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Review article

Age changes in pain perception: A systematic-review and meta-analysis of age effects on pain and tolerance thresholds

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ABSTRACT

Demographic changes, with substantial increase in life expectancy, ask for solid knowledge about how pain perception might be altered by aging. Although psychophysical studies on age-related changes in pain perception have been conducted over more than 70 years, meta-analyses are still missing. The present meta-analysis aimed to quantify evidence on age-related changes in pain perception, indexed by pain thresholds and pain tolerance thresholds in young and older healthy adults. After searching PubMed, Google Scholar and PsycINFO using state-of-art screening (PRISMA-criteria), 31 studies on pain threshold and 9 studies assessing pain tolerance threshold were identified. Pain threshold increases with age, which is indicated by a large effect size. This age-related change increases the wider the age-gap between groups; and is especially prominent when heat is used and when stimuli are applied to the head. In contrast, pain tolerance thresholds did not show substantial age-related changes. Thus, after many years of investigating age-related changes in pain perception, we only have firm evidence that aging reduces pain sensitivity for lower pain intensities.

Contents

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1. Introduction

Age changes in pain perception have been of growing interest for many years (Gagliese, 2009). Primary catalysts for this increasing interest have been the demographic changes in the developed countries, with substantial increases in life expectancy as well as high prevalence rates of clinical pain among older people (Gagliese, 2009). In parts due to these epidemiological phenomena, a number of experimental studies have accumulated over the years, in which age changes in pain perception – mainly in pain thresholds (PT) and pain tolerance thresholds (PTT) – have been studied in cross-sectional designs. These studies have repeatedly been reviewed (Edwards, 2005; Gibson and Farrell, 2004; Lautenbacher, 2012) and certain believes about the essential findings have been developed. For example, the pain threshold is supposed to increase with age whereas the tolerance threshold is assumed to decrease, which are two opposite changes that may, as a result, narrow the pain range in elderly individuals (Lautenbacher, 2012). Thus, on the one hand, age might dull the pain sense (at least for low pain intensities) as it dulls vision and audition; as a consequence, external threats may be detected later and older adults may run higher risks of injuries. On the other hand, older adults might tolerate strong pain intensities less well, possibly due to ineffective pain inhibitory processes. Consequently, pain complaints become more likely (Lautenbacher, 2012). Although the latter interpretation fits well with clinical findings of high pain prevalence rates in older adults (Gagliese, 2009), it is not undisputed because findings have repeatedly been contradictory (e.g. Cole et al., 2010; Edwards and Fillingim, 2001).

Given the great empirical interest in the topic, the sufficient number of relevant studies and the easy accessibility of the data, it is the rather surprising that meta-analytic attempts have been scarce and not published in peer-reviewed journals. Gibson (2003) previously published a meta-analysis in a book chapter. We presented in a review article (Lautenbacher, 2012) results from a meta-analysis being conducted as part of a Master Thesis. Although these meta-analytic results roughly corresponded with the narrative reviews, some ambiguities prevailed. These ambiguities mainly resulted from differences and inaccuracies as regards the weighting of studies according to the widely varying samples sizes, the statistical handling of strongly deviating results as well as inclusion criteria used for study selection. Therefore, the present meta-analysis aimed to quantify evidence on age-related changes in pain perception using a transparent and replicable operationalization. Furthermore, we tried to search for explanations for the differences between results of primary studies in a systematic fashion. To find possible moderators with explanatory value, we grouped the primary data into different categories that might be critical:

(i) The *mean age difference between the age groups* classified as young and old participants may matter. It is likely that the larger the age gap is, the more likely age effects on pain perception can be picked up even if linear relationships cannot be assumed. Thus, we categorized studies into those with small and those with large age gaps. (ii) The *type of physical stressor* (noxious stimulation based on temperature, pressure, electrical current, etc.) determines which nociceptive mechanisms are engaged, which time course and quality of pain sensations are associated and how physical threat is perceived by the individuals (Chapman et al., 1985; Gracely, 1999; Kumar Reddy et al., 2012). These factors may be differently affected by age, which makes the type of physical stressor chosen an important category to be considered. (iii) The *site of stimulation* determines which body tissue is stimulated. This in turn influences the nociceptor density in the stimulated area and the length of nociceptive fibers for impulse transmission from the periphery to the central nervous system. Even the psychological threat level can be affected by the site of stimulation because pain stimuli applied in the face are experienced as more threatening than at the lower limbs (Essick et al., 2004; Lautenbacher and Strian, 1991; Schmidt et al., 2016). These factors may undergo site-specific age changes, qualifying the site of stimulation as another relevant category for this meta-analysis.

In sum, the present meta-analysis aimed at determining age changes in pain perception indexed by changes in pain (PT) and tolerance thresholds (PTT). PT and PTT values were chosen as indicators of pain perception because they are psychophysical parameters – although not undisputed – of proven validity; furthermore, a sufficient number of primary studies are available investigating these variables in different age groups. Finally, it was examined whether the categorization of the primary studies according to (i) the mean age difference between groups (young and old participants), (ii) the type of physical stressor, and (iii) the site of stimulation, helps to explain differences between primary study outcomes.

2. Methods

The systematic review and meta-analysis were performed following the "Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015" (Moher et al., 2015).

2.1. Search strategy and study selection

Literature search: An extensive search of literature published until January 2016 was conducted using the databases PubMed, Google Scholar and PsycINFO. We set no restrictions with regard to the earliest year of publication. In our search, we combined with a logical AND keywords for age (aging, aged, elderly, age difference, age related, geriatric, gerontolo*, senior, older; connected with a logical OR) with keywords for experimental pain sensitivity (pain threshold, pain tolerance; connected with a logical OR).[1] Given that we were interested in age-related changes in pain sensitivity, which occur in older age and are not confounded by age-related diseases, we excluded the following keywords by setting a NOT qualification: child, adolescen*, pediatric, neonat*, fetal, disease, intervention. Additionally, reference lists from identified articles and reviews on pain and aging (Gibson and Farrell, 2004; Lautenbacher, 2012) were screened for missing articles. The systematic search was limited to human subjects and articles published in English.

Eligibility criteria: We selected only those studies (i) that assessed pain and/or tolerance thresholds, (ii) that reported the chronological age of the participants, (iii) that included at least two age groups, (iv) with one of the age groups having a mean age >60 years and (v) an age difference of at least 10 years between age groups (mean difference), (vi) with a minimum sample size of $N = 20$, (vii) and that provided a clear description of statistics. Furthermore, we only included studies focussing on healthy participants and, thus, we excluded studies of populations restricted to specific diseases, pathological conditions, or metabolic disorders as well as studies where participants took medications that could alter the processing of pain (analgesics, psychotropic drugs). Thus, the selected data should be representative for true non-pathological aging effects on pain sensitivity. We excluded non-original research, conference proceedings, and doctoral theses. Two independent reviewers (MH, JS) screened the titles and abstracts for the eligibility criteria. We retrieved full texts of all studies that were potentially relevant or where exclusion could not be determined based on the study title or abstract. In case of discrepancies/disagreement between the 2 reviewers, a third

[1] Precise search terms and combinations are available from the authors upon request.