MUSCULOSKELETAL COMPLAINTS AND HUMAN ASSUMED CENTRAL SENSITISATION IN INDIVIDUALS WITH BRACHIAL PLEXUS INJURY AND UPPER LIMB ABSENCE

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ABSTRACT

Background: Musculoskeletal complaints (MSCs) are a highly prevalent problem in subjects with upper limb absence (ULA) and Brachial Plexus Injury (BPI). Single-handed individuals often experience pain in multiple locations. Human Assumed Central Sensitisation (HACS) can be present in single-handed individuals. This study aims to determine the presence of HACS in single-handed individuals with MSCs compared to individuals without MSCs as well as two-handed controls.

Methods: This study aims to include 20 individuals with ULA, 20 with BPI, and matched two-handed controls. All participants filled in the Central Sensitisation Inventory (CSI) questionnaire (range 0-100, cut off value for CS ≥ 40). Furthermore, they underwent a Quantitative Sensory Testing (QST) protocol. Seven sensory tests were executed to quantify the function of the sensory nervous system: dynamical mechanical allodynia (DMA, range 0-100), mechanical detection threshold (MDT, range 0.125-1024mN), mechanical pain threshold & sensitivity (MPT, range 8-1024mN & MPS, range 0-100), wind-up ratio (WUR, ratio), and pressure pain threshold & sensitivity (PPS in N & PPT, range 0-100).

Results: Data collection is ongoing. At present, data of seven individuals with BPI are collected. CSI mean is 24 (SD 11.0). QST: DMA [1.0], MDT [1.3-1024.0mN], MPT [19.2-1024mN], MPS [0.6-25], WUR [1.33-4.5], PPS [27.5-138.0N], and PPT [1-50].

Conclusion: Preliminary results indicate that CS may be present in a subgroup of single-handed individuals with MSCs. This study sheds light on the role of CS in single-handed individuals and could give more insight in the frequently occurring MSCs in such individuals.

INTRODUCTION

Many individuals with one functional hand, such as individuals with upper limb absence (ULA) and brachial plexus injury (BPI), complain about musculoskeletal complaints (MSCs). The prevalence of MSCs in individuals with ULA is nearly twice as high as compared to two-handed controls (35% vs. 65%) [1]. A higher prevalence is also shown in a sample with BPI (49%) compared to a non-impaired control group (35%) [2]. They experience pain more often, but also in more bodily locations [1,2].

Pain can be described by three mechanistic descriptors according to the International Association for the Study of Pain (IASP): a) nociceptive pain, pain that arises from actual or threatened tissue damage to non-neural tissue and is due to the activation of peripheral nociceptors; b) neuropathic pain, pain caused by a lesion or disease of the somatosensory nervous system; and c) nociplastic pain [3]. Nociplastic pain is pain that arises from altered nociception despite that there is no clear evidence of actual or threatened tissue damage causing the activation of peripheral nociceptors or evidence for disease or lesion of the somatosensory system causing the pain [3]. However, in individuals with pain, multiple simultaneous mechanisms can play a role, described as mixed pain [4]. Central sensitisation (CS) is related to all three pain descriptors. CS is defined by the IASP as “the increased responsiveness of nociceptive neurons in the central nervous system to their normal or sub-threshold afferent input” [3]. Although CS has some overlap with nociplastic pain, it differs in the fact that CS refers to a neural mechanism and nociplastic pain to a pain

mechanism [5]. CS has been proven in animal studies, but not yet in humans, therefore CS should be regarded as a concept and therefore we used the term Human Assumed CS (HACS) [6]. Currently, no golden standard for HACS is available, and investigating HACS can be done by identifying reference clinical symptoms and signs [6]. Instruments like the Central Sensitisation Inventory (CSI) and the Quantitative Sensory Testing (QST) protocol are often used to assess the indicators of HACS [6]. An indicator for HACS is allodynia, a hypersensitivity to normally subthreshold innocuous stimuli [3,7]. Another indicator is hyperalgesia, an increased responsiveness to noxious stimuli [3,7]. Furthermore, temporal summation is another indicator, which is described as an increased response to repetitive noxious stimuli over time [7].

HACS has been researched in persons with other diagnoses, such as fibromyalgia and chronic low back pain [8], but not in single-handed individuals, despite the fact that it is known that many single-handed individuals suffer from musculoskeletal pain [1,2]. Knowledge about the presence of HACS could give additional insight into the development and persistence of MSCs, and could help clinicians in the treatment and prevention of those complaints [9]. This study aims to examine the presence of HACS in individuals with ULA and BPI with and without MSCs and healthy two-handed individuals, by performing the QST protocol [10] and evaluating results of the CSI [11]. We hypothesized that individuals with MSCs showed some indicators for HACS compared to individuals without MSCs. Within participants, we expected to see differences between a painful area and a non-painful area, showing more indicators in the painful area.

METHODS

The Medical Ethics Review Board of the University Medical Center Groningen (METc UMCG) approved the study (METc 2019/425). All participants signed an informed consent before the start of the study.

Three samples were included: individuals with ULA, either due to congenital transversal reduction deficiency or an acquired amputation, individuals with BPI, and matched controls. Participants were recruited via a list of adult eligible patients composed by clinicians of the UMCG, Center for Rehabilitation. Individuals with ULA were also recruited via the Dutch patient organization for persons with ULA. Controls were recruited via the network of the researchers through advertisements.

At the start of the measurements, participants filled in a survey with demographic and clinical characteristics (i.e. age, gender, handedness, cause of injury, affected side, level of injury, aid use). All participants also filled in the CSI questionnaire [11]. This is a self-reported questionnaire consisting of two sections (A and B) to assess the presence of HACS-related symptoms. In section A, 25 questions about how often a symptom occurred were rated on a 5-point Likert scale (range 0-100). A score higher than 40 could indicate HACS. Section B asked participants about previously diagnosed CS syndromes (CSS) and/or conditions related to HACS, such as restless legs syndrome or fibromyalgia.

Furthermore, all participants underwent the QST protocol. This protocol is composed of several sensory tests to quantify the function of the sensory nervous system [10]. Five sensory tests were executed resulting in seven outcomes. These were all performed on four body locations: thigh on the non-dominant/affected side as a control site, thigh on the dominant/unaffected side as a reference site, the most painful location of the upper extremity, and the location contralateral to this most painful location. The following tests were executed: 1) Dynamic Mechanical Allodynia (DMA): pain rating of a brush stroke (range 0-100); 2) Mechanical Detection Threshold (MDT): stimulus intensity of a Von Frey filament when touch was no longer perceived (range 0.125-1024mN); 3) Mechanical Pain Threshold (MPT): stimulus intensity of a pinprick when it becomes sharp (range 8-1024mN); 4) Mechanical Pain Sensitivity (MPS): the pain rating of the MPT (range 0-100), 5) Wind-Up Ratio (WUR): the ratio between pain rating of repeated stimuli and a single stimulus; 6) Pressure Pain Threshold (PPT): intensity in Newtons of pressure algometer; and 7) Pressure Pain Sensitivity (PPS): pain rating of the PPT (range 0-100).

Data records from the different tests and questionnaires were collected and imported into the database RedCap. The records were then exported that SPSS, where the analyses were performed. Before analysis, the ratio of the DMA and the WUR was calculated. A mean of the five repetitions of the MDT, MPT, and MPS was calculated, given that there were at least three valuable data points. Descriptive statistics of the sample characteristics and the main test results were calculated as median and range. Because data collection is ongoing, no statistical tests were performed.

RESULTS

Participants

Seven participants (six males) with BPI were included so far, since due to the COVID-19 regulations measurements were delayed. The median age of the participants was 65.3 years (range 36.3–74 years). The side of the BPI was right in four cases. The participants were diagnosed with BPI between 7 and 45 years ago (median 30 years). All seven had an accident that caused the BPI. Four individuals experienced MSCs in the previous year, while three did not. Of these four participants, three experienced MSCs during the last four weeks. The median duration of MSCs was 13 years (range 1.5–30 years). The location of the pain varied, in three of the participants with MSCs the most painful area was the affected shoulder/neck region. One participant experienced pain in the unaffected hand and fingers.

CSI outcomes

The mean (SD) of the CSI was 24 (11.00). Previously diagnosed CSS were jaw complaints (n=1), migraine (n=1) and neck injuries (n=2).

QST outcomes

The results for the QST are presented in Table 1. The DMA, an assessment for allodynia, was missing in almost all participants, indicating no pain from a single brush stroke. In the MDT, on the most painful site the intensities of the Von Frey hairs were higher compared to the contralateral site, indicating that the stimuli with lower intensities (i.e. thinner Von Frey hairs) were not felt and thus a decreased responsiveness. This was also seen in the MPT; a higher value meant that the pinprick was considered painful with a higher intensity (i.e. thicker pinprick), so less sensitive to the stimulus. Additionally, the stimuli were rated as less painful with the MPS. The WUR remained relatively similar between the test sites. All participants experienced more pain after the stimulus series in comparison with the single stimulus.

Table 1: QST test results for each test site.

QST Test (n=7)	Reference test site	Most painful test site	Contralateral test site (to most painful test test)[b]
1) DMA[a]	1.0 [1.0] (n=2)	1.0 [1.0] (n=1)	1.0 [1.0] (n=1)
2) MDT in mN	6 [3.2–11.2] (n=7)	9.6 [1.3–1024.0] (n=7)	3.1 [1.0–16.0] (n=6)
3) MPT in mN	115.2 [19.2–115.2] (n=7)	108.8 [16.0–1024.0] (n=7)	64.8 [19.2–454.2] (n=6)
4) MPS	3.4 [0.8–25.0] (n=7)	1.5 [0.6–7.5] (n=6)	3.5 [0.8–20.0] (n=6)
5) WUR[a]	2.5 [1.33–4.0] (n=7)	2.8 [2.0–4.0] (n=5)	2.67 [1.4–4.5] (n=5)
6) PPT in N	81 [45.0–138.0] (n=7)	46.5 [33.0–73.0] (n=6)	61.5 [27.5–93.0] (n=6)
7) PPS	4 [1.0–40.0] (n=7)	9.5 [2.0–50.0] (n=6)	16 [2.0–45.0] (n=6)

Legend: All results were reported as median [range] (n=). [a] The DMA/WUR cannot be calculated if the pain rating of the single stimulus was zero, those were registered as missing value. [b] One participant was not tested on the CTS. Abbreviations: QST, Quantitative Sensory Testing; DMA, dynamic mechanical allodynia; MDT, mechanical detection threshold; MPT, mechanical pain threshold; MPS, mechanical pain sensitivity; WUR, wind-up ratio; PPT, pressure pain threshold; PPS, pressure pain sensitivity;

DISCUSSION

Several individuals with ULA or BPI experience MSCs [1,2], which may indicate the presence of HACS in these people. Until now, knowledge on HACS in these populations remained underreported and this research aims to bridge that gap by using the CSI and QST protocol to assess indicators for HACS. In this study, seven individuals with BPI have participated. None of the participants reported a score above>39 points on CSI, which represents an often used cut-off point for the presence of HACS [11]. However, while often used, the validity of this cut-off is debated, and recently a clinically relevant cut-off of 30 points was suggested (males 25, females 33; [12]). Based on the newest cut-off, the presence of HACS is feasible in a subgroup in this study.

Regarding the QST results, differences were seen between the test sites, this could be explained by the fact that different body locations have different sensitivity to stimuli [10]. We did not find more indicators in the most painful site in comparison with the contralateral site. Almost all participants showed no values on the DMA, suggesting that allodynia is not present in these participants. Results on hyperalgesia, assessed with the MDT, MPT, and MPS, showed that the most painful site was less responsive and less painful than the contralateral side. Temporal summation is considered positive when the pain intensity increases with repeated stimuli, so this might be present [6]. However, there were no differences seen between the test areas. These surprising results might be explained because these QST tests consist of cutaneous stimuli and might not be very adequate for musculoskeletal conditions [13]. Another explanation could be that HACS was not present, but that the pain could be described as nociceptive, neuropathic, and/or nociplastic pain. These pain descriptors have to be examined with other tests and physical examinations. Furthermore, due to the lack of cut-off values for the QST, it is difficult to interpret the data [6].

This is to our knowledge the first study to examine the presence of HACS in single-handed individuals. The CSI and the QST are quite easily adapted into clinical practice and could give additional insight into individuals with ULA or BPI experiencing MSCs. However, individuals with ULA and BPI may also suffer from phantom pain and neuropathic pain. As we did not examine these pain conditions, this may have influenced the results. Currently, there is no golden standard for HACS and due to the lack of cut-off values for the QST, the presence of HACS is difficult to determine. Other QST measures, such as conditioned pain modulation (CPM) and thermal stimuli were not included in this study due to practical reasons. Adding these tests could give a broader insight into HACS in this population. As this is an ongoing study, only preliminary results were reported. More participants (also with ULA) will be included and we expect to be able to present more results at the congress. Hopefully, this will show explanations for the findings. Analysing the group with ULA and the controls could also show similarities and differences between the three samples.

In conclusion, this preliminary data showed possible HACS in a subgroup of BPI participants, depending on the applied cut-off score of the CSI questionnaire. Variability between subjects was considerable. This suggests that an individual approach could be more efficient. With more results, this study could shed light on the role of the pain mechanisms and CS in single-handed individuals. This could give more insight into MSCs in individuals with ULA and BPI, and could aid in the treatment and prevention of these complaints.

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