WEDNESDAY, 14 JUNE 2017

Fibromyalgia: a disease of the peripheral or central nervous system

SP0019 SIGNS, SYMPTOMS AND CO-MORBIDITIES OF FIBROMYALGIA

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In the beta browser version of ICD11, fibromyalgia is listed as a chronic primary pain syndrome (Treede et al. 2015). It is categorized as chronic widespread pain, and is distinguished from other chronic widespread pain by a) tender point counts (American College of Rheumatology 1990 criteria), or b) psychosocial distress (ACR 2010). Both ACR definitions are problematic for research purposes: mechanisms of tender points are poorly understood, and using distress as inclusion criterion may lead to circular arguments.

Chronic primary pain is characterized by significant emotional distress and functional disability. It is multifactorial: biological, psychological and social factors contribute to the pain syndrome. The diagnosis is appropriate independently of identified biological or psychological contributors unless another diagnosis would better account for the presenting symptoms. Chronic Primary Pain can occur in any body site (face, low back, neck, upper limb, thorax, abdominal, pelvis, urogenital region), or in a combination of body sites (Widespread pain). In general, multiple sites of pain are associated with higher distress and disability than single sites. Chronic Primary Pain is also often associated with sleep disturbance, adverse side effects of treatments (such as medication dependence), and comorbidities (such as depression, anxiety, anger, guilt, fear, and a range of chronic medical conditions).

As part of the research consortium LOGIN we have compared the pathophysiology of fibromyalgia, other chronic widespread pain and chronic localized pain in the lower back. In those datasets, fibromyalgia patients showed higher comorbidity of anxiety and depression and more functional impairment than the other groups (Gerhardt et al. 2016). A deficit in conditioned pain modulation (CPM) was related to the spatial spread of ongoing pain, consistent with the neurobiology of endogenous pain control systems. FMS differed from CWP with respect to psychosocial burden, consistent with the shift in clinical diagnostic criteria. Tender point counts (an evoked pain measure) were still useful to identify the FMS patients (Gerhardt et al. 2017). A study using the childhood trauma questionnaire suggests that early stress exposure is associated nonspecifically with lowered pressure pain thresholds which may be related to tender points (Tesarz et al. 2016).

Experimental sleep deprivation in healthy subjects or rodents leads to symptom profiles reminiscent of fibromyalgia (e.g. widespread hyperalgesia, anxiety), suggesting a potential vicious circle of pain, hyperalgesia and sleep disturbance in fibromyalgia.

In summary, fibromyalgia is a chronic primary pain syndrome characterized by widespread pain and major comorbidities. A combination of predisposition plus an initiating painful event seem to play a role in its genesis; according to the dual hit hypothesis, traumatic events during childhood may contribute to the predisposition.

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References:

[1] Gerhardt A, et al. (2016) Clin J Pain 32: 568–579.
[2] Gerhardt A, et al. (2017) Pain: in press.
[3] Schuh-Hofer S, et al. (2013) Pain 154: 1613–1621.
[4] Tesarz J, et al. (2016) Pain 157: 1799–1809.
[5] Treede RD, et al. (2015) Pain 156: 1003–1007.

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SP0020 PERIPHERAL PATHOLOGY IN FIBROMYALGIA

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The pathophysiology of pain in fibromyalgia is complex. In recent years, an involvement of the thinly myelinated nerve fibers of the A-delta type and the unmyelinated C-fibers has been reported in fibromyalgia patients. Independent research groups have published consistent findings of objective injury to these "small nerve fibers". These included disturbances in function, electrical properties, and morphological integrity of these nerve fibers. While the reasons for this small fiber pathology and its contribution to FMS pain are still unclear, a new research field has emerged that will focus on uncovering the underlying pathophysiology. In this talk, I will summarize current findings and discuss their significance for the understanding of the fibromyalgia syndrome.

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SP0021 CENTRAL PATHOLOGIES IN FIBROMYALGIA

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Fibromyalgia is characterized by widespread, mainly muscular pain that is exacerbated during and following physical activity. Although mechanisms such as muscle ischemia and peripheral nerve fibre pathology have been implicated in fibromyalgia, currently no known peripheral pathology can fully account for the pain. Therefore, the pain in fibromyalgia is most likely explained by a complex interaction between peripheral and central mechanisms. Fibromyalgia patients are characterized by a multimodal, widespread, increase in pain sensitivity and a dysfunction of endogenous pain inhibitory mechanisms. Imaging studies have revealed functional as well as structural cerebral abnormalities in fibromyalgia. During painful stimulation, fibromyalgia patients exhibited an inability to activate cerebral structures associated with the descending pain inhibitory system, i.e., rostral anterior cingulate (rACC) and thalamus[1]. There was no association between depression or anxiety and cerebral processing of evoked pain, indicating segregated mechanisms for mood and pain processing[2]. Furthermore, FM patients had less pain related functional connectivity within the brain's pain inhibitory network and structural changes such as decreased cortical thickness and reduced brain volumes[3]. Longer duration of FM pain was associated with more pronounced functional and structural abnormalities suggesting a time-dependent progress of cerebral pathology, even when controlled for age and mood[3]. In addition, FM patients had elevated interleukin-8 in the cerebrospinal fluid indicating neuro-inflammation[4], possibly due to glia cell activation. Interleukin (IL)-8 is co-localized with translocator protein (TSPO) in glia cells. During glia activation, the production of TSPO is increased and TSPO agonists are involved in the regulation of the expression of IL-8 and it's receptor, thus affecting glia to neuron signalling and central sensitisation. We have recently documented that FM patients who are carriers of the genetic functional polymorphism associated with high TSPO binding affinity report higher pain intensity and more severe fibromyalgia symptoms compared to genetically inferred TSPO low affinity binders and that this genetic polymorphism also affects cerebral pain processing[5]. To our knowledge, this is the first finding of genetic mechanisms associated with symptom severity in FM.

Finally, the effect of different treatments on central pathology in FM will be discussed. Short pain duration was predictive of a positive response to a 12 weeks treatment with a serotonin-noradrenalin re-uptake inhibitor (SNRI)[6]. The degree of symptom improvement and reduced pain sensitivity in SNRI treated FM patients corresponded to the degree of increased pain related activation of cerebral areas associated with pain modulation and the default mode network[6]. In contrast, cognitive behaviour therapy did not affect clinical pain or pain sensitivity but increased activations of cerebral regions implicated in executive cognitive control during painful stimulation and thus likely reappraisal of painful stimuli[7]. Finally, 15 weeks of physical exercise partially normalized resting state activity in FM[8]. The results demonstrated that different treatment modalities affected specific brain mechanisms, indicating that at least some of the cerebral abnormalities in FM are reversible.

References:

[1] Jensen et al. Pain 2009;144:95–100.
[2] Jensen et al. Arthritis Rheum 2010;62(11):3488–3495.
[3] Jensen et al. Arthritis Rheum. 2013 Dec;65(12):3293–303.
[4] Kosek et al. J Neuroimmunology, 2015 Mar 15;280:49–55.
[5] Kosek et al. Brain Behav Immun. 2016 Nov;58:218–227.
[6] Jensen et al. J Pain, 2014 Dec;15(12):1328–37.
[7] Jensen et al. Pain 2012:153(7):1495–503.
[8] Brain Connect, 2015 Aug 18;9:134–9.

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Chondrocyte channels (role in mechanotransduction)or "channeling the chondrocyte"

SP0022 TRPA1 CHANNELS IN OSTEOARTHRITIS

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Osteoarthritis (OA) has long been viewed as a degenerative "wear-and-tear" disease of cartilage. There is, however, increasing evidence to confirm that inflammation has a critical role in the pathogenesis and symptoms of the disease. Inflammation in osteoarthritis is distinct from that typical for rheumatoid arthritis; it is generally low-grade in its nature but characterized by exacerbations with joint effusions and more severe symptoms. Osteoarthritis shares many features of innate immunity but the inflammatory mechanisms eventually leading to anatomical and functional changes and symptoms typical for osteoarthritis are not known in detail; but their further understanding is essential for the development of disease-modifying treatments for osteoarthritis.

Transient receptor potential ankyrin 1 (TRPA1) is a ligand-gated membrane-bound cation channel. It has been widely studied in sensory neurons where it acts