



LEEDS
BECKETT
UNIVERSITY

Citation:

Astita, R and Tashani, OA and Sharp, D and Johnson, MI (2015) Argument for the need of investigation of the relationship between body fatness and experimental pain sensitivity. The Libyan journal of medicine, 10 (1). -. ISSN 1993-2820 DOI: <https://doi.org/10.3402/ljm.v10.28457>

Link to Leeds Beckett Repository record:

<https://eprints.leedsbeckett.ac.uk/id/eprint/1894/>

Document Version:

Article (Accepted Version)

Creative Commons: Attribution-Noncommercial 3.0

This is an Accepted Manuscript of an article published by Taylor & Francis in The Libyan journal of medicine on 16 June 2015, available online: <http://www.tandfonline.com/10.3402/ljm.v10.28457>

The aim of the Leeds Beckett Repository is to provide open access to our research, as required by funder policies and permitted by publishers and copyright law.

The Leeds Beckett repository holds a wide range of publications, each of which has been checked for copyright and the relevant embargo period has been applied by the Research Services team.

We operate on a standard take-down policy. If you are the author or publisher of an output and you would like it removed from the repository, please [contact us](#) and we will investigate on a case-by-case basis.

Each thesis in the repository has been cleared where necessary by the author for third party copyright. If you would like a thesis to be removed from the repository or believe there is an issue with copyright, please contact us on openaccess@leedsbeckett.ac.uk and we will investigate on a case-by-case basis.

LETTER TO THE EDITOR

Argument for the need of investigation of the relationship between body fatness and experimental pain sensitivity

Rehab A. Astita*, Osama A. Tashani, Duncan Sharp and Mark I. Johnson

Centre for Pain Research, Faculty of Health and Social Sciences, Leeds Beckett University, Leeds, UK

In this communication, we argue about the need for an extensive investigation of the relationship between body fatness and fat distribution and experimental pain to explore the factors that might contribute to the increased prevalence of pain conditions in obese individuals.

Keywords: *obesity; chronic pain; experimental pain; body fat; cytokines*

*Correspondence to: Rehab A. Astita, Centre for Pain Research, Faculty of Health and Social Sciences, Leeds Beckett University, City Campus, LS1 3HE, Leeds, UK, Email: R.Astita@leedsbeckett.ac.uk

Received: 21 April 2015; Accepted in revised form: 6 June 2015; Published: 16 June 2015

Obesity and pain are significant public health problems and contribute to significant disability worldwide (1). There appears to be tentative evidence that individuals with a high body mass index (BMI), which is often used as a proxy measure of obesity, report higher pain intensity compared with individuals with normal BMI (2). However, the relationship between obesity and pain has received little attention and the potential mechanisms underlying a putative relationship is not well understood (3, 4).

Obesity is defined as an increase in body weight as a result of an excessive accumulation of body fat and is associated with increased morbidity and mortality (5). Obesity is commonly measured using the BMI, with obesity characterised as a BMI greater than 30 kg/m², overweight between 25 and 29.9 kg/m², and normal weight from 18 to 24.9 kg/m² (6, 7). The World Health Organization (2013) reports that more than 1.5 billion adults worldwide are overweight and approximately 500 million adults meet the criteria for obesity. In the United States, approximately 78 million adults and 12.5 million children and adolescents are obese (8).

Obesity and chronic pain

Obesity is usually associated with comorbidities (9, 10) such as diabetes. There is very strong evidence that obesity is a high-risk factor for elevated cholesterol, heart disease, type 2 diabetes, cancer, and stroke (10). Obesity may be influenced by genetic and physiological factors, such as a thyroid disorder, growth hormone and leptin deficiency, and lifestyle factors including overeating, especially excess

consumption of sugary and processed foods, and lack of exercise associated with a sedentary way of life (11).

Obesity is also associated with painful conditions, including low back pain, fibromyalgia headache, and osteoarthritis (12). It has been estimated that approximately 50% of people who are obese regularly experience pain (13). The International Association of the Study of Pain (IASP) defines pain as 'an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage' (14). It is unclear whether obesity causes chronic pain or chronic pain could cause increased weight, or some other factor(s) cause both conditions concurrently (2, 15). It has been assumed that pain in obese people could be the result of the excessive weight, causing mechanical stress to weight-bearing structures, particularly joints of the back and lower limbs (16). More recently, attention has been on the possibility that obesity produces a pro-inflammatory state and that inflammatory substrates may contribute to the development of pain (2).

Body fatness and experimental pain

Laboratory investigations into the pain sensitivity response of healthy individuals has been used extensively in pain science to investigate relationships between pain sensitivity and sex, gender, ethnicity, and other factors that may influence pain experience. To date, the mechanisms underlying the supposed relationship between obesity and an individual's pain sensitivity response has received little attention (3, 4, 16, 17). Pain sensitivity is the level at which an individual reacts to a noxious stimulus and is measured using controlled experimental stimuli (18).

Laboratory investigations into the pain sensitivity response of obese pain-free individuals would be useful to determine whether obesity contributes to pain experience, in addition to other factors already known to influence pain sensitivity response, including age, sex, gender, ethnicity, and psychological factors such as anxiety and catastrophising. These factors should be accounted for in any study of pain sensitivity (19).

The role of pro-inflammatory cytokines

Susceptibility to pain in obese individuals may be affected by increases in the concentrations of pro-inflammatory cytokines in the blood (2, 17). Cytokines are proteins secreted by cells to regulate the immune response to infection and trauma (17, 20, 21). Some cytokines promote the healing of wounds; pro-inflammatory cytokines increase inflammation and cause diseases to progress; anti-inflammatory cytokines suppress the activity of pro-inflammatory cytokines (20). Inflammatory responses in the peripheral and central nervous systems play key roles in the development and persistence of the hallmarks of pain: redness, swelling, temperature rise, and pain (22). Cytokines are regulators of adipose tissue metabolism and are secreted by many cells in the body. Pro-inflammatory cytokines are predominantly produced by activated macrophages and are involved in the up-regulation of inflammatory reactions. There is abundant evidence that certain pro-inflammatory cytokines such as IL-1 β , interleukin-6 (IL-6), and tumour necrosis factor- α (TNF- α) are involved in the process of pathological pain (23). The significance of cytokines in the development of pain and hyperalgesia as well as their mechanisms of action on nociceptors has been realised only during the last decade (24, 25). Adipose tissue releases inflammatory mediators, including prostaglandin, histamine, and interleukin (25). Visceral adipose tissue in particular is a rich source of pro-inflammatory cytokines, which appear to be major regulators of adipose tissue metabolism. There is evidence that obese individuals have elevated circulation levels of pro-inflammatory cytokines, such as TNF- α , IL-6, and C-reactive protein (CRP). IL-6 is a circulating cytokine secreted from different types of cells, including activated macrophages and lymphocytes. The biological activity of IL-6 is elevated in the presence of systemic infection or inflammation (26), and it is known that IL-6 and TNF- α play key roles in chronic pain conditions (27).

Obese individuals may be in a pro-inflammatory state (17). It is unclear whether an increased prevalence of pain conditions and pain sensitivity in obese individuals is the result of the inflammatory mediators associated with adipose tissue or else some other factors, such as body size and accumulation and distribution of fat, are also linked to pain sensitivity responses (28).

Conclusion

One way of investigating whether inflammatory mediators in obese people are associated with pain sensitivity is to correlate the concentrations of biomarkers of systemic inflammation in pain-free individuals using experimental pain induction techniques. However, before undertaking experimental studies, it is necessary to review the current status of research literature to contextualise the prevalence of chronic pain among obese individuals and the current understanding of the mechanism by which fat content of the body affects pain. It is also necessary to conduct a systematic review of research on experimental pain sensitivity response and body fatness to determine the status of current research on the topic and to inform the design of the experimental studies. Therefore, there is a need to investigate the relationship between pain sensitivity, body fat distribution, and levels of pro-inflammatory cytokines. Such a study should be based on an experimental investigation of the relationship between pain sensitivity, body fat distribution (measured by a state-of-the-art device), and blood levels of IL-6, CPR, TNF- α , and leptin.

Conflict of interest and funding

The first author was supported by The Medical Technology Higher Institute, Al-Bayda, Libya.

References

1. Finucane MM, Stevens GA, Cowan MJ, Danaei G, Lin JK, Paciorek CJ, et al. National, regional, and global trends in body-mass index since 1980: systematic analysis of health examination surveys and epidemiological studies with 960 country-years and 91 million participants. *Lancet*. 2011; 377: 557–67.
2. Ray L, Lipton RB, Zimmerman ME, Katz MJ, Derby CA. Mechanisms of association between obesity and chronic pain in the elderly. *Pain*. 2011; 152: 53–9.
3. Hitt HC, McMillen RC, Thornton-Neaves T, Koch K, AG C. Comorbidity of obesity and pain in a general population: results from the southern pain prevalence study. *J Pain*. 2007; 430: 6.
4. McVinnie DS. Obesity and pain. *Br J Pain*. 2013; 7: 163–70.
5. Haslam D. Obesity: a medical history. *Obesity Rev*. 2007; 8: 31–6.
6. Wright LJ, Schur E, Noonan C, Ahumada S, Buchwald D, Afari N. Chronic pain, overweight, and obesity: findings from a community-based twin registry. *J Pain*. 2010; 11: 628–35.
7. WHO. 2010. Available from: <http://www.ic.nhs.uk/statistics-and-data-collections/health-and-lifestyles-related-surveys> [cited 25 August 2014].
8. Ogden CL, Carroll MD, Curtin LR, Lamb MM, Flegal KM. Prevalence of high body mass index in US children and adolescents, 2007–2008. *JAMA*. 2010; 303: 242–9.
9. Brown CD, Higgins M, Donato KA, Rohde FC, Garrison R, Obarzanek E, et al. Body mass index and the prevalence of hypertension and dyslipidemia. *Obes Res*. 2000; 8: 605–19.
10. Pischon T, Nöthlings U, Boeing H. Obesity and cancer. *Proc Nutr Soc*. 2008; 67: 128–45.

11. Wijga AH, Scholtens S, Bemelmans WJ, de Jongste JC, Kerkhof M, Schipper M, et al. Comorbidities of obesity in school children: a cross-sectional study in the PIAMA birth cohort. *BMC Public Health*. 2010; 10: 184.
12. Kim SW, Mintz GS, Escolar E, Ohlmann P, Pregowski J, Tyczynski P, et al. The impact of cardiovascular risk factors on subclinical left main coronary artery disease: an intravascular ultrasound study. *Am Heart J*. 2006; 152: 7–12.
13. Kerns RD, Otis J, Rosenberg R, Reid MC. Veterans' reports of pain and associations with ratings of health, health-risk behaviors, affective distress, and use of the healthcare system. *J Rehabil Res Dev*. 2003; 40: 371–80.
14. Mersky H, Bogduk N. (Eds.) *Classification of chronic pain: descriptions of chronic pain syndromes and definitions of pain terms*. Seattle, WA: IASP Press; 1994, p. xi. Available from: <http://www.iasppain.org/files/Content/ContentFolders/Publications2/FreeBooks/Classification-of-Chronic-Pain.pdf> [cited 9 September 2014].
15. Shiri R, Karppinen J, Leino-Arjas P, Solovieva S, Viikari-Juntura E. The association between obesity and low back pain: a meta-analysis. *Am J Epidemiol*. 2010; 171: 135–54.
16. Ray L, Lipton RB, Zimmerman ME, Katz MJ, Derby CA. Mechanisms of association between obesity and chronic pain in the elderly. *Pain*. 2011; 152: 53–9.
17. Stolzman S. The influence of cytokines on obesity-associated pain. 2013. Available from: <http://epublications.marquette.edu/cgi/viewcontent.cgi?article=1010&context=dittman> [cited 9 September 2014].
18. Nielsen CS, Stubhaug A, Price DD, Vassend O, Czajkowski N, Harris JR. Individual differences in pain sensitivity: genetic and environmental contributions. *Pain*. 2008; 136: 21–9.
19. Caldwell J, Hart-Johnson T, Green CR. Body mass index and quality of life: examining blacks and whites with chronic pain. *J Pain*. 2009; 10: 60–7.
20. Charles A, Dinarello MD. Proinflammatory cytokines. *Chest*. 2000; 118: 503–8.
21. Coppack SW. Pro-inflammatory cytokines and adipose tissue. *Proc Nutr Soc*. 2001; 60: 349–56.
22. Watkins LR, Milligan ED, Glial MS. Proinflammatory cytokines mediate exaggerated pain states: implications for clinical pain. *Adv Exp Med Biol*. 2003; 521: 1–21.
23. Zhang J-M, An J. Cytokines, inflammation and pain. *Int Anesthesiol Clin*. 2007; 45: 27.
24. Koltzenburg M, Kress M, Reeh P. The nociceptor sensitization by bradykinin does not depend on sympathetic neurons. *Neuroscience*. 1992; 46: 465–73.
25. Fain JN. Release of interleukins and other inflammatory cytokines by human adipose tissue is enhanced in obesity and primarily due to the nonfat cells. *Vitam Horm*. 2006; 74: 443–77.
26. Yudkin JS, Kumari M, Humphries SE, Mohamed-Ali V. Inflammation, obesity, stress and coronary heart disease: is interleukin-6 the link? *Atherosclerosis*. 2000; 148: 209–14.
27. Puglisi MJ, Fernandez ML. Modulation of C-reactive protein, tumor necrosis factor- α , and adiponectin by diet, exercise, and weight loss. *J Nutr*. 2008; 138: 2293–6.
28. Tashani OA, Alabas OA, Johnson MI. Cold pressor pain responses in healthy Libyans: effect of sex/gender, anxiety, and body size. *Gend Med*. 2010; 7: 309–19.