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The predictive relationship between activity change and functional disability in acute low back pain: A prospective cohort study. P Hendrick¹, L Hale¹, M Bell², S Milosavljevic¹, D Hurley-Osing³, S McDonough⁴, D Baxter¹. ¹Centre for Physiotherapy Research, School of Physiotherapy, University of Otago, ²Department of Preventive and Social Medicine, Dunedin School of Medicine, University of Otago, ³School of Physiotherapy and Performance Science, University College Dublin, Ireland, ⁴Health & Rehabilitation Sciences Research Institute, School of Health Sciences, University of Ulster, Northern Ireland.

Activity advice and prescription are commonly used in the management of low back pain (LBP). However, no research has assessed whether objective measurements of physical activity predict outcome, recovery and course of LBP.

One hundred and one patients with acute LBP were recruited. Activity levels at baseline and 3 months were measured with an RT3 triaxial accelerometer and the Seven Day Physical Activity Recall (7d-PAR) Questionnaire (n = 83). Habitual activity levels prior to the onset of LBP and at 1 year were measured with Baecke Physical Activity Questionnaire (BPAQ). Each participant completed the following LBP outcomes: Roland Morris Disability Questionnaire (RMDQ), Visual Analogue Scale (VAS) pain measurement and a “simple” activity question, detailing resumption of “normal” activities (Y/N), at baseline and 3 months. At 1 year seventy seven participants returned completed VAS, RMDQ, BPAQ and modified Nordic LBP Questionnaires.

There was no significant change in activity levels measured with the RT3 ($P = 0.56$) or the 7d-PAR ($P = 0.43$) from baseline to 3 months or BPAQ activity levels from baseline to 1 year ($P = 0.70$). Objective physical activity change (RT3) did not predict RMDQ change in multivariate analysis at 3 months ($P = 0.84$) or 1 year ($P = 0.77$). A patient report of a return to full “normal” activities at 3 months ($P < 0.0001$) predicted RMDQ change at 3 months. A higher VAS score at 3 months ($P = 0.02$) predicted chronic LBP (Nordic LBP Questionnaire) at 1 year.

None of the objective or questionnaire activity measures at baseline, 3 months or 1 year predicted functional recovery in acute LBP. These results question the role of activity in LBP recovery and stress the importance of the patient’s perception of activity ‘normalisation’ in recovery from acute LBP.

Effectiveness of a sleep hygiene programme, developed with youths, on sleep hygiene, daytime somnolence, sleep quality and body mass index. E Tan, B Galland, P Cleland, C Lobb. Department of Women's and Children's Health, Dunedin School of Medicine, University of Otago, Dunedin.

Childhood sleep disturbance, often due to poor sleep hygiene (or habits), can negatively impact on daytime functioning. Although effective, few sleep hygiene interventions target youth specifically and none, as we know, have been developed in consultation with youth. We aim to evaluate the effectiveness of a novel 20 week F.E.R.R.E.T (an acronym for Food, Emotions, Routine, Restrict, Environment and Timing) sleep programme, developed in consultation with 21 youths, in improving sleep, sleep hygiene and daytime functioning.

Youths (aged 10-18 years) with self-identified sleep problems (e.g. initiating and/or maintaining sleep) were recruited and the programme delivered by one researcher. An education pack, ongoing telephone and outpatient support was provided. Participants completed the Pediatric Daytime Sleepiness Scale (PDSS), Adolescent Sleep Hygiene Scale (ASHS) and Pittsburgh Sleep Quality Index (PSQI) twice before (5 and 1 week) and three times after intervention (6, 12 and 20 weeks). Body mass index (BMI) Z-scores were also obtained.

Thirty-three youths (mean age 12.9 years; M/F = 1.2) enrolled and retention was 100%. We found significant improvements in daytime sleepiness, sleep hygiene and sleep quality. PDSS scores (mean = 16.69) improved (-4.87, 95% confidence interval or CI -6.45 to -3.29; $P < 0.001$) as did ASHS scores (mean = 4.72) post-intervention (0.20, CI 0.07 to 0.32; $P = 0.002$). PQSI scores (mean = 7.75) also improved (-3.16, CI -3.90 to -2.42; $P < 0.001$) after intervention. BMI Z-scores (mean = 0.8) decreased significantly post-intervention (-0.13, CI -0.20 to -0.05; $P = 0.001$), despite no height change.

The F.E.R.R.E.T sleep programme is effective in improving sleep and daytime sleepiness, and might prove feasible for weight management as seen in the BMI reduction - we will now target obese youth, a group which often experience disturbed sleep. The consultation process might have accounted for the positive outcomes and high retention.

Direct regulation of *c-Myc* by cohesin. J Rhodes, F Bentley, J Horsfield. Department of Pathology, Dunedin School of Medicine, University of Otago, Dunedin.

Cohesin is a multi-protein complex that plays an essential role in sister chromatid cohesion. Recently it has emerged that cohesin also functions in regulating gene expression, sometimes in combination with CCCTC-binding factor (CTCF). Our work has revealed that cohesin positively regulates the *c-Myc* oncogene. In zebrafish, loss of cohesin subunits *rad21* and *smc3* reduced the transcription of *myca* (zebrafish *c-Myc*), indicating that cohesin is required for normal *myca* expression. Cohesin regulation of *c-Myc* is conserved in *Drosophila*, mouse and human. We aim to understand the mechanism by which cohesin regulates *myca* expression.

Chromatin immunoprecipitation (ChIP) performed on 1-day-old zebrafish embryos revealed that the Rad21 subunit of cohesin binds to the transcriptional start site of *myca* (4.4 ± 0.5 , fold enrichment relative to site where no Rad21 binding is predicted \pm SEM) and an upstream CTCF binding site (8.9 ± 1.9). Although CTCF has been shown to recruit cohesin, Rad21 still bound these sites in *ctcf* knockdown embryos in which *myca* expression was unaltered. Greater enrichment of Rad21 was detected at the upstream site in the absence of *ctcf* ($P = 0.0098$, two sample *t*-test, $n = 5$).

To determine if the Rad21 binding site upstream of *myca* affects chromatin structure at the *myca* locus, ChIP was performed using antibodies specific for active and repressive histone modifications. From 10 kb upstream of *myca* to the start of the gene, there was no difference between the chromatin structure of *rad21* mutants and wild type embryos. However, repressive chromatin marks (reduced acetylated H3K9 and increased trimethylated H3K27) were observed at the transcriptional start site of *myca* in *rad21* mutant embryos.

In conclusion, the regulation of *myca* by cohesin is direct and appears to be independent of CTCF. Down-regulation of *myca* transcription by cohesin depletion is associated with repressive histone marks at the *myca* gene.

A model system for heterologous expression of cysteine-rich secretory proteins, antigen 5 and pathogenesis-related group 1 proteins in *E. coli*. A Nguyen¹, T Milne², B Monk², J Tyndall¹. ¹National School of Pharmacy, ²Department of Oral Sciences, Faculty of Dentistry, University of Otago, Dunedin.

The Cysteine-rich secretory proteins, Antigen 5 and Pathogenesis-related 1 proteins (CAP) superfamily appears ubiquitous in eukaryotes. Most CAP proteins are multidomain proteins rich in disulfide bonds. Some CAP proteins are proposed to have essential roles in mammalian reproduction, others have been linked to gliomas and prostate cancer, but their biochemical functions are poorly understood. Tex31, a protein isolated from the venom of *Conus textile* (Cloth of gold cone), is the only CAP member identified with an enzymatic activity. In an effort to further understand the structure and function of CAP proteins, we have expressed the pathogenesis-related domain of Tex31 (PRD_{Tex31}) in soluble form.

PRD_{Tex31}, the N-terminal truncated PRD (NdelPRD_{Tex31}) and the disulfide mutant constructs of NdelPRD_{Tex31} were heterologously expressed in *E. coli* strain DH5 α using maltose-binding protein (MBP) as a fusion partner and purified using amylose-affinity chromatography and size-exclusion chromatography (SEC). A significant fraction of each Tex31 chimera (~80%) was affinity-purified. Disulfide bonds in the PRD_{Tex31} constructs caused the formation of aggregated soluble complexes. Ablation of a specific disulfide bond in recombinant NdelPRD_{Tex31} constructs plus the addition of the mild detergent n-dodecyl- β -D-maltoside together with sonication prior to SEC eliminated small heat-shock proteins IbpA/B from the preparation and 50% of the MBP-NdelPRD_{Tex31} was recovered in soluble, monodisperse form. Crystallisation of MBP-NdelPRD_{Tex31} using hanging-drop vapour-diffusion gave non-diffracting, 10 – 30 μ m diameter crystals within 6 weeks. Optimisation of crystallisation conditions for MBP-NdelPRD_{Tex31} chimeras is needed to obtain crystals that produce suitable X-ray diffraction data.

This expression protocol can now be applied to other members of this protein superfamily in an effort to understand their function.

Permanent spatial memory deficits after bilateral vestibular deafferentation and the effects of cannabinoids. J-H Baek, Y Zheng, C Darlington, P Smith. Department of Pharmacology and Toxicology, Otago School of Medical Sciences, University of Otago, Dunedin.

Previous studies of rats with bilateral vestibular deafferentation (BVD) have demonstrated spatial memory deficits. In this study, we investigated whether rats exhibited spatial memory deficits at 14 months following BVD and whether these deficits could be exacerbated by the administration of cannabinoid (CB) drugs.

Twenty-eight adult rats were divided into 4 groups: 1) sham surgery + vehicle (n = 8); 2) sham surgery + the CB₁/CB₂ receptor agonist WIN55,212-2 (WIN) (n = 7); 3) BVD + vehicle (n = 6); and 4) BVD + WIN (n = 7). WIN, at a dose of 1 or 2 mg/kg/day, or vehicle was administered (s.c.) on days 1 – 10 and 11 – 20 (respectively), 30 min before the rats performed in a foraging task to test spatial memory.

Unexpectedly, the BVD animals were impaired in using the visual cues in the light during the probe trial, where the home location was changed to a novel position. Sham animals made significantly more visits to the old home compared to the BVD animals ($P = 0.02$, ANOVA). In the dark, when visual cues were unavailable, BVD animals were unable to use self movement cues to remember the correct home location ('homing'), which was demonstrated by their significantly longer homing distance and time (both $P = 0.000$, ANOVA). Whereas the sham animals had a clear orientation toward the correct home ($P < 1 \times 10^{-12}$, Rayleigh's test), BVD animals did not. However, WIN at 2 mg/kg/day significantly reduced the homing time ($P = 0.000$, ANOVA) and number of errors ($P = 0.004$, ANOVA) of BVD animals.

These results suggest that at 14 months post-BVD, the animals are not only impaired in a spatial memory task when visual cues are unavailable, but even when they are available. The involvement of the CB system is more complicated than expected.

Lessons for patient safety in primary care from the 'no-fault' treatment injury database. K Wallis, S Dovey. Department of General Practice and Rural Health, Dunedin School of Medicine, University of Otago, Dunedin.

Legislative reforms in 2005 removed 'error' from medical injury compensation in New Zealand and provided for the creation of a unique 'no-fault' treatment injury database. This study aimed to analyse the first four years of data from the 'treatment injury' claims database to identify targets for improvement in patient safety in primary care.

There were 6007 primary care treatment injury claims lodged and 3853 were accepted (64%). Most claims were 'minor' (83%), but there were 729 'major' (12%), 244 'serious' with 'the potential to result in death or permanent loss of function' (4%), and 58 'sentinel' 'resulting in death or major permanent loss of function' (1%). 'Serious'

and 'sentinel' events are reported to the Director General of Health and sometimes also the Medical Council or Medsafe. Medication caused most injuries (45%) and most 'serious' and 'sentinel' events (62%). Injuries included haemorrhage from warfarin (13), renal failure (7) and gastric bleeds (5) from anti-inflammatory drugs, strokes (4), thromboembolism (3) from oral contraceptives, avascular necrosis from steroids (7) and pulmonary fibrosis from nitrofurantoin (5). 'Injections and vaccinations' caused 12% of injuries and 11% of 'serious' and 'sentinel' events. Delay / failure to diagnose caused few injuries overall (2%) but a disproportionate number of 'serious' and 'sentinel' events (15%) for missed cancer (15), infection (6), testicular torsion (5), and fatal cardiac conditions (4). Spinal / neck manipulation by chiropractors and physiotherapists caused 3% of injuries and 2% of the 'serious' and 'sentinel' events including strokes (4). Ear syringing caused 3% of injuries including 78 perforated eardrums.

Analysis of the treatment injury database identifies targets for improvement in patient safety in primary care. Information about the type, prevalence and impact of injury can be used to guide injury prevention initiatives and educate practitioners about the dangers and pitfalls in practice and also to inform 'consent' discussions with patients.