

Australian Pain Society NEWSLETTER



**2020 AUSTRALIAN PAIN SOCIETY
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In the IASP Global Year for the Prevention of Pain



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2020 RISING STAR



Dr Samuel Robinson

Dr Samuel Robinson is a Postdoctoral Research Fellow at the Institute for Molecular Bioscience, University of Queensland. He is the 2020 Australian Pain Society Rising Star Award Winner.

His research expertise is in the discovery of new plant and animal toxins and investigation of their structure, function, and potential for biomedical applications. Sam is an expert on plants and animals that sting, and the biology, chemistry, pharmacology, and pathophysiology underlying those stings.

His research is providing new understanding on the mechanisms of chemical defense and predation used by animals and plants. The new toxins he has discovered are being used as tools for improving our understanding of the human body and designing new and better treatments for certain diseases.

ABSTRACT **GAIN FROM PAIN: USING VENOMOUS ANIMALS TO EXPLORE NEW NOCICEPTIVE PATHWAYS**

Animal venoms are complex mixtures that typically contain hundreds of peptide and protein toxins. A primary role of venom for many animals is predation, where specific toxins act to subjugate prey by targeting vital processes in one or all of the nervous, musculoskeletal, or cardiovascular systems. But almost all venomous animals also use their venoms for defensive purposes—many solely. Defensive envenomations are often associated with intense pain and my hypothesis is that this pain is produced by toxins that directly target sensory neurons, hijacking or overstimulating neuronal transmission. The goal of my research

has been to identify the responsible pain-causing (algogenic) toxins from a range of pain-producing animal venoms and to determine their mechanism of action.

Venom samples were acquired from numerous species with characteristically painful stings and the composition of several venoms was determined using a combination of venom proteomics and venom-gland transcriptomics. High-content calcium imaging of mammalian sensory neurons was used to guide the isolation of algogenic toxins. Calcium imaging and electrophysiology were used to determine cellular and molecular mechanisms of action.

I have identified new algogenic toxins from a range of venoms. Different venomous animal lineages employ distinct structural classes of algogenic toxins. A common convergent mechanism of action is the targeting of cell membranes to generate a leak in ion conductance. In excitable cells, such as mammalian sensory neurons, this leak in ion conductance shifts the membrane potential to threshold, initiating neuronal depolarisation, an action, which on nociceptors, results in immediate pain. Other more specific mechanisms also exist, including the activation (or delayed inactivation) of specific ion channels and receptors involved in normal sensory reception and transduction.

The identification and characterisation of new algogenic toxins has provided new knowledge about methods of chemical defence by venomous animals and has the potential to elucidate new components of mammalian pain signalling pathways. A better understanding of our own pain physiology may ultimately lead to the development of new or improved pain treatments.

ANTINOCICEPTIVE ACTIVITY IN MICE OF A SYNTHETIC PEPTIDE FROM LATIN AMERICAN WASP *PARACHARTERGUS FRATERNUS*

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Background and Aims

Pain is a health problem around the world and this condition can be disabling with some patients do not responding to the treatments. Venomous animals have an arsenal of compounds with promising activities in relief of pain. The peptide Agelaia-MPI isolated from Latin American wasp *Parachartergus fraternus* showed antinociceptive activity in mice and to improve the activity we did structural modifications. So, the objective was to evaluate the antinociceptive activity in mice of the synthetic peptide, neuroVAL.

Methods

Male Swiss mice (n=5/group, 18-25g) were used. Assays were performed using neuroVAL at the dose of 5 µg/animal diluted in a solution of water with 5% DMSO. For writhing test, the peptide was injected via subcutaneous (s.c., 0.1 mL) and after 30 min, acetic acid (0.6%, v/v) was injected via intraperitoneal (i.p., 0.5 mL). Positive control was dipyron (500 mg/kg, s.c., 0.1 mL). Antinociceptive activity was expressed as writhing scores over a period of 30 min. The second assay, formalin test, consisted again in s.c. injection of peptide 30 min before intraplantar injection of formalin (1.2%, v/v, 40 µL/paw). Positive control was morphine (5 mg/kg, i.p., 0.5 mL). Time of licking the injected paw was recorded in seconds (s) in neurogenic phase (phase 1; 0-5 min) and inflammatory phase (phase 2; 15-30 min). Negative control of both assays was 5% DMSO (s.c., 0.1 mL). The

experiments was approved by Animal Care and Ethics Committee and is in accordance with the National Council for Animal Experimentation Control. Results expressed as mean ± SEM; ANOVA; Bonferroni; $p < 0.05$.

Results

In writhing assay, acetic acid induced 108.8 ± 4.3 writhing episodes in animals of negative control. Dipyron reduced this response in 66.9% (36.0 ± 3.8 writhing) and neuroVAL reduced 38.2% (67.3 ± 4.6 writhing) ($p < 0.001$). In formalin test, neuroVAL showed antinociceptive activity in both phases. In first phase, the animals of negative control licked the paw during 57.2 ± 4.8 s, morphine reduced 90.7% of this response (5.3 ± 0.7 s, $p < 0.001$) and the peptide reduced 31.3% (39.3 ± 3.0 s, $p < 0.01$). In phase 2, the recorded data of negative control was 239.4 ± 11.3 s, morphine almost abolished the response with 99.7% of reduction (0.8 ± 0.6 s, $p < 0.001$) and neuroVAL showed a little activity of 16.8% (199.1 ± 9.2 s, $p < 0.05$).

Conclusions

For writhing and formalin assays, we choose a via (s.c.) that is less invasive than commonly used in animal models (intracerebroventricular) and neuroVAL showed antinociceptive activity similar with the parental peptide Agelaia-MPI. These results indicate that neuroVAL has activity in neurogenic and inflammatory pain, however we do not know the mechanism of action and more assays are necessary to characterize better this activity and to understand how this peptide triggers the antinociception.

SPINAL CORD INJURY IS NOT A FEATURE OF CHRONIC WHIPLASH ASSOCIATED DISORDER: A MAGNETIC RESONANCE SPECTROSCOPY STUDY

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Background and Aims

Neurophysiologic processes underpinning chronic whiplash associated disorder (WAD) are not well understood. Incomplete injury to the cervical spinal cord has been suggested as a mechanism that could underlie ongoing pain and disability in this condition, considering the traumatic mechanism, observations of widespread sensory disturbances (hypoesthesia, hyperalgesia), and reports of fatty infiltration of cervical spine muscles in this population. Tissue metabolic changes may indicate pathophysiology without detectable structural alterations. The primary aim of this study was to assess metabolite concentrations indicative of neuronal injury or pathology in the cervical spinal cord in people with chronic WAD. A secondary aim was to explore the relationship between spinal cord metabolite profiles and clinical variables.

Methods

Forty-one people with chronic Grade II WAD (mean [SD] age 39.6 [11.0] years, 25 females) and 14 healthy controls (39.2 [12.6] years, 9 females) participated in this cross-sectional study. Participants underwent cervical spinal cord magnetic resonance spectroscopy to assess metabolite concentrations: N-acetylaspartate (NAA), creatine (Cr) and choline (Cho). Chronic WAD group participants completed clinical questionnaires regarding pain (0-10 visual

analogue scale [VAS]), disability (Neck Disability Index [NDI]), post-traumatic stress symptoms and pain catastrophising. Chronic WAD group participants also underwent cervical range of motion assessment and pain threshold testing to cold and pressure stimuli. Data were analysed using Wilcoxon rank-sum testing and Spearman correlations ($p < 0.05$).

Results

Chronic WAD patients were median (IQR) 3 (1.5, 5.5) years post-injury. Mean (SD) pain intensity was 4.3 (2.0) VAS, and median (IQR) NDI was 32% (22, 44). There were no differences between the WAD and control groups for any of the three metabolite ratios assessed: NAA:Cr (median [IQR] WAD 1.73 [1.38, 1.97], controls 2.09 [1.28, 2.89], $p = 0.37$), NAA:Cho (WAD 1.50 [1.18, 2.01], controls 1.57 [1.26, 1.93], $p = 0.91$) or Cr:Cho (WAD 0.84 [0.64, 1.17], controls 0.76 [0.60, 0.91], $p = 0.33$). There were no significant correlations observed between NAA:Cr, NAA:Cho or Cr:Cho and any clinical variable ($p \geq 0.06$).

Conclusions

Cervical spinal cord metabolic profile did not differ between people with chronic WAD and pain-free controls, implying spinal cord injury does not underlie symptoms in this population. Metabolite ratios were not correlated with any clinical or questionnaire outcomes in the WAD group. These findings are not consistent with spinal cord metabolic changes, measured by MRI *in vivo*, providing an independent clinical grading for ongoing symptoms of patients with chronic WAD.

CLINICIAN EDUCATION TO SUCCESSFULLY REDUCE OPIOID DISCHARGE PRESCRIBING IN OPIOID-NAÏVE SURGICAL PATIENTS: A CLUSTER-RANDOMISED CONTROLLED TRIAL

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Background and Aims

Opioid analgesics are associated with harm, and prescribing variability persists. We tested whether clinician education optimised prescribing on discharge in opioid-naïve and tolerant surgical patients.

Methods

A pragmatic cluster-randomised controlled trial was undertaken of 13 surgical units of a major Melbourne hospital. Interns, residents and clinical pharmacists from intervention units received face-to-face pharmacist-led education in February 2019. Prescribing was evaluated for patients discharged home from surgical units before (baseline: February-April 2018) and after education (follow-up: February-April 2019). Patients receiving opioid agonist therapy were excluded. Opioid-naïve (no regular pre-admission opioids) and opioid-tolerant patients (≥ 1 regular pre-admission opioid/s) were analysed separately. The primary outcome was change in proportion of opioid-naïve patients prescribed regular opioids at discharge. The proportion of opioid-tolerant patients prescribed regular opioids above their pre-admission level was evaluated along with quantities supplied. Multivariable regression included interaction terms and confounding factors; mixed-effects models tested for variations between clusters. The study received ethics approval from the participating institution (226/18) and was prospectively registered on the Australian New Zealand Clinical Trial Registry (ACTRN-12618000876291).

Results

Overall, 4062 opioid-naïve patients were evaluated (baseline 2383; follow-up 1679). In the intervention arm, an absolute reduction in regular opioid prescribing of 15.1% was observed, compared to a reduction of 6.3% in the control arm from baseline ($p=0.005$). Opioid-naïve patients in the intervention group were 49% less likely to be discharged on regular opioids compared to the control group following mixed-models analysis (odds ratio (OR) 0.51, 95% confidence interval (CI) 0.28 to 0.90). Reductions were demonstrated for immediate-release/'as required' opioid prescribing (OR 0.69, 95% CI 0.51 to 0.93), regular daily dose (oral morphine equivalence (OME), mean difference -2.49; 95%CI -4.33 to -0.65), and quantity supplied (-1.18, 95%CI -2.33 to -0.04). Discharge without opioids (OR 1.7, 95%CI 1.3 to 2.4) and with documented de-escalation plans (OR 2.4, 95%CI 1.3 to 4.5) was higher in the intervention arm. There were 330 opioid-tolerant patients discharged during the period (Baseline 189; Follow-up 141). No differences were observed in the likelihood of being discharged with opioid above admission levels following the intervention (OR 0.29, 95%CI 0.07 to 1.11). No differences were observed between arms for discharge quantities (-3.01, 95%CI -11.94 to 5.91) or regular daily dose (OME, -0.16, 95%CI -16.0 to 15.7).

Conclusion

Clinician education was associated with significant reductions in discharge prescribing for opioid-naïve patients, highlighting the value of education to optimise prescribing. Lack of prescribing change in opioid-tolerant patients reflects the complexity of chronic pain management and the need for further research in this cohort.

EFFECT OF HAND DOMINANCE ON IMPLICIT MOTOR IMAGERY PERFORMANCE (MIP): META-ANALYTICAL REVIEW

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Background and Aims

People in pain have impaired implicit MIP for bodily images. When shown pictures of the painful body part, they are less accurate or slower at identifying left or right orientation – findings thought to indicate changes to attentional allocation and function of motor-related brain maps. Whether differences in motor function (via hand dominance) influence MIP is largely unknown. Such information is critical to untangle the effects of pain on MIP impairment. This is the first review to synthesise empirical evidence on the effect of handedness on MIP.

Methods

Databases were searched from inception to March 2018. Eligible studies evaluated a left/right hand recognition task in healthy adults. Two independent reviewers performed screening, data extraction, and critical appraisal. For each primary outcome (response time; accuracy), five meta-analyses were conducted: three between-group [(1a) left- versus right-handers overall; (1b) left- versus right-handers for right hand images; (1c) left versus right-handers for left hand images] and two within-group [(2) for right-handers: left versus right images; (3) for left-handers: left versus right images].

Results

The search identified 6867 publications with 42 studies (56 datasets) eligible for meta-analysis (n=224 left-handers; n=2545 right-handers). Risk of bias was high due to small sample size, lack of blinding, and inadequate control of previous task exposure.

Meta-analyses showed:

- (1) Overall, right-handers were faster [114.47ms (95%CI: 48.81, 180.14) N=5], but less accurate [-0.92% [(95%CI: -1.51, -0.33) N=4], than left-handers. For right hand images, right-handers were faster than left-handers [220.05ms (95%CI: 154.56, 285.53) N=4], but no more accurate [-0.73% (-2.58, 0.50) N=2]. For left hand images, right-handers were faster [69.38ms (95%CI: 2.92, 135.84) N=4] and more accurate than left-handers [3.21% (95%CI 1.42, 4.99) N=2].
- (2) Right-handers were faster [42.14ms (95%CI 21.51, 62.77) N=50] but no more accurate [-0.10% (95%CI -0.62, 0.42) N=34] at identifying right hand images over left.
- (3) Left-handers were no faster at identifying left versus right hand images [3.13ms (95%CI -44.62, 50.87) N=3], nor more accurate [1.63% (95%CI -0.45, 3.71) N=2].

Conclusions

Limited evidence showed that right-handers are faster than left-handers at recognising hand laterality, regardless of whether the image is of a right or left hand. Such findings suggest that cerebral dominance may play an overarching role in MIP. However, within right-handers the effects of hand dominance on MIP were somatotopically-specific: they were quicker at recognising images of right hands than images of left hands. This did not occur within left-handers: they were no quicker at recognising images of left versus right hands. Such findings may reflect the comparatively reduced hand dominance of left- versus right-handers (i.e., left-handers are typically more ambidextrous). There is a relative paucity of information for left-handers and evidence for accuracy differences was conflicting. Collectively, handedness appears important to consider/control for in MIP.

ALTERED REGIONAL BRAIN ACTIVITY AND HYPOTHALAMIC CONNECTIVITY PRECEDING A MIGRAINE

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Aims

The mechanisms underlying migraine pathogenesis remain hotly debated. A large body of evidence suggests that the development of migraine-pain is dependent on the activation of the trigeminal sensory afferents that innervate meninges and their large blood vessels. More recently it has been hypothesised that increased sensitivity of the central nervous system is also needed for migraine initiation, although few studies have explored the brain immediately prior to a migraine attack. During the 24-hour period preceding a migraine headache, symptoms such as altered sleep, appetite and thirst often present, which likely result from altered hypothalamic function. It is possible that an altered hypothalamic network is involved in the initiation/expression of a migraine attack. Indeed, we have recently shown increases in resting infra-slow oscillations in regions of the hypothalamus, periaqueductal gray, dorsal pons and spinal trigeminal nucleus in this period. In this study, we aimed to investigate whether individuals in the 24-hour period preceding a migraine attack would exhibit alterations in cerebral blood flow and hypothalamic connectivity, reflecting both neural and vascular changes. Given this, we hypothesise that the same areas displaying changes in resting activity patterns immediately prior to a migraine attack, will show significant blood flow and hypothalamic connectivity alterations.

Methods

In 7 migraineurs preceding (within 24 hours) a migraine (5 female, mean age 32yrs), 13 migraineurs following (within 72 hours) a migraine (9 female, mean age 32yrs), 22 interictal migraineurs (15 female, mean age 31yrs) and

26 controls (22 females, mean age 32yrs) we measured arterial spin labelling (ASL) (108 volumes, TR=5.3 seconds) and resting blood oxygen level dependent functional magnetic resonance imaging (fMRI) (180 volumes, TR=2 seconds) over the entire brain. Using SPM12, ASL images were realigned, cerebral blood flow maps calculated and spatially normalized to the Montreal Neurological Institute template. fMRI images were realigned, intensity normalized and spatially normalized to the Montreal Neurological Institute template. Significant differences in resting blood flow, as well as in hypothalamic connectivity were determined using a two-sample random effects procedure ($p < 0.05$ false discovery rate corrected and $p < 0.002$ respectively).

Results

There were significant decreases in cerebral blood flow in the period immediately preceding a migraine attack in the regions encompassing the lateral hypothalamus, visual cortex and retrosplenial cortex. Using a cluster of reduced blood flow as a seed, hypothalamic connectivity was assessed and decreases occurred only during the period preceding a migraine. Reductions in hypothalamic connectivity occurred in the rostral ventral medulla, midbrain periaqueductal gray, dorsal pons, spinal trigeminal nucleus and anterior cingulate cortex.

Conclusion

These findings provide evidence that in the 24-hour lead up to a migraine, the activity of the hypothalamus and descending pain modulatory system is disturbed. As the descending control of the trigeminal nociceptive pathway is altered, hyperexcitability develops along the trigeminovascular pathway. Further investigations exploring the role of the hypothalamus and its complex network preceding a migraine is needed.

A DYADIC PERSPECTIVE ON COPING WITH CHRONIC PAIN AND ITS EFFECTS ON RELATIONSHIP QUALITY AND PSYCHOLOGICAL DISTRESS

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Background and Aims

Dyadic coping is the process of coping that transpires between couples when challenged with a common stressor such as one partners' illness. Dyadic coping is intended not only to support the patient but also to maintain equilibrium in the relationship. There has been considerable conjecture on the role dyadic coping plays in couples' coping with chronic pain. Given that partners are often the primary caregivers and emotional support for patients; and make adjustments to their daily living and long-term life plans it is important to understand the process of dyadic coping from both patient and partners' perspective. This study applies the dyadic conceptualization of coping which recognizes the interdependence between intimate relationships. Aim. To examine the effect of dyadic coping on relationship quality and psychological distress, over time, from patient and their partner's perspective.

Methods

Recruitment: Members of Pain groups (e.g. Flemish Pain League) in Belgium were invited via a letter to participate. To be eligible patients had to be experiencing pain for at least 3 months and living together with a partner for more than a year. Three measurements over six months were collected from each couple. Measures: (i) Dyadic coping was measured using pain-specific Dyadic Coping Scale, (ii) Relationship quality was measured using Dyadic Adjustment Scale and (iii) Psychological distress was measured

using the Depression, Anxiety, Stress Scale. All couples' demographic information and patients' pain rating (using Graded Chronic Pain Scale) was also collected. Analysis. The effects of dyadic coping were examined together by treating data from both members of the dyads as a unit, using an innovative statistical model, the Actor-Partner Interdependence Model.

Results

139 couples participated, 82% of patients were female and 81% of partners were male. All couples identified as Caucasian, with 82% cohabitating, with mean length of relationship 25.2 years. The mean pain intensity for patients was 6.90 (SD= 1.41). Both patient and partner's relationship quality, was strongly associated with the patients' own perception of received dyadic coping. Similarly, both patient and partners' psychological outcomes, should strong association with patients' perception of received dyadic coping. Partner reported dyadic coping did not show statistically significant association with their own and patients' relationship quality, and patients' psychological distress.

Conclusions

As compared to partner report, patient perception of dyadic coping seemed to be a better predictor of patient and partners' relationship quality, and psychological outcomes, over time. These findings may have clinical implications, appropriate appraisal of patients' expectation from dyadic coping may be central to the couple's overall wellbeing. Incorporating interventions to teach adaptive and open communication skills to the couples may directly improve their individual psychological outcomes and indirectly their relationship quality.

MICROSTRUCTURAL CHANGES IN THE TRIGEMINAL NERVE OF INTERICTAL MIGRAINEURS

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Background and Aims

Migraine is a common debilitating neurological disorder affecting approximately 15% of the global population. While neuroimaging studies have revealed altered trigeminal nerve volumes and diffusivity in chronic pain conditions such as trigeminal neuralgia, the structure of the trigeminal nerve has not been explored in migraine sufferers. Evidence from one histological investigation, however, found that the altered structure of the zygomaticotemporal nerve in migraineurs may be indicative of disrupted axon alignment. This study aimed to determine whether structural alterations of the trigeminal nerve contribute to migraine pathophysiology. We hypothesised that the trigeminal nerve volume may be similar between the left and right trigeminal nerves of migraineurs and controls, but that indicators of altered fibre alignment such as free water diffusion will be reduced.

Methods

Thirty-nine subjects with migraine (mean age: 29.97 years, 29 females) and 39 healthy controls (mean age: 30.70 years, 23 females) were recruited for the study. In all subjects, T1-weighted anatomical images and diffusion tensor images (DTI) of fractional anisotropy (FA), mean diffusion (MD), axial diffusion (AX) and radial diffusion (RD) were collected. Using SPM12, these images were resampled and the left and right trigeminal nerves within the root entry zone were isolated. Using the T1 image, a volume of interest encompassing the trigeminal root entry zone was

created and the nerve volume (mm³) from each voxel inside this isolated region was extracted and averaged. Additionally, maximum coronal cross-sectional area value (mm²) was calculated from the cross-sectional volume of the nerve in each coronal slice. Further, DTI parameters were calculated from trigeminal nerve volumes. The nerve was divided into caudal, middle and rostral thirds based on voxel location in the coronal plane and the FA, MD, AX and RD values for the caudal, middle and rostral thirds of the trigeminal root entry zone were calculated.

Results

The left and right trigeminal nerve volumes revealed that the left nerve showed a significantly greater volume than the right nerve in both the control and migraine group. Additionally, MD, AX and RD were significantly greater in the left nerve compared to the right nerve of migraineurs. However, regional analysis of the trigeminal nerve revealed that FA differences between the left and right nerves of controls were significantly greater than that of the left versus right nerve in migraineurs in the middle and rostral segments of the nerve.

Conclusions

This data revealed that migraine pathophysiology may be associated with microstructural abnormalities in the trigeminal nerve. Migraineurs exhibit differences between the left and right nerve, however this change is not significantly different to the controls. Furthermore, migraineurs display microstructural alterations in FA which may be indicative of demyelination and/or axonal loss within the middle and rostral, more myelinated portion of the trigeminal nerve.

MUSCLE FUNCTION AND POWER BUT NOT MASS PROTECT AGAINST MORE SEVERE KNEE PAIN TRAJECTORIES

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Background and Aims

Evidence suggests that periarticular muscles have a role in the pathogenesis of pain, but results have not been consistent. We recently reported that pain population is heterogenous and consists of different subgroups of which the causes and mechanisms differ. Study has not been performed yet to investigate whether muscle function, power and mass are risk factors for worse pain trajectories. The aim of this study was to examine the association of leg strength, knee extensor strength, low-limb muscle quality (power), total and local muscle mass with knee pain trajectories over 10.7 years.

Methods

This study utilised the data from a population-based older adult cohort study. 1,099, 875, 768 and 563 participants attended baseline, follow-ups at Year-2.6, 5.1 and 10.7, respectively. Leg strength in both legs and dominant knee extensor strength were measured at baseline. Dual-energy X-ray absorptiometry was used to assess total muscle/fat and lower-limb muscle/fat mass. Low-limb muscle quality (power) was calculated (i.e. leg strength divided by lower-limb muscle mass). The Western Ontario and McMaster Universities Osteoarthritis Index pain questionnaire was used to measure knee pain at each time-point. Radiographic knee osteoarthritis (ROA) was assessed by X-ray. Group-based trajectory modelling was applied to identify pain trajectories. Multi-nominal logistic regression was used for the analyses.

Results

A total of 975 participants [Mean±SD: age 62.2±7.4 years, body mass index 27.8±4.6 kg/m² and 51% females] were included in the analysis. Three distinct pain trajectories were identified: 'Minimal pain' (53%), 'Mild pain' (34%) and 'Moderate pain' (13%). In multivariable analyses, both greater total and low-limb muscle mass were associated with an increased risk of 'Mild pain' [total muscle mass: relative risk (RR): 1.45 per SD increase, 95%CI: 1.11–1.90; low-limb muscle mass RR: 1.30 per SD increase, 95%CI: 1.05–1.61] and 'Moderate pain' [total muscle mass: RR: 2.09 per SD increase, 95%CI: 1.42–3.08]; low-limb muscle mass: RR: 1.65 per SD increase, 95%CI: 1.22–2.23] compared to the 'Minimal pain' trajectory group. After adjustment for fat mass, these associations disappeared. In relative to the 'Minimal pain' trajectory, leg strength, knee extensor strength and power were associated with a reduced risk of being in more severe pain trajectories after adjustment for covariates (RR=0.59 to 0.73 per SD increase, all P<0.05). Similar results were observed in those with ROA.

Conclusions

Muscle strength and power, but not mass are associated with a reduced risk of more severe pain trajectories, suggesting that loss of muscle function and power are of more clinically relevance to preventing the development and maintenance of worse pain trajectories. Disappeared association between muscle mass and pain trajectories after adjustment for fat mass indicates that detrimental effects of muscle mass on pain are caused by fat mass. These results underscore that training/exercise specifically for strength should be recommended to improve pain symptom in general practice.

IDENTIFICATION OF EFFECTIVE ANALGESICS FOR DYSTROPHIC EPIDERMOLYSIS BULLOSA (DEB)

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Background and Aims

Epidermolysis Bullosa (EB) is a group of genetic blistering skin disorders caused by mutations in genes encoding structural adhesion proteins within the skin. Pain is a major clinical problem that contributes substantially to the disease burden in EB, reducing quality of life of these patients. Due to the heterogeneous manifestation of pain and the ad hoc nature of analgesic prescribing, knowledge of the most effective analgesics in the treatment of EB-related pain remains limited. Using Col7a1 Δ mutant mice from a novel model for dominant dystrophic EB (DEB) (a major subtype of EB) that we recently developed and validated, we aimed to objectively compare the effectiveness of existing analgesics commonly used to treat EB-associated pain.

Methods

DEB mice were treated with different classes of analgesics currently used in EB patients including: buprenorphine, an opioid; meloxicam, a non-steroidal anti-inflammatory drug; and bupivacaine, a local anaesthetic, and paw withdrawal thresholds (PWTs, reported as mean \pm SEM) assessed in DEB and wildtype control mice using a standard von Frey assay.

Results

After 1 hour of systemic administration of 0.1 mg/kg buprenorphine (s.c.), PWTs of DEB mice (n=5) significantly (p \leq 0.0001) increased from a baseline value of 0.24 \pm 0.03 g to a post-treatment value of 0.67 \pm 0.06 g, with 41.2 % reversal of pain-like behaviour compared to wild-type controls. After 1 hour of systemic administration of 2 mg/kg meloxicam (s.c.), PWTs of DEB mice (n=5) significantly (p \leq 0.0001) increased from a baseline value of 0.22 \pm 0.03 g to a post-treatment value of 0.7 \pm 0.07 g, with 47.1 % reversal of pain-like behaviour. After 20 min of local administration of 0.1 % bupivacaine (i.pl.), PWTs of DEB mice (n=5) significantly (p \leq 0.0001) increased from a baseline value of 0.21 \pm 0.03 g to post-treatment value of 1.24 \pm 0.1 g, with 99 % reversal of pain-like behaviour. At the given doses, none of the drugs significantly affected the PWTs of wildtype control mice, suggesting absence of any impaired motor reflexes.

Conclusions

Analgesics currently used to treat EB-associated pain differ in their efficacy and potency. These data (and ongoing experiments in this area) are likely to inform and assist with more rational prescribing of analgesic drugs for the relief of EB-related pain, and also provide important mechanistic insights into the processes that are driving pain in this condition.

EMBEDDING LOW INTENSITY COGNITIVE BEHAVIOURAL THERAPY IN A TERTIARY CHRONIC PAIN SERVICE: A PILOT STUDY

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Background and Aims

Chronic pain affects 1 in 5 Australians in their lifetime, and costs billions of dollars annually in lost productivity and care. While providing adequate pain management remains difficult, with long waiting lists for specialist pain units, CBT-based pain management can improve pain, disability, and quality of life. Low-intensity CBT (LICBT) more accessible as it is administered via phone by various tertiary-trained professionals, and has reduced mental illness and improved functioning in chronic illness patients, but has not been trialled for chronic pain. The aim of our pilot study was to assess the effectiveness and feasibility of embedding LICBT within a chronic pain outpatients unit.

Methods

Clinical Masters students administer LICBT in-person or over-the-phone. Six manualised sessions address goal setting, psycho-education, brain retraining, weakening the pain cycle, activity scheduling, pacing, and thought disputation. We are trialling two LICBT modalities (using convenience samples): (1) following a mandatory pain education program and prior to further pain unit contact, to improve self-management (as a pilot 2-group parallel RCT); and (2) alongside pain unit appointments, to enhance standard care. Depression (using the PHQ9), anxiety (using the GAD7), pain catastrophising (using the PCS), and pain intensity/severity (using the BPI) are assessed at the start and end of therapy. Preliminary data are available for these 2 modalities: (1) 9

treatment-as-usual (66% female) and 3 LICBT (66% female) participants, and (2) 42 pain unit patients (64% female). Descriptive statistics, along with repeated measures t-tests for pain unit patients, have been calculated.

Results

For pain unit patients (n = 42), depression (M=14.21, SD=7.11, vs. M=11.36, SD=7.74), anxiety (M=11.83, SD=6.67, vs. M=9.31, SD=7.03) and pain catastrophising scores (M=29.59, SD=12.67, vs. M =21.82, SD=16.05) significantly (i.e., $p < .05$) decreased from pre- to post-LICBT, being small to moderate in effect size ($d = .37$ to $.54$). Pain severity and intensity showed very small, non-significant decreases. Results were similar when limiting analyses to those undertaking the recommended 6+ sessions (n = 22). RCT descriptive statistics appear to support these changes among LICBT participants, while treatment-as-usual scores remained the same/increased. Following education, uptake was low, and dropout high (80%), with LICBT more readily accepted alongside pain unit appointments. Patient and clinician feedback suggested many post-education patients were focussed on medical intervention and/or not in an active stage of change. Qualitative feedback patient highlighted several beneficial components of LICBT.

Conclusions

LICBT is a feasible and promising option for chronic pain sufferers, with results supporting improvements seen for other chronic illness sufferers. Psychological rather than functional benefits may reflect mechanisms of engagement/validation. Our ongoing RCT will provide more rigorous effectiveness results, including longer-term 'maintenance' outcomes.

THE DEVELOPMENT AND PSYCHOMETRIC EVALUATION OF A MULTIFACETED SELF-REPORT OVERACTIVITY ASSESSMENT IN CHRONIC PAIN

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The Australian eHealth Research Centre, CSIRO, Herston, Queensland

Background and Aims

Overactivity in the context of chronic pain (i.e. activity engagement that significantly exacerbates pain) is an important clinical issue that has gained empirical attention in the last decade. Current assessment concepts of overactivity tend to focus on merely frequency to quantify the severity of the pain behaviour. The aim of this study was to develop a more comprehensive self-report overactivity assessment tool, the Overactivity in Persistent Pain Assessment (OPPA), and examine its psychometric properties.

Methods

The overactivity concept was first deconstructed using theories, qualitative data and clinical observations. Five quantifiable and progressive severity features were identified: Severity of the Pain Exacerbation, Maladaptive Coping Strategies Used, Impact on Occupational Performance, Recovery Time and Frequency. A single-item format was adopted to quantify each of these five features in OPPA. After initial clinician and consumer feedback was gathered, a sample of 333 individuals with chronic pain completed the OPPA. A subset of 202 individuals also completed a set of existing measures of pain-related outcomes and activity patterns. The remaining 131 participants were provided with a second copy of the OPPA to fill in one week following their initial assessment. A principal component analysis (PCA) using direct oblimin rotation was

first conducted. Next, the construct validity of the OPPA was evaluated by correlating the OPPA scores to the scores of pain-related measures. A series of hierarchical linear regression models were also performed to evaluate whether the OPPA had superior ability to predict pain severity, pain-related disability and psychological functioning, when compared with the other existing overactivity scales after controlling for age, gender and activity avoidance. To examine the test-retest reliability of the OPPA, interclass correlation coefficients (ICC) with 95% confident intervals were calculated based on the 2-way mixed-effects model with absolute agreement. The internal consistency was calculated using Cronbach's alpha coefficient.

Results

The principal component analysis confirmed that the OPPA items were best represented by a single construct (labelled overactivity severity). The OPPA was found to correlate with pain-related measures in an expected way that is supported by both theory and qualitative data. When compared to existing overactivity measures, the OPPA was the only measure to contribute significantly to the regression models predicting higher levels of pain severity, more pain interference and lower levels of activity participation. In addition, the OPPA scale exhibited acceptable internal consistency and good test-retest reliability.

Conclusions

The results of this study reinforce the important role of overactivity in the maintenance of pain-related suffering and supports a corresponding assessment tool with preliminary psychometric evidence for clinical and research applications.

DIGITAL ABSTRACTS



2020 AUSTRALIAN PAIN SOCIETY 40TH ANNUAL SCIENTIFIC MEETING

In the IASP Global Year for the Prevention of Pain

It was disappointing that the accepted free paper and poster abstracts were not able to be presented at the 2020 ASM. Therefore, the APS Board and Scientific Program Committee are pleased to provide Members and interested delegates with another prominent means for these abstracts to be viewed.

APS 2020 Digital Abstracts Website

The APS offered all authors who had their abstract accepted, either as a free paper or poster, into the APS 2020 program the opportunity to have their presentation included in the APS 2020 Digital Abstracts Website (<https://aps2020.paperlessevents.com.au/>). Over 50 submissions are now available to view. These submissions will be online for the next 12 months.

Explore, connect, discover – and enjoy.

2020 APS DISTINGUISHED MEMBER AWARD



A/Prof David Champion AM

*A/Prof G David Champion AM
MBBS, MD, FRACP, FFPANZCA*

Associate Professor G David Champion AM has had a singular career. Well-known for his clinical evolution from rheumatologist to clinical pharmacologist to pain physician. In adult, and especially paediatric spheres, what distinguishes David is his remarkably long-term involvement in research while working full-time in private practice – a very uncommon combination in the modern era. As a private practicing physician, it was brave and costly to spend long hours on unpaid research. However, David is the first to acknowledge that his achievements and publications reflect collaboration and teamwork. Less than 10% of his personal contribution to research since 1975, almost 140 listed publications, has been funded externally; the remainder has been pro bono.

David established the modern Department of Rheumatology at St Vincent's Hospital, Sydney, in 1974. Having trained also in paediatric rheumatology in the UK and the USA, David began a Paediatric Rheumatology Clinic at Prince of Wales/Sydney Children's Hospital in 1975, collaborating with Prof John Ziegler and Dr John Feller, and continued that for about 35 years.

In 1986, David founded the Pain Research Unit at Sydney Children's Hospital. The early focus of this group was primarily children's self-report and behavioural measures of pain intensity. Its first publication, in 1990, introduced the internationally acclaimed Faces Pain Scale which became a classic citation - the third most cited publication in paediatric pain between 1975 and 2010. The derivative paper, developed in collaboration with Canadian colleagues, established the international standard of paediatric pain measurement (The Faces Pain

Scale – Revised: toward a common metric in pain measurement. *Pain* 2001; 93:173-183). Over many years, the team used the needle pain model for examining child and parental influences on children's pain outcomes. Children's ability to draw distinction between pain-related anxiety and pain intensity was considered. The team found parental influences on pain-related distress following immunisation injections to be strongly evident as early as 4 to 6 months of age, and that brief parental guidance could improve outcomes. Under David's leadership, the now internationally recognised Unit's research interests diversified into areas such as twin studies in paediatric pain, children's attention and distraction, information provision, somatosensory testing in children, and pain and the family. He was a co-convenor of the 6th International Symposium on Paediatric Pain in Sydney in 2003.

In 1998, David was awarded a Doctorate in Medicine from the University of Sydney on the basis of his published work in the pharmacology and therapeutics of rheumatic disease – again achieved from outside hospital- or university-based academic structures. In 1999, he was inducted as a Foundation Fellow of the Faculty of Pain Medicine of the Australian and New Zealand College of Anaesthetists. Since 2003, he has held a conjoint appointment as Associate Professor in the School of Women's and Children's Health at UNSW Sydney. In 2008, David retired from adult medical private practice, maintaining a medicolegal practice in pain medicine that – characteristically – has also spawned a research component.

This long-standing clinical and research activity has been the source of David's prolific presentations at Australian Pain Society (APS) meetings over more than three decades, on

ANNUAL GENERAL MEETING (AGM)



THE
AUSTRALIAN
PAIN SOCIETY

**will be held via Zoom video conference
from 5:30 – 6:30pm AEST
on Thursday 28 May 2020**

A General Business Meeting (GBM) will immediately follow the AGM.

The AGM Information Pack was emailed to members and includes:

- Notice of AGM
- AGM Agenda and following GBM Agenda
- Proxy Form
- Minutes from previous AGM and GBM
- Office Bearer Nominee Information
- APS constitution, adopted on 10 April 2019
- By-Laws to support the APS constitution

The financial accounts for the year ended 31 December 2019 are available on the Members Only area of the APS website.

If you are unable to attend the AGM please send your apology via the RSVP link sent by separate email and proxy form to the Secretariat by email to aps@apsoc.org.au by 5:30pm AEST Tuesday 26 May 2020.



2021 AUSTRALIAN PAIN SOCIETY 41ST ANNUAL SCIENTIFIC MEETING

In the IASP Global Year Against Back Pain

18 - 21 April 2021 • National Convention Centre Canberra, ACT

APS 2021 will be held from 18-21 April 2021 at the National Convention Centre, Canberra.

Please visit the conference website here:
www.dconferences.com.au/aps2021

Further information on APS 2021 will be sent out in the coming months, but we have some exciting speakers already confirmed and we can't wait to catch up with you all next year.

IMPORTANT DATES FOR YOUR DIARY

Wednesday 8 July

Topical Session Submissions Open

Wednesday 29 July 2020

Rising Star Award Applications Open

SPC Scholar Position Applications Open

Free Paper/Poster Abstract Submissions Open

Wednesday 4 November 2020

Registrations Open

If you have any questions please contact the APS Conference Secretariat: aps2021@dconferences.com.au