were used to make comparisons. This method is novel because it is the first time that the age of cells has been reversed by so many years and without the loss of function.

This idea of tampering with the developmental clock is not new by any means. Shinya Yamanaka was awarded the Nobel Prize in 2012 for genetically reprogramming mature skin cells in mice to become the famous induced pluripotent stem cells (iPSCs), which are fundamental in the field of regenerative medicine research. These are cells that have been reprogrammed back to their pluripotent state and that are capable of becoming any type of human cell. This was achieved by manually reversing multiple factors, such as telomere attrition and oxidative stress.

MTPR follows the same principle as induced pluripotent stem cell reprogramming and utilises the four Yamanaka factors- Oct3/4, Sox2, Klf4, c-Myc, which are molecules that are highly expressed in embryonic stem cells. However, the crucial difference is that iPSC reprogramming takes much longer and is characterised by a loss of function. MTPR enables the cell to retain its original characteristics and behave as it originally would.

The key to the preservation of function is to not subject the cells to complete reprogramming. MTPR exposes the cell to Yamanaka factors for just 13 days until the point of rejuvenation. The cells were subsequently removed and grown in normal conditions, upon which the cells regained fibroblast markers. Thus, a fine balance is struck between restoring the cell's youthfulness and allowing them to preserve their specialised cell function.

Whilst the mechanism by which this is achieved is not yet completely understood, it was observed that MTPR had positive effects on the APBA2 gene which is associated with Alzheimer's disease. APBA2 codes for a protein that interacts with the precursor of Alzhemier's disease called amyloid precursor protein (APP) and stabilises it. Further, the reprogrammed cells have been shown to be better at healing wounds as they produce higher levels of collagen, a property that can have many uses in clinical practice.



Even though this method cannot be used clinically at present, it will have widespread applications, especially if it can be replicated in other cell types. It could be used to potentially identify the genes involved in rejuvenation after which gene therapy can be used to target them directly. Several prolific people, including Bill Gates, have expressed their disapproval, claiming it to be an egocentric endeavour to try to prolong lives when there are infectious diseases that are yet to be eliminated from the more developing parts of the world. However, the wider consensus is that this technique must be harnessed for good, to prolong healthy lives and prevent neurodegenerative diseases that occur with age. Research is proceeding full-throttle to investigate therapeutic applications, albeit with caution. How would these partially reprogrammed cells behave in living organisms? Could there be adverse effects upon injecting these cells into the recipient? Could they be cancerous? There is much to be discovered in this arena but the implications of the discovery are enormous and will lay the foundation for many potential valuable discoveries.

Nobody is illegal:

How British tabloids' fear-mongering tactics create a false view of migrants

Written by Kate Hodgson

Art by Moeno Sugiyama

'GPs told: you must treat foreigners'
'Migrants milking Britain's benefits'
'BRITAIN MUST BAN MIGRANTS'

Frequently spotlighted across the front pages of British tabloids, headlines such as these are all too familiar. The consequence is a very frosty attitude towards migrants in the UK from British natives. A study by British Social Attitudes found that 55% of Britons believe that the main reason migrants travel to the UK is to claim benefits, and 47% of Britons believe that migration in the UK has negatively affected the economy. But how many of these negative perceptions can be backed up by scientific evidence?

Many headlines that concentrate on the 'strain' that migrants put on British benefits centre around the National Health Service. In 2014, the Immigration Act was implemented, redefining what it means to be an "ordinary resident" in the UK and restricting the entitlement to healthcare for many migrants. The laws were further escalated in 2015 when non-native patients would have to pay for the services provided by the NHS. Immigrants would be confronted with a 150% surcharge if deemed ineligible. From 2017, migrants wanting to receive treatment from the NHS would have to pay for the service before even receiving it. If the patient is unable to pay the upfront cost, medical care could be withheld unless deemed urgent or immediately necessary.

The effects of these regulations were devastating. A quarter of maternal deaths in the UK from 2015 to 2017 occurred in women born outside of the UK. What is deemed "urgent" or "immediately necessary" creates blurred boundaries, ultimately relying on the individual judgement of the doctor. The doctors involved have taken an oath not to harm any patient - it could be argued that refusing such care would violate the Hippocratic oath. Furthermore, the onset of illness or accidents is unpredictable, which makes preparing for any possible future events impossible and financially draining for migrants.

Migrants make up 14.4% of the UK population yet only contribute to 1.83% of NHS expenditure. Social discrimination against migrants is prolific, yet few laws protect them from hostility relating to their migrant status. This culture of fear prevents migrants from seeking care and maintaining follow-up appointments. Frighteningly, the relative mortality associated with assaults is higher for international migrants in high-income countries. Furthermore, evidence by the UCL-Lancet commission discovered that, in advanced economies such as the UK, each 1% increase of migrants in the adult population increases the GDP per person by up to 2%. These statistics suggest that allowing international migrants to live and work in the UK, along with reaping the benefits of the NHS, could be beneficial for the UK economy.

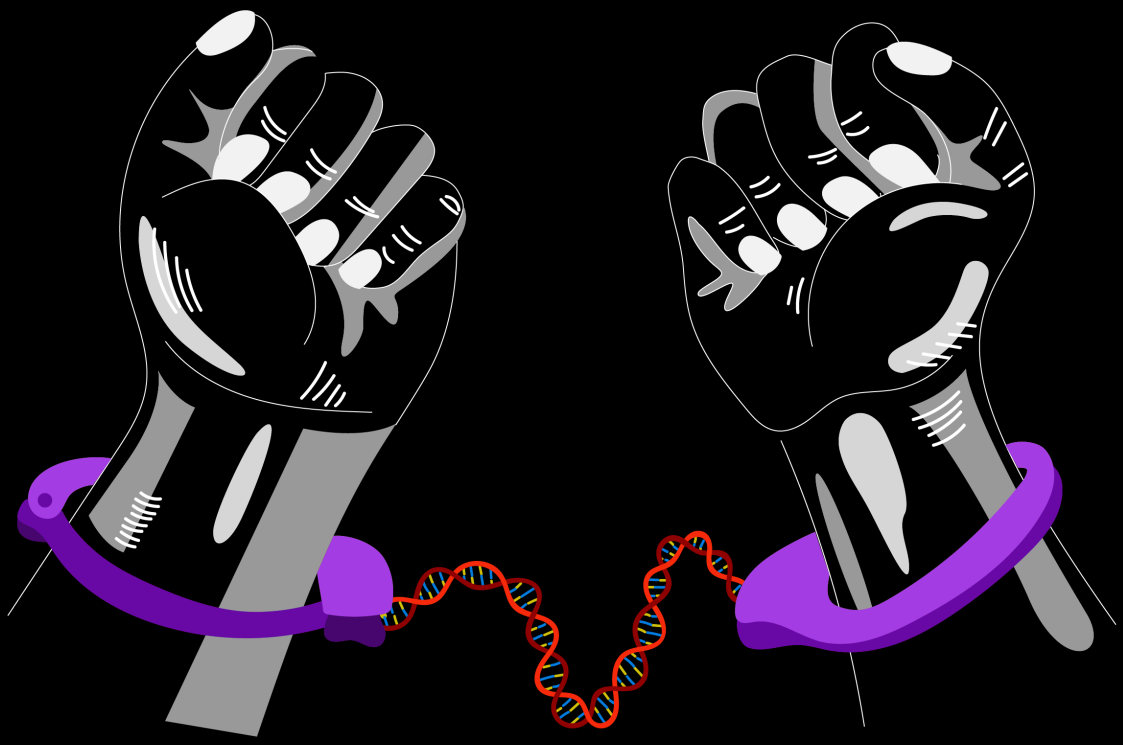
A study by the UCL-Lancet commission released in 2018 exploring the mortality patterns of international migrants suggested that there is a reduced mortality rate among international migrants. Xenophobia-based articles in UK tabloids would like you to believe that migrants are a burden to our healthcare systems. Migrants actually had a lower frequency of death compared with the general populations of high-income countries. It is important to note that this study focused only on international migrants from high-income countries so this study is likely to be representative of international migrants who are studying, working, or have joined family members. Infectious disease relative mortality was higher in migrants for viral hepatitis, tuberculosis, and HIV. The increased rate of deaths from preventable diseases highlights the reluctance of migrants to seek medical care. The mortality advantage could also be attributed to the "salmon bias", a phenomenon in which international migrants return to their country of origin upon the onset of poor health or close to death. This perhaps disputes the claim that the sole reason for migration to the UK is to seek free medical care.

The evidence presented is a direct contradiction to the three negative headlines quoted. It is widely believed that migrants travel to the UK with the sole purpose of claiming benefits yet countess regulations restrict them from accessing healthcare. Although nearly half of Britons believe that immigration has negatively affected the economy, only a tiny proportion of the NHS budget is attributed to migrants, and migrants themselves increase GDP directly just by living and working in the UK. If the government and general population can put their xenophobic biases aside, the outcome would be a wealthier and healthier Britain.

RACIALISED GENES

AND THEIR DANGEROUS APPLICATIONS IN POLICING

DOES THE USE OF GENETICS IN POLICING REALLY MAKE US SAFER?



WRITTEN BY NIRU VARMA
ART BY NIRVAN MARATHE AND RAHEL KISS

Picture a wanted poster for a dangerous criminal. Emblazoned with a picture of their face and a description of the crime committed.

Now imagine that the face on the poster isn't really the face of the suspect at all. Rather, it's a probability-based estimation of what their face might look like according to their DNA.

That describes the image tweeted out by the Edmonton Police Department in Alberta, Canada. They had used DNA phenotyping, a way of deducing an individual's appearance from their DNA to assign this face to the perpetrator of a violent sexual assault.

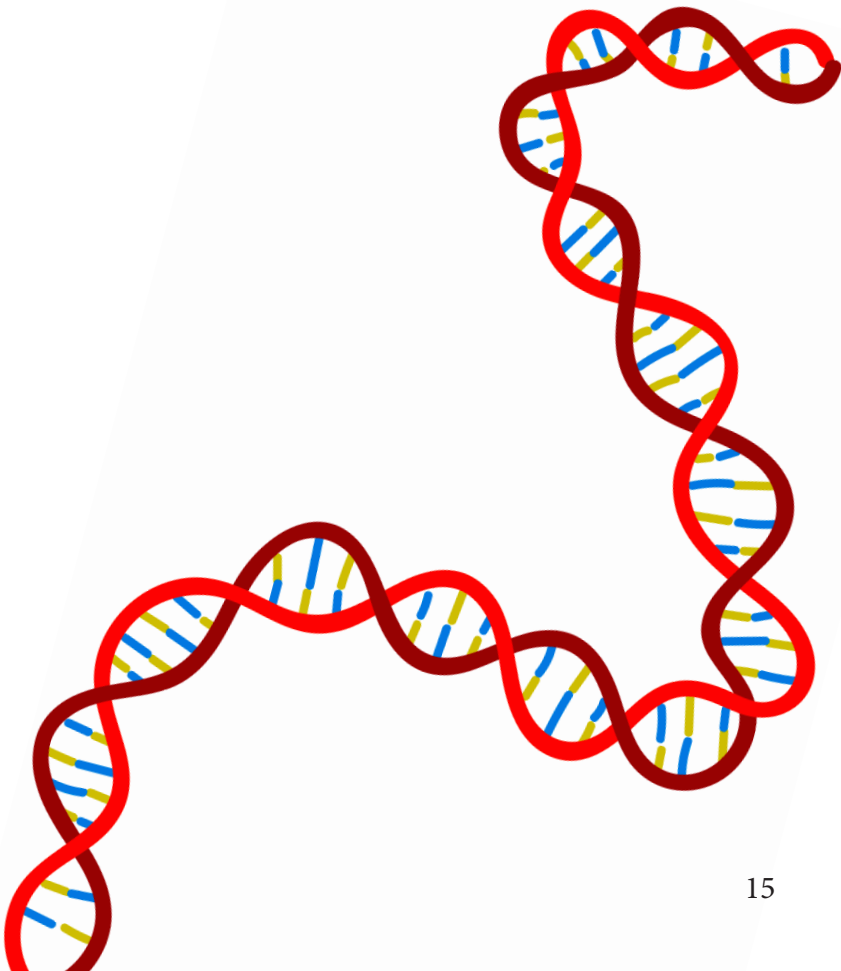
The forensic DNA phenotyping (FDP) apparently determined the suspect to be a Black male (as previously described by the survivor to the police) of East African descent with brown or dark brown skin, brown or black eyes, and black hair. Alongside this information was a portrait, a computer-generated image of a young Black man, claimed to be an approximation of the suspect's appearance based on a DNA sample.

The big issue? There is absolutely no evidence to suggest that DNA phenotyping can be used to predict individual faces. As an extremely complex trait, it is likely that facial morphology is determined by a large number of DNA variants, each with a small effect, making them difficult to identify and therefore mostly unknown. Parabon Nanolabs, the company behind the Snapshot commercial phenotyping service, has never put out peer-reviewed publications validating their methods nor disclosed what markers they use for establishing facial characteristics, casting doubt on whether there is any validity to their methods at all. While their predictions of skin colour, eye colour, hair colour, and biogeographic profile (often simplified as denoting ethnicity) are based on established methods and markers with evidence to support their accuracy, these are simply predictions of a range of phenotypes based on probability as opposed to a definitive description of the suspect. Additionally, unlike a typical facial composite composed from eyewitness testimonies, an FDP image cannot depict distinguishing features like scars, blemishes, facial hair, hair style, or tanning.

All of this means that the image produced is very generic, bearing a possible resemblance to a large number of individuals, whilst not even necessarily representing the suspect with any degree of accuracy. An informal test by the New York Times showed how many individuals misidentified FDP images of their coworkers, with one image having a 0% correct identification rate. This perfectly demonstrates the potential consequences of publishing these images claiming them to be the faces of dangerous criminals. The labelling of the image as an "approximation" does not necessarily prevent scrutiny and even harm towards individuals who may resemble it — after all, the purpose of the image is to incite suspicion towards those who fit the description. If those viewing the image are truly not supposed to treat it as an accurate image of a potentially dangerous criminal, then what is the point of it?

Even outside of the questionable use of FDP to predict faces, its use in determining the race and skin, eye, and hair colours can also be called into question. Some would say that instead of identifying a specific suspect, they instead create a suspect population. This, of course, is nothing new; even before the advent of DNA technology, security cameras and eyewitness accounts could testify that the suspect was, for example, a white man with brown hair — but FDP is unique for being unable to show any other identifying characteristics and instead flattening suspects into just a race and colour profile. In the Edmonton case, the FDP did not reveal any new solid information that could help to catch the suspect given that the survivor had already identified the suspect as a Black male. In a case where even less is known about the suspect, it could be argued that creating a suspect profile by means of FDP results in police treating a whole demographic as potential perpetrators as opposed to helping them to find a singular perpetrator, increasing the risk of harm towards that demographic.

While the Edmonton Police apologised and took down the image as a result of a spike of public backlash, claiming to have only used it as a last resort, they are far from the first police department to use this tool and will likely not be the last. Parabon Nanolabs point to the customer satisfaction from police departments using their service as evidence of its effectiveness. With their appeal to public safety and to the comforting notion of having dangerous criminals taken off the streets, many will side with FDP providers and the police that use their services, believing FDP keeps them safer. This is bolstered by the fact that FDP is (supposedly) based in science and data — this, in the eyes of some, makes it automatically objective and free from human biases and error. A composite sketch may not be accurate because human memory isn't always accurate — the idea of an objective image based on cold hard evidence is an appealing one. Lack of understanding of and misplaced belief in science can, in some cases, be as damaging as denial of it. It's for this reason that those in the field of genetics have a responsibility to ensure that knowledge of this highly socially relevant technology does not remain in the ivory tower and is spread as widely as possible, so that the public and lawmakers can be better informed about genetic technologies like FDP, and their potentially dangerous consequences on society.



The Scientist Complex

The complex relationship between scientists and the public

Written by Obomate Briggs
Art by Qiwen Liu

From as early as I can remember, I knew that to be a scientist was to be held in high esteem. Like many kids deciding what to do with their life, I was 'gently encouraged' to pursue occupations that were advertised as financially stable and that held a certain prestige and power within our society: Lawyer, Doctor, Engineer, Scientist (whatever that means).

For me, the role of the 'scientist' was shrouded in mystique, but I was aware of the characteristics attributed to those who held the position. They were smart. They were important. They were a necessity.

Cut to 2020, and Nature magazine has published an article exposing the anonymous emails containing the harrowing statements 'I hope you die' and 'I would shoot you' received by an epidemiologist.

These emails were received in response to his stance on the anti-parasite drug Ivermectin — controversially promoted as a potential COVID-19 treatment without evidence that it was effective. An extreme, but telling, example of the shift in much of the public perception.

The outbreak and ongoing ramifications of the COVID-19 pandemic have thrust our healthcare and scientific industries into the spotlight and under increased scrutiny. Though we came together as a nation to applaud those working on the frontlines in our NHS, those behind the scenes were not privy to the same reverence, and it begs the question as to why?

In attempting to tackle this question the ideas of perception versus reality play a key role. Within the scientific community, there is an overwhelming sense of being misunderstood by the public and the idea that any negative public attitude is a result of fear or a void in the knowledge of what it is that they do and/or the processes through which science is reviewed and verified.

This is evidenced in a 2015 study carried out by The Royal Society of Chemistry (RSC), in which they investigated what they call 'chemophobia'. What was particularly telling about the RSC's findings is not that the public doesn't understand chemists, but that chemists don't understand the public. The RSC started by asking its members how they felt Chemistry was perceived, and sure enough most expected them and their work to be perceived in a negative light.

But what could be worse than a negative opinion? For some scientists; not having one at all. Everyone has a stake in science, whether that be financially, physically, or otherwise and therefore, everybody has a right to it. But they also have

the autonomy to not engage with it at all. There is a temptation for scientists to categorise those that do not actively engage with technoscientific content as an uninformed group. The RSC study found that rather than a majority of the public holding a negative stance towards science, the consensus was one of neutrality. This alludes to the somewhat egoic nature of scientists in pushing the ancient idea of science and its progression as a 'Universal Light', that has the potential to solve every possible problem.

Perceptions such as these formed the early foundations of the endeavour to relate with, and inform, the public, effectively known as 'Science communication.' Scientific communication has been viewed by many for millennia as a didactic enterprise. Didactics make sense only on the assumption of a knowledge deficit, and democratically this becomes problematic when many science-related public affairs are seen as being aimed at a 'knowledge deficient' public.
STS scholar Corina Cortassa suggests that this idea of a deficit public will always return. The idea is an simplistic coping mechanism when attempting to remedy the gap created between science and society and the asymmetric dynamic that resides between the two.
Epistemic asymmetry is a normative concern in seeking and giving advice, a dialogue that is dependent on trust. 'Trust is a legitimate part of knowledge acquisition,' suggests Philosopher Maya Goldenberg. She offers a view that purposes we have mischaracterised how we come to know things, by failing to take into account the influence of this vital relationship on our understanding. Epistemic Trust is an individual's willingness to consider new knowledge as trustworthy and relevant, and therefore worth integrating into their lives.

The public is instructed to trust, with no eye or involvement in the innermost practices. The mechanisms used to ensure the trustworthiness of scientific information are internal to the scientific community, shielded from public view, therefore requiring a certain 'leap of faith'. But, for communities that have, and continue to, experience medical racism or those that have been spurned by the commercialisation of healthcare, this 'leap of faith' may seem like a large vault, made difficult through the acquiring of social and historical knowledge, which informs their decision-making.

Trust is difficult to bestow when one is susceptible to the effects of the power yielded by another. Scientists are deemed a necessity in our society but with that necessity comes a dependency that can be uncomfortable to be subjected to. The inherent power imbalance of a relationship founded on informational authority and undemocratic (or perhaps one-sided) assertion of values of honesty, transparency and integrity, leaves the public in a vulnerable position - with high stakes and risk potential when such science enters the public sphere.
This power was perceived to be wielded irresponsibly during the COVID-19 pandemic. The politicisation of science was brought to the forefront - particularly evident in the US government, where there was a clear trend between the party one was affiliated with (Democratic or Republican), and the likelihood of adhering to the mask mandate or social distancing guidelines. Science was being weaponised to drive an agenda, so how can we place full trust in scientists when we see them being used as pawns?

The dynamic between the 'public' and the 'scientist' is complex. One that likely does not benefit from the harsh distinctions between the two. It is likely that no matter how well-intentioned or rigorously studied the art of science communication is, people will continue to make meaning out of their own reality.

However, that does not mean efforts should cease, nor are they entirely futile. We are seeing science communication evolve from unilateral dissemination of 'fact' to multidirectional dialogue. Relying on public engagement and participation with science and technology to give representative publics an input on the direction of science, and the ways in which its products are integrated into society (whether they be informational, system or physical product-based). Identifying the interdependence between scientists and the public, and acknowledging their interactions as a relationship, is a start in the right direction towards bridging the gap.

Why are the numbers of full time GPs dwindling?

Written by Altay Shaw
Art by Zach Ng

The Doctors' Association UK (DAUK) wrote an open letter to Health Secretary Therese Coffey on September 20, warning that inaction to support health services and general practitioners will result in a shortfall of up to 8000 GPs within the next ten years. This statistic was somewhat overshadowed within the letter by the DAUK bringing light to the tragic suicide of Dr. Gail Milligan, who had taken her life due to the overwhelming pressures she was placed under.

The tragic passing of Dr. Milligan highlighted a large divide between the profession as a whole and an outdated viewpoint that GPs are seen as "lazy part-timers," despite working long hours to meet the needs of patients across the country, leading to increased burnout and the incidence of mental health disorders. But how has the profession reached this situation in the first place?

What are the challenges being faced?

In 2021, the GP Worklife Survey discovered that 84% of physicians surveyed were working over the scheduled hours, as stated within their contracts with practices. While critics may point out that the majority of those polled work part-time, the hours spent managing, developing, and even teaching students and colleagues are typically substituted. As such, many doctors are being forced to work outside of their contracted hours, causing fatigue within their roles. It should also be noted that this is not an attempt to gain additional hours or salary in most cases. The Royal College of General Practitioners found that the desire to leave the profession for pay or the desire to move abroad was lower than the average for clinical specialties.

In addition, the average GP practice is now caring for 9596 patients, more than 2000 more than at the same time in 2015. With a higher number of GP partners leaving the profession due to the stress of both managing complex patient lists and trying to achieve typically high goals for community care, the number of practices has reduced by nearly 1200 in the same time period. With an ever-increasing population living with a greater number of morbidities and ongoing health concerns, including the Season Flu and COVID-19, GPs are having to treat a higher number of patients with fewer full-time doctors in primary care than ever before. As a result, they have too much work to do because they have to put together referral letters, blood tests, and appointments.

What is currently being offered to GPs?

The Department of Health and Social Care published "Our plan for patients" on September 22nd, reviewing approaches to supporting health care services. Some parts of the press release talked about doctors and making less use of general practitioners (GPs), but it didn't go into enough detail to explain the extra help that would be given to reduce burnout. Rather, it focused on the need to reduce waiting times. No mention was made in regards to supporting the development or training of new GPs. Nor was there any mention of what streamlining approaches would be offered to allow pharmacists to have autonomy within their practise, and not require GPs to constantly approve minor changes, even when the only difference was the brand name.

Previously, the government had offered support to GPs through the use of the GP retention scheme. The main goal of the scheme, launched in 2021, focused on reducing the number of individuals seeking to leave the profession through targeted financial support and flexibility in regards to furthering education, e.g., seeking additional qualifications to aid their professional development. This scheme was intended to complement the already-established flexible pay premia for junior doctors completing GP training,

which is worth more than £9000 per year (provided they work full-time and not locum).

While the scheme does allow GPs to earn up to £4,000 more per year, it does not provide much in the way of long-term support. The scheme ultimately lasts for only 5 years, with provisions to extend for an additional 2 years in exceptional circumstances. It is unclear whether any of the pay increases seen would continue into a full-time salaried position within most GP practices. It is intended to help doctors with care responsibilities or academic pursuits because the standard NHS allocation of leave and timetabling does not allow for the necessary time off to ensure GMC registration requirements are met.

However, to access the scheme, doctors need to have actively signalled their intent to leave the profession. In which case, this approach to support seems to be a desperate attempt to stop the haemorrhaging of doctors from the register. Furthermore, the scheme attempts to incentivise the practices to retain the GPs over the doctors themselves. Practices can earn up to four times as much as their physicians do by simply having them participate in the scheme. No guidelines have been disclosed as to how the practices are meant to use the funds, suggesting an even wider gulf is emerging between those disenfranchised and those running the practices.

Prospects for the Future

The NHS faces an uncertain period in regards to GP numbers and support eligible within the primary care setting. While a record number of medical students both enter and graduate each year, the numbers required to go into General Practice are not being met.

With the little support currently offered, it is hard to see how any government targets can be tackled in the short term. To prevent any further loss of individuals from the medical register, harsh reviews and reforms must be implemented.

"A Hug Without 'U' is Just Toxic" - it's fun until it's not!

A very short introduction to toxicology and drug interactions

Written by Rachel Nguyen
Art by Rahel Kiss

On an autumn day in 1996, Karen Wetterhahn, a Dartmouth chemistry professor and toxic heavy metal researcher, was working with dimethylmercury, when she accidentally spilled a few drops on the back of her latex glove. Five months later, she presented at the emergency room with an array of neurological deficits, from ataxia to visual blurriness and hearing difficulty. Further investigations later revealed those few dimethyl mercury drops that she had been so unwary of had penetrated through her latex gloves, diffused through her skin, and travelled to the liver, where it is metabolised into methylmercury. Methylmercury then rapidly infiltrated fat tissues, most importantly the brain and the myelin sheath, which wraps around axonal bodies. This lipophilic molecule induced neuronal loss and gliosis observed across her frontal lobe, cerebellum, and visual and auditory cortices; the radical damage and oxidative stress was so extensive that it sent her into episodes of extreme agitation and ultimately, an irreversible coma.

Although only a very small percentage of the world population might come into contact with dimethyl mercury, the rest of us are constantly exposed to toxins everyday - from the food we consume, the medication we take, and the air we breathe in. In fact, paracetamol poisoning is one of the leading causes of acute liver failure in Western countries, primarily due to its combined use with either alcohol or other prescribed medications. A concept far more familiar among the general public is food poisoning. In 2008, a 20-year-old college student from Belgium was found to be hypoglycemic and in fulminant liver failure after unknowingly consuming pasta that had been left unrefrigerated for 2 days. A post mortem autopsy confirmed traces of Bacillus cereus toxin in his liver and bile, which was responsible for fatty acid buildup and liver necrosis. It is noteworthy that, although this is an extreme case of food poisoning, understanding the pathogenesis of common toxicological responses will save many of us from unnecessary trips to the emergency room and, in the worst case, death.

Factors affecting toxic response

One of the factors affecting the toxic response is its variation between different species. For instance, cats are more vulnerable to paracetamol-induced liver damage because they lack the enzymes responsible for converting paracetamol to a non-toxic, soluble metabolite, (discussed in more detail below). Moreover, different inbred strains of an animal might demonstrate a range of toxic responses. A similar phenomenon is observed in humans, primarily due to genetic polymorphisms that result in less functional metabolic enzymes. Perhaps one of the most well-known examples of such a polymorphism is alcohol flush reaction, where a variation in the aldehyde dehydrogenase gene (encodes for the enzyme responsible for converting acetaldehyde produced by alcohol breakdown), results in little to no aldehyde dehydrogenase. This leads to a buildup of alcohol metabolite, causing increased blood flow via vasodilation.

Genetic polymorphisms in other enzymes can have far more significant consequences. For instance, polymorphisms in cholinesterase genes can reduce the metabolic rate of succinylcholine, a muscle relaxant. As a result, muscle relaxation is prolonged and can quickly accelerate from being therapeutic to being fatal.

Important drug profiles in clinical toxicology

Any medications, after oral ingestion, will be metabolised in the liver via two pathways:
Phase 1: a functional group is added to be further conjugated in Phase 2. These reactions include: oxidation (catalysed by the enzyme family cytochrome P450) reduction, and hydrolysis.
Phase 2: a polar functional group is added to make the compound hydrophilic and easier to be excreted by the kidneys

It is important to note that the CYP450 family can be induced by a number of exogenous substances, namely alcohol and anti-epileptic drugs (i.e barbiturates). It is extremely important to remember not to take paracetamol at the same time as taking these substances.

The case of paracetamol:
Paracetamol is one of the most common painkillers given to the general public. 95% of ingested paracetamol is metabolised via conjugation by glucuronidase, forming hydrophilic products that can be excreted in the urine. The remaining percentage of paracetamol undergoes oxidation by CYP450, producing the toxin NAPQI. Fortunately, in a healthy individual, NAPQI is rapidly converted by glutathione into non-toxic, soluble paracetamol conjugates. However, when alcohol consumption occurs in tandem with paracetamol ingestion, the balance shifts towards CYP450, causing a buildup of NAPQI. More potently, as this NAPQI accumulates, the activity of glutathione is also overridden. Unconjugated NAPQI disrupts the hepatocellular membrane and depletes the level of glucuronidase enzyme, resulting in a vicious cycle, which causes hepatocellular injury.

Fortunately, there are alternatives. Ibuprofen, an equally-popular NSAID for headache treatment, is absorbed by the gut into the bloodstream and rapidly excreted into the urine. This process relies only marginally on liver metabolism. Therefore, those looking for a remedy to their hangover headache should consider switching to ibuprofen.

Alcohol is not the only exogenous compound that can induce a lethal reaction. Grapefruit juice, a seemingly harmless food product, was confirmed to prolong the QT interval in both individuals with long QT syndrome and those being treated for it. This can lead to lethal arrhythmias and,in some cases, sudden cardiac arrest. One study found that a plausible culprit could be furocoumarins. When absorbed by the enterocytes, furocoumarins are converted to reactive intermediates that bind to and inactivate CYP3A4, a member of (you guess it) the CYP450 family. This increases the oral bioavailability of cardiovascular medications (e.g. nisoldipine, used to treat hypertension), which means a higher-than-recommended amount of active drug is found in its intended tissues, potentially causing overdose.

Conclusion

What is the key takeaway from this? While science is heading towards a personalised medicine model, where every individual's genetic profile is filtered for any defects (for example, in the CYP450 enzyme) that might affect their pharmacotherapy, this approach is far from being widely implemented. What you can do instead, when picking your over-the-counter medicine (or in fact any kind of medicine), is to 1) check for their route and (primary) site of metabolism (i.e. paracetamol versus ibuprofen), 2) consult with your GP about any underlying medical condition and whether your diet could potentially interfere with your prescribed medications (you can also take extra precautions and read the neatly folded medical instruction sheet inside the cover of your prescription). Oh, and while you're at it, toss away those leftovers that have been at the back of your fridge for 3 days.

COULD HYDROCORTISONE BE THE KEY TO ERASING TRAUMATIC MEMORIES?

Written by Leonie Hellwich
Art by Zach Ng

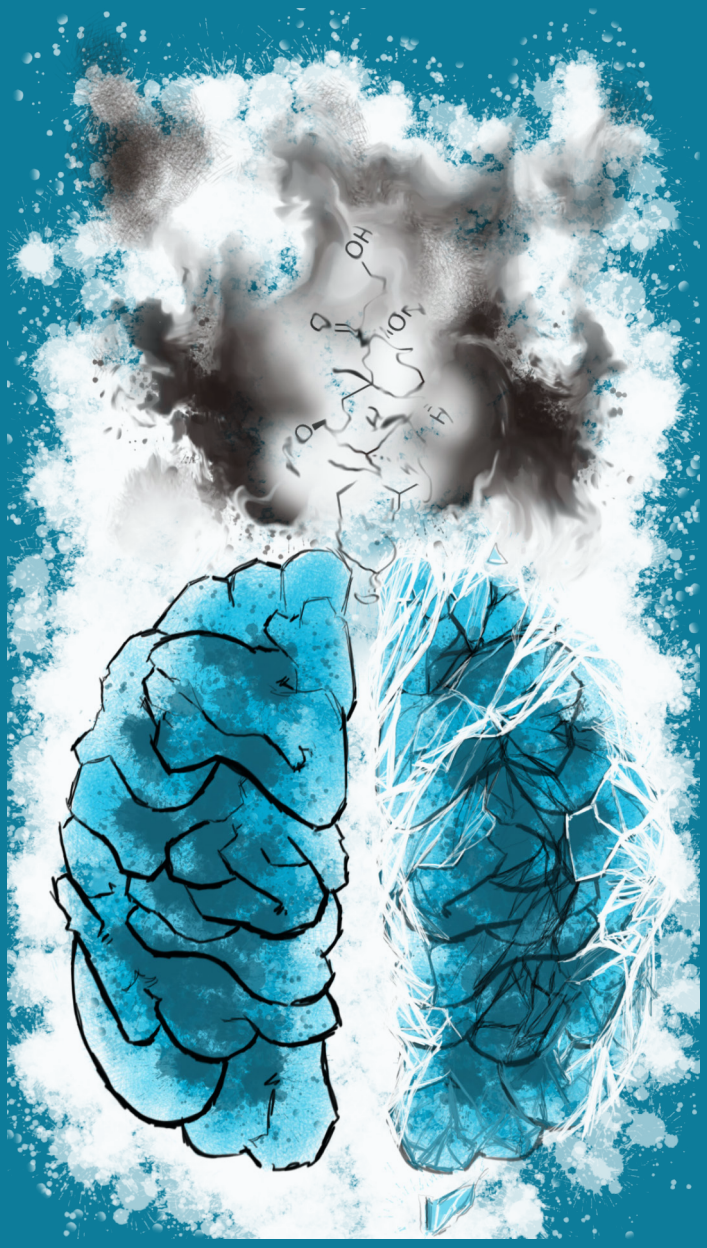
Post-traumatic stress disorder (PTSD) can be described as one of the most impactful disorders known nowadays that presents various challenges for clinical practitioners. The disorder usually arises by experiencing or witnessing an anxiety-inducing traumatic event, characterised with coping difficulties including panic attacks, flashbacks, intrusive memories and nightmares. Intrusive memories are described as emotional impressions based on other senses that come to mind involuntarily and often transport the affected individual back to the time of the traumatic event, leading to the illusion of a persistently active threat. The term panic attacks refers to spells of sudden and intense anxiety which can take forms of difficulty with breathing, shaking or hyperventilating.

Common causes of PTSD include abuse, assault, severe accidents, or war events. Having PTSD can affect various areas of life and have grave consequences for the affected individual, for instance result in distancing themselves from friends and families, developing irrational fears of everyday behaviours or struggling to remain optimistic about the future.

Thus, it becomes evident how crucial it is to develop an effective strategy to tackle PTSD symptoms and allow affected individuals to continue their life as undisturbed as possible. Unfortunately for the 4% estimated to be affected by PTSD in the United Kingdom, the current field lacks broader availability of therapeutic approaches that focus on trauma. Exploring new treatment options is therefore essential.

While previously reviewed as not recommended for PTSD treatment, a recent paper by Hennessy et al. (2022) questions those past results. They are concentrating on the trend for PTSD patients to have low levels of the hormone cortisol, usually associated with stress. This may be associated with a decreased capacity to react to and maintain physical functioning during episodes of heightened stress. Since previous studies obtained unclear and conflicting results also in regards to sex differences in the effectiveness of hormone-based PTSD treatment, Hennessy et al. (2022) investigated the effect of hydrocortisone on men and women after they had experienced analogue trauma in the form of a trauma film, consisting of two scenes that showed extreme violence. Hydrocortisone refers to the hormone cortisol when administered to an individual as tablets.

To accurately test the impact of hydrocortisone, it was crucial to have a control group, a group that receives a void medication instead of the drug which should not cause any effect. In research like this, one needs to factor in the placebo effect, which describes the phenomenon where people who expect an effect after taking medication will feel an effect or notice an effect even when the medication has none. If the observed effect on the experimental group exceeds the effect on the control group, it can be assumed that the medication has a valid and significant effect. Hydrocortisone or the placebo were randomly administered to the participants one hour after seeing the film.



Firstly, participants in the study completed various self-report questionnaires assessing their characteristics and whether they showed symptoms of personality disorders. Following the exposure to the film the participants were instructed to complete online diaries which included reports of their intrusive memories for seven days. Each memory was to be briefly described and the number of its repetitions on the day reported. Additionally, their vividness and the distress level they caused were rated on a scale.

The results obtained in the study are highly interesting. Measurements of heart rate and blood pressure during the day of the trauma film exposure showed that both increased from pre-film to post-film measurement, but recovered within an hour. Administering hydrocortisone was reflected by increased levels of cortisol in the participants' saliva.

While accounts of immediately recorded intrusive memories in the post-film hour did not differ between the groups, meaningful results were obtained when testing the effects of time, sex and drug (hydrocortisone or placebo) on the number of memory intrusions. The hydrocortisone group reported a faster reduction of intrusive memories, especially between day 1 and day 2 after watching the trauma film. Vividness and distress, nevertheless, decreased slightly faster in the control group. Now, what conclusions can we draw from these observations? The accelerated decline in memory intrusions in the hydrocortisone group mark this medication as potentially promising in the development of an effective PTSD treatment. Evidence to highlight the role of female sex hormones in memory functioning in men and women was observed and should be further investigated.

Of course, the results of this study do not allow us to apply them to real-life scenarios. Compared to the trauma response that was artificially created by exposing participants to the trauma film, real-life trauma is highly individual and complex., PTSD can stem from extremely diverse situations and experiences, and is therefore difficult to sum up or develop a suitable treatment that can be generalised to all possible causes. The convergence between the impact on healthy participants with artificially created trauma and the impact on clinical participants remains unclear.

What can we take away from this paper?

Treating PTSD with prescribed hydrocortisone appears promising in terms of reducing memory intrusions early on. Which type of memory is affected by the medication, the impact on clinical populations, and the effectiveness on real-life complex trauma remains to be investigated in future studies, which could lead to novel and life-changing improvements in PTSD treatment.

Dear Maladaptive Daydreamers,

A glimpse into a lesser-known mental health condition and why it is not recognised

Written by Hannah Balane *Art by Irina Pirvu*

We've all experienced daydreams to a certain extent – from staring off into space in the lecture hall and wishing we were somewhere else, to pretending we are world leaders speaking giving public speeches, to even reimagining a discussion from several years ago in the shower (but this time with a better argument). Daydreams are so common, in fact, research suggests that we spend about 47% of our waking hours distracted by our daydreams.

However, maladaptive daydreaming (MD) is sometimes referred to as a "daydreaming disorder" and it describes a condition where a person regularly, whether intentionally or not, experiences vivid complex daydreams from hours to days at a time. These are often so intense and sometimes addictive that they can disrupt daily life. For some people, these daydreams can be relatively harmless and are triggered as a form of entertainment in the safety of their home, using stimuli such as music, recent events or even books. For others, it can strike when they least expect it: halfway through a conversation, walking on the way to work but somehow getting lost or in the silence of a funeral perhaps.

The daydreams often start small. From personal experience, it starts with one group of characters with a singular plot. They then start to develop their own personalities, make their own decisions, and live their own lives and before you know it, you've created a second (or third or multiple parallel) universe in your head, and you are unable to write it down because it would be akin to writing down the whole of human history from start to finish. While you can control some aspects of the 'plots' or 'actions' of your characters, I generally prefer to watch how things play out and let them decide how they live. I can make that life (quite literally) everything I have ever dreamed of.

But that is not everything MD is. It is not as wonderfully fanciful as it may seem. No one fully understands the causes of MD, though experts and community members alike have agreed that it may be a coping strategy in response to trauma or stress where it is 'safer' to be in an imaginary

world than to deal with the reality of things. All the hours spent away from reality means hours away from developing core life skills such as socialising, career or academic progression or simply adapting to living with an undetermined future. An unfortunate truth for many people is that these daydreams start to control their real lives; where weeks may have passed but they still choose to live their daydreams. Although we may

be aware of our dreams and their consequences, the temptation of it all can be far stronger.

It has only been recently proposed as a psychological disorder yet has not been officially identified

in the International Statistical Classification of Diseases and Related Health Problems (ICD-11) – the current and approved standard list of clinical diagnoses in England. Upon review of the limited literature on MD, there are indeed reported shared traits with other psychological conditions such as Obsessive-Compulsive Spectrum Symptoms (OCSS) including repetitive movements like pacing, unconscious facial expressions and whispering. It can include features of behavioural addiction; where habit becomes an obligation like an unstoppable urge to daydream. These acts could provide evidence that a separate diagnosis for MD is necessary as it does not fully align with more common types of neurodivergence such as autism, attention deficit hyperactivity disorder (ADHD) and bipolar disorder.

A proposed diagnostic tool called the "Maladaptive Daydreaming Scale (MDS)" has been studied in Italian and Turkish populations, with both studies concluding that its use is suitable in their respective populations. The MDS was developed to differentiate between MD and non-MD using three key factors: yearning - the need or urge to spend time daydreaming; impairment - how much disruption and distress it causes; and kinaesthesia - how movement facilitates daydreaming. Naturally, more structured clinical studies would be required to form a proper diagnosis, which in turn could lead to more specific treatment options to be explored.

Overall, there is a distinct lack of formal studies into this condition (perhaps due to its recent emergence) and like other psychological conditions, it is complex and affects a spectrum of people. Maladaptive daydreaming is an escape for many, a hobby for some and a unique experience for each individual.

The Joker: A Deep Dive

T.W: Mention of abuse, blood, and murder

"The worst part about having a mental illness is people expect you to behave as if you don't..."

Written by Madhumila Killamsetty
Art by Zach Ng

The Joker is a popular DC supervillain who, according to some canonical versions, fell into a vat of chemical solutions that left him disfigured and 'crazy'. However, in the 2019 film, Joker, we see a different origin story of this iconic character. The movie provides insight into what made Arthur Fleck, the Joker. It uses the context of his background — his mental illness, personality disorders, lack of resources, and the lack of empathy from the people around him — to show how Arthur Fleck transitioned into the Joker.

Our first glimpse of one of Arthur's disorders is when he sits in his therapist's office. He breaks into a burst of laughter that visibly pains him and almost chokes him. These outbursts of laughter are observed throughout the film creating an uncomfortable atmosphere as nobody around him seems to understand his struggle. He carries around a laminated card to let people know about his condition but is always met with scorn and disdain. His mannerisms gain unwanted attention from three drunk men in the subway who beat him to a pulp. This uncontrollable laughter is symptomatic of a real disorder called Pseudobulbar Affect (PBA).

In PBA, there is a disconnect between the frontal lobe of the brain (controls emotions) and the cerebellum (mediates reflexes) which causes sudden, uncontrollable, and intense episodes of laughter or crying due to the inability to control facial muscles. In Arthur's case, this delicate connection was probably disrupted when his abusive foster father caused severe trauma to his head during his childhood. This disorder makes people feel alienated from society, often leading to anxiety and depression. This is exactly what we see with Arthur: His loneliness, negative thoughts, and constant need for love and acceptance explain his delusions about Murray, the talk show host, being his fatherly figure, or his neighbor being romantically interested in him. Throughout the film, Arthur yearns for acceptance, for people to be proud of him and give him attention. He imagines being on the Murray Franklin show, receiving the audience's appreciation for taking care of his mother, and receiving fatherly warmth and affection from Murray. This is a case of Narcissistic personality disorder (NPD), in which people have an inflated sense of self and a deep need for attention and admiration. This stems from Arthur's need to bury his feelings of low self-esteem and self-worth. NPD likely arose in Arthur as a psychological defense against his traumatic childhood where he was repeatedly abused and starved. It could have also been inherited since NPD is known to have a genetic component.

Things go downhill when Arthur kills two men on the subway in self-defense and the third one deliberately. This is the turning point in his life. He enjoys the sudden surge in attention from the masses for these actions. He finally feels seen, as if his existence has meaning. We see him imagining fake scenarios to validate his actions, like his "girlfriend" glorifying the person who killed the three men. During the climax, we witness Arthur's extremely fragile ego when he reveals a "joke" to the talk show audience that he was the murderer of the three men on the train. When nobody finds this funny and he is met with hate and disapproval, he snaps and murders Murray, the host. People with NPD, genuinely struggle to make intimate connections with people and have a deep sense of loneliness and insecurity. Arthur coped with these issues by eliminating people who demeaned him. With compassion, we need to encourage people with NPD to seek help to address feelings of low self-esteem, and shame, so that they do not yield to the harmful compensatory strategies that emerge from the disorder as Arthur did.

Finally, Arthur is an extreme case of psychopathy. Psychopathy is not a mental illness; it is a collection of traits, including not feeling remorse and being callous and uncaring. Following the murder on the subway, Arthur locks himself in the bathroom and performs a slow dance which is the first sign of the 'Joker' in him emerging. He confides in his therapist that he never felt better. We never see him questioning his actions or feeling remorse, which further points to his underactive neocortex. He believed that they deserved it. He doesn't think about what is morally or lawfully correct and demonstrates irritable and aggressive behavior. Even when his friends visit him, he brutally murders one of them for getting him fired from his job. With blood splattered all him, he casually diverts the topic to his appearance on the Murray show. His iconic dance at the staircase is symbolic of him completely embracing his new identity, fully transitioning into the Joker. He mentions stopping his medications, implying that he has given up, intending to no longer fit in. With an eerie smile on his face, he whispers, "Isn't it beautiful?", as he watches his city burn.

Contrary to popular notions, most psychopaths are not criminals. They might use their psychopathic traits to get what they want at the expense of others in everyday life such as in the workplace. Some inherited genetic and environmental factors such as bad parenting and birth complications

increase the risk of developing psychopathy. These factors influence the brain, in particular the amygdala which affects empathy, social responsiveness, and outcomes related to fear. Although we don't know the Joker's birth family history, environmental factors such as the torture in his childhood could make a case for Arthur's psychopathy.

Despite Arthur most likely developing his disorders because of childhood abuse and traumatic brain injury, his mental illnesses do not justify his violent tendencies. In the real world, people with disorders and mental illnesses are more likely to be victims of violence rather than perpetrators. In the film, the Joker's heinous crimes are depicted as consequences of a failed society. It provides us with potential results of pulling out funding from mental health institutes and mistreating people with mental disorders. Pop culture's representation of mental illness is almost always associated with violence and the film Joker does not try to fix that. It was neither made to vindicate mentally ill people nor to educate society about mental illness. Rather, it was made to tell us a story about one man, Arthur Fleck, who became the Joker because of his choices, situations, and society.

CAN THE GYM MAKE YOU SMARTER?

How working out can improve your memory, concentration and potentially delay the onset of Alzheimer's disease

Written by Jasmine Bains *Art by Minjia (Erin) Pan*

We've all been taught about the physiological benefits of exercise, ranging from improved cardiovascular health to decreased obesity rates. These benefits reduce the risk of developing diseases, such as cancer and diabetes. Some of us might even be aware of the psychological benefits of physical activity due to its ability to trigger an immediate release of neurotransmitters, such as dopamine and serotonin, which almost instantly improve mood. However, did you know that the gym can actually make you smarter?

BETTER CONCENTRATION AND FOCUS?

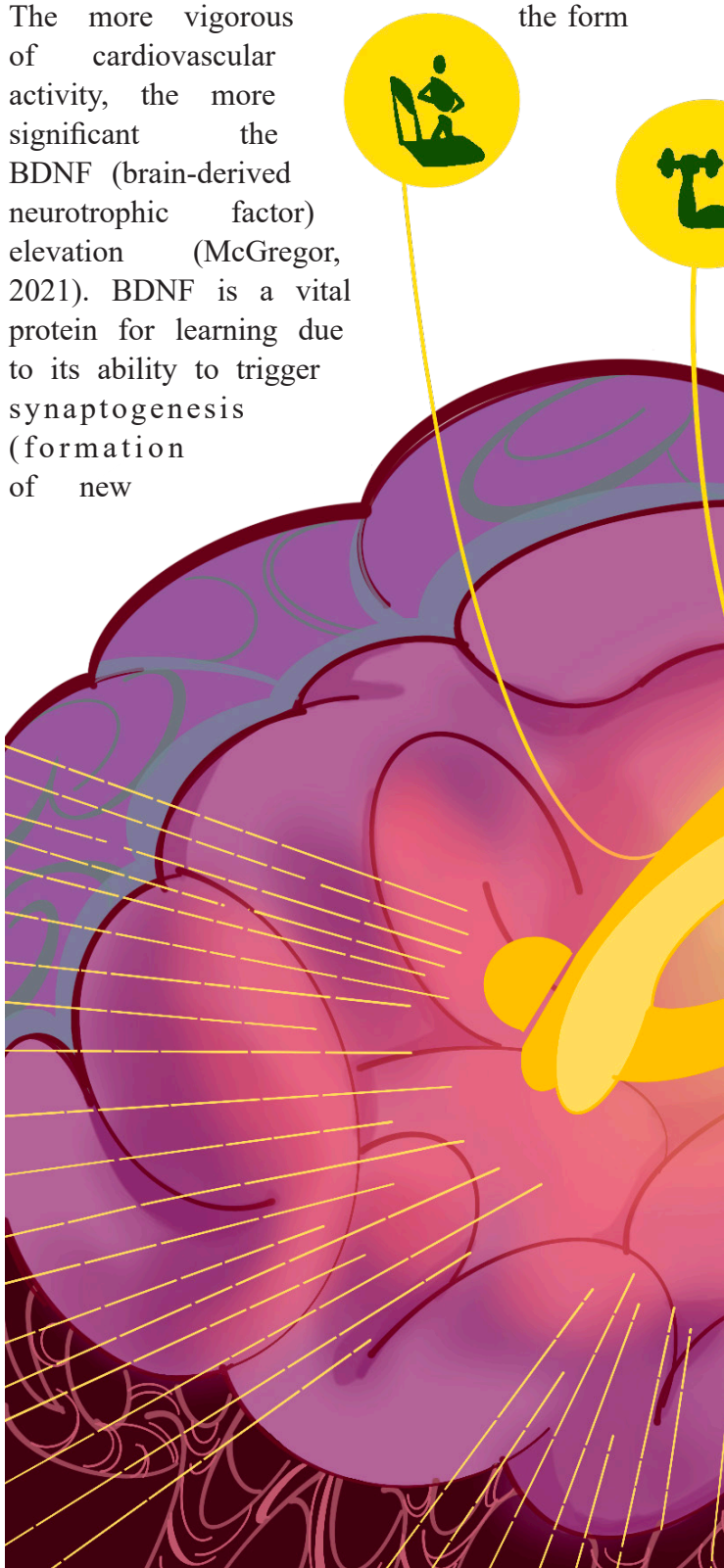
Cardiovascular activity increases your heart rate, therefore pumping blood at a faster rate around your body, including to your brain . This increase in blood flow to the brain "fires up neurons",so that they become more ready for neuronal activity and neurotransmitters can diffuse across synapses more quickly. This helps to promote cell growth especially in the hippocampus, thereby increasing its volume. This increase in volume of the hippocampus is extremely important, and has many short- and long-term benefits. Simultaneously, this increase in blood flow also helps maintain a steady influx of nutrients into the brain, which helps improve cognition and promote brain functions that are vital to learning, such as memory. As a result, studies have shown that a single workout can improve your concentration and focus for the next two hours of studying .

IMPROVES SHORT TERM MEMORY

The temporary increase in size of the hippocampus after a work-out can enhance short-term memory. The hippocampus is an important area in the temporal lobe in the limbic system, which plays key roles in memory and learning. Therefore, if you learn new information straight after a workout, you have a better chance of recalling it later on.

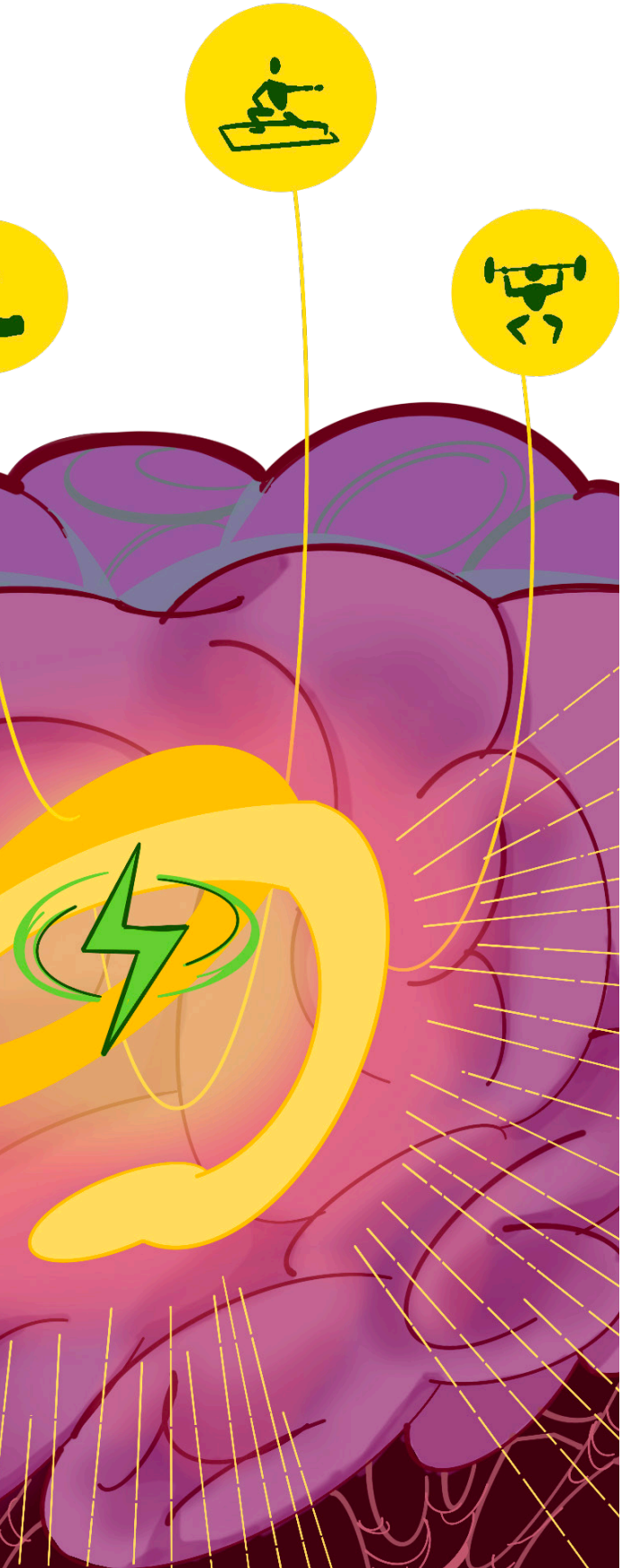
BOOSTS LONG TERM MEMORY

Exercise can also boost long-term memory and increase synaptic plasticity. The more vigorous the form of cardiovascular activity, the more significant the BDNF (brain-derived neurotrophic factor) elevation (McGregor, 2021). BDNF is a vital protein for learning due to its ability to trigger synaptogenesis (formation of new



synapses) and increase synaptic plasticity. This allows the formation of new memories, as well as strengthening connections of pre-existing synapses by permanently increasing the volume of the hippocampus and prefrontal cortex.

Can exercise delay the onset of Alzheimer's disease and could it be a potential form of treatment in the future?



So far we've only explored the neurological effects of exercise that create minor benefits for students like ourselves – but what if these simple lifestyle adjustments could support long-term effects and help delay the onset of neurodegenerative diseases?

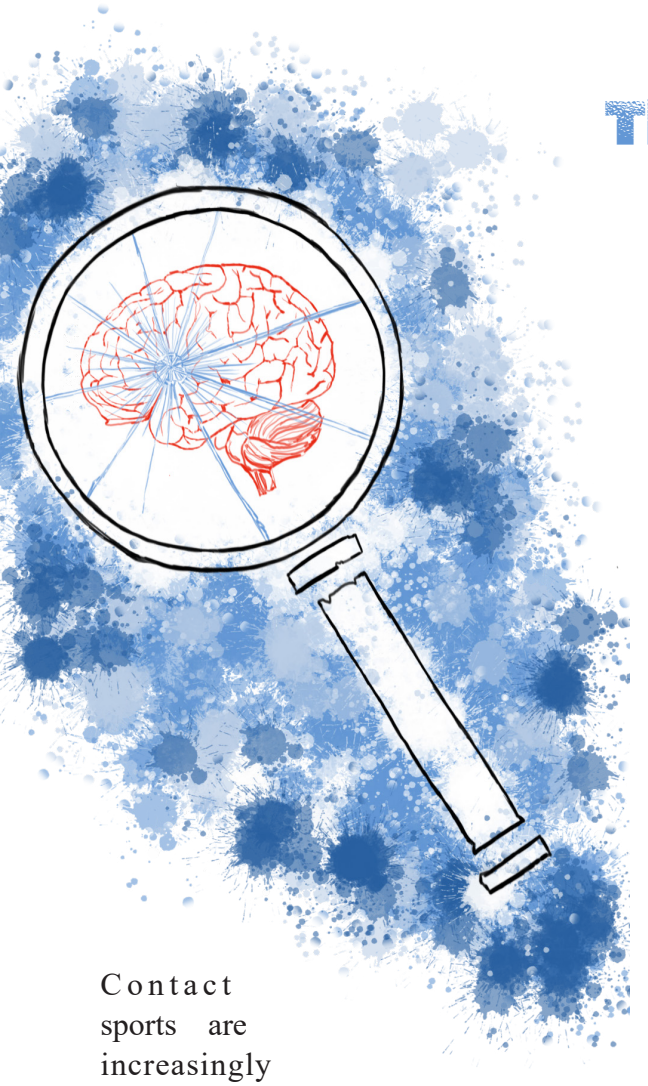
Alzheimer's disease often develops due to the accumulation of beta-amyloid and tau protein which form plaques and neurofibrillary tangles respectively. This leads to the overactivation of microglia and astrocytes in an attempt to clear the accumulating cellular debris. However, as a result, this mechanism also causes chronic inflammation and instigates the degeneration of synapses. These aggregations and deteriorations seem to target the neocortex and hippocampus - the brain regions most associated with memory. This drives memory loss - one of the typical symptoms of Alzheimer's disease.

However, since exercise is able to increase the volume of the hippocampus by increasing synaptogenesis and neuroplasticity, it takes longer for these synapses to be attacked. This helps delay the onset of symptoms of neurodegenerative diseases. Exercise is also being considered as a potential treatment for Alzheimer's disease. Studies have shown that some patients already diagnosed with memory problems not only experienced a decrease in rates of memory decline, but actually showed improvements. For example, a study in which people aged 60 or older, who had been diagnosed with memory problems, underwent 12 months of aerobic exercise training found that 47% of these participants showed an improvement in memory scores compared to the rest of the participants who did not undergo the aerobic activity programme. Brain imaging studies of the first group of participants showed an increase in blood flow to the anterior cingulate cortex and the hippocampus, thus displaying the improvement in memory function (Thomas, 2020). Scientists are now looking to conduct further research specifically involving Alzheimer's disease patients in order to determine the extent to which exercise could be considered an effective treatment for this neurodegenerative disease.

Whilst going to the gym might not make you 'smarter', it can definitely improve your short and long-term memory, concentration and perhaps even delay the onset of neurodegenerative diseases. So, the next time you are struggling to find the motivation to work-out, maybe you will remember some of these neurological benefits alongside all the typical physiological gains and decide to head to the gym.

ImPact?
The Ongoing Investigation of Concussion and Neurodegenerative Disease

Written by Olivia Kehoe
Art by Zach Ng



Contact sports are increasingly attracting attention: not from spectators, but from the scientific community. Once considered an injury you could "rub some dirt on" and return to the field, repetitive head impacts are now considered to be the cause of a neurological disease afflicting many contact sports athletes. What has emerged over the last decade of research is a contentious link between repetitive head injury, and the development of early symptoms of dementia. At the heart of this issue are ex-professional athletes who have voiced their experiences of developing symptoms in the years after their retirement, some ultimately leaving their brains to research. While at first lone voices, stifled by the stigma of their conditions and denial by powerful sports governing bodies, this issue stands at a tipping point. The largest biomedical research agency, the US National Institute of Health, has now formally recognised a causal link between repetitive head injuries and Chronic Traumatic Encephalopathy (CTE), a distinct neurodegenerative disease.

Where it all began

Concern about the long-term effects of repetitive brain injury has existed in medical literature for at least a century. Tracing back to 1920s boxing, the term 'punch drunk' was coined in relation to prize fighters who presented with altered behaviour. Memory loss, confusion, a Parkinsonian gait and dramatic changes in personality, such as higher levels of aggression, were among the symptoms progressively observed in individuals sustaining 'considerable head punishment' during matches. However, there remains debate about whether historical reports of repetitive brain injury, and modern CTE characterisations refer to the same condition.

Modern CTE has its roots in a ground-breaking paper published by Dr Bennet Omalu and colleagues in 2005, detailing the autopsy of a retired professional American football player with distinct neuropathological features in their brain that were similar, but not identical, to features observed in Alzheimer's patients. Among the cases published since then include athletes from internationally popular sports such as rugby, football, ice hockey, boxing and wrestling, as well as non-athlete groups such as military veterans with blast exposure and victims of physical abuse. An array of clinical symptoms and associated neuropathology have followed to characterise this novel disease.

Written in pathology

The hallmark of CTE in brains post-mortem is the abnormal phosphorylation and accumulation of the protein tau into neurofibrillary tangles that clog up neurons and astrocytes. General atrophy (shrinkage) of the cortex and enlargement of the

brain's ventricles are also characteristic, and similar to the shrinking seen in other forms of dementia. Altered mood, movement and behavioural disorders have also been reported and related to CTE. Yet crucially, these individuals developed cognitive symptoms much younger than is typical for age-related dementias, such as Alzheimer's disease.

What makes CTE particularly intriguing, is that it is emerging as a neurodegenerative disease with an environmental aetiology. This means that external events, such as head impacts, could be the trigger for disease, rather than genetic origins.

Ongoing Research

One of the biggest debates in the area of CTE is if it's even a concept at all. Many ask the question: "Can head injuries from contact sports really lead to early onset neurodegeneration?" Those driving the research, such as Dr. Anne McKee of Boston's CTE Centre, maintain that there is an irrefutable correlation, while others stand strongly in denial. Sceptics cite the lack of reliable control groups, confounding factors in the studies that may introduce bias, the fact that diagnosis is so far only possible post-mortem (often meaning a reliance on retrospective interviews with next-of-kin), and the lack of a clear mechanism between head trauma and the onset of clinical symptoms. Despite the announcement from the NIH, alongside efforts to understand the nature and prevalence of the disease, uncertainty remains on many other fronts. How do later-life symptoms progress? What is the relationship between pathology in the brain and clinical presentation? Is there overlap with other neurodegenerative diseases and comorbidities?

Media Controversy

Characterising CTE has become not merely the pursuit of medical understanding, but an increasingly high-profile political battle fought between researchers, athletes and governing bodies such as the National Football League (NFL). The spotlight has been on the latter, not least for the book, League of Denial, and its film adaptation starring Will Smith. Told as the story of a public health crisis, such narratives have shaped societal understanding of CTE in relation to sport. Given the influence of NFL as a multi-million dollar industry, it would appear necessary to ensure that research remains independent of external bodies, so that political or financial interests do not bias future studies or the researchers working on them.

A caution for more balanced and unbiased reporting was not made more forthcoming than in an article in The Lancet, Neurology, titled 'Primum non nocere' (Latin= do no harm). In the article, researchers of brain injury and neurodegeneration voiced concerns about the narratives and tone of the coverage on CTE cases by media outlets in the past decade. Moreover, they emphasised that where much of the characterisation so far of clinical and pathological outcomes is still in its infancy, this nuance and uncertainty is often neglected in media reporting. Clarity in communicating the nature of this relationship is crucial for public safety, by developing a better understanding of risk, prevention strategies and the possibility for future therapeutic targets.

In Harm's Way

In the absence of any disease-modifying treatments, prevention remains the most effective strategy for managing CTE. Public perception and popular reporting of the disease will thus prove increasingly important for developing and implementing preventative measures and policy changes in contact sport. Suggestions for protecting at-risk groups include introducing safe practice techniques in game play, while also penalising dangerous tackles or manoeuvres. More broadly, this requires a cultural shift in the way that sports and activities involving repetitive head impacts are perceived, which can be achieved through consideration of the socio-political and financial implications surrounding diagnosis. Most importantly, an environment among players, coaches, physicians and the public that prioritises players' safety above all may promote better transparency in reporting symptoms. This must start in school and youth league sports, all the way to understanding the incentives around injured professional athletes wanting to return to the field.

Given how common concussive injuries and head impacts are, those in the line of fire deserve to know the risks they face when stepping onto the field. With a causal link now recognised, it is undeniably important for research to push on, to prevent future cases of CTE.

Can animals feel empathy? Observations of rescue behaviour

Written by Rachel Cooper
Art by Laila Kandil

What is rescue behaviour?

A common occurrence in humans, but extremely rare in animals, rescue behaviour is shown when an individual is in distress, and physical harm will come to them if they don't escape the situation. Another individual acts to help, putting themselves in a dangerous position even if no immediate benefit will come to the rescuer. This behaviour in non-human animals has so far only been demonstrated in a small handful of species, so the full extent is vastly unknown. It is nonetheless a significant discovery which leads us to question, why? Isn't deliberately risking their lives to save others going to hinder their own survival rate? Or is it possible that an evolutionary development of empathy could increase the species' chances of survival as a whole?

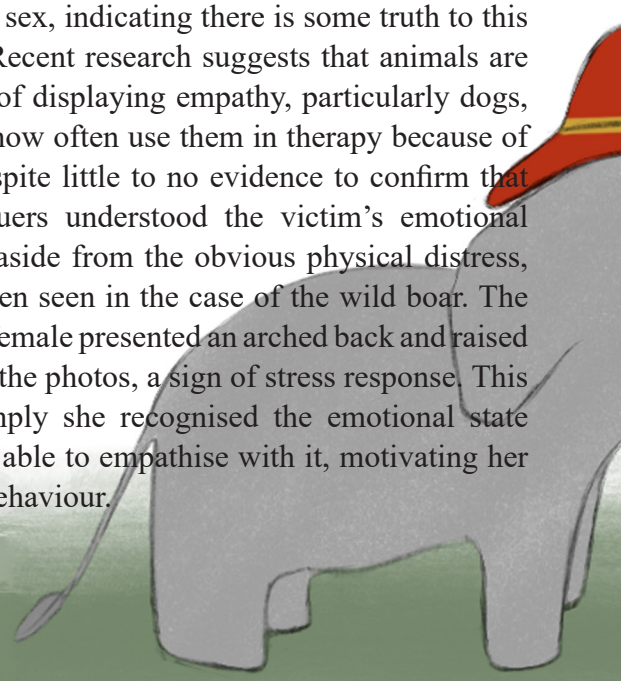
There are a handful of cases of species presenting this behaviour, across different animal groups. One example was shown by the removal of sticky 'bird catcher tree' seeds by a group of Seychelles warblers. These species can become caught in seed clusters of Pisona trees (also known as bird catcher trees); the seeds attach to their feathers, weighing them down and preventing flight which may cause mortality. In some cases, Seychelles warblers were observed removing the seeds from other individuals in the group, even if it meant they risked entangling themselves. Another observation involves an adult female wild boar rescuing two younger boars from a wooden cage trap. It captured the adult boar removing logs that sealed the cage door, allowing the juveniles to escape. The trapped boars had shown clear signs of distress such as charging at the cage walls, and the adult female put herself at risk by spending a significant amount of time at the site of the trap during the rescue. In a study of elephant behaviour, a case was recorded of an adult elephant removing a tranquiliser dart out of another adult male.

Empathy as an evolutionary trait

The question hereby presents itself whether or not these incidents of rescue behaviour were driven by empathy. This ability to recognise and respond to emotions that other individuals express is a behaviour which has been integral for human evolution. Our species has dominated the planet, with the main attribute of population success being our highly complex brain development. We evolved empathy to facilitate cooperation, improving the survival of individuals, and by extension the population as a whole. It is hypothesised that selective pressures aided this evolution. early human ancestors had to develop strong teamwork to survive in their small numbers. They had to compete for resources, find shelter and avoid numerous predators. Without many physical adaptations, we benefited from helping each other, resulting in the development of empathy.

So could this same idea apply to animals?

In the theory of natural selection, species evolve and pass on traits that aid their ability to survive and reproduce. Traits that aren't useful wouldn't be passed on as successfully, and considering rescue behaviour puts individuals in dangerous situations, this is surely unbeneficial to them. Despite this, there is a case to be made for strength in numbers. Maintaining the survival of a group could benefit reproductive success due to a larger gene pool. In the case of the warblers, all four cases of rescue behaviour were recorded between members of the opposite sex, indicating there is some truth to this theory. Recent research suggests that animals are capable of displaying empathy, particularly dogs, and we now often use them in therapy because of this. Despite little to no evidence to confirm that the rescuers understood the victim's emotional distress aside from the obvious physical distress, it has been seen in the case of the wild boar. The rescuer female presented an arched back and raised mane in the photos, a sign of stress response. This could imply she recognised the emotional state and was able to empathise with it, motivating her rescue behaviour.



Discovering that animals display rescue behaviour, perhaps stemming from a development of empathy, gives us an idea of their evolutionary potential to ensure collective survival. We shouldn't underestimate the capabilities of animals, and since they are put under more and more stress by human actions, there is heightened pressure to adapt to changing environments. We may see further displays of rescue behaviour, along with new survival strategies, as their brains evolve and develop to catch up.

Seaweed farms: a tasty solution to climate change?

Written by Amelia Elamradi
Art by Sylvia Tsai

Seaweed farms are the latest trend in climate change solutions, with Europe investing millions into them in the hope that they will absorb and store carbon.

Within a decade, a boat trip in European waters might just involve a view of expansive rows of seaweed attached to ropes under the ocean's surface. This is because of the European Commission's new goal to create large-scale seaweed farms, specifically to farm 8 million metric tons of seaweed annually by 2030. Funding for seaweed farm projects has increased in the past couple years, including the €1 million provided by the EU for the AlgaeDemo project planned to cover up to two hectares of the North Sea.

Why the need for seaweed?

Part of the current seaweed demand is that seaweed is extremely versatile, as it can be used in food such as sushi, medicinal products, natural fertilisers, packaging, biofuel production and carbon sequestration.

However, the benefit most talked about is seaweed's ability to capture carbon from the air during photosynthesis and store it within its biomass, lowering the carbon dioxide levels in our atmosphere. Less carbon dioxide means we can reduce the amount of heat trapped in our air by this greenhouse gas, and prevent further global warming.

The benefits do not stop there: the carbon captured can remain fixed into the seaweed. When this aquatic plant dies, it drifts to the ocean floor and is buried as deep sea sediments. Deep in the ocean, little oxygen means that the seaweed with stored carbon takes centuries, or potentially millions of years, to decay, therefore keeping that carbon in the ocean, and not in our atmosphere. This is the plan for seaweed farms focused on carbon credit schemes, in which investors compensate for the carbon they release by investing in projects that sequester carbon.

For other seaweed farms, even though carbon isn't sequestered via the natural process of seaweed detritus sinking, and is instead harvested for production, the use of seaweed may prevent environmentally-damaging practices. If seaweed is harvested to be used as a biofuel, we can avoid relying on fossil fuels, which led to the release of 36.3 billion tonnes of carbon in 2021. If seaweed is used to create packaging, we can reduce plastic use. Traditional plastics take centuries to decay and eventually end up in our ecosystems as microplastics. Furthermore, if seaweed is used as a fertiliser, there will be less need for artificial fertilisers, which cause environmental damage when they run off into our waterways. Most notably, this run-off causes excess growth of algae, taking oxygen and sunlight from other animals and plants, in a process called eutrophication.

Is there a catch?

Whilst seaweed farms offer substantial benefits, there may be other factors to consider. For example, marine biologists have highlighted the possible risk of introducing diseases that may accompany large-scale seaweed farms, and the need to maintain genetic diversity. Seaweed farming methods must remain sustainable for the seaweed crop to be environmentally favourable.

Furthermore, seaweed farms may actually be a carbon source instead of a carbon sink. Researchers have proposed that the surrounding ocean waters will bring in plankton and other organic material, therefore creating an ecosystem with an abundance of food for various species. Eventually, if this reaches the scale of a whole ecosystem, there will be many creatures releasing carbon dioxide as they respire, perhaps even more carbon than the seaweed is able to absorb.

Are seaweed farms the answer to climate change?

Considering its many uses, seaweed may be very promising as an alternative to other very environmentally damaging practices and materials, such as plastic and artificial fertilisers. In terms of the effect on climate change, further research would be useful to ensure the many farm developments can continue with confidence in its benefits. However, if it turns out seaweed farms aren't as beneficial as we thought, authorities would need to take a step back to reevaluate, and put a hold on the mountain of investments being piped into them. Nevertheless, the majority of public opinions and scientific studies praise seaweed farming and it's reassuring to see authorities such as the European Commission beginning to take action to tackle climate change.

Can Plants See?

Written by Miranda Hitchens
Art by Lola Artiles

Over a century ago, a theory was proposed by botanist Gottlieb Haberlandt, which subsequently fell into relative obscurity. The idea he devised was a method by which plants may be able to see, not in an abstract way, but by a similar mechanism as an animal's eyes. He posited that the epidermis of many leaves was suspiciously lens-shaped, focussing light onto a light-sensitive mesophyll below, much like our eyes to our retinas. The validity of this theory has been debated by botanists ever since, but a key discovery has reignited interest in so-called 'plant ocelli'.

The Boquila Trifoliolata, a climbing vine native to South America, has a remarkable ability to mimic the leaves of a wide range of plants; climbing and disguising itself to avoid predation. However, the plant doesn't need to climb, or even contact the plant that it mimics. It is also capable of a range of transformations, including colour, shape and vein pattern changes, with quite remarkable accuracy. The question is, how?

Ernesto Gianoli and Fernando Carrasco-Urra, the researchers who discovered the plant in 2014, have introduced several theories by which it may mimic its hosts. In 2016, it was proposed that the vine may be receptive to volatile chemicals which arise from the host plant, from which it can determine information about the host's phenotypes and commence its shape-shifting.

However, it was not confirmed if enough genetic information could be conveyed by these volatiles.This theory was later superseded by the possibility of bacteria transfer between the Boquila Trifoliolata and its host. The bacterial communities on the leaves of the host, the mimicking Boquila Trifoliolata plant and another Boquila Trifoliolata plant which was not mimicking were studied, showing the non-mimicking vine had very different bacterial content than the other two.The mimicking vine had a large cross-over with the host, indicating that there may be exchange of genetic information via the common microorganisms.

These findings seemed convincing given this evidence, but what if there were no bacteria to transfer? In 2020, an experiment showed that the Boquila Trifoliolata could mimic the leaves of an artificial plastic plant - a host with no genetic information to offer. This indicates that the vine has some degree of sensory capability, which lended much more credence to the plant ocelli theory. The shape of the leaves of all vines placed significantly close to the plant showed some degree of mimicry, though the vines improved their ability to mimic the shape of the host as time went on, seemingly learning and even demonstrating an ability to remember the shapes over the months of exposure.

This study leaves plant ocelli as potentially the only theory standing, as there are limited options beyond sensory perception that could explain this phenomenon. However, further studies of the Boquila Trifoliolata and leaf anatomy will be essential to explore this enigmatic plant and the extent to which the similarities between leaf cells and lenses can be shown. We may not have definitive proof that plants can see, but it looks remarkably similar.

CRYPTIC CEPHALOPODS THE ECOLOGICAL BASIS OF CAMOUFLAGE

Written by Emily Vialls
Art by Shangyu Chen

In their early evolutionary history, the common ancestor of modern-day squids, octopuses and cuttlefish made one of the largest U-turns in evolution. 400 million years ago, in the late Devonian period, Coeloid cephalopods did away with their shells, favouring better motility, and the ability to squeeze into small spaces. But there was a catch: reducing themselves to a squishy piece of nutritious muscle would make them an easy score for predators. In response to this new selective pressure, cephalopods adapted to some of nature's most novel and challenging niches, including complex cognition, diet generalism, and adaptive camouflage. In particular, their adaptive camouflage (a.k.a. metachrosis) system possesses complexity unlike any other animal, making it a unique research target.

The Biological Benefits of metachrosis camouflage

In tandem with their well-developed cognitive abilities, cephalopods use metachrosis in hunting, communication, and, primarily, as an antipredatory weapon. To fend off predators they can mobilise several camouflage mechanisms including countershading (a gradient colouration matching their oceanic backdrop), masquerade (resembling an inedible object), and mimicry (disguising themselves as an entirely different animal).

Another notable use of adaptive camouflage is in interspecies communication - specifically antagonistic and courtship displays. Male cuttlefish have been observed using honest and deceptive signals simultaneously to fool a rival male. The male presented typical female patterns towards the rival, whilst presenting normal male patterns towards a receptive female. The rival was confused, providing the two-faced cuttlefish with an opportunity to mate. This example elucidates how cuttlefish decision-making used alongside their metachrosis capabilities can give them a selective advantage.

The mechanisms underpinning cephalopod metachrosis

Ironically, cephalopods are colour-blind! Somehow cephalopods interpret colour in the surrounding environment without using their eyes. Individual colour-changing cells are thought to be capable of detecting light and responding by altering colour expression independently. It is thought that light-detecting proteins (known as opsins) in cephalopod skin, which only differ from proteins in the eyes by a single amino acid, can detect the presence and wavelength of peripheral light and signal the brain. After processing this visual information, the brain responds with both hormonal and neuronal cues. These signal myriads of light-refraction-altering cells, with each puzzle piece integrating seamlessly to produce a cohesive and convincing disguise. These specialised cells alter wavelength by either light reflection or refraction:

Light reflection involves chromatophores. Described as biological pixels, these consist of radial muscle cells arranged around a pigment-containing electric sac. Following a neural impulse, these muscles contract to stretch out the central sac, spreading out the pigment molecules. This amplifies the expression of the pigment colours – reds, yellows, and browns. Reflector cells called leucophores scatter the full spectrum of light, producing white by similar mechanisms that produce the polar bear's fur colour. Leucophores match the light level of the surroundings, producing a backdrop that aids the appearance of patterns.

Light refraction works through the iridescent iridophores - cells which change colour as the angle of view changes. The layers of protein in these cells selectively reflect different wavelengths of light, due to differences in the refractive index between layers and the spaces separating them. From above these appear blue, but reflect red light if viewed from a more oblique angle. Mediated by neurohormones, or another diffusible cue, the position and orientation of these in a cell can change.

Different combinations of these substituent elements can alter wavelength collectively, individually, or not at all. Getting a pixel-by-pixel match would be impossible, nonetheless, cephalopods' well-developed cognitive and visual systems extract an approximation of their environment, and then use this to select a camouflage out of an in-built library of patterns. The camouflage does not have to be perfect – just sufficient to fool any potential predators.

Applications in research

The nervous and camouflage systems in cephalopods are highly interconnected. Cephalopod neural networks have long been favourable research targets, providing some of the earliest insights into the inner workings of the brain, with continued use in modern neuroscience. Cephalopod studies could provide a window into another form of intelligence – one possessed by animals whose lineage split from humans 540 million years ago.

A multitude of mysteries still confound cephalopod metachrosis and its association with their complex neuronal systems. Most recently, scientists have utilised the activity of chromatophores to give direct insight into the activity of cuttlefish motor neurones and visualise extensive populations of neurones in free-living animals. Future studies could help us define a more precise link between brain activity and behaviour (a field called neuroethology), or perhaps be utilised in the growing discipline of computational cognitive neuroscience.

A damaging partnership:

How does the climate crisis further enforce gender inequality?

Climate change might be far less gender-neutral than we thought.

Written by Azita Vatandost
Art by Rahel Kiss

The climate crisis, as universally felt as it is, unfortunately shows gestures of bias by targeting certain groups in society. As much as the climate crisis, through our general perspective, is the melting of the ice caps and the rising of the sea levels, it is also equally the enforcement of gender inequality. The interface between climate change and gender inequality is predominantly visible in low and middle-income countries as a result of cultural norms that support bigotry of men. Therefore, there is unequal opportunity in the accessibility of education, healthcare and employment.

The majority of the agricultural sector in developing countries is women, such as within the regions of Eastern Africa and South Asia. In particular, ⅔ of small-scale farming in South Asia is constituted by women. Women's heavy presence in agriculture and being subsistence farmers can be explained by how 75% of women are a part of the informal economy because of unequal employment rights. Consequently, to support their wellbeing and their family, they become increasingly more dependent on acquiring natural resources. In the instances of drought and fluctuating rainfall, there will be pressure for women to work more in order to obtain these necessary resources. Due to unpredictable weather conditions, food sources are threatened which in turn threatens the livelihoods of women.

We see natural disasters as genderless—they do not take place for the purpose of discrimination or at least, they shouldn't. However, the aftermath is regrettably sexist. Women are less likely to survive and seek out assistance after natural disasters because of pre-existing inequalities in social mobility that prevent their accessibility to disaster planning and evacuation response. To illustrate, the aftermath of the Indian Ocean tsunami in 2004 showed that 70% of deaths were women. With an increase in natural disasters by five-fold over 50 years, the disparity in deaths between men and women continues to amplify gender inequality.

Within extreme climate hazards, women's health is further threatened. Extreme heat can significantly increase the occurrence of still birth and the transmission of vector-borne illnesses. Meanwhile, displacement due to natural disasters limits pregnant women's right to receive sufficient aid to support pre and post-natal care. Ultimately, 68% of women were recorded to suffer adverse health effects out of 130 studies conducted.

But then again, climate change shouldn't cherry pick who needs to suffer more or less, it should not have to cause suffering: but, why does it?

It all boils down to policymakers in government. The gender balance or lack thereof in government is essentially a direct reflection of gender inequality enforced by the climate crisis. If we are unable to have a balance of gender in our respective governments across the globe, how are we meant to eliminate the adverse aftermath that climate change continues to cause? Across the world, 21% of women are government policymakers. In the EU alone, only 26.8% of policymakers for environment and sustainability are women. Thus, information on climate adaptation strategies are inevitably catered towards men, which can be seen in agriculture. This is prevalent in Uganda and Senegal where men have more awareness in the implementation of climate-smart agriculture. Therefore, having gender balance in government would potentially ensure that needs for all genders could be adequately met.

There is a dire need for policymakers to adopt more gender-responsive climate adaptation strategies to combat gender inequality. Could policies that focus on implementing briefings towards marginalized women affected by climate change become the next step?

WHY CAN'T WE POWER THE WORLD WITH BIOFUELS YET?

Written by Toma Ogawa *Art by Nirvan Marathe*

Biofuels are fuels made from living matter, and they are an important alternative to traditional fossil fuels. As fossil fuels contribute around 90% of global carbon dioxide emissions, there is a huge incentive to develop viable biofuels. The ideal biofuel must be close to carbon neutral, meaning that the gases released when the fuel is burned equal the gases absorbed in its production. To be able to replace fossil fuels, the biofuel must be energy-dense, producible in large volume and affordable. The potential of biofuels for creating a sustainable future is immense. So, why don't we have a reliable biofuel yet?

Over the years, researchers have come up with three generations of biofuels. The first-generation biofuels, ethanol, are produced from edible biomass like corn and sugarcane through fermentation by yeast. There is an interesting debate about the use of food crops for biofuel production. As discussed in the Green Alliance Report, the invasion of Ukraine has exacerbated concerns of worldwide undernourishment, making this debate even more important. According to the report, about 3.5 million people could be fed per year if the production of crop-based biofuels in the UK ceased. Second-generation biofuel solves this problem by using non-edible plant dry matter, known as lignocellulosic biomass.

The ingredients for these fuels are non-food crops and non-traditional commodities.

However, both first- and second-generation biofuels are not able to power aircrafts and heavy automobiles as they are less energy-dense and often get diluted by water. According to David Pimentel, an agricultural scientist, to produce 1 litre of ethanol by corn, you would require 6600 kcal of energy; this is highly inefficient considering that a litre of ethanol contains just 5130 kcal. This is essentially a negative energy process, so it could be argued that this is not a green technology. Furthermore, harvesting crops for an energy inefficient process wastes scarce resources, such as freshwater. Research by the University of Twente found that the water footprint of biomass production (m3/GJ) is approximately 72 times more than crude oil and 240 times more than solar. Ethanol comes with additional disadvantages. For instance, its corrosive properties mean it cannot be readily used in engines and is expensive to ship.

A more complicated form of alcohol has been sought as an alternative, such as butanol. Butanol, as a result of its longer carbon chain, wouldn't mix with water and is less corrosive. Producing large volumes of butanol is the limitation as yeast has long been adapted to produce ethanol. There are other organisms that produce more complex alcohol but only in small quantities.The challenge is to devise a method to equal ethanol production

The last form of biofuels, also known as third-generation biofuels, are produced from algal biomass. Chlorella vulgaris is a popular choice because of its high lipid composition of more than 40% and its fast rate of generation. Although some of these algae can be grown using saltwater or wastewater, it requires large amounts of water and energy to harvest the algae and extract lipids. Currently, algae-based fuel costs 300-2600 USD per barrel, which is significantly higher than petroleum. Despite the current limitations, biofuels have the potential to be the fuels of the future. Much more research is needed to make these fuels affordable and energy-dense. Every development in this field brings us a step closer to a world that can be powered by biofuels.

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