



New light on bone formation in CRPS?

MAY 13, 2014 BY [BIM](#)

The variability of signs and symptoms of Complex Regional Pain Syndrome (CRPS), may represent between-patient variability in the pathological mechanisms at work. One often forgotten CRPS feature is impaired bone formation yet this has been found in up to fifty percent of patients regardless of disease duration [1]. German Surgeon Paul Sudeck (1866-1945), one of the founding fathers of CRPS, first described impaired bone formation in cases he called “Acute Inflammatory Bone Atrophy” [2]. Recently, Kramer et al. [3] have given



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HELP NEEDED FOR PAIN RESEARCH SURVEY

Please consider taking this online survey to help close the gap in our understanding of pain. You are likely eligible if you over 18 and suffer from neck pain, whiplash, low back pain, fibromyalgia, rheumatoid arthritis, migraines (will take only 15-minutes).

If you have no current pain or history of persistent pain (a pain problem that lasted more than 3 months) then you are also eligible to take the survey as a control subject (takes 5-minutes only).

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this idea impetus with their discovery of elevated markers for bone remodelling in CRPS patients. They found that Osteoprotegerin (OPG) levels were significantly increased in CRPS patients than in either healthy controls or patients with a fracture, but without CRPS.

Osteoprotegerin protects the skeleton from excessive bone destruction [4], but the role of OPG does not stop there. OPG is closely involved in reducing NF- κ B activation [4]. NF- κ B is a key factor in the inflammatory response to tissue damage and is thereby involved in general physiological mechanisms that play a role in CRPS, such as inflammation, oxidative stress and sensitization [5]. Mind you, just like inflammation, oxidative stress and sensitization, OPG upregulation is what is *supposed* to happen after trauma. It is the exaggerated nature of the response in CRPS that causes us to view these mechanisms as pathologic. In a sense, the increased levels of OPG in CRPS might be sign of a counter reaction to a derailed inflammatory response. Therefore, the findings of Krämer et al. may have to be viewed in a broader context. Other biomarkers supposed to

survey.

REHABILITATION FOR CRPS. WHAT DOES CURRENT CLINICAL PRACTICE LOOK LIKE?

Researchers at Brunel University London and the University of Oxford are conducting a survey to try to get a sense of what therapists involved in the rehabilitation of patients with complex regional pain syndrome (CRPS) do with their patients. The need for this research is clear. All recent international clinical guidelines recommend rehabilitation therapies as the core treatment for CRPS, yet there is little clinical evidence to guide practice. If we are to develop a clear model of best practice and rigorously evaluate it then we first need a clearer sense of what current practice is.

So if you are a clinician currently working in a rehabilitation context and you are currently involved in the management of patients with CRPS (types I or II) then it would be great if you could take the time to complete our survey which can be found here:

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play a role in CRPS, including TNF- α , IL-1, IL-6 [6], glutamate and glycine [7] and possibly many others we have yet to investigate, need to be included in a balanced approach to the assessment of mechanisms underpinning the clinical manifestation of CRPS patients. In addition, it is important to establish whether these findings also apply to CRPS patients with other limb trauma such as sprains, minor lesion or even spontaneous onset.

Notwithstanding these questions, Krämer et al's findings lend support to existing treatments that address the exaggerated inflammatory response and altered bone remodeling in CRPS, such as free radical scavengers, corticosteroids [8] and bisphosphonates [9], although the evidence for these treatments remains inconsistent. Furthermore, we should not forget the very important role of activity and weight bearing exercise for CRPS patients which may serve to activate bone formation processes related to this pathway.

About Roberto Perez

Roberto Perez was trained as a physical

[Go to the CRPS Rehabilitation survey here.](#)

CONGRATULATIONS TO DR TASHA STANTON, SOUTH AUSTRALIA'S TALL POPPY!

We are all very proud here at BiM to announce to the world that Dr Tasha Stanton has been judged South Australia's Tall Poppy for 2015.

The Tall Poppy Campaign was created in 1998 by the Australian Institute of Policy and Science (AIPS) to recognise and celebrate Australian intellectual and scientific excellence and to encourage younger Australians to follow in the footsteps of our outstanding achievers.

It has made significant achievements towards building a more publicly engaged scientific leadership in Australia. Congratulations to Tasha for what is a thoroughly deserved recognition of her outstanding contributions.



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therapist and human movement scientist and is currently Associate Professor for pain, pain therapy and palliative care research at the **Anesthesiology department of the VU University Medical Center in Amsterdam**, The Netherlands. His fields of expertise are in chronic pain (in particular CRPS and neuropathic pain) and palliative care, with a focus on clinical patient based research, diagnostic and clinimetric aspects of pain and palliative care. He is chairman of the taskforce for the development of multidisciplinary guidelines for CRPS in The Netherlands. He is also a member of the steering committee of the knowledge consortium TREND, where he is program leader for clinical trials. In addition Roberto is also a steering committee member of NeuroSIPE and NeuroControl, and a faculty member of the special Interest Group “Complex Regional pain Syndrome” of IASP. In his spare time Roberto plays double bass and soccer, although his enthusiasm for these substantially exceeds his skill.

References



Dr Tasha Stanton posing with His Honour Justice AO, Governor of South Australia

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The Art of Pain was a great success. You can listen to **Professor Michele Sterling's excellent talk on whiplash by clicking here**

DO YOU HAVE BACK PAIN? WE NEED YOU!

We are looking for people who have back pain that has persisted for more than 3 months. Our study in Adelaide is investigating the relationship between chronic back pain and poor sleep, and the contributions of general mood and beliefs about pain.

We are asking that you complete a questionnaire about your general health, pain and sleep characteristics.

[1] Veldman, P., Reynen, H., Arntz, I., & Goris, R. (1993). Signs and symptoms of reflex sympathetic dystrophy: prospective study of 829 patients *Lancet*, *342* (8878), 1012-1016 DOI: [10.1016/0140-6736\(93\)92877-V](https://doi.org/10.1016/0140-6736(93)92877-V)

[2] Sudeck P (2005). On acute inflammatory bone atrophy. *Hand Surg Br*, *30* (5), 477-81 PMID: [16122585](https://pubmed.ncbi.nlm.nih.gov/16122585/)

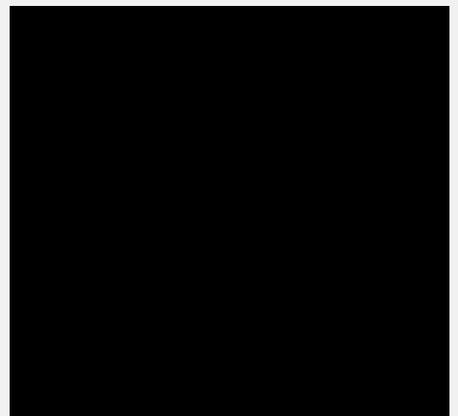
[3] Krämer HH, Hofbauer LC, Szalay G, Breimhorst M, Eberle T, Zieschang K, Rauner M, Schlereth T, Schreckenberger M, & Birklein F (2014). Osteoprotegerin: A new biomarker for impaired bone metabolism in complex regional pain syndrome? *Pain*, *155* (5), 889-95 PMID: [24447513](https://pubmed.ncbi.nlm.nih.gov/24447513/)

[4] Boyce, B., & Xing, L. (2007). Biology of RANK, RANKL, and osteoprotegerin *Arthritis Res Ther*, *9* (Suppl 1) DOI: [10.1186/ar2165](https://doi.org/10.1186/ar2165)

[5] de Mos M, Laferrière A, Millecamps M, Pilkington M, Sturkenboom MC, Huygen FJ, Coderre TJ. Role of NFkappaB in an animal model of complex regional pain syndrome-type I (CRPS-I). *J Pain*

You will also be asked to wear a wristwatch type device that records your activity levels for one week while also maintaining a pain and sleep diary. If you choose to participate, you will be given a report on your sleep quality. This research has been approved by the UniSA Ethics Committee Ref. 0000033839 "Chronic Back Pain and Sleep study".

If you are interested, please contact Danny on 8302 1432 or email danny.camfferman@unisa.edu



2009; 10: 1161-9

[6] Heijmans-Antonissen C, Wesseldijk F, Munnikes RJ, Huygen FJ, van der Meijden P, Hop WC, Hooijkaas H, & Zijlstra FJ (2006). Multiplex bead array assay for detection of 25 soluble cytokines in blister fluid of patients with complex regional pain syndrome type 1. *Mediators Inflamm*, 2006 (1) PMID: [16864900](#)

[7] Wesseldijk F, Fekkes D, Huygen FJ, van de Heide-Mulder M, & Zijlstra FJ (2008). Increased plasma glutamate, glycine, and arginine levels in complex regional pain syndrome type 1. *Acta Anaesthesiol Scand*, 52 (5), 688-94 PMID: [18419723](#)

[8] Fischer, S., Zuurmond, W., Birklein, F., Loer, S., & Perez, R. (2010). Anti-inflammatory treatment of Complex Regional Pain Syndrome *PAIN*, 151 (2), 251-256 DOI: [10.1016/j.pain.2010.07.020](#)

[9] Marinus, J., Moseley, G., Birklein, F., Baron, R., Maihöfner, C., Kingery, W., & van Hilten, J. (2011). Clinical features and pathophysiology of complex regional pain syndrome *Lancet Neurol*, 10 (7), 637-648 DOI: [10.1016/S1474-4422\(11\)70106-5](#)



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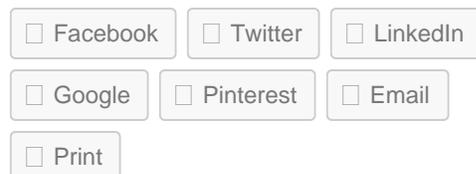
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PARTICIPANTS NEEDED – ADELAIDE

Do you live in Adelaide? Are you female between 25 and 70 and have good hearing? Do you have fibromyalgia or would you like to help someone who has by being a participant in a very

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Comments

stuart miller says:

May 14, 2014 at 1:41 pm

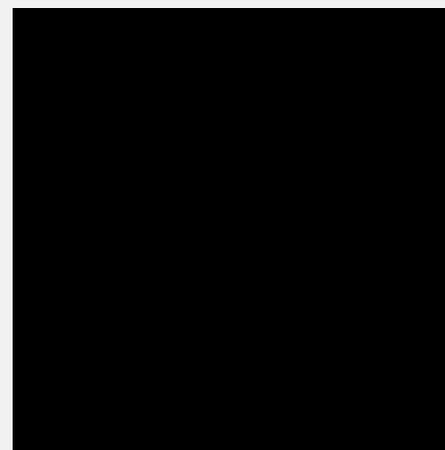
Roberto, thanks for this interesting study from Kramer. Would there be increased OPG upregulation in patients post stroke with disuse and dependent edema ? Does facilitated neurogenic inflammation dictate the response ? I think that Neil O'Connell's systematic review didn't lend support to corticosteroids but did for bisphosphonates. Any updates on the randomized, double-blind placebo controlled study by Varenna (2013) on treatment of CRPS type 1 with neridronate ? Has this led to any improvement in treatment ? Finally, activity is important but getting under the radar to recognize that movement despite the pain is a good strategy is a tough sell as is increasing weight bearing with swollen joints (except with slow graded progression: brain exercises -> physical exercises sometimes) – how would you utilize this new finding re OPG upregulation in your education

interesting and painless study we are conducting at the University of South Australia.

The study examines sensory processing in people with fibromyalgia and those without by recording your eye blink responses to some sounds. You also need to complete several questionnaires that ask about your health and well-being so we need up to 2 hours of your time.

Compensation of \$20 per hour up to a maximum of 2 hours is offered. If you are interested, please contact Carolyn.berryman@unisa.edu.

BRAINMAN STOPS HIS OPIOIDS



BRAINMAN CHOOSES



(especially when it is supposedly a response to trauma) ?

stuart miller says:

May 24, 2014 at 1:01 pm

Roberto, if OPG up regulation prevents bone destruction then is it protective (homeostatic) ?

Sandra Martineau says:

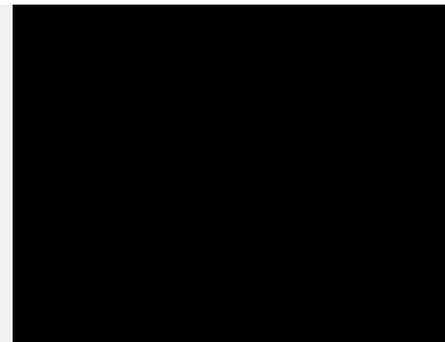
July 8, 2014 at 3:54 am

Is CRPS actually a protective (immune related?) response to trauma (or suspected/assumed trauma) that has gone awry in some people?

That makes a lot of sense, and so do a lot of CRPS symptoms when you consider their potential uses as warning of danger in our early days of development as a species, I am not just talking about the flight or flight system (SNS) but even the types of pain patients with CRPS feel.

I have CRPS myself for 9 years now and I read all the research I can find and pass on any breaking news and new (requested) research to people with CRPS on a Facebook page.

We have over 7500 members who read the links we provide that lead to great sources of information such as the above explanation of



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- [Jennifer Gait](#) on [Art of Pain Exhibition is a hit;](#)

the published Kramer research.

I can say for all of us, that we very much appreciate write ups like these, thank you.

_ Sandra Martineau
RSD/CRPS R&D.

'Whiplash – to treat or reassure?'

 **MOTORIMPAIRMENT BLOG**

- **Knee extensor power as it relates to mobility performance in people with knee osteoarthritis**

Osteoarthritis (OA) is a chronic, progressive condition characterized by a loss of articular cartilage and leads to chronic pain, disability and psychological effects in adults living with the disease. As there is no cure, researchers are concerned with identifying modifiable factors that could improve physical and psychological functioning for adults suffering with OA. The knee [...]

- **Does deep brain stimulation improve balance in people with Parkinson's disease?**

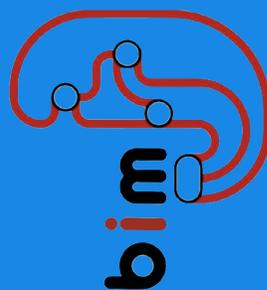
Poor balance is common in people with Parkinson's Disease (PD). This can significantly impact on quality of life. The ability to generate a step quickly and accurately after a loss of balance is critical to avoid falling. The most effective medical treatment for PD

(levodopa) seems to offer no benefit to these balance responses (King [...])

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