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Research Showcase 2016

ABSTRACTS

Contents

Comparing the innate immune response in patients with varying degrees of Non Alcoholic Fatty Liver Disease

Stephan Abdallah

Non alcoholic fatty liver disease (NAFLD) has emerged as the most common cause of chronic liver disease in the world. It has increased in prevalence in line with the rise in obesity and has a strong association with insulin resistance, affecting up to 75% of those with type 2 diabetes. It is characterised by a deposition of fat in the liver, in the absence of excessive alcohol consumption. NAFLD is benign in the majority of instances, but around 15% of people will experience fibrosis and hepatocyte death and this is known as non alcoholic steatohepatitis (NASH). Around 20% of those with NASH will experience cirrhosis which can lead to eventual liver failure and mortality. The factors that underpin the progression from benign NAFLD to deleterious NASH aren't clear, but inflammation caused by commensal translocation, reactive oxygen species and adipokines has been suggested as the key early driver.

Transcriptional events during the initial stages of vertebrate heart development in vivo

Mai Baalbaki

Transcriptional events during the initial stages of vertebrate heart development in vivo remain poorly understood. Mesp1, a bHLH transcription factor, has been described as the earliest transcriptional regulator of cardiac progenitor cells in multiple species, and represents an excellent candidate for the investigation of relevant transcriptional targets during cardiovascular development. We report here that both depletion and mutation of Mespaa, the zebrafish homolog of mammalian Mesp1, lead to randomization of cardiac looping, together with significant cardiac morphogenesis defects. These disruptions are preceded by a defect in cardiac left-right asymmetry. We show that Mespaa regulates miR-430 expression during gastrulation to modulate the levels of Nodal signaling, and that this regulation is required for asymmetric laterality signaling in the prospective heart field. Ectopic expression of miR-430 is sufficient to induce cardiac laterality defects, and consistent with Mespaa over-expression in this system, the reduction of miR-430 leads to cardia bifida. This study reveals a novel transcriptional regulation of miR-430 by Mespaa and a role for this pathway in cardiac laterality during gastrulation.

How do stiffness and pain impact on daily activities in a primary care polymyalgia rheumatica cohort?

James Cawley

Background
Polymyalgia rheumatica (PMR) is a common inflammatory condition of older people, characterised by bilateral stiffness and pain in the shoulder and hip girdles, often with raised inflammatory markers and treated with glucocorticoids. Stiffness is an important part of the core domain set suggested by OMERACT and a key symptom for patients' that impacts on daily activities. Our aim was to examine the relationship between the symptom experience of stiffness and pain, and the functional ability of patients newly-diagnosed with PMR.

Methods
Baseline analysis of a prospective inception cohort study of patients with PMR from primary care. Patients aged ≥50 years, with a new diagnosis of PMR, were recruited from 382 English general practices. Patients were sent a baseline questionnaire, which included several measures of stiffness and pain, an overall score (numerical rating scale (NRS) of 0 (no pain/stiffness) to 10 (severe pain/severe stiffness)) and separate stiffness and pain mannequins to indicate affected body areas (44 site maximum). Assessment of patients' function in undertaking their usual daily activities was recorded using the modified Heath Assessment Questionnaire. Linear regression analysis was used and results reported as regression co-efficients (95% confidence intervals), initially crude and then adjusted for age, gender, deprivation status, smoking status, BMI, anxiety, depression and current steroid dose.

Results
654 patients responded to the baseline survey (90.1%). The mean age of responders was 72.5 years (SD 8.9), the majority were female (61%) and approximately two-thirds reported high (NRS ≥8) overall levels of stiffness (60%) and pain (66%). Crude linear regression analysis demonstrated that high levels of overall stiffness (0.22 (95%CI 0.13 to 0.31)) and pain (0.24 (0.15 to 0.34)) were associated with significantly lower usual activities scores compared to those with low levels of pain or stiffness (**Table 1**). These were maintained after adjustment (stiffness 0.18 (0.91 to 0.26); pain 0.19 (0.11 to 0.28)). There was also an association between a greater number of body sites with stiffness (0.17 (0.04 to 0.30)) or pain (0.20 (0.07 to 0.32)) and a lower usual daily activities score. Though crude analysis showed that bilateral shoulder stiffness and pain were both associated with a lower usual activities score, after adjustment, this was only retained in those with shoulder pain ((0.15 (0.01 to 0.30)). A high rating of hip stiffness or pain was not associated with a lower usual daily activities score.

Conclusion
Patients with incident PMR who experience symptoms of pain or stiffness are more likely to have reduced ability to conduct daily activities during this early disease phase, independent of steroid use. An initial poor functional status may impact on several other future health outcomes, including mental health, quality-of-life and healthcare costs. Early management to assess and improve function may be needed.

Investigating The Influence of Episodic Memory on Examiner Score Accuracy

Natasha Cleaton

Background

This paper documents research into rater cognition exploring judgements examiners make on student performance in order to gain an understanding of problems within the process, including bias and score variability.[1] Sensory memory, the shortest term memory, lasts ~30seconds, however, examiners must retain observations they make about students in their memory for typically 5-10minutes before using them, therefore using 'episodic memory' that relies on encoding, processing and retrieval of information[2] . This research explores how examiners' episodic memory impacts the accuracy of scores they give, an issue that has not yet been directly investigated. Various factors influence an individual's episodic memory including previous experience, gender[3], delay time between observation and recall due to interference[4], and encounters individuals have directly before observations (contrast effect)[5].

Method

This study used secondary data analysis on a study including n=159 participants; the participants were divided into 2 orders (order-1:n=79, order-2:n=80) and watched 3 sequential videos (labelled-A,C,D) in opposing orders. The videos were standardised with scripts demonstrating different set levels (high: +,low: -,or mixed) of knowledge(K) and communication(C) in the performance.

	Video-A: K+, C-	Video-C: K-, C+	Video-D: mixed K & C
Order 1	3rd	2nd	1st
Order 2	1st	2nd	3rd

Following the videos, participants completed a recollection test for video-D including 20 real statements that were in the performance and 20 invented statements that were not. Half of the statements were knowledge-based, half communication-based.

Hypotheses

1. Participants with better recollection will be more accurate in scoring.

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2. Participants with better recollection will be more able to distinguish between domains of performance, i.e. between scores for communication and scores for knowledge.
3. Participants with a longer delay between observation and recall will have a lower score on the recollection task.
4. Participants who have more years of experience in examining OSCEs will have better recollections.
5. Female participants will perform better in the recollection task than male participants.
6. Participants with better recollection will be less influenced by the contrast effect.

Definitions

- Recollection accuracy: Proportion of real statements marked true minus the proportion of invented statements marked true.
- Score accuracy: Score variance from the median score.

Results

No association was found between: recollection and score accuracy; duration as an OSCE examiner and recollection accuracy; or gender and score accuracy. Susceptibility to contrast effects was not influenced by recollection accuracy. Univariate anova found a shorter delay between observation and recollection improved recollection accuracy (short-delay accuracy:44.68(41.31,48.06); long-delay accuracy: 35.00(31.62,38.38), $F(1,157)=16.3$ $P<0.001$. Pearsons' correlations supported the hypothesis that examiners with better recollections discriminated between domains better:

Correlation Analysis between Domain Difference and Recollection Accuracy.			
		r values	p values
Order-1	Video A (k+/c-)	NS (0.070)	NS (P=0.540)
	Video C (k-/c+)	0.292	P=0.009
Order-2	Video A (k+/c-)	0.386	P=0.00
	Video C (k-/c+)	0.289	P=0.009

Conclusion

Episodic memory declined in accuracy over time. While episodic memory was not found to directly impact score accuracy, improved episodic memory was associated with improved distinction between domains, indicating that there are differences in the way raters make judgements on students' scores. Some raters appear to process and integrate students' performances into their episodic memory, enabling them to award marks accurately, others appear to make general judgements, both resulting in accurate scoring. More research is required to confirm this.

Using advanced biomaterials to augment cellular therapies for chronic spinal cord injury

Alex Delaney

Olfactory ensheathing cells promote axonal regeneration and improve locomotor function when transplanted into the injured spinal cord. A recent clinical trial demonstrated improved motor function in companion dogs with traumatic spinal injury, following autologous olfactory mucosal transplants (Granger et al; 2012, Brain). Their utility in canine subjects offers considerable promise to human translation as they are highly comparable to human patients in terms of spinal lesion heterogeneity, genetic/environmental variation and management strategies. However, major translational challenges still exist: (1) Cell loss during transplantation due to mechanical stress and clumping within injection solutions (2) Incomplete corticospinal tract regeneration. To address this, we have combined two next-generation nanotechnologies: Advanced 3-D hydrogel technology could function as a protective and implantable cell delivery system, but its utility for olfactory mucosal cell delivery has never been investigated. We demonstrate for the first time the feasibility of safely encapsulating canine olfactory mucosal cells within a 3-D implantable hydrogel matrix. We also demonstrate the ability to safely genetically engineer this population to express a major neurotrophic factor, to augment therapeutic capacity, using magnetic nanoparticles combined with Magnetofection Technology (magnetically-assisted transfection) and novel DNA minicircle vectors. Our results suggest this combination of technologies could enable delivery of a therapeutic “plug” of nano-engineered cells within an implantable matrix into sites of neurological injury, a strategy with considerable clinical potential.

The Upper Tendinous Part of the Sternocleidomastoid: A Landmark for the Spinal Accessory Nerve

Michael Eastwood

Background

The Spinal Accessory Nerve (SAN) has a complex and variable course through the neck leaving it prone to injury during surgical neck dissections. Most landmarks to aid its identification are situated in the posterior triangle of the neck (neck level V) which is often avoided in selective procedures. The nerve may also be identified in the anterior triangle as it passes through neck level II. Few landmarks have been described to identify the SAN in this region, although anecdotally the upper tendinous part of the sternocleidomastoid muscle has been used.

This study aims to identify whether the tendon represents a reliable landmark for the SAN and how it compares to other existing landmarks in the literature.

Methods

18 cadavers from Keele University Anatomy Department underwent bilateral neck dissection to identify the; SAN, tendon, Sternocleidomastoid Branch of the Occipital Artery (SBOA) and the Great Auricular Nerve (GAN). Variations and relationships between structures were recorded and quantifiable measurements taken. Digital Photographs and image-J analysis software were used to measure the angular relationships between these structures.

Results

The tendon was found in all specimens (Mean length 44.08mm), terminating in one, two or three slips. Its relationship to the SAN was found to have some variation. The SAN was deep to the tendon in 89% of cases and level in 11% (Mean depth 1.82mm SD 1.64). The SAN inserted above the tendons termination in 25% of sides, level in 25% and below it in 50% (Mean distance 2.56mm SD 4.09). Other landmarks also showed variation the SBOA had one branch in 50% of specimens, two in 46% and three in 4%, the mean distance from the SAN being 3.65mm. Its position of insertion relative to the SAN was also found to be variable. With regard to the GAN the SAN exited above it in 86% of cases, level in 3% and below in 11% (Mean distance 6.60mm SD 4.54). The SBOA, digastric muscle and tendon formed a triangle containing the SAN, although angles between structures varied.

Conclusions

The tendon was a constant feature and was found to be closer to the SAN and less variable than other landmarks studied. From the results of this study a simple approach has been developed to identify the SAN which may be used during surgical procedures. As head and neck cancers are increasing in prevalence and surgery is a mainstay of treatment, this landmark and knowledge of variants could reduce the risk of iatrogenic SAN injury and its associated morbidity.

Does repeated activation generate an ‘experienced’ microglial phenotype, with altered pro-inflammatory responses?

Tiggs Gholamian

Microglia, the brain’s immune cells, play critical roles in resolution of disease. These beneficial behaviours are mediated by appropriate switching between phenotypes (M0: ‘inactivated’; M1: pro-inflammatory; M2: pro-repair). However, inappropriate microglial activation is increasingly implicated in onset and progression of neurological diseases such as Alzheimer’s and Parkinson’s disease. The pro-inflammatory M1 form can arise as a result of certain ‘triggers’, including infection, trauma and aging. This can become problematic, such as reacting over-aggressively or remaining activated even after removal of the ‘trigger’. Recent evidence suggests that although the activated microglia appear to return to their original ‘inactivated’ phenotype, they are actually slightly altered; these are considered to be a distinct ‘experienced’ microglial phenotype (Figure1).

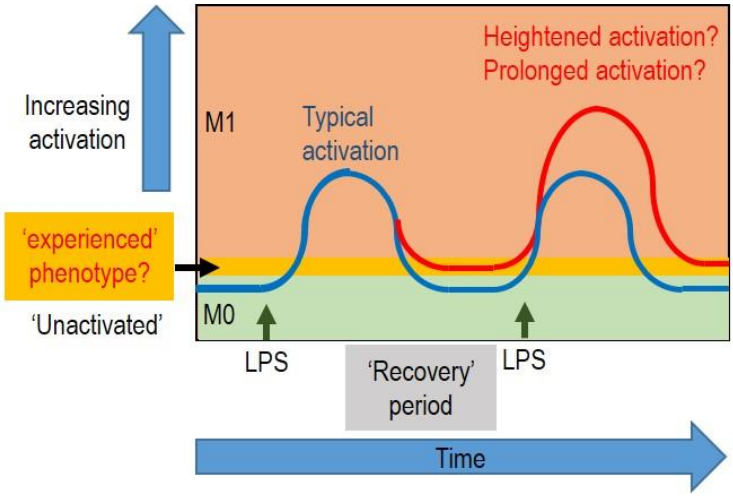

Figure 1 - Hypothesis of ‘experienced’ microglial phenotype, showing altered response to secondary activation.

Experienced’ microglia may exhibit differences in their inflammatory responses (2^{o} secondary activation event), compared to their naïve microglia counterparts (1^{o} primary activation event). If these responses are greater and/or more prolonged in the former, the data would be supportive of the theory that episodes on of neuro-inflammation can influence risk and progression of subsequent neurodegenerative events. Hence, determining whether a simulated infection could generate an ‘experienced’ microglial phenotype, with a heightened or continuous expression of pro-inflammatory markers following repeated infection (Figure 2).

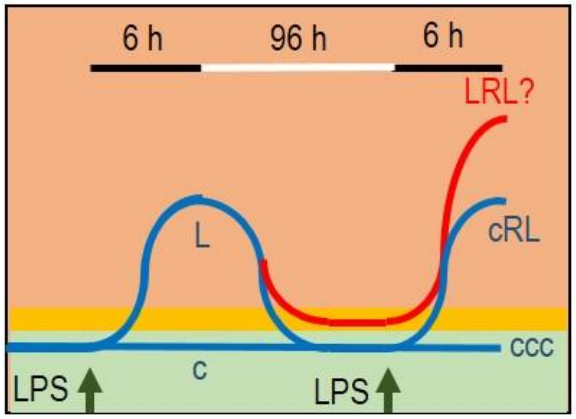

***Figure 2* - Experimental treatment groups**.

c = untreated control (6 h)
L = LPS (6 h)
ccc = control: untreated, 'recovery', untreated
cRL = untreated, 'recovery', LPS
LRL = LPS, 'recovery' (or, hypothesised experienced phenotype develops), LPS (repeated activation)

This aim was investigated by treating environment-controlled microglial cultures with lipopolysaccharide (LPS, a bacterial fragment to simulate 'infection') in order to induce pro-inflammatory activation. They were allowed to recover to return to their 'inactivated' form, then re-challenged with LPS (Figure2). The cultures were processed and fixed, followed by immunocytochemistry staining and imaging to produce micrographs to assessed for changes in cell morphology and marker expression (Arg1 and iNOS, which indicate activation status). The Preliminary data is suggestive of altered cell morphology and an elevated iNOS expression with LPS-stimulation (Figure 3). Furthermore, repeated LPS exposure, i.e. the activation of 'experienced' phenotype, appears to show a greater effect than a single LPS-induced activation (Figure 3). Although further experiments analyses are required, this data at the early stages data is are consistent with the theory of an altered microglial phenotype with induced by repeated LPS treatment.

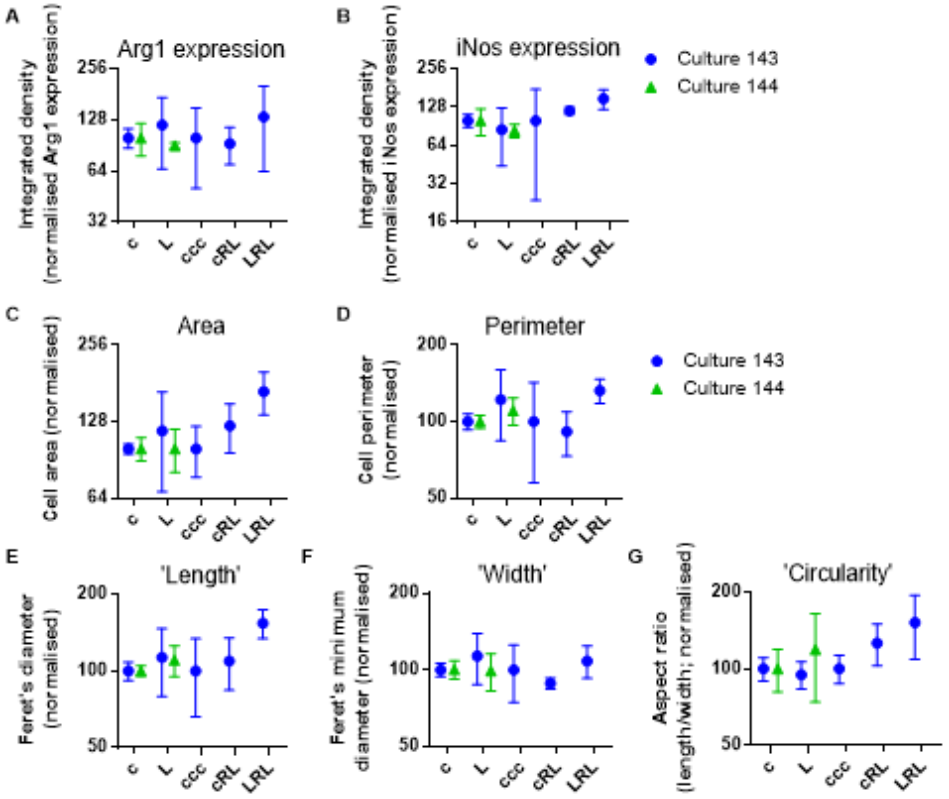

Figure 3 - **Effects of repeated activation on microglial marker expression and morphology**. Data analysed so far are insufficient for statistical analysis. Arg1 expression (A) was not obviously altered, but the iNOS expression (B) in the 'experienced' (LRL) group was potentially elevated. Most morphological measures (C, D, E and G) suggested elevated values in the 'experienced' (LRL) group. However, more data are required to determine whether these observations are consistent with an altered, 'experienced', phenotype.

Normalised data: 100% = *matches control;* **>100%** = *increase;* **<100%** = *decrease*

Expression of HMG-CoA reductase in ovarian cancer

Samuel Kalu

The aim of this project was to develop a method that to measure HMG-CoA reductase (HMGCR) in ovarian tumours and to subsequently evaluate whether this enzyme is expressed more highly in ovarian cancer than normal ovarian tissue. HMGCR normally catalyses the conversion of HMG-CoA to mevalonic acid and to isoprenoids, these have been theorised to facilitate oncogenic GTPase activity.

Ovarian cancer samples were obtained as commercially available tissue microarrays. These consisted of 200 ovarian cancer and normal cancer cell samples annotated with pathology findings and disease stage. A monoclonal HMGCR antibody was obtained from Atlas Antibodies but no studies have been reported validating this antibody from immunohistochemistry. To confirm that this antibody was specific for HMGCR the ability of the peptide antigen to block the immunostaining was also measured.

Methods

1) Deparaffinization of the ovarian cancer microarray slide
Microarray slides were washed in a sequence of solvents ranging from xyelene to 100% ethanol and then eventually 50% ethanol

2) Antigen retrieval
The microarrays were boiled in sodium citrate buffer in a pressure cooker

3) Blocking:
The microarray was treated with diluted Fetal calf serum

4) Antibody Incubation
The HMGCR antibody was diluted in antibody dilution buffer and incubated for 16 hours at 4ºC.. Following this a secondary antibody tagged with a peroxidise enzyme was subsequently added to the microarray.

5) Slide staining
-A hydrogen peroxide solution containing Diaminobenzidine substrate was added to the slide and the reaction stopped after the brown stain developed. Hematoxylin (H&E) was then added to the slide in order to stain the sample's nuclei. Following this the slide was washed in bluing agent which was required to counterstain the hematoxylin.

6) Slide Fixing
The slides were washed in a sequence of solvents ranging from 50% to 100% ethanol and finally eventually xylene and then mounted on a glass slide for visualization by microscopy.

Results

Our first attempts of this staining process yielded poor staining and insignificant results. Subsequently the method had to be altered. The initial suggested incubation time for antigen retrieval was eventually increased from 10 mins to 60 mins and the temperature was increased from 100ºC to 200ºC. The primary antibody incubation time was increased from 30 mins to an overnight incubation and the secondary incubation time was increased from 30 mins to 60 mins.

The specificity of the antibody was supported by the blocking experiment. When the antibody was used alongside along the blocking peptide no staining was seen in ovarian cancer cell samples unlike the unblocked condition.

Having established an appropriate method I next evaluated two microarrays containing 400 ovarian cancer samples in total. Staining was observed in the cytoplasm of ovarian cancer samples (where HMGCR is normally located) and no staining in the normal ovarian tissue samples. The data is currently being evaluated by a pathologist but initial interpretation supports the hypothesis that abnormally high HMGCR are present in ovarian cancer.

To assess the health outcomes in a population in North Staffordshire more than 50 years old with osteoarthritis following a change in socioeconomic circumstances: an observational cohort study

Kiran Kaur

Background

Osteoarthritis is the most common joint condition, the fourth leading cause of disability globally and the fastest increasing major health condition. The temporal relationship between osteoarthritis and physical and psychological comorbidity is unclear and may differ by levels of socio---economic status. The aims of this study were to (i) identify if osteoarthritis was associated with the onset of depression, anxiety, cognitive impairment, widespread pain, insomnia, social restriction and neurosis, and (ii) determine if these relationships were moderated by education, area level deprivation or change in income.

Methods

Prospective cohort study combining data collected by questionnaire at two time points (2005, 2008) in the North Staffordshire Osteoarthritis Project (NorStOP) and medical record data (n=3910). Osteoarthritis was defined by consultation to primary care for osteoarthritis between 2000 and 2005, and the indication of moderate to extreme pain interference in the questionnaire (2005). Logistic regression was used to examine the association between osteoarthritis and the onset of seven comorbidities (between 2005 and 2008), first unadjusted and then adjusting for putative confounders (comorbidity, socio---demographic and lifestyle factors). Moderation of the association between osteoarthritis and new onset comorbidity by change in income, education and area---level deprivation was examined by including interaction terms in regression analyses and stratified analyses. Results were reported as odds ratios with a 95% Confidence Interval (OR; 95%CI).

Results

Mean age was 63, 55% were female, and 942 (24%) had osteoarthritis. In the unadjusted analysis, osteoarthritis was significantly associated with new onset of all seven comorbidities ($p<0.05$). After adjusting for confounders, osteoarthritis was associated with the onset of depression (OR 1.35; 95%CI 1.02---1.79), cognitive impairment (1.36; 1.03---1.81), widespread pain (2.49; 1.96---3.17) and insomnia (1.58;1.14---2.19); it was not associated with new onset of anxiety (OR 1.29; 0.97---1.72), social restriction (OR 1.14; 0.86---1.49) or neurosis (OR 1.31;0.86--- 1.97). There was a significant non---multiplicative interaction between osteoarthritis and change in income and new onset cognitive impairment ($P=0.047$), and between osteoarthritis and education and new onset widespread pain ($P=0.012$). There was no significant interactions between osteoarthritis and change in income, education or area---level deprivation with new onset of depression, anxiety, insomnia, social restriction or neurosis ($p<0.05$).

Conclusion

Consulters to primary care for osteoarthritis were more likely to develop new physical and psychological comorbidities than those in the community that do not consult for osteoarthritis. Although this association with the onset of anxiety, neurosis and social restriction is explained by comorbidity, socio---demographic and lifestyle factors, those who consult for osteoarthritis represent a group who may benefit from more proactive strategies to prevent further morbidity. Despite no significant multiplicative interactions, there were differences in the prevalence of new onset of morbidity in those with osteoarthritis when stratified by socio--- economic status (e.g. onset of cognitive impairment was higher in people with an inadequate income than in those with an adequate income (Figure 1). Osteoarthritis and baseline morbidity were higher in lower socio---economic groups and further exploration across the life--- course will help to establish the role of socio---economic status on the natural history of osteoarthritis and its impact.

Molecular interactions of the vaccine candidate HASPB in the protozoan parasite *Leishmania Major*

Bridget Kemball

Background

Leishmaniasis is a neglected tropical disease caused by infection with the protozoan parasite Leishmania. There are an estimated 2 million new cases per year, many localised to areas of poverty and conflict. Currently there are no vaccines to prevent infection and the few drugs available for this disease are toxic and expensive. The parasites life cycle involves a motile promastigote stage in the midgut of the sand fly vector and an obligate intracellular amastigote stage inside host macrophages. A greater understanding of mechanisms involved in parasite differentiation and survival could aid the development of new tools for disease treatment and prevention.

Aims

This project focuses on the molecular interactions of a *Leishmania major* protein, hydrophilic surface protein B (HASPB), which is known to be important in the progression of the parasite through the sand fly vector. HASPB is highly expressed on the surface of infective stage parasites and is being studied as a potential vaccine candidate. The main aim of this project is to identify proteins that interact with HASPB to better understand the function of this surface protein.

Methodology

Transgenic parasite lines were generated which express HASPB in fusion with a biotin ligase tag BirA. A suitable plasmid construct was generated by amplifying the HASPB gene from L. major genomic DNA using PCR and inserting this into a *T. brucei* plasmid containing BirA. The HASPB-BirA fusion was then amplified and inserted into a plasmid suitable for transfection into *L. major*. The plasmids were checked by DNA sequencing to ensure the insert was correct. The final construct was then transfected into *L. major* using nucleofection. Three transgenic lines were isolated and expression of the HASPB-BirA fusion was confirmed using immunofluorescence and Western blot. Biotin identification (Bio ID) was then used to try and identify interacting partners of HASPB. In the presence of a biotin reagent, proteins immediately adjacent to the HASPB-BirA fusion were biotinylated, enabling streptavidin-based capture to be performed. The samples were then separated on an SDS PAGE gel and transferred onto nitrocellulose. Control samples were also used: wild type L. major parasites and parasites with BirA fused to an unrelated protein (BBS1). Western blots were probed with fluorescent streptavidin to detect biotinylated protein bands.

Results

Plasmid constructs were successfully generated for transfection into L. major. Transfection was also successful and Western blotting confirmed that the HASPB-BirA fusion protein was expressed in resulting transgenic L. major lines. The results of the Bio ID were inconclusive as the Western blot showed no clear bands. We plan to reprobe the blots with HRP-

conjugated streptavidin as an alternative means of detecting protein bands, which will be a step closer to identifying proteins that interact with HASPB.

Conclusion

HASPB plays an important role in the progression of Leishmania through its insect vector, the sand fly, and is highly expressed on the surface of infective stage parasites. Bio ID is a tool that may allow us to better understand the mechanism of action of this protein. Transgenic lines of L. major have been successfully produced which express HASPB fused to a biotin ligase tag and further research on these lines may help us to identify interacting partners of this important protein.

Anti-inflammatory and immunoregulatory effects of mesenchymal stem cells conditioned media in inflammatory arthritis

Bhagat Manku

Background

Rheumatoid arthritis (RA) is a chronic debilitating autoimmune disease. Despite its unknown aetiology, a painful inflammatory catabolic environment is created within the joint, which can lead to cartilage destruction, bone changes and joint damage[1]. In addition RA is a systemic condition affecting multiple organs, which can increase morbidity and mortality rates in patients[2]. In the UK, approximately 690,000 people have RA, with 20,000 new cases diagnosed each year[3]. This has significant financial implications, costing the UK between £3.8 and £4.75 billion per year[4]. Existing treatment consists of disease modifying drugs and biologic therapy[5]. Although their primary aim is to treat the inflammatory symptoms, they are not directly involved in repairing damaged joints. Moreover, many patients are not responsive to treatment and half of patients end drug therapy after 2 years[2]. Therefore further research needs to be conducted to help overcome these current problems.

One attractive therapeutic approach is considering the use of mesenchymal stem cells (MSCs) because they have shown huge promise in several pre-clinical models of arthritis[2].

The prevalent mechanism by which MSCs aid tissue repair is through a paracrine activity[6], as they secrete trophic factors[7] (IL-10, TGF- β), which help to reduce tissue degradation.

Aims

This project aimed to investigate the mechanism of immunoregulatory effects of mesenchymal stem cells conditioned media (MSC-CM) as a novel strategy into treating RA. We hypothesised that intra-articularly injected MSC-CM promotes the shift of M1 (pro-inflammatory)/M2 (anti-inflammatory) macrophage balance within the arthritic joints synovium.

Methodology

Arthritis was induced in C57Bl/6 mice[2] and 15µl of CM-MSC at peak swelling (after one day) was injected[8]. Animals receiving injections of serum free medium (SFM) were used as controls. M1 and M2 macrophages phenotypes were detected by immunostaining, using paraffin-embedded sections of joints previously collected from MSC-CM treated and control treated mice. Sections were immunostained with antibodies for mice pan-macrophage

marker F4/80, CD86 and CD206 for M1 and M2 macrophages respectively. For semi-quantification, positive signals in 5 random fields of view were counted and expressed as percentage of total F4/80-positive cells (mean±SEM).

Results

Positive staining for F4/80 in SFM controls averaged 50.03% +/- 3.6 whilst MSC-CM treated averaged 49.6% +/- 5.1**.** Healthy F4/80 knees averaged 14.7% +/- 3.4 for F4/80. For CD206, SFM averaged 46.4% +/- 4.3 and MSC-CM averaged 49.8 +/- 3.0%, whilst healthy CD206 knees averaged 27.8% +/- 7.5 (Figure 1).

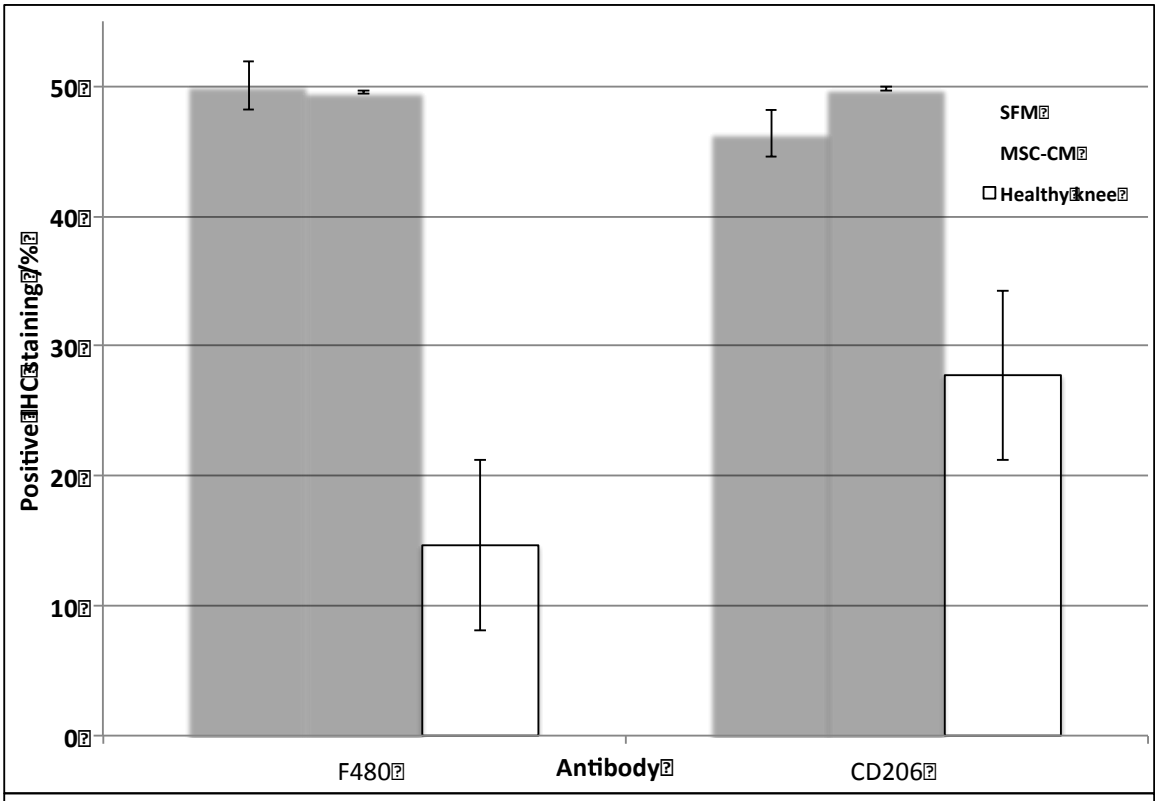

Figure 1: *Average number of M1/M2 macrophages detected by F480 and M2 macrophages by CD206 in C57Bl/6 arthritic mice synovia treated with serum free media (SFM), mesenchymal stem cells conditioned media (MSC-CM) and healthy controls expressed as percentage of total F4/80-positive cells (mean±SEM). F480: SFM 50.03% +/- 3.6, MSC-CM 49.6% +/- 5.1 and healthy synovia 14.7% +/- 3.4. CD206, SFM 46.4% +/- 4.3, MSC-CM 49.8 +/- 3.0%, healthy synovia 27.8% +/- 7.5. There was no significant difference (p<0.05) between SFM and MSC in either condition.*

Conclusions

MSC-CM treatment did not increase the proportion of M2 macrophages in inflamed joints. Analysis of the M1/M2 balance (CD86/CD206) was limited due to unsuccessful CD86 response. Overall, antibody specificity was not high enough to draw firm conclusions on the M1/M2 balance. Although F4/80 antigen is an excellent marker for mature macrophages, other cell types (peritoneal eosinophils, Langerhans cells, dendritic cells) also express this

antigen, whilst CD206 is also present on dendritic, liver and lymphoid endothelial cells. Further investigation of M1:M2 ratios needs to be carried out using more specific antibodies with the inclusion of a successful CD86 antibody, to elucidate the effect of MSC-CM treatment on RA joints.

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The impact of unfractioned heparin sulphate as a novel method of inhibiting the zika virus replication and infection within the Aedes genus of mosquito, primarily Aedes aegypti

Ben Nyemi-Tei

Introduction

Zika virus infection of pregnant mothers is currently a major problem in South America and is a growing problem in North America also. Zika virus (Zika) is not particularly harmful to the infected mother, but alters development of a growing foetus via vertical transmission. Evidence is gowning to suggest that Zika virus results in congenital microcephaly and global developmental delay in children born to mother's who had been infected throughout their pregnancy. The Zika virus outbreak in Brazil in 2015 resulted in an increase of babies born with microcephaly by a factor of 20. In early 2016 the World Health organisation declared the Zika virus to be a "public health emergency of international concern".

Zika Virus is part of the *Flaviviridae* family, which also includes several other pathogenic viruses, for example; Chikungunya Japanese encephalitis, yellow fever and dengue. Like these other viruses, Zika infects and spreads to human hosts via vector born transmission using the Aedes genus of mosquito, primarily Aedes aegypti. Transmission occurs when a female mosquito injects Zika virus whilst taking a blood meal from a mammal. There is also evidence to suggest that zika virus can be passed via sexual intercourse or transfusion of contaminated blood products, But vector born transmission is undoubtedly the most common route. Zika virus infection may be asymptomatic, meaning that the first time a pregnant female realises that she has contracted the the virus is at delivery, when her baby has microcephaly. Clinically Zika virus presents similar to influenza virus, with pyrexia, arthralgia, myalgia, rash, malaise, gastrointestinal disturbance and headache. These clinical features last from 2-8 days.

Current management for Zika virus infection is Supportive and via education on the disease as there is no available antiviral therapy. Likewise there are no available vaccines against Zika virus and thus, primary prevention using mosquito nets, removing stagnant water and mosquito replication sites, appropriate clothing and insect repellent are the only current control measure.

Objective

The aim of this research is to evaluate and understand whether unfractioned heparin sulphate can inhibit the replication of Zika virus inside the gastrointestinal system of Aedes aegypti mosquito. Therefore preventing the transmission of the virus and controlling the spread of disease.

Methods

Infection assays were performed on two groups of Aedes aegypti mosquitos. Two groups of mosquitos where starved and then infected with Zika virus via a blood meal (human blood). One group of mosquitoes were fed a blood meal that also contained heparin sulphate (test sample), while the other group were fed a blood meal that had no heparin sulphate (control sample). After a period of incubation the mosquitos were dissected at different time points post infection. The viral load was then determined and compared to assess the efficacy of heparin sulphate to inhibit replication of Zika virus.

Results & Conclusion

Currently no results are available due to the delay in starting the research in Brazil. The research is ongoing I hope to hear from the UNESP institute for Biotechnology (IBTEC) at Botocatu in the near future.

Limitations

- Achieving adequate number of successful blood meal fed mosquitos
- Delay in the acquisition of heparin sulphate, which delayed the start of the project significantly.
- The spontaneous death of mosquitoes throughout the experiment.

Formative moments in education that inspire careers

Lawrence Oligbo

Background

To achieve seniority in academic Primary Care requires commitment, hard work, and a consistent contribution to the development of research in the field. Exploring the career path and education of senior academics can provide inspiration and insight for more junior colleagues and may have implications for undergraduate and postgraduate education, as well as for institutions wishing to support a culture of staff and student continuing development.

One way of exploring a career path is to understand "formative moments" within an individual's education that critically inspired them. Analysing formative moments may aid in the understanding of the motivating factors, opportunities and challenges that contribute to career growth.

Objectives

To explore the critical moments in education that have inspired and shaped the careers of senior academics in Primary Care to help understand possible pathways that can be taken and to identify implications for undergraduate and postgraduate education.

Method

Senior Primary Care academics were invited to present their “careers in context” as part of an Athena Swan initiative aimed at inspiring emerging researchers. From this group, a purposive sample of six staff from a range of backgrounds and professions, including four male and two female academics, was selected. These senior academics were invited to send their presentation slides and take part in an interview discussing formative moments in their career. Participant consent was gained for interviews to be recorded and anonymised quotes to be used for thematic analysis.

Discourse analysis of the presentation slides formed the basis for a matched semi-structured interview with the participants. Participants’ interviews were arranged at a suitable time and location. Interview questions focused on salient education events including the accompanying thoughts, feelings and context as well as who or what influenced them in their career. Themes of motivation, challenges and opportunities were also explored. Interviews were transcribed, with the recordings and transcripts stored in secure drives to ensure confidentiality. Transcribed data was analysed and coded into separate themes in order to flag similarity and differences in formative moments between participants.

Results

The routes taken to a career in academic Primary Care varied greatly and information on how to become a researcher was not always readily available prior or during undergraduate study. Four recurring themes were identified along with a fundamental interest in partaking in research. These included: ‘characteristics’ of the person considering research; ‘research

training' received during work or education; 'role models and support' from both individuals and organisations, and 'serendipity' and taking advantage of it.

Discussion

The study highlighted a broad range of ways a career in academic primary care can develop. Personal characteristics that complement the nature of the career, included the ability to recognise the need for and the social impact of primary care research. The importance of having some research training either at undergraduate or masters level was alluded to. The need for role models and institutions to provide opportunities, guidance and support was often critical. Serendipitous life events and meetings with influential people also gave chances for research, collaboration and new employment.

A review of newborn screening results and anthropometric measurements in infants diagnosed with cystic fibrosis in the West Midlands

Katie Patterson

Introduction

Newborn screening (NBS) for cystic fibrosis (CF) was implemented nationally in 2007. It has significantly reduced the age of diagnosis and has been associated with improved clinical outcomes, particularly related to nutrition. We reviewed the demographic data of a screened cohort within the West Midlands, over a 7-year period. The anthropometric and nutritional progression of infants with confirmed CF were subsequently assessed. From this, we have developed a model for predicting height and weight of CF patients in the first 2 years of life, based on information available at first clinic visit.

Methods

Data were collected from the West Midlands NBS Laboratory on babies screened between November 2007-October 2014. A retrospective case notes review was performed on all confirmed cases, collecting anthropometric and nutritional data. Cluster analysis, classification and polynomial regression modelling were used to analyse these data. Models were validated using the 5 fold cross-validation method.

Results

507,608 infants were screened. 200 had a positive NBS and 144 had confirmed CF (birth prevalence 1/3525) giving a positive predictive value of 72%. There were 9 missed cases. Of the confirmed cases, there was no difference in birth weight (BW) z scores between pancreatic sufficient (PS) and pancreatic insufficient (PI) children (-0.05 v -0.36, p=0.29) however a significant difference was observed in rate of weight gain from birth weight to first clinic visit (-0.1 vs -0.33 p=0.007). Time taken for children to reach a z score of 0 for weight was 65 weeks compared with 90 weeks to reach a z score of 0 for length. Cluster analysis identified two distinct groups of patients, faecal elastase being the main determinant of class with a cut off of 212µg/g. Our models can predict weight z score at 1 and 2 years with a mean absolute error of 0.51 and 0.67 and length z scores at 1 and 2 years with an accuracy of 0.7 and 0.85. The most important factor when predicting future nutritional parameters was birth weight z score.

Conclusions

The birth prevalence of CF in the West Midlands is lower than the UK, which is likely to be due to the ethnic diversity within this region. Babies born with CF have a normal birth weight but lose weight by the first clinic visit. Infants with CF achieve catch up weight faster than length, which agrees with previous studies. We have developed and validated models that can provide a good estimate of weight and height z scores in the first two years of life for children diagnosed with CF by NBS. These models only require data available at first clinic visit. Clinicians can potentially use this tool to identify children at risk of poor nutritional outcomes thus, encouraging closer monitoring and earlier intervention.

How does Diabetes Compromise Renal Function and Result in Diabetic Nephropathy?

Previn Philippiah

Diabetic nephropathy is a slow progressing microvascular complication of diabetes mellitus (DM), which is the leading cause of End-Stage Kidney Disease (ESKD). As a result of the increasing prevalence of DM world-wide, the incidence of diabetic nephropathy is also predicted to increase. Furthermore, the associations of diabetic nephropathy with ESKD and cardiovascular mortality, highlight the importance in understanding the pathophysiology of diabetic nephropathy, to inform treatment. This review, will outline the current understanding of the pathophysiology of diabetic nephropathy; and attempt to explain the contribution of hyperglycaemia in the formation of AGEs and oxidative stress; which have been implicated in diabetic nephropathy.

There are numerous risk factors associated with the development of diabetic nephropathy, these include; hypertension, hyperglycaemia, hyperlipidemia, smoking, obesity, dietary protein and genetic factors. Furthermore, diabetic nephropathy is associated with increased cardiovascular mortality. This highlights the importance of a clear understanding of the pathophysiology of diabetic nephropathy, in order to inform treatment options.

Hyperglycaemia plays an important role in the development and progression of diabetic nephropathy, as suggested by the UKPDS and DCCT. These trials indicate that, intensive glycaemic control, prevents the progression of diabetic nephropathy; as shown by the reduction in the occurrence of microalbuminuria and macroalbuminuria.

The potential mechanisms by which hyperglycaemia induces renal impairment, namely the AGE-pathway and oxidative stress; have shown that receptor independent AGE-mediated damage results in the increased expression of collagen IV by mesangial cells and podocytes, which alters the structural components of the GBM and ECM. Furthermore, receptor independent AGE-mediated damage cause covalent intermolecular and intramolecular cross-links to form between glycated ECM proteins, together preventing the maintenance of tissue integrity, thus affecting the filtration barrier within the human kidney.

Moreover receptor dependent AGE-mediated damage, results in the production of ROS and the release of adhesion molecules, growth factors and pro-inflammatory cytokines. These ultimately act to increase endothelial permeability, cellular injury and fibrosis [26]. Thus potentially, promoting the progression of diabetic nephropathy from microalbuminuria to proteinuria within the kidney. This suggests that inflammation may play a pivotal role in the progression of diabetic nephropathy.

In addition, hyperglycaemia increases oxidative stress via increased production of O2-. This modulates the activity of PKC, Ang-II and TGF-β1; these in turn affect the synthesis of ECM components which may contribute to GBM thickening and glomerular sclerosis. However, the fact that the AGE-pathway produces ROS such as O2-, which contribute to oxidative stress; suggests that there may be possible synergistic interplay between these two mechanisms. Further investigation, is required, to determine this possible synergistic

interplay, and interaction between the several metabolic processes implicated in diabetic nephropathy.

In addition, the fact that 30-40% of diabetic patients, develop diabetic nephropathy, of which only 1-2% progress to ESKD; suggests that other factors may also influence the non-development of this disease in the other 60-70% of diabetic patients, and 98-99% of patients who fail to progress from CKD to ESKD. Thus, further research is necessary, to determine why some diabetic patients develop diabetic nephropathy, and why only a small percentage progress to ESKD.

The role of intracellular [Ca^{2+}] in the onset of atrial tachyarrhythmias

Patrick Quinn

Atrial fibrillation (AF) is commonly triggered by ectopic electrical activity within the sleeve of cardiomyocytes found in the pulmonary veins. This effect is enhanced in heart failure through adrenergic phosphorylation of calcium-handling proteins. The release of Ca^{2+} is therefore central to the triggering of AF, underlying the aberrant signalling which occurs within the pulmonary veins. Decreasing the open probability of the intracellular Ca^{2+} release channel reduces the amplitude of Ca^{2+} leak from the sarcoplasmic reticulum, and can mediate the ectopic electrical activity. This is possible using K201, a drug which stabilises the cardiac ryanodine receptor (RyR2) by preventing phosphorylation-dependent dissociation of RyR2 structural proteins. Autonomic regulation of Ca^{2+} is also achieved through the SERCA transporter, with phosphorylation of its inhibitory proteins increasing its activity and exposing RyR2 to greater Ca^{2+} concentrations. K201 can also act here to reduce this effect. The experiments proposed here employ a rabbit model of heart failure, studying induced arrhythmic activity to better understand the potential role of stabilisation of RyR2 and SERCA inhibition in arrhythmogenesis prevention. Structural investigations aim to explore how the Ca^{2+} channel is phosphorylated in heart failure, and how the K201 molecule acts. This work could contribute to future, pulmonary vein-specific treatments of the early activity that triggers the cascade of AF cellular pathology.

Consultation patterns of knee pain in children: an observational study

Amit Rajani

Introduction

Musculoskeletal pain is a common experience for children and adolescents. The knee is one of the most commonly affected regions and up to 60% of children and adolescents with knee pain seek care. General practitioners (GPs) are usually the first to assess, treat and manage children and adolescents with knee pain. Despite this, we currently know very little about the range of knee problems children and adolescents consult for, how GPs document consultations or if consultation patterns vary according to age and gender. The aim of this study was to describe the range of knee problems children and adolescents aged between 3 and 19 years consult GPs about, how these consultations are documented by GPs (i.e. symptom codes or diagnosis codes e.g. trauma and non-trauma) and how consultation patterns may differ when stratified by age and gender.

Methods

Consultations specific to the knee were extracted for children and adolescents aged 3-19 years from the recorded consultations at eleven general practices contributing to a general practice consultation database (CiPCA) in 2010. Two authors independently categorised the list of knee Read codes into ‘Symptom’ or ‘Diagnosis’ categories. Diagnosis codes were further sub-categorised into ‘Trauma’ or ‘Non-Trauma’ categories. Descriptive statistics (raw values and percentages) were used to describe consultation patterns overall and when stratified by age and gender. Chi squared tests were used for significance testing.

Results

Knee problems accounted for 10.8% (n=550) of all consultations for musculoskeletal problems involving 327 patients (mean age 13.9 years), and were documented using 42 of the 375 knee Read codes. Overall, the number of patients and consultations for knee problems increased with age until 12-15 years old, after which there was a slight decrease. Symptom codes (e.g. knee pain) were most commonly used to document consultations for knee problems regardless of age or gender. Symptom code usage decreased with age and there was an increase in the use of diagnosis codes. Within the diagnosis category, consultations were more frequently documented using trauma codes for males (males 37.3%, females 24.2%) and there was a trend for non-trauma codes to be used more frequently for females (males 2.8%, females 5.2%). Stratified by age and gender, consultations were more frequently coded with symptom codes for males until age 15 years, after which time diagnosis codes were more frequently used. For females, the patterns were generally more stable, the exception being for 12 to 15-year age band where there was an increased proportion of symptom codes used and an equivalent reduction in the proportion of diagnosis codes used.

Conclusions

The category of Read codes used by GPs to document consultation for knee problems was found to be influenced significantly by age and gender. An improved understanding of the epidemiology of knee problems in children and adolescents can inform training and assessment priorities in general practice, and encourage the development of targeted injury prevention programs. Further work is needed to describe how knee problems are managed by GPs and how this management may differ depending on how consultations are documented.

Information needs in patients presenting with a fragility fracture or osteoporosis: a systematic review

Grace Raybould

Background

Osteoporosis is a condition characterised by a reduced bone density that if poorly controlled can lead to a higher risk of fragility fractures. Fragility fractures are an economic burden, reduce quality of life and are a significant cause of mortality. A number of these fractures are preventable with the correct investigations and treatment. Current guidelines in the UK indicate that following a fragility fracture all patients should receive secondary prevention including a bone health assessment. In practice only 20% of cases meet these guidelines.

Aims

To identify the expressed information needs of patients with osteoporosis or fragility fractures. To find out how patients think problems can be addressed to reduce further fractures.

Methods

A systematic review was conducted, looking at qualitative papers from the last 20 years. Databases searched included CINAHL, EMBASE MEDLINE, PsycINFO, HMIC, AMED and Web of Science. Papers were also found using citation tracking. This produced nine suitable articles to review. These articles were quality assessed and underwent data extraction.

Results

Several themes emerged across multiple papers. Findings were separated into headings; barriers to information needs being addressed (discussing ethnicity, gender, age, physician and patient attitudes, lack of knowledge), suggestions to address information needs (support groups, style of consultation, quality of explanation, progress report). Three overarching themes emerged, outcomes, barriers and solutions and were incorporated into a theoretical model.

Conclusion

This study not only identifies where osteoporosis or fragility fracture patients feel like information is lacking but also offers practical solutions to these issues. This information is important for clinicians managing osteoporosis patients aswell as guiding the direction for new patient information literature.

Safe areas for placement of external fixator pins, within the distal femur and proximal tibia

Lucy Reipond

With external fixation of the femur and tibia, iatrogenic injury to neurovasculature from self-drilling tips of fixation pins is an important consideration in pin placement. Precise knowledge of the neurovascular anatomy in the distal femur and proximal tibia is important to limit potential pin misplacement. Six pin placement sites on 6 cadaveric legs were used in accordance with current placement techniques. After pin placement, the soft tissue around each pin was dissected and distances between the pin and surrounding neurovasculature were measured. The resultant data allows for a description of safe and unsafe corridors which can be used for external fixator pin placement. Safe sagittal insertion into the distal femur should consist of 2 pins: 1) 90mm+ proximal from the base of the patella and 3mm+ medially, 2) 55mm + proximal from the base of the patella and 2mm+ laterally. Safe coronal insertion into the distal femur should consist of 2 pins: 1) 30mm + proximal to the lateral epicondyle, 2) 100mm+ proximal to the lateral epicondyle. Safe proximal tibial pin placement should be at an oblique angle, 20mm+ below the tibial tuberosity and 2mm + medially and 35mm + distal to the tibial tuberosity and 2mm+ medially.

This study forms an investigation into the safe areas for placement of external fixator pins, within the distal femur and proximal tibia. In specifically, detailing best practice for pin placement in relation to the tips of the external fixation pins.

Femoral nerve entrapment syndrome: a new perception due to muscular compression

George Solomou

Aberrant descriptions of femoral nerve compression as a consequence of indirect trauma, ischemia and stretch injury have been previously reported. Latest insights suggested a muscular compression of the femoral nerve due to abnormal variations of the iliopsoas muscle. Despite the fact that the femoral nerve is ubiquitously described in the literature to be formed either through or lateral to the psoas major muscle or even formed posterior to the muscle and subsequently pass through the muscle as a single nerve, no articles to our knowledge have demonstrated its pathway in a cadaveric study.

The aim of this study is to provide a detailed description of the course of the femoral nerve passing through the psoas major muscle and propose a femoral nerve entrapment syndrome that has not been described before.

During the bilateral dissection of six male and female cadavers, six unilateral examples of femoral nerve formation inside the psoas major muscle were observed. In addition, six unilateral examples of the femoral nerve passing through the psoas major muscle have also been found. Multiple photographs have been taken during the dissection procedure, which can be used to demonstrate the formation of the femoral nerve as well as to show a step by step guide of the method used to delineate the anatomical relationship of the femoral nerve and its surroundings.

Moreover, 12 more cadavers have been identified to be dissected in order to provide a reasonable statistical significance of our findings. Future research directions to visualize the femoral nerve inside the psoas muscle, such as using ultrasonography or magnetic resonance neurography will also be discussed.

Scouting for suicide - Ethical considerations of social media surveillance to identify users at risk of suicide

Sahdeea Sultana

With the advent of social media, our way of communication has changed and with it, so have the patterns of suicide communication. Where previously, the suicide note was a physical entity, often discovered after the act, the ease of accessibility and instant delivery of messages via social media has meant it is becoming increasingly common for users to express such intentions during moments of distress in real time (Jashinsky (2014); Sueki (2015); Won (2013)). This has been recognized as a promising window of opportunity to provide intervention for those in crisis and is rapidly gaining momentum within literature and real life applications. However, as we adapt our prevention strategies to harness this potential of social media, ethical concerns will inevitably arise. A contemporary example is the *Radar* app, launched by the UK charity Samaritans in 2014, which quickly surmounted a negative response and was discontinued within days because of concern from social media users it intended to help (Orme (2015)). This presentation will explore the relationship between social media and suicide, it's applications in suicide prevention and the bioethical issues which present.

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Renal disease in Pregnancy

Tony Talhat

Background

Pregnancy related Acute Kidney Injury (PRAKI) is a rare condition in the developed world, however it is associated with high mortality and adverse outcomes for both mother and baby (1). PRAKI is still a significant problem in the developing world due to septic termination of pregnancy and limited access to care; especially prenatal care (2).

Aim

We aimed to examine the link between renal disease in pregnancy and perinatal outcomes. We initially undertook a systematic review of studies on PRAKI in order to better understand the prevalence of adverse outcomes in PRAKI. We then examined a cohort of women with renal disease in pregnancy at University Hospital of North Midlands over the last 3 years to determine their pregnancy outcomes and comparing these to healthy women.

Methodology

Systematic review: We searched EBMASE and MEDLINE for studies using search terms of: pregnancy AND PRAKI, acute kidney injury (AKI) and acute renal failure since inception. After screening the abstracts, we then chose the most common outcomes to conduct our systematic review: caesarean delivery, complete renal recovery, partial renal recovery, irreversible renal damage, maternal mortality, and perinatal mortality. Data were analysed via RevMan.

Retrospective cohort study: An anonymised list of women with renal disease and women without renal disease who delivered on the same date was generated through the hospital coding system with their perinatal outcomes (maternal age, blood loss at delivery, birth weight, length of gestation, mode of delivery and smoking). All data were analysed in GraphPad Prism.

Results

Systematic review: 459 studies were initially identified. 145 duplicates were removed. After screening the titles and abstracts of 306 studies, 52 full text articles were selected. The rate of adverse outcomes after PRAKI were: maternal mortality 13.8%, perinatal mortality 31.7% and C-section 43%. The rate of renal recovery after PRAKI were: complete recovery 58.9%, partial recovery 13.9% and irreversible damage 10.5%. We conducted meta-analysis in outcomes with studies that had separate AKI and control groups and with more than 1 study. This showed that AKI increased the risk of maternal mortality by 22-fold (OR 21.74, 95% CI 1.65-286.12), however there was high heterogeneity. The result for Caesarean section rate was non-significant (OR 1.51, 95% CI 0.37-6.15).

Retrospective cohort study: 78 women with renal diseases and 1361 control women were included. T tests showed significant differences (p<0.05) in the following outcomes between women with renal disease and healthy pregnancies: age, blood loss, birthweight and duration of gestation. For mode of delivery, women with renal disease had more Caesarean

sections and instrumental deliveries and fewer normal deliveries compared with healthy women (Caesarean sections: 51% vs 25%, Instrumental deliveries: 16% vs 11%, normal deliveries: 33% vs 64%).

Conclusion

Systematic review and meta-analysis showed significantly higher rates of maternal mortality in PRAKI. Our own data showed that women with renal diseases were more likely to face adverse outcomes such as a low birthweight and shorter gestations. The mode of delivery was also more likely to be invasive methods such as Caesarean and Instrumental deliveries.

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Perceptions of third sector workers providing care for older patients with depression: analysis of a qualitative data-set

Maatla Tshimologo

Introduction

Older people have complex health needs because of co-morbid physical and mental health problems. The commonest mental illnesses in older people are dementia, anxiety and depression. Depression is the commonest mental illness in the 65 years+ age group with a prevalence rate 25 %. Despite the high prevalence of depressive symptoms and the increased usage of primary care services by this age group, depression is still inadequately managed in older people. This may be due to patient, practitioner and/or system factors. Third sector organisations offer services that support older people with depression and anxiety.

This study aimed to explore the perceptions of third sector workers working with older people with depression and anxiety.

Methods

A qualitative study utilising interview data collected for the Non-Traditional providers to support the management of Elderly people with Anxiety and Depression (NOTEPAD) primary study. The data comprised nine transcripts of interviews conducted with third sector workers about their experiences working with older people with depression and anxiety.

The interviews were conducted using a topic guide, audio recorded and then transcribed.

A thematic analysis of the transcripts was conducted. All were transcripts coded by the three researchers (MT and supervisors) and major themes identified through a process of continuous comparison between different transcripts to refine themes and discussion amongst the research team. Through an iterative analysis process five main themes were identified.

Results

Eight out of the nine interview participants were female. Four out of the nine participants were volunteers, which means they weren't paid, while five were employed by the third sector services. The main themes that were identified from the workers' transcripts are; services provided, roles and responsibilities, training, support and supervision, challenges and suggested solutions.

The types of services provided, reported by workers included social groups, such as walking groups and knitting groups, telephone befriending, signposting the clients they receive to other relevant services. They are aimed at combating loneliness and isolation which the third sector workers linked to or believed trigger depression in older people. Workers reported a wide range of responsibilities, some held leadership positions and were responsible for coordinating the organisations' daily activities. Other roles reported include advocacy and counselling.

The workers reported having good support networks which they used for debriefing, guidance, and mutual support. Workers reported lack of training, short-term funding, poor relationships with primary care, staff shortage and transport difficulties for older people hinder service provision. Formal training, service integration, and long-term funding are some of the suggestions made by workers to improve service delivery.

Conclusions

Third sector organisations reported that they support older people with anxiety and depression, but receive little training to support this aspect of their work. GP awareness of such services should be increased to improve relationships between practices and third sector services. Clinical Commissioning Groups need to be aware that short-term funding reduces the sustainability of third sector services.

In sickness and in health: A cross-sectional analysis of concordance for depression and anxiety in 13,507 couples in primary care

James Walker

Background

Depression and anxiety are common and have significant impacts on individuals and wider society. This impact is acutely felt in primary care, not only because most depression and anxiety conditions are treated there, but also because depression and anxiety can detrimentally influence other common chronic illnesses. One theory, with growing research interest, used to understand increased risk in depression and anxiety is concordant influence between family members, particularly the level of affective concordance (shared mood) in couples (e.g. spouses, cohabiting partners). Previous studies have shown concordance between partners for various health conditions (heart disease, hypertension, diabetes, severe psychiatric illness). However little attention has been given to primary care populations, and less is known about what factors (e.g. shared; environment, behaviours, life experiences) may explain why concordance is present. The aims of this study were to test for affective concordance in couples, and examine possible theoretical reasons for concordance.

Methods

This is a 1-year cross-sectional study of anxiety and depression consultations in primary care. Data was obtained from the Consultations in Primary Care Archive (CiPCA), a validated primary care database of recoded consultations from GP practices in North Staffordshire. The outcome was the presence of an anxiety or depression Read Code (GP-recorded reason for consultation) in the female within the couple dyad, and the exposure was a recorded Read Code of anxiety or depression in the male of the couple dyad. Logistic regression was used to test associations with odds ratios (OR) and 95% confidence intervals (95% CI) reported. Statistical adjustment was carried out on potential influences of concordance; shared age, shared environment (deprivation), shared healthcare behaviour (consultation frequency), and shared comorbidity (cardiovascular, musculoskeletal).

Results

In total 13,507 couples were included within the analysis, with 2.2% of males and 4.7% females receiving a Read Code for anxiety, and 1.2% males and 2.8% females receiving a Read Code for depression. Logistic regression analysis showed a 3 times increase in odds of an anxiety consultation (OR 2.98; 95% CI 2.2 to 4.1), and an increase in over 4 times the odds of a depression consultation (OR 4.45; 95% CI 2.8 to 7.1) by females if their male partner had also consulted. There was no notable reduction in these Odds Ratios for the adjustment of each of the shared experiences (age, environment, healthcare behaviour, comorbidity). However, collectively within a multivariable model, concordant anxiety was reduced to 2.6 times odds (OR 2.57; 95% CI 1.8 to 3.7) and depression to 3.8 times odds (OR 3.84; 95% CI 2.4 to 6.3).

Conclusion

Results show a significantly large effect of concordant influence on consultations for anxiety and depression in females whose male partners had also consulted. Examination of potential influences on this concordance showed minor collective effects, however electronic health record databases are limited in the key shared lifestyle information that may further explain this concordant effect and more research is required. Given the clear effects shown for concordance, clinicians may wish to be aware of potential external home influences on their patients' mental health state.