

# ASPIRE Showcase 2017

## ABSTRACTS

Abstract book designed by medical intercalaters  
Louise Finch and Marrigje Nell

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## GP perspectives of perinatal anxiety in women: Implications for medical education

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*Jacquelyn Walsh-House*

### **Background**

Perinatal mental health conditions are those that arise during pregnancy and the first-year post-partum. Depression and anxiety disorders are the most common conditions; research indicates around 22% of women are affected by anxiety during this period (Somerville *et al.*, 2014). Research suggests that perinatal anxiety (PNA) is underdiagnosed in primary care and that actual prevalence is greater than that of perinatal depression, which is estimated to affect 13% of women (Somerville *et al.*, 2014). However, research and clinical attention seems disproportionately focussed on the latter (Matthey *et al.*, 2003). Undetected and poorly managed PNA is associated with a negative impact on both maternal health, the child's cognitive and emotional development, and to increasing demand on services (Somerville *et al.*, 2015). Currently the National Institute for Health and Care Excellence (NICE) have not developed guidelines for the identification and management of PNA in women; therefore, NICE identify PNA as a research priority. In the UK, the identification and management of PNA falls under the responsibility of General Practitioners (GP's) (Ford *et al.*, 2017).

### **Aims**

This study aims to explore GP experiences of, and perspectives on, current practice in the provision of care to women with PNA in order to identify implications for contemporary medical education.

### **Methodology**

A secondary qualitative analysis of semi-structured interviews with GPs in the West Midlands about their experiences and perceptions of managing women with PNA. Consent to use research data in future research was obtained in the original study and transcripts were already anonymised. Thematic analysis using principles of constant comparison was conducted with key themes agreed with the supervisory team.

### **Results**

Nine transcripts were analysed identifying key themes: awareness of PNA and use of diagnostic tools; relationships between GPs and other health care practitioners; communication with women, and need for training. These themes are displayed using a conceptual map in figure 1 (Page 2). Qualitative data supporting the key themes identified in this study are displayed in tables 1,2 and 3 (see page 3, 4 and 5).

### **Conclusions**

The secondary analysis of GP interview transcripts has several implications for current undergraduate and postgraduate medical education. Firstly, the importance of integrated professional education (IPE) and practice was evident throughout all transcripts as an

essential aspect in the ability of GPs to identify and manage PNA in women. Additionally, the use of informal communication methods between services was noted; suggesting that a flexible and adaptive approach to communication is beneficial between GPs and service providers. The role of continuous reflective and experiential learning was emphasised in facilitating relationships between service providers and patients.

This study also identified the need for introduction of specific training in order to increase GPs ability to distinguish between PNA and perinatal depression. Furthermore, establishing a standardised referral framework and improving understanding and use of available diagnostic tools were identified as key review issues. Several GPs raised issues over being uncertain over which tool to use and how to appropriately interpret results providing a potential future target in the postgraduate GP training.

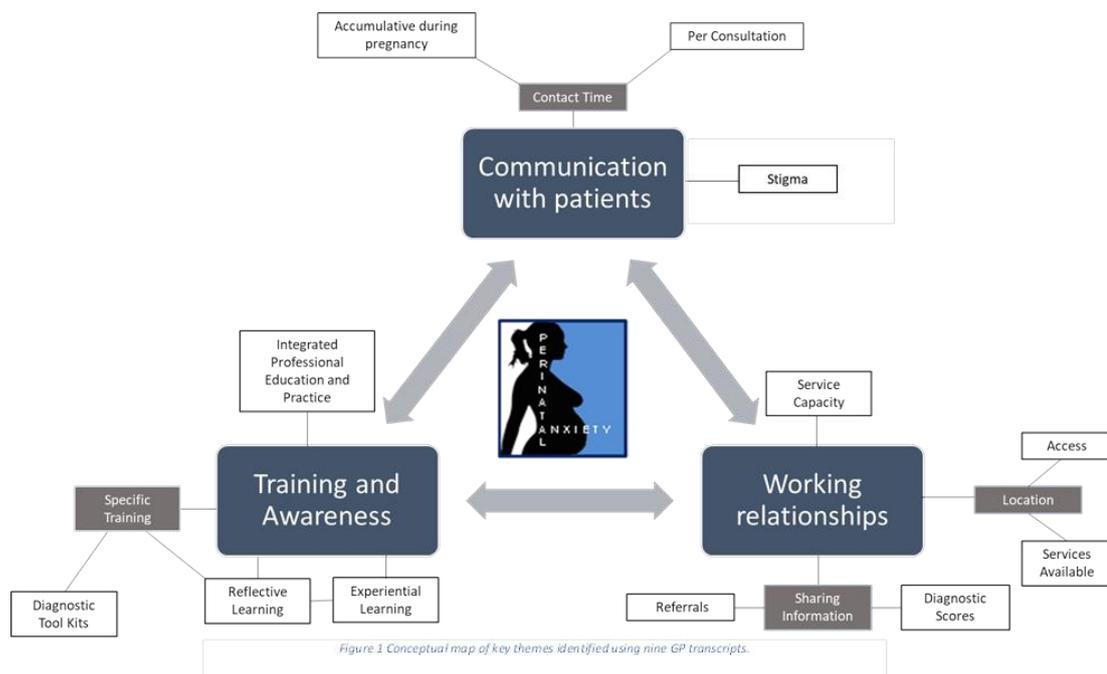


Figure 1 Conceptual map of key themes identified using nine GP transcripts.

Table 1 Supporting qualitative data for the theme 'Communication with Patients'. Interview transcripts are references via [GP(number)] refers to the transcript source reference

Communication with Patients: How GPs interact with the patients and factors that affect this.	Contact time (Accumulative over perinatal period and per appointment)	"So I suppose there are those two formalised definite moments of involvement." "The first one may last ten minutes, the second one may last half an hour." [GP008]
	Resources (Use of resources to support information giving)	"as part of the CCG requirements, we see women at about 29 weeks, as part of their Antenatal Care but that would be the only time." "Postnatally, I'm involved in ad hoc 6-8 week checks" [GP010]
		"some women can sail through pregnancy and we barely see them. But if there is an anxiety or depressive element, then we probably see more." [GP001]
	Stigma (Perceptions held by both GP and patient)	"they get this enormous book when they've had a baby, they get so much paperwork given to them and that's almost in lieu of things being said perhaps but you get that 0 to 5 it's like an encyclopedia given to you." [GP008]
"Probably there is definitely a social taboo as with any anxiety issues, isn't it?" [GP009]		
"The stigma I mean it prevents people from seeking help from family, friends and perhaps more objective access in the process." [GP008]		
		"worried that if they're seen as feeling depressed or weak or anxious or crying a bit more, that this could be picked up maybe by somebody else and they're deemed as not being a fit parent" [GP006]

Table 2 Supporting qualitative data for the theme 'Working Relationships'. Interview transcripts are references via [GP(number)] refers to the transcript source reference

<b>Working Relationships:</b> The Interaction and collaboration between GPs and other service providers.	<b>Location</b> (Availability of and access to services)	"midwives and the district nurses were based in the health centre but they've now been centralised and you have to leave a message on an answerphone to get into contact and that's not as good as it used to be." [GP007]
		"in most areas, GPs are completely removed from any routine Antenatal Care" [GP010]
		"being a bigger practice and being a well-structured maternity midwife attached with the practice, works with us I think we have slightly less role than single handed and smaller practices where the midwives are more central and they don't have any direct contact on a day to day basis." [GP009]
	<b>Sharing Information</b> (Referrals, sharing diagnostic scores)	[On communication with secondary psychiatric services] "I don't recall getting a lot of, um, up to date information from them. [GP001]
		"So, I have an informal way of communication because they're locally based or based in the building and we've got this formal way of coming and getting advice into practice and also emails." [GP009]
		"The patient yeah just turns up actually so we don't, I don't think I've ever had a letter from the health visitor, it's pretty much word of mouth or if they're very concerned they would I'm sure call. But generally, it's fed back through the patient actually yeah. And I know they've got their red book, I'm trying to think if they, I mean they're very good at documenting things in there but generally it's through the patient that they refer." [GP004]
	<b>Service Capacity</b> (GPs perception of services ability to accommodate patients)	[on wanting more routine appointments] "No, not really. What do I think? Two things about that. First of all, workload is high enough as it is and there's a GP crisis, so do I want to see more often and gain rapport? That would be nice but I seriously don't have the time." [GP005]
		"If we were seeing every mother or every mother to be an extra time or two that would be quite a lot of extra appointments. And it just sort of adds a potential burden and then reduces the opportunity to be able to pick up those people who do need our attention" [GP008]

Table 3 Supporting qualitative data for the theme 'Training and Awareness'. Interview transcripts are references via [GP(number)] refers to the transcript source reference

<b>Training and Awareness:</b> The Individual GPs preparation and influences for managing these patients.	<b>Integrated Professional Education and Practice</b> (working with and awareness of other service providers)	"say it should be the role of the midwife in uncomplicated pregnancies to support the woman." [GP006]
		[Regarding being more involved with the care pathway of women in the perinatal period] "I've no desire to find out what goes on with that care because I'm happy with the midwives looking after the patients well enough; just in the same way that patients see a Nurse Practitioner, a nurse or a Healthcare Assistant. As long as they're seeing people within their skill set and looking after them well enough, then that's fine." [GP005]
		"Midwives stand a better chance to identify and review developing problems" [GP003]
	<b>Specific Training, Reflective and Experiential Learning</b> (Professional and personal development to practice)	"I don't think there is particularly antenatally a protocol but I think postnatally we're all a bit more aware" [GP001]
		"I don't think you get extra training for that [Prescribing for PNA]. It's just, like, part of your training and then part reading up to make sure you pick the right one" [GP006]
		"I think you've got your experiential learning from a personal perspective and a clinical perspective" [GP008]
	<b>Diagnostic Tool Kits</b> (Awareness of tools, uses and interpretations)	"we don't use anything which identifies anxiety in the absence of depression." [GP004]
		"I quite commonly use the PHQ9 score which is just a general look at sort of depression markers really. I know there is a postnatal depression score that we can use but I haven't accessed that one for quite a long time actually so I haven't used that one recently anyway. I can't remember what that one's called formally" [GP003]
		"Hmm. I personally don't [use diagnostic tools] and I don't like mental health score cards and things where you have to get a number and then you are, then you're diagnosed as whatever. I think with experience and skill, you can pretty much pick it up yourself." [GP007]

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## ‘No decision about us without us?’: The extent to which the metaphors used in poetry written about illness and medical care challenge

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**Corinne Dignan**

The noun ‘patient’ is derived from the adjective, which describes a person capable of enduring an affliction without complaint. Over the last thirty years the nature of the patient role has changed, with an increasing emphasis on promoting the active role of the patient alongside the medical practitioner in decisions concerning the patient’s medical care. This emphasis on shared decision-making raises the question of whether the term ‘patient’, with the connotations of passivity and disempowerment that it holds, is still an appropriate label for today’s recipients of healthcare. This study examines the use of metaphors in poetry written by published poets about their experiences of illness and the medical care that they

received. It includes only poems written during or after the year 1990, as this is when the NHS initiative of shared decision-making started to percolate into clinical practice. The medium of poetry was chosen due to its inherently reflective nature, and the unguarded insight it provides into patients' perceptions of the state of ill health. Metaphors lend themselves to the expression of complex or emotionally charged thoughts and feelings, and therefore particularly suit lay explanations of illness and healthcare. The study explores the use of extended metaphors in the thirty-three poems that were found to fulfil the inclusion criteria of the study, and analyses the extent to which they conform to the connotations of the term 'patient'. This study finds that the metaphors fall into a spectrum of reactions to the patient role, which can be divided into three main categories. The first category includes metaphors that emphasise a feeling of passivity, which is in accordance with the connotations of 'patient'. The second category includes metaphors that suggest that the patient is taking some ownership over their body by engaging with their illness and attempting to increase their own understanding through metaphor. The third category includes the metaphors that are used by the patient to show active engagement with their own care. The study finds that the majority of metaphors fall into the first category, echoing the passive connotations of the term 'patient'. Although this may be a true reflection of patients' feelings about their illness and the medical care they received, this could also be due to the nature of the poetic medium, which tends to lend itself more to lament than to challenge. The results of this study demonstrate the value of medical professionals engaging with alternative forms of patient communication, in addition to the conventional clinical history, to gain a different perspective on patient wellbeing. It may also suggest that further initiatives, either NHS or third-sector, may be beneficial in order to further promote patient empowerment within the UK healthcare system. Finally, this study also highlights that engaging with the arts and humanities may be a valuable way for patients to develop their understanding and acceptance of their illness.

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## **Interventions for the Management of Distal Intestinal Obstruction Syndrome in Cystic Fibrosis.**

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*Jessica Green*

Cystic fibrosis is the most common, life-limiting, genetically inherited disease. It affects multiple organs, particularly the respiratory system. However, gastrointestinal problems such as distal intestinal obstruction syndrome (DIOS) is also an important complication in cystic fibrosis. DIOS arises when thick mucus and viscid faecal material combine in the bowel, commonly at the terminal ileum or caecum, leading to partial obstruction (incomplete DIOS) or complete obstruction (complete DIOS). There is limited evidence for the efficacy and safety of laxatives used to manage DIOS and insufficient knowledge of current practices used to treat it; consequently, my project aimed to evaluate these matters in children and adults. In order to analyse the efficacy and safety of various interventions used in the management of DIOS, I conducted a Cochrane review on the interventions for the prevention of DIOS. The second aim of my project was to evaluate the current practice for the treatment of DIOS. I did this by conducting a nationwide survey for both adult and paediatric CF clinicians. In the Cochrane review, there were 2631 studies identified, but only 1 study was included. This meant that meta-analysis could not be performed. The study was

a double-blind, placebo-controlled, crossover trial investigating the efficacy of cisapride (a prokinetic drug) in 17 patients with a history of DIOS. Radiograph scores revealed no difference between cisapride and placebo. There were no adverse effects. However, total gastrointestinal symptom scores favoured cisapride with a mean difference of -7.60 (95% CI -14.73 to -0.47). However, cisapride is no longer licenced due to cardiac side effects, limiting its clinical applicability. A quantitative survey was conducted to establish the current treatments for constipation and DIOS in UK CF centres. Results varied greatly, especially for the treatment of DIOS: incomplete DIOS had 23 different 1st line combinations in adults and 22 in children; complete DIOS had 25 1st line combinations in adults and 17 in children. Over 99% respondents recognised limited evidence for their treatment decisions. My project demonstrated that there is a lack of evidence for the prevention of DIOS and little consensus for the treatment of DIOS, highlighting a need for research, which at present is pitifully lacking. The results of the survey and review should also signal that there is no consensus or evidence base for the management of DIOS in clinical practice. There is a great deal of importance placed on respiratory complications in CF, but not enough on the gastrointestinal problems that commonly arise.

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## **Marital status and the risk of cardiovascular diseases: A systematic review and meta-analysis.**

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*Chun Wai Wong*

**Background:** Cardiovascular disease (CVD) is the commonest cause of mortality worldwide. There is great interest in understanding sociodemographic risk factors associated with CVD to enable healthcare providers to identify high risk individuals for targeted interventions. Whilst individual studies have evaluated the relationship between marital status and future CVD risk, the literature reports inconsistent relationships, with no clear consensus around whether a relationship between marital status and incident CVD and outcomes exists.

**Aims:** We aimed to perform a systematic review of the literature and meta-analysis to quantify the association between marital status and incident CVD and outcomes after CVD.

**Methods:** A systematic search of MEDLINE and EMBASE was performed to identify relevant studies that evaluated the association between marital status and risk incident CVD or outcome after CVD. The outcomes of interest were death, coronary heart disease (CHD) and stroke. Only studies published since 2000 were included and retrospective and case-control studies were excluded. We used Review Manager to conduct random effects meta-analysis stratified by the type of population which were either general population, post stroke, post myocardial infarction or post percutaneous coronary intervention (PCI).

**Results:** Our analysis included 38 studies with 2,263,876 participants (age 25-80 years) and the mean follow-up period ranged from 30 days to 34 years. The results for the general population are summarized in Table 1. Compared to married participants, unmarried participants were more likely to die from all causes (Risk ratio (RR) 1.31 95%CI 1.19-1.45,  $p < 0.001$ ), develop CVD (RR 1.43 95%CI 1.01-2.02,  $p = 0.04$ ) and develop CHD (RR 1.12 95%CI 1.02-1.23,  $p = 0.02$ ) but no difference was observed for incident stroke ( $p = 0.23$ ).

Gender effects were observed for all-cause mortality and CHD where significant differences were only observed for men and not women. Being divorced was associated with increased risk of all-cause mortality (RR 1.43 95%CI 1.20-1.71,  $p<0.001$ ) for both men and women and CVD for men only (RR 1.93 95%CI 1.22-3.06,  $p=0.005$ ). Widowed participants were more likely to develop a stroke (RR 1.16 95%CI 1.09-1.23,  $p=0.01$ ). For participants with CVD (Table 2 and 3), mortality was significantly higher for unmarried patients who underwent PCI (RR 2.09 95%CI 1.66-2.64,  $p<0.001$ ) and men and women who sustained a myocardial infarction were more likely to die (RR 1.36 95%CI 1.17-1.58,  $p<0.001$ ). Gender effects were observed where men who underwent PCI were more likely to have a myocardial infarction ( $p=0.010$ ) and men who have myocardial infarction are more likely to die ( $p=0.001$ ).

**Conclusions:** Marital status appears to be associated with mortality and incident CVD in a general population and in patients after PCI and myocardial infarction. For some outcomes, gender effects were present where men who are unmarried show higher risk compared to women. While current evidence may demonstrate an association between marital status and mortality and CVD, lack of social support might be a mitigating factor. Future work should focus around whether marital status is a surrogate marker of other adverse health behaviours or cardiovascular risk profiles that underlies our reported findings and whether targeted interventions should focus on such high risk groups.

**Table 1:** Risk of adverse outcomes for not married vs married in a general population

Outcome or Subgroup	Studies	Risk ratio [95% CI]	p-value
<b>All-cause mortality not married vs married</b>	<b>4</b>	<b>1.31 [1.19, 1.45]</b>	<b>&lt;0.001</b>
<b>Men only</b>	<b>3</b>	<b>1.45 [1.26, 1.66]</b>	<b>&lt;0.001</b>
Female only	3	1.12 [0.96, 1.30]	0.16
<b>Men and women</b>	<b>1</b>	<b>1.33 [1.28, 1.38]</b>	<b>&lt;0.001</b>
<b>All-cause mortality divorced vs married</b>	<b>2</b>	<b>1.43 [1.20, 1.71]</b>	<b>&lt;0.001</b>
<b>Men only</b>	<b>2</b>	<b>1.39 [1.15, 1.68]</b>	<b>&lt;0.001</b>
<b>Female only</b>	<b>1</b>	<b>1.86 [1.07, 3.24]</b>	<b>0.03</b>
All-cause mortality widowed vs married	1	1.02 [0.70, 1.48]	0.45
Men only	1	0.87 [0.50, 1.52]	0.62
Female only	1	1.16 [0.70, 1.93]	0.57
All-cause mortality separated vs married men only	1	1.24 [0.98, 1.57]	0.07
CVD death not married vs married	2	1.20 [0.55, 2.65]	0.65
Men only	2	2.07 [0.72, 5.94]	0.17
Female only	2	0.63 [0.18, 2.26]	0.48
CVD death widowed vs married	2	0.96 [0.43, 2.16]	0.93
Men only	2	1.38 [0.27, 6.99]	0.70
Female only	2	0.70 [0.26, 1.90]	0.48
CVD death divorced vs married	3	1.56 [0.95, 2.56]	0.08
<b>Men only</b>	<b>3</b>	<b>1.93 [1.22, 3.06]</b>	<b>0.005</b>
Female only	2	0.56 [0.07, 4.37]	0.58
<b>CVD death separated vs married men</b>	<b>1</b>	<b>1.43 [1.05, 1.95]</b>	<b>0.02</b>
<b>CVD not married vs married</b>	<b>2</b>	<b>1.43 [1.01, 2.02]</b>	<b>0.04</b>

Female only	1	1.82 [0.18, 18.40]	0.61
Men and women	1	1.42 [1.00, 2.01]	0.05
<b>CHD death not married vs married</b>	<b>5</b>	<b>1.43 [1.28, 1.60]</b>	<b>&lt;0.001</b>
<b>Men only</b>	<b>3</b>	<b>1.28 [1.13, 1.45]</b>	<b>&lt;0.001</b>
<b>Female only</b>	<b>4</b>	<b>1.44 [1.16, 1.78]</b>	<b>&lt;0.001</b>
<b>Men and women</b>	<b>1</b>	<b>1.60 [1.50, 1.71]</b>	<b>&lt;0.001</b>
CHD death widowed vs married	2	0.78 [0.48, 1.25]	0.29
Men only	2	0.50 [0.19, 1.34]	0.17
Female only	2	0.92 [0.52, 1.60]	0.76
<b>CHD, IHD and AMI not married vs married</b>	<b>7</b>	<b>1.12 [1.02, 1.23]</b>	<b>0.02</b>
<b>Men only</b>	<b>4</b>	<b>1.18 [1.09, 1.28]</b>	<b>&lt;0.001</b>
Female only	5	1.10 [0.96, 1.26]	0.19
Men and women	1	1.05 [0.69, 1.60]	0.82
CHD death separated vs married men only	1	1.31 [0.76, 2.26]	0.33
<b>CHD, IHD and AMI divorced vs married</b>	<b>2</b>	<b>1.30 [1.13, 1.49]</b>	<b>&lt;0.001</b>
<b>Men only</b>	<b>2</b>	<b>1.28 [1.08, 1.51]</b>	<b>0.004</b>
<b>Female only</b>	<b>1</b>	<b>1.36 [1.04, 1.78]</b>	<b>0.02</b>
<b>CHD, IHD and AMI in remarried vs married</b>	<b>1</b>	<b>1.21 [1.02, 1.44]</b>	<b>0.03</b>
Men only	1	1.13 [0.96, 1.34]	0.15
<b>Female only</b>	<b>1</b>	<b>1.35 [1.07, 1.70]</b>	<b>0.01</b>
<b>Stroke death not married vs married</b>	<b>2</b>	<b>1.55 [1.16, 2.08]</b>	<b>0.003</b>
<b>Men only</b>	<b>2</b>	<b>1.55 [1.15, 2.11]</b>	<b>0.005</b>
Female only	1	1.52 [0.53, 4.34]	0.43
<b>Stroke death divorced vs married</b>	<b>1</b>	<b>2.33 [1.11, 4.89]</b>	<b>0.03</b>
<b>Men only</b>	<b>1</b>	<b>2.40 [1.03, 5.59]</b>	<b>0.04</b>
Female only	1	2.11 [0.45, 9.86]	0.34
Stroke death widowed vs married women only	1	1.52 [0.53, 4.34]	0.43
Stroke not married vs married	3	1.23 [0.88, 1.72]	0.23
Men only	2	0.95 [0.76, 1.19]	0.68
Female only	1	1.27 [0.95, 1.69]	0.10
<b>Men and women</b>	<b>1</b>	<b>1.93 [1.34, 2.78]</b>	<b>&lt;0.001</b>
<b>Stroke widowed vs married</b>	<b>3</b>	<b>1.16 [1.09, 1.23]</b>	<b>&lt;0.001</b>
<b>Men only</b>	<b>2</b>	<b>1.16 [1.03, 1.29]</b>	<b>0.01</b>
<b>Female only</b>	<b>2</b>	<b>1.12 [1.04, 1.22]</b>	<b>0.004</b>
<b>Men and women</b>	<b>1</b>	<b>1.33 [1.12, 1.57]</b>	<b>&lt;0.001</b>
Stroke divorced vs married	3	1.13 [0.99, 1.28]	0.06
Men only	2	1.17 [0.93, 1.48]	0.19
Female only	2	1.09 [0.86, 1.39]	0.47
Men and women	1	0.94 [0.62, 1.43]	0.77

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## Cluster Headache: Impact and Perceptions Study (CHIPS)

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*Yachna Mehta*

**Background:** There is only one qualitative study of cluster headache (CH) patients' perceptions (Palacios-Cena et al 2016). The perceptions and experiences of migraine patients, on the other hand, have been studied via a social science approach by a number of teams (for a Flemish study see Dikomitis et al 2013; for a UK-based study see Peters et al 2003; Peters et al 2004; Peters et al 2005 and for a study in the Netherlands see Dekker et al 2012b). Because there are almost no qualitative studies of cluster headache, we have little in-depth understanding of the perceptions and experiences of cluster headache patients and the health professionals who treat them. I worked with an existing data set, which included 26 qualitative interviews conducted by Dr. Dikomitis for an NHS funded study (CHIPS).

**Aims:** The overall objective of this ASPIRE studentship was to gain insight into the perceptions, experiences and understandings of cluster headache (CH) from the perspective of the cluster headache patients. Two sub-objectives (1) examining the barriers to and facilitators of awareness of CH by patients, GPs and neurologists; (2) mapping the time to diagnosis and identifying the factors affecting the patient pathway from first symptom to start of treatment.

**Methodology:** The QSR Nvivo 11 software was used throughout the project. Analysis was guided by the research objectives. Regular analysis meetings were held between Dr. Dikomitis and myself to discuss the themes emerging from the analysis. To ensure a transparent and in-depth coding process we applied a systematic approach to the data analysis. This included a first phase in which a repeated close reading of each interview transcript took place. This in order to develop a detailed coding framework. In a second coding phase, memoing and focused coding led to the translation of the descriptive codes into analytical codes.

### Results

Five themes emerged from analysis:

- (1) Experiences of living with CH  
Patients described in infinite detail the intense pain during an attack. Some study participants said they would rather die than have another attack. This ties in with earlier findings, which show CH is nicknamed the 'suicide headache'. The data highlights the extent of the pain experienced and identifies a loss of self-control.
- (2) Diagnostic challenges  
This theme revolves around misdiagnosis, delay in diagnosis and patient delay.
- (3) Patient interaction with healthcare professionals  
It is clear that doctor patient interaction has a huge impact on the diagnostic journey and adherence to treatment plan.
- (4) Communication between primary and secondary care  
This theme highlights the challenges with regards to delay with referrals and communication neurologists and GP post-diagnosis.

(5) Impact of cluster headaches.

Here we grouped the data around impact on family life, employment and the high occurrence of social isolation experienced by CH sufferers.

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**An observational study of Entrustable Professional Activities undertaken by Y5 students during assistantships and how they contributed to preparation for practice.**

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**Sreya Sam**

*“Not had much practice with IM injections since year 2/3. The way I did it was rather clumsy. Had I not caught myself at the last moment (with the doctor supervising me also reminding me about that last step of the procedure at the same time) this may have been a potential harm to the patient”* student 5, Block: GP

This project is an observational study aiming to acquire insight into the transition between final year medical students to foundation year junior doctor. Currently medical students undertake a mandatory student assistantship during the final year of the course in the UK. An assistantship is a shadowing model of apprenticeship where 5<sup>th</sup> year students gain experience of working within the clinical settings in which a foundation year 1 doctor works<sup>[1]</sup>. This study aimed to analyse year 5 student logs and classify them in terms of entrustable professional activities [EPA]. An EPA is a unit of professional practice to be entrusted to a trainee once sufficient competence has been reached<sup>[2]</sup>.

### **Methods**

The data for this study were collected as part of Keele Medical Education Research Group's Transitions Study. Ethical approval was granted by Keele University School of Medicine Ethics committee on 4.8.13.

The daily student learning logs analysed for this study were collected during the final year assistantship of 32 participating Keele medical students. Each student logged their learning activities of the fourth week of one of their 5-week blocks in hospital and general practice [GP] in the academic year 2013-14. Students were asked to categorise each learning activity by the following categories:

1. Learned by observing
2. Learned by doing
3. Listened to a talk or read about
4. Discussed

They were advised that an activity may be categorised in one or all of these categories. Students also made a daily audio recording during that week of their immediate reflections on new, interesting and significant experiences. They commented on perceptions of value and for what purposes this value is. Students were then interviewed to debrief them. The activities named by the students were categorised by EPA type following the Utrecht classification (box 1).

**Box 1: Utrecht core EPAs <sup>[3]</sup>**

- 1. The Clinical Consultation**
  - History, physical examination, measuring vital signs, creating a differential diagnosis, ordering and interpreting diagnosis tests, designing a management plan, documentation
- 2. General Medical Procedures**
  - Preparing and executing medical procedures including communication with the patient
- 3. Informing, Advising & Guiding Patients and Families**
  - Discussing diagnostic options, test results or a management plan and documentation
- 4. Communicating & Collaborating with Colleagues**
  - Writing discharge summary/letter, oral patient hand-overs, patient & research presentations, collaborating with health care workers are contributing to interprofessional teams
- 5. Extraordinary Patient Care**
  - Basic life support, establishing death

For each EPA logged the degree of entrustment was determined by the student's log record of 'learned by observing' or 'learned by doing', interpreting any further descriptive text indicating whether learned by doing was supervised directly or indirectly

Table 1 <sup>[2]</sup>: EPA Supervision scale for residents appropriate for medical school (level 1-3) showing how we mapped them to the study data

EPA supervision scale for medical school	Study data
1. Be present and observe	Learned by observing
2. Act with direct proactive supervision.	Learned by doing
3. Act with indirect reactive supervision.	Learned by doing
4. Act with supervision not readily available	Learned by doing
5 Permission to supervise others in practice of this EPA.	Doing (Teaching)

## Results

32 year 5 Keele medical students consented. Each logged one week, in which there were 15 students in GP blocks 1-5 and 17 in hospital blocks 1-6. Within hospital, 6 were in medicine, 5 in surgery and 6 in critical care.

The total number of activities logged per student per week in GP: 29.9 Of these 69.4% were EPAs. (fig 1)

The total number of activities logged per student per week in hospital: 30.5 Of these 77.0% were EPAs.

Some examples of non EPAs include: cluster project, audit, reflection, self-study and weekly seminars.

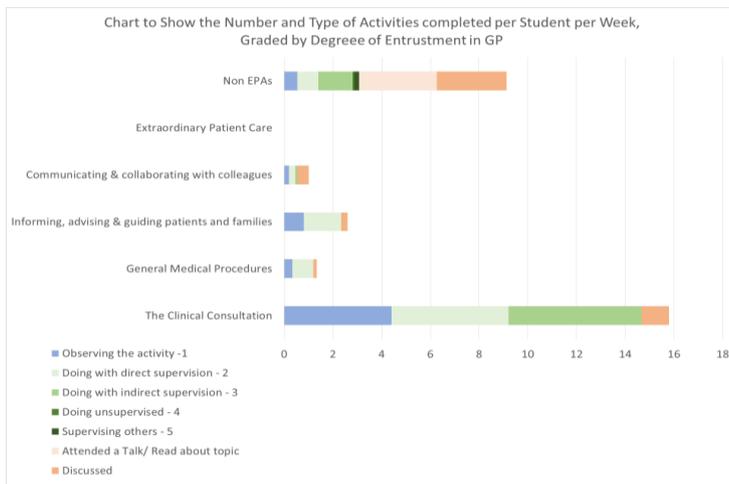


Fig 1: Activities logged in hospital (numbers in Appendix 1)

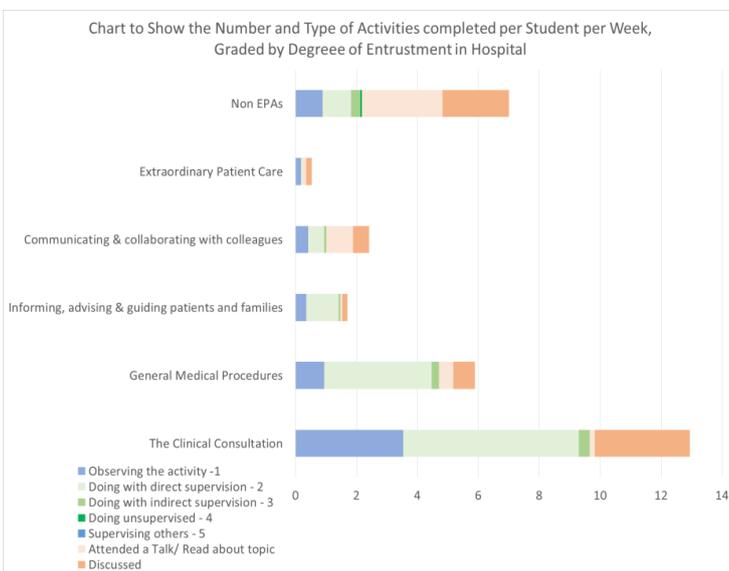


Fig 2: Activities logged in GP (numbers in Appendix 2)

**Conclusions:**

Final year medical students at Keele logged more EPAs than non-EPAs in their learning logs. This may reflect the significance which they afford to EPAs as learning worthy of recording, but it does also indicate that students are being allowed to do some of the activities of doctors. The types of activities logged were largely consultations and it might be possible to increase the numbers of procedures, advising patients, collaborating with colleagues and extraordinary patient care EPAs.

**References:**

Available

at:[http://www.gmcuk.org/How\\_Prepared\\_are\\_UK\\_Medical\\_Graduates\\_for\\_Practice\\_SUBMITTED\\_Revised\\_140614.pdf\\_58034815.pdf](http://www.gmcuk.org/How_Prepared_are_UK_Medical_Graduates_for_Practice_SUBMITTED_Revised_140614.pdf_58034815.pdf) [Accessed 24 Sep. 2017].

1. ten Cate, O., Chen, H., Hoff, R., Peters, H., Bok, H. and van der Schaaf, M. (2015). Curriculum development for the workplace using Entrustable Professional Activities (EPAs): AMEE Guide No. 99. *Medical Teacher*, 37(11), pp.983-1002.

2. ten Cate, O. (2017). *Keynote - Keele University School of Medicine Annual Medical Education Conference March 29 2017.*

Appendix 1: Activities logged by students in the GP block, categorised into EPAs, Non-EPAs and Degree of Entrustment

Degree of entrustment	Utrecht Core Entrustable Professional Activities					
	The Clinical Consultation	General Medical Procedures	Informing, advising & guiding patients and families	Communicating & collaborating with colleagues	Extraordinary Patient Care	Non EPAs
Observing the activity -1	66	5	12	3		8
Doing with direct supervision - 2	72	13	23	4		13
Doing with indirect supervision - 3	82			1		21
Doing unsupervised - 4						1
Supervising others - 5						3
Attended a Talk/ Read about topic	17	2	4	7		48
Discussed	123	3	8	7		43

Degree of entrustment	Utrecht Core Entrustable Professional Activities					
	The Clinical Consultation	General Medical Procedures	Informing, advising & guiding patients and families	Communicating & collaborating with colleagues	Extraordinary Patient Care	Non EPAs
Observing the activity -1	60	16	6	7	3	15
Doing with direct supervision - 2	98	60	18	9	1	16
Doing with	6	4	1	1		5

indirect supervision - 3						
Doing unsupervised - 4						1
Supervising others - 5						
Attended a Talk/ Read about topic	3	8	1	15	2	45
Discussed	53	12	3	9	3	37

Appendix 2: Activities logged by students in the Hospital block, categorised into EPAs, Non-EPAs and Degree of Entrustment.

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## The effectiveness of an elite rugby union player, coach, medical professionals and referee concussion education programme.

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**Edward Smith**

**Objective:** To assess the effectiveness of the Welsh Rugby Union (WRU) concussion education programme offered to elite players, coaches, medical professionals and referees by assessing their knowledge of various aspects of concussion recognition and management.

**Design:** Online, role specific questionnaires for players, coaches, referees and medical professionals.

**Setting and Participants:** 152 players, 25 coaches, 35 medical professionals and 37 referees from elite rugby union in Wales.

**Interventions:** Baseline concussion knowledge in elite and semi-professional rugby union in Wales was surveyed in 2015.<sup>1</sup> Over the following 2-years the WRU instituted an education programme for the stakeholders consisting of annual presentations, courses and online information.

**Main Outcome Measures:** Knowledge on various aspects of concussion including concussion symptom recognition, the return to play protocol and consequences of concussion compared to the baseline.

**Results:** The WRU education programme has been effective in increasing concussion knowledge in all stakeholder groups. Ninety six percent of participants reported receiving concussion education. Participants showed a greater knowledge of; concussion symptom recognition ( $p < 0.001$ , *cohen d* = 0.30), the graduated return to play protocol ( $p < 0.001$ , *cohen d* = 0.54) and the consequences of concussion ( $p < 0.001$ , *cohen d* = 0.92) compared with the baseline study. Players and coaches wish to continue to receive education from their team's medical professionals. Referees and medical professionals identified online resources as preferable future education sources.

**Conclusions:** The findings of this study demonstrate the education programme offered by the WRU has been effective in increasing knowledge on concussion in players, coaches, medical professionals and referees.

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## **Barriers and facilitators to the uptake and adherence of pre-exposure prophylaxis (PrEP) in adolescent girls and young women in Sub-Saharan Africa: a mixed methods systematic review**

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*Aliza Hudda*

Adolescent girls and young women aged 15-24 years are at the epicentre of the HIV epidemic in Sub-Saharan Africa. The biological, structural and behavioural risk factors for HIV acquisition in this age and sex category have been widely reported; these include gender-based violence, age-disparate relationships and risky sexual behaviours. However, despite randomised-controlled trials that demonstrate the efficacy of daily oral tenofovir disoproxil fumarate (TDF) or TDF combined with emtricitabine as pre-exposure prophylaxis (PrEP), there have been major discrepancies in the efficacy of HIV prevention amongst young women due to low adherence, inconsistent or incorrect use. Thus, adherence has been coined the 'Achilles heel' of PrEP use in adolescent girls and young women. As part of my intercalation in Global Health, I conducted a mixed-methods systematic review to identify barriers and facilitators to the uptake and adherence of PrEP in adolescent girls and young women in Sub-Saharan Africa.

This is the first study to systematically review the barriers and facilitators to the uptake and adherence of PrEP from both a quantitative and qualitative perspective. Published literature was systematically searched in seven databases in March 2017. The search strategy contained four key concepts: 'barriers and facilitators to the uptake and adherence', 'PrEP', 'girl or woman' and 'Sub-Saharan Africa' with no publication date or language restrictions. Titles, abstracts and full text articles were screened with a broad inclusion and strict exclusion criterion. Reference lists were hand-searched to include other relevant articles and experts were consulted to make sure that all appropriate articles could be included in this review. The initial search returned 692 titles; after deduplication and review of abstracts, 46 were selected for full text review, and 21 included in the final analysis (11 qualitative, 5 quantitative and 5 mixed-method studies). Overall, the studies were conducted in eight countries within Sub-Saharan Africa: Ghana(n=1), South Africa(n=13), Uganda(n=5), Kenya(n=8), Zimbabwe(n=1), Botswana(n=1), Nigeria(n=1) and Cameroon(n=1) between 2010-2017. A total of 10,609 women are represented, with the majority of papers are from clinical trials with three PrEP regimes: oral, topical or both(n=3), oral(n=11) and topical n=4). Two qualitative papers explored hypothetical oral PrEP barriers and facilitators to adherence and one mixed-methods retrospective study explored participants' preferences to oral, topical and other potential PrEP technologies such as the implant, injectable and cervical barrier.

The identified barriers and facilitators to the uptake and adherence of PrEP were summarised into four key areas of an adapted socio-ecological model: individual,

interpersonal, organisation and sociocultural factors. Individual factors include: age, PrEP product, side effects and regimen, location and fertility desires, alcohol use and HIV risk perception. Interpersonal relations such as partner and family dynamics influence uptake and adherence of PrEP, particularly the notion of privacy. Organisational facilitators include the healthcare facilities whereas employment and migration were barriers to PrEP uptake and adherence. Finally, wider socio-cultural practices, stigma and fear as well as gender norms and social relations play a significant role in young women's adherence to PrEP.

The findings of this review emphasise the complexity and multi-factorial nature of PrEP preference, uptake and adherence. This is because facilitators of PrEP adherence included positive partner dynamics, social support programmes such as 'adherence buddies' and an open environment to discuss PrEP. However, as the arsenal of PrEP products expands, it is not just access to PrEP technologies that is required; it is essential to enable multi-layering interventions so that adolescent girls and young women are empowered to access healthcare.

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## **Developing the chick embryo as a novel standardised neurological injury model**

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*George Solomou*

50,000 people are living with a spinal injury in the UK with an estimated a cost of £1bn per annum in addition to wider psychological impact to themselves and their support network. As a result, there is a global need for therapeutic developments to restore function and improve patient's quality of life. Researchers tend to employ live mammalian models in pre-clinical studies of neurological injury to test novel therapies in the complex cellular, structural and pathological environment of adult injury sites. Despite their advantages, live animal models are technically complex and time consuming, require multiple animals to generate statistically significant data which can be expensive and have additional ethical implications.

The chick embryo, a well-defined substitute to the mammalian nervous system, which has been extensively employed in neurodevelopmental research can be an alternative. Moreover, its major central nervous system cell types have been established. Notably, studies have shown that it can display nerve outgrowth and neural progenitor proliferation in response to injury.

### **Aims:**

We aimed to establish a standardised neurological injury protocol to be utilised for therapeutic testing. Moreover, we aimed to develop methodologies for visualising the injury site in whole-mount embryos using immunofluorescent and histology stains.

## Methods:

Ten chick embryos were incubated at 37.5 ° C, 68% humidity and operated on at embryological-days (E)3,4,5,6 and 7. A microscope-guided microsurgery was performed on all viable embryos at the lower spinal cord region adjacent to the main embryological vessels. At each time point, half of the embryos were fixed and half were incubated for a further 24 hours. The embryos were cleared of their embryonic membrane and subsequently labelled with i) Borax-carminine ii) Tuj-1 (immunostaining), for nuclear and neuronal tubulin staining respectively.



## Results:

Two chick embryos for each embryological day were successfully injured. One embryo was successfully stained for Tuj-1, facilitating detection of nerve fibres. In addition, Borax-carminine staining allowed clear delineation of the injury site and surrounding tissue. Finally, we demonstrated nanoparticles could be delivered to the lesion and detected 48h post injection.

## Discussion:

The project was able to usefully provide a protocol for inducing a spinal cord injury at E3-7 and introducing potential therapeutic agents. Use of this protocol could allow testing of the mechanism of actions and toxicity of a range of nanotechnologies such as implantable hydrogels and multifunctional nanoparticles in sites of an *in vivo* spinal cord injury. Moreover, its principles can be used to generate more dissecting protocols for later developmental stages in chick embryos (where the spinal cord exhibits less regeneration) or even adapt the technique to develop similar protocols in other 'egg-derived' animals such as reptiles or amphibians.

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## Resolution of comorbidities in the morbidly obese patient after bariatric surgery: A Case report and focused literature.

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### *Jessica Aggrey-Akyeampong*

The prevalence of obesity worldwide continues to escalate and imposes a challenge for the public health sector and health services to reduce and manage long term health risks successfully. Obesity, is defined as a body mass index (BMI) of 30 or more and increases the risk of complex chronic conditions whilst reducing life expectancy and consequently, an impact on NHS resources. In 2006/7, the direct cost to the NHS for people overweight and obese was £5.1 billion and is projected to increase to £7.1 billion by 2050.

The aim of this report is to discuss the case of a 62 year old female who presented to the bariatric clinic via referral from primary care with comorbidities and symptoms of cardio-respiratory compromise secondary to morbid obesity (Patient A). Achievements after bariatric surgery are explored with focused literature supporting findings.

Results from non-surgical interventions, show that the vast majority of patients relapse and regain weight often within a year. Majority of weight lost from exercise and diets are short term and only show a maximum of 5-10% of initial weight loss achieved. There are hardly reports of 'successful' cases, showing immediate resolution of metabolic dysfunctions and long term cures of associated comorbidities. These findings however are found in patients who have undergone bariatric surgery such as the more popular laparoscopic gastric bypass, laparoscopic gastric sleeve and gastric band (no longer offered by the National Health Service).

Bariatric surgery has become a growing area of interest, is becoming understood for its upper hand in short term and long term benefits and is considered a safe and effective method for successful weight loss surgery. There is evidence supporting its cure for type 2 diabetes, gastro-oesophageal reflux disease (GORD) and depression. This report documents Patient A's journey encompassing these changes. Although there are current arguments for and predominantly against bariatric surgery, we must recognise the increase in individuals diagnosed with obesity annually. There is a growing demand to manage complex comorbidities, and the undoubtable financial implications of treating each condition associated with obesity in primary and secondary care.

One surgical operation rectifies and improves these burdens. It is possible that social pessimism and stigma are holding us back from witnessing and accepting the phenomenon of bariatric surgery for morbid obesity.

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## **How Does Savant Syndrome Help Us Understand The Capabilities Of The Brain?**

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### ***Mai Baalbaki***

Savant syndrome is a rare condition typified by extraordinary abilities. These abilities range from rote memorization of one topic, such as historical dates, to extraordinary artistic skills. The drawback is that savant syndrome is usually displayed alongside severe neurological disabilities of varied forms. Neuroimaging studies on savants and dementia patients suggest that damage to the left anterior temporal lobe is key to the onset of savant syndrome. This is hypothesized to be due to a release of inhibition on the right hemisphere, allowing "rewiring" of localized neural connections. It is from this that new cognitive abilities develop, categorized as savant skills. Savant-like abilities have been induced in neuronally normal individuals through magnetic inhibition of the left anterior temporal region. From current evidence, the hypothesis of savant syndrome occurring through inhibition of the left anterior temporal lobe seems promising. Understandably, due to the rarity of savant syndrome, some areas of this research are lacking. Future research needs to focus on longitudinal studies, genetic basis of congenital savants, and additional neuroimaging studies, before an accurate model of savant syndrome can be elucidated.

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## Introduction: Heparan Sulphate biochemistry

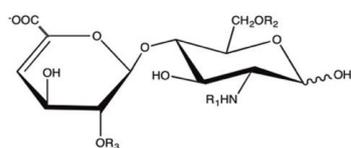
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*Kirsty Clarke*

Heparan sulphate (HS) is a linear polysaccharide comprised of repeating heterogeneous structures of  $\alpha$ 1-4 linked glucuronic acid and N-acetylglucosamine disaccharides. During HS biosynthesis, the backbone is modified by a plethora of enzymes, resulting in the fine chemical patterning of the polysaccharide chain <sup>[1]</sup>. Modification of the primary structure thus is thought to modulate target biomolecule binding, exerting a direct influence upon a multitude of discrete biological functions, including growth factor expression and secretion of extracellular matrix proteins <sup>[2]</sup>. HS is highly abundant in humans and other higher organisms, and plays a role in a multitude of cellular processes, however, due to difficulty in labelling and marking HS, its role in disease pathogenesis remains largely unexplored. Development of a multiplexed method to characterise HS patterning will enable analysis of a wide variety of biologically derived heparan sulphate preparations. For example, HS samples from numerous strains of leishmaniosis, where variations in its abundance and behaviour may correlate with the manifestations and prognosis of disease, could be studied using these techniques. Eight major HS disaccharide species exist (fig 1), providing heterogeneous mixtures for compositional analysis and AminoxyTMT isobaric tags for labelling glycans enables the simultaneous analysis of multiple experiments by mass spectrometry.

**Aim:** To develop a new method for the LC separation and MS detection of aminoxyTMT-tagged HS disaccharides, comparing RP- and HILIC-LC-MS

**Methodology:** Disaccharides (table 1) and a maltose control were derivatized using aminoxyTMT<sub>0</sub> with minor modifications from the manufacturer's protocol. Clean-up of the derivatized sample performed using an Oasis HLB column. Samples analysed by static ESI-MS or LC-MS, using a QToF Premier and Dionex U3000, with Reprosil Gold (RP) and Accucore amide (HILIC) columns, with various gradients.



(e.g. ~OH in 1A).

Fig 1. A) Generalised structure of HS disaccharide. R groups vary according to Table 1. B) aminoxyTMT<sub>0</sub> reagent, showing reporter ion component, mass balance and reactive group. This reacts with the reducing sugars

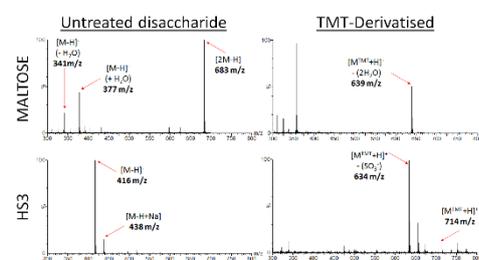
### Results

Successful HS TMT labelling was achieved for a number of disaccharides, Both HILIC and RP showed some ability to separate labelled disaccharides

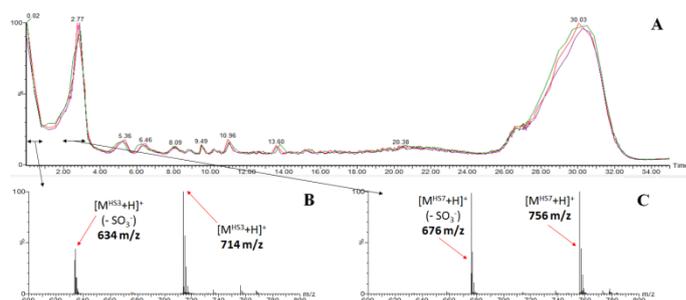
Disaccharide standard	Unit Formula	R1	R2	R3
1	$\Delta$ -UA-GlcNAc	Ac	H	H
2	$\Delta$ -UA-GlcNAc(6S)	Ac	Sulf	H
3	$\Delta$ -UA-GlcNS	Sulf	H	H
4	$\Delta$ -UA-GlcNS(6S)	Sulf	Sulf	H
5	$\Delta$ -UA(2S)-GlcNS	Sulf	H	Sulf
6	$\Delta$ -UA(2S)-GlcNS(6S)	Sulf	Sulf	Sulf
7	$\Delta$ -UA(2S)-GlcNAc	Ac	H	Sulf
8	$\Delta$ -UA(2S)-GlcNAc(6S)	Ac	Sulf	Sulf

Prior to TMT derivatisation, UA-GlcNS was observed as deprotonated/sodiated molecular ions (416 and 438 m/z respectively in negative ion mode). Derivatisation enabled facile analysis in positive ion mode: TMT<sub>0</sub>-US-GlcNS was detected (714 m/z, +ve ion mode) with labile neutral loss of sulphate ( $\Delta m$  -80; SO<sub>3</sub>) at 634 m/z. UA-GlcNAc and UA(2S)-GlcNAc were also tagged with reasonable efficiency and similar neutral losses from parent observed.

**Fig. 2: AminoxyTMT0 tags reducing sugars with high efficiency:** Negative ion mode ESI-MS spectra of underivatized maltose (top left) and HS3 disaccharide (bottom left). Positive ion mode ESI-MS spectra of derivatised ( $[M+H]^+$ ) maltose (top right) and HS3 disaccharide (bottom right). Comparison between native and derivatised spectra shows high labelling efficiency of aminoxyTMT

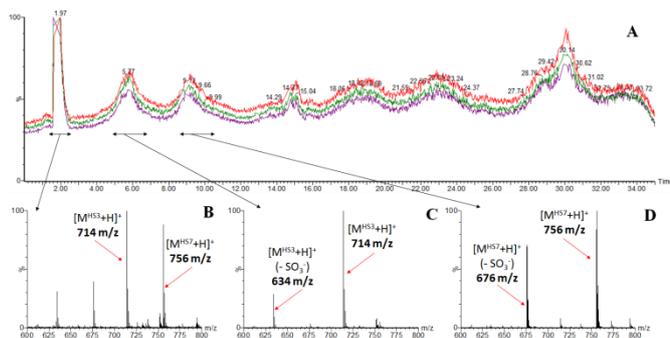


Using reversed phase chromatography, UA-GlcNS and UA(2S)-GlcNAc were separated from a mix of three disaccharide standards, with good reproducibility. UA-GlcNS was poorly retained by RP column, (0.02 min. elution), whilst UA(2S)-GlcNAc showed longer retention (2.77 min.), UA-GlcNAc (predicted Mr. 694) was undetected by this method.



**Fig. 3: Total Ion Chromatogram and MS spectra from HS separation using LC-MS:** Overlaid TIC showing retention time stability (A) HS3 elutes rapidly (B) HS7 shows longer retention (2.77 min) (C) from the mix

Using HILIC chromatography UA-GlcNS and UA(2S)-GlcNAc also separated by HILIC from a mix of three disaccharides (UA-GlcNAc, UA-GlcNS and UA(2S)-GlcNAc) with good reproducibility (N=3 replicates). Distinct peaks observed for UA-GlcNS (~6 min) and UA(2S)-GlcNAc (~9 min).



**Fig. 4: Total Ion Chromatogram and associated MS spectra from HS mix separation using HILIC: TIC showing retention time stability (A) Two HS disaccharides observed in breakthrough peak at (~2 min) (B), distinct elution maxima observed for HS3 (~6 min) (MS: C) and HS7 (MS: ~9 min) (D). Product ion spectrum**

**Conclusion:** HS disaccharides can be successfully labelled with aminoxyTMT<sub>0</sub>. Development of aminoxyTMT-labelled disaccharide separation and analysis will enable application of the technology to biologically-derived material.

## References

- 1) Sasisekharan, R.; Venkataraman, G. Heparin and heparan sulfate: biosynthesis, structure and function, *Current Opinion in Chemical Biology* 2000, 4, 626-631.
- 2) Gill V.; Rao, S.; Pohl, C.; Zaia, J. Disaccharide Analysis of Glycosaminoglycans Using Hydrophilic Interaction Chromatography and Mass Spectrometry, *Analytical Chemistry* 2013 **85**, 1138-1145.

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## Adult-derived microglia: validation of protocol and identity

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**Samuel Coleman**

### Background

Glial cells (astrocytes, oligodendrocytes and microglia) make up an estimated 50% of the cells in the brain. Microglia act as the immune cells of the CNS, responding to injurious stimuli, and generate inflammatory responses including cytokine production. They are critical in the development and potential resolution of neurodegenerative diseases. Most in vitro studies of neurodegenerative disease employ neonatal microglia, but these cells are recognised as being more resistant to simulated pathology, and show greater recovery/regeneration than is observed in patients. Patients with neurodegenerative conditions have microglia best described as adult, or aged, with a stronger tendency to be pro-inflammatory, and often exhibiting altered morphology. To accurately simulate neurodegenerative diseases in vitro, it is important not only to ensure the diseases are modelled on aged microglia, but also establishing a high-yield protocol producing such cells and make testing feasible.

### Aims

This study aimed to validate a protocol for the growth of adult-derived microglia.

### Methodology

Potential species-specific antibodies were identified through manufacturer websites and gene/protein sequence comparisons. Astrocyte cultures were established from neonatal mouse cerebral cortices to act as a feeder layer. Adult rat mixed glial cultures were added. After 8-10 days, a confluent layer of astrocytes forms at the base of the flask, allowing

microglia to be separated by shaking the flask for two hours, 220 rpm. High purity microglia cultures were stained for various markers: Arg1, iNos, OX42, TLR-4, CD206 and Lectin.

### **Results**

Several candidate markers were identified that might distinguish rat from mouse microglia. However, all were found to be non-specific, with staining found in cells from both species. Although microglia were not definitively shown to be adult-derived, cultures derived using adult tissue did exhibit far greater expression of various microglial markers: Arg1, iNos and OX42 all provided stronger staining in our suspected adult-derived cells compared to the neonatal expression. These greater levels of expression suggest these cultures more closely resemble adult/mature microglia.

### **Conclusions**

Successful establishment of this protocol for growing adult-derived microglia could allow the opportunity to study adult and aged microglia in vitro, more relevant to neurodegenerative disease. How these changes in function then also incorporate into the progression of neurodegenerative diseases, and the more accurate simulation of therapy options on modelled disease in-vitro. Therapy options including the modulation of increased microglial activation, or the upregulation of antioxidant pathways lost with age. It may be possible to confirm the adult origin of microglia in this system by gene expression analyses, or sex-specific markers, to distinguish adult male microglia, from neonatal female, for example. The greater levels of marker expression seen in adult cultures here suggests these cells are genuinely of adult-derivation, more closely resemble the behavior of adult microglia in vivo, and so warrants further investigation.

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## **To Examine the Relationship Between Parenting and Executive Function (EF) in Children Diagnosed with a Neurodevelopmental Disorder or Special Educational Need (SEN)**

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### ***Catherine Graham***

Executive Function (EF) is an umbrella term for complex cognitive processing, which requires the co-ordination of several sub-processes to achieve goal-directed behaviour (Best & Miller, 2010). The higher level cognitive processes associated with EF include problem-solving and attention shifting. There is convincing evidence that EF plays an important role in child functioning. Typically, the development of EF is demonstrated through the biological development of the prefrontal cortex (PFC). However, until recently research on EF has neglected the impact of social interaction on development, specifically the role of parenting on PFC development (Matte-Gagne & Bernier, 2010). Research addressing this relationship between parenting and EF in school-aged children diagnosed with a neurodevelopmental disorder and special educational need is limited (Bernier, Carlson, Deschênes, & Matte-Gagné, 2011). In the present study, we examined the relationship between parenting and EF in 65 families using a range of measures. We also examined the relationships between EF and children's behaviours and IQ score. EF was measured using a composite, derived from three cognitive tasks completed by the children and a previously validated parent report measure of behaviour. Parenting was measured using the parenting scale, specifically

measuring laxness and overreactivity, and emerging parenting strategies from an open-ended question. Results show that increased laxness and overreactivity are associated with higher EF scores. There was an association between parents who use more positive parenting strategies when dealing with challenging behaviours, and lower EF scores. Furthermore, more executive dysfunction is displayed in children with behaviour problems. Finally, results revealed that a higher EF score is related to a higher IQ score. This study, along with previous research, concludes that parenting does play a vital role in a child's EF development.

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## **Peer Teaching: perceived challenges faced by students and posed to teaching staff**

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*Yeo Hea Su*

**BACKGROUND:** Peer teaching is defined as 'People from similar social groupings who are not professional teachers helping each other to learn and learning themselves by teaching' (Topping, 1996: p.322). Peer teaching is recognised as an effective educational tool that provides additional educational opportunities and a platform for students to develop and refine their teaching skills; it has consequently been increasingly implemented by Medical Schools. However, to date, no research explores the challenges in peer teaching experienced by both students and staff. This study aims to explore the perceived challenges and unintended consequences of peer teaching amongst students and staff across two disparate Medical Schools.

**METHODS:** Student focus groups and semi-structured interviews with staff were conducted across the two institutions. Peer tutors from Years two to five with experiences in organising peer teaching, and staff who current teach the undergraduate curriculum were recruited by snowball sampling. The recordings were transcribed and analysed using thematic analysis.

**RESULTS:** Fifteen students and four staff members participated in this study. Six main challenges with subsequent sub-themes were identified: Staff engagement, Recruitment, Regulation of peer teaching, Curricular integration, Impact on staff, and Organisational support. The staff concerns regarding 'misinformation', lack of regulation, and exam focused teaching affected the educational culture within each institution, subsequently shaping the challenges experienced by students. Staff concerns arose from their increasing awareness of 'separate schooling' amongst students whereby students were prioritising peer teaching over similar faculty led teaching sessions, reflected by the contrasting attendance rates.

**CONCLUSION:** Despite the disparity in the educational culture and regulation of peer teaching across the two institutions, similar challenges were experienced amongst staff and students. The discrepancies between staff and students' perspectives on the same challenge added depth to the study and helped build upon findings in existing literature. Findings from this study provide an insight into an aspect of peer teaching that is poorly understood, and highlights areas in need for further research.

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## **Are Mindfulness-based Mind Body Practices (M-MBP) more effective than Eye Movement Desensitisation and Reprocessing (EMDR) therapy for Post-Traumatic Stress Disorder (PTSD) in adults?**

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*Arie Hawazie*

### **Background:**

Post-Traumatic Stress Disorder (PTSD) is a detrimental anxiety disorder that can affect anyone. One domain of Complementary and Alternative Medicine (CAM) known as Mind Body Practice (MBP) involving the aspect of altering physiological function using the mind is a potential therapy to treat PTSD. Could the characteristic of mindfulness be another unique therapy that has potential for efficacy in comparison to Eye Movement Desensitisation and Reprocessing (EMDR), an established first line therapy that had major scepticism when initially introduced?

### **Aim:**

This study analysed the efficacy of Mindfulness based Mind Body Practices (M-MBP) and EMDR therapy in treating PTSD in adults to observe the full potential of mindfulness through statistical analysis. Also, different models have been theorised for the understanding of EMDR, thus this dissertation will provide a statistical analysis into one of these leading theories known as the 'working memory model'. This analysis observes if this model is taxed by 'mindfulness' in M-MBP and 'eye movements' in EMDR.

### **Objective:**

This analysis compared the efficacy of M-MBP to EMDR statistically to treat total symptomatology in PTSD. Also analysed the efficacy of the two therapies to reduce two specific symptoms separately measured; re-experience and avoidance to show evidence for the working memory model.

### **Methods:**

Through using the databases; PubMed, Medline, EBSCO, EMBASE and Cochrane, the database search found 24 articles, of which 11 for M-MBP and 13 studies were for EMDR. These studies were analysed for efficacy of reducing total PTSD symptomatology and specifically treating re-experience and avoidance.

### **Results:**

Both EMDR and M-MBP was significantly more effective to treat PTSD against wait-list controls, but statistically EMDR was more effective than M-MBP to treat overall symptoms for PTSD. Reduction in re-experience and avoidance was statistically significant in both therapies compared to wait-list controls.

### **Conclusion:**

The two therapies are effective to treat PTSD symptomatology compared to control, suggestively EMDR more than M-MBP. Furthermore, the statistical analysis conducted supported the working memory model, as re-experience and avoidance were reduced in both therapies.

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## Role of hMSCs secretome in modulation of hemoxygenase-1 anti-inflammatory pathway

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*Jordan Higgs*

**Background:** The potential of Mesenchymal Stem Cells (MSCs) as therapeutics is only just beginning to become understood. With heavy ties to immuno-regulation, inflammatory and repair processes, human MSCs (hMSCs) have become a cell type of great interest over the last decade. Characterised by their origin in the mesoderm and their ability to differentiate into multiple progenies such as osteocytes and chondrocytes, as well as myogenic precursors giving rise to adipocyte or myocytes, hMSCs are tailor made to repair and replenish damaged and decrepit cells and tissues of these types.

It is well known that haem containing proteins use haem as a co-factor, and when inappropriately exposed inter-cellularly often facilitate a pro-inflammatory environment as haem is capable of free radical generation, leading to local tissue damage. Haemoxygenase-1 (HO-1) is a bespoke enzyme designed perfectly to catalyse the breakdown of haem containing compounds down to iron, carbon monoxide and biliverdin. Most antigen presenting cells (APCs), such as dendritic cells or macrophages, express high levels of HO-1, and for this reason it has been extensively studied. Understanding if there is a link between hMSCs and HO-1 expression in these APC is yet to be elucidated, but could provide improved anti-inflammatory therapies.

**Aim:** The main focus of this study was to highlight any anti-inflammatory or immuno-regulatory properties between hMSC secretomes (via cultured media) and K562 cells. K562 cells, are an immortalised Human Chronic Myelogenous Leukaemia (hCML) cell-line, capable of evolving granulocyte and monocyte (APC) like properties.

**Study design:** 1. Culture hMSC. 2. Serum Free Condition Media (SF-CM) generation. 3. Using 2 different oxygen saturations (21% and 2%), collection of K562 cell pellet cultured in SF-CM and control group media [Serum Free Non-Condition Media (SF-NCM), and Growth Media (GM)] after exposure to hemin (a haem containing compound). 4. Isolation and quantification of K562 RNA. 5. Electrophoresis and qPCR primer design for gene of interest (GOI) HO-1 and vs control (GAPDH). 6. Quantitative PCR to evaluate GOI fold change vs control.

**Results:** Fold change of HO-1 in hemin exposed K562 cells:

**SF-CM/21% O<sub>2</sub>:** 32.5, 95% CI 21.3 - 49.5 (1dp); P value: 0.00000000489.

**SF-CM/2% O<sub>2</sub>:** 20.0, 95% CI 11.3 - 35.2 (1dp); P value: 0.000000162.

**SF-NCM/21% O<sub>2</sub>:** 27.4, 95% CI 18.0 - 41.5 (1dp); P value: 0.0000000074675.

**SF-NCM/2% O<sub>2</sub>:** 1.0, 95% CI 0.01 - 20.4 (1dp); P value: 0.98.

**GM/21% O<sub>2</sub>:** 1.2, 95% CI 0.4 - 3.5 (1dp); P value: 0.74.

**GM/2% O<sub>2</sub>:** 0.00435, 95% CI 0.00003 - 0.71207 (5dp); P value: 0.000000162.

**Conclusion:** At both 21% and 2% O<sub>2</sub> saturations, hMSC secretome (SF-CM) cultured K562 cells drastically increased expression of HO-1 (some 20 to 30 times) after hemin exposure compared to controls, both with statistically significant P values. This quantitatively shows

that hMSC secretomes have the ability to interact with monocyte like cells and stimulate their HO-1 expression, improving their propensity to respond to a harsh pro-inflammatory haem containing environment into a more hospitable anti-inflammatory and anti-oxidative iron, carbon monoxide and biliverdin containing milieu.

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## **Nature vs Nurture: is it really our genetics that are responsible for mental illness?**

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*Shannon Kelly*

The exact cause of mental health problems is unknown due to its multivariate nature. This study focuses on bipolar disorder and generalised anxiety disorder – which both have established risk factor genes associated. This research aims to find whether the mental illnesses bipolar disorder and generalised anxiety disorder are mainly caused by genetic factors or whether they are influenced more by environmental factors. By analysing numerous family, twin and adoption studies (where available), it was evident that genetics play a large role in these mental health conditions – particularly bipolar disorder. It was noted that there were some confusions between research papers in regard to the impact of environmental factors with some researchers placing a larger emphasis on the impacts. Overall both disorders appear to have strong genetic influences indicated by the research conducted and individuals with risk factor genes may be at higher risk of developing the disorders. Anxiety disorder had no papers available for adoption studies which may be a good area for future research into the true cause of generalised anxiety disorder. Isolating environmental risk factors appeared to be a challenge when carrying out research due to the same risk factors being present for a number of diseases.

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## **Glenoid labral cysts: a rare cause of shoulder pain**

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*Connor Moore*

### **OBJECTIVES:**

Shoulder pain is a leading cause of morbidity. Tears of the glenoid labrum (GL) are a common pathology, and can result in glenoid labral cysts (GLCs). Suprascapular neuropathy and quadrilateral space syndrome (QSS) are potential complications of GLCs. This is due to compression of the suprascapular and axillary nerves respectively. If undetected, permanent atrophy and weakness of the associated muscles can occur. Due to the infrequency of complications from GLCs, they are often overlooked in favour of more common shoulder pathologies. This review collates current information on the relevant anatomy, etiology, and management of GLCs resulting in neuropathy.

### **METHODS:**

An extensive literature search was conducted to collate all information on the anatomy, etiology and management of GLCs resulting in neuropathy. Two dissections were created to illustrate the complete path of the suprascapular and axillary nerves.

## **RESULTS:**

GLCs are commonly thought to be due to a one-way valve mechanism allowing fluid to leak into surrounding tissue from the glenohumeral joint. Magnetic resonance imaging is used in combination with electromyography to diagnose labral pathology and GLCs resulting in neuropathy. Surgery is avoided if possible. However, when required the preferred approach is to fix the labral pathology and remove the cyst arthroscopically, and if this fails by open excision.

## **CONCLUSIONS:**

Suprascapular neuropathy and QSS are rare occurrences which are under-diagnosed. GLCs as a cause of these compression neuropathies should be included in the differential diagnosis of shoulder pain, especially when more common causes have been excluded.

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## **Perceptions of self-management in people with Type 2 Diabetes: a qualitative analysis.**

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*Nathan Nikoloff*

### **Background**

People with type 2 diabetes are encouraged to play a major role in managing their own care. People with a diagnosis of type 2 diabetes for less than 5 years can reverse HbA1c to sub-diabetic levels through self-management (calorie-restricted diet and weight maintenance). People with diabetes are now educated about making lifestyle changes at diagnosis. However, education alone does not necessarily lead to self-management. Behavioural interventions are suggested to increase engagement in self-management when combined with education.

### **Aims**

The aim of this qualitative study is to explore perceptions of patients with type 2 diabetes about self-management, with a secondary analysis using the framework of Contextual Behavioural Science (CBS).

### **Method**

A data-set comprising transcripts of semi-structured interviews with people with type 2 diabetes for less than 5 years, was used. Participants had been recruited from primary care; interviews were facilitated using a topic guide, lasted one hour, in the participant's home.

A thematic analysis was conducted, with data management using Nvivo. Commonalities were generated during open coding, with flow diagram and memo writing to track emerging thematic relationships. Codes were consolidated during axial coding and comparatively analysed with similar qualitative analysis to improve validity. Themes were then mapped on to the model of psychological flexibility and data were further analysed using CBS to demonstrate the validity of relationships with psychological flexibility. Contextual behaviorism is the underlying science of acceptance commitment therapy and the model of psychological flexibility. It is based on verbal behaviour and therefore is appropriate for analysis of perceptions.

## Results

Data from interviews with 21 patients were analysed. Data supported three main areas of CBS:

- Adapting (rule governed behaviour, communal commitments, reinforcing self-care, reinforcement via medical care)
- Experiential avoidance (confusion and anxiety, guilt, paternalism, losing track)
- Identifying values (valuing a healthy diet and self-management, valuing exercise and an active lifestyle)

## Conclusions

Relationships between themes of perceptions of self-management and CBS were found. Adaption to self-management involves reinforcement of operants to develop rule governed behaviour. Encouraging patients to monitor bio-markers (e.g. blood glucose) and make family commitments, allows patients to reinforce positive self-management strategies or rules.

People with diabetes commonly relate negative feelings, feelings of failure, guilt and anxiety to diabetes and self-management. Avoidance of negative feelings results in avoidance of self-management, denial and reinforcement of problematic eating. Literalising negative self-perceptions is related to poor self-management of the disease and reliance on medication.

People with diabetes have values of managing diabetes with diet and not with medication, leading an active lifestyle, and eating a healthy diet. If patients set goals that relate these values to positive health behaviours, a powerful reinforcement of self-management relational responding proceeds. This is due to contextual and historic intrinsic reinforcement: a shortcut to self-management, rather than learning new behaviours.

Conclusions suggest that individualised acceptance, mindfulness and commitment interventions and value based goal setting; on these themes and reinforced by the clinician; could predict and influence self-management and subsequently HbA1c.

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## Effects of Hydric Stress on the FoxO Pathway and Microbiota

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*Jacob Oguntimehin and Seeta Shah*

### Introduction:

Dengue Fever (DF) is a neglected tropical disease, effecting approximately 390 million people annually. It consists of four serotypes; DEN-1, DEN-2, DEN-3 and DEN-4. It is transmitted by the *Aedes aegypti* mosquito which is present in tropical areas of the world. The symptoms of DF can be mild and death is usually due to dengue haemorrhagic fever or dengue shock syndrome. In 2015 in Sao Paulo, Brazil, an endemic of DF broke out at the same time of the country experiencing a major drought. A link was therefore put forward between the susceptibility of the vector and 'hydric stress'- a term used to describe the

mosquitos having lack of water during this period. The FOXO pathway would be used as it is present during a stress response.

#### **Methods:**

*Aedes aegypti* mosquitoes of the Rockefeller laboratory strain were obtained. Eggs were placed in water until hatched and larvae were separated till they reached the pupae stage, after which they were placed in cages. This was done over a period of two days. Mosquitos were kept in an insectary with the temperature and light being controlled. Once hatched, the mosquitos were allowed to mature before being separated again with 30 females and 20 males in each cage. Three replicated were made. They underwent hydric stress for 8-hour periods. This involved removing the sugar water soaked cotton wool from the top of the cage and replacing this with dry sugar cubes inside the cages. RNA extraction, purification and cDNA synthesis was done followed by qPCR for each replicate to see the effect of hydric stress on gene expression (16s RNA and PP2A).

#### **Results:**

Hydric stress analysis was done considering fecundity and mortality. There was no change in egg laying capability whereas there was an increased mortality in those mosquitos which underwent hydric stress. An increase in 16s RNA and PP2A expression in the hydric stress group was seen. However, both P values showed an insignificant difference between the two groups; hydric stress and non-hydric stress.

#### **Discussion:**

The results obtained showed that undergoing hydric stress did impact the mosquitos, however did not show any significant effect on their fecundity or mortality. Previous studies in this area suggest that the more well fed mosquitos are, the greater their egg laying ability. Another study was done regarding temperature, which showed little to no difference in fecundity between temperature ranges. The FOXO pathway is present during times of stress and PP2A is a key regulator of this pathway. Hence, it would be thought that under stressful periods there would be a higher expression of PP2A, which was seen from the results.

#### **Conclusion:**

We were able to see the effects that hydric stress has on gene expression and the ability of the mosquitos to lay eggs and their mortality rate. It shows us the complexity in the *Aedes Aegypti* mosquito in tolerance to hydric stress. However, further investigations need to be done to help develop control and preventive measures against dengue fever.

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## **Musculocutaneous - Median nerve communication: lessons derived from a case report**

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### ***Francis Osuji***

As per standard Anatomy textbook, there are no peripheral communication branches between the musculocutaneous and the median nerves. Ignorance of anatomical variation of the musculocutaneous - median nerve intersection or the lateral cord of the brachial plexus may lead to inadvertent injuries during clinical procedures. **Objective:** To document anatomical variations of the brachial plexus terminal branches, including novel inter-

communications, in a single cadaver. **Methods:** A cadaveric dissection of the neck and axilla on both sides was conducted exposing the brachial plexus and its terminal branches. **Results:** A communicating branch between the musculocutaneous and the median nerves was observed on the left side of the cadaver. The communicating branch of the musculocutaneous nerve was located 8.5cm after the lateral cord branching of the brachial plexus. The communicating branch was 6cm in length and distal to the coracobrachialis muscle. **Conclusion:** The presented variation can be a potential vulnerability for neural or neurovascular compression, in addition to surgical approaches at the axilla and arm level. The presence and incidence of anatomical variations of the brachial plexus is of the utmost importance clinically for surgeons and anaesthetists performing pain management treatments, anaesthesia or surgical approaches to the upper limb.

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***What is chronic traumatic encephalopathy, and how does it cause the symptoms seen in sports with repetitive sub-concussive hits to the head?***

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***Simran Parmar***

My project is a literature review about chronic traumatic encephalopathy (CTE), which is an umbrella term that is used to describe the neurodegenerative disease that is thought to result from repetitive traumatic brain injuries. CTE is characterized by a tau protein pathology, very similar to Alzheimer's disease. CTE primarily affects former athletes who participated in sports such as American football, boxing, and rugby. In 2013, a group of nearly 4,000 former National Football League (NFL) players won a \$765 million settlement from the league, claiming they were not adequately informed of the risks of developing CTE as a result of playing American football.

It was originally thought that CTE arises only when one gets hit with enough force to cause a concussion. Recently however, CTE has been diagnosed in people with no history of concussion, but with an extensive history of repetitive sub-concussive hits to the head. CTE presents with a very wide range of signs and symptoms, including memory loss, aggressive behaviour, depression, dementia, and Parkinsonism. Interestingly, the symptoms of CTE only start to develop after a latent period of years to decades after the discontinuation of the exposure to brain trauma.

The defining pathology of CTE is the accumulation of hyperphosphorylated tau protein neurofibrillary tangles (NFTs). The exact same type of tangles have been identified in Alzheimer's disease, and are thought to destabilize microtubules and contribute to axon cell death. The precise mechanism of how repetitive head trauma leads to NFTs is not yet known, however there are a few proposed mechanisms. One explanation is that repetitive head injuries promote the activation of microglia, causing them to release pro-inflammatory cytokines, and neurotransmitters such as glutamate. These substances can alter membrane permeability to allow calcium to enter the axon, which in turn activate calpains and caspases, promoting apoptotic and necrotic pathways. These same substances also inhibit phosphatases, leading to the hyperphosphorylation of tau proteins and the accumulation of NFTs.

There has been a recent increase in the number of diagnosed cases of CTE across many contact sports. A recent study performed by the Department of Veterans Affairs and Boston University found that 96% of NFL players who received post-mortem autopsies were diagnosed with some form of CTE. This is a potential threat to public health, as there are millions of mild traumatic brain injuries each year in the United States, putting those who play contact sports at risk of developing CTE later on in life.

Most of the literature that was reviewed was consistent in saying that repetitive head trauma leads to CTE. However, because CTE diagnosis can only be made during an autopsy, it is worth noting that there may be a selection bias towards those afflicted with CTE, as individuals are more likely to receive an autopsy if CTE symptoms were present before death. It is also worth noting that there is only one prominent CTE researcher, Dr Joseph Maroon, who consistently refutes the link between repetitive head trauma and CTE. However, this could be due to a conflict of interest, as he has been the team neurosurgeon for the Pittsburgh Steelers, an NFL team, for the last 25 years.

The next steps in CTE research include trying to find a biomarker for the disease, as this could allow it to be diagnosed in a living patient. Confirming the pathophysiology of CTE is another important area of research, as this could help with diagnosis and management of the disease.

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## Quality of life in patients who underwent patent foramen ovale closure, left atrial appendage closure or mitralclip procedure

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*Chantal Patel*

**Aim of study** To assess patients quality of life (QOL) pre and post patent foramen ovale (PFO) closure, left atrial appendage (LAA) occlusion or Mitraclip procedures, in a single centre.

**Material and Methods** We analysed 148 patients who underwent one of the above procedures from October 2014 to October 2016 at RSUH. The mean age of patients who underwent PFO closure was 46 years, whilst in the LAA closure and Mitraclip procedure groups, the mean age was 78 and 82 years respectively. Data was entered into the NICOR database as part of the *Commissioning through Evaluation* process. We collected data using the EQ-5D-5L questionnaire, either in person or over the phone.

**Results** 67 patients underwent PFO closure, out of which 32 responded pre op and 22 post op, despite multiple repeated attempts. 30 patients out of 54 who underwent LAA closure responded pre-procedure and 27 post procedure. 19 and 18 patients out of 27 who underwent Mitraclip procedures responded pre op and post op respectively; 6 deceased (MitraClips only).

There was no improvement of QOL post PFO closure in terms of walking, dressing, conducting ADL's, pain and global health score. However, we demonstrated an improvement in the level of anxiety and depression.

In the LAA closure group of patients there was also an improvement in anxiety and depression, but similarly no improvement was seen in the other categories.

There was a significant improvement globally in the QOL in patients who had undergone the Mitraclip procedure. Additionally, their global health score showed almost a two-fold increase.

**Conclusion** Patients in the PFO and LAA closure groups showed no improvement in QOL, other than in anxiety and depression. This result was expected because both procedures are performed to prevent a further thromboembolic event (PFO and LAA) or further bleed on an anticoagulant (LAA). We were surprised that anxiety and depression were improved, but further questioning revealed patients had high levels of worry that a further event could occur without treatment, and that treatment mitigated the risk.

There was a dramatic improvement in QOL after Mitraclip procedure, as expected in a disease modifying procedure. The mortality was due to pump failure (2) and non-cardiac causes (4).

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## **Intrathecal Nusinersen: A novel treatment for Spinal Muscular Atrophy**

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***Toni Robinson***

I completed a case report and literature review during my year 3 SSC in the paediatric intensive care unit. I found the case of an infant with spinal muscular atrophy (SMA) type 1 particularly interesting due to the fact that she was one of the first patients in the UK to be receiving a new drug, Nusinersen approved by the FDA in 2017; it is the first treatment for SMA. I was fortunate to be able to consult with the patient and her family prior to initiating treatment and well as in the initial stages of treatment then a follow up after 3 months of treatment. My case report comprises of the case presentation and a literature review exploring the evidence base for Nusinersen and other potential future treatments for SMA. The case report summaries a case of a 1 year old girl who presented with floppy baby syndrome at 2 months old. This followed an obstetric history of reduced movements in utero resulting in an induced vaginal delivery at 39+6 weeks. A diagnosis of Spinal Muscular Atrophy (SMA) type 1 was made at 6 months of age.

Until June 2017, management of the patient reported, was supportive with the aim of preserving pulmonary function, ensuring adequate nutrition and regular physiotherapy. In June 2017, Nusinersen was licensed for use as a treatment for SMA for patients on the expanded access programme (EAP).

This case study and literature review explores the previous management of SMA, the role of Nusinersen as a treatment for SMA and its effects on patients so far. The key learning points from this case report included the importance of recognising SMA in neonates because initiating treatment early on can drastically improve outcomes, the significant advances in SMA management and the impact of the new treatment on the patient and their families.

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## The revolution of glaucoma surgery - the associated fibrosis risk of devices/ procedures and mechanisms.

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*Salman Sadiq*

**Introduction:** Glaucoma is a progressive optic neuropathy caused by raised intraocular pressure (IOP) and is the leading cause of irreversible blindness worldwide. The efficacy of the current gold-standard treatment, surgical trabeculectomy, reduces over time primarily due to fibrosis and scarring of the surgically filtering bleb. This has resulted in a 5-year failure rate of 46.9% despite the use of the toxic antimetabolites mitomycin C (MMC) and 5-fluorouracil (5-FU) intra-operatively.

The field of minimally invasive glaucoma surgery (MIGS) has gained considerable popularity over the past decade. The Xen Stent, a new MIGS device, has been utilised clinically to reduce the IOP as an alternative to trabeculectomy. However, despite its gelatinous properties, the device may still be susceptible to fibrosis. Hence, a greater understanding of the mechanisms underpinning fibrosis following MIGS and surgical trabeculectomy is required, as both procedures disturb the conjunctiva resulting in fibrosis and therefore failure. In this project, a 3D tissue-engineered conjunctival model has been developed and used to identify the factors involved in fibrosis.

**Materials and Methods:** The 3D tissue-engineered conjunctival model was composed of collagen type 1 and porcine conjunctival fibroblasts obtained from freshly dissected porcine conjunctiva to best replicate the native human conjunctiva. Two isolation techniques, explant outgrowth and enzymatic digestion, were compared. Specially located conjunctival tissue was utilised to study the Tenon's capsule structure and its potential role in post-operative fibrosis. Using the 3D model, the effects on fibroblast behaviour following application of the growth factors TGF- $\beta$ 1 and VEGF and the antimetabolites MMC and 5-FU were studied. The effect of antimetabolite delivery method, injection or topical application, along with dose and application time were also investigated. The cellular interaction with the implanted Xen Stent was examined with and without the addition of VEGF.

**Results:** Enzymatic digestion was a more effective method to obtain fibroblasts in a greater quantity with a shorter culture time as compared to explant culture. Histological analysis demonstrated the disorganised structure of the Tenon's capsule as compared to the conjunctiva. 3D conjunctival tissues were constructed and cultured up to 14 days successfully. The addition of growth factors in the culture promoted the proliferation of conjunctival fibroblasts. Both MMC and 5-FU application resulted in a significant reduction in fibroblast proliferation ( $p < 0.05$ ) with a time-dependent relationship observed following MMC application. The Xen Stents were successfully inserted into the 3D model and conjunctival fibrosis was visualised after just five days when provided with VEGF media.

**Conclusion:** The 3D tissue-engineered conjunctival model is versatile and can act as a platform to study the mechanisms involved in fibrosis. This is one of the first reported uses of a conjunctival model with a MIGS device whilst also demonstrating early fibrosis, suggesting the potential need for adaptation of the Xen Stent design or the continual use of MMC intra-operatively. More research is required on the mechanisms affecting fibrosis, such as shear

stress and other growth factors influencing fibrosis, to help define better future specific anti-fibrotic treatments whilst moving away from the toxic antimetabolites that currently plague glaucoma surgery.

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## **Is there an association between dementia and cardiovascular disease? A systematic review and meta-analysis.**

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*Bethany Seale*

### **Background**

Dementia is a disabling disease which results in cognitive decline and loss of independence. Age is a recognized risk factor for dementia and with the ageing population, dementia will pose an increasing burden on the National Health Service. While dementia is currently incurable, there are medicines that slow its progression so there is significant interest in identifying patients at risk. Several studies have linked cognitive decline with conditions such as stroke and atrial fibrillation but there evidence for other conditions such as coronary heart disease and heart failure is less clear. Furthermore, it is unclear if cardiovascular diseases (CVDs) independently increase dementia as they both share common risk factors such as high blood pressure and hyperlipidaemia. Therefore, we conducted a systematic review and meta-analysis to evaluate the association between cardiovascular disease and cognitive decline or dementia.

### **Methods**

We included prospective cohort studies which evaluated CVD (coronary artery disease, myocardial infarction, atrial fibrillation, stroke, peripheral artery disease, transient ischaemic attack, heart failure, heart valve disease and arrhythmia) and its association with cognitive decline or dementia. Studies had to exclude patients with the prevalent CVD studied at baseline and there was no restriction based on definition of cognitive decline or dementia. Conference abstracts were included to reduce risk of publication bias. A search was performed on EMBASE and MEDLINE using the search terms in Supplement 1. The bibliography of included studies and relevant reviews were searched for additional studies. The search results were independently screened by two reviewers and extracted onto preformatted tables with information on study design, patient characteristics, quality assessments, follow-up and results. Statistical analysis was performed on Review Manager and statistical heterogeneity was assessed using the  $I^2$  statistic. The analyses with more than ten studies were stratified by duration of follow up.

### **Results**

Our search yielded 2,477 studies and after detailed screening and searching for additional studies from existing systematic review 53 prospective cohort studies were included with 1,116,858 participants (Figure 1). The results are summarized in Table 1. Atrial fibrillation (Risk ratio (RR) 1.63 95%CI 1.35-1.97,  $I^2=89%$ ,  $p<0.001$ ) and stroke (RR 2.12 95%CI 1.88-2.39,  $I^2=94%$ ,  $p<0.001$ ) were found to be associated with increased risk of dementia.

Coronary artery disease (p=0.90), myocardial infarction (p=0.65) and transient ischaemic attack (p=0.52) were not associated with increased risk of dementia. While there was only a few studies, peripheral artery disease and heart failure appeared to be associated with increased risk of dementia (2 studies, RR 1.52 95%CI 1.37-1.69,  $I^2=0\%$ ,  $p<0.001$  and 4 studies, RR 1.54 95%CI 1.07-2.22,  $I^2=40\%$ ,  $p<0.001$ , respectively).

## Conclusion

Atrial fibrillation and stroke appear to be associated with dementia and there is some evidence that heart failure and peripheral artery disease may also increase risk of dementia. However, coronary artery disease and myocardial infarction do not appear to be associated with dementia. More studies are needed to understand mechanisms of developing dementia and its relationship with cardiovascular risk factor and CVD so that patients at high risk of dementia could be identified earlier and preventative measure for dementia be considered.

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## Investigating the potential of human umbilical cord derived-stem cells for wound healing in the skin.

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**Sandesh Shrestha**

### Introduction

Pressure ulcers commonly develop as a complication of spinal cord injuries (SCI). These lead to reduced quality of life and increased mortality in SCI patients, and are costly for health services. Existing evidence supports the potential of mesenchymal stem/stromal cells (MSC) for use in novel therapies to manage pressure ulcers (Walter *et al.*, 2010).

### Aim

To investigate whether umbilical cord-derived MSCs can be used for cutaneous wound healing in an *in vitro* model system.

### Method

An *in vitro* 'scratch assay' was used to simulate cutaneous wound healing. Monolayer co-cultures and individual mono-cultures of HaCaT (keratinocytes) and L929 (fibroblast) cell lines representing the cutaneous layers were established as the skin model. Both cell types were grown at  $0.85 \times 10^6$  cells/cm<sup>2</sup> in a standard culture medium of DMEM/F12 medium with 10% foetal calf serum and antibiotics (penicillin/streptomycin), at 37°C in a humidified atmosphere and 5% CO<sub>2</sub>. MSCs were obtained from human umbilical cords (UC) from three patients. These were cultured in media, as above, for 24 hrs, either with or without 25ng/ml interferon-gamma (IFN- $\gamma$ ) to create conditioned media (CM).

The cultured L929s and HaCaTs were seeded at a combined and individual densities of 100,000 cells/well into 24 well plates. They were maintained for 24 hours at 37°C and 5% CO<sub>2</sub> for cell adhesion and confluent monolayer formation. A ~0.5mm wide 'scratch' was performed in each well using a 20 $\mu$ l pipette tip to simulate a wound. Six different experimental conditions were created: normal/control with standard medium, (ii) conditioned

media (CM) from IFN- $\gamma$ -stimulated and (iii) CM from unstimulated UC-MSCs, (iv) UC-MSCs placed on scratch, (v) L929 and (vi) HaCaT mono-cultures.

Wound closure was observed via the Cell IQ Imaging System (Chip-Man Technologies, Finland) which captured images at regular intervals (every ~20 minutes) until complete wound closure. Parameters to compare the different treatment groups encompassed total time taken to close the wound and wound percentage coverage.

## Results

Cells cultured with CM from UC-MSCs without IFN- $\gamma$  stimulation took the shortest time to close the scratch assay completely ( $\bar{x}$ =18 $\pm$ 2 hours). The control and IFN- $\gamma$  stimulated UC-MSC CM treatments showed slower wound closure times  $\bar{x}$ =32 $\pm$ 13 and  $\bar{x}$  =35 $\pm$ 11 hours, respectively, although the differences were not significant (Fig.1). UC-MSCs placed on scratch assays completed closure at  $\bar{x}$ =20 $\pm$ 2 hours. L929 and HaCaT mono-cultures (with UC-MSC CM added) resulted in scratch assay closure at  $\bar{x}$ =25 $\pm$ 2 hours and  $\bar{x}$ =36 $\pm$ 6 hours, respectively.

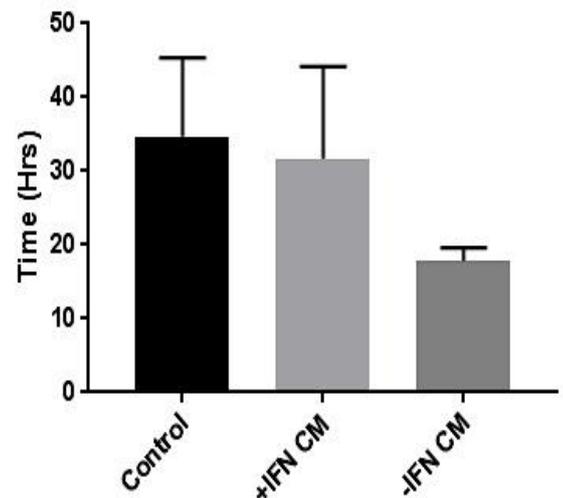


Fig.1 Time taken for control media and CM to stimulate complete wound closure.

## Discussion

The results support UC-MSCs' ability to enhance wound healing through their secretions in CM, especially without IFN- $\gamma$  stimulation. IFN- $\gamma$  may promote a pro-inflammatory environment impairing wound healing. UC-MSCs offer a potentially novel therapy for pressure ulcers.

L929s appear to play a greater role than HaCaTs in cutaneous wound healing, as reported by Walter *et al.*, (2010). These cell types need further study in co-cultures to determine the mechanism of action on wound healing. If pro-wound healing factors produced by each cell type are identified they could make ulcer therapies more efficacious. To simulate human skin more closely a poly-layered skin model could be used to study wound closure activity.

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## Mesenchymal stem cells secretome modulate antigen presentation markers in an oxygen dependent manner

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### Haleema Siddique

A number of haematopoietic cell types have been suggested to present antigens on major histocompatibility complex II (MHCII) molecules to CD4 +T cells, including dendritic cells, mast cells, basophils, eosinophils. Professional APCs intrinsically synthesize and express MHCII. MHCII is encoded by the human leukocyte antigen gene complex and is composed of 4 subunits ( $\alpha_1$ ,  $\alpha_2$ ,  $\beta_1$ , and  $\beta_2$ ) of which the most common is HLA-DR. PMN including neutrophils lack surface expression of MHCII under standard conditions, however, recent

reports confirmed that neutrophils could express MHCII and subsequently present antigens leading to propagation of immune responses through the activation of T<sup>CD4+</sup> cells.

**Aim:** The aim of the present study is to identify the paracrine role of MSCs on antigen presentation using a myeloid progenitor cell line model (K562 cell line). K562 cells were pharmacologically activated in the hMSCs secretome, collected as SFCM from both hypoxic and normoxic cultured hMSCs. Preliminary results confirm that the secretome collected from normoxia cultured MSCs induces HLADR expression while hypoxia inhibits HLADR marker expression.

The HLADR expression by K562 was confirmed through co-culturing K562 with natural Killer cells (NKL) which lysis any cell not expressing HLADR markers, while protect those which are HLADR positive.

**Methods:** 1- Culturing hMSCs. 2-SFCM generation. 3- Culturing K562 in SFCM collected from hypoxia (10% O<sub>2</sub>) and normoxia (21% O<sub>2</sub>) cultured MSCs 4 -Co-culturing K562 cells, after their exposure to SFCM, with NKL to determine their lysis by NKL 5- apoptosis assay to confirm k562 cell lysis by NKL.

RT-PCR gene expression by K562 cells in SFNCM versus SFCM in both hypoxia and normoxia. qRT-PCR conducted on RNA isolated from K562 exposed to PMA in GM, SFNCM, and SFCM versus PMA non-treated control group, using primers designed through NCBI gene browser. CD10 is a megakaryocytic marker, and CD44 is PMA-induced activation marker in both hypoxia and normoxia.

Flow cytometry were conducted K562 cells exposed to PMA in GM, SFNCM, and SFCM versus PMA non-treated control group, using human PE-conjugated primary antibodies.

NRF group have already created a model for assessment of HLADR expression using K562 as an in vitro model. This subsequent step will demonstrate that the expression of HLADR by K562 is protecting them from lysis by NKL.

**Results:** To confirm antigen presentation of K562 cells as a model for neutrophils, HLA-DR and CD197 were used as a marker plus CD10 as a megakaryocytic marker and CD44/CD61 as PMA-induced activation markers. Results showed that SFCM collected from normoxia induces significant upregulation of HLA-DR in comparison to their negative expression in hypoxia collected SFCM or control groups. CD197 expression is significantly induced in SFCM in an oxygen independent manner in comparison to the control groups. CD10 showed negative expression in all culture conditions. CD44 and CD61 were significantly upregulated by PMA particularly in SFC in an oxygen independent manner when compared to GM and SFNCM whether polarised or in a resting state. Results suggest that MSC's may contribute to the resolution of infection and inflammation through the promotion of anti-microbial activity in PMNs.

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## **Are there commonalities between the molecular changes that occur in spinal muscular atrophy and amyotrophic lateral sclerosis?**

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*Joanne Stock*

### **Background**

Unravelling the molecular pathways responsible for motor neuron degeneration in amyotrophic lateral sclerosis (ALS) and spinal muscular atrophy (SMA) remains a persistent challenge. Interest is growing in the potential similarities between these diseases, with the hope of better explaining motor neuron pathology for the guidance of therapeutic development. The aim of this study was to compare the proteomic profiles of ALS and SMA, seeking common molecular changes to be prioritised as future therapeutic targets.

### **Methods**

Comparison of studies reporting the proteomic changes across a range of ALS associated samples allowed identification of conserved molecular changes across patient and animal models. These key proteins were then compared with results from a similar meta-analysis of SMA studies. Bioinformatics platforms (DAVID and STRING) were used to explore processes likely involved in pathology. Upstream regulators of dysregulated proteins were also sought to identify drugs for future investigation.

### **Results**

27 studies were included and split into eight analysing patient CSF and 19 analysing cell/tissue samples. 16 proteins demonstrated consistent change in CSF representing processes such as inflammation and cell death. 42 proteins showed consistency in cell/tissue studies. Many represent those previously overlooked for their role in ALS, including the top result aldolase A which was upregulated in five studies. Other top results included upregulation of antioxidant proteins, including superoxide dismutase (SOD) 1 and 2 and peroxiredoxin 2. Comparison with SMA revealed upregulation of calreticulin and SOD1 as commonalities between the two diseases. Furthermore, bioinformatics results revealed overlap by way of antioxidant activity, RNA-binding functions and proteome homeostasis. Finally, a number of drugs were identified as regulating proteins involved in both ALS and SMA.

### **Discussion**

The study has drawn attention to metabolic processes, oxidative stress and protein misfolding in ALS pathology. The upregulation of antioxidant proteins, specifically SOD1, in both ALS and SMA suggests a response to oxidative stress experienced by motor neurons in both diseases. Furthermore, upregulation of calreticulin, which prevents release of misfolded proteins, appears to be a conserved molecular change in ALS and SMA and may represent an attempt to rescue motor neurons. It seems ALS and SMA do indeed share common molecular changes and pathological processes and a drug for use in both diseases may be an achievable goal. What is more, it seems increasingly likely that multiple

processes interact to play a role in motor neuron diseases; future approaches to treatment may require multiple therapeutics agents, targeting different pathological components.

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## An ultrastructural evaluation of multicellular neuromimetic hydrogels by electron microscopy

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*William Swadling*

Neuro-regenerative therapies are emerging as a key line of research in the development for treatment of spinal cord injuries. Although these therapies may prove to be effective, research is currently limited by our ability to test these therapies and research has previously focussed on 2D cell cultures and in vivo animal models. In vivo animal studies are useful but suffer drawbacks in terms of safety and efficacy. In vitro cultures are often monocellular and propagated on highly artificial plastic/glass surfaces meaning that they fail to replicate the native environment of the CNS.

As an alternative, developing protocols to more reliably and consistently replicate features of neurological tissue may be achieved by propagating multiple neural cells in hydrogels which are more representative of the 3D and soft mechanical environment of the CNS.

The aim of this project is to establish procedures for examining the ultrastructural features of neural cells within the collagen matrix using scanning electron microscopy (SEM); demonstrate the presence of all 3 major neural cell types (astrocytes, neurons and oligodendrocytes) within the hydrogel; and conduct a basic qualitative assessment of the membrane activity of the differentiated cells. To achieve this, multicellular hydrogels containing the 3 cell types from the CNS were generated by differentiating neural stem cells for 1 week prior to fixing for electron microscopy analysis. From here, they were processed through the OTOTO fixation methodology then imaged.

Cells were identified by their appearance and a basic assessment of aspects of membrane activity was conducted. These were namely the relative abundancies of nanopodia, filopodia, circular ruffles, pitting, and membrane ruffles. Each feature was scored between 0 and 3 depending on the relative abundancy of that feature: 0 signified no or negligible presence of that feature on the cell, 1, some presence, 2, abundancy across half the visible cell surface and 3, high abundancy across the whole cell surface.

Twenty cells were identified and recorded, 9 neurons, 9 astrocytes and 2 oligodendrocytes. Cells showed relatively low activity on average but with high standard deviation of the

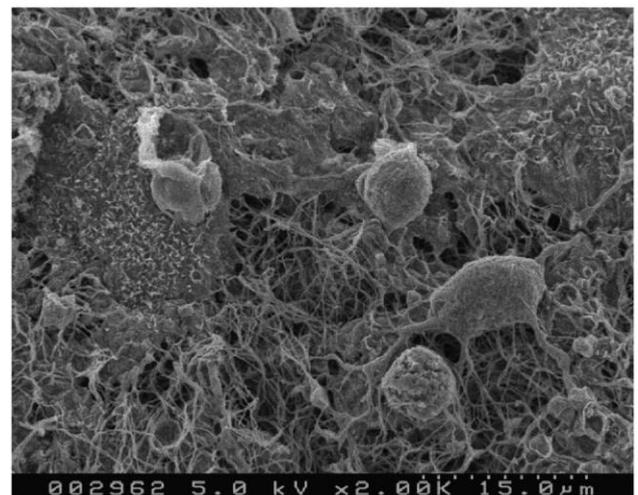


Fig 1. SEM image demonstrating presence of an astrocyte, neuron and oligodendrocyte

values. Neurons showed similar activity to Astrocytes which both exhibited more activity than the Oligodendrocytes although the data set was too small to make any conclusions.

The results demonstrate the presence of all cell types as shown in figure 1 and would benefit from being repeated with a hydrogel containing microglia in addition to the established 3 cell types to fully establish protocols to produce images with ultrastructural detail in cell-cell and cell-matrix interactions which could provide valuable information on synapse formation, myelination and membrane activity and responses to neuro-regenerative therapies such as interaction with nanomedicines.

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## Anti-inflammatory effects of extracellular vesicles on activated CD4+ cells

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*Kane Treadwell*

**Introduction:** Rheumatoid arthritis (RA) is a chronic inflammatory autoimmune disorder affecting many tissues and organs, characterised by inflammation and subsequent destruction of the synovium in the joints<sup>1</sup>. The prevalence of RA is between 0.3-1.1% and varies between geographical populations<sup>2</sup>. Currently there is no cure for RA, with treatment options limited to steroids, DMARDs and monoclonal antibodies, however these treatments can only slow disease progression and are often accompanied with side effects<sup>3</sup>. There is currently an urgent need for novel treatment options. Mesenchymal stem cells (MSCs) are multipotent adult stem cells with a differentiation potential and the ability to self-renew<sup>4</sup> and show therapeutic potential in preclinical inflammatory disease models, including rheumatoid arthritis<sup>5</sup>. MSCs possess anti-inflammatory and immunosuppressive properties modulated by the secretion of biologically active molecules and extracellular vesicles (EVs)<sup>6</sup>. EVs are immunologically active mediators as they suppress proliferation of activated T cells and their IFN- $\gamma$  secretion, inhibit B cells proliferation and induce high levels of anti-inflammatory cytokines IL-10 and TGF- $\beta$ <sup>7</sup>. The aim of this in-vitro study was to investigate if, and how, EVs can directly modulate activated T cell (CD4+) activity and proliferation cycles.

**Methods:** EVs were isolated from conditioned medium of human bone marrow MSCs by differential ultracentrifugation and characterized by flow cytometry. CD4+ cells were harvested from healthy spleens of mice and isolated using the Miltenyi T cell isolation kit. After activation, CD4+ cells were exposed to either EVs or MSCs. Proliferative cycles and IL-17a expression was quantified using flow cytometry.

**Results:** We found that the EVs decreased IL-17a expression (signal intensity per event) in CD4+ cells. MSCs reduced the number of proliferative cycles of activated T cells, however EVs did not.

**Conclusion:** Our results demonstrated an anti-inflammatory effect of EV on activated T cells (decreased IL-17a expression leads to a less pro-inflammatory environment). This shows that EVs may have a modulatory effect on inflammation. MSCs also have an anti-inflammatory effect on activated CD4+ cells. RA is CD4+ driven with IL-17a playing a role in the polarisation of CD4+ cells to Th17 cells<sup>8</sup>, therefore this research suggests that there is a

possible therapeutic role for EV's when treating inflammatory diseases such as inflammatory arthritis although further work is required to examine the mechanisms involved.

#### References:

1. Smolen JS, Aletaha D, McInnes IB. Rheumatoid arthritis. *Lancet* 2016;388(10055):2023- 2038.
2. Alamanos Y, & Drosos AA Epidemiology of adult rheumatoid arthritis. *Autoimmunity reviews* 2005;4(3), 130-136.
3. van Vollenhoven RF. Unresolved issues in biologic therapy for rheumatoid arthritis. *Nat Rev Rheumatol.* 2011;7(4):205-15.
4. Maumus M, Jorgensen C, & Noël D. Mesenchymal stem cells in regenerative medicine applied to rheumatic diseases: role of secretome and exosomes. *Biochimie* 2013; 95(12), 2229-2234.
5. Wang LT, Ting CH & Yen ML Human mesenchymal stem cells (MSCs) for treatment towards immune- and inflammation-mediated diseases: Review of current clinical trials. *J Biomed Sci* 2016;23:76.
6. Baglio SR, Pegtel DM, Baldini N. Mesenchymal stem cell secreted vesicles provide novel opportunities in (stem) cell-free therapy. *Front Physiol.* 2012;3:359.
7. Mokarizadeh A, Delirezh N, Morshedi A, Mosayebi G, Farshid AA, & Mardani K. Microvesicles derived from mesenchymal stem cells: potent organelles for induction of tolerogenic signaling. *Immunology letters* 2012;147(1), 47-54.
8. Gaffen SL. The role of interleukin-17 in the pathogenesis of rheumatoid arthritis. *Current rheumatology reports* 2009;11(5), 365-370.

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## Health inequalities and the NHS transition

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*Ben Walters*

### BACKGROUND

Regional health inequalities within England are widening: since 1965 the English north-south health divide in terms of premature mortality has continued to expand. Indeed, in England, with premature deaths each year as a result of health inequalities would otherwise have enjoyed, in total, between 1.3 and 2.5 million extra years of life. The underlying causes of premature death are both social and economic. To help address these statistics we need new ways of thinking and working to ensure that professionals in the reformed National Health Service (NHS) rise to the challenges posed by health inequalities.

Since 1st April 2013 the manager-led Primary Care Trusts have been replaced by the Clinical Commissioning Groups (CCGs), with local GPs driving these. An important aspect of the reforms is that responsibility for public health has moved to the local authorities and the new Health and Wellbeing Boards (HWBs). The CCGs have many challenges to face as they take on commissioning responsibility and liaison over public health issues with these two groups.

## **AIMS**

The aim of this APIRE studentship was to analyse interview data with GPs, Directors of Public health, Lay CCG and HWB board members and local politicians. In my analysis, I explored how CCGs are formulating their strategies and new partnerships. A focus was health inequalities, a key issue for the north of England, where the interviews were conducted. This is particularly relevant to the problem of health inequalities, a key issue for the north of England, where fieldwork was conducted.

## **METHODOLOGY**

I analysed with the QSR NVivo 11 software for qualitative data analysis the interview data set ( $n=39$ ). I created with my supervisor, Dr Lisa Dikomitis, a coding framework and performed a thematic data analysis to those 39 interviews. Alongside data analysis, I familiarised myself with relevant academic literature which aided me in interpreting the analysed data set.

## **RESULTS**

There are 5 emerging themes from my analysis: (1) recruitment to the CCG and HWB boards; (2) managerial roles and budgets; (3) tackling health inequalities; (4) access to healthcare and health literacy; (5) social determinants of health.

## **CONCLUSIONS**

My analysis demonstrated the challenges for these new NHS organisations with regards to health inequalities. If the new structures are to succeed in both the legal and self-set duties to reduce health inequalities, attention will need to be paid to overcome the cultural divide between the different professional groups involved (managers, politicians and clinicians).

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## **Exploring factors contributing to poor pregnancy outcomes in a low risk obstetric population.**

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*Matthew Watson*

### **Introduction**

Pre-eclampsia, fetal growth-restriction (SGA) and spontaneous preterm birth (SPB) are leading causes of perinatal morbidity and mortality. This research focused on identifying factors associated with preeclampsia, SGA and PTB in a low-risk obstetric population.

### **Methods**

Demographic and biomedical data were extracted from medical records of women under the care of University Hospital of the North Midlands and Shrewsbury and Telford Hospital. Women were selected based on them not having any known risk factors for preeclampsia, SGA or PTB. SPSS was used to identify and measure association between identified factors

and pre-eclampsia, SGA and SPB. Statistical tests used were chi-squared, independent-samples two-tailed t-tests and relative risk calculations.

## Results

Five-hundred and fifty-seven, primarily white-British (93.7%) women aged 18-42 were selected. 2.4% developed preeclampsia (n=13), 8.1% of births were SGA (n=44), and 2.7% of births had SPB (n=15).

Having excluded SGA and PTB cases, we examined pre-eclampsia as an outcome. Of the population that did *not* take pre-pregnancy folate supplements, 4.7% (n=13) developed preeclampsia. Of the population that did take pre-pregnancy folate supplements (n=212), none developed preeclampsia (n=212), (relative risk (RR)=1.05, 95% CI: 1.02–1.08, p<0.001). Next, we looked at the SGA outcome, after excluding preeclampsia and PTB cases. 19.4% of those using  $\beta_2$ -agonists during pregnancy gave birth to SGA babies (n=6) compared to 7.8% of those not using  $\beta_2$ -agonists that gave birth to SGA babies (n=38) (RR=2.48 95% CI: 1.14–5.42, p<0.05). Glucocorticoid use during pregnancy was also significant for increased risk of SGA (RR=3.72 95% CI: 1.38–10.02, p<0.02), with 30% of those using glucocorticoids (n=3) becoming SGA cases, compared to 8.1% (n=41) of those not using glucocorticoids becoming SGA cases. However, we did not find any association between a history of asthma with SGA. For the SPB outcome, we found that women who had SPB spent statistically significantly (p<0.02) more days in hospital postnatally ( $\mu$ =5.07) compared to mothers of non-SPB babies ( $\mu$ =2.04).

## Discussion and Conclusions

Asthma as a risk factor for SGA is a contentious issue in current literature. Further work is needed to measure the association between asthma severity and SGA, as we found that 47.7% with a history of asthma did *not* use  $\beta_2$ -agonists during pregnancy. It could not be determined if the increased length of postnatal hospital stay for women with PTB is due to their own medical condition or the mother's will to stay near her premature baby in the hospital.

In summary, even in a low risk population, potential risk factors for poor outcomes can be identified. However, further research is need to understand the underlying mechanism and to further identify prognostic factors in both low risk and high risk obstetric population

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## An enhanced Microsoft HoloLens® Augmented Reality Platform for Training in Acetabular Cup Implant Orientation: A Randomised Controlled Trial

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*Luke Western*

### Background:

Complications such as dislocations, impingement and early wear following total hip arthroplasty (THA) increase with acetabular cup implant malorientation. These errors are more common with low-volume centres or surgery in novice hands. Currently, this skill is

most commonly learnt during real surgery with an expert trainer, but simulated training may offer a safer and more accessible solution. This study investigated if a novel MicronTracker® enhanced Microsoft HoloLens® augmented reality (EAR) system was as effective as one-on-one expert surgeon (ES) training for teaching novice surgeons hip cup orientation skill.

### **Methods:**

Twenty-four medical students were randomly assigned to EAR or ES training groups, which had statistically equivalent demographics and initial orientation errors. Participants used a modified sawbone/foam pelvis model for hip cup orientation simulation. A validated EAR system measured the orientation of acetabular cup implants. Learning curves were measured over four sessions, approximately one week apart. Error in orientations of non-taught angles and during a concealed pelvic tilt were measured to assess translation of skills. Six different inclination and anteversion combinations, related to hypothetical patient-specific anatomy, were used as targets. A post-test questionnaire was used for qualitative analysis of procedure understanding and participant experience.

### **Results:**

Both groups significantly improved (ES:  $15.7^{\circ} \pm 6.9^{\circ}$  to  $8.15^{\circ} \pm 4.6^{\circ}$ ,  $p < 0.001$ ; EAR:  $14.24^{\circ} \pm 7^{\circ}$  to  $9.59^{\circ} \pm 5.7^{\circ}$ ,  $p < 0.001$ ) and session baseline values were statistically equivalent, except between session three ( $p = 0.034$ ). EAR achieved significantly lower orientation error than ES in teaching sessions (ES:  $5.96^{\circ} \pm 3.4^{\circ}$ , EAR:  $1.14^{\circ} \pm 0.89^{\circ}$ ,  $p < 0.001$ ). There was no orientation error change with pelvic tilt (ES:  $p = 0.345$ ; EAR:  $p = 0.408$ ) and non-taught angles improved (ES:  $p < 0.001$ ; EAR:  $p = 0.011$ ). In post-training evaluation, ES was preferable to EAR for learning orientation skills and related visuospatial and procedure-specific skills. 79% of participants indicated future simulation with EAR and ES in combination would be their preference.

### **Discussion:**

A novel head-mounted EAR platform was shown to deliver training to novice surgeons more accurately than an expert surgeon. Both EAR and ES enabled novices to acquire and retain skills on a learning curve to orientate the implant. These skills were successfully translated to non-taught orientations and in the presence of a pelvic tilt.

### **Conclusions:**

EAR could provide a cost-effective simulation to improve a novice surgeon's orientation skills. Reducing orientation error and moving toward patient specific angles may reduce complications and increase patient care.

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## Investigating the feasibility of using the chick embryo as a traumatic spinal cord injury model.

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*William Woods*

**Background:** Spinal cord injury (SCI) is currently a life-long debilitating condition dramatically impacting the lives of patients and their support networks. It has an estimated cost to the UK of £1 billion per annum, and furthermore there are no available treatments which restore function to the injured spinal cord (SC). Current SCI research is often conducted on small rodents, which despite providing an invaluable insight into potential human treatments, have substantial disadvantages. Rodents are expensive to buy and house in quantities needed to generate statistically significant data, involve technically challenging and time consuming manipulations and pose considerable ethical issues when introducing an injury into the SC. As an alternative, chick embryos are widely used for neurodevelopmental research and could be used as a model to replicate some features of the mammalian SC and injury. For example, the spinal cord displays typical neuroarchitecture, such as corticospinal tracts, with all major CNS cell types within a vascularised SC by embryonic day 8 (E8). In addition, the embryos are inexpensive to maintain, relatively straightforward to manipulate and have limited ethical issues before E14. However, they have not yet been used as a SCI model within which potential therapies can be tested.

**Aim:** The aim of this project was to assess whether the chick embryo can be used as a SCI model to facilitate further research into hydrogels or nanoparticles which have shown promise as potential treatments.

**Methods:** Fertilised chick eggs were incubated at 37.5°C in 45% humidity. Two chick embryos were taken each day (E4-E7) for lesioning by micro-scissors in the lumbosacral region. Fixation was either performed immediately or 24 hours post lesioning by immersing in 4% paraformaldehyde for 2 hours. Fixed embryos were cryoprotected using a 30% sucrose solution overnight at 4°C before cryosectioning (20 micrometre sections). Un-lesioned E11 spinal cords were also fixed and cryoprotected using the same protocols. Immunostaining was carried out using 5 antibodies; Tuj-1 (neurones), Sox-2 (stem cells), NG-2 (oligodendrocytes precursor cells), GFAP (glial cells) and MBP (oligodendrocytes). Fluorescent microscopy was used for detecting neural cells and neuroarchitecture of the chick embryo SCs.

**Results:** E4 and E5 embryo SCs were cryosectioned successfully. Neural progenitor cells and immature neurons could be reliably detected in the developing SC. E6 and E7 embryos were less successfully cryosectioned where folding and breaking occurred using the same protocols as earlier developed embryos. In contrast to younger tissue, GFAP and MBP staining was observed in longitudinal sections of an E11 spinal cord although it was difficult to reliably detect individual cells. In the limited period of time for this project, the SCI could not be robustly identified. See figure 1.

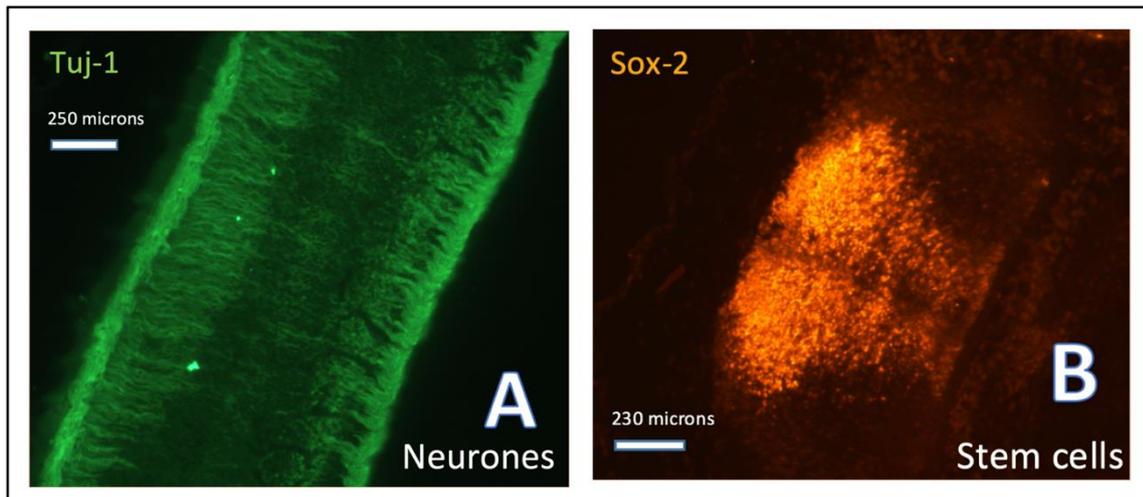


Figure 1; immunofluorescent stained chick embryo spinal cords. Representative fluorescent images of Tuj-1 (A) stained neurones in an E5 immediately fixed embryo spinal cord. Sox-2 (B) in stem cells show activity of a proliferating somite in an immediately fixed E5 embryo spinal cord.

**Discussion:** Initial data shows the injured chick embryo can be processed for immunocytochemistry where major neural cell types (associated with healthy tissue and responses to injury) can be reliably detected within the spinal cord. Protocols need to be optimised to facilitate identification of the lesion site within cryosections. In addition, as key cells (oligodendrocytes and astrocytes) were only detected at late time-points, it needs to be investigated whether trialling the protocols at different embryo ages can be more relevant to adult like SCI.

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## Calcitriol shows a neuroprotective effect while nicotinamide shows a neurotoxic effect on primary neurones of the substantia nigra

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*Yasemin Zaremba*

### Introduction

Parkinson's Disease (PD) is neurodegenerative; depleting dopamine neurones of the substantia nigra (SN) in the midbrain. 4% of the world's population suffer from PD. Vitamins play an important role in health and development throughout life. Calcitriol (D3) has been shown to attenuate neurotoxicity in dopamine neurones<sup>1</sup>. Nicotinamide (B3) has recently been identified as a possible neuroprotectant<sup>2</sup>.

### Aims

The aim of this research was to use primary SN cells as an in vitro model to determine whether or not vitamins D3 and B3 have a neuroprotective or neurotoxic effect on midbrain dopamine cells that had been selectively injured with 6-hydroxydopamine (6-OHDA) to mimic PD.

## Methods

Primary neurones of the SN were obtained from embryonic day 14 rats. Cells were cultured for seven days with 10mM nicotinamide and/or 10nM calcitriol. Cells were then treated with either 100mM 6-OHDA dissolved in 0.015% ascorbic acid vehicle or the ascorbic acid vehicle alone for 25 minutes. A control that received only media changes with no treatment was also included. Cells were then left to recover for 2 days in their conditions. Cover slips were then fixed with 4% paraformaldehyde and stained for  $\beta$ -III-tubulin, tyrosine hydroxylase (TH) and mounted in 4',6- 2 diamidino-2-phenylindole (DAPI) mounting medium. Imaging was carried out and cell numbers under each condition were counted and analysed.

## Results

There were clear differences in cell morphology between conditions. Under both vehicle and 6- OHDA conditions, neurones treated with D3 were significantly higher in quantity with long, thick, complex processes (figure 1). However, in conditions treated with B3, neurones were much lower in number with thinner less complex processes (figure 2). A two-factor ANOVA revealed that vitamins significantly altered total cell and neurone number,  $p < 0.05$  (figure 5).

## Conclusion

The cell and neurone count was much higher for D3 treated cells than cells treated with B3 or B3+D3. D3 appeared to have a neuroprotective effect on overall cell, neurone and TH number whilst B3 had a neurotoxic effect at the concentration of 10mM. Repeat experiments need to be carried out to confirm results. Further work could involve treating cells with lower concentrations of B3 to determine an accurate neurotoxic concentration. This suggests that supplementing PD patients with D3 may protect dopamine SN neurones from degeneration, while excessive quantities of B3 may be a risk factor.

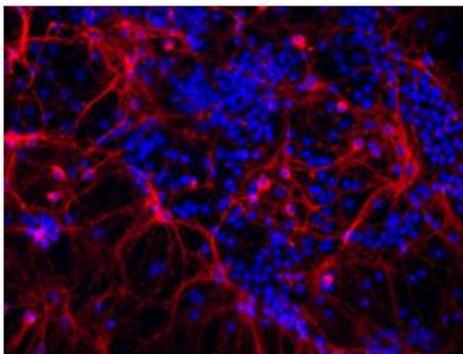


Figure 1: 6-OHDA treated primary cells with D<sub>3</sub>,  $\beta$ -III-tubulin red, DAPI blue

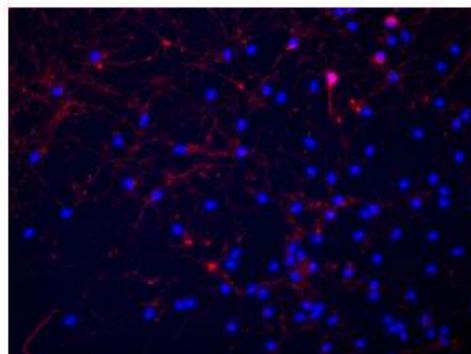


Figure 2: 6-OHDA treated primary cells with B<sub>3</sub>,  $\beta$ -III-tubulin red, DAPI blue

## References

1. Wang, J.-Y. et al. Vitamin D attenuates 6-hydroxydopamine-induced neurotoxicity 3 in rats. *Brain Res.* 904, 67–75 (2001).
2. Anderson, D. W., Bradbury, K. A. & Schneider, J. S. Broad neuroprotective profile of nicotinamide in different mouse models of MPTP-induced parkinsonism. *Eur. J. Neurosci.* (2008).

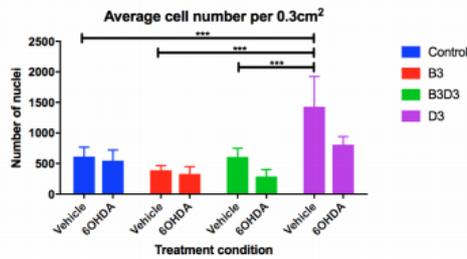


Figure 3: average cell number per 0.3cm<sup>2</sup>

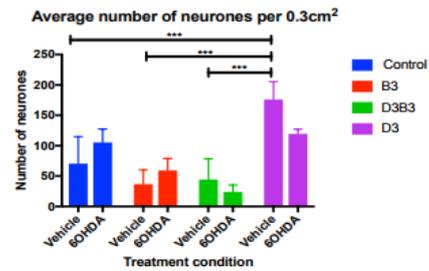


Figure 4: average number of neurones per 0.3cm<sup>2</sup>

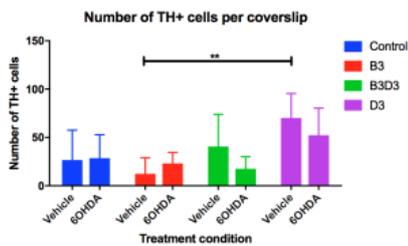


Figure 5: number of TH+ cells per coverslip