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by Christopher Little & Jo Flynn
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About
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EDITOR’S EPILOGUE
173 | Russell Crawford, Managing Editor of JADE
Before thanking our wonderful students, it is important to note the tremendous role that JADE has had in helping to establish this conference as a permanent option for our undergraduate students. As far as we can tell we are among the first undergraduate conferences to offer a direct route to publication and this would not be possible without the support and encouragement of Dr Russell Crawford who plays a key role in the selection of papers and putting this very journal together.

After its first successful year, JSLUG was essentially homeless. This is where the wonderful team in Keele’s Institute of Liberal Arts and Sciences (ILAS) stepped in. They saw how this could mirror their postgraduate conference offering and spoke to their values around the value of interdisciplinary conversations and rigorous research. Huge thanks, therefore, must go to Professor Jonathan Wastling, Pro-Vice Chancellor for Postgraduate Studies, Executive Dean for Natural Sciences and Director of ILAS. The conference simply wouldn’t happen without the hard work of Professor Wastling’s team of Jo Flynn, ILAS Manager, and Stephen Kilner, ILAS Coordinator. Huge thanks must go to ILAS for their vision, unending support and for giving this wonderful conference an equally wonderful home at Keele Hall.

The most significant thanks, however, must go to the inspirational and intellectual students of Keele. Every year my colleagues and I are blown away by the incredible professionalism and rigour of the presentations they deliver at JSLUG. As you will see, the abstracts, posters and papers that make up this edition of JADE are of an excellent quality, showcasing the students at Keele. They also represent the breadth of academic programs we have at Keele and show the interdisciplinary breadth of the JSLUG Conference hosted in June 2018.

In previous editions of JADE, I have waxed lyrical about the benefits of engaging with JSLUG. We have proven that students gain incredible confidence from presenting at and attending JSLUG. Additionally, we have shown that students presentation and research skills as well as their ability to conceptualise their own disciplinary identity. Crucially, we know that students who engage with JSLUG go on to become much more engaged students and are significantly more likely to go on to present at other external conferences during their undergraduate degrees. As you will see from the quality of the papers here, these quantum leaps in skills and communication are apparent for all to see.

I will keep these opening remarks brief but will take this final opportunity to highlight that JSLUG will return on Thursday 30 May 2019, so keep an eye on the ILAS website for details of information sessions and calls for abstracts. I hope you enjoy reading his edition of JADE as much as we have enjoyed compiling it and we’ll see you at JSLUG2019.
Oral Presentations

Temitayo Adeyemi, Pharmaceutical Science Technology and Business
Advancement of Regenerative Medicine and Tissue Engineering using Artificial Intelligence

Every day, hundreds of thousands of surgical procedures are performed to replace or repair tissues that have been damaged through disease or trauma. However, due to the limitations of these procedures, many patients are not promised a better quality of life after surgery. Regenerative Medicine (RM) promises to override these limitations and provide less invasive surgical procedures by aiding the body to heal itself. The three main strands of RM are: cell therapy, gene therapy and tissue engineering. This paper will discuss the various aspects of RM and investigate current medical adaptations of RM that is radically transforming modern medicine.

Leah Cooper, Midwifery
Vaginal Seeding: Is it worth it?

During vaginal delivery, exposure to normal vaginal flora has been well documented as imperative to the development of the neonate’s immune system and gut flora. However, with the UK Caesarean Section rate now at 26%, millions of infants are not introduced to these essential microorganisms during delivery. Attempting to mimic this, ‘vaginal seeding’ is becoming an increasingly new phenomenon, involving placing swabs in the vagina during Caesarean Section and then rubbing them onto the baby’s body. This presentation will collate the limited research to determine the benefits of ‘vaginal seeding’ and its comparison to the exposure achieved through vaginal delivery.

Kathryn Dickins, Chemistry and English
The Ethics of Discussing Eating Disorders in Literature

As eating disorders become more prevalent in society it is natural that their prevalence in literature would also increase, but to what extent? This presentation will examine the portrayal of eating disorders in narrative literature, and consider whether these portrayals may be construed as informative or instructive: further glamourising and fetishising these illnesses or providing useful and valid insights into what is often a poorly understood topic. This presentation will examine a range of texts from the last decade and determine how and if it is possible to write responsibly about this topic.

Ahmed Elkady, International Relations
The Spirit of Boycott: A Comparative Analysis between Anti-Apartheid Struggles

This article seeks to examine the Palestinian Boycott Divestment Sanctions movement, and how it relates in spirit and practical application to the South African Anti-Apartheid Movement, from which it claims inspiration and kinship. Historians have documented the important contributions of boycott activists, whose grass-roots initiatives helped build the moral consensus upon which governments rejected apartheid. Whether Palestinian efforts will be similarly successful is not immediately apparent. This article will explore the likely efficacy of the BDS movement by determining the contextual similarities and differences to the original anti-apartheid struggle. It is my hope that the article will not only tell us something meaningful about the necessary course of the Palestinian liberation movement, but also more generally about the character and spirit of organised action and morality-driven grass roots movements.

Luca Filippi, History with International Relations
Habemus Papam! A Short History of Papal Power and the Vatican City

With a population of less than 600 and easily circumnavigable in 40-minutes, the Vatican City may be small. However, the Pope is frequently described as one of the most powerful people in the world. Not only is he the supreme sovereign of the Vatican and the spiritual leader of one billion Catholics across the globe, the Pope is also a very important actor in international affairs and the office has played a very influential role in world history. This presentation will address the origins, sources, and influence of the Pope’s power on the global stage.

Raidah Gangji, Biomedical Science
Any hope for Alzheimer’s?

Approved treatment for Alzheimer’s disease currently revolves around treating symptoms and slowing progression of the neurodegenerative disease. The brain is a complex organ with the invested power of controlling the entire human body. A disease that effects the brain has detrimental effects not only on the patient but also family, friends and carers that are constantly with the patient. Therefore, to what extent is exploring and understanding a healthy brain function compared to Alzheimer’s disease brain is important for targeting next-generation drug therapies targeting cure disease instead of maintaining progression of disease.

Edward Hopkins, History
Personal Warfare: Paul von Lettow-Vorbeck and the First World War in East Africa

The First World War in East Africa is relatively unknown as a theatre of war. This is particularly the case in the career of Paul von Lettow-Vorbeck, who was essentially undefeated in the field and was the only German commander to invade British Imperial soil. This presentation will primarily consider the impact of his guerrilla campaign in east Africa on the course of WWI, as it necessitated the Entente powers sending thousands of troops from other fronts to deal with it. It will also consider the impact of this campaign on Africa itself as a colonial theatre of warfare.
Lucy Jones, Psychology
The effects of parental confidence of water and swimming on children’s behaviours during a swimming lesson

The purpose of this study was to determine whether there was an association between parental confidence and children’s behaviour during a swimming lesson. Children from the Hannah Jones Academy of Swimming were observed during their swimming lesson and parents completed a questionnaire concerning their levels of confidence towards water. Parents with higher levels of confidence were observed to have children with a higher swimming confidence score. A positive correlation was found between parental confidence and children’s positive behaviours. A negative non-significant correlation was found between children’s negative behaviours and parental confidence. No gender differences were found for children’s swimming confidence.

Rebekah Leftley, Biology
A Wolf in Sheep’s Clothing: Can Cells Recognise ‘Self’?

Our bodies are subjected to all kinds of environments which requires a complex system to defend us from whatever comes our way. Its common knowledge that the immune system plays this role, protecting us from harmful bacteria, toxins, and the like. The many thousands of white blood cells pumping through our bodies can effectively recognise ‘self’ and ‘non-self’, and then eliminate anything determined as potentially dangerous. This presentation will explore the fascinating techniques our bodies have to recognise when our own cells pose a threat, such as with viral infection and cancerous cells, and how this might be applied to modern medicine.

Robert Mannix, History with American studies
How is Russia’s territorial expansion and influence on other nations perceived from the end of the Second World War to the present day by Russia and its allies in comparison to NATO?

When contemplating the Soviet Union’s and Russia’s territorial expansion and influence on other nations there are two perspectives to be considered. The first being from the NATO point of view, whereby Russia is seen as an aggressive state and is seen as trying to gain as much land as possible and gain influential leverage on the captured land. The second perspective to be examined would be from the Russian viewpoint. By gaining land and influence to create a buffer of protection. I will be examining both perspectives and analysing the viewpoints of each.

Caroline Millett-spicer, Medicine
The Power of PowerPoint or PowerPointless in Education?

Originally designed to provide visuals for group presentations within business organisations PowerPoint has become so synonymous with briefings, assignments and lectures that death by PowerPoint has become a part of public, and student lexicon. However with increasing use in the delivery of education is a tool originally designed to be a visual aid for the presenter a good medium to deliver 3+ years of course material? This talk aims to discuss this question and discuss some faults and strengths of PowerPoint historically then present some ways for powerpoint use to be improved both in education and the wider work place.

Thomas Nelson, Liberal Arts and Sciences
Democratising Mass Media’s (final?) Secret Weapon: The Future of Grassroots Transmedia Storytelling

Since its emergence twelve years ago, ‘Transmedia storytelling’ - the practise of building fictional worlds across multiple media, telling multiple connected stories that contribute to a single narrative - has impacted all forms of communication, traditionally suited to creative practice or otherwise. The presentation will examine the grassroots scene that emerged with transmedia in its early days from an interdisciplinary perspective. Some argue this scene has recently declined for favour of larger, corporate efforts. The speaker will examine this issue, while drawing on case studies not limited to their own experiences conducting zero-budget transmedia to highlight possibilities for the future.

Harry Nevard, History
The Lost Vikings: Disappearance of the Greenlandic Norse in the 15th Century

Greenland: an unforgiving arctic island of striking black earth and white ice. It features some of the world’s most inhospitable conditions and ranks high for bleak weather. Nevertheless, it was home to one of the most remote European settlements for over 500 years. In 1721, missionary Hans Egede travelled north to convert the long-isolated settlers to Protestantism. However, there was nothing left but ruins. Egede questioned, ‘Were they destroyed by an invasion of the natives … [or] perished by the inclemency of the climate, and the sterility of the soil?’. This presentation will attempt to answer his question.

Rebecca Pierce, History
Hidden Lesbianism? Why female homosexuality was never criminalised in Britain

The year 2017 marked the 50th anniversary of the Sexual Offences Act, which partially decriminalised homosexuality in Britain. This act, however, only decriminalised male homosexual activities, for female same-sex relations were never unlawful. Male-male sex was considered a criminal offense in England for over 500 years, so why then were women never legally targeted? Past explanations have hinged on the incorrect assumption that society was entirely oblivious to female-on-female sex. This presentation will dispel the myth that all lesbian activity occurred behind tightly locked doors, whilst also questioning how women were still able to largely avoid legal persecution.
Encryption in today’s society

Our ever-evolving technological world is a topic that is often discussed in the media. One aspect that is continually overlooked in articles about terror attacks and the like, is how these attacks are coordinated and managed secretly. Encryption plays a major role in our every day life, from protecting login information to secure messaging. I would like to briefly delve into what encryption is, and how it is used on a day-to-day basis in our communications and interactions with technology. I will also touch on how encryption prevents challenges with respect to gathering intelligence; and how this affects anti-terrorism objectives.

Olu Ijiitimihin, Law
Understanding The Child Protection Law and Its Difficulties

Child Law is the principal vehicle for protecting children. The child law is contained in the Children Act 1989 which was amended by the Children Act 2004, and was later amended by the Child Care Act 2006. After the child protection policy, an important theme was created from the Children Act 1989.

The act promoted cooperation between parents and local authorities in order for them to work together to achieve anything that is in the best interest of the child. The Child Protection Law was created to prevent child abuse and to sanction anyone that abuses a child.
US along with a historical study of previous monetary cycles; finally through financial modelling, scenario analysis will be conducted to get a feel of how high and quick rates can be raised.

**Poster Presentations**

**Nma-EIIEta Abdul-Obitayo, Chemistry and Physics**

*Healing and harming: metallic compounds in medicine*

When one thinks of a metal, one’s first thought may be a block of shiny silver solid, and one certainly would not think it edible. However, my presentation wishes to challenge this perception and demonstrate that at a molecular scale metals come in many shapes and types, allowing them to affect the body in fascinating ways. These vary from chelating agents and pioneering anti-cancer platinum complexes to deadly dimethylmercury. I take inspiration from a similar topic taught in Year 2 Inorganic Chemistry but include more of the compounds’ biological effects, and current research in this area.

**Danielle An’Mai, Adult Nursing**

*Let’s All Go to the Emergency Department! A time for empowerment and intervention*

As patient volume exceeds capacity in busy Emergency Departments (EDs), congestion ensues creating crowded conditions. This does not make for comfortable viewing. Extended waits combined with stress levels can aggravate bodies already impacted by illness or injury. There are no rest stops for resolution as 2016/17 saw 23.4 million attendances to the ED; an average of 63,000 per day (King’s Fund, 2017). Incidentally, the NHS Mandate on the four-hour standard has not been met nationally since 2013/14 (Op cit., 2017). Multi-factorial dilemmas require multifaceted solutions. This is a global issue. This is huge. A change in tack is a necessity.

**Laura Brennan, Psychology and Sociology**

*Becoming you’re worth it? Consumption of cosmetics and identity*

For many, wearing makeup is part of a daily routine. However, use of makeup carries negative perceptions, including associations with vanity, arrogance or insecurity. Through thematic analysis of interviews, this presentation will discuss the complex and sometimes contradictory ways in which young adults view makeup and their motivations for using it. Preliminary findings suggest that participants use makeup to present themselves as competent in social or professional situations, to “make an effort” as a crucial part of their feminine identity, and to compensate for negative feelings. Therefore, highlighting important ways in which makeup use relates to self-confidence, identity, and well-being.

**Kathryn Dickins, Chemistry and English**

*Transuranium Elements: Past, Present, Future*

Transuranium elements rarely make headlines. Decades on from the Manhattan project and the opening of the world’s first nuclear reactor, what else has research into transuranic elements contributed to both the world and to science as a whole? From Glenn Seaborg to the recently discovered Nihonium, Moscovium, Tennessine and Oganesson, and the work that is being done to progress further up the shores of the island of stability, this literature review will consider the advancements that have been made in the field of nuclear chemistry leading us up to the present day and consider the future of this fascinating field.

**Christos Evangelides, Applied Environmental Science and Physical Geography**

*Post-fire regeneration assessment in Cyprus: A case study in Evironchou*

Post-fire revegetation dynamics were ascertained using Remote Sensing and GIS techniques for a big fire event in Cyprus in 2016. This was the first post-fire study to be conducted in Cyprus and focused on producing severity maps based on the NDVI and a DEM to investigate topographical parameters (aspect, slope steepness). The results have shown a progressive increase in the vegetation index indicating the improvement in vegetation health, that vegetation recovered mostly during spring and on north-facing and less steep slopes. Lastly, the study highlighted the ability to conduct a rapid and cost-effective post-fire assessment.

**Mairead Hampton, Mental Health Nursing**

*The experiences of second year pre registration Mental Health Nursing students taking part in KUF*

Current prevalence of personality disorder is believed to be 5-13% (ONS 2000), with inpatient populations estimated at 15-40% (Westwood and Baker 2010). The knowledge and understanding framework commissioned by Departments of Health and Justice aim to support greater effectiveness in working with this client group. In the second year, part of the undergraduate syllabus is to undertake the three day nationally accredited course, a component not provided in every university.

The purpose of the study is to explore student perspectives of the KUF including changes to knowledge and attitudes and gather information on the subjective experience of completing the course.

**Hazel Meades, Music technology and Psychology**

*Music Therapy and Autism: Techniques and Outcomes*

Music therapy was developed after world war 2 by French cellist Juliet Alvin. Initially used to assist the mental and physical recovery of hospitalised soldiers, the field has progressed considerably, enabling a variety of techniques to be applied to clients through a person-centred framework. Although music therapy is well known for its positive effects on dementia patients, studies have
investigated using music therapy with autistic individuals. This presentation explores the work of music therapy with autistic children and provides an overview of common approaches, based on interviews with music therapists, parents of autistic children and a literature review.

Gracious Mupfuuri, Brian Tangara & Temitayo Adeyemi, Pharmaceutical Science Technology and Business

Treating Amyotrophic Lateral Sclerosis

Amyotrophic Lateral Sclerosis (ALS) is a progressive neurodegenerative disease that is caused by gradual deterioration and death of motor neurons in the brain and the spinal cord. Motor neurons are cells that extend from the brain to the spinal cord and to muscles throughout the body.

With voluntary muscle action progressively affected, ALS patients may lose the ability to speak, eat, move and breathe. Riluzole is the only drug that has been shown to extend survival. This paper will explore the pathophysiology of ALS and the on-going pharmaceutical discoveries that could be used to inhibit it’s neurodegenerative pathways.

Cristal Collado Rojas, Biochemistry and Human Biology

Cancer: Origins, hallmarks and implications for treatment

Cancer is a collection of over 100 related diseases and is a leading cause of morbidity and mortality worldwide. All cancers arise from a single cell and ultimately result in increased cell divisions, thereby leading to the development and formation of tumours. Cancer is complex and heterogeneous, which suggests that finding a single cure is very unlikely. Advances in our understanding of cancer have allowed the development of current local and systemic approaches to therapy, however, there are several implications that hinder the efficacy of treatment. Perhaps, the focus should be shifted towards understanding cancer first, rather than treating cancer.

Madeleine Shackleton, Midwifery

Saving babies’ lives: Why are parents putting babies in boxes?

For the past 75 years, the Finnish government have given new parents ‘baby boxes’, which can be used as a bed and contain sheets, clothes and toys. Many people believe this scheme has contributed to Finland having one of the lowest infant mortality rates in the world. Education surrounding prevention of cot death is given to each family postnatally, yet 250 babies and toddlers still die in the UK each year. With the scheme currently piloting in certain areas of the UK, this study will analyse whether the lower infant mortality rate is due to the boxes or better parenting education.

Henry Simpson, Physical Geography with Biology

The Battle of Habbaniya 1941

The Battle of Habbaniya in May 1941 saw the repelling of the Iraqi army’s siege of RAF Habbaniya. It was accomplished by the largely obsolete aircraft of an underprepared and overstretched force and is undoubtedly one of the most unsung chapters of the Second World War. This presentation will look at the battle which proved decisive not just for the war in Iraq, but also for Axis designs on the Middle East and North Africa with implications throughout the European theatre. It will also explore why the significance of this vital action became so lost in the annals of war.

Sabah Sirajuddin, Medicine

Immunity and Ageing

Immune Risk Phenotype (IRP) is defined by poor T-cell proliferation, low B-lymphocytes and an inverted CD4:CD8 ratio, potentially predicting morbidity and mortality. The project aims to understand the ageing immune system. IRP is associated with killer-cell immunoglobulin-like receptors (KIR) and is enhanced by cytomegalovirus. 25 blood samples underwent immunophenotyping, involving blood isolation, cell-count and fluorescent-activated cell sorting. Serology and DNA extraction were performed for KIR evaluation. Naïve T-cells, CD8 effector memory T-cells and CD28- immunosenescent markers were significantly affected with ageing. Further analyses were unable to define a trend, however this data collection is a part of a wider study.

Ryan Stanyard, Neuroscience and Psychology

Assessing the Utility of Hydrogels for Neural Stem Cell Transplantation Therapy

Hydrogels are pragmatic biomaterials with growing potential for neural stem cell transplantation therapies. As a result of decades of disease model research and in vitro studies, biogels and synthetic gels are being produced which may offer therapeutic efficacy in facilitating neural stem cell growth, enabling neuronal repair in cases of disease and injury (e.g. spinal injury). Successful models would offer a transformational transplant tool for patients, but crucially, potential commercial gels must be scrutinised to ensure long-term patient benefit, tolerance, and toxicity. This research assesses whether a series of bio and synthetic gels are suitable candidates for further therapeutic testing.

Pamela Sturges & Thomas Bestwick, Medicine

Primary care in Primary schools

With very little emphasis on lifestyle choices and their health consequences in the primary school curriculum, The Junior Health Society (JHS) was created with the aim to be a preventative intervention. Our interactive stations cover topics including: dementia, disabilities, exercise, obesity, long-term conditions, alcohol and smoking. This project has now been running for six months having reached over 350 students. With over a quarter of children aged 2-10 years being overweight or obese, it is imperative
to create a positive behaviour change to prevent further co-morbidities. The JHS is a unique scheme reaching a large community to do just this.

Brian Tangara, Neuroscience
Investigating the clinical utility of allosteric inhibitor VP 0.7 to GSK 3 in neurogenesis from Neural Stem Cells (NSCs)

Glycogen Synthase Kinase-3 (GSK-3), is a protein kinase expressed in all tissues and a regulator of diverse cellular functions. Aberrant GSK-3 participation in many signalling pathways has been implicated in several neurodegenerative diseases that have driven research to focus on identifying prospective therapeutics using GSK-3 inhibitors. Allosteric inhibitors are very specific and remotely modify orthosteric binding sites of a biological target. Using VP 0.7 on GSK 3, we reveal promotion of neuronal differentiation from NSCs which can be transplanted into neurodegenerative brains. This can shift the balance from neurodegeneration to neurogenesis and neuronal plasticity in disease such as Alzheimer’s.

UNDERGRADUATE POSTER URLs

History

On 23rd January 1912 the first international drug treaty was signed. This was a treaty signed in The Hague in the province of South Holland banning Opium. This was the first national banning of a substance, and was the first step towards what is now commonly referred to as The War on Drugs. Its mission was to create a drug free world. The term War on Drugs was only officially used in 1971 when Richard Nixon declared the term in a hard line project to get rid of drug use in America. Since 1912 there have been many further acts to restrict drug usage, the most notable in the UK being the 1964, 1971, and 2016 Acts.

Since 1964 literally trillions of dollars worldwide have been spent on this war, but it has done anything but end drug usage. The War on Drugs is the main cause of creating the largest illegal commodity market in history; in fact, some estimates put the value of the illegal drug market at between $400 and $600 billion (May, C 2017). The prohibition of drugs has been implemented in the USA and to begin with the consumption alcohol usage fell to an estimated 30% of its previous level. However over the next few years it grew sharply to around 60-70% and by the end of prohibition it was virtually the same level as pre-prohibition (Miron, J & Zwiebel, J. 1991).

Prohibition also led to the rise of gangs and corruption in the police force. We know that prohibition does not work; we know that banning alcohol does not stop the consumption of alcohol so why should we think it would work for other drugs.

Why prohibition will never work

We know that prohibition does not work. In the 1920’s and early 30’s prohibition was implemented in the USA and to begin with the consumption alcohol usage fell to an estimated 30% of its previous level. However over the next few years it grew sharply to around 60-70% and by the end of prohibition it was virtually the same level as pre-prohibition (Miron, J & Zwiebel, J. 1991).

The way in which the War on Drugs has been implemented bears striking resemblance to the failed prohibition in 1920’s and ignores the basic economics of demand and supply. The War on Drugs has tried to get rid of the sourcing and trafficking and sale of drugs, however they have done very little to reduce the demand for drugs. If you attempt to reduce drug supply without attempting to reduce demand, prices will rise. This may reduce the demand for some products but not for drugs, because drugs are not price sensitive, people will consume drugs no matter the price. Therefore, the war on drugs pushes prices up but does not reduce demand. This incentivises production of more drugs and employment of more traffickers as there is higher profit margins. Furthermore, shutting down drug producers does not stop production; it just ends up moving it to a new location. This is called the balloon effect.

We know all this is true because of Crystal Meth. The US attempted to reduce the supply of Crystal Meth by regulating chemicals commonly used its production; these were products that contained ephedrine, pseudoephedrine, or phencyclidine. However production did not fall. What happened was that many large scale Meth producers in the US went out of business, and Meth producers in Mexico took over and simply transported it across the border. Also since this “war” began many street dealers have been arrested, between 35,000 to 45,000 traffickers each year (EMCDDA 2013), and even large scale productions have been closed down, yet it has never been easier to get illegal drugs, more proof of the balloon effect.

Our understanding of addiction is flawed

Our understanding of addiction mainly refers back to tests performed in the 1960’s. In the 1960s, researchers at the University of Michigan created devices that allowed rats to self-administer drugs by pressing a lever. (Woods, J. H, 1978), How the test is done is that you put a rat in a metal cage and then teach the rat to press a lever to receive heroin or morphine.

Given the choice between fresh water and heroin the rat will get addicted and will overdose and die. This was used as evidence that human will be the same and we must ban the usage of heroin and other similar opioids in order to protect people from becoming addicts as heroin was uncontrollably addictive.

However, in the 1970’s Bruce Alexander noticed that the rats used in this experiment were in the cage alone, sometimes in very small metal cages called Skinner Boxes. The rats had no stimulation or social interactions, and so the rat has nothing else to do but to take the drugs. So he decided that instead he would create a new experiment; he built Rat Park. Rat Park was a place where many rats would live and have pipes to climb through, coloured balls to play with and have many other rats to socialise with. The amazing thing was that “the rats living in Rat Park had little appetite for [heroin]” (Alexander, B. 2012), and no rats overdosed on it, this was because they were in a happy and healthy environment; they were able to bond with others. The rats had no need for heroin, as they were no longer isolated they chose interaction instead of heroin.

Of course rats and humans are different; it would be folly to claim results from rat tests would be identical to human. To make any
claims about the effects of addiction on humans we require a human version of Rat Park. And we have one; it was called the Vietnam War. During the war nearly 20% or 1/5 of troops were addicted to heroin. “35% of army enlisted men actually tried heroin while in Vietnam, and 19% became addicted” (Robins, L et al 2010). It was feared that after the war ended there would be an army of heroin junkies returning back home. However, when the war ended, the troops were monitored and “only 5% of them became re-addicted to heroin” (Clear, J 2018) hardly any of them continued using, and they did not even suffer from withdrawal symptoms.

If we follow the standard view on addiction then this would make no sense, the old rat studies found that heroin is uncontrollably addictive, how is it possible that after leaving the war almost all soldiers gave up heroin, after all 90% of people in the US that go to rehab for heroin addiction will relapse. However, if you follow Bruce Alexander and Rat Park experiment then it makes perfect sense. They left the distressing conditions of war and went back to their nice houses with their family and friends. They went from the equivalent of the Skinner Boxes into a human version of Rat Park. “In both [rats and people], the drug only becomes irresistible when the opportunity for normal social existence is destroyed.” (Alexander, B. 2010).

Our current War on drugs has failed, it had led to huge numbers of young people being arrested for simple possession, their actions were not going to harm anyone, yet they now have a criminal record. We arrest people with drug problems and put them in literal cages. In America alone “there are 207,847 people incarcerated in federal prisons. Roughly half (48.6%) are in for drug offenses…. There are 1,358,875 people in state prisons. Of them, 16% have a drug crime as their most serious offense” (Roeder, O. 2015). This is over 320,000 people in jail for non-violent drug related offenses. In the UK 15% of all people in prison are in prison for drug related offences (Allen, G. Watson, C. 2017).

After they are released we make it harder for them to get certain jobs and harder to reconnect with society and just expect them to stop taking drugs when they are physically excluded from society, we take away benefits if we find them with drugs, we make it harder for them to find housing and give them harsher sentencing for further crimes. The War on Drugs actively ruins the lives of people with addiction problems. These are people who have never raped, murdered, or abused anyone.

Our current system takes those with a drug addiction problem and puts them in cages and tells them they are criminals instead of helping to rehabilitate them. We are taking away their chances to live a clean life.

Why many drug users do not get help

The main issue that we have with the war on drugs is that it actively stops people with drug problems from getting help. If you are addicted to a substance, which the law says that by using it you are a criminal, you are going to be less likely to want go and get help because of the fear of arrest. But if you are addicted to a drug in a country where they assist people with drug addictions then people are more likely to get help as they know they will not get arrested and can receive treatment.

We can also easily fund this softer approach to drug laws. We spend about £16bn each year fighting this war on drugs (Politics.co.uk 2009), would not that be better invested in our NHS by helping people with drug addictions rather than hindering them. People that are addicted to drugs should never be treated as criminals, drug addicts need help, they do not need prison cells.

People who are sentenced to prison find it incredibly hard to find a job as “only around a quarter (26.5%) of prisoners enter employment after release” (Kirstie B. 2017). This is because many employers commit illegal acts of discrimination against felons as even though employers are not allowed to refuse jobs to convicted felons who have served their sentence.1 “A YouGov survey commissioned by the Department for Work and Pensions in 2016 found that 50% of employers would not consider employing an ex-offender, regardless of the offence or sentence received” (Kirstie B. 2017). People coming out of prison find it extremely hard to find a job; we take away benefits from them if they are caught with drugs. Due to this they will return to drugs as a destructive coping mechanism and so are very likely to reoffend. Instead of arresting those with drug addictions we should be helping them to get clean, get a job, and get a safe place to live.

A different approach to drugs

We need a different approach, the old system has incarcerated hundreds of thousands of people worldwide, had not reduce drug usage and has failed its objectives. Countries that have a hard war on drugs have high rates of overdoses and drug related crimes The US, the leaders of the War on Drugs also leads the world as having the highest rate of Overdoses in the world, 245.8 Overdoses per million inhabitants, Germany and England account for over half of all drug overdoses in Europe (EMCDDA. 2017).

In 2000, 1 in every 100 (or 1%) of Portugal’s population were addicted to heroin (Ferreira, S. 2017). Portugal had tried to follow what the US had done, having a hard war on drugs, increasing punishments

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1. With the exception of jobs which require a DBS check.
for possession and selling drugs, more officers tracking down drug dealers and generally reducing peoples freedoms. However, in 2001 the government had had enough and put together a panel of experts derive a new plan; the political parties agreed they would do whatever the panel suggested. The panel’s response? End the War on Drugs, decriminalise possession, and all the money that was being spent on the war to be put into providing treatment for drug addicts.

This radical new plan was put into place to exchange prisons with rehab for addicts, a softer approach, and it worked. Since 2001 drug usage of drugs from weed to heroin among teenagers and adults has fallen. Since decriminalisation HIV rates among heroin users fallen, the amount of overdoses has fallen to one of the lowest in the EU and the people that are suffering from addiction are getting treatment and rehab all paid for with the money that Portugal was spending on the War On Drugs (EMCDDA 2017).

Switzerland had a similar problem in the 1980s with heroin usage and HIV rates among users were rising. In response they opened up free heroin maintenance centres where they would be given clean needles, high quality heroin, and medical supervision on site (Citizens Opposing Prohibition, 2018). This has led to a huge decrease in heroin overdoses, HIV rates among users has fallen, and crime rates have fallen 60% among users.

Legalising weed in America has had similar results. Scientific America reported that after legalisation in Colorado, marijuana usage fell among teenagers; other US states have experienced no increase post legalisation. (Gorman, S and Craft, D. 2015).

Countries that are moving away from punishment and moving towards, decriminalisation, regulated legalisation, and harm reduction have lower rates of overdoses, lower HIV rates and lower rates of drug related crime.

So there are methods of reducing drug problems that are not only cheaper, but actually do work instead of just creating more problems, drug prohibition has led to hundreds of thousands of innocent citizens in prison and makes it harder for drug addicts to get clean.

After 40 years of the War on Drugs it is time to finally end the war on drugs and move onto something better. We need to change our society to feel a lot more like Rat Park, and a lot less like a Skinner Box.

Bibliography


In 2003, media analyst Henry Jenkins published an essay in MIT’s ‘Technology Review’ (Jenkins, 2003) in which he coined the term ‘transmedia storytelling’ to describe a newly emerging technique being used to communicate mass media entertainment narratives at the time. In his 2008 book ‘Convergence Culture: Where Old and New Media Collide’ (Jenkins, 2008), he put these techniques into the wider context of our culture, and elaborated on them. Since then, transmedia has been used by a wide variety of franchises, and in a wide range of contexts very successfully. Notable examples of its success include the ratification of the credit ‘transmedia producer’ by the Producers’ Guild of America (Anon, 2010). This was the first occasion in its history that the Producers’ Guild had ratified a new credit. Jenkins’ book describes how transmedia, alongside other features of a convergence culture may be read into movements in politics, religion, entertainment and education.

Although it is a system hailed for its capacity to evoke participation, this capacity is innately one-sided and determined almost exclusively by the media producer. On the other side of this issue, the grassroots communities transmedia projects are designed to exploit could benefit greatly from understanding these tools— for example cross-media arts collaboration, conversion rates, and examples of the uses of transmedia in education and training—that appear to have been reserved almost exclusively for media professionals. From increasing participation in democracy, to building local community initiatives, this term ‘transmedia’ is little-known among the people for whom the collections of artefacts it describes are intended. Therefore, this field—originally hailed as a democratising influence—could greatly benefit from further democratisation.

‘Transmedia storytelling’ describes the process whereby an ‘influencer’ takes a story, or multitude of stories that occur within the same ‘universe’, and tells them across multiple media, playing each medium or delivery method to its own unique strengths. Key examples of transmedia include the Marvel Studios ‘Avengers’ franchise, (Whedon, 2012) and ‘The Matrix’ (Wachowski and Wachowski, 1999).

Screenwriter Houston Howard notes that entertainment companies will pay much greater sums for scripts that make use of transmedia (Howard, 2017), and have occasionally been known to pay for transmedia world-concepts that do not even have completed scripts associated with them.

Transmedia franchises vary from traditional franchising in a few key ways. Firstly, there’s more than just one ‘story’. Undergraduate Article #2

Title
Democratising Mass Media's (Final?) Secret Weapon: The Future of Grassroots Transmedia Storytelling

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Key words
Transmedia storytelling; grassroots activism; interdisciplinary arts.

Abstract
Since its emergence in the first years of this millennium, Transmedia storytelling—the practice of building fictional worlds across multiple media, telling multiple connected stories that contribute to a single narrative—has impacted all forms of communication, traditionally suited to creative practice or otherwise. Some argue that the art scene that sprung up around this practice in its early years has declined for favour of larger, corporate efforts. The paper will examine this issue in relation to recent concepts in politics such as Bond and Evely’s ‘Big Organising’ and Monbiot’s ‘Politics of Belonging’. The paper draws on the writer’s own work conducting zero budget transmedia to propose a model for an amateur art collective that approaches the issues raised.


In 2003, media analyst Henry Jenkins published an essay in MIT’s ‘Technology Review’ (Jenkins, 2003) in which he coined the term ‘transmedia storytelling’ to describe a newly emerging technique being used to communicate mass media entertainment narratives at the time. In his 2008 book ‘Convergence Culture: Where Old and New Media Collide’ (Jenkins, 2008), he put these techniques into the wider context of our culture, and elaborated on them. Since then, transmedia has been used by a wide variety of franchises, and in a wide range of contexts very successfully. Notable examples of its success include the ratification of the credit ‘transmedia producer’ by the Producers’ Guild of America (Anon, 2010). This was the first occasion in its history that the Producers’ Guild had ratified a new credit. Jenkins’ book describes how transmedia, alongside other features of a convergence culture may be read into movements in politics, religion, entertainment and education.

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Transmedia franchises vary from traditional franchising in a few key ways. Firstly, there’s more than just one ‘story’.
There’s one ‘world’ or ‘event’ with numerous stories in that world. Secondly, participation is encouraged. Playing games with a strong reliance on narrative, attending real-life events, and commenting on online content is encouraged, and often rewarded with further instalments of the story. What would have been a simple trip to the cinema, or evening ‘binge’ a TV series becomes a unique and lasting participatory experience that rewards curiosity.

It is clear to see, therefore that consuming transmedia storytelling places a range of new demands on its audience, and as such, it is very much a product of the wider convergence culture in which we find ourselves, according to Jenkins.

As the roles of media producer and media consumer converge as fan-like behaviour becomes more widely accepted within society, and online platforms such as YouTube facilitate the broadcasting of grassroots-created content to over a billion users monthly (YouTube, 2018) so too do grassroots communities gain access to greater tools with which to communicate, though as will be explained later, this has not been observed to be the case with transmedia.

Using transmedia as a more general philosophy may bring one to some intriguing conclusions. Jenkins notes similarities between the communication of religion, and political campaigns and the transmedia model.

This was mirrored in a talk by writer George Monbiot at Keele University (Monbiot, 2018), who proposed that to enact political change an understanding of political movements as narratives played out across all available media could be beneficial. Monbiot proposed that a narrative of localism and grassroots collaboration could be successful in facing the challenges faced by today’s society. When taking questions, Monbiot indicated that while he was aware that the role of connectivity technology in political narratives is very likely to increase in significance for anyone attempting to take advantage of, or research this theory, he himself had not pursued that angle. It seems intuitive therefore to analyse his ideas according to transmedia, due to the pervasive, immersive, and participatory nature of political media.

If a voter hears about a political figure in a news story, in a world designed ideally for that political figure, that political figure will know and control exactly what media text will follow what, according to the private opinions held by each individual voter, to best win each voter around to their point of view. Such a system would, by the very nature of our society feature many different media, and many different narratives all contributing towards a single ‘world’; the life of this single political figure. Its hypothetical adaptability (which is of course the key impossible element of this thought experiment) would be the participatory element of the transmedia—the uniqueness of each individual’s experience of politics would require this.

Perhaps fortunately however, this thought experiment is so far impossible. The individual’s experience of each political figure is determined by so many influences that it would be impossible for any campaign manager to achieve this for even a single voter. However, this does not prevent the model from being at least in part applicable, especially when one draws on one of Monbiot’s central sources.

In Bond and Exely’s ‘Rules for Revolutionaries’ (Bond and Exely, 2016), the writers describe their process regarding the rallying of volunteers as a substitute for a trained campaign team while they managed Bernie Sanders’ campaign in 2016. Sanders’ campaign was hailed at the time for its then-unique approach to grassroots organisng (Gambino and Jacobs, 2015). He then went on to further argue the case for attempts by grassroots groups and community initiatives to bear more influence on our wider society, in and through, but also beyond politics.

It should be noted that engagement in such transmedia campaigns will likely be the only political contact experienced by many voters. Although a campaign may have measures in place to simulate the impression of a conversation, they by no means equate to such a conversation. By contrast, Bond and Exely’s concept of ‘Big Organising’ does generate genuine conversation, but additionally it requires grassroots communities to direct transmedia, or at the very least a transmedia-like system.

So, we see that there is a need for transmedia to be more widely understood and practised beyond the mass media circles in which it is currently practised. As objects, advertisements, films, and television become increasingly deliberately placed in relation to each other, so grows the need for the average citizen to be somehow literate in the techniques that govern this deliberation if there is to be a rise in participation in local community enterprises or initiatives utilising these techniques.

So, specifically, there is a need for grassroots-created transmedia.

On her blog, author and transmedia producer Andrea Phillips (Phillips, 2016) writes that the grassroots transmedia scene has recently declined, almost out of existence. In response to this, Caitlin Burns of a similar profession proposed that this was because “People simply no longer need a term to describe experimenting with multiple platforms creatively the same way they did 10 years ago.”
This writer would propose that while this may be the case for the people Burns most readily associates with requiring use and understanding of the term, this is not the case for the groups of people who, perhaps unknowingly require use and understanding of the term for very different reasons, in very different new and emerging contexts. Due to what Burns describes as the term’s ‘niche’ nature, it is highly unlikely that these groups overlap in any significant manner.

One method for the understanding of transmedia to increase within grassroots communities would be for it to be practised for personal enjoyment by individuals within such communities, and shared and interacted with by others in those communities. These could be the geographically local communities as Monbiot describes, or online niche communities.

This writer’s own project ‘Phomestory’ (Nelson, 2017) is an example of one such project. Completed as part of an extended research project at sixth form level, it is proof that an amateur with minimal training or understanding of transmedia can, with no funding of any sort complete a transmedia franchise and successfully entertain a handful of friends, though even then the breadth of expertise, as well as the time commitment required for such an undertaking is not accessible for most.

The goal of ‘Phome’ was to prove that zero-budget transmedia is feasible. Corners were cut at every opportunity to allow the project to be completed within a very strict time limit before the complete lack of budget was taken into account. These restrictions proved highly exacting, both on the creator’s skills, and on the quality of the final product, though as the final product was primarily consumed by friends who had been involved in its creation the audience was, to an extent aware of this and as such made allowances that would not necessarily be afforded by the wider public.

In 2013, Will Coldwell wrote in the Guardian newspaper that ‘The role of the graduate collective is now being played by the student one’ (Coldwell, 2013) in relation to a growing scene of young, student art collectives. Towards the end of June 2017, in the wake of completing ‘Phome’, this writer and between two and six other collaborators began an art collective in this vein. Although similar in the eventual goal of leading to or encouraging the growth of or progression into a sustainable creative career, this collective differed, and continues to differ in a myriad of other ways, most of which have arisen from favouring the research that contributed towards this paper over convention.

‘Unredacted Productions’ (Nelson et al, 2018) was intended as a ‘sandbox’ through which members could distribute their current work in a manner akin to how a small independent record label might publish the work of musicians, to produce an ongoing document of each member’s abilities, and progression in their respective crafts. Music composition is the best represented discipline among members of the group, and so music has become the central focus of the group’s output, although visual art, short films or animation, and pieces of creative writing are often published in conjunction with these musical releases.

This cross-media collaboration is not just encouraged, but necessary to the survival of the collective. Though capable of running smoothly on a zero budget the collective does have a few minimal expenses which are paid through the revenue acquired when the collective collaborates internally. At most three times a year every member of the collective is asked to contribute towards a compilation release. The artists do not receive any compensation for these contributions, as they act as a substitute for membership fees; in effect, membership fees are paid with work rather than with money.

This cross-media collaboration contributes in turn to a wider transmedia story world. Each compilation serves as a chapter in said story world. This model serves to encourage collaboration and productivity by enforcing both as a requirement of membership. For example: for the online domain to remain registered, the story world must continue, and the artists must continue to produce material.

This model is intended to act as an incentive for artistic development, and features transmedia both as a supportive mechanism for this, and of course as an additional marketing tool.

Now a year old, ‘Unredacted Productions’ is not a perfect experiment, nor has it by any means concluded. Insufficient data exists regarding its activities to draw any empirical conclusions regarding its effectiveness in terms of attracting impressions or financial gain, though success may be judged qualitatively according to the activity level of members relating to upcoming output: to gauge the success of the model one need only measure the continued existence of the enterprise as an online entity. If it continues to exist due to its initially planned business model, the enterprise may be regarded as successful as it is serving its purpose as an ongoing document. If a member chooses to become inactive, but substitutes their regular contributions for a small payment, the enterprise may be regarded as successful, as it is clear that they value the document they created and wish to see it sustained. As the collective heads towards its second summer, the designing of a new website, among continued activity on social media can only indicate success according to its original criteria. Since becoming acquainted with Monbiot’s work
however, the potential for this collective model to assist in the formation of his ‘politics of belonging’ has become increasingly clear. ‘Unredacted Productions’ is a potentially repeatable model. It requires next to no financial investment, and the only thing that differs between ‘Unredacted’ artists and any others is the drive to publish, and to improve at their respective art forms through collaboration; other than this, artistic practise has continued as it would have done otherwise. Members are connected by geography, and the nature of their collaboration can only eventually result in a raised awareness of transmedia within geographically local/similarly niche grassroots communities. Additionally, the model is not a complete plan - there is a lot of freedom to be had with much of the rest of a hypothetical group’s operation that may be determined by such a group's membership according to their unique aims or abilities.

For little over ten years, transmedia has served as a buzzword, and a creative ‘Wild West’ for those aware of its existence. As utilising the capabilities of the ‘grassroots’ becomes more significant to influencers of all descriptions, so grows the need for our culture’s grassroots to be privy to the techniques used by the people that aim to sway them, and to make use of these techniques in their own work. This paper’s proposed model for an arts collective is one possible way of increasing this ‘transmedia literacy’ among such communities, as it draws on the same ‘politics of belonging’ that Monbiot suggests may be entailed by the very movements such communities, as it draws on the same ‘politics of belonging’ that Monbiot suggests may be entailed by the very movements that are bringing about the requirement for transmedia initially, and relies on minimal changes to a hobbyist’s current mode of practise. Convergence culture has brought media consumers and producers closer together than ever before, increased media literacy, and democratised paradigms that were once reserved for a very select group of corporate entities. But still this flagship array of creative potential remains little known to non-specialists. This paper has argued that for this to cease to be the case could be beneficial to communities of all descriptions, and therefore to society more broadly. It is proposed to the grassroots communities of today—be they local or digital—that they democratise mass media’s final ‘secret weapon’.

References


Introduction

Drowning is one of the most frequent causes of injury-related death in children across the globe (Brenner, Saluja & Smith, 2003). By undertaking frequent formal swimming lessons such risks can be lessened (Brenner, Saluja & Smith, 2003). Children aged between one and four who attend frequent swimming lessons were found to be 88% less likely to be at risk of drowning and for children between the ages of five and nine, a 64% reduction (McIntosh, 2009).

The Swimming Teachers’ Association (STA) focuses on making children aware of swimming and lifesaving skills. STA conducted a survey with more than 2,000 parents with children aged between zero and 16 (Burgham, 2017) and found that one in three children living in the UK could not swim. In response to this, 25% of parents admitted they do not like the water themselves or cannot swim, impacting their decision. Additionally, although nine out of ten parents agreed that swimming is a life skill, almost 50% reported that they do not go swimming with their children. The survey also indicated that approximately 75% of parents were worried that their child is not confident in water (Burgham, 2017).

Previous research suggests that children have the ability to experience a wide range of fears throughout childhood (King, Eleonora & Ollendick, 1998). In most cases, fears are suggested to be temporary. Despite this, some children display fear and phobias that are maladaptive, persistent and prove to cause a great deal of distress longitudinally, thus affecting their day to day lives by causing increased heart rate, respiration rate and also avoidance of the situation (King et al., 1998). Fears that have the ability to cause children significant amounts of distress are most commonly referred to as either clinical fears, or specific phobias; with water being an example.

Menzies and Clarke (1993) conducted a study that investigated children’s fears towards water in relation to Rachman’s pathways to fear. Rachman (1991; 1997) proposed that children’s fears can be caused by classical conditioning, vicarious conditioning and threat talk. The findings of Menzies and Clarke (1993) indicated that only one parent from the study recalled an episode of classical conditioning to be the main contributing factor of the onset of their child’s water phobia. With this in mind, a large majority of parents (56%) reported that their child’s concern with water had always been apparent.

Similarly, Graham and Gaffan (1997) compared water fearful children to non-water fearful children of similar swimming abilities. Findings indicated that parents most commonly reported that their child’s initial onset of fear towards water began at their child’s primary contact with water, thus supporting the findings of Menzies and Clarke (1993) who argued that classical conditioning was unlikely to be the cause of water phobia, as first contact with water would suggest that no prior conditioning took place. It was also found that in both the fearful and non-fearful samples, parent-offspring and sibling resemblances were found for the fear of water. However, further analysis revealed that parents suggested that the effects of social learning theory in fact lowered the chances of their children displaying fears towards water rather than heightening their child’s risk of water phobia. Graham and Gaffan (1997) concluded that when both parent and child reported to have a fear of water, the similarities could also be indicated by genetics, as well as the effects of parental influences as suggested in Rachman’s (1991;1997) three pathways to fear.

The present study aimed to investigate a gap in psychological research into the effects of parental confidence towards water and swimming on children’s behaviours during their swimming lessons, and whether there is an association between parental level of confidence and the behaviours their children displayed. A better understanding of this can help support children in learning to swim.

Method

Participants

The study involved 64 children and one of their parents. Of the 64 child participants that actively took part in the experiment, 33 were female and the remaining 31 were male. All were aged 3 to 6 years. The mean age of participants was 4.046 and the standard deviation was 0.998.

Materials

The materials consisted of a questionnaire concerning parents’ feelings towards swimming and water, which was from a pre-existing scale (Cheng, 2004). The original scale was used to identify second language writing anxiety and was thus adapted to measure the levels of confidence that parents have towards water and swimming. The consisted of 24 questions related to swimming and water. For example, participants were asked to respond to statements such as ‘I often feel panic when near water’ and ‘I usually do my best to avoid going swimming’. Participants responded to each of the items within the scale by providing an answer on the Likert scale (1–5) between strongly agree and strongly disagree. Parents were given the questionnaire during their child’s swimming lesson and asked to complete it by the end of the swimming lesson.
The children were observed during their swimming lesson and behaviours were coded from zero to five, in relation to the following behaviours: smiling and laughing, crying, positive verbalisation, negative verbalisation, positive physical behaviours, negative physical behaviours and jumping in. When each of the following had been given a score between zero and five all scores were added up. Negative behaviour scores were then taken from the positive behaviour scores to provide each child with their own, individual swimming confidence score. A score of 0 would reflect that that particular behaviour was not apparent during the swimming lessons, whereas 5 would suggest that that particular behaviour was performed repeatedly during the lesson.

Design

The design used in this experiment was a correlational study. To measure the co-variables within this study, both observations and surveys were used. The observation involved observing children’s swimming lessons for 30 minutes, whilst the survey involved parents completing a 24-item confidence questionnaire. The children were observed for positive and negative physical and verbal behaviours. The co-variables in this study were the levels of confidence in both parent and child. Therefore, this study was looking for an association between the level of confidence towards water between parent and child.

This study also involved a pseudo-experiment, looking at the effects of the sex of a child and their behaviours during a swimming lesson. This involved a single independent variable (sex of the child) with two levels (male or female). The dependent variable was the amount of behaviours observed that was calculated to be the swimming confidence score of each child.

Procedure

Parental participants formally agreed to participate by reading the information sheet and consent form provided in advance and were required to say yes in order to participate (opt-in). Consent forms were then collected and questionnaires were given out to the parents who had consented to take part in the experiment during their child’s next swimming lesson. Parents of the children who were not being observed but were in the same class as one of the observed children, were also given an information sheet to explain what was taking place and why. This gave them the opportunity to say if they did not wish the observation of their child’s class to take place, despite their child not being observed at that time.

At the beginning of the swimming lesson the individual child was made aware by their parent that they were going to be observed and if they had any concerns they could speak to either the observer or their parent. The researcher also reminded parents that if they wished to withdraw from the experiment, they must do so before leaving the swimming lesson as their results would be anonymous and there would be no way of knowing which set of results and observations were theirs. The experimenter would then observe the child for any behaviours they displayed during their 30 minute swimming lesson, whether that be positive or negative, physical or verbal. During this time, parents completed the confidence questionnaire provided. To conclude the experiment, completed questionnaires were collected and both parent and child were thanked.

Results

Hypothesis 1: The parental participants who demonstrate high levels of confidence towards swimming and water will have children who will be observed to have a high swimming confidence score.

Hypothesis 2: The parental participants who demonstrate low levels of confidence towards swimming and water will have children who will be observed to have a low swimming confidence score.

The initial correlation performed compared the parental confidence towards water and swimming and children’s swimming confidence score in which a significant, medium-sized, positive correlation was obtained $r (62) = .37, p =.002$. This suggests that as levels of parental confidence towards water and swimming increased, children’s swim confidence score also increased. This does not necessarily mean that the level of parental confidence of water and swimming directly affects a child’s swimming confidence score but rather that there is a positive relationship between the two.

There was a small effect size for children’s swimming confidence scores ($r^2 = .137$).

Hypothesis 3: Amongst parents who have a low level of confidence towards swimming and water, their child/children will produce more negative behaviours during their swimming lesson.

A Pearson’s correlation test found a small-sized, negative, non-significant correlation between children’s negative swimming behaviours and parental confidence $r (62) = -.017, p =.175$. This demonstrated that there was no relationship between the levels of parental confidence and the amount of negative behaviours that children displayed during their swimming lesson. Power analysis power = 0.271. With this in mind, the power of this correlation is small, which could be due to a small sample size and so a possible type-two error.
Hypothesis 4: Parents who demonstrate a high level of confidence towards swimming and water, their child/children will display more positive behaviours during their swimming lesson.

The third and last Pearson correlation performed was between parental confidence, and the amount of positive swimming behaviours observed in the children, in which a significant, medium-sized, positive correlation was obtained $r(62) = 0.42, p < .001$. This revealed that there was a positive relationship between the level of parental confidence towards water and swimming, and the amount of positive behaviours that the children displayed during their swimming lesson. This does not mean that the level of parental confidence directly affects the amount of positive behaviours that children display during their swimming lesson but rather, there is a positive association between the two.

Again, the effect size for children’s positive swimming behaviour scores ($r^2 = .180$) indicated that a small proportion of the variability in parents’ levels of confidence towards swimming and water accounted for children’s behaviour.

Hypothesis 5: Female participants will have a lower swimming confidence score than male participants, as observed during their swimming lesson.

Table 1 shows that there is no overall difference in children’s swimming confidence score when analysed by gender. Females had a higher swimming confidence score (M= 7.00, SD= .85) in comparison to males (M= 5.97, SD= 1.10). To analyse any potential differences between gender and a child’s swimming confidence score, an independent t-test was performed. The result of the t-test revealed that there was no significant difference between gender and children’s swimming confidence scores $t(62) = -0.748, p = .46, r^2 = .0187$. This suggests that there is no effect of gender on children’s swimming confidence.
Discussion
The current study is the first to look at parents level of confidence towards water and swimming and to determine whether or not there was an association between that and children’s swimming behaviours. The results for the first, second and fourth and hypotheses were statistically significant and thus revealed significant positive correlations. However the third and fifth hypotheses were not found to be significant.

The present study confirms the findings of Graham and Gaffan (1997), who found that parents suggested that the effects of social learning theory in fact lowered the chances of their children displaying fears towards water, rather than heightening their child’s risk of water phobia. The present study found that there is an association between parental level of confidence towards water and swimming on children’s behaviour during their swimming lesson, in particular with reference to the positive behaviours they exhibited. However, there was no association found for the negative behaviours and thus social learning theory cannot be put forward as an explanation for such negative behaviours exhibited by the children during their swimming lesson.

In contrast, the present study contrasted with that of Menzies and Clarke (1993). Whilst their study produced no findings that would suggest Rachman’s three pathways theory to childhood phobias to be true, the present study did. The present study showed that there is an association between a parent’s level of confidence towards swimming and water and children’s swimming behaviours, thus suggesting that there are parental effects, which to some degree, have the ability to affect the child’s behaviour during swimming lessons. However, this was only found to be associated with children’s positive behaviours and not negative behaviours.

Whilst correlations can allow us to identify if there is a relationship between variables, they cannot be taken to imply causation; even if there is a strong association between any two variables, we cannot assume that one causes the other. It could be that the cause of the relationship between the two variables is due to a third variable—in this study it could be the swimming teacher.

It is also important to question the \( r^2 \) for both child swimming confidence scores and parental confidence levels (137) and children’s positive behaviours and parental confidence levels (180). Whilst both found a significant positive correlation it is clear from the \( r^2 \) that there are other variables interacting and affecting a child’s behaviour during their swimming lesson. Thus, future research should consider focusing on other possible variables.

Additionally, the present study relied on parental responses to a questionnaire to measure confidence. Parents may have responded with socially desirable answers. This would therefore affect the credibility of the study as the responses provided may not be an accurate representation of their levels of confidence. In order to reduce the effects of socially desirable answers, future research should consider implementing a social desirability bias scale, such as the Marlowe-Crowne Social Desirability Scale (Crowne & Marlowe, 1960).

Despite the limitations, the present study found that there was in fact no significant correlation between gender and the swimming confidence score obtained, thus the findings do not support those of Costello and Angold (1995), but instead follows the suggestions of Ferrari (1986) who proposed that whilst previous research has indicated there to be sex-related differences in fear, yet it is not irrefutable that girls are more fearful than boys. However, the previous literature has only investigated phobias and fears as a whole and not individually, as in the present study.

In conclusion, children’s swimming confidence seems to be increased by parental confidence, but not reduced by a lack of parental confidence. There is no effect of gender on children’s confidence in water. This implies that working with parents to increase their confidence may facilitate children in learning to swim.

References
Introduction

Earlier this year, financial markets within the US were shaken by a sell off nicknamed black wednesday by media pundits (Forbes, 2018). With indices such as the Dow jones industrial average losing as much as 12% over the course of the week (Investing.com, 2018). The market sell off was triggered by an NFP figure that was higher than market expectation, leading many market participants to speculate a faster and more periodic monetary tightening regime might be adopted by the federal reserve.

Unemployment figures such as Non Farm Payrolls (NFP) data are an important indicator for central bank policy, when production is increased to meet growing demand this leads to lower unemployment rates further fueling demand. When wages increase this allows consumers to spend more freely, which in turn leads to higher GDP (Consumer spending is a large proportion of GDP) combined with inflation.

Monetary tightening is a central bank policy whereby short term interest rates are increased, this results in higher borrowing costs for companies slowing down investment activities and as a result slows GDP growth. This has the effect of closing the gap between actual and potential GDP, helping reduce inflation which is directly related to this gap (equation 1.1).

\[ \pi = k (GDP_{\text{ACTUAL}} - GDP_{\text{POTENTIAL}}) \]

Equation 1.1 (Saunders, 2017)

Much of this sell off was driven on the prospect that higher interest rates would increase interest expenses on company balance sheets, this in turn increases the default probability of these companies whose highly leveraged capital structure can make higher interest expenses difficult to pay. Corporate debt has grown exponentially within the US since the 2008 financial crisis. Figure 1 demonstrates this, showing how as rates are lowered to near 0%, corporations within the US have capitalised on the environment by leveraging on cheap loans. This cycle of monetary easing led to greater investment, which in turn increased production and employment helping drive economic growth and strengthen the recovery of the US economy.

This brings us to the essence of this article, based on the assumption of greater short term interest rates in the coming monetary cycle, what is the fair value of equity markets given the increased default risk. In order to conduct a fair assessment of this question, we will begin by studying two fundamental models for equity pricing, namely the Dividend discount model and book value per share. Which based on efficient market hypothesis will give us an understanding of the disconnect between fundamental value and market...
value for US indices. Finally an econometric model will be built to study the relationship between Federal Funds rates and the S&P 500, allowing us to make predictions on the best course of action for a monetary tightening cycle to be pursued.

Figure 1: US interest rates & Corporate Debt 1950-2018 (Bloomberg, 2018)

**Risk Assessment: building models of fair value**

**Dividend Discount Model**

According to semi-strong efficient market hypothesis (EMH) the market price of an asset is equal to the information set provided by previous prices and all publicly available information (Fama, 1965), as such it is impossible for investors to use fundamental and technical analysis to predict future prices. Based on this hypothesis it would be unwise to suggest the models that will be developed in this paper can be points of reference for investment decisions. They can however provide accurate models of value based on sound financial theory. For example, a critical foundation to investment valuation is Net Present Value (NPV). This argues the value of an investment is equal to its cash flows adjusted for the time value of money (inflation). Within the Dividend Discount Model (DDM) this is equal to arguing the present stock price or value of company equity is equal to future cash flows in the form of dividends adjusted for time value (see equation 1.2). (Gordon, 1959) who proposed the model argued that investors gain value from equity investment in two ways, dividends and future expected price. According to a study conducted by (Shapiro, 1956) as n→∞ we see Pn→0, that is to say no company remains forever and so we can assume based on the law of large numbers that the future stock price of any company is equal to 0. Allowing us to adjust equation 1.2 to equation 1.3, which is very similar to the NPV equation.

\[
P_0 = \frac{D_1}{r} + \frac{D_2}{(1+r)^2} + \cdots + \frac{D_n}{(1+r)^n}
\]

**Equation 1.2**

\[
P_0 = \sum_{i=1}^{n} \frac{D_i}{(1+r)^i}
\]

**Equation 1.3**

(Gordon, 1959) extended this model to account for expected growth in dividends, presenting equation 1.4 nicknamed the gordon growth model.

\[
P_0 = \sum_{i=1}^{n} \frac{D_i}{(1+r+g)^i}
\]

**Equation 1.4**

If we apply this to the SP500 stock indices in the US based on historical expected return, mean dividend growth rate and mean earnings per share (data shown below in table 1a). We get a stock price of £2,378.70, more than 17% below current market price of £2,800.23 (Bloomberg, 2018).

| Earnings Per Share (EPS) | 30.21 |
| Dividend Growth Rate (g) | 5.92% |
| Cost of Equity (r) | 7.19% |

Table 1: Data generated from (Bloomberg, 2018)

The Standard & Poor’s 500, often abbreviated as the S&P 500, or just the S&P, is an American stock market index based on the market capitalizations of 500 large companies having common stock listed on the NYSE or NASDAQ (Investopedia.com, 2018). It is one of the most commonly followed equity indices, and many consider it one of the best representations of the U.S. stock market, and a bellwether for the U.S. economy. As such it is a good place to start in studying the current divergence between fair value and market prices we see in corporate valuations.
Book Value per share

The second fundamental model we will study is that of Book value per share. According to (Abuzayed, 2009) book value per share is the value of a company based on the equity available to common shareholders. The term book value is used as the equation uses information collected from the financial statements or ‘books’ of a company. It is calculated as the total value of a company’s assets minus its liabilities and is sometimes referred to as shareholders equity, this is then divided by the total number of shares on float to give book value per share.

The book value per share is often used by investors to determine the equity in a company relative to its market value, as represented by the share price. For example, a company that has a share price of £80 but a book value per share price of £40 is currently trading at twice its equity. This is often referred to as price to book value (P/B), a ratio commonly used to analyse stocks.

The SP500 index currently has a book value per share of £826.52 and a price to book value (P/B ratio) of 3.39, meaning its market value currently trades at 3.39 times its book value (Bloomberg, 2018).

Both the dividend discount model and the book value valuation price show a large disconnect between fundamental models and current market prices. It should be noted as was discussed before that these valuations are rarely accurate, but do provide investors with a solid grounding for understanding the value of stocks. Other valuation models such as the Arbitrage Pricing Theory (APT) might be more accurate, however require large economic data sets which extend beyond the scope of this article. As such it could be concluded that despite the sell offs exhibited early this year within US markets, market indices such as the SP500 are still trading comfortably above their fundamental value suggesting remaining optimism and confidence despite monetary prospects.

Econometric modelling: studying the relationship between US short term interest rates and equity markets

An Econometric model is a statistical model used in econometrics that specifies a statistical relationship between economic quantities pertaining to a particular economic phenomenon (Investopedia, 2018). In this case the economic quantities are short term interest rates and equity markets as represented by the SP500, the phenomenon being studied is the role of monetary tightening in equity market valuations.

We will begin my building a simple model for the period 1970–2018 using correlations between the economic factors, and then modelling the residuals using an appropriate moving average (MA(q)) model.

A simple model for studying the role of interest rates on equity markets

Figure 2 shows US interest rates and SP500 price levels from 1970 to 2018 on a monthly basis. Some observations that can be made include periods of positive correlation, negative correlation and no correlation. This is best explained by Arbitrage Pricing Theory which argues for a range of economic factors as determinants of an asset’s price. Using this theory we could argue that during economic cycles certain economic factors take precedence over others, their beta factors increase causing the asset to become more sensitive to certain data releases. For example in 2008 following the housing crisis, indices became more sensitive to new residential construction (Bloomberg, 2018). This is because investors were paying closer attention to the data release, hoping to capture signs of an economic recovery. Nonetheless we will begin by constructing the following model to represent periods 1970–2018:

\[
\text{SP500\_return} = -4.567816 + 1.222\text{Interest\_rate\_change} + e
\]

SP500 returns and interest rate changes were used here using data from (Bloomberg, 2018) and regression function on STATA software, this was to ensure the model built represented consistent units for the purpose of analysis. With an \(R^2\) of 0.005 this is a very poor model to study and even make deductions about, so instead we will separate
out the data set for interest rates and instead focus on building a model for studying historic periods of monetary tightening.

An econometric model to study relationship between monetary tightening and equity markets

For the monetary tightening period of 1977-1983 shown in figure 2 we get the following model using SP500 returns data (period JAN 1977–JAN1983) from (Bloomberg, 2018) and regression function on STATA software:

\[ \text{SP500}\_\text{returns} = -1.0027 -0.451\text{Interest}\_\text{rate}\_\text{Change} + e_i \]

Model 1.0

The Adj R\(^2\) here was 0.783, which shows most of the variables that determined equity prices during this period are included by the model. As such it could be assumed that given a 1% increase in interest rates we would expect a 0.451% decrease in equities. This is in line with modern economic theory that monetary tightening works to slow business activity and investment by making debt funded investments more difficult to pursue. We can then extend this model by modelling its residuals (\(e_i\)) using an appropriate moving average model (MA(q)), which should strengthen the predictive capabilities of the model.

The following MA(4) model was found to best fit the residuals of model 1.0, using the same SP500 returns data from (Bloomberg, 2018) and MA(q) function on STATA software:

\[ \text{SP500}\_\text{returns} = -1.009 +0.4453L +0.0636L^2 -0.0874L^3 -0.1492L^4 + e_i \]

Here L=e\(_{i-1}\), L\(^2\)=e\(_{i-2}\). These are referred to as lags in econometric modelling.

This model leads to the final predictive model shown below:

\[ \text{SP500}\_\text{return} = -2.0117 -0.451\text{Interest}\_\text{rate}\_\text{Change} +0.4453L +0.0636L^2 -0.0874L^3 -0.1492L^4 + e_i \]

Model 2.0

Sensitivity analysis: analysing the optimal monetary tightening policy given equity market stability

In order to begin this section of analysis, it is important to first gain an understanding of the term financial stability. It is one of the key roles of central bank policy; maintaining financial market stability and confidence. (Praet, 2017) argues stability is best quantified through studying market volatility, where policy response has low market volatility while also achieving policy objectives, market stability is achieved. In order to do this we will first begin by building a model relating SP500 return volatility and interest rate change volatility along the same methodology used for model 2.0. Volatility returns of the SP500 index can then be used to build a GARCH(p,q) model that accurately predicts the future volatility of the indices based on historic volatility changes. These two models can then be linked to predict the effects of an increase in interest rate volatility on future SP500 return volatility, and thus make conclusions regarding financial stability of such central bank policy routes.

The following model demonstrates the relationship between Interest rate volatility and SP500 volatility using data from (Bloomberg, 2018) [SP500 return\(^2\) 1970–2018] and regression function on STATA software:

\[ \text{SP500}\_\text{Return}\_\text{Volatility} = 0.05 + 0.38\text{Interest}\_\text{Rate}\_\text{Volatility} +e_i \]

Model 3.0

Model 3.0 has an Adjusted R\(^2\) value of 0.83 which shows greater accuracy in modelling volatility than the return modelling conducted in Model 2.0.

We can now build a Gaussian Autoregressive Conditional Heteroscedastich (p,q) (GARCH(p,q)) model for studying the volatility of returns of SP500. We get the following results with a GARCH(1,1) model by using the STATA GARCH(1,1) function on SP500 return volatility data from (Bloomberg, 2018) [JAN 1970–2018]:

\[ \sigma_t^2 = 0.1168 + 0.124R_{t-1}^2 + 0.048\sigma_{t-1}^2 \]

Model 4.0

This gives us a predictive volatility of:

\[ Y_t = \frac{0.1168}{1-0.124} = 0.141 \]

Model 4.1

This model is said to be converging, so an increase in volatility dies down very quickly which shows the role of the central bank in maintaining market stability in the US to be historically positive. An increase in SP500 return volatility of 1 converges to 0 at a rate 0.141. SP500 returns volatility on a quarterly basis has a mean of 0.0359 (Bloomberg, 2018), assuming this is the long term stable value for the indices. We can use this value for model 3.0 to give us an optimal interest rate volatility of:
This volatility comes out to an interest rate change per quarter of 0.4754:
\[
\sqrt{0.226} = 0.4754
\]
So while maintaining financial market stability, the US Federal Reserve can raise rates by up to 0.4754 basis points per quarter. With volatility dying out at a rate of 0.141 per month, this means it would take roughly 1.95 months for the volatility effects of a base change to die out (assumed at 0.005):
\[
0.226 \times 0.141^n = 0.005 \\
\ln \left( \frac{0.005}{0.226} \right) = \ln(0.141) = 1.945
\]
Which fits comfortably within the time frame of each quarterly federal reserve meeting.

Conclusion

To conclude, this essay has tried to outline the causes for the selloff world markets experienced in February of 2018 (Investing.com, 2018). By building fundamental models (namely Dividend Discount Model and Book Value per Share) we were able to assign a fair value to the main US stock market indices (SP500), which allowed us to make a reasoned judgement about whether or not the behaviour exhibited in February was an over reaction. The fair value found by the Dividend Discount Model was found to be £2,378.70, which is more than 17% below current market price of £2,800.23 (Bloomberg, 2018). SP500 was found to have a book value per share of £826.52 and a price to book value (P/B ratio) of 3.39, meaning its market value currently trades at 3.39 times its book value (Bloomberg, 2018).

Both these models suggest that despite the sell off, the stock market indices are still trading comfortably above their fundamental value suggesting remaining optimism and confidence despite monetary prospects. Sensitivity analysis was then used to build a model to predict the optimal monetary tightening regime the Federal Reserve could pursue while keeping markets stable. By using historical volatility responses to monetary tightening, a volatility model was built to demonstrate the expected response. Using the assumption that Central bank policy aims to reduce market volatility, it was found that the US Federal Reserve could raise rates by up to 0.4754 basis points per quarter. With volatility dying out at a rate of 0.141 per month, this means it would take roughly 1.95 months for the volatility effects of a base change to die out. Meaning the safest monetary tightening route that could be taken was a maximum rate hike increase of 0.4754 basis points per quarter.

References

Bloomberg, 2018, Terminal.
Introduction

The maternity packages known as ‘baby boxes’ have been widely promoted as the reason for Finland’s low infant mortality rate, however on closer inspection there are multiple other factors to consider. These include greater wealth in the country, better parental education, better nutrition and child care by families or medical advancements. The UK currently has double the infant mortality rate than that of Finland. In Finland, women and their families are well supported financially by the state and through a well-established health system and parent education system. This article will study whether the low infant mortality rate in Finland is due to the maternity packages or better parental education.

Maternity Packages

(‘baby boxes’)

Since 1937, the Finnish government has been actively providing maternity grants for new mothers. Although the scheme initially started in order to provide extra help to low-income families, it has grown into a national project, providing either a cash sum or a maternity package for all families. The scheme was set up to increase birth levels and decrease the infant mortality rate. In 1930 approximately 1 in 10 babies born in Finland would die in their first year of life (Hakulinen and Gissler, 2017).

The maternity package was made available to all mothers in 1949 and since 1994 has been administered by the Social Insurance Institution, Kela (Kela, 2016). Kela (2016) state that only a third of mothers opt for the cash benefit (€170 in 2018) with more than 40,000 maternity packages being given out each year. For the past few years, the maternity packages have been provided in neutral colours with a different design each year. This ever-changing design allows mothers to recognise other mothers with children born in the same year (Lee, 2013).

The maternity package contains a number of items to aid the mother with the first year of having a newborn infant. This includes a mattress and bedding to be used in the box which doubles as a crib, clothes suitable for both cold and hot weather, romper suits, toiletries such as nappy cream, nail scissors and a toothbrush, muslin squares, cloth nappies, a picture book, teething toy, bra pads and condoms (Lee, 2013). The content of the boxes is ever changing with new trends and more availability of objects. During the 1930s and 40s, the mothers were provided with fabric rather than ready-made clothes so that the mothers could make their own clothes for their baby. Ready made clothes entered the box in the 1950s and by the 1970s they were made of stretchy materials. In 1968 disposable nappies were included but by 2000 these were replaced with the more environmentally friendly cloth nappies. Bottles and dummies were removed from the box to promote breastfeeding. The box contains a book about how to breastfeed (The Globe and Mail, 2013). It is recommended that all babies sleep in their own bed and not share with their parents (Lullaby Trust, 2018b). The box which can also be used as a bed was a way to encourage this safer sleep mechanism.

The maternity package is provided by the government as a gift to new mothers. Antenatal women must have attended at least one prenatal check and apply for either the package or the cash sum two months before the due date. A certificate stating that the pregnancy has lasted at least 154 days and the mother has attended an antenatal check is presented on application. This persuades nearly all women to access medical care throughout their pregnancy. The mothers-to-be are also provided with milk and fresh fruit to promote a healthy lifestyle (The Globe and Mail, 2013). Parents who have multiple births are eligible for extra maternity packages and cash sums depending on how many children they have. Adoptive parents are also able to apply for a maternity package providing the child they are adopting is under 18 months old (Kela, 2016). This non-discriminatory method of providing the maternity packages enables more families to practise safe sleep with their infant and therefore could be the reason for the low infant mortality rate. Mothers are also visited by a lactation consultant and receive 9 months of benefits. The women are given free childcare regardless of whether the mother is working, and if it is not required the women can get a cash sum instead (Ridky, 2016). Each box is scribed with the words ‘Every child matters. Every family matters’ (The Globe and Mail, 2013). This symbolic gesture is the cornerstone which Finland has built its public policy on. Arguing that the Finnish children are the future of their country and thus providing them with the best start in life proves that Finland truly cares about their residents.

Safe sleep practices

The number of infant deaths globally was 33 deaths per 1000 births in 2015 (United Nations, 2017). Finland had a rate of 2 per 1000 births in the same year, and the UK had double the amount at 4 per 1000 births (United Nations, 2017). Although there can be many different reasons why a young infant may not survive past early infancy, the most common reason is Sudden Infant Death Syndrome (SIDS) which is when a seemingly healthy baby would die for apparently no reason. Around 89% of SIDS happens in the first 6 months of a baby’s life (Lullaby Trust, 2018a). Although the cause is unknown, there are a number of environmental factors which can lead to SIDS, such as tobacco and bed-sharing with parents (Lullaby Trust, 2018b).
Numerous studies since 1956 have shown that breastfeeding babies can halve the risk of SIDS (Ford et al., 1993). Exclusive breastfeeding provides more protection than partial breastfeeding but there are various reasons why this may be the case. Some researchers believe it is because breastfed babies have better arousal from sleep, or the breastmilk promotes the development of the brain in the new-born infant and provides the infant with natural immunity passed through mum to baby (Dieterich et al., 2013). Many promotional tools produced in the UK aimed at reducing the risk of SIDS omit this link to breastfeeding. This omission could influence maternal decisions over the feeding of her infant.

Smoking cessation can also lower the risk of SIDS (Best, 2009). In some regions of the UK, 27.8% of women smoke at delivery (NHS Digital, 2018). Smoking during pregnancy not only increases the risk of SIDS postnatally, but can cause an increased risk of premature labour, intra-uterine growth restriction (IUGR) and increased risk of miscarriage (NhS, 2018). It is estimated that up to a third of all SIDS-related deaths could be eliminated if all women stopped smoking during pregnancy (Mitchell and MileraD, 2006). In Finland, although it is the highest percent out of the Nordic countries, smoking at the end of pregnancy is only 8.2% (The National Institute for Health and Welfare (THL), 2016).

The Lullaby trust, a UK charity based around educating members of the public in safe sleep methods and preventing SIDS states that bed-sharing or co-sleeping is a risk factor for SIDS (Lullaby Trust, 2018b). This is especially true with parents who are under the influence of alcohol or drugs or parents who smoke. The infants can suffocate on bedding or be squashed by parents. A study done in Bristol, UK aimed to find the benefits versus the risks found with co-sleeping. It found that SIDS was caused in part by poor maternal education regardless of co-sleeping or not (Fleming, Pease and Blair, 2015). Although SIDS has a positive correlation with co-sleeping, there are benefits associated with initiation of breastfeeding (Blair and Ball, 2004). The initiation of breastfeeding is associated with a reduced risk of SIDS, thus counteracting the risk of co-sleeping.

Parental Education

All parents-to-be in the UK are given information on the birth process and the postnatal period. Each trust in the UK differs in how they give this information, but National Institute of Clinical Excellence (NICE) Antenatal Guidelines for uncomplicated pregnancies says that all women and partners should be provided with the same information (NICE, 2008). Often this information can be given in the form of leaflets from the community midwife, or some trusts offer antenatal classes where they can teach the skills and information in a more practical manner. Unicef UK have produced a leaflet about ‘caring for your baby at night’, outlining various ways to keep an infant safe during sleeping (Unicef, 2017). Learning theories state that teaching information in multiple ways aids more people to understand it (Lujan and DiCarlo, 2006). There are multiple learning types which should be covered during the antenatal period to aid parents to make appropriate decisions about the birth and the postnatal period.

From the 1980s, the UK produced a ‘back to sleep’ campaign to promote the supine (back) position for infants sleeping in their cots (de Luca and Hinde, 2016). This position has been proven to be the safest position for sleep as the infant can breathe easily and not suffocate on the sheets. However, as a result of the promotion of the supine position, it was found that healthcare professionals were not aware or teaching the risks of the prone (front) position (de Luca and Hinde, 2016). In Hong Kong in 1985, the parental education was that the infant should be put to sleep in the supine position and SIDS was very rare (Davies, 1985). On the contrary in the USA, the prone position for sleep was promoted until 1992 and the SIDS rate was much higher (Kattwinkel et al., 2000). It was believed that the prone position aided infants who had gastro-oesophageal reflux and reduced the likelihood of aspiration. It took until 2011 until the supine position was exclusively recommended in the USA. The SIDS rate in USA still remains at 5 infant deaths for every 1000 infants (Kattwinkel et al., 2000).

Since starting the ‘back to sleep’ campaign in the UK in 1986, the SIDS rate has decreased rapidly, however in recent years has plateaued. Whilst the ‘back to sleep’ campaign clearly has helped parents in remembering to place their infant in the supine position to sleep, some researchers worry that such a small statement does not provide all the necessary information (Moon et al., 2010). Many parents would still have questions surrounding the positioning for sleep, such as the risk of choking in the supine position. Some parents require to know the rationale before committing to practise a recommended health procedure. The health belief model suggests that a person believing they are immune to a certain illness directly impacts on their motivation to alter their behaviours (Becker, 1974). This can also be true in safe sleep. Parents who believe their infant is unlikely or immune to die from SIDS as it is always something that happens to another person, are unlikely to alter their behaviours such as smoking, sleep positioning or bed-sharing (Moon et al., 2010). A study performed in Brazil found that an antenatal class where the parents had the ability to get their questions answered were more likely to adhere to the promotional message and place their infant on their back to sleep (Moon, Oden and Grady, 2004).
In Finland, all new parents are provided with an information book which covers everything from the antenatal period, through birth and into the postnatal period (National Institute for Health and Welfare, 2012; Hoppu and Talasniemi, 1997). Although the booklet does not use different learning types to aid more women to understand the information, the booklet contains more information than could be achieved through midwife antenatal appointments alone and is regarded as playing a vital role in reducing the infant mortality rate. Parents will feel more empowered to be able to take care of their child if they have had all the information and knowledge given to them by a health professional they respect (Fisher, 2001). Finland also offers fathers extended paternity leave with high income replacement to aid with the parenting in the first few months and help the family to bond (O’Brien, 2009).

Finland set up Maternity and Child health service centres in the 1920s (Hakulinen and Gissler, 2017). These provide the service of health checks at predetermined times in the child’s life, focussing on preventing and diagnosing illnesses early to achieve the best outcome. Therefore, 99.6% of women used the maternity services in Finland in 2014 (Hakulinen and Gissler, 2017). As these were started at a similar time to the maternity package scheme, some academics believe the boxes and prenatal information together to be the cause for the reduction in infant mortality rate (Cassin, 2017). In the UK, children’s health records are passed through the midwife to the health visitors and then the school nurses. However, once the children are school age, the health checks become less frequent and are more focussed on treatment of an illness than prophylaxis.

Conclusion

Throughout the UK and Finland, the parental education schemes seem matched in quantity and quality of information. These schemes will differ throughout the regions and hospitals and depend on financial backing and educational levels of the residents. The maternity package provides the women with an excellent start to life for their infant and lasts them up to 1 year of age. This would enable the parents to practise recommended health promotion schemes such as safe sleeping and would reduce the infant mortality rate further if introduced into the UK. Murphy, Ewers and Wood (2015) hypothesised that the ‘baby boxes’ would aid parents with learning difficulties to look after their own infant, as up to 50% of infants of parents with learning difficulties are taken into care (The Nursing Times, 2007). Companies are also selling similar maternity packages worldwide (The Baby Box Co., 2018).

Some regions in the UK are already trialling a similar scheme to the one in Finland. In 2017, Scotland rolled out a baby-box scheme which mothers-to-be can register for and have the box sent to their home. Although there were initially concerns about the requirements to meet the safe-sleep guidelines, the baby boxes have been popular with the new mothers (BBC News, 2017). However, Scottish leaders claimed that the baby box had been scientifically proven to reduce infant mortality, whereas Finnish suppliers, Kela, simply state that the boxes improve the healthcare the women receive, thus inadvertently reducing infant mortality (Carrell, 2018). The boxes have also been introduced in Birmingham, Liverpool and Wigan in the UK (Gill, 2018). In 2015, it was announced that Mexico were introducing the Qunita Plan to distribute similar style baby boxes to all new parents (Bio, 2016). In 2017, New Jersey became the first US state to initiate a maternity package scheme (Alroy, 2017).

Although the maternity packages have great benefits, the reduced infant mortality rate is understandably caused as a result of better healthcare provision, better education surrounding parenthood and an instinct to care for each and every child and family.

References


MADELEINE SHACKLETON


SAVING BABIES’ LIVES: WHY ARE PARENTS PUTTING BABIES IN BOXES?
### 1.0 Introduction

#### 1.1 Immune Function

The immune system is essential for health as it protects the human body from pathogens. T-lymphocytes are a component of the immune system which recruits immune cells and reshapes its function to mitigate infections (Cole et al. 2014). T-lymphocytes differentiate to express proteins on their cell surface which determines the cell function according to the presenting infection. For example, CD4 proteins classify T-lymphocytes as CD4 T-helper cells (Th) which enhances the immune response. Further differentiation of T-helper cells results in Th1 and Th2 cells. Th1 promotes cell-mediated immunity whereas Th2 allows humoral immunity encompassing antibody production (Rammos & Kondomerkos 2007) (Boren & Gershwin 2004). Another type of T-lymphocytes are cytotoxic T-cells which feature CD8 proteins and function to directly destroy infected cells. Pathogens are digested by immune cells by phagocytosis. These fragments are subsequently displayed as antigens by major histocompatibility complex (MHC) found on T-cells. CD8 T-cells identify antigens displayed by MHC-I, whereas CD4 T-lymphocytes display MHC-II. T-lymphocytes are activated by a series of signals (Cole et al. 2014) allowing for survival, development and clonal expansion (Rammos & Kondomerkos 2007). The antigen binds to the T-cell receptor which instigates a second signal (Chan et al. 2014). Co-stimulatory signals involving CD28 receptors and CD80/CD86 completes the fusion between the two cells.

#### 1.2 Immune Homeostasis

Undifferentiated T-cells are known as naïve T-lymphocytes which are produced within the bone marrow and subsequently develop in the thymus. Immune homeostasis maintains the T-lymphocytic pool during an individual’s lifetime. This involves checkpoints that are implanted throughout the cell cycle where dysfunctional immune cells are discarded from the immune system (Dondi et al. 2014). As a result, a balance is attained between T-cell production and cell death in order to preserve the population of naïve T-cells.

#### 1.3 Ageing and Immunity

##### 1.3.1 Immunosenescence

Immunosenescence describes the reduction in immune function with ageing (García Verdecia et al. el. 2013). As we age, the thymus involutes reducing the production of T-lymphocytes (García Verdecia et al. el. 2013). Genetics and lifestyle factors additionally influence the ageing process (García Verdecia et al. el. 2013). In particular, cytomegalovirus (CMV) is a common infection in the elderly, which largely contributes to the development of immunosenescence.

Aged CD8 T-cells inevitably lack the expression of CD28, therefore CD28- is known as an immunosenescent marker (CD8+CD28-). These are terminally differentiated cells which are largely found in the elderly population (Plonquet et al. 2011) (Rammos & Kondomerkos 2007). Several cell surface proteins such as CD45RA, CDS7 and CCR7 (Fülöp et al. 2013) contribute to T-cell activation, proliferation and cytokine production. However, as we age many protein alterations occur reducing the overall efficiency of the immune system (Fülöp et al. 2013).

##### 1.3.2 Immune Risk Phenotype

“Immune Risk Phenotype” (IRP) is defined by poor T-cell proliferation in response to mitogens, reduced B-lymphocyte and an inverted CD4/CD8 ratio. This concept was derived by the Swedish OCTO Immune Longitudinal Study (OCTO study), involving elderly participants (Ferguson et al. 1995) and subsequently confirmed by the NONA Immune Longitudinal Study (NONA study), involving the original participants (Strindhall et al. 2007). To calculate IRP the CD4/CD8 ratio must be <1. It was found that 16% of participants, who were IRP positive, had a higher mortality risk than other candidates. Immunosenescent markers, including CD8CD28-, CDS7 expansion and (Plonquet et al. 2011), a reduction in CD4+ and CD19 T-cell populations (Boren & Gershwin 2004) are similarly associated with the development of IRP.

#### 1.4 Hypothesis and Aims

The aim of this study is to investigate the influence of ageing on T-cells, specifically to:

1. Estimate IRP frequency in our study’s population.
2. Evaluate the relationship between IRP status and expression of immunosenescent markers.

### 2.0 Methodology

#### 2.1 Recruitment

25 participants were recruited from the osteoporosis and rheumatology clinic in a hospital setting, over a two month period. A consent form was completed prior to participation. Research and Development (R&D) approval was obtained from the London West Research Ethics Committee.

#### 2.2 Phlebotomy

A 20ml blood sample was obtained from each participant, where...
10ml was collected in vacutainers containing an anticoagulant and the remaining 10ml was sent for serological analysis.

2.3 Blood Isolation

15ml of Ficoll-Paque was allocated using a glass pipette into a 50ml conical tube. The 10ml blood sample was diluted by a factor of two into a separate 50ml conical tube, using phosphate buffered saline (PBS). The sample was overlaid on top of the Ficoll-Paque using a pipette, resulting in a total volume of 35ml and spun using the Thermo Scientific Heraeus Multifuge X3R centrifuge. Within the density gradient centrifuge, the sample was balanced using another tube of a similar volume and locked in the rotator. The sample was spun at 400xg for 25 minutes, with no brakes. Blood isolation allows for dense material to gravitate towards the bottom of the tube and subsequently separate into four layers. Approximately 10ml of the plasma was removed to provide access to the peripheral blood mononuclear cell (PBMC) layer. This layer consists of the desired cells, lymphocytes. A few millilitres of PBS were added to a new 50ml conical tube. The PBMC layer was removed using pipettes and added into the conical tube. Disinfectant was added to the remaining layers of blood and was appropriately discarded.

The sample was spun at 300xg for 10 minutes with the brakes on. The supernatant was subsequently discarded, leaving behind a white pellet. This pellet was gently disturbed and resuspended in 1ml of PBS. PBS was then added to the conical tube, totalling the volume of the sample to 20ml. The sample was centrifuged again and after the second wash, the supernatant was removed. The pellet was dispersed and the cells were resuspended in 1ml of PBS. This volume was then equally aliquotted between two fluorescent-activated cell sorting (FACS) tubes. Once more, the tubes were placed within the centrifuge and spun at 300xg for 5 minutes.

2.4 Staining Cells

Samples were processed by BD FACSCanto machine on the same day as the sample was collected. Fluorochromes were added to the FACS tubes with 100µl of PBS. Fluorochromes are dyes which bind to complementary antibodies. These are light sensitive; therefore the tubes were wrapped in foil and incubated in the refrigerator for 30 minutes.

2.5 Staining Beads

Compensation beads, OneCompE beads, were prepared to overcome the overlapping spectra of fluorochromes. Compensation beads was added to 8 labelled FACS tubes with 100µl of PBS, including a negative control. These were wrapped in foil for 30 minutes and incubated in the refrigerator. The beads were processed before the cell samples, in order to set up the parameters for FACS analysis.

3.0 Results

3.1 Gating Strategy

Gating isolates lymphocytes and its subpopulations enabling an in-depth analysis of each cell type. Health conditions may interfere with cell surface protein expression which allows for immunophenotyping to distinguish between healthy and diseased cells. Immunophenotyping was conducted for each blood sample using BD FACSDiva 6.0, producing a series of dot plots and contour graphs (Figure a, Figure b).

Figure a: Dot plot devised by FACS analysis with the CD4 and CD8 T-lymphocyte population gated, using the appropriate fluorochromes; Amcyan-CD4 and APC-Cy7-CD8.
3.2 Age Associations

**Naïve T-Lymphocytes**

The effect of age on the percentage of naïve T-lymphocytes.

![Proportion of naïve T-lymphocytes against increasing age](image)

Figure b: The effect of age on the percentage of naïve T-lymphocytes.

Figure b displays a significant negative correlation of naïve T-cells as age increases ($P=0.0183$, $R^2=0.2191$).

**CD8$^+$ T-Lymphocytes**

There is no significant association between CD8$^+$ expression and age, ($P=0.64$, $R^2<0.01$).

**CD4$^+$ T-Lymphocytes**

There is no significant change within the CD4$^+$ T-lymphocytes as age increases ($P=0.9642$, $R^2<0.001$).

**CD4/CD8 Ratio**

8 out of 25 participants were IRP positive and 17 volunteers were classified as IRP negative. The range of IRP in this data set varied from 61-83 years of age. The most elderly of participants were IRP negative ($P=0.7216$, $R^2=0.005674$).

**CD8CD57$^+$ T-Lymphocytes**

There was a weak trend towards CD57$^+$ expression on effector memory T-cells (TEM) and on central memory T-cells (TCM). This was not significant for TEM ($P=0.2977$, $R^2=0.04703$), although significant for TCM ($P=0.0370$, $R^2=0.0757$).

**CD4CD57$^+$ T-Lymphocytes**

CD4 T-cells expressed CD57$^+$ much more marked on TEM than on TCM cells. Further analysis found insignificant trends in the CD4CD57$^+$ TEM and TCM population (CD4CD57$^+$ TCM $P=0.432$, $R^2=0.02169$ and CD4CD57$^+$ TEM $P=0.3495$, $R^2=0.03814$).

3.3 Predictors of Immunosenescence

**CMV and IRP**

There was no correlation between CMV status and IRP ($P=0.1670$, Chi-squared=0.9333). 4 participants were CMV$^+$ and IRP positive, 16 participants were CMV$^-$ however IRP negative.

**CMV and CD57$^+$ T-Lymphocytes**

CD8 T-lymphocytes generally expressed a high concentration CD57$^+$ with age, however CMV$^+$ participants largely expressed CD57$^+$ in comparison to CMV$^-$ participants ($P=0.1928$, $R^2=0.0595$).

Similarly, CD4 T-cells expressed a higher number of CD57$^+$ in CMV$^+$ participants. However, CD4CD57$^+$ in comparison to CD8CD57$^+$ T-cells ($P=0.0051$, $R^2=0.3054$).

**CMV and CD28$^-$ T-Lymphocytes**

There was a higher concentration of CD8CD28$^-$ T-lymphocytes in participants who were CMV$^+$, in comparison CMV negative participants. ($P=0.0023$, $R^2=0.3511$). A significant difference occurred between those who were CMV$^+$ in CD8CD28$^-$ cells, compared to those who were CMV negative ($P=0.0469$, $R^2=0.1751$).

### Statistical Analysis Summary

<table>
<thead>
<tr>
<th>Variables</th>
<th>P Value</th>
<th>R-Squared Value</th>
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</thead>
<tbody>
<tr>
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</tr>
<tr>
<td>CD8 Expression</td>
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<td>CD4/CD8 Ratio</td>
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<td>CD8CD57 TCM</td>
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Figure c: Table displaying a summary of the statistical analyses performed throughout the data.

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<td>CMV and IRP</td>
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</table>

4.0 Discussion

From the results obtained several conclusions can be derived contributing to current concepts exploring immunity and ageing.

4.1 Naïve T-Lymphocytes and Ageing

Naïve T-lymphocytes are undifferentiated immune cells that are maintained by immune homeostasis. These cells develop into the required cell type necessary to combat the invading infection. Naïve T-cells are one of the most prominent markers of ageing. Results show the number of naïve T-cells largely reduces with age which can be explained by thymic involution (Appay & Sauce 2014).

4.2 CD8, CD4 T-Lymphocytes and Ageing

CD4 and CD8 T-cells are types of immune cells within the T-cell subset. With age, an expansion in CD8 T-lymphocytes occurs resulting in an inverted CD4/CD8 ratio. This contributes to a positive IRP status. Results obtained from this study found a statistically insignificant increase within the CD8 and CD4 T-lymphocytes. According to other studies, CD4 T-cells should display a decline in number as age increases (Wikby et al. 1998). However similar to this investigation, a study conducted by Yan et al, found no significant change within CD4+ T-cells and ageing. (Yan et al. 2010). This suggests ageing may not necessarily have a prominent impact on CD4+ T-lymphocytes.

4.3 CD4/CD8 Ratio and Ageing

A positive IRP status suggests that an individual may be at a higher risk of mortality and morbidity than those who are IRP negative. The definition of IRP includes an inverted CD4/CD8 ratio, however the CD4/CD8 ratio in this investigation was statistically insignificant. Furthermore, the distribution of IRP throughout the data set was not as expected where the most elderly subject, an 89 year old was IRP negative and the youngest participant at 61 years was IRP positive. This variation suggests the CD4/CD8 ratio is not a definite marker of ageing.

4.4 Immunosenescent markers and Ageing

Ageing cells possess characteristics which define them as immunosenescent, reducing the performance of the immune system. An expansion in CD57+ on CD8 and CD4 T-cells was found however proved to be statistically insignificant. Although, results from other studies agree with this expansion, confirming CD57+ as an immunosenescent marker (Pawelec et al. 2009) (Wikby et al. 1998).

Another immunosenescent marker, CD28−, proved to be statistically significant within the CD8 T-cell population (Weng et al, 2010) however, insignificant within CD4 T-lymphocytes. This suggests the lack of CD28 expression particularly favours CD8 T-cells over the CD4 population. Furthermore, CMV infections were found to enhance the development of immunosenescent markers, therefore supports the fact that CMV should be included within the IRP definition.

4.5 T-Lymphocyte Populations and Ageing

Cytotoxic T cells which express CD8 and CD57+ cell surface proteins are noted as CD8CD57+. After an infection, T-cells remember the invading pathogen in order to prevent future infections from the same organism. These are known as T-memory cells which can be further categorised into central memory (TCM) and effector memory (TEM) T-cells. The expression of CD57+ was particularly significant within the TEM subpopulation in comparison to TCM. Additionally, this observation appeared to largely influence CD8 T-cells as opposed to CD4 T-lymphocytes.

The majority of lymphocyte expansions are located in the CD8 TEM populations (Pawelec et al. 2009), as agreed by our findings. Similar observations were made within the CD4 T-lymphocyte population but to a lesser extent. TCM cells differentiate into mature TEM cells, resulting in the loss CD28 expression. (Moro-garcia et al. 2013). Therefore as we age, T-cells become more differentiated resulting in a significantly higher TEM population. Additionally, a study found that CD4 T-cells have a greater susceptibility to apoptosis; suggesting CD8 T-cells become apoptosis-resistant causing them to accumulate with age (Pawelec et al. 2009).

Results have shown that CD8 T-lymphocytes are more susceptible to ageing. Macaulay et al suggests remodelling within the immune system is more dominant within the CD8 T-lymphocyte compared to CD4 T-cells (Macaulay et al. 2013). These differences can be explained by the age-resistance properties of CD4 T-lymphocytes.
making them less prone to change. Nonetheless, a slight increase in CD4CD28− expression occurs with ageing which can occupy up to 50% of the CD4 T-cell compartment in some individuals older than 65 years (Vallejo et al. 2000).

4.6 Cytomegalovirus (CMV) and Ageing
CMV causes cells to age earlier than expected. It particularly is responsible for CD8 expansion (Koch et al. 2007) as the immune system attempts to maintain the virus in its latent state. This potentially contributes to IRP development, inverting the CD4/CD8 ratio. However results were statistically insignificant which suggests there may be no relationship between CMV and IRP status. 4 CMV positive participants were additionally IRP positive and 16 CMV positive participants were IRP negative. However other immunological investigations suggest CMV contributes to IRP development (Koch et al. 2006). It may be suggested with a larger sample size, this trend may become more apparent.

CMV did not appear to have any association with CD57+ expression as CMV negative participants had no significant difference in CD8CD57+ T-cells than those who were CMV positive. In comparison to CD4CD57+, those who were CMV positive had significant CD57+ expression. However the same cannot be said for those who are CD4 negative and CD4CD57+ T-cells as data was insignificant.

A significant correlation was found between CMV and CD28-. Those who were CMV positive had a significantly higher proportion of CD8CD28- T-cells. This is because clonal expansion of CD8 T-cells and CD28- occurs with age. Similarly significant results were seen in the CD4CD28- population, where CMV positive participants largely expressed CD28- cells than those who were CMV negative. Despite there being no direct correlation between CMV and IRP, these results supports that CMV enhances the expression of immunosenescent markers leading to IRP development.

4.7 Limitations and Amendments
The sample size of this investigation consisted of only 25 individuals. This is a very small data sample; despite the significance of the results, the findings would not have been applicable to a much wider audience unless repeated on a much larger scale. In addition, results which were calculated to be statistically insignificant, may potentially have been improved in a larger dataset. A larger sample size may reduce the age gaps between the participants and minimise individual variation. Furthermore an intra-assay variability could have been performed identifying a variation range within the dataset.
Chang, D. V et al., 2014. Differential CTLA-4 expression in human CD4 \(^+$\) versus CD8 \(^+$\) T cells is associated with increased NFAT1 and inhibition of CD4 \(^+$\) T cell proliferation. *Genes and Immunity, 15*(1), pp.25–32.


Introduction

Glycogen Synthase Kinase-3 (GSK-3), is a serine/threonine protein kinase expressed in all tissues and a regulator of diverse cellular functions (Ugolkov et al., 2016). GSK3 phosphorylates by transferring a phosphate group to either serine or threonine residue of its substrates, and therefore it initiates, regulates, inhibits and enhances the activity of many biological processes including cell signalling, glucose regulation on metabolism, apoptosis, proliferation, protein structuring, and intracellular communication (Pandey and DeGrado, 2016). The involvement of GSK-3 in many cellular processes has emerged as an essential and fascinating target for drug development in severe unmet human diseases, such as diabetes type II, bipolar disorders, chronic inflammatory diseases, and neurodegenerative pathologies (Finkelman and Martinez, 2011). There are two highly homologous forms of GSK-3 in mammals, GSK-3α and GSK3β (Lange et al., 2011). In rodents and humans an alternative splice variant of GSK3β — GSK3β2 — has been reported. This could shift the balance from neurodegeneration to neurogenesis and neuronal plasticity in diseases such as Alzheimer’s.

The two main signalling pathways known to impinge on GSK-3 are the insulin and Wnt pathways which are the most studied (Beurel, Grieco and Jope, 2015). These pathways specifically Wnt play a significant role as a regulator of neurodevelopment processes in the nervous system such as neurogenesis, migration, neuronal migration, neuronal polarisation and axonal growth and guidance (Hur and Zhou, 2010). GSK-3 Regulating Neuron differentiation

During brain development, GSK signaling is essential in coordinating neuron differentiation. GSK-3 promotes neuronal differentiation evidenced by the elevated levels pro proliferation factors prior differentiation in-vivo (Hur and Zhou, 2010). Activating GSK-3 phosphorylates and degrades pro proliferation factors such as cMyc and β-catenin allowing neuron differentiation to follow (Hur and Zhou, 2010). The high basal activity of GSK-3 shifts cell cycle from cell proliferation to differentiation in-vivo. However, in in-vitro studies, GSK-3 activity maintains NSCs in progenitor form limiting neuronal differentiation (Lange et al., 2011). Pharmacological in-vitro inhibition of GSK-3 increases proliferation and enhances neurogenesis. Garcia et al., (2016) study on in-vitro GSK-3 inhibition on NSCs resulted in an increase in number and size of neurospheres generated as well as an increase in migration and induced neuronal differentiation of NSCs. This is particularly beneficial in guiding NSC towards desired lineages such as neurons that potentially could be used in cell transplant therapy.


SABAH SIRAJUDDIN

UNDERGRADUATE ARTICLE #7

Investigating the clinical utility of GSK-3 Inhibitor (VP 0.7) to control neurogenesis from neural stem cells

Title

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Key words

Small molecule inhibitors; VP 0.7; GSK-3; Neural stem cells.

Abstract

Glycogen Synthase Kinase-3 (GSK-3), is a serine/threonine protein kinase expressed in all tissues and a regulator of diverse cellular functions (Ugolkov et al., 2016). Aberrant GSK-3 participation in many signalling pathways has been implicated in several neurodegenerative diseases that have driven research to focus on identifying prospective therapeutics using GSK-3 inhibitors. Allosteric inhibitors are very specific and remotely modify orthosteric binding sites of a biological target. Using VP 0.7 on GSK-3, we reveal promotion of neuronal differentiation from neural stem cells (NSCs) which can be transplanted into neurodegenerated brains. This could shift the balance from neurodegeneration to neurogenesis and neuronal plasticity in diseases such as Alzheimer’s.
Small Molecule/ GSK-3 Inhibitors

GSK 3 inhibitors are of diverse types with different mode and mechanism of actions. These include inhibitors isolated from natural sources, cations, and small synthetic molecules. Regarding the mechanism of inhibition, we find ATP (Adenosine triphosphate) -competitive inhibitors, non-ATP-competitive inhibitors, and substrate-competitive inhibitors (Finkelman and Martinez, 2011). The two isoforms of GSK 3, GSK-3α and GSK-3β, indicate the expected specificity and selectivity of GSK-3 inhibitors. Inhibition of GSK-3α has been found to be more potent in GSK-3β that in GSK-3α in pathological models of AD (Alzheimer’s disease) (Avrahami et al., 2013). The underlying mechanism that allows this unique mechanism probably involves differential subcellular localisation or interaction with different protein partners that act at other sites of the kinase by alternative molecular approaches (Avrahami et al., 2013). Nevertheless, designing drugs that effectively target specific kinases is challenging because of the conserved nature of the ATP binding sites across the kinase family (Pandey and DeGrado, 2016).

GSK 3 Inhibitors on NSCs

The growing interest in GSK 3 inhibitors or small molecules led to their adoption in neurodevelopment research examining their effects under both normal and pathological conditions. These small molecules are applied in stem cell derivation, maintenance, production and differentiation in-vivo and in-vitro. Small molecules regulating signalling pathways involved in cell proliferation and maintenance, e.g. Wnt signalling pathway have facilitated long-term maintenance of undifferentiated pluripotent stem cells by inhibiting GSK-3 (Lee, Atala and Yoo, 2016). They have also played a key role in determining cell lineages by modulating signalling pathways involved in stem cells differentiation such as transforming growth factor-β (TGF-β) and Wnt. Guided differentiation reduces the risk of tumour formation in-vivo courtesy of the pluripotency of the cells. Small molecules also improve the safety of pluripotent derived cells. Pluripotent stem cells carry the risk of over proliferation leading to tumours; thus, differentiated cells should be free of pluripotent stem cells (Lee, Atala and Yoo, 2016). Therefore, small molecules have been used to get rid of pluripotent stem cells from differentiated cells to improve safety during transplantation. Previously, pluripotent stem cells had to be genetically modified to express suicide gene that would metabolise in contact with a prodrug and kill the cell. Cell therapy is quite challenging to achieve in the CNS, but small molecules can promote neurogenesis in-vivo. Inhibition of GSK-3 has a profound effect on neuroprotection and self-renewal pluripotency of stem cells. However, for all these inhibitors to be successful in their mode of actions, they need to be more specific on GSK 3 targeting.

Recently, data has shown that only a selective subtle modulation of GSK is needed to provide an effect on without interfering with other cellular signalling (Martinez, Gil and Perez, 2013). This is made possible through allosteric sites which are distinct sites from the active enzyme site. These compounds act by inducing conformational change on the enzyme modulating the kinase without competing for the catalytic domain with ATP. These allosteric modulators offer several benefits over other inhibitors. First, they provide higher selectivity because they target unique sites in kinases rather than the ATP binding domain (Palomo et al., 2017). Secondly, besides inhibition of GSK3, allosteric modulators can simultaneously activate the intracellular catalytic activity of specific kinases such as growth factor receptors. Growth factors such as BDNF and NGF support neuronal survival which reduces neurodegeneration and disease progression in AD and Parkinson’s (Eglen and Reisine, 2011). Presently, very few allosteric modulators of GSK-3 have been described, one of them is the quinoline-3-carbohydrazide 1 (VP0.7) (Palomo et al., 2011). Given the potential advantage of GSK-3 inhibition through the use of allosteric modulators, this study aims to test the ability VP 0.7 to control daughter cells from NSCs and its application in clinical utility. Specifically, this study will investigate neuronal differentiation and maturation by investigating the proportion of neurons obtained after inhibiting GSK-3 activity.

Methods

Primary antibodies were purified donkey anti-β-tubulin (TuJ1) (Biolegend UK), biotinylated anti-rabbit secondary antibodies (UK) were prepared using 10 ml PBS and 0.3% Triton mixed with normal blocking serum (Vector Laboratories, USA). VP 0.7 was synthesised at the Institute of Medical Chemistry-SIC following described protocols (Palomo et al., 2011). CDI strain Postnatal mice (n=4) of between one and three days old were used in this study.

NSCs were derived by mechanically dissociating the subventricular zone of CDI mice and maintained in suspension at 37°C/5% CO2 in complete medium supplemented with growth factors that preferentially select for NSCs (EGF and FGF2). The NSCs proliferated and formed neurospheres that were fed every 2-3 days and passaged weekly. To determine the effect of VP0.7 on NSC differentiation, NSCs were seeded onto poly-ornithine/laminin-coated coverslips. They were incubated for 48 hours and switched to a differentiation medium (Neurosphere medium, minus the growth factors) alone or differentiation medium containing a different concentration of VP0.7. The four groups were control (differentiation medium alone), 0.1, 1.0 and 10.0 µM VP0.7. Differentiating NSCs were cultured for a further seven days with medium changes (using the appropriate...
medium, e.g. 0.1 µM VP0.7) every 2-3 days. After seven days, cells were washed with PBS and fixed in 4% paraformaldehyde for 20 mins at room temperature (RTP).

Immunostaining was conducted as usual using 200µl donkey anti-β-tubulin (Tuj-1) primary antibodies and 200µl diluted biotinylated anti-rabbit secondary antibodies at RTP. For staining, the wells were then incubated in peroxidase substrate (DAB) (Vector Laboratories, Southgate UK) solution and counterstained using filtered hematoxylin then washed in graded ethanol solutions of 70% and 100 % concentration. They were inserted in Xylene for 30 seconds and fixed on a slide using DPX. Imaging was conducted using SP150 microscope (Brunell Microscopes, UK), processed using ToupView software (China) and cells were counted using FIJI (ImageJ).

Statistical analysis was done using GraphPad (version 4.03; Prism software, USA).

**Results**

To investigate whether small molecule inhibitors of GSK-3 can be utilised clinically to promote neurogenesis from NSCs, we measured the number of differentiated neurons in the presence of the different concentrations of the small molecule inhibitor VP 0.7. The four groups were control (differentiation medium alone), 0.1, 1.0 and 10.0 µM VP0.7. Cells were stained with neuronal marker Tuj-1, and the proportion of Tuj1 immunoreactive neurons were quantified. A one way anova was carried out and the average proportion of differentiated neurons in 0.1µM and 1µM increased significantly \( F(3, 66) = 3.40 ,p < 0.002, \) by 19.95% (M=50.48,SEM=3.82) and 15.13% (M=48.41,SEM=1.71) respectively compared to the control (M=42.05 SEM=2.87) while neuron population in the 10µM decreased by 5% (M= 39.94,SEM=1.89) (Fig 1a). The proportional increase in neurons after VP 0.7 administration indicate that GSK-3 inhibition results differentiation of neural stem cells toward mature neurons.

Specifically, to determine the specific concentration of the inhibitor VP 0.7 that induces more neurons, multiple comparisons tests were carried out between the controls and the three concentrations and also in between the concentrations. Only the 0.1µM concentration of VP 0.7 was significant when compared to controls and other concentration (p<0.05). The effect VP 0.7 concentration of 10 µM reduced the number of neurons contrary to the population increase trend indicating an opposing effect on neuronal differentiation and maturation. Furthermore, the low percentage of variance (r=13.5%) explained in this study indicate the involvement of other factors in the signalling pathways of NSCs differentiation.
To investigate the length of the neuron projections, we measured the DAB stained neurites, but no significant changes were observed (Fig 1b). All the measured lengths were found similar in all the conditions including the controls. However, one observation made in the 10µm/l on neurite lengths different from other concentration was the elongated neurites (Fig 2d) in the fewer matured neurons. The high concentration of VP 0.7 appears to have an increasing effect on neurite projection and an antagonistic effect on neuron population. Finally, we investigated the cell population to ascertain the health of the cells (Fig 2). The total number of cells in all the concentrations of VP 0.7 including the differentiated neurons remain unchanged 29 (p> 0.0.5) when compared to control even though they increased in the 0.1µm/l. However, the neurons were visible with all the neurites expressed and no pyknotic nuclei observed in all the three concentration of VP 0.7 suggesting obvious toxicity of the introduced drug.

Discussion

Results revealed that the selective allosteric non-competitive GSK-3 inhibitor, VP 0.7, enhanced neuron differentiation from NSCs in vitro. Our findings are consistent with results on previous studies showing that inhibition of GSK-3 with small molecules inhibitors with similar molecular structure induces neurogenesis in-vitro and in-vivo in the hippocampus, dentate gyrus, of adult rats (Garcia et al., 2016). These results reaffirm the potential use of GSK 3 inhibitors therapeutically. Deficiencies in NPCs (neural precursor cells) and impaired neurogenesis has been implicated in the aetiology of many neurodegenerative and psychiatric patients suffering from depression, schizophrenia and bipolar disorder (Eom and Jope, 2009). Therapeutic interventions such as antidepressants, mood stabilisers, and antipsychotics in part facilitate activation of neurogenesis while enhancing remission. The differentiated neurons in this study could potentially be transplanted to replace lost cells from TBI, neurodegeneration or in spinal cord injuries. The active involvement of GSK in CNS diseases can, therefore, be ameliorated courtesy of the regenerative capacity of the brain induced by VP 0.7 which can shift the balance from neurodegeneration to neurogenesis and neuronal plasticity in disease such as Alzheimer’s.

Certain morphogens are implicated in determining neuronal differentiation which VP 0.7 maybe acting on to result in the differentiated neurons observed. Morphogens such as Bone morphogenetic proteins (BMPs), Notch, Wnt and sonic hedgehog (SHH), are important for a variety of cellular processes, including cell survival, proliferation and fate specification during development (Bong, Ming and Song, 2015). Despite this promising potential, VP 0.7 has not yet reached clinical trial phase unlike other small molecule inhibitors such as tideglulsib that has no clinical safety concerns in patients with supranuclear palsy and Alzheimer’s disease even after long-term treatment (Somesh, 2016). Nevertheless, it has shown promising efficacy and safety results in preclinical models of Multiple sclerosis (MS) by diminishing the severity of the chronic phase of Experimental autoimmune encephalomyelitis (EAE), which models the debilitating progressive stage of MS (Beurel et al., 2013). Irrespective of the three different concentrations of VP 0.7, none of them promoted the growth of neurites. However, the cytoarchitecture of the cells appeared normal with intact cell structure with neuronal polarity. This result reveals that VP 0.7 does not break cell cytoskeletal or cause cell death and therefore neurons can survive.

Several lines of in-vitro studies suggest that inhibition of GSK-3 kinase activity is important for morphological functions such as neuronal polarity, axonal growth and branching (Morgan-Smith et al., 2014). Thus, the observed neuronal polarity in the differentiated neurons could be the direct effect of GSK-3 inhibition by VP 0.7. However, one of the reasons for the limited neurite processes could be the small surface area in monolayer cell cultures used in this study. Finally, the total number of cells in some conditions remained unchanged and reduced in other conditions. This could be explained in two ways. Either the cells undergo apoptosis, or they stopped proliferating to begin differentiation. Considering apoptosis was not present in the neurospheres, we conclude that the cell would rather stop the cell cycle for self-renewal in favour of differentiation. One limitation of this study was the lack of specific staining for other cell types, e.g. astrocytes to be quantified. Staining of other cells could confirm exclusive specificity of VP 0.7 on NSCs differentiation to neurons and further identify alternative ways of improving its effect.

In conclusion, GSK-3 is involved in the various signalling pathways affecting neurogenesis, and its aberrant phosphorylation has been implicated in several diseases driving research to focus on identifying prospective therapeutics targeting this pathway. In this study, VP 0.7, an allosteric GSK-3 inhibitor was used to control neurogenesis from NSCs for clinical utility. VP 0.7 inhibited GSK3 differentiating NSCs to mature neurons which can be transplanted to be utilised in a clinical setting. Besides, VP 0.7 did not interfere with the cell health or the cell cytoarchitecture indicates its tolerance in the cell. This discovery is likely to shift the balance from neurodegeneration to neurogenesis and neuronal plasticity in disease such as Alzheimer’s. Cell replacement therapies with the endless source of NSCs could potentially adopt VP 0.7 in generating desired cell phenotypes specifically neurons.
Acknowledgement
I wish to sincerely thank my supervisor, Dr Chris Adams for his gallant support, guidance, and encouragement throughout the research. My appreciation goes to my family and friends both in Kenya and the UK.

Funding
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References


Introduction

Aromatherapy is a known method of using essential oils as alternative treatment to some medicines and for use in calming the mind (Sayorwan et al., 2012). In the experiment carried out, essential oils were used to see their effect on alpha brain waves. This was measured through an electroencephalogram.

Electroencephalograms (EEGs) are used to monitor brain activity in a non-invasive manner which can be used for a number of different purposes. Medically, it is most often used to monitor seizures and epileptic fits to analyse wave patterns to see if there is abnormal activity. This is done by picking up neuronal firing known as waves and are then shown in a programme which enables researchers to analyse the waves. Through this, they are able to see the state the brain is in. For example, beta waves (13-30 Hz) are mostly found in people who are awake with their eyes open. Theta waves (4-8 Hz) are found in children who are awake while not usually found in adults.

Alpha waves are predominantly present in relaxed individuals with their eyes closed. This is further discussed by Schwabedal et al. (2016) as they stated that participants without insomnia showed a greater alpha wave variability and greater alpha power than those participants with sleep deprivation. Alpha waves are usually present only in relaxed individuals, so those with insomnia are not as relaxed which then leads to the difficulty in sleeping, resulting in lesser alpha waves. Alpha waves were chosen to be analysed in this experiment as essential oils are suggested to be useful in relaxation. If this is the case, a relaxant in the form of an essential oil should increase alpha power as alpha waves are usually present in relaxed individuals. The oils were chosen as they would provide olfactory stimulation, which according to Hadara et al. (1998), is a basis for EEG changes. They found that changes in olfactory stimulation in a participant resulted directly in changes in alpha and delta wave power.

The odorants used in the experiment were in the form of an essential oil and are known to be relaxants. The hypothesis of the experiment was that the use of relaxing odorants would directly correlate to an increase in alpha activity. One of the odorants used was lavender. This is a known relaxant and in a study carried out by Kouiviland et al. (2013), it was suggested that lavender had an effect on brain waves, as inhaling lavender at a 10% dilution significantly increased alpha power in all regions of the brain, showing that lavender is a successful relaxant. This is also prevalent in a study by Sayorwan et al. (2012), who tested the lavender at a 10% dilution as well and found that participants were significantly more relaxed after inhaling the lavender oil than before inhaling it as well as increasing alpha wave activity in all

Materials and Method

For this experiment, we recruited a participant (male, aged 21) from the undergraduate neuroscience second year class, and it was made sure that they were comfortable with partaking in the experiment. The participant was to sign a consent form which allowed the participant to have a record of their participation and that they consented to being subject to the experiment. They were able to opt out at any time. The consent form is in the appendix. The reason for using the consent form is to allow there to be a record of the

regions of the brain. For this reason, it is thought that lavender would increase alpha wave activity in the participant in the experiment.

The other odorant used in the experiment was Olbas oil, which was hypothesised to have similar effects on the brain as lavender, as it is marketed as being soothing, relieving and aids relaxation for better sleep. The hypothesis of the experiment was that the use of both odorants, lavender and Olbas oil, would directly correlate to an increase in alpha activity.
participant’s willingness to be part of the experiment, and for them to be debriefed before partaking in the experiment. At this point they were asked if they had any questions and if they were comfortable still taking part. The entire experiment was conducted in one of the science labs in Huxley building at Keele University.

The volunteer was first put into a comfortable position and was lying down with their eyes closed. Distractions were minimised through making sure sound and visual cues were not able to be a distraction through the participant wearing an eye mask and ear plugs. EEG electrodes were attached to the participant’s head using electrode gel to ease contact between the electrodes and the scalp. Face masks were used to hold each different type of odorant by having a few drops of the odorant being dropped onto the mask for 30 seconds at a time. After 30 seconds, the mask was swapped with a new one and another odorant was used. PowerLab, a programme used for acquiring data in life sciences by converting signals into readable data, was used to record the waves after each different type of odorant was applied. The different odorants used were lavender and Olbas oil, both in the form of essential oils. The data was then displayed on PowerLab and the alpha waves were then analysed and the wavelength was looked at more closely. To analyse the data, a section of the wave was cropped and enlarged to be able to see the frequencies and alpha power more closely. From there, it was possible to record each figure and compare data.

Results

![Figure 2: Baseline before applying Lavender oil](image)

![Figure 3: After applying Lavender oil](image)

![Figure 4: Baseline before applying Olbas oil](image)
The baseline before lavender oil was applied was at a frequency of 9.375Hz and had a wave power of 19.687pV². After lavender oil was applied the frequency of the alpha wave was 9.766Hz and the wave power was 36.953pV², indicating that although before and after the oil was applied, there were alpha waves present as the frequency is between 8-12Hz, lavender oil was a relaxant as the alpha wave power increased. The baseline before the Olbas oil was applied was at a frequency of 9.766Hz, whilst the wave power was 26.883pV². After applying Olbas oil, the frequency of the waves 9.766Hz and the alpha power was 22.399pV². This shows that the alpha power decreased after the Olbas oil was applied, indicating that the oil was a stimulant. The graph shows a visual representation of the data.

**Discussion**

The hypotheses that the lavender oil would have an effect on EEG rhythms by generating greater alpha power had failed to be rejected. However, the hypothesis that the Olbas oil would have an effect on EEG rhythms by generating greater alpha power had failed to be accepted. Instead, the Olbas oil was a stimulant and decreased alpha power.

The lavender being a relaxant suggests that lavender has a significant effect on brain activity, more specifically on alpha wave activity. This points to lavender being successful at allowing an individual to be more relaxed. According to a study by Souwndhararajan and Kim (2016), smell plays a big role in stress relief and mood and has done so for thousands of years dating back to ancient Egyptian, Chinese and Indian civilisations. The reason as to why smells have an effect on EEG rhythms is described to be because of the olfactory system having ‘relatively direct’ connections to the brain that are involved in emotion and memory. Some of these regions are known as the thalamus, hippocampus and the frontal cortex. This suggests that olfactory stimulants have a direct effect on cognitive function, and this can be seen as alpha waves are associated with cognitive performance. Souwndhararajan and Kim (2016) also suggest that the reason why lavender has an effect on EEG rhythms is due to it increasing drowsiness, having sedative properties. This points to Lavender being a successful treatment of various psychological disorders, due to its soothing effects. It could perhaps be used clinically, for use in soothing erratic patients or those with anxiety and difficulty staying calm. On the other hand, it could be used for use in home, for those who feel they could benefit from feeling soothed and calm in massage therapy or for use before bed to unwind.

The Olbas oil, although hypothesised to also be a relaxant was a stimulant. It was thought to be a relaxant due to it being marketed...
as a soothing and relaxing oil for use when ill or having blocked sinuses. However, the reason for it being a stimulant could be due to its strong odour when used undiluted. The Olbas oil had been used undiluted in this experiment. A suggestion by Brauchli et al. (1995) suggested that an unpleasant odour would lead to cortical deactivation. They also suggest that repetitive olfactory input results in less cortical activity. The Olbas oil used in this experiment was used after the use of lavender oil on the participant, so by then the use of essential oils may have become repetitive. The lessening of alpha power could also be correlated to the strong smell of the Olbas oil and rather than it being relaxing, it could have been irritating for the participant, making them uncomfortable and the alpha waves would not have been as strong if the participant was not sufficiently relaxed. The Olbas oil may be more effective as a relaxant if it had been sufficiently diluted.

References
be attached, and a small elastic bandage will be applied around the electrodes to hold them in place.

If I take part, what do I have to do?
You will be expected to lay down on the bench, with electrodes attached, and remain relaxed whilst the recording is conducted. Sensory input will be reduced through the wearing of an eye mask and earplugs, though in the initial setup stage you will be required to move your eyes, and head in response to commands to calibrate the equipment.

What are the benefits (if any) of taking part?
EEG recordings are a fairly uncommon form of standard clinical investigation. Therefore, you will be able to visualise your EEG trace.

What are the risks (if any) of taking part?
Minor risk associated with the use of products on the skin, could result in mild reaction to the electrode gel, cleaning wipes, or electrode adhesive.

How will information about me be used?
The data collected will be used by you and your group to produce your laboratory report and oral presentation.

Who will have access to information about me?
Once you have collated your data we will erase the files from the computer used during the practical. Therefore, access to the data will be yourself and your group work colleagues.

What if there is a problem?
If you have a concern about any aspect of this study, you may wish to speak to the tutor who will do their best to answer your questions. You should contact the Module Manager David Mazzocchi-Jones on 33051 d.mazzocchi-jones@keele.ac.uk. Alternatively, if you do not wish to contact the module manager you may contact our School UG/TPG Practicals/Projects Ethics Committee Chair Trish Proctor on p.proctor@keele.ac.uk. If you remain unhappy about the research and/or wish to raise a complaint about any aspect of the way that you have been approached or treated during the course of the study please write to the Head of the School David Hosie on d.hosie@keele.ac.uk who is the University’s contact for complaints regarding practicals.

Contact for further information
Normally only Keele telephone numbers and e-mail addresses should be used in all study documentation. If there are reasons to depart from this then these must be explained in your Ethical Review Panel documentation.

CONSENT FORM
Title of Practical: EEG Recording Practical
Module name and code: LSC-20078 Neuroscience Research
Methods
Name and contact details of Module Manager: Dr David Mazzocchi-Jones
Tel:33051 Email: d.mazzocchi-jones@keele.ac.uk

Please tick box if you agree with the statement

1 I confirm that I have read and understand the information sheet for the above study and have had the opportunity to ask questions. □

2 I understand that my participation is voluntary and that I am free to withdraw at any time. □

3 I agree to take part in this practical. □
The Battle of Habbaniya in May 1941 saw the repelling of the Iraqi army's siege of RAF Habbaniya. It was accomplished by a politically pressured pre-emptive assault by obsolete RAF aircraft of an underprepared and overstretched force and was undoubtedly an unsung chapter of the war. Lasting for five days the assault took hundreds of sorties, thousands of rounds and tonnes of explosives. By ingenuity, tenacity, fortitude and sacrifice, the battle proved decisive, not just for the war in Iraq, but also for Axis designs on the region to gain oil supplies and geographical advantage. However, its significance became lost due to a combination of factors including insufficient press reports and attentions focussed on events closer to home. Arguably it was a political embarrassment; a base left underdefended, aggravated by failures of commanders and civil servants and post war it may have been seen by politicians as unwise to hail victory whilst simultaneously establishing a friendly government in Iraq.

Context
Royal Air Force (hereafter referred to as RAF) Habbaniya was an airbase situated nearly 60 miles from Baghdad on the west of the Euphrates River (Dudgeon, 2000). It was selected in 1931 and completed in 1936. Iraq was viewed as a friendly country hence the base was left vulnerable; no substantial defensive positions, shelters or duplicate services (Dudgeon, 2000). Despite this at the outbreak of the Second World War in 1939 it constituted the major British military base in Iraq. Iraq, a former colony of Britain, had been a British ally, although anti-British sentiment led to “The Great Iraqi Revolution” of 1920 (James, 2009). Britain and Iraq came to an agreement in 1930 and signed the Anglo-Iraq Treaty of Alliance and Mutual Support, this granted Iraq greater autonomy with Britain recognising the “independence and sovereignty” of Iraq and its government and in return Britain was permitted to hold two military bases within the country (Dudgeon, 2000).

Rashid Ali al-Gaylani, (hereafter referred to simply as Rashid Ali), was an outspoken pro-axis Iraqi nationalist and politician during Iraq’s dynamic political landscape of the 1920’s and 30’s. Fostering ties and support through the German Legation in Baghdad, he spread anti-British propaganda (Dudgeon, 2000). On April 1st 1941 seven months after the Battle of Britain, Germany and the Axis powers occupied vast swathes of Europe and North Africa. With the United States and Russia not yet involved in the conflict, Britain stood alone under increasing pressure with the invasion of Greece underway, the siege of Malta and fortunes turning against them in North Africa. However, Prime Minister Churchill recognized the threat that an Axis power in Iraq would pose to the war; depriving Britain of crude oil, severing its air link with India and encouraging further anti-British uprisings already of concern in Egypt. Britain’s first response was to send the 2nd Brigade of the 10th Indian Division who landed at Basra on the night of April 29th, with the rest of the division to follow along, and the aircraft carrier Hermes and two cruisers (Dudgeon, 2000). On learning of this, Rashid Ali mobilized the Iraqi army and dispatched them to seize Habbaniya.

Title
The Battle of Habbaniya 1941: Why was this action so significant and yet so forgotten in the history of the Second World War?

Author
Henry Simpson

Abstract
Iraq was politically thought be an ally of Britain, but politicians, distracted by the occupation of Europe, did not foresee Rashid Ali, a nationalist and Axis ally, gaining support and military influence. The Battle of Habbaniya in May 1941 saw the repelling of the Iraqi army's siege of RAF Habbaniya. It was accomplished by a politically pressured pre-emptive assault by obsolete RAF aircraft of an underprepared and overstretched force and was undoubtedly an unsung chapter of the war. Lasting for five days the assault took hundreds of sorties, thousands of rounds and tonnes of explosives. By ingenuity, tenacity, fortitude and sacrifice, the battle proved decisive, not just for the war in Iraq, but also for Axis designs on the region to gain oil supplies and geographical advantage. However, its significance became lost due to a combination of factors including insufficient press reports and attentions focussed on events closer to home. Arguably it was a political embarrassment; a base left underdefended, aggravated by failures of commanders and civil servants and post war it may have been seen by politicians as unwise to hail victory whilst simultaneously establishing a friendly government in Iraq.
An Audax Biplane sent to reconnoitre at daybreak on April 30th discovered 2,000 troops, fieldpieces and armoured vehicles, digging in on the plateau above the camp, with many more en route from Baghdad. At 6am an Iraqi officer delivered a warning to the camp: 'For the purpose of training we have occupied the Habbaniya Hills. Please make no flying or the going out of any force of persons from the cantonment. If any aircraft or armoured car attempts to go out it will be shelled by our batteries, and we will not be responsible for it.' (Dudgeon, 2000, p48).

Air Vice Marshal Smart, base commander replied: “Any interference with training flights will be considered an ‘act of war’ and will be met by immediate counter-offensive action. We demand the withdrawal of the Iraqi forces from positions which are clearly hostile and must place my camp at their mercy.” (Dudgeon, 2000, p48). In response to the threat, ground crews dug trenches with machine gun pits around the base and aircrew armed and fuelled aircraft which were put in safe locations and 4 makeshift squadrons were formed as part of the “Habbaniya Air Striking Force.” It was judged that if the Iraqi force was to strike, the underdefended base would be overrun. The only solution was to strike first, Churchill himself messaged Smart; “if you have to strike, strike hard.” (Lyman, 2006 p42). The scene was therefore set for the battle to commence.

The Battle began at 05:00 hours on May 2nd when the “Habbaniya Air Striking Force,” supported by Vickers Wellington twin engine bombers, from Shaiba, attacked the entrenched Iraqi positions on the plateau. The Iraqi army quickly responded with strong anti-aircraft fire and by launching a continuous shell bombardment of the camp which ironically helped the striking force to identify their positions. The Iraqi Air Force later responded by launching hit and run raids against the camp and in return the RAF units put up a continual air assault; as aircraft landed, engines were kept running whilst one crew reported their attack and the other oversaw repairs, refuelling and re-arming.

The RAF perimeter blockhouses took sustained fire throughout the day but remained in action thanks to an Assyrian company which repelled armoured forays towards the camp by Iraqi armoured cars and light tanks (Lyman, 2006). The RAF air assault lasted around 14 hours and at the close of day, 22 out of 64 RAF aircraft were out of action and ten pilots where dead or hospitalised. The Wellingtons had attracted the majority of ground fire resulting in one crash and nine unserviceable (Dudgeon, 2000).

On May 3rd the relentless programme of bombing Iraqi positions continued, as did the intense bombardment of the camp. A decision was taken to “take the fight to the enemy” and the RAF began to target Iraqi Air Force bases with the first attack being on Rashid Air Base catching many of the Iraqis by surprise and damaging 29 aircraft on the ground (James, 2009). A raid on Baquba followed which destroyed a further 14 aircraft seriously reducing the Iraqi air potential. A rifle factory at Al Musayib was also bombed and set on fire although the main targets remained the Iraqi positions on the plateau (Dudgeon, 2000). Gloster Gladiator, 1934 biplane fighters, were proving effective in air combat against the Iraqi Air Force and DC-2 twin engine airliners of No.31 Squadron were able to evacuate civilians and deliver supplies (Lyman, 2006).

During the second night limited night bombing raids were carried out by the RAF and fighting patrols began to range out under the cover of darkness to find outlying Iraqi positions and deter any advance on the camp. On May 4th the Habbaniya Air Striking Force was now working in a pattern of attacks alongside the Wellington Bombers, although a shortage of pilots was the major concern. Fortunately Bristol Blenheim bombers, converted into interim fighters from No. 203 Squadron were sent in support and the arriving pilots were staggered to see ground crew trying to wave them in behind the hangars until bursting shells revealed exactly why (Dudgeon, 2000).

Amazingly two 18 pounder vintage guns of First World War were removed from display, cleaned and pressed into action. A cheer went up from the defenders as they opened fire and, with the Iraqis now receiving return shell fire, they feared further British reinforcements had arrived (James, 2009). On May 5th bombing and shelling continued with a conspicuous air to air victory for a Blenheim over the camp which rallied the defenders and further dented Iraqi morale. The Iraqi air bases were also targeted again and their return raids dropped off sharply. By this stage only four RAF Oxford trainers, converted to act as bombers, of 27 remained airworthy and the pilot situation became even more critical; four of the student pilots were suffering nervous exhaustion and almost every man was carrying some sort of wound and facing severe fatigue (Dudgeon, 2000).

By May 6th, suffering high casualties and with shattered morale from continuous attack, the Iraqi troops withdrew from the plateau abandoning much of their remaining equipment just as an armoured column containing reinforcements headed towards them from Falluja. Their meeting mid retreat in a vulnerable position resulted in a disaster for the Iraqis that would prove the decisive blow of the battle. An Audax on reconnaissance spotted the bottleneck of men, vehicles and equipment and swiftly relayed the information back to Habbaniya. The result was the launch of a “maximum effort strike,” every aircraft that could be coaxed off the ground was launched fully loaded with bombs and ammunition and under instructions not to return until that was exhausted. Some 40 aircraft launched and over the course of two hours of attack, 139 sorties (missions flown) were recorded, resulting in the destruction of the Iraqi column...
the Middle East and North Africa.

Access to the oil would also have strengthened the Germans’ impossible, thus allowing the Axis powers to control vast swathes of occurring) and would have made the victory at El Alamein vital for the North African theatre (a place in which military action would not have been able to dislodge. This was a suitable base in Iraq, one that the underprepared troops of the Habbaniya fallen, then the Axis powers would have established back under British control with Raschid Ali’s pro-Axis government then on the Iraqi armed forces were on the back foot with direct ground and in combat.

Discussion

The outcome of the Battle of Habbaniya was decisive for Iraq as from then on the Iraqi armed forces were on the back foot with direct Axis support arriving too late to turn the tide. By May 31st Iraq was back under British control with Raschid Ali’s pro-Axis government removed. However, the impacts were much wider reaching. Had Habbaniya fallen, then the Axis powers would have established a suitable base in Iraq, one that the underprepared troops of the Kingcol relief column would not have been able to dislodge. This would have denied Britain access to Iraq’s oil fields which were vital for the North African theatre (a place in which military action is occurring) and would have made the victory at El Alamein impossible, thus allowing the Axis powers to control vast swathes of the Middle East and North Africa.

Access to the oil would also have strengthened the Germans’ positions in Russia and the European theatre. Lord Tedder, air officer commanding RAF Middle East command, recognised the importance of this action to the conflict and said of the battle in 1943 “If the school had been overcome, ...the whole course of the European war would have changed drastically, if we had not lost it altogether.” (Dudgeon, 2000, p139).

But why has a battle of such importance become so lost in the annals of war? Dudgeon (2000) argued that the absence of press reporters or photographers, due to the region being some 1,000 miles from the nearest fighting front in April 1941, resulted in there being few accounts recorded about the battle and no story officially published. This view does cover a main factor about the lack of coverage, but it should also be noted that this was enhanced by other events in the west that grabbed public and media attention around the time of the battle. On May 10th deputy führer Rudolph Hess defected to the United Kingdom, attracting significant media attention, as did the invasion of Crete on May 20th and the sinking of HMS Hood and the subsequent pursuit of the Bismarck at the end of the month. Whilst these occurred just after the Battle of Habbaniya itself any claim of victory in the immediate aftermath could have been said to be premature as the battle for Iraq was still continuing with a Luftwaffe unit heading to reinforce the Iraqi Air Force and the relief column not yet at Habbaniya. Many more skirmishes would need to be fought before peace was declared in Iraq at the end of the month.

When fighting in Iraq finally ended the public attention was then likely still focused on the aforementioned events to the west and with the Iraqi theatre of the Second World War one of the shortest, the public scarcely had time to learn of the fighting before it was over. Without public awareness the event never became entrenched in the public mind set as would the victories in the Battle of Britain, El Alamein and the siege of Malta.

There is however a political argument behind why the battle was so hidden: The whole incident had been a political embarrassment for the strategically important Habbaniya had been left vastly underdefended in the face of an underestimated enemy. Dudgeon 2000, refers to the understandable desire for the failings of civil servants and military commanders to be kept hidden from the public for morale purposes in time of war. There would also be cause for the events to be further buried after the war whilst Britain helped to establish a friendly government in Iraq. It could have been seen by politicians as unwise to hail the victory and stir up anti British sentiments and subsequently the event was side-lined for many years as “The Iraq Revolt” suppressing the vitality of the action to the outcome of the Second World War (Dudgeon, 2000).

While modern historians now recognise the battle more so than their predecessors and more published works are raising the profile of the battle, some did appreciate the significance of the battle early on. Winston Churchill wrote in his memoirs that “The spirited defence of Habbaniya by the Training School was a prime factor in our success.
The Germans had at their disposal an airborne force which would have given them Syria, Iraq and Persia, with their precious oil fields...” (Dudgeon, 2000, p137). Denis Richards, the senior narrator of the Air Ministry’s historical section from 1943 to 1947 also wrote “But no one who has studied the story of the Iraqi Revolt has forgotten, or is likely to forget the achievements of No. 4 Flying Training School; for the rout of an organised army and air force by makeshift crews in training machines, who in less than a month flew some 1,400 sorties against the enemy, a feat unprecedented in the brief but crowded annals of air warfare.” (Dudgeon, 2000, p140). His wording highlights the Ministry of Defence doctrine to refer to the theatre as the “Iraq Revolt” in the years following the conflict.

Conclusion

Overall however, with little public knowledge about the battle it was all too easy for victory at Habbaniya to be buried among other events and for it to remain buried willingly or unwillingly after the war and as a result it remains a poorly recognised engagement to this day.

Sources


Context

Makeup is a widely functional and diverse product which has been around for centuries (Adams, 2011), with the market becoming increasingly saturated in recent years. In a survey of 2,496 women, it was found that on average women spend two years of their life, nine days a year putting on makeup (Haria, 2016). This means that it is not an accidental behaviour and deserves studying (Batres, Russell, Simpson, Campbell, Hansend, and Cronke (2018) measured time spent applying makeup, the amount of disposable income spent on makeup, and level of sociosexual orientation. Makeup was not found to be an accurate predictor of someone’s sociosexual orientation, meaning they were not more overtly sexual. It was suggested this could be different for evening makeup, a comparison of evening and day makeup would have made this result more useful. A flaw with this theory though is that women do not see makeup as sexual. Loegel, Courrèges, Morizot, Frédérique, and Fontanye (2017) conducted a study using free association, and women did not change their tipping behaviour. This shows that it may be beneficial to wear makeup in a work setting, especially customer service. This research may have been adapted by asking the waitresses whether they know of this behaviour and wear makeup accordingly. This does not just apply to social situations. Klett et al. (2015) found that women who wore makeup in the hiring process came across as determined, confident and more likely to be considered for leadership roles. However, they were also seen as cold, which would be a disadvantage for them if they intervieaw for a caring role. This means studies of makeup may be important to shift stereotypes of makeup wearers.

Let us now consider why men and women may wear makeup. More recent studies contest whether makeup is worn to elicit attraction from other people. Batres, Russell, Simpson, Campbell, and Cronke (2018) measured men’s responses to wear makeup accordingly. This research may only apply to how the women feel after they have applied rather than why they...
decided to put it on. A study with a more conclusive answer to this question is Logel et al. (2017) who found that sportswomen would use makeup to balance between their multiple identities, one in a more masculine role of sportsperson and another, their feminine identity. Another perception of people wearing makeup is that they are insecure which can be seen in the study as women said ‘well-being’ and ‘camouflage’, this suggests that makeup makes women feel secure and hidden. This can also be seen in the therapeutic use of makeup that it helps cover insecurities improving well-being, this can then lead to better social relationships (Sagehashi, Ito, Ohtake, Nakamura, Yagi, Ogawa, Katsuyama, Yoshida, Oshiro, Aoki, 2009).

In another study, 420 Japanese women between the ages of 40-59 were participants in a study to see how makeup was used, Oi and Ohi (2012) found that during menopause these women used makeup to compensate for negative feelings such as depression, anxiety and wanting to be alone. A strength of this study is that it shows makeup can be used throughout a lifetime, which may include changing motivations to wear makeup.

Because of this gap in the knowledge about makeup this study aims to investigate the motivation behind makeup use and how people use it to show their different identities. Previous research has many limitations, four of which I will highlight here. Firstly, there has been a focus on professional makeup beauticians. Secondly, makeup has been treated as a homogenous group and not focused on the different types of makeup, such as daytime and evening differences. Thirdly, most of the previous research has been quantitative, this has not left room for new motivations and feelings about makeup to emerge. Lastly, the focus on asking others what they think of an individual’s makeup has not allowed makeup users to tell the story of why they wear makeup.

Therefore, this study uses a qualitative design, and thematic analysis of interviews with nine women and one man, to ask the questions (1) What are the social and psychological motivations behind makeup use? and (2) How is the consumptions of make-up implicated in the construction of identity?

Method

Participants

Ten 19 to 21-year-olds (M=20) who self-certified that they used cosmetics at least once a week. This included nine women and one man. Eight undergraduate students and two in full-time work. Opportunity sampling was used to obtain participants. Participation in this study was on a voluntary basis with no compensation for taking part. However, some were recruited by offering reciprocal participation in their final year projects.

Materials

An interview schedule of 26 questions with prompts was designed for the pilot study. Including questions such as “Do you wear different makeup for different occasions?” and “Has wearing makeup changed how you feel over time?”. Questions were placed under three categories ‘General, personal, and makeup use’, ‘Motivations’, and ‘Perceptions of makeup use’. This was printed off on one-sided paper to lay out questions in front of the researcher. All interviews were recorded with an Olympus digital voice recorder WS-852. Audacity digital audio editor 2.1.0 was used to transcribe.

Ethics

Informed consent was gathered by giving all participants the information sheet. They were then asked to sign consent forms, one acknowledging they had agreed to take part in the study and one giving permission to use quotes. They were also reminded in the debrief about their right to withdraw up to a month after data collection. To ensure anonymity of participants they were given pseudonyms and all personal information was removed from the transcripts. Their real names were then kept on a separate document.

Pilot Work

Two pilot interviews were conducted to ensure the questions were easy to understand and prompted answers which were relevant to the research question. The second pilot interview gave unexpected and interesting insights into gender and empowerment. Questions around this were then added to the interview schedule.

Procedure

Interviews could last up to a maximum of one hour, the ten interviews averaged 33.9 minutes. Transcription was done verbatim, this started during the data collection process. Audacity digital audio editor 2.1.0 was used to play interviews as they were transcribed manually into Microsoft word. Data was anonymised during this. Any identifiable data such as name or home city was redacted in transcription and replaced with a description of the identifying data in square brackets. A research journal recorded to note thoughts during data collection.

Design and analyses

All interviews were used in data analysis. Thematic analysis was used to analyse data. Complete coding was used to identify any points of interest relating to the research questions. This was used to
minimise the researcher’s effect on the data and to create as varied a database as possible. Both data-derived and research-derived codes were employed. These codes were then sorted into groups which were given subheading, these were then brought together to create themes and subthemes.

Results

5 themes were found.

• Growing up girly
• Orange struggle
• Not just girl talk
• Blending in
• Femininity at ‘work’

For the purposes of this article, the focus will be on Femininity at ‘work’. This theme was mentioned by every female participant multiple times during their interview and therefore established a much more complete picture of their makeup use than the other themes.

Femininity at ‘Work’

This theme captures how femininity was portrayed in the data. The majority of participants felt that as women they needed to construct and maintain femininity. This can be seen through the repeated use of phrases such as ‘put together’. This can also be interpreted through how the women perceive they are viewed in a work setting. Although they felt they had to wear makeup to be seen as acceptable, they also remarked that wearing makeup was ‘worth it’ because of the reaction they get from others when wearing makeup. This theme shows how femininity is work, work needs femininity, and how femininity can work for you.

First of all, 21-year-old third-year student Shay talks about how she feels that society has put a pressure on her to make an effort in order to look feminine.

“It makes you feel more girly when you put more makeup because you’re making more effort in yourself so you feel more of a girl... yeah I think if you went out without makeup on erm and people just said oh you haven’t made much effort with yourself.” – Shay, 21, page 4.

Shay feels as though she needs makeup to seem feminine, without this she would leave a bad impression because she has not made an effort in herself. Interpreting this, femininity needing effort into the self can be seen as an expectation that women must perform self-reflection and focus on self-improvement to become feminine women. However, being a not so feminine woman is also not an option for Shay, which is why she must put in daily effort to maintain her femininity. “Being a girl you’ve just gotta like get stay up to expectations kind of thing being a girl.” (Shay, 21 page 4). Shay feels women have expectations to keep up with, this highlights how femininity takes persistent work to ‘keep up. From these two extracts there is a picture building of femininity as work.

Liz talks about how she uses makeup to make a good impression on people.

“When you’ve got important things to do yeah like I think it makes everyone look more put together, rather than you’ve just rushed out the house and not put anything on ... especially if you have an interview or something, to look more awake and put together, puts a really good impression on people.” – Liz, 21, Page 1.

In this, we can see that Liz feels it’s important for her to show she is awake and prepared, in contrast to looking flustered. This can also be shown in previous studies where makeup has been linked to looking competent and confident (Klatt et al, 2015). This is significant as Liz feels she needs makeup to meet those expectations.

If this theory were true we would be able to see the positive effects of women wearing makeup. June, a 21-year-old undergraduate, talks about the difference between wearing and not wearing makeup to work.

“I remember I went to work one day and I wasn’t wearing makeup and my mam was like ooh you look so tired and other people were going ooh you look ill, I remember another time when I did have makeup on one man did a double take at the door when I was sat on the floor putting out strawberries and he turned around and went “you’re beautiful”– June, 21, page 12.

June has shown us the stark contrast between wearing and not wearing makeup. Without it, others are worried she is not prepared for the day, either being too tired or unwell. This also shows a positive effect of wearing makeup. As June describes it “it’s just shit like, that like people are a bit nicer to you if you look nice.”. This shows how women have knowledge of the ‘what is cared for is beautiful’ stereotype (Dion, Berscheid, & Walster, 1972). Mia, a 21-year-old student tells us she knows makeup can work in her favour. “I can get resting bitchface so I look more approachable when I have makeup... I prefer it cause I’m quite quiet... so people talking to me I like.” (Mia, 21, page 9). This can be understood as Mia viewing makeup as a tool to help her with social interaction.
Discussion

In summary, this study has opened up the knowledge about makeup use by asking the users themselves why they put it on. This included women wearing makeup to appear feminine. Although, it is important to remember that the majority of participants did not regret wearing makeup and that they did find joy in it at times. This is significant to this research as this study is designed to ask the makeup users how they feel about makeup rather than asking others how they perceive those in makeup.

In relation to the research question, this study has found some motivations behind makeup use. Such as, a pressure the women felt to appear feminine by applying makeup. The social benefits of wearing makeup can also be seen in the theme femininity at work where the women felt they were treated more nicely when they were wearing makeup compared to without. From this analysis, makeup can be seen as affecting identity by improving self-confidence in social situations and self-efficacy in challenging ones. However, whether the long-term effects of makeup use, such as being overcritical needs future research. It can be suggested that encouraging critical thinking about makeup use to those who use it would be useful, this was seen in the interviews where one participant, Kim, even acknowledged that the interview made her think about whether she should be using makeup in the way she did.

The implications of this research for the topic is that we can see some real life experiences of how makeup has affected how people feel and think of themselves. This shows that there is something to be said about makeup, that it is important and relevant for social psychological research. For the individual there are implications also, the participants in the study felt they learned new things about themselves and their makeup habits by taking part. This may also provide a platform for other individuals to reflect off and ask why they wear makeup and if they agree they should be.

Conclusion

The research on motivations behind makeup use and how this affects how the wearer sees themselves are still relatively new. This study has shed light on some motivators such as blending in with others, feeling pressure to show femininity. Through further social psychological research, there will be a more complete answer to how and why people wear makeup.

References


Acknowledgments

I would like to thank my supervisor Dr. Kirsty Budds for guiding me through this project. My final year project group who have been fantastic moral support. Finally, all the participants who dedicated their time to take part in my study.
Introduction
Eating disorder incidences have been increasing worldwide since the 1930s (Hoek, 2016). Whilst this increase has been partly attributed to changes in diagnostic practices, ‘exposure to western media’ has also been cited as a contributing factor (Makino, Tsuboi and Dennerstein, 2004). The media’s role in eating disorder development has long been debated, with the general conclusion that it is ‘media-exposure promoting the Western beauty-ideal’ (Beat, 2018) that is leading to higher incident rates. However, despite this conclusion, Beat (2018) has produced a comprehensive media guidance for reporting on eating disorders that goes beyond concerns of the ‘beauty-ideal’, suggesting that responsible writing about eating disorders must consider a wider range of factors. Additionally, they also identify ways in which the media can engage constructively with the topic. Using the Beat guidelines as a basis, this study aims to identify how a selection of recent eating disorder novels engage with eating disorders and whether this engagement can be considered harmful or responsible.

Method
The Diagnostic and Statistical Manual of Mental Disorders (DSM-V) defines eating disorders as ‘a persistent disturbance of eating or eating-related behaviour that results in the altered consumption of or absorption of food and that significantly impairs physical health or psychosocial functioning’ (2013, p.329), with specific criteria for each disorder. For the purposes of this research, however, ‘eating disorder novel’ has been defined as any piece of narrative literature where the author identifies at least one of the protagonists as having an eating disorder.

The five novels explored in this study are Believarexic (Johnson, 2015), Life Hurts (McNaught, 2017), Snap Out of It (Crilly and Illiffe-Pollard, 2017), The Time In Between (Tucker, 2015), and Wintergirls (Halse, 2009). Each of the novels were selected according to the following criteria: first, that they fulfilled the aforementioned definition of eating disorder novel and, second, that they were first published within the last decade. The criteria the novels were judged against were adapted from the Beat Media Guidance for reporting Eating Disorders. How the novels engaged with these criteria was determined analytically. The following four components will be used to structure the discourse of this research.

Potentially Harmful Features (adapted from the BEAT Media Guidelines):
- Perpetuating stereotypes
- Sensationalise, glamourise or trivialise (exaggerating, unrealistic portrayal)
- Tips and tricks (specific behaviours and how to engage in them)
- Triggering content (descriptions of emaciated bodies, fixation on specific body parts, numbers)

Analysis
Perpetuating Stereotypes
Despite the five books in this study being selected based on just two predetermined factors, there transpired to be further similarities. Most notably, all of the books adhered to the stereotype of the archetypal anorexic, perpetuating the misconceptions that eating disorders only affect white, middle class, teenage girls, and that to have an eating disorder someone must be underweight. Four of the novels in this study concern protagonists who suffer from anorexia nervosa, whilst the fifth, Believarexic, centres on an underweight character with bulimia nervosa. The National Institute for Health and Care Excellence (NICE) estimates the percentage of eating disorder sufferers with anorexia nervosa to be as low as 5%, with the most common condition, other specified feeding and eating disorders (OSFED) affecting 50% of suffers (Figure 1). Quite clearly these books do not accurately represent the broad spectrum of eating disorders that exist.

Figure 1: Pie chart breakdown of the percentage of sufferers with the four most common eating disorder, based on NICE date (NICE Guideline: Eating disorder final Scope, 2015).
Although this particular study has only considered a very small selection of eating disorder novels, the same trend is apparent more widely. Of GoodReads’ 100 top rated young adult eating disorder novels, 73% are focused on anorexia, 13% on bulimia, one on OSFED, and none on binge eating disorder. Giving disproportionate attention to anorexia may contribute to the myth that anorexia is the most common eating disorder and that to have an eating disorder a sufferer must be underweight.

The five novels in this study ranged from entirely fictitious to autobiographical. Both The Time In Between and Life Hurts are memoirs by women who suffered from anorexia in their adolescence. McNaught is now a medical doctor and it is from this perspective that she writes. Conversely, Nancy Tucker writes from the voice of her youth. Wintergirls is fiction written by an established teen author, as is Snap Out of It, albeit co-written by Crilly, a mental health counsellor whose daughter suffered from anorexia. Believarexic identifies itself as an ‘autobiographical novel… the fictionalized story of actual events in [the author’s] life’ (Johnson, 2015), which is a useful view to take of all autobiographies, due to the incomplete, and subjective nature of recollection. Considering that eating disorder sufferers, and in particular those with anorexia, struggle to lay down and retain memories more so than people without eating disorders, it is probable that there are more in inaccuracies within eating disorder memoirs than in memoirs generally (Nandrino et al., 2006). Whilst within autobiographies generally this may not be particularly notable, when discussing eating disorders accuracy is of the utmost importance. Presentation of inaccuracies as fact, as in Nancy Tucker’s The Time In Between, can set unattainable precedents to vulnerable readers. Most concerning is the assertion that when already severely underweight she survived more than ‘three months - with no food at all. Not a crumb’ (Tucker, 2015). Tucker presents this implausible assertion as fact, telling her readers that it is possible to stop eating for almost four months and survive, which may encourage them to emulate this behaviour. Whilst, in many cases, the inaccuracies in autobiographies will not be meant to intentionally deceive, a caveat that ensures the reader is aware that the novel may contain these inaccuracies would be advisable.

**Sensationalise, Glamorise or Trivialise**

There is a balance to be struck between what is accurate and what is necessary, particularly in relation to sharing disordered thoughts. Eating disorders often skew a person’s perspective, leading them to hold untrue and harmful beliefs in relation to weight and body image, among other things. Whilst it is important to capture a realistic representation of an eating disorder, much of which is manifest through psychological symptoms, there is also a need to protect one’s readers. Focus on thoughts pertaining to anxiety and self-doubt are useful in providing an accurate portrayal, but do not risk sensationalising eating disorders in the same way as comments on the illness itself. ‘Except from being hungry and cold, most of the time I feel like I can do anything. It gives me superhuman powers of smell and hearing’ (Anderson, 2009, p.189). These words portray anorexia as something empowering rather than disabling. Similarly, Believarexic gives an idealised image of anorexia as ‘flawless./Anorexics are iron-clad in their willpower’ (Johnson, 2015, p.107). Whilst these comments may not reflect the thoughts or beliefs of their respective authors, the inclusion of them is a potential hazard to vulnerable readers who may internalise the comments as mantra. To mitigate this danger Snap Out of It utilises dual narration to counter the disordered voice with a more objective one, whilst Life Hurts, being written in the past tense, uses a rational, retrospective to counter any potentially problematic comments. Unfortunately, the other three novels studied did not address this issue at all.

**Tips and Tricks**

Similarly, the inclusions of ‘tips and tricks’—the sharing of potentially harmful behaviours and ways in which one can engage in them—needs to be balanced. Although often encompassing many fundamental characteristics of eating disorders, detailing behaviour and ways they can be engaged in poses a real possibility that the books will be used as ‘instruction manuals: diet tips, weight loss ideas’ (Johnson, 2015, p.249). This is a reality that many of the authors seem acutely aware of. ‘My biggest fear in writing this book—and writing it honestly—was that it would serve the same “cheat sheet” purpose that eating disorder memoirs served during my own struggle’ (Tucker, 2015, p.ix). Similarly, two of the authors refer to specific instances where the power of suggestion had an impact on them during their own illnesses. McNaught writes:

“Do you make yourself sick?” she asked. Until that point I’d not thought about that way of losing weight, but now the idea had been suggested to me, by a doctor, I couldn’t get the notion out of my mind.’ (2017, p.47)

Likewise, Tucker notes: ‘not accessing pro-anorexia websites on the internet (... I didn’t know such things existed, but will definitely investigate them now).’ (2015, pp.217-8) These specific moments are not necessarily inappropriate themselves, however they serve to demonstrate how impressionable vulnerable people can be, and why it is imperative that the inclusion of ‘tips and tricks’ be kept to a minimum. Yet, despite the apparent awareness of this hazard,
excluding this potentially harmful content has not occurred. The Time in Between, the novel that makes the biggest point in the foreword about not providing this information, is the worst offender.

Life Hurts is the only novel that makes a consistent effort to exclude ‘tips and tricks’. Rather than explain how she ‘learned to cheat the system’ and ‘avoid[ed] eating the food’ (McNaught, 2015, p.80, p.39), McNaught simply states that she did. There are, however, a few occasions within the novel where a ‘tip’ or a ‘trick’ is included. Whether this is a calculated risk, ensuring that the reality of eating disorders is not sanitised, cannot be determined by only looking at the text. However what is clear is that ‘tips and tricks’, and triggering content more widely, are far less prevalent in McNaught’s Life Hurts than in the other novels included in this study.

**Triggering Content**

Triggering content is defined for the purposes of this study as anything that may cause the relapse, development or worsening of an eating disorder, and has been broken down into three countable factors as detailed in Figure 2. Each of the novels has engaged with these factors to different degrees: forming an integral part of the plots of both Wintergirls and The Time In Between, whilst McNaught’s Life Hurts omits them entirely.

Given the highly competitive nature of eating disorders and a common feeling that one is not ‘ill enough’ for treatment, including specifics against which sufferers can compare themselves can be extremely dangerous. This is equally relevant in relation to numbers as it is to descriptions. Whilst ‘diet soda (2) + lettuce (15) + 8 tablespoons salsa (40) + hard-boiled egg white (16) = lunch (71)’ (Anderson, 2015, p.76) allows for someone to directly compare their own diet and caloric intake with a character’s, so too does a description without the calories stated, ‘I tin tuna/ I tin sweetcorn/ I apple’ (Tucker, 2015, p.288). As such, both instances are considered equal in their potential to cause harm, reinforcing the idea that physical health is a marker for mental wellness. This is both incorrect and potentially invalidating to the majority of eating disorder sufferers who are not underweight and by this measure do not look ill (Beat, 2018). Ironically, this is something that the authors of the novels appear to be aware of, but continue to perpetuate regardless. One of Anderson’s character asserts ‘it’s not about the number. It never was’ (2015, p.116), yet progresses her novel by periodically stating the protagonist’s weight and using the same number format as she uses for weights to number the chapters, quite literally progressing the novel through the use of weights. Tucker echoes this process, naming the sections of The Time In Between as ‘Small’, ‘Smaller’, ‘BIG’, and ‘In Between’ (2015), the longest section by far being ‘Smaller’. Poignantly, it is both of these novels that include the most references to ‘numbers’, with 62 and 73 respectively, they also both include the most references to ‘bones’ and ‘tips and tricks’. The Time In Between includes significantly more ‘physical descriptions’ than do any of the other books, with 37 instances, compared with less than 10 references in each of the other novels. Towards its end, Tucker’s novel briefly explores a period of bulimia within Nancy’s life. Nancy states, ‘I’m not better. Yes, I’m heavier and less malnourished and slightly more able to cope with day-to-day life’ (Tucker, 2015, p.281). However despite including moments of binging, Tucker still continues to use restriction as a marker of greatest sickness, focusing most prominently on restriction rather than on binging and purging, behaviours that are the indicative markers of bulimia.

This body checking routine, whilst not including any numbers, provides the same opportunities for comparison as weights or BMIs would. Although Tucker is careful not to include many stated numbers, there are several instances of this ilk that can be considered equally harmful; her use of physical appearance, including 37 extended ‘physical descriptions’, is used to track the decline of the protagonist’s health.

Using physical health and appearance as a marker for mental wellness is a technique employed by all of the authors included in this study, again with the exception of McNaught whose focus is primarily on the protagonist’s psychological decline, including no references to ‘numbers’, ‘bones’, or inclusion of protracted ‘physical descriptions’ of her characters. Psychological symptoms are also present in the other four novels, albeit to a much lesser degree, focusing instead on what is visible and perhaps more easily understood, reinforcing the idea that physical health is a good marker for mental wellness. This is both incorrect and potentially invalidating to the majority of eating disorder sufferers who are not underweight and by this measure do not look ill (Beat, 2018). Ironically, this is something that the authors of the novels appear to be aware of, but continue to perpetuate regardless. One of Anderson’s character asserts ‘it’s not about the number. It never was’ (2015, p.116), yet progresses her novel by periodically stating the protagonist’s weight and using the same number format as she uses for weights to number the chapters, quite literally progressing the novel through the use of weights. Tucker echoes this process, naming the sections of The Time In Between as ‘Small’, ‘Smaller’, ‘BIG’, and ‘In Between’ (2015), the longest section by far being ‘Smaller’. Poignantly, it is both of these novels that include the most references to ‘numbers’, with 62 and 73 respectively, they also both include the most references to ‘bones’ and ‘tips and tricks’. The Time In Between includes significantly more ‘physical descriptions’ than do any of the other books, with 37 instances, compared with less than 10 references in each of the other novels. Towards its end, Tucker’s novel briefly explores a period of bulimia within Nancy’s life. Nancy states, ‘I’m not better. Yes, I’m heavier and less malnourished and slightly more able to cope with day-to-day life’ (Tucker, 2015, p.281). However despite including moments of binging, Tucker still continues to use restriction as a marker of greatest sickness, focusing most prominently on restriction rather than on binging and purging, behaviours that are the indicative markers of bulimia.
Figure 2: Numerical analysis of triggering elements in the novels studied.
‘Numbers’ refers to any inclusion of BMI, weight or calories, and any descriptions that would allow for one of these to be easily calculated.
‘Bones’ refers to any references to ‘bones’, ‘skeleton’ or a specific bone. ‘Physical Descriptions’ are descriptions of a character’s physical appearance that exceed two sentences in length. ‘Tips and Tricks’ is the sharing of potentially harmful behaviours and ways in which one can engage in them.

<table>
<thead>
<tr>
<th>Novels</th>
<th>Numbers</th>
<th>Bones</th>
<th>Physical Descriptions</th>
<th>Tips and Tricks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Believarexic</td>
<td>13</td>
<td>7</td>
<td>4</td>
<td>15</td>
</tr>
<tr>
<td>Life Hurts</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>5</td>
</tr>
<tr>
<td>Snap Out of It</td>
<td>2</td>
<td>9</td>
<td>7</td>
<td>8</td>
</tr>
<tr>
<td>The Time In Between</td>
<td>73</td>
<td>69</td>
<td>37</td>
<td>42</td>
</tr>
<tr>
<td>Wintergirls</td>
<td>62</td>
<td>25</td>
<td>4</td>
<td>17</td>
</tr>
</tbody>
</table>

Conclusion

Overall, adherence to the guidelines derived for this study varies between the five novels considered. It is difficult to portray the horrors of eating disorders without providing a how-to-guide, but it is certainly possible. Both Crilly and Iliffe-Pollard (2017) and McNaught (2017) have succeeded in writing broadly responsible eating disorder novels, however the other authors have produced works that have the potential to cause serious harm, especially Tucker’s The Time In Between (2015).

Despite the predominant focus of the guidelines on harmful elements to exclude, it is evident that a responsible eating disorder novel must seek to contain positive elements as well. All of the novels studied contained some of these positive elements: the clear portrayal of symptoms both physical and psychological, realistic pacing of eating disorder development and recovery, and the all-encompassing nature of eating disorders. However, it is also pertinent to note that whilst there are a number of positive actions an individual author can take, there are also a number of actions that must be taken by authors as a collective. Ensuring that a range of characters, illnesses, and eventual outcomes are included across this genre of writing must be a concerted effort.

Many vulnerable readers come to these novels looking for ‘tips and tricks’, so whilst support may not be what they seek, it is important that they be able to find it, even if it is included separate to the narrative. Ultimately it is the responsibility of the publisher and the author to protect their vulnerable readers, as is the case for screenwriters and television broadcasters. This study does not suggest censorship or wish to curtail the conversation on eating disorders, but an amount of professional guidance would go a long way to ensuring that eating disorder novels do more good than harm.

References

Anderson, L. H. (2009), Wintergirls, Croydon, UK: Scholastic Ltd.
Abstract

Biomaterials offer the potential to enhance CNS regeneration, potentially providing limited recovery of neurological function for patients, with emerging animal models of spinal cord injury (SCI) showing promise. Hydrogels—cross-linked polymer structures comprising of ~95-99% H₂O—are emerging biomaterials with the potential to support neural stem cell (NSC) scaffolds, allowing replenishment of endogenous stem cell populations depleted at the site of injury. The experiments described herein assessed the utility of Biogels (RM, R20) and Self-Assembling peptides/SAP's (PepGel, a1) for scaffolding NSC growth. Biogels RM and R20 failed to support cell growth in 3-D experiments, whereas SAP's were more stable and supportive of NSC growth. Fluorescence imaging revealed that nuclei and neurons were more abundant and mature in PepGel versus a1 during 2-D slice experiments, therefore PepGel was explored as the primary gel-plated assay candidate. The average Nuclei:Neuron Ratio (NNR) was higher in 0.5% versus 0.1% PepGel solutions, with greater average neurite numbers and more extensive neurites, suggesting 0.5% PepGel is more conducive to NSC growth and development than 0.1% solutions. However, PepGel's mechanical stiffness remains to be elucidated, as does the optimal polymer density for culturing extensively arboured neurons, closer to lengths observed in the literature, enhancing in-vivo transplantation potential.

Repair in the CNS

In the endogenous Central Nervous System (CNS), neural stem cell (NSC) recruitment functions to restore oligodendrocyte and neuronal populations during postnatal life, however, our innate capacity for repair is limited, increasingly strained as we age, and even more if injured or exposed to disease. In pathologies such as Spinal Cord Injury (SCI) or Alzheimer's Disease (AD), toxic microenvironments contain high levels of reactive oxygen species (ROS) leading to premature cell death and molecules inhibitory to regeneration, such as myelin fragments. Myelin debris has been shown to activate RhoA protein cascades resulting in stunted axonal growth (Yiu & He, 2006). Promisingly, synthetic microenvironments contain toxic agonists like TLR4 (which enhance myelinophagy) show evidence of encouraging remyelination in rodent models (Church et al., 2017). These microenvironments are more conducive to nerve regrowth (McKenzie et al., 2014). These agonists lead to premature cell death and molecules inhibitory to regeneration, such as myelin fragments.

Injecting therapeutic molecules in situ comes with its own complications, with short-lived benefits due to degradation or signal interference at the injury site (Ziembka & Gilbert, 2017). One key concern for therapeutic molecules is their off-target migration due to cell washout. Direct intervention at the injury site, through vectors (e.g. retroviruses) or combinatorial therapies are the main methods of intervention (Church et al., 2017; Führmann, Anandakumaran & Shoichet, 2017; Trounson & McDonald, 2015).

Cell transplantation is a popular versatile strategy which can be utilised with other approaches, particularly with a class of biomaterials known as hydrogels. Hydrogels are biological or synthetic cross-linked polymer substrates composed of 95-99% H₂O. These long-chain polymers can be either natural Biogels (e.g. glycosaminoglycans), similar to cartilage (Pan et al., 2014), or synthetic self-assembling peptides (SAP's) (Pakulska et al., 2015).

Having been the subject of research since the early 60's (El-Sherbiny & Yacoub, 2013) hydrogels are becoming a biologically-relevant therapeutic tool (Mata et al., 2017). Biological (chitosan, cellulose, collagen) and synthetic substrates (poly-ethylene-glycol, poly-lactic acid) can be used independently or in mixed constructs to utilise the biological compatibility of biological substrates with the mechanical tuneability and manufacturing pragmatism of synthetic substrates (Koutseopoulos, 2016).

These polymers can gelate reversibly or irreversibly in response to pH or temperature as desired (Zhu & Marchant, 2011), evidencing physiologically appropriateness. Gel properties such as tunability (modifiability) and biodegradability are key modalities for sustainable functional group release as the gel degrades and may offer long-term potential for personalised therapies (Ahmed, 2015).

At present, lab-grown and commercially sourced gels are undergoing research to explore their in vitro and in vivo potential for neural stem cell (NSC) regeneration. These constructs will be evaluated in terms of cell viability in terms of cell morphology, process length and cell counts.
Figure 1: Common tissue engineering approaches used in bioengineering/biomaterial research. Novel bioengineering/biomaterial approaches generally involve isolating cells from the body, increasing the cell number and seeding them onto media, either onto pre-gelated scaffolds or onto injectable scaffolds which gelate in response to a stimulus (such as temperature, pH etc.). Diagram sourced from El-Sherbiny & Yacoub (2013).

The hardness of the substrate affects the relative proportion of given cell types: neurons versus oligodendrocytes versus astrocytes and so on, in line with the physiological stiffness of native tissues (Amer et al., 2017; Engler et al 2006). Culturing appropriate levels of these cells may aid neurons forming connections within and around the lesion site (Mauri et al., 2018), whilst glia (predominantly astrocytes, oligodendrocytes) support synaptic formation, and clear lesion debris, sustaining neuronal function (Franklin & Ffrench-Constant, 2008).

A second combinatorial benefit comes in the form of releasing drugs (e.g. growth factors, immunosuppressants) as the gel degrades, potentially bolstering cell survival, and ameliorating disease (Führmann, Anandakumaran & Shoichet, 2017). Furthermore, identifying pre-clinical candidates for these combinatorial treatments may provide traction towards personalised medicine solutions, where tailored therapies target pathology-specific and person-specific components of disease to yield therapeutic efficacy (mitigating allergies or intolerance to given drugs).

The present research examines the suitability of a number of hydrogel candidates in culturing NSC’s in both 2-D and 3-D with respect to cell morphology, process length and cell counts.

Method

Primary progenitor cells were extracted from the sub-ventricular zone of CD1 mice at P0-P3, providing a stem cell source for NSC culture. Ethical permission for cell harvesting was attained through the School of Life Sciences Student Project Ethics Committee.

Hydrogels candidates were produced in two 500 µL solution concentrations (0.1%, 0.5%) for PepGel, acquired from [PepGel, U.S.A] and α1, RM and R20 from [BiogelX Ltd, U.K.] respectively. Three experiments explored neuronal growth hypotheses, listed as Experiment One [3-D assessment of the utility of Biogels and SAP’s for NSC’s]; Experiment Two [2-D assessment of PepGel utility for NSC’s] and Experiment Three [2-D gel-plated assay on PepGel concentration effect on neuronal growth]. Gel concentrations for experiments as follows: Experiment One, Two (0.1%), Experiment Three (0.1%, 0.5%).

Cells were cultured in neurosphere medium for four days followed by three days in differentiation medium as described previously.
(Adams et al., 2015) before being seeded onto the surface of hydrogels at concentrations of 1 x 10^5 cells/mL. To examine whether NSCs could be supported in 3-D constructs of PepGel (and other test gel formulations) 1 x 10^6 NSCs/mL were mixed with 0.1% PepGel to distribute cells throughout the matrix. The cell/gel mixture was allowed to gelate for 30 mins at 37°C and once set, culture medium was layered on the gel. NSC and differentiated NSC protocols were then the same as above until fixation. 2-D seeding was used to assess cell viability on individual sections [Experiment Two] and the effect of PepGel concentration on the behaviour of NSCs using 0.1% and 0.5% PepGel (500 µL) hydrogels [Experiment Three]. Hydrogels were set for 30 mins at 37°C for both experiments, as per manufacturer’s instructions. Following culture and feeding, cells were fixed in 4% paraformaldehyde (PFA) for 30 mins (2-D) or 1h (3-D) at room temperature before transferal into PBS and storage at 5°C.

DAB Staining was used for gels in Experiment Two, but not in other experiments. Fluorescent immunostaining was used for all experiments, using DAPI [Experiment One and Two] and Hoescht [Experiment Three] for labelling nuclei, alongside mouse β-Tubulin/FITC as the primary antibody for all experiments. Blocking solution (10% NDS in 0.3% Triton X-100) was applied for 30 minutes prior to overnight primary antibody incubation (β-Tubulin in blocking solution at 1:200 dilution). After washing and blocking, the secondary antibody was applied (Donkey-Anti-Mouse β-Tubulin in blocking solution at 1:200 dilution), for DAB staining [Experiment Two] and fluorescence staining using FITC [all experiments].

DAB samples underwent an immunohistochemical wash procedure prior to DAPI coating, whilst fluorescence samples were only coated in DAPI. In Experiment Two, PBS was replaced with 30% sucrose in PBS (1ml) as a cryoprotectant for freezing at -80°C until later retrieval and cryosectioning at 45µm. Slices were stored on poly-lysine slides at -20°C for immunostaining. For Experiment Three, solutions were prepared as above in eight experimental wells; four for each concentration (0.1%, 0.5%).

Brightfield analysis was completed prior to freezing and after DAB staining to assess NSC visibility in the hydrogel. A Leica AX10 Fluorescence Microscope was used to visualise DAPI/Hoescht (Blue channels) and FITC/β-Tubulin (Green channels) channels using ZEN software. Micrographs were processed using Adobe Photoshop CC 2018 to enhance basic features (e.g. contrast, brightness) and merge planes. Merged images and Z-Stacks from ZEN were processed in ImageJ to analyse cell counts to explore nuclei:neuron ratios. Neurite numbers were counted using ImageJ, and NeuronJ was used as an add-on to trace neurites in 8-bit images (converted from original 64-bit images in-software) to determine neurite length. Neurite length conversions from pixels to micrometres was made using the scale bar reference. One-tailed two-sample t-tests were to analyse statistical differences in the average of nuclei:neuron ratio (NNR), neurite length, and neurite number.

### Results

Bright field analysis of the hydrogel compounds showed neurosphere development in all gels, with greater development in α1 and PepGel versus Biogels. Further examination using fluorescence microscopy highlighted neurospheres were present and well-supported in PepGel and α1 wells, whereas the RM and R20 Biogels showed few visible early neurospheres, and high background fluorescence, thus were removed as candidates. PepGel and α1 gels showed acceptable levels of background fluorescence and seemed conducive to neuronal culture. However, image analysis showed evidence of blurred nuclei and neurons, as if out-of-phase. This did not necessarily indicate that the gels were not conducive transplant materials, but rather that the 3-D gel stack is not necessarily well-distributed.

Alternatively, the gel may have obscured visualising the neurons, meaning projections were unclear in the 3D model, limiting evaluation of its support for neuronal growth. Images from Experiment One were thus unclear, which prompted the use of a 2-D model to assess PepGel utility. Average slice data is given in Table 1, providing a summary of neuronal growth indicators in the 2-D PepGel slices, including the average nuclei:neuron % (NNR), designated as the DAPI:FITC (β-tubulin) ratio, alongside the average neurite length in each section.

Section one and two averages fall within 7µm of the average NNR, whereas section three illustrates a lower NNR, indicative of a higher quantity of neurons being visible in the slice, a promising indicator of early neuronal growth.

<table>
<thead>
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<tr>
<td>1 [180µm]</td>
<td>37.62</td>
<td>24.56</td>
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<td>2 [225µm]</td>
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<td>3 [315µm]</td>
<td>20.58</td>
<td>31.58</td>
<td>5.71</td>
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Table 1: Extent of neuronal growth in 2-D PepGel slices [Experiment Two]
Table 2: Extent of neuronal growth in plated 2-D PepGel slices [Experiment Three]. N.B. Standard Error of the Mean indicated as appropriate [SEM]

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<th>Gel Concentration</th>
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<td>55.19 (52)</td>
<td>51.33 (46)</td>
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<td>52.58 (46)</td>
<td>45.75 (46)</td>
<td>45.05</td>
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<td></td>
<td>3</td>
<td>68.56 (49)</td>
<td>48.50 (49)</td>
<td>42.55</td>
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<tr>
<td></td>
<td></td>
<td>x-bar = 58.77           [±4.20]</td>
<td>x-bar = 48.53 (49)          [±6.00]</td>
<td>x-bar = 42.57               [±2.60]</td>
</tr>
<tr>
<td>0.5%</td>
<td>1</td>
<td>53.38 (49)</td>
<td>81.67 (82)</td>
<td>45.74</td>
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<td></td>
<td>2</td>
<td>85.12 (76)</td>
<td>76.00 (76)</td>
<td>48.64</td>
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<tr>
<td></td>
<td>3</td>
<td>123.27 (70)</td>
<td>69.33 (70)</td>
<td>60.25</td>
</tr>
<tr>
<td></td>
<td></td>
<td>x-bar = 87.26               [±19.00]</td>
<td>x-bar = 75.67 (76)          [±8.00]</td>
<td>x-bar = 51.54               [±3.80]</td>
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<td></td>
<td>x-bar = 73.02               [±11.60]</td>
<td>x-bar = 62.10 (63)          [±7.00]</td>
<td>x-bar = 47.06               [±3.20]</td>
</tr>
</tbody>
</table>

Similar trends were also observed for the neurite length, though in section three, a broad dispersion from the mean is observed, indicating larger neurite processes than seen in other slices, 8µm larger than average.

This dispersion indicates neurons embedded in deeper slices of the PepGel solution are building more extensive processes than those closer to the apex of the gel.

In Experiment Three, the difference between the average NNR of 0.1% and 0.5% PepGel solutions was determined to be statistically significant by a t-test; t(22) = -1.84, p < .05.

This difference is illustrated in Figure 4(C), as is the difference in the average number of neurites in 4(D); t(22) = -2.19, p < .05. As evident in Table 2, there is trivial difference between the SEM values for neurite length, 2.5 (-5% of the average neurite length across conditions).

Figure 3: (A-B) The dense core of the neurosphere evidences dense aggregation of β-tubulin, with multiple developing somas visible on gel and around the neurosphere borders. The abundance of neurons and associated neurites suggests the gel is supportive of neural stem cell development. A higher quantity of β-tubulin stained neurons is visible in the (B) 0.5% versus the (A) 0.1% PepGel. Stained nuclei are visible within the gel and in close proximity to the neurosphere, with limited migration away from the neurosphere itself. Trapped neuronal bodies such as this pose interesting transection injury models in severing axonal connections and investigating the degree of regrowth.

On the pages overleaf, Figure 5. shows neurons and nuclei stained for β-tubulin and DAPI respectively, with particular attention drawn to the developing dendrite (bottom layer, right panel) and to numerous sprouting axonal collaterals.
Figure 4(E) illustrates this difference in the neurite length across the 0.1% and 0.5% concentrations respectively, with a t-test indicating a highly significant difference in the neurite length of 0.1% and 0.5% PepGel; t(22) = -2.39, \( p < .001 \).

**Discussion**

The experiments described assessed the utility of Biogels (RM, R20) and SAPs (PepGel, a1) for NSC culture. PepGel appeared to support NSC differentiation into neurons in 2-D experiments generating a higher number of neurons in the 0.5% PepGel concentration (as indicated by the higher NNR). This demonstrates PepGel can be optimised to influence NSC differentiation and may potentially be useful for in-vivo NSC transplantation. However, in preliminary 3-D experiments, Biogels did not appear to enable 3-D NSC growth, with limited neurosphere development comparative to a1 and Pepgel.
displayed lower levels of neurosphere development and arborisation compared to PepGel, therefore, PepGel was selected as the main candidate for later experiments.

During Experiment One, neurons were indistinct, with less neurosphere development than predicted. As Mauri et al., (2018) and Zhang et al., (2017) suggest, 3-D gels are essential assays for recapitulating native parenchyma, thus it is vital to understand whether PepGel did not support NSC differentiation in 3-D culture. In the case of Mauri et al., (2018), cells cultured in 3-D gels had 6x higher survival rates versus 2-D gels, with overall numbers 40% higher in 3-D versus 2-D gels at active phases, suggestive that 3-D gels provide better cultures for NSC’s. Therefore, it is unclear why findings were not recapitulated with PepGel in Experiment One. Further investigation with live-dead ki67 staining may be useful in follow-up research to elucidate why PepGel displayed poor survival in 3-D, and to explore whether PepGel concentration affects survival/proliferation in 2-D.

Secondary experiments assessing PepGel’s utility for culturing NSC’s showed modest 2-D growth with homogenous distribution across differing PepGel concentrations (0.1%, 0.5%). Higher PepGel concentrations increased the number of neurons, neurites and the length of arborous. Overall, the data suggests 0.5% PepGel was more conducive to NSC growth and differentiation on all three metrics, potentially offering greater number of functional groups for NSC binding, which Lampe, Antaris and Heilshorn (2013) evidence increases the rate, length and density of neurite outgrowth in elastic-protein hydrogels.

Hydrogel matrix stiffness may also influence NSC culture and can be tuned close to that of the endogenous ECM (Rauner et al., 2017), supporting not only 3-D growth, but drug/molecule-of-interest release. To better understand how the stiffness of the 3-D model affected NSC culture, the exact stiffness of PepGel needs to be determined via mechanical testing (Adams et al., 2016) or Atomic Force Microscopy (Nalam et al., 2015).

The poor neuronal survival evident in the Biogels in Experiment One was likely a result of the fact that Biogels generally have a specific optimal pH and temperature range upon which to gelate (Ziembka & Gilvert, 2017; Pakulska et al., 2015). NSC’s grown under such conditions may experiences factors detrimental to cell survival and proliferation, particularly for neuronal species. Gel acidity would have buffered in situ under physiological pH, however, in vitro, the survival rate of NSC’s was low.

It may be advantageous to use pH-tolerant self-healing nanofiber gels to protect NSCs from damage. Sun et al., (2016) highlight their nanofiber hydrogel is functional at neutral pH (valuable as a physiological pH probe) supporting NSC differentiation. In contrast, SAPs are reversible hydrogels, with greater mechanical stiffness variability, and more tuneable mechanical and chemical properties.

Applications of 3-D hydrogels/scaffolds are promising, with potential long-term prospects of “battery” technology integration (Sun et al., 2016; Balint, Cassidy & Cartmell, 2014), helping to power next-generation devices (e.g. biosensors). Such technologies could integrate electroactive properties into hydrogels (i.e. PepGel) to yield conducive polymer-hydrogels to stimulate encapsulated tissues, creating rudimentary biosensors or drug-release devices (Schroeder et al., 2017; Thompson et al., 2014; Green et al., 2010; Small, Too & Wallace, 1997). Hydrogels can also mitigate drug-release via nanoparticles, as in, as in chitosan-derived hydrogels releasing antimicrobials (Babu et al., 2010). Similar models have been suggested for 3-D printed hydrogels for liver detoxification (Gou et al., 2014), providing other therapeutic avenues for hydrogels, alongside NSC scaffolding.

Currently both commercial and laboratory hydrogel formulations need to be refined to improve in vitro efficacy, prior to implantation in vivo. Candidates will be modelled in physiologically representative 3-D systems (Zhang et al., 2017), and will be tuneable, biodegradable, and compatible with combinatorial therapies. Hydrogels need to be optimised for CNS implantation, targeting concerns including gel toxicity, and poor gelation (Sun et al., 2016; Shoichet, 2009). In conclusion, the present research highlighted of the initial candidate hydrogels, only PepGel adequately supports NSC differentiation into neurons, and may warrant further in vitro testing as a potential research candidate.

References


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For those concerned with achieving universal social and political justice, the sordid state of human affairs must not obscure the tangible gains acquired through decades of principled activism. Indeed, it is our recognition of this progress which incentivises and inspires the necessary work still to be done. It is no small feat that the populations of the most powerful nations in the world now overwhelmingly express their disgust and horror at the historical atrocity of apartheid, mere decades after its collapse. “Why?” is the question typically posed. “Why did the world tolerate such a grotesque regime based on segregation, discrimination and abuse?” For those more intimately familiar with apartheid South Africa, the question becomes yet more perplexing. “Why did liberal, democratic Western nations make themselves complicit in perpetuating this awful injustice” (The Intercept, 2018). The examples provided by the Apartheid Convention do not necessarily disqualify a system from being apartheid. Two further clarifications should be made in order to dispel certain prevalent misconceptions about apartheid. While in the cases of South Africa and Rhodesia, the white settler minority ruled over the indigenous black majority, the Apartheid Convention does not stipulate that minority rule is a necessary feature of apartheid. Secondly, and perhaps more surprisingly, extending the right to vote to the disempowered party does not necessarily disqualify a system from being apartheid. The negotiation of this does not automatically deliver an “innocent” verdict to the accused party. The examples provided by the Apartheid Convention do not mention the right to vote (Kattan, 2011). With these qualifications, this definition provides the required clarity to assess the case of Israel. The universal definition of apartheid was outlined in the Convention for the Suppression and Punishment of the Crime of Apartheid (1973 Apartheid Convention) before examining the case of Israel. The universal definition of apartheid was outlined in the Convention for the Suppression and Punishment of the Crime of Apartheid (1973 Apartheid Convention) as follows: a crime “which shall include similar policies and practices of racial segregation and discrimination as practised in southern Africa.” (Kattan, 2011, p.2). The Convention elaborates that apartheid includes “inhuman acts committed for the purpose of establishing and maintain domination by one racial group over any other racial group of persons and systematically oppressing them” (Kattan, 2011, p.3). It is important to highlight the use of the term “southern Africa” as opposed to South Africa here. The system of Apartheid was infamous in South Africa but also in Namibia (between 1948–1990) with a similar system existing in Rhodesia (now known as Zimbabwe) (between 1965–1979). Under international law, apartheid may constitute a crime against humanity. Two further clarifications should be noted in order to dispel certain prevalent misconceptions about apartheid. While in the cases of South Africa and Rhodesia, the white settler minority ruled over the indigenous black majority, the Apartheid Convention does not stipulate that minority rule is a necessary feature of apartheid. Secondly, and perhaps more surprisingly, extending the right to vote to the disempowered party does not necessarily disqualify a system from being apartheid. The negotiation of this does not automatically deliver an “innocent” verdict to the accused party. The examples provided by the Apartheid Convention do not mention the right to vote (Kattan, 2011). With these qualifications, this definition provides the required clarity to assess the case of Israel. Earlier this year, the United Nations Economic and Social Commission for West Asia (UNESCWA) published an official report documenting various discriminatory abuses and condemning Israel for establishing “an apartheid regime that dominates the Palestinian people as a whole” (The Intercept, 2018). Immediately, the United Nations Secretariat came under immense pressure from the United States and Israel, causing them to expunge the document from their website. While this is the first time a document carrying the United Nations emblem has levelled the charge of apartheid against Israel, it is certainly not the first organisation of repute to do so. The
Russel Tribunal, originally established by renowned philosopher and mathematician Bertrand Russel to galvanise public opposition to the Vietnam war, established a mandate to determine the character of the Israel's occupation the Occupied Palestinian Territories and the treatment of Palestinians within Israel proper. The Russel Tribunal on Palestine was formed in response to the massive destruction wreaked on Gaza during Israel’s Operation Cast Lead in 2008, resulting in the deaths of over 1400 Palestinians and enormous damage to civilian infrastructure. The jury consisted of figures of international repute, including British Barrister Michael Mansfield QC, Spanish Supreme Court judge Martin Pallin, Jewish member of the African National Congress Ronnie Kasrils and holocaust survivor and French diplomat Stéphane Hessel (who contributed in writing in the Universal Declaration of Human Rights.) (Kattan, 2011). While the Israeli government was invited to present their case, they refused and did not engage in correspondence with the tribunal. The verdict issued was damning: “Israel subjects the Palestinian people to an institutionalized regime of domination amounting to apartheid as defined under international law” (Kattan, 2011, p.3). This conclusion was reached after careful examination of a wide range of evidentiary sources including reports issued by international human rights organisations. Below are passages from the Human Rights Watch report titled “West Bank: Separate and Unequal”:

“In most cases where Israel has acknowledged differential treatment of Palestinians - such as when it bars them from “settler-only” roads - it has asserted that the measures are necessary to protect Jewish settlers and other Israelis who are subject to periodic attacks by Palestinian armed groups. But no security or other legitimate rationale can explain the vast scale of differential treatment of Palestinians, such as permit denials that effectively prohibit Palestinians from building or repairing homes, schools, roads, and water tanks” (my emphasis.)

“Palestinians face systematic discrimination merely because of their race, ethnicity, and national origin, depriving them of electricity, water, schools, and access to roads, while nearby Jewish settlers enjoy all of these state-provided benefits,” said Carroll Bogert, deputy executive director for external relations at Human Rights Watch. “While Israeli settlements flourish, Palestinians under Israeli control live in a time warp - not just separate, not just unequal, but sometimes even pushed off their lands and out of their homes.” (my emphasis.)

If the measure of apartheid is “inhuman acts committed for the purpose of establishing and maintain domination by one racial group over any other racial group of persons and systematically oppressing them” (as stipulated by the Apartheid Convention) then the conclusion reached by the Russel Tribunal and UNESCWA appears inescapable. The fact that “Palestinians face systematic discrimination merely because of their race, ethnicity, and national origin” (my emphasis) satisfies the Apartheid Convention’s conditions.

The discriminatory practice of limiting Palestinian access to “electricity, water, schools, and...roads” based on ethnicity constitutes the “physical faces of apartheid” but Abdelnour (2013) elaborates on its “ideological face” within Israel. Abdelnour (2013, p.5) notes that “ideology dehumanises: propagated myths of ‘a land without a people for a people without a land’ or the imaging of Palestinians as parasites and savages”. This charge of an ideological face is carried out by the statements of Israeli officials such as current Defense Minister Avigdor Liberman who callously asserted that “there are no innocent people in Gaza” (The Jerusalem Post, 2018) to justify Israel’s lethal response to the “Great Return March” – an unarmed protest moved organised by Gazan civil society to secure the right of return and an end to the blockade of Gaza). Another example is former Prime Minister Yitzchak Rabin who bewailed “if only Gaza would just sink into the sea” (The Intercept, 2018) during the first intifada—a largely non-violent, Palestinian popular uprising against occupation. In a grotesque demonstration of this ideological face, emergency medical services were provided for Israeli pets and street animals “traumatised by rocket fire” while Israel bombed Gazan medical facilities and UN premises harbouring Palestinian refugees, using white phosphorus during Operation Cast Lead (a war crime under international law) (Kattan, 2011). These attitudes are not limited to Israeli officials alone. While a United Nations fact-finding mission concluded that Cast Lead was “a deliberately disproportionate attack designed to punish, humiliate and terrorise a civilian population” (Kattan, 2011, p.1), polls found that between 80–90% of Israeli Jews supported the operation leading up to it. According to another poll conducted by Tel Aviv University, 60% of respondents agreed that human rights organisations should not be allowed “to operate freely” (Finkelstein, 2018). As recently as this week, Israel passed a controversial bill which asserts that “the realization of the right to national self-determination in Israel is unique to the Jewish people” and the “state sees the development of Jewish settlement as a national value and will act to encourage and promote its establishment and consolidation” (Haaretz, 2018).

In response to the diplomatic failures of the Oslo Accords, and the horrors wrought on Palestinian society during the second Intifada, the Boycott Divestment and Sanctions movement emerged as a tactic towards achieving Palestinian rights. During the 2001 World Conference Against Racism in Durban, South Africa, Apartheid activists from across the globe “equated Israel’s racially
discriminatory policies throughout Israel proper and the Occupied Territories with apartheid and advocated BDS as a strategy of choice for fighting back” (McMahon, 2014, p.67). A similar call was issued by the newly formed Palestinian Campaign for the Academic and Cultural Boycott of Israel (PACBI) in 2004. This resulted in a unified call unanimously endorsing BDS by 170 civil society organisations representing Palestinian refugees, Palestinian under occupation in the West Bank (including East Jerusalem) and Israeli-Arabs within Israel proper. The document issued required Israel “recognize the Palestinian people’s inalienable right to self-determination” by “1. Ending its occupation and colonization of all Arab lands and dismantling the Wall; 2. Recognizing the fundamental rights of the Arab-Palestinian citizens of Israel to full equality; and 3. Respecting, protecting and promoting the rights of Palestinian refugees to return to their homes and properties as stipulated in UN resolution 194” (McMahon, 2014, p.67).

Having reviewed the origins of the movement and the ideology it seeks to dismantle; a closer examination of its mechanisms is important. The Boycott, Divestment and Sanctions movement seeks to bring significant economic pressure to bear on Israel until it complies with the above demands. These tactics are “academic, cultural, consumer and sports boycotts, divestments and sanctions” (McMahon, 2014, p.68). While boycott of goods produced on illegal Israeli settlements in the Occupied West Bank is quite uncontroversial among progressives, the academic boycott is often perceived as inherently discriminatory as it appears to ostracise Israeli academics based merely on their nationality. The PACBI has undertaken to clear up this misconception by clarifying that academics attached to Israeli institutions are not automatically the target of boycott, however the individual academics must “recognise internationally sanctioned and inalienable rights of the Palestinians” while the objective of the association with these academics/institutions must be “resisting the occupation and/or apartheid” (Barghouti, 2014, p.408). McMahon (2014) highlights that the third demand of BDS (the right of return for Palestinian refugees) subverts traditional discourse about Palestine by insisting that the conflict between the two parties does not start with the occupation of the West Bank and Gaza in 1967 but originates in the forced mass expulsion of the indigenous Palestinian population in 1948, and allows us to negotiate with the issue in a way more faithful to the reality of the Palestinian experience. By initiating a mass grass roots movement with the objective of securing Palestinian rights, co-founder of the movement, Omar Barghouti envisions that the momentum of the movement will bring about a state of affairs where “under severe and daunting pressure from within and without, the natural, human quest for normalcy, for a peaceful and economically viable life, will lead many of those Israelis to withdraw their support for Israeli apartheid” (Barghouti, 2014, p.409). The collapse of the apartheid regime will follow swiftly after as in “South Africa, despite the obvious differences” (Barghouti, 2014, p.409).

Despite the wide-ranging support for BDS across Palestinian society, the movement also faces considerable challenges. Even reputable figures generally sympathetic to the Palestinian cause have expressed significant doubts about the potential efficacy of the movement. Perhaps most notable among them is renowned linguist and intellectual Noam Chomsky who pointed to the seeming hypocrisy of boycotting Israeli academic institutions but not other universities equally complicit in Israel’s human rights abuses: “If you boycott Tel Aviv University, then why not Harvard? ... If Tel Aviv University is targeted for an academic boycott, it can rally Harvard and a whole array of equally-complicit universities to its defence” (McMahon, 2014, p.72). BDS is also “agnostic” on the debate over the one state/two solution. By refusing to directly recognise the Israeli state, many critics claim that BDS only serves to alienate those who would otherwise be sympathetic to the tactic (McMahon, 2014). BDS has also failed to obtain significant state support until now, with Ireland being the only country to adopt boycott of settlement goods into legislation. Lawmakers in Israel have also taken a firm stance against BDS, adopting legislation “effectively criminalising support for any boycott against Israel or its institutions under threat of heavy penalties” (Barghouti, 2014, p.409-410).

Despite these setbacks, the Boycott Divestment Sanctions movement enjoys support among a number of Israeli organisations including: The Alternative Information Centre, the Israeli Committee Against House Demolitions, Who Profits from the Occupation? And Boycott from Within and has had several significant victories among artists (Elvis Costello, the Pixies, Carlos Santana, Shakira have all refused to perform in Israel.) It is difficult to gauge at this point how BDS’s will negotiate the significant challenges it faces if it is to succeed in bringing international pressure to bear on Israel. The first step, however, seems clear. Activists, human right organisations and intellectuals must do the necessary work of establishing a consensus about the apartheid character of the Israeli regime, it is only then that BDS can gain the necessary momentum it requires to achieve it ends. From the available evidence, the apartheid nature of Israel’s current structure seems clear. As former Israeli Environment Minister once put it “what acts like apartheid, is run like apartheid and harasses like apartheid, is not a duck — it is apartheid” (Intercept, 2018).
Ahmed Elkady

References


Reitz, Brayne and Mayeux, 2011).

The rates are doubled every five years after 60years of age, with 3% of 65–74 years, 19% of 75–85 years and 47% of 85+ years old population suffering from AD in the U.K. (Kravitz, Schmeidler and Schneider Beeri, 2012). Factors associated with ageing such as changes of nerve cells, cell structure, hormones and immune system which may contribute to development of late onset AD (Launer, 2002; Reitz, Brayne and Mayeux, 2011).

Several studies indicate environment factors increase the risk of dementia (Adlard, 2006; Wang et al., 2006; Kravitz, Schmeidler and Schneider Beeri, 2012). A study conducted on mouse models by Adlard (2005) suggested direct influence of active physical activities to brain functionality, plasticity and structural aspects showing decrease in amyloid-beta (Aβ) plaques, which is one of the...
hallmarks of AD contributing to neuron degradation in the cerebral cortex and hippocampus in the brain. This study proposes that low levels of physical activity may increase Aβ-plaques developing AD. In addition, bad eating habits such increased alcohol consumption, caffeine and fatty and processed foods reflect high alarming body mass index (BMI) reflect prevalence of late onset AD (Wang et al., 2006; Kawahara and Kato-Neigishi, 2011). However, mechanisms explaining pathophysiology of AD with vascular pathology is undefined (Launer, 2002). Recent evidence also demonstrates that elevated traces and accumulation of aluminum in the brain obtained from canned foods and aluminum plated cooking pans also contributes to the late onset AD (Kawahara and Kato-Neigish, 2011, Mirza et al., 2017).

Sex determines the brain development, structure, function and biochemistry making it an important risk factor for AD. The clinical presentations of AD in men are more aggressive in behaviour, comorbid in nature and have higher mortality rates compared to women who present more affective and debilitative symptoms and have lower mortality rates (Mazure and Swendsen, 2016). In contrary, twice as many women as men over the age of 65+ are diagnosed with AD (Dementia Statistics Hub, 2015). The hormone, oestrogen has beneficial effects on the brain tissue providing neuroprotection, which is decreased overtime due to menopause (Behl et al., 1995). Oestrogen promotes growth and survival of cholinergic neurons increasing cholinergic activity and antioxidant properties, favouring non-amyloidogenic metabolism of the Amyloid Precursor Protein (APP) (Janicki and Schupf, 2010). The longitudinal Cache County Study initiated in 1995 recruited 5000 elderly Utah, US residents for over twelve years to participate in the study focusing on the memory in aging women and contributing risk factors (Tschanje et al., 2013). Amongst other investigations, the study also investigated the risk of AD depending on the timing of Hormone Replacement Therapy (HRT). Out of the 5000 women, 1150 women used oestrogen-HRT. The analysed data indicated women who began oestrogen-HRT within 5-years of menopause were 30% less likely of developing AD compared to non-HRT users (Tschanje et al., 2013). However, women who began combined HRT of oestrogen and progestin showed increased risk of developing AD compared to non-HRT users (Tschanje et al., 2013). This suggests the critical window of time before a reduction in endogenous levels of oestrogen as a result of reduced numbers of variants in genes involved in oestrogen biosynthesis and receptor activity increases the risk of developing AD (Henderson, 2005). Nonetheless, this theory must be further investigated as small sample size in a remote region in US is limited as the conclusion maybe extrapolated (Faber and Fonseca, 2014).
JADE plaques interacting with microglial and astrocytic neurons activating complement factors and cytokines (Spies, 2012). This injures the neurons increasing oxidative stress altering kinase and phosphatase activities forming neurofibrillary tangles: insoluble twisted fibres primarily consist of the protein tau (Roberts et al., 2014). These sequences lead to neuronal death and eventually dementia (Suzhen et al., 2012).

Therapies
Currently, established treatments for AD are treating the symptoms instead of the cause. Cholinesterase inhibitors are oral, or patch treatment given to mild to moderate AD patients (Sadowsky et al., 2010). The cholinergic systems in the basal forebrain are affected of patients in the early process of the AD losing function of acetylcholine neurons resulting in memory loss and deterioration of cognitive function (Yiannopoulou and Papageorgiou, 2012). Thus, to enhance cholinergic transmission, cholinesterase inhibitors are provided to delay the degradation of acetylcholine in the synaptic clefts (Grossberg, 2003). Additionally, N-methyl-D-aspartate antagonist (memantine) are given to moderate to severe AD patients (Folch et al., 2016). Memantine, is administered orally which aims to protect against chronically elevated concentrations of glutamate, protecting neurons from excitotoxicity (Farrimond, Roberts and McShane, 2012; Bullock, 2006). Memantine improves cognition and aggressive behaviour in AD patients within 6 months (Cummings et al., 2016). Tariot et al., 2004 showed significant benefits in cognitive function, language and behaviour from combination therapy of cholinesterase inhibitor and memantine in moderate to severe categorised AD patients. However, additional benefits were not recorded such as a reversal in phases such as severe to mild (Tariot et al., 2004; Farrimond, Roberts and McShane, 2012).

Possible therapeutics
Recent research progress by immunohistochromical examination indicate Heparin and Heparan Sulphate (HS) play an important role in Aβ-plaque pathogenesis (Zhang et al., 2014). Heparin and HS are glycosaminoglycans (GAGs) which are heavily glycosylated, linear polysaccharide chains covalently attached to proteoglycans which are specialised proteins (Yanagishita, 1993). Proteoglycans are located on the cell surfaces and matrix surrounding of virtually all mammalian cells, essential for biological processes (Yanagishita, 1993; Kondo et al., 2016). Proteoglycans are synthesised in the ribosomes and translocated to the rough Endoplasmic reticulum and GAGs components are synthesised in a complex, multi-step process in the Golgi apparatus (Godfrey, 2009). Mutation defects in most genes of GAGs biosynthetic enzymes in vertebrates lead to severe disorders such as mutations in EXT1 and EXT2 genes encoding glycosyltransferase responsible for HS biosynthesis causes bone disorder characterised by multiple benign cartilage-capped tumours (Wuyts and Van Hul, 2000; Mizumoto, Ikegawa and Sugahara, 2013).

Heparin and Heparan Sulphate (HS) are polysaccharide GAGs. Heparin is widely used as anticoagulant drug isolated from Porcine Intestinal Mucosa and Bovine Lung (John, 2006). HS interacts with the β-site APP cleaving enzyme (BACE 1) regulating BACE cleavage of APP. Inhibitory activity is dependent on saccharide size and specific structural characteristics and mechanism of action involved in inhibiting substrate access to active site (Hunt and Turner, 2009). HS and Heparin are nominated as BACE 1 inhibitors as it specifically inhibit BACE 1 APP cleavage but do not interrupt alternative cleavage by α-secretase (Striher et al., 2011).

β-secretase (enzyme BACE) is responsible for the initiation of the amyloid cascade in the amyloidogenic metabolism of APP (John, 2006). Interruption of the metabolic amyloid cascade could potentially reduce the amyloid burden slowly and could even reverse the symptoms. Therefore, identification for selective BACE inhibitors which can cross the blood-brain barrier can be future targets for pharmaceutical drug development (Mullard, 2017). Study conducted by Roberds et al (2001) on BACE knockout mice to determine
physiological effects of lacking BACE has out on the brain. The study conducted by Roberts et al. (2001) was carried out on 29 wild type, 77 heterozygous BACE allele knockouts and 29 homozygous BACE knockouts mice. Homozygous and heterozygous BACE knockout mice developed normally and showed no phenotypic changes with normal brain tissue morphology and biochemistry and normal blood and urine chemistry with no distinct difference behaviour compared to the wild mice. The brain samples obtained from BACE knockout mice showed no β-secretase activity and decreased amounts of sAPPß. There is also a significant 2-fold increase in the α-secretase activity metabolically synthesising APP in the non-amyloidogenic pathway. Thus, nominating BACE inhibitors as a potential therapeutic treatment for AD. This study has had a significant impact on the neuroscience and human molecular genetics opening avenues for in-depth research in modified GAGs in treating the root cause of AD.

Study carried out by Scholefield et al. (2003) in Birmingham U.K. further investigated modified HS and Heparin to obtain optimum level to be administered as potential therapeutic. Heparin directly interacts with BACE1 with a strong physiological bond at pH 7.0 and pH 4.5. At pH 7.0 a maximum of 60% of BACE1 is tightly bound to HS displaying a high level of inhibition of BACE1. At pH 4.5 which is the optimum pH of BACE1, the extent of HS binding to BACE1 is ~25% lower than pH 7.0. The interaction at pH 4.5 is weaker, but still significant to exude an effect. Scholefield et al. (2003) also investigated the size specificity of HS and Heparin to bind to BACE1 for inhibition. Depending on the saccharide fragment size, no inhibitory activity was recorded under 10 monosaccharide units. 24 monosaccharide units and larger displayed inhibitory activity similar to full length HS and Heparin including anticoagulant properties. Saccharide of 12 monosaccharide units and larger can cross the blood brain barrier. The size specificity is important when selecting the correct fragment size with the ability to inhibit BACE1 activity and developing drugs; outlining its administrate routes. Heparin intravenously administered in the human body: 18% is found in liver and 33% is excreted in the urine. This suggests that modifying HS and Heparin size and using alternative administrative routes are determined. Scholefield et al. (2003) also emphasises on modifying the anticoagulant activity of HS and Heparin because as therapeutic agents against BACE1 would prevail severe side effects such as internal bleeding, impaired blood clotting mechanism and heparin-induced thrombocytopenia.

In conclusion, HS and Heparin are physiological regulators of BACE1 in vivo. However, to maximise the inhibitory ability and reduce consequent side effects, chemical modification to HS and Heparin chains, further research and investigation needs to be invested, to produce a potential therapeutic for AD (Shriver et al., 2011). The most important feature that requires modification is attenuating anticoagulant property of heparin-based drugs without disturbing the core Heparin structure (Rabenstein, 2002). Thus, current research in modifications of heparin-based drugs are showing positive results in the development of potential therapeutics for AD, which could theoretical reduce Aβ-plaques and eventually reversing the damage caused in the brain by AD. In the future, the impact of these research can recue the alarming rate of affected population suffering from AD.

References


Amyotrophic lateral sclerosis (ALS) was first described in 1869 by French neurologist Jean-Martin Charcot (NINDS, 2010; Talbot, 2002; Wijesekera et al., 2009, Rowland et al., 2001). However, this disease became well known in 1939 across the United States when baseball player Lou Gehrig was diagnosed with it. ALS is also known as Charcot disease in recognition of Jean-Martin Charcot (the first person to comprehensively describe the disease). ALS is a motor neuron disease (MND) and one of the five other MNDs namely: Primary lateral sclerosis (PLS), progressive muscular atrophy (PMA), progressive bulbar palsy (PBP), and pseudobulbar palsy (Talbot, 2002; Wijesekera et al., 2009).

In the 19th century, neurologists (Charcot and Joffroy) recognised that the muscle weakness in ALS could be primarily due to disorders of muscle or secondarily due to loss of neuromuscular integrity, as happens when peripheral nerves are cut or when motor neurons degenerate (NINDS, 2010; Talbot, 2002). It was further observed that some patients presented with motor neuron degeneration which selectively affected upper motor neurons or lower motor neurons (Talbot, 2002; Wijesekera et al., 2009, Rowland et al., 2001). However, the combination of upper and lower motor neuron dysfunction was named amyotrophic lateral sclerosis (ALS) by Charcot and Joffroy.

Introduction

ALS is one of the most devastating neurodegenerative disorders resulting in dysfunction and subsequent degeneration of both the upper (motor neurons in the cortex) and lower motor neurons (motor neurons in the spinal cord) (Sebastião, Rei and Ribeiro, 2018). These degeneration causes a deficiency of input from the motor neurons resulting in progressive skeletal muscle atrophy causing muscle weakness in...
the arms, legs and body. Its onset below 40 years is rare and tends to predominantly affect ages between 55 and 65 years old and the median survival upon diagnosis is 3–5 years (Van et al., 2017). The initial cause of ALS is unknown but majority of the cases are sporadic (sALS) (90–95%) and the remaining have a positive familial history (fALS) (5–10%) (King et al., 2016). In fALS, More than 30 different genes have been linked and the inheritance is autosomal dominant, but the penetrance is variable however, both forms, sALS and fALS, present similar pathological and clinical features (Van et al., 2017). The mechanisms underlying ALS pathophysiology is not fully understood but some molecular and cellular process have been implicated. These include toxic protein aggregation, decreased neurotrophic support from non-neuronal cells, RNA toxicity, hypermetabolism, inflammation, mitochondrial dysfunction, prion-like spreading, excitotoxicity, oxidative stress and impaired protein degradation (Van et al., 2017).

ALS has many variants that share similar neuropathology but differ on the anatomical distribution of the pathological burden (Saberi et al., 2015). Progressive Muscular Atrophy (PMA) is characterized by its lower motor neuron pattern with little or no upper motor neuron involvement as in Primary Lateral Sclerosis (PLS). Spinal Muscular Atrophy (SMA) is similar to PMA but has a predisposition of genetic involvement such as mutations in the SMN1 gene. Hereditary Spastic Paraparesis (HSP) has a late onset with progressive spasticity of the lower limbs and axonal degeneration is centred on the lumbar region of the spinal cord (Saberi et al., 2015). Besides intercellular pathological processes altered excitatory neurotransmission is observed in ALS patients. ALS patients have higher glutamate levels and low levels of the excitatory amino acid transporter 2 (EAAT2) in their plasma and cerebrospinal fluid (Patai et al., 2017). Other studies reveal alterations in the AMPA type glutamate receptor allowing influx of normally impermeable calcium into the postsynaptic motor neuron resulting in excitotoxicity.

There is no cure for ALS and the modulation of other pathological mechanisms remain unsuccessful therefore, understanding excitatory alterations in ALS and their contribution to excitotoxicity is currently explored in seeking potent therapy for ALS (King et al., 2016). ALS also has no prevention or vaccination due to its etiology being unknown, the treatment goal is the management of symptoms and to help improve patient’s quality of life. Currently the only approved treatment for ALS is riluzole that reduces neuronal excitability by inactivating sodium channels, inhibiting glutamate release and blocking excitatory amino acid receptors in a non-competitive manner has been shown to increase life expectancy by 3–6 months (Fattore et al., 2015, Dorst et al., 2017). Riluzole-treated animals reveal functional recovery, improved neurobehavioral outcomes, reduced inflammation and improved axonal conduction (Siddiqui, Khazaei and Fehlings, 2015). Despite the promising results, Riluzole only extends the average life expectancy for 3–6 months at most, therefore, research into novel compounds for ALS progression delay and treatment including non pharmacological strategies is of utmost urgency (Fattore et al., 2015).

Epidemiology

Over the past decades, studies have shown (with a 95% confidence percentage) that the number of reported cases of ALS has not increased (Zarei et al, 2015). ALS cases have been reported to be between 1.5 and 2.7 per 100,000 in Europe and North America since the 1900s (Logroscino et al., 2010; O’Toole et al., 2008; Worms PM 2001). However, as of 2008, the prevalence of ALS was 0.32
per 100,000 with an equal risk proportion in male to female ratio (Kiernan et al., 2011; Logroscino et al., 2008; O’Toole et al., 2008). With only 5% of recorded cases recorded with an onset age less than 30, the mean age of onset of ALS varies from 50 to 65 years with the median age of onset of 64 years old (Sarah et al., 2017; Zarei et al., 2015). More so, studies have indicated that the incidence of ALS is most pronounced in people in their late 70s, 80s and older; with an incidence rate of 10.2 per 100,000 in men and 6.1 per 100,000 in women (Zarei et al, 2015). Whilst this might not seem like a lot, the lifetime risk of developing ALS is about 1 in 300 by the age of 85, with the risk increasing steadily, at least until about the eighth decade of life (Johnston et al, 2006, Sarah et al., 2017; Alonso et al., 2009). This is very similar to the risk for multiple sclerosis in the UK. Although it has been hypothesized that the reason for this drastic increase in the incidence rate in older population is related to the variation in care for these patients.

There are also some forms of ALS that are geographical and region specific where prevalence can vary between 50 to 100 times in certain locations than others throughout the globe (Sarah et al., 2017; Zarei et al, 2015, Johnston et al., 2006, Alonso et al., 2009). These population include; but is not limited to parts of Japan, Kii Peninsula of Japan, Guam, and South West New Guinea. Although evidences for this hypothesis are not widely accepted, it is believed that the reason for this is due to environmental factors (Zarei et al, 2015, Sarah et al., 2017; sorenson et al., 2007). This has been specifically narrowed down to be a ‘neurotoxic nonprotein amino acid, β-methylamino-L-alanine (BMAA) in the seeds of the cycad Cycas microsperma produced by a symbiotic cyanobacteria in the roots of the cycad that are commonly found in these areas’ (Zarei et al, 2015, Johnston et al., 2006, Alonso et al., 2009).

**Pathophysiology of Amyotrophic Lateral Sclerosis**

The aetiology of ALS remains unknown although it has been identified that some genetic factors could put an individual at risk. Recent reviews on environmental factors have also indicated that there is no consistent association between one environmental factor and risk of developing ALS (Zarei et al, 2015). Most scientist however, favour a hypothesis of complex interplay between multiple pathogenic cellular mechanisms of genetic-environmental interaction as the causal factor for ALS. Factors that contribute to the pathophysiology of ALS include:

**Genetic factors**

Copper-Zinc superoxide dismutase (SOD1) gene has been shown to be mutated in more than 20% of cases of patients with autosomal dominant FALS and 2% of patients with SALS (Zarei et al, 2015, Dangoumau et al., 2014). It was suggested that this mutation cause disease through a toxic gain of function rather than causing impairment of the antioxidant function of the SOD1 enzyme involved. More so, mutations in TARDBP gene (encoding the TAR-DNA binding protein TDP-43) (fig. 2) located on chromosome 1p36.22 have also been linked to be a casual of familial and sporadic ALS (Zarei et al, 2015, De Vos et al., 2007; Ivanov et al., 2014). Furthermore, mutations associated with ALS have been identified in the KSP repeat region in NEFH gene (encoding neurofilament heavy subunit), apolipoprotein genotype (APOE), decreased expression of EAAT2 protein, and alterations in the vascular endothelial growth factor (VEGF) gene (Dangoumau et al., 2014; De Vos et al., 2007; Ivanov et al., 2014).

Excitotoxicity

This is a condition in which neuronal injury is induced by excessive glutamate which causes induced stimulation of the postsynaptic glutamate receptors such as cell surface NMDA receptors and AMPA receptors (Lin et al., 2000; Honig et al., 1998). The over stimulation of glutamate receptors is thought to result in excessive influx of calcium into neurons which leads to increased nitric oxide formation and thereby neuronal death (fig. 2) (Zarei et al, 2015). The levels of glutamate in cerebral spinal fluid (CSF) are elevated in some patients with ALS. This has been suggested to be due to the loss of the glial cell excitatory amino acid transporter EAAT2 (Lin et al., 2000; Honig et al., 1998; Zarei et al, 2015).

Oxidative stress

Oxidative stress is known as accumulation of reactive oxygen species (ROS) that cause cell death (Simkó et al., 2004) (fig. 2). This has been longed linked to neurodegeneration. Since mutations in the anti-oxidant enzyme superoxide dismutase 1 (SOD1) gene can cause ALS, there has been an important interest in the mechanism underlying the neurodegenerative process in ALS (Zarei et al, 2015). This has led to findings of biochemical changes reflecting free radical damage and abnormal free radical metabolism in CSF and post mortem tissue samples in ALS patients. In addition, fibroblasts cultured from ALS patients show increased sensitivity to oxidative damage controls (Simkó et al., 2004; Martinez-Sámano et al., 2012; Zhou et al., 2012; Barber et l., 2010).

Mitochondrial dysfunction

Mutation in Mitochondria DNA has been identified in patients with ALS. This has been accompanied with elevated calcium levels and decreased activity of respiratory chain complexes I and IV, implicating defective energy metabolism (Zarei et al, 2015). More so, in sporadic ALS patients, SOD1 transgenic mice, and cellular models, numerous disorders and damages have been reported in mitochondrial morphology and biochemistry (fig. 2) (Boillé et al., 2006; Chung et al., 2007; Echaniz-Laguna et al., 2002; Magrané et al., 2009; Manfredi et al., 2005; Sasaki et al., 2007).

Impaired axonal transport systems

Motor neuron axons could be as extended as one metre in length in humans and they rely on efficient intracellular transport systems (fig. 2) (De Vos et al., 2007). There are two main transport systems called anterograde (slow and fast) and retrograde. They depend on molecular ‘motors’, which are the kinesin complex of proteins (for anterograde) and the dynein-dynactin complex (for retrograde) (Zarei et al, 2015, Duffy et al., 2007). Mutations in the kinesin genes have been observed to cause neurodegenerative motor nerve diseases in humans and dynactin complex mutation cause a lower motor neuron disorder with vocal cord paralysis. However, studies (haven’t been done in humans with ALS) have reported that SOD1 transgenic mouse models of ALS show findings of slowed anterograde transport and retrograde transport ((De Vos et al., 2007; Duffy et al., 2007; Ferraiuolo et al., 2011; Zarei et al, 2015)

Neurofilament aggregation

‘A toxic isoform of peripherin (peripherin 61), has been found to be toxic to motor neurones even when expressed at modest levels and is detectable in spinal cords of ALS patients but not controls’. (Zarei et al, 2015). Several neurodegenerative conditions including SALS and FALS present with an abnormal assembly and accumulation of neurofilaments (fig. 2) (Ikenaka et al., 2012; Zarei et al, 2015). Furthermore, in the neurofilament heavy (NFH) gene, mutation is found in about 1% of sporadic cases in the KSP repeat sequence. All these aggregations may be present in ALS cases, and this can be used in its differential diagnosis (Ikenaka et al., 2012).

Inflammatory dysfunction and contribution of non-neuronal cells

Numerous studies have shown and proven that there are that inflammatory processes and non-neuronal cells may play a part in the pathogenesis of ALS (fig. 2) (Zarei et al, 2015) Although ALS is not known to be an autoimmune disease, activated non-neuronal cells produce inflammatory cytokines such as TNFα, interleukins, COX-2, and MCP-1. More so, evidences of the upregulation of this activation are found in CSF or spinal cord specimens of ALS patients or in vitro models (Zarei et al, 2015).

Deficits in neurotrophic factors and dysfunction of signalling pathways

ALS patients have been shown to have decreased levels of neurotrophic factors like GDNF, CTNF, BDNF, and IGF-1). Furthermore, in mice, motor neurone was caused by the deletion of the hypoxia-response element in the vascular endothelial growth factor (VEGF) gene (Zarei et al, 2015). This has been shown to be true in humans where three mutations in the VEGF gene were found to be associated with increased risk of developing sporadic ALS (Philips et al,1998). In the final stages of cell death in ALS motor neurones, it has been observed that this is similar to a programmed cell death pathway (apoptosis) (Philips et al,1998). During this occurrence, biochemical markers of apoptosis are detected in the terminal stages of human and models of ALS (Zarei et al, 2015).
Clinical Features & Diagnosis of Amyotrophic Lateral Sclerosis

Clinical Presentations

The symptoms of the onset of ALS can be so subtle that they are overlooked but gradually, they develop into more obvious weaknesses or atrophy that may suggest to a physician that a patient is at risk of ALS (NINDS, 2018; Zarei et al, 2015). Some of the early symptoms include:

Difficulty chewing or swallowing, fasciculations (muscle twitches) in the arm, leg, shoulder, or tongue, muscle cramps, spasticity, persistent fatigue, uncontrollable periods of laughing or crying, tight and stiff muscles (spasticity), muscle weakness affecting an arm, a leg, neck, or diaphragm, slurred and nasal speech (dysarthria), and breathing (dyspnea) (NINDS, 2018; Zarei et al, 2015; Sarah et al., 2017).

Clinical presentations of amyotrophic lateral sclerosis

<table>
<thead>
<tr>
<th>Classifying feature</th>
<th>Name of phenotype</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Motor neuron involvement</td>
<td>Amyotrophic lateral sclerosis (ALS)</td>
<td>• Mixture of upper and lower motor neuron signs on clinical examination.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Degree of certainty of diagnosis based on El Escorial criteria.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• May involve up to all regions.</td>
</tr>
<tr>
<td>Primary lateral</td>
<td>Progressive bulbar palsy</td>
<td>• Condition involving the bulbar region and predominantly lower motor neurons.</td>
</tr>
<tr>
<td>Motor neuron</td>
<td></td>
<td>• May progress to other regions.</td>
</tr>
<tr>
<td>predominant ALS</td>
<td>Pseudobulbar palsy</td>
<td>• Condition involving the bulbar region and predominantly upper motor neurons.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• May progress to other regions.</td>
</tr>
<tr>
<td>Spinal onset</td>
<td>Flail arm</td>
<td>• Predominantly lower motor neuron proximal symmetrical involvement in the upper limbs.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Some upper motor neuron signs may be seen in the lower limbs.</td>
</tr>
<tr>
<td>Site of onset</td>
<td>Flail leg</td>
<td>• Lower motor neuron distal symmetrical involvement restricted to the lower limbs.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• May affect one side only.</td>
</tr>
<tr>
<td>ALS with cognitive</td>
<td>ALS with cognitive impairment</td>
<td>ALS with some cognitive involvement below the threshold criteria for frontotemporal dementia.</td>
</tr>
<tr>
<td>involvement</td>
<td>ALS with frontotemporal dementia (ALS-FTD)</td>
<td>ALS with frank frontotemporal dementia.</td>
</tr>
</tbody>
</table>

**Figure 3:** Figure showing the clinical presentations of amyotrophic lateral sclerosis (Sarah et al., 2017. What causes amyotrophic lateral sclerosis? Maurice Wohl Clinical Neuroscience Institute. F1000Res 2017; 6: 371.).

Diagnosis

No one test has been proven to provide a definitive diagnosis of ALS. ALS is primarily diagnosed based on detailed medical history of the signs and symptoms observed by a physician during physical examination through a series of tests (to rule out other similar diseases) (Zarei et al, 2015). It takes an average of 13–18 months after onset of patient’s symptoms to confirmation of the diagnosis of ALS (AlSarraj et al., 2014), due to its complexity and heterogeneity (Chiò et al., 1999; Andersen et al., 2012).

However, the presence of upper and lower motor neuron symptoms strongly suggests the presence of the disease (Zarei et al, 2015). To make effective diagnosis, physicians will review an individual’s medical history and conduct a neurological examination at regular intervals to assess whether symptoms such as muscle weakness, atrophy of muscles, and spasticity are getting progressively worse (Zarei et al, 2015).
Appropriate tests for making a differential diagnosis of ALS will usually include: muscle and imaging tests (electromyography (EMG)), spinal tap (also called a lumbar puncture), X-ray, magnetic resonance imaging (MRI) (neuroimaging studies), muscle and/or nerve biopsy (Brooks et al., 2000; de Carvalho et al., 2008; Hardiman et al., 2017; Mitsumoto et al., 1997; Hortobágyi et al., 2014).

However, other similar diseases and disorders like human immunodeficiency virus (HIV), can, in some cases, cause ALS-like symptoms. Post-polio syndrome, multiple sclerosis, multifocal motor neuropathy, west nile virus, human T-cell leukaemia virus (HTLV), polio, and spinal and bulbar muscular atrophy (Kennedy’s disease) can also imitate the clinical presentation of ALS (Zarei et al., 2015).

Prognosis

Majority of ALS patients die from respiratory failure, usually within three to five years from the onset of symptoms (Sarah et al., 2017). However, with appropriate treatments, approximately 10 percent of those individuals with ALS survive for 10 or more years (Sarah et al., 2017; Lee et al., 1995).

Treatments & Ongoing Pharmaceutical Discoveries of Amyotrophic Lateral Sclerosis

Riluzole is prescribed to many patients for modifying disease progression in ALS (Europeans Medicines Agency, (EMA), 2015). Riluzole slows the disease progression in some people with ALS. Riluzole is, well tolerated and the most common side effects include asthenia, nausea, gastrointestinal upset and liver dysfunction, therefore, liver function should be regularly monitored during therapy (Bensimon and Doble, 2004). The recommendation dose of Riluzole is 50 mg twice daily for patients with definite or probable ALS for duration <5 years, an FVC >60%, and no tracheostomy (Miller et al., 2009).

Edaravone (Radicava) was approved in 2017 by the Food and Drug Administration. It was originally developed as an acute stroke treatment and it was later studied in two separate trials in Japan to assess its efficacy in treating people ALS (Chang and Ross, 2017). The first clinical trial found no treatment benefit and second clinical trial identified a subgroup of mildly symptomatic participants whose decline seemed to slow down on Edaravone treatment. It is a nootropic and neuroprotective agent that is used for neurological treatment. Edaravone mechanism of action is that it works as a free radical scavenger and it have protective effects against oxidative...
stress (Takei et al., 2017). Edaravone can exert antioxidant effects because it can quench hydroxyl radicals and hydroxyl radical-dependent lipid peroxidation (Inokuchi et al., 2009). The drug is available as a 60mg dose and it is administered by intravenous infusion.

Edaravone was developed by Mitsubishi Tanabe (MT) Pharma Corporation in Japan. Edaravone side effect include acute renal failure, liver dysfunction, acute allergic reactions, disseminated intravascular coagulation, thrombocytopenia, and leukocytopenia, are occasionally observed by >5% of patients during Edaravone treatment (Higashi et al., 2006). Edaravone because it contains sodium bisulfite it can cause serious allergic reactions to patients with sulfite sensitivity. Edaravone has demonstrated to slow the decline in clinical assessment of daily functioning in persons diagnosed with ALS.

Pimozide is also a new drug which has been found to be safe and preliminary data in animal models shows that it could stabilize the progression of ALS. However, more studies need to be conducted to confirm the results. Many drugs have been tested for the treatment of ALS and several are in clinical trials. Riluzole still remains the only drug that has impact on survival for patients with ALS, it does slow ALS progression but only marginally. Patients who are most likely to benefit from Riluzole treatment are those who have had symptoms for less than five years and have very little respiratory impairment.

**Conclusion**

This study encompassed a broad range of information regarding ALS its epidemiology to the treatment of the disease. Unfortunately, ALS has been categorized as an incurable disease although there are handful of medications available to treat it. These medications do not substantially increase life expectancy. Since the approval of riluzole nearly all the clinical trials done have failed to achieve clinically significant efficacy or therapeutic effects. Although three potentially efficacious treatments (Masitinib, Pimozide and edaravone) have claimed to benefit ALS patients to a clinically significant endpoint. More so, even though edaravone has received marketing authorisation in Japan, due to mixed results from numerous clinical trials, Japanese patients are still reluctant to use the medication.

There have been recent advancements in the understanding of the pathophysiology of ALS with nineteen genes and genetic loci been found to be associated with ALS. Furthermore, researchers and authors are cautiously optimistic that one or more of the above-mentioned medication—for ALS treatment—will be improved in the near future following the better understanding of the pathophysiology of the disease. Thus, current discoveries of the mechanism underlying ALS have helped to slow down the progression of the disease. Hence, future treatments and medications would aim towards preventing neuronal damage, as a patient progresses from their initial onset.

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I am delighted to introduce the postgraduate work from the ILAS conference in this special student JADE edition. Despite an unseasonably hot April day, over 130 presenters and visitors attended the ILAS annual interdisciplinary conference, Turning Heads: Changing Minds. The Keele Hall ballroom was abuzz and the day was a fantastic celebration of the diversity and quality of postgraduate research across the university, which included 62 posters from 14 schools and 12 Three Minute Thesis presentations. Here you will find all of the conference abstracts, plus three additional contributions from poster presenters Joanne Moore, School of Politics, Philosophy, International Relations and Environment (SPIRE), Lloyd Myatt, School of Law, and Claire Melia, School of Psychology. Joanne and Lloyd both reflect on their personal experiences of the conference; Joanne's article focuses on how interactions on the day helped her to locate and strengthen her purpose for her own research. Lloyd highlights how the enhanced his appreciation of the differences between disciplines and their contribution to real world issues. In her article Who is to blame for alcohol addiction? Claire extends the work presented in her wonderful poster, which was awarded first prize by the judging panel in the poster competition.

Researcher skills and Impact
In her welcome address Pro-Vice-Chancellor Professor Helen O’Sullivan emphasised the importance of researchers opening up their work to critical conversations with other disciplines, noting the value of the skills that they would develop through this process. This theme was further developed by our visiting keynote speaker Jonathan Lutwyche, CEO of Yordas Group, a leading provider of environment consultancy, located at the Lancaster Environment Centre at Lancaster University. His engaging talk Inspiring Impact in Industry shared a number of stories highlighting the importance of postgraduate research skills and how they have contributed to the evolution of the Yordas Group. From a modest ‘start up’ with just three staff, Yordas now employs 60 people, most of whom were former master’s and PhD students at Lancaster.

At the heart of research is the desire to ensure that the work has impact beyond academia and contributes to improving the health, prosperity and well-being of people and society. This involves researchers communicating their work in ways that make it accessible and interesting to different audiences and often to those outside their own disciplines. The ILAS conference is a great opportunity to meet and talk with people from different fields and alternative perspectives and to become more confident and skilled at discussing the ‘so what’ question about your own research.

Joanne Moore’s article is a fascinating reflection on this very challenge. Her work focuses on philosophical understandings of the nature of the soul and the quest for self-realisation and in her (first) poster presentation she had not drawn out of the significance of her work and why it is important. On the day however, conversations with fellow researchers prompted her to think more deeply about this and this led to a firmer sense of the ways her work continues to be relevant and contribute to greater understanding of many of the contemporary problems being tackled in other research areas.

Keele Three Minute Thesis Competition (3MT)
Now in its third year, the Keele 3MT, continues to go from strength to strength. This year, in addition to the ILAS conference heat, 3MT heats were offered at symposia across the university and overall there were 23 entrants with representation from all three faculties. Six participants were selected for the final round which was again held at the KPA Bob Beattie Postgraduate Student of the Year awards evening in the Salvin Room Keele Hall; Alison Aries, (School of Health and Rehabilitation), Angela Blanchard, (School of Health and Rehabilitation), Angela Blanchard, (School of Psychology) Annabelle Machin (Institute for Primary Care and Health Sciences) Kara Holloway (School of Psychology), Sarah McKevitt (Institute of Primary Care and Health Sciences) and Grant Mitchell (School of Politics and International Relations and Environment). The winner was Angela Blanchard with her presentation; Through fog: An autoethnography of childhood emotional neglect and she was put forward to represent Keele at the national VITAE virtual semi-final.
Getting conference ready

The Academic Development Team with ILAS offered a full programme of support for all elements of conference preparation and this included workshops with the Listening Project, an innovative HEFEC funded initiative which focused on developing skills for effective dialogue, particularly listening, in order to explore others’ viewpoints. Feedback from conference participants reported on the many ways that the conference had been both enjoyable and contributed to their learning and development; emphasising particularly how participating in the conference had contributed to strengthened confidence and skills in communicating with lay audiences and increased interdisciplinary understanding.

Enjoy the conference outputs here and also on the ILAS website where you can see the videos of the 3MT presentations (www.keele.ac.uk/ilas) and photographs of the winning posters (www.keele.ac.uk/ilas/conferences/ilaspostgraduateconference/turningheadschangingminds2018). I hope that they inspire you to think about different ways of communicating your work and getting involved in the conference next year. Save the date, 29 April 2019, and look out for more information on the ILAS website and Twitter over the coming months.

To view the all of the abstracts for the ILAS conference, please visit the following web address:
I am a part-time PhD student in my first year with the School of Politics, Philosophy, International Relations and Environment (SPIRE) (Faculty of Humanities and Social Sciences). As I live and work near Birmingham and am not on campus very regularly, the conference presented a new challenge and an opportunity for me in several ways. It was an opportunity to spend time with fellow post-graduate research students and to find out more about the range of post-graduate research at Keele through the poster displays and the ‘3-minute Thesis’ competition. It was also a challenge for me to try to capture my research in the concise visual form of a poster and convey my enthusiasm to peers with very different interests and areas of expertise.

This was the first time I had designed a poster and although I had no expectations of winning one of the prizes, it was with a feeling of pride that I picked up the finished article on the day before the conference. It was modest in comparison with some of the very professional, innovative and interactive posters in the hall but, nevertheless, I had managed to capture some of what I wanted to convey about quite a traditional, academic subject area in visual form.

The conference was a great opportunity to talk to fellow research students about subjects I knew little to nothing about and to engage in some stimulating conversations. It also highlighted the challenge involved in explaining my own topic is a way that was interesting, made sense to someone from a different discipline, and captured the most important elements of the research. Being at an early stage of the research, with an element of exploration into possible routes I may want to take, I also found producing and talking about the poster encouraged me to interrogate my Thesis proposal and the ground covered so far; when you are asked to distil and portray the main elements of something, you are forced to strip it back to essentials and then build it back up, which is a very useful focusing exercise.

As the day went on however, I realised the one thing that I had not done successfully on my poster was to explain why the research was important. I also began to be increasingly aware of this as I spoke to people about it. My research is in Ancient Greek Philosophy and Yoga, a comparative study into Indian and Greek thought about the nature of the soul and the practical aim in both systems to achieve Self-Realisation, a state of union with the universal ‘One’. In the company of research into debilitating disease, or more ethical ways of conducting lab research, or mental health, or current political issues, I began to ask myself why anyone should care very much about some long dead philosophers and their speculative spiritual adventures. My own passion for the subject suddenly did not feel enough; could it really have interest or relevance beyond the limited circle of Classicists or Historians of Philosophy? Why was the research worth doing?

The realisation came quite late in the day. A poster close to mine about the legality of military intervention under International Law was generating some interesting discussions about contemporary political, moral and ethical dilemmas and the changing face of warfare in an age of drone technology. It made me consider whether these issues are ever truly surmountable? Will there, or can there, be lasting political, military or social solutions or will human nature always get in the way? Greece’s ancient thinkers were not dismissive of politics or law or social order, but, as in the traditions of India, there was a consistent theme of seeking inner transformation. They recognised a reality beyond the reality we live in, a reality of realisation of the spiritual Self which would overturn the misguided, human perception of life. Furthermore, the comparative nature of the research implies that this seeking for transformation was a universal pursuit, independent of cultural or religious background.

Looking for a moment through the lens of ancient philosophy and the yogic tradition, the root of human problems is revealed as ignorance of our true nature, the solution its realisation. We are limited by our enslavement to the ego and super-ego, our sense of ‘I’-ness and separation, the weight of our conditionings and habits. To gain liberation is to transcend these limitations and to negate the desire for power or domination or the fear of the ‘other’. If enough individuals are transformed, then society itself is transformed. The aspirations of the ancient philosophers and yogis may therefore have far more relevance than we give them credit for and are certainly worth understanding better if nothing else.

I benefitted in several ways from the Turning Heads, Changing Minds conference. I built my own confidence in presenting my ideas in an unfamiliar format, I learned about a range of research projects, I engaged in interesting and stimulating conversations which made me examine my own views on a range of topics and I networked with my peer group. But perhaps the greatest learning I took from the day was a deeper understanding of the purpose of my research, why it is worth doing and what it can contribute.
Introduction

There is no doubt that alcohol is a common substance within Western society. It is well known that there are many pleasant effects of alcohol consumption including tension reduction, confidence in social situations, and even suppressing negative emotions (Read, Wood, Kahler, Maddock & Palfai, 2003). Due to these pleasant associations with alcohol it is a very commonly used substance. Whether celebrating an anniversary, having a meal with friends, or relaxing after a long day at work, alcohol is often present. The ever-present nature of alcohol reflects its culturally acceptability within the UK culture.

However, whilst many people enjoy alcohol in moderation, there are also many who rely more heavily on this substance. With an estimated 595,131 dependent drinkers, 8,758 alcohol-related deaths, and a cost of £3.5 billion annually to the NHS (Alcohol Concern, 2016), alcohol clearly has a major impact in the UK. Although there have been significant increases in treatment provisions in recent years, the treatment engagement rate remains low at approximately 18% (Alcohol Concern, 2016). Although a clinical definition of alcoholism and dependency exists (NICE, 2011), many individuals may not view their drinking as problematic. If individuals have a different perception of what constitutes problematic drinking to clinicians, this will likely hinder treatment efforts. Given that popular opinions about alcohol can shape how alcohol use is thought about within society, it is important to explore common descriptions and accounts. This research identifies the common explanations that are available across multiple sources, for different audiences and from different perspectives. Ultimately, this will provide a comprehensive understanding of how alcohol use is depicted and how these perspectives are shared through discourse.

Methods

This project gathered text-based documents written by professional and general public authors. Professional documents were written by individuals or organisations such as clinicians and academics to convey information. The general public included a broader range of authors and sources which were not written for professional audiences. In line with the latest alcohol use issue guidance (APA, 2013) collected data was published between 2013 and 2017 to ensure the data reflected any changes in guidance. The data was initially identified through keyword searches including ‘alcohol addiction’, ‘alcoholism’ and other similar terms. The data was then condensed to create a more manageable dataset including the richest sources. Excluding data was predominantly based on relevance as many sources were identified which used the key terms only once. Further refinement of the data set included choosing newspaper articles with the most comments, national (NICE) and international (WHO) policy documents widely used in the UK, and the most relevant and most recent journal articles. Again, general public sources were inclusive and the only exclusion was that data was not written by professionals or organisations.

Table 1: Overview of sources and data collection

<table>
<thead>
<tr>
<th>Professional</th>
<th>General Public</th>
</tr>
</thead>
<tbody>
<tr>
<td>Policy Documents</td>
<td>5 Documents (142 Pages)</td>
</tr>
<tr>
<td>Journal Articles</td>
<td>5 Articles (78 pages)</td>
</tr>
<tr>
<td>Newspaper Articles</td>
<td>45 Articles from 3 newspapers (98 pages)</td>
</tr>
</tbody>
</table>

Analysis

The analytic approach of Critical Discursive Psychology (CDP) was used which argues that language is not a neutral resource for communicating information. Instead, we construct different versions of reality through our use of language. That is, we draw upon different techniques and discourses within language to portray a certain viewpoint, for specific actions and purposes. In addition to exploring the discourses presented through language, CDP also considers the broader context in which they are set (Edwards, 2005). Within this project, CDP allows for the analysis to consider the context of the sources in terms of who the author is. For example, this would allow the analysis to explore whether there are systematic differences in the way professionals and the general public discuss alcohol use issues.

In terms of analysis I have drawn upon Potter and Wetherell (1987), where they propose ten stages which guide the researcher through developing research questions and collecting data through to analysis. In terms of analysis, the first stage is coding in which the researcher systemically categorises data into smaller data sets. The researcher analyses the coded transcripts to understand how specific discourses are constructed through systematic uses of linguistic techniques. Following analysis, the researcher conducts validation. These steps of analysis and validation are often conducted in tandem, with numerous re-analysis until the analysis provides a coherent understanding of the construction of these discourses.
Results
Overall, there appear to be three distinct ways in which problematic alcohol use is accounted for. The first is individual in which it is explained that humans are rational and able to make informed choices. In addition, normalisation of alcohol use is often cited, explaining that since many individuals can drink moderately, addiction must be a personal weakness. This is consistent with the theory of moral weakness which has been linked to stigmatisation and heavily places blame on the individual. Under this discourse, it was clear that if individuals are rational, then policy makers and practitioners should focus on improving awareness and helping individuals make rational decisions.

Secondly, there was a construction of alcohol use as a medical disorder which cannot be controlled and requires treatment, rather than choosing to stop drinking. Since a medical disorder is not within individual control, the individual cannot be blamed or held responsible for their addiction. As such, this leads to less stigmatisation of the individual compared to the previous discourse. In addition, this discourse is much more open minded, reduces stigmatisation of those with alcohol use issues and advocates for improved access to treatment. However, it also takes power from the individual and places them as a victim of their own disorder.

Finally, culture and policy are implicated as extremely influential in alcohol use issues. Individuals discussed how government policies such as longer opening hours, supermarket licences and cheap alcohol have diminished the social rules around alcohol. As these social expectations have changed, it has promoted a culture of excess. Some people find this problematic and consider this cultural normalisation of alcohol use to be a possible cause of addiction. Individuals feel that drinking alcohol is expected and encouraged and that a change in policy and culture may help reduce rates of alcohol addiction.

Conclusion
In summary, this project has analysed text-based documents from a range of sources. From analysis, three dominating discourses are used to construct blame regarding alcohol addiction. Although the prominence of these discourses varies across sources, they appear prevalent across all data sites, both professional and public. Future steps for this project will include conducting world cafés and focus groups, again with professional and public groups, to further explore these initial discourses. Upon completion, this project will provide insight into how problematic alcohol use is discussed within society. In addition, this insight can be used to help stakeholders adapt awareness and treatment campaigns on the basis of these discourses, ultimately guiding individuals towards sensible drinking choices or engaging with treatment.

Acknowledgement
This PhD project is fully-funded by Keele University School of Psychology within the Faculty of Natural Sciences. Thank you also goes to my supervisory team of Dr Alexandra Kent, Dr Alex Lamont, Dr Richard Stephens, and Dr Joanne Meredith. In particular, Dr Kent has provided exceptional support and advice during this stage of the project and Dr Lamont has been an excellent source of expert advice and guidance throughout.

References
Our feet were made for walking: can you imagine what it would be like if you were suddenly unable to move one side of your body, and your foot was no longer “made for walking”? This is exactly what can happen if you experience a stroke. Strokes are usually caused by a blood clot in the brain: a bit like a heart attack—but a brain attack. Frighteningly, every two seconds somebody in the world has a stroke; strokes cause difficulty with movement, but can also cause a loss of feeling. If you are unable to feel the floor with your feet, it is very difficult to balance and walk.

I am a physiotherapist specialising in stroke rehabilitation. I know from my own experience that therapy to increase feeling, movement and control of the foot can help to give someone the ability to walk again after a stroke. This was my motivation for undertaking a National Institute for Health Research (NIHR) doctoral fellowship exploring the feasibility of delivering treatment to increase feeling and movement in the foot early after stroke in a mixed methods (experimental, focus groups and daily diaries) feasibility study.

I truly believe my research relating to sensory stimulation to the foot and ankle after stroke is important; if taken forward it could benefit stroke survivors in the future. I know it is important to disseminate my work widely, and when I heard about the three minute thesis (3MT) competition I felt this was another opportunity to raise the profile of my work.

My initial thoughts relating to the 3MT competition were “how difficult could that be?...I have the gift of the gab, surely I could do this!” However, I did not rush into the decision to apply. On Thursday 19th April I went and watched the entrants for the 3MT competition during the Institute for Liberal Art and Sciences Postgraduate Conference. I was in awe of how people managed to summarise several years of work into a three minute speech, delivering it with passion and beating the ever-dwindling, very daunting timer! I was not sure that I could manage to achieve the same results, but felt it was worth giving it a go. Despite my feelings of anxiety, when the call from the Institute for Science and Technology in Medicine (ISTM) came out on the 24 April, I decided to be brave and enter the competition.

My round of the 3MT competition was taking place on the 15th May during the ISTM postgraduate conference. I knew I had to work hard to pull something together and be able to deliver it within just 21 days... I must be mad! However, hard work is not something I am afraid of or shy away from; this was an opportunity which could not be missed. I prepared ‘the speech’ with the help of my supervisor Dr Sue Hunter and set to achieving the challenge.

I practiced and practiced, my daughter helping me learn it sentence by sentence. I discovered learning lines was not a skill I find easy, but perseverance paid off. Once I had learnt it, I practiced it everywhere and to anyone! Emptying the dishwasher was undertaken with the three minute timer on, and so was pretty much every activity I undertook! We had friends round for a barbeque and they were subjected to the compulsory three minute thesis (which I delivered with no script after several gins), I was ready.

I was extremely nervous on the day of the ISTM postgraduate conference. I was practicing with a friend in the corridor and managed to recite it all the way through with people walking past me. I went up to the podium and delivered my speech with as much passion as I could; I was absolutely thrilled to receive both the judge’s vote and the peoples’ vote - what an accolade! I felt great! However, it meant I had to do it all over again at the Keele 3MT final on 18 June at the Bob Beattie Award Evening.

It was another month of hard graft; I practiced and practiced, making sure I knew not only the words, but the appropriate actions and gesticulations, driving my family mad with my relentless reciting! I really wanted to deliver a presentation with passion and enthusiasm, and knowing how I feel about my research I knew this was possible. Journeys to work in the car became an opportunity to recite it over and over again.

The night of the 18 June 2018 was a lovely evening. It was an opportunity to celebrate the success of the many postgraduates receiving the awards, and to share and enjoy hearing about the research undertaken by the other 3MT competition entrants. It was nice to share this experience with both my husband and my supervisor; we all enjoyed the lovely meal in Keele Hall.

I was nervous on the night, but took my laminated 3MT speech up to the front with me (just in case I froze)!... I had no intention of using it, and did not need it. I felt that I delivered my speech with confidence and passion and I was content that I had achieved my best. Several people came up to me and complimented me, or asked about what my research had entailed after I had delivered my speech. Unfortunately, I did not win on the night; however, I had maximised another opportunity to raise the profile of my research, presenting to many eminent people within Keele University. Perhaps not winning was a good thing, I could now settle down and concentrate on the other important aspect that I need to complete—writing up my thesis!

Although time-consuming the 3MT was a positive experience; I feel if I was able to do it, anyone would be able to manage it if they set their minds to it. So, if you are reading this and wondering if you should give it a go next year, my advice would be—just go for it. What do you have to lose? This is another great forum for raising both your own profile and that of your research.

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'No matter what people tell you, words and ideas can change the world'. This is a quote from the late Robin Williams, whom is credited with taking ideas and utilising them to achieve joy, laughter, and happiness. This is true with any idea, however, once created, it can never be stopped. That was the aim of my idea, not to change minds but to create new avenues of thought and consideration. I would never attempt to place my ideas in another, only to let them observe and bear witness to a new idea; landscape, and atmosphere. This is what I always set out to achieve. I believe this is also the beauty of learning, not to discard but to appreciate difference.

This was reflected in the diversity of subjects offered from the participants, ranging from drones to fracking to spirituality. These are not only issues that are of the greatest importance in the twenty-first-century but are questions that have forever entertained humanity. For example, how does one fight in armed conflict? Is the environment important? Do we have a soul? These are questions that would have run through at least one person’s mind at the conference. Therefore, this emphasises the innovation and enterprise of participants to identify real-world issues that affect every one of us.

Through this experience and questioning these issues, I have an appreciation for disciplines that I may not know or fully understand. This is again, the beauty of learning. Knowledge should be treated as a privilege to be used for the good of humanity so that we develop, achieve and move forward together. This is the position that I am at now. I know a lot but also, so very little. There is always so much more to knowledge than a set path; rules are only there to guide, never constrain.

I am at the stage where I am no longer ticking boxes but creating the box, the space, and instrument with which to fulfil it. There will be those that will come after who will do the same but it is always imperative to ensure that the foundations that we build are solid. This is what I felt that the conference did. It solidified my ability to not only communicate my knowledge to specialists but to those who are not specialists. It is a skill that enables a more profound understanding of your discipline but also other’s disciplines.

Finally, to go back to the quote given at the start of the piece by the late Robin Williams, I will utilise one of his iconic roles to deliver my last analogy. Like an idea, once the genie is out of the bottle, there is no putting it back. I hope that with this, I have not changing minds but opened them to new and exciting ways to view the world. It is always a privilege to be at the forefront of what I do and my ability to display within a medium such as a poster, only furthered this point.
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