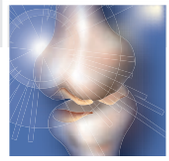
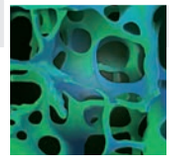


Bulletin Board

Cognitive behavioral therapy improves sleep and pain in people with osteoarthritis

Results published in the Journal of *Clinical Sleep Medicine* revealed that a successful treatment for older patients with osteoarthritis and comorbid insomnia is behavioral therapy for insomnia (CBT-I).

Cognitive behavioral therapy is a form of psychotherapy that emphasizes the important role of thinking in how we feel and what we do. Patients with osteoarthritis and comorbid insomnia were reported to have responded well to the therapy and both their immediate and self-reported sleep appeared to without directly addressing pain control. Patients demonstrated significant decreases in sleep latency and wake after sleep onset; reduced pain was observed and sleep efficiency rose.

The study was carried out using a comparative method involving 23 patients with an average age of 69 who were treated by CBT-I and 28 patients, with a mean age of 66.5 years, were treated through stress management and wellness control group. All patients were required to be over 55, demonstrate insomnia symptoms and have been diagnosed with osteoarthritis. The control group was reported to have no significant improvements.

Michael Vitiello, leading author and a professor at the University of Seattle, WA, USA, claims that insomnia and osteoarthritis are coexisting diseases as opposed to the common perspective that insomnia is a symptom of osteoarthritis. He explained that if you improve sleep, this will have a knock-on-effect and improve osteoarthritis. Insomnia, at least in adults, generally does not exist on its own and rather coexists with other illnesses and depression. For this reason, if patients are able to improve their sleep this will have a long last effect on their illness. Vitiello added "study after study has shown that the improvement persists for a year or more."

The CBT-I regime were made up of 8 weekly 2 hour classes, which were spread throughout the calendar year in an academic medical center. Sleep and pain were reviewed through self-report at the beginning of the treatment and at the end of one year.

Initially sleep latency dropped by 16.9 minutes and a year after treatment it was found to have decreased by 11 minutes. Wake after sleep onset was initially reduced by 37 minutes, which also dropped to 19.9 minutes a year after treatment. Pain improved by 9.7 points initially and 4.7 points a year later and sleep efficiency increased by 13 and 8% a year on. These sustained improvements were observed in 19 out of 23 patients that received CBT-I.

The study described sleep quality as a central concern for patients suffering from osteoarthritis and indicated that 60% of people suffering from the disease experienced sleep disturbance during the night due to chronic pain. This in turn caused prolonged sleep disturbance as the insomnia maintained the feeling of pain.

Vitello believes that CBT-I could be incorporated into behavioral interventions for pain management in osteoarthritis. He concluded by explaining that the treatment of sleep disturbance could ultimately improve the quality of life for patients with chronic pain conditions.

Source: Vitiello MV, Rybarczyk B, von Korff M, Stepanski EJ: Cognitive behavioral therapy for insomnia improves sleep and decreases pain in older adults with co-morbid insomnia and osteoarthritis. *JCSM* 5(4), 355–362 (2009).

http://www.nacbt.org/whatiscbt.htm

in the news...

IRF-8 protein thought to be involved in causing gum disease, osteoporosis and arthritis

The interferon regulatory factor-8 (*IRF-8*) gene has been found to be involved in diseases including periodontitis (gum disease), rheumatoid arthritis and osteoporosis. Scientists at the Hospital for Special Surgery, New York, USA, collaborating with researchers from other institutions, published their findings in *Nature Medicine*.

Dr Baohong Zhao, the lead author of the study, explained that the discovery "…doesn't have immediate therapeutic applications, but it does open a new avenue of research that could help identify novel therapeutic approaches or interventions to treat diseases'.

It was demonstrated that by downregulating the gene, which codes for the IRF-8 protein there was an increase in proliferation of cells called osteoclasts. Osteoclasts are cells responsible for breaking down bone and osteoblasts for the formation of bone. These two types of cell work closely to remodel and fortify bone tissue. Consequently, if there is an increase in osteoclast development, canals and cavities can form causing diseases such as periodontitis, osteoporosis and rheumatoid arthritis.

Reserachers demonstrated that *IRF-8* expression in osteoclast precursors was downregulated during the initial phase of osteoclast differentiation induced by receptor activator of nuclear factor-κB ligand (RANKL), which is encoded by the *Tnfsf11* gene.'

The scientists used microarray technology to identify the downregulation of the *IRF-8* gene. *IRF-8* expression was reduced by 75% in the primary stage of osteoclast formation.

The researchers demonstrated this using *IRF-8* deficient mice; when analyzed, the mice were found to have decreased bone mass and severe osteoporosis. While there was no decrease in osteoblast numbers, there was seen to be a significant decrease in osteoclast numbers.

Enhanced levels of oesteoclasts were also observed in humans when IRF-8 mRNA in human osteoclast precursors was silenced. Moreover, in the absence of *IRF-8*, NFATc1, a protein that interacts with *IRF-8*, appeared to lose its function and no longer be expressed.

"We hope that the understanding of this gene can contribute to understanding the regulatory network of osteoclastogenesis and lead to new therapeutic approaches in the future" Zhao concluded.

Source: Zhao B, Takami M, Yamada A *et al.*: Interferon regulatory factor-8 regulates bone metabolism by suppressing osteoclastogenesis. *Nat Med.* 15(9), 1066–1071 (2009).

About the Bulletin Board

The Bulletin Board highlights some of the most important events and research in the field of rheumatology.

If you have newsworthy information, please contact:

Christine Forder, Commissioning Editor,
International Journal of Clinical Rheumatology, Future Medicine Ltd,
Unitec House, 2 Albert Place, London N3 1QB, UK
Tel.: +44 (0)20 8371 6090;
Fax: +44 (0)20 8343 2313;
c.forder@futuremedicine.com

in brief…

Adverse events and factors associated with toxicity in patients with early rheumatoid arthritis treated with methotrexate tight control therapy (the CAMERA study).

Verstappen SM, Bakker MF, Heurkens AH *et al. Ann. Rheum. Dis.* (2009) (Epub ahead of print).

Assesses toxicity profiles in rheumatoid arthritis patients treated with methotrexate (MTX) in an intensive or a conventional strategy. The study also looks at factors associated with MTX-related toxicity. Results from a previous study were used where intensive MTX treatment strategy was more advantageous along with new data of adverse events compared between each treatment group. Factors causing MTX withdrawal or liver toxicity at follow-up were examined with Logistic regression analyses. The research showed a higher proportion of patients in the intensive group experienced MTX-related adverse events but in every case the effects were milder. Higher BMI and a correlation with creatinine clearance were discovered in MTX withdrawal. An immediate increase in serum liver enzymes was associated with liver toxicity. The study concluded in favor of intensive treatment strategy when studying toxicity profiles.

Disease activity and damage are not associated with increased levels of fatigue in systemic lupus erythematosus patients from a multiethnic cohort: LXVII

Burgos PI, Alarcón GS, McGwin G Jr, Crews KQ, Reveille JD, Vilá LM. *Arthritis Rheum.* 61(9), 1179–1186 (2009).

Establishes factors relating to enhanced fatigue in systemic lupus erythematosus (SLE) patients from Lupus in minorities: nature versus nurture, a longitudinal multiethnic cohort. The study included patients of Hispanic, African–American and Caucasian ethnicity who, when the study began, had an SLE disease duration of less than 5 years and were aged 16 or more. By means of generalized estimating equations the association between a variety of different factors and characteristics for fatigue were examined. A significant majority of the 515 patients were female with the highest percentage being Puerto Rican–Hispanic and the lowest Hispanic. Variables such as ethnicity, weight loss, fever, pain levels and abnormal behavior were found to be associated with increased fatigue. Conversely, disease activity and damage related to SLE were not.

Number of US veterans to develop rheumatoid vasculitis drops significantly

Researchers at the University of Wisconsin School of Medicine and Public Health (WI, USA) have discovered that there has been a substantial decline in the prevalence of rheumatoid vasculitis (RV) in US patients at the national Veterans Health Administration (VHA). Following peak prevalence in the 1980s, the decline was found to be steady throughout the 1990s. Between 2000 and 2001 a significant decline in RV of approximately 53% among inpatients and 31% among outpatients was observed.

Rheumatoid vasculitis occurs in approximately 2– 5% of patients with rheumatoid arthritis (RA). RV is an extra-articular disease, causing inflammation of the blood vessels and can be found throughout the body.

The authors conducted a cross-sectional study involving more than 37,000 RA patients admitted to VHA hospitals over a 22-year period, in order to determine the prevalence of RV in this population (as defined by the International Classification of Diseases). Over 90% of the patients were men with a mean age of 64.9 years. Commenting on the study, lead author Christie Bartel remarked: "Our study is the first to examine a national US population for RV prevalence among both inpatients and outpatients."

> "The treatment for RA improved throughout the 1990s and researchers suggest this as one possible explanation for the decline in the number of RV cases."

Previous research in California hospitals has shown a similar decline in RV hospitalization since 1980. However, owing to the fact that previous studies have only had data for inpatients, the accuracy of the results may be questionable since there may have been RV cases that went undetected owing to changing outpatient management of the disease.

The treatment for RA improved throughout the 1990s and researchers suggest this as one possible explanation for the decline in the number of RV cases. In addition, they suggest the decline in RV reported in the current study may be attributed to a decrease in the number of RV incidences, a disease cure in some patients, patients discontinuing VHA services or dying, or error.

The authors note that while the influence of smoking had been taken into consideration, and a system-wide effort had been made to decrease tobacco use, further studies would have to be carried out on the correlation between tobacco and RV.

Sources: Bartels C, Bell C, Rosenthal A, Shinki K, Bridges A: Decline in rheumatoid vasculitis prevalence among US veterans. *Arthritis Rheum.* 27, 60(9), 2553–2557 (2009).

Rheumatism video discloses center of inflammation at an early stage

Researchers at the Technische Bundesanstalt (PTB), Berlin Institute (Berlin, Germany) have developed an optical imaging method for the detection of early-stage rheumatoid arthritis.

This new technique uses fluorescent dye which is stimulated by near-infrared light. The procedure could potentially be very important in the initial detection of the disease, as it is capable of revealing more centers of rheumatism at an earlier stage than with x-ray apparatus. Furthermore, the method is harmless and cost effective in comparison to the use of a magnetic resonance tomography.

Approximately 1% of the population experience rheumatoid arthritis and the causes are still not completely understood. It is most commonly found in people aged between 30–50 years, but it can affect anyone. It is an autoimmune disease that usually begins with inflammation of the finger joints and progresses from there. If discovered and treated in time the effects of this potentially debilitating disease can be prevented.

> "This study will bring hope to all sufferers of rheumatoid arthrisis as this breakthrough sets the foundations for further research in the identification and cure of the disease"

The medical technology company 'Mivenio' (Berlin, Germany) recently obtained licensing rights from PTB in order to launch a large-scale study to further the promising results this research has shown. In addition, the financial benefits of this comparatively low-cost imaging technique have warranted great interest by statutory health insurance companies, as this may well be the future of rheumatism diagnostics and treatment. This study will bring hope to all sufferers of rheumatoid arthrisis as this breakthrough sets the foundations for further research in the identification and cure of the disease.

Source: www.ptb.de/en/aktuelles/archiv/presseinfos/pi2009/pitext/pi090820.html
www.nhs.uk/Pathways/RheumatoidArthritis/Pages/Avoiding.aspx