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Low back pain: Moving toward mechanism-based management

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ABSTRACT

Low back pain is a complex, multifactorial, and heterogeneous condition, but this does not make it an exception in medicine. Management of low back pain based on a mechanistic approach and developing more effective multidisciplinary treatment is possible and would finally implement the biopsychosocial model of care.

1. Introduction

Low back pain (LBP) remains the leading cause of disability worldwide (GBD, 2016 Disease and Injury Incidence and Prevalence Collaborators., 2017), and the most expensive health problem in many countries (Dagenais et al., 2008). While attempts to address this growing problem centred on reform of the current management of LBP, parallel evidence from basic sciences and advanced imaging indicates that management of LBP may significantly benefit from a mechanistic approach toward pain classification and treatment in the foreseeable future. We define a mechanism-based approach to LBP as one that goes beyond anatomical and pathological factors, attempting to identify mechanisms at different levels of peripheral and central nervous system and provide individualized treatments targeting relevant inflammatory factors and molecules, especially when directed toward patients with distinct pain states and mechanisms; i.e., nociceptive, neuropathic, peripheral sensitization, and central sensitization (Vardeh et al., 2016). Here, we highlight several signs that we believe point to such changes in hopes to begin a discussion among clinicians and researchers to give rise to a new, improved approach toward care.

2. The problem

The current approach to LBP management classifies more than 85% of patients as having non-specific low back pain (NSLBP), defined as LBP without a specific physical cause, and diagnostic procedures to reduce this percentage are discouraged by current clinical guidelines. Over the last three decades, several factors have led clinicians and clinical researchers to embrace the term NSLBP for use in practice and research without the need to identify the exact origin of pain. First, the prior pathoanatomic approach was too simplistic as it proved impossible to find the origins of pain in the majority of patients. Importantly, degenerative and pathological findings, suspected causes of LBP, were frequently reported in asymptomatic subjects. Consequently, the bio- aspect was lost from the biopsychosocial model, largely because of unfulfilled promises of the biological approach. Second, an optimistic view about potential spontaneous recovery of LBP expedited the trend of refraining from diagnostics and treatment in acute pain and led to the idea that treatment and hence diagnostics were not needed. Finally, a shift in focus from acute to chronic LBP, which accounts for the bulk of the costs associated with LBP, strengthened this paradigm shift to NSLBP.

3. The transition

While managing NSLBP and its related disabilities as a multidimensional problem was successful in some ways, recommended treatments for NSLBP show small effect sizes, adherence to evidence-based clinical guidelines is low, and use of imaging, medication, and physicians' referrals are increasing (Mafi et al., 2013). To address this problem, subgrouping of NSLBP patients (based on neuromuscular, psychological or prognostic factors or treatment-based classifications) and directing specific treatments to the targeted subgroups has been proposed and may have marginally improved treatment effect sizes. However, evidence for the effectiveness of this approach is still inconsistent.

Several key factors are now in favor of the management of LBP based on mechanistic diagnosis and targeted treatment. First, recent evidence indicates that we may now be closer than ever to identifying underlying mechanisms in many more cases of LBP (Table 1). Second, there is a preference among patients to understand the diagnosis of their problem over simply managing their pain and maintaining function. In fact, acute LBP is in many cases not as self-limiting as previously thought (Wirth et al., 2017), so that a lack of specific diagnosis might

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Table 1
Examples of recent evidence on biological factors that may provide targets for treatment in LBP.

Central neurological factors.	fMRI studies have revealed clear evidence of altered and reversible changes in pain processing in the brain of chronic LBP patients (Nijs et al., 2017). Glial activation, which plays a key role in persistent pain, has been demonstrated in the thalamus and somatosensory areas representing the lumbar spine of chronic LBP patients (Loggia et al., 2015).
Peripheral neurological factors.	A link between sensory nerve ingrowth into the inner layer of intervertebral discs (IVDs), a potential source of LBP, and degeneration of the (IVD) has been proposed (Ohtori et al., 2015). TNF-Alpha in nucleus pulposus and interleukins may induce this sensory nerve growth (Hayashi et al., 2008). There is also evidence of association between painful intervertebral disc degeneration and nerve injury (Lim et al., 2017).
Inflammatory factors.	Higher serum levels of interleukin-6 (IL-6) were found in patients with degenerative disc disease or spinal stenosis compared to control subjects (Weber et al., 2016). There is also evidence of elevated levels of C-reactive protein and IL-6 in acute LBP, which were correlated with symptom severity (Klyne et al., 2017).
Genetic and molecular factors.	Several single-nucleotide polymorphisms (SNPs) were identified as potential risk factors for intervertebral disc degeneration (Martirosyan et al., 2016). Molecular profiles of human annulus fibrosus and nucleus pulposus cells were identified that can facilitate cell-based therapies for lumbar discogenic pain (Tang et al., 2016).
Structural factors.	Significant associations were found between MRI findings such as Modic changes and episodes of severe and disabling LBP, persistent LBP, disc pathology and endplate abnormalities (Luoma et al., 2016; Määttä et al., 2015).

have negative psychological consequences that would contribute to pain becoming chronic. Third, and more optimistically, mechanism-based classification and treatment of LBP may receive more research and clinical attention by the advent of novel treatments such as regenerative therapies that require early detection of degenerative changes (Sakai and Andersson, 2015), and the rise of personalized and precision medicine that aims to use biomarkers to select patients for targeted, personalized treatment (Collins and Varmus, 2015).

4. The path forward

A close multidisciplinary collaboration between clinicians and researchers could lay the ground for such a movement leading to more effective treatment: 1) with appropriate targeting, exercise might assume new roles in facilitating repair of early degenerative changes (with low load, dynamic exercises) (Belavý et al., 2017) and reducing inflammatory components of LBP, 2) pharmacologic therapies could move from symptomatic to causal, targeting relevant inflammatory factors and molecules, especially when directed toward patients with distinct pain states and mechanisms (Vardeh et al., 2016), and 3) surgical intervention would be more effective if it could target the structures and mechanisms underpinning LBP with greater precision. Advances in electronic health records are also important infrastructures to integrate these efforts and support development of new diagnostic procedures and treatments for LBP. The time is also right for such a transition, as healthcare and treatments for various conditions begin to consider more directly each individual patient's needs based on genomics, biomarkers, function, and lifestyle (Collins and Varmus, 2015).

In conclusion, we propose that the time is appropriate to re-assess mechanism-based diagnosis and treatment of LBP. Controversies surrounding mechanistic and non-mechanistic causal explanations of diseases and medical outcomes continue in the philosophy of medicine (Reiss and Ankeny, 2016). However, in such a complex phenomenon as LBP, with basic science pointing to previously unknown mechanisms, it seems likely that doing so would change LBP management for the better. Obviously, this claim is open for debate and discussion and should be tested in thorough clinical studies.

Conflict of interest

The authors have no conflict of interest to declare.

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