

NOTICE: this is the author's version of a work that was accepted for publication in Archives of Physical Medicine and Rehabilitation. Changes resulting from the publishing process, such as peer review, editing, corrections, structural formatting, and other quality control mechanisms may not be reflected in this document. Changes may have been made to this work since it was submitted for publication. A definitive version was subsequently published in Archives of Physical Medicine and Rehabilitation, Vol. 96, no. 2 (2015).
DOI: 10.1016/j.apmr.2014.09.015

1 **Title: Divergent sensory phenotypes in non-specific arm pain:**
2 **comparison with cervical radiculopathy**

3 Moloney, N^{1,2}

4 Hall, TM³

5 Doody, C¹

6 ¹UCD School of Public Health, Physiotherapy and Population Science, University College
7 Dublin, Belfield, Dublin 4, Ireland

8 ² Discipline of Physiotherapy, Faculty of Health Sciences, The University of Sydney, PO Box
9 170, Lidcombe, NSW 1825, Australia.

10 ³School of Physiotherapy, Curtin University of Technology, G.P.O. Box U1987, Perth, WA
11 6845, Australia

12 ⁴Manual Concepts, P.O. Box 1236, Booragoon, WA 6954, Australia

13

14

15

16

17

18 Corresponding author: Niamh Moloney, Discipline of Physiotherapy, Faculty of Health
19 Sciences, The University of Sydney, PO Box 170, Lidcombe, NSW 1825, Australia.

20 Email: niamh.moloney@sydney.edu.au

21 Tel: +61 2 9351 9266

22 |

23 **Title: Divergent sensory phenotypes in non-specific arm pain:**
24 **comparison with cervical radiculopathy**

25 **ABSTRACT**

26 Objective: The primary research question under review was whether distinct sensory
27 phenotypes were identifiable in individuals with non-specific arm pain (NSAP) and if they
28 differed from people with cervical radiculopathy. A secondary question considered whether
29 the frequency of features of neuropathic pain, kinesiophobia, high pain ratings, hyperalgesia
30 and allodynia differed according to sub-groups of sensory phenotypes.

31

32 Design: A cross sectional study

33

34 Setting: Higher education institution

35 Participants: Forty office people with NSAP, 17 with cervical radiculopathy, and 40 age-
36 gender-matched healthy controls.

37

38 Interventions: Nil

39

40 Main Outcome Measures: Participants were assessed using quantitative sensory testing (QST)
41 comprising thermal and vibration detection thresholds, and thermal and pressure pain
42 thresholds; clinical examination and relevant questionnaires. Sensory phenotypes were
43 identified for each individual in the patient groups using z-score transformation of the QST
44 data.

45

46 Results: Individuals with NSAP and cervical radiculopathy present with a spectrum of
47 sensory abnormalities; a dominant sensory phenotype was not identifiable in individuals with
48 NSAP. No distinct pattern between clinical features and questionnaire results across sensory
49 phenotypes was identified in either group.

50

51 Conclusion: When considering sensory phenotypes, neither individuals with NSAP nor
52 cervical radiculopathy should be considered homogenous. Therefore, people with either
53 condition may warrant different intervention approaches according to their individual sensory

54 phenotype. Issues relating to the clinical identification of sensory hypersensitivity and the
55 validity of QST are highlighted.

56

57 **Abbreviations: QST: quantitative sensory testing; NSAP: Non-specific arm pain;**

58 **LANSS: Leeds assessment for neuropathic symptoms and signs**

59

60 **Keywords:** Sensory threshold; pain threshold; non-specific arm pain (repetitive strain
61 injury); cervical radiculopathy; musculoskeletal arm pain.

62

63 INTRODUCTION

64

65 Work related upper limb disorders are a significant public health problem with a prevalence
66 of 29% (Eurostat),¹ 50% of which are described as non specific.² Non-specific arm pain
67 (NSAP) commonly affects computer users and is frequently associated with poor prognoses.³
68 The absence of consistent information regarding the pathology and pathophysiology
69 underlying NSAP has obvious implications for clinical decision making. Given growing
70 computerisation of the global workforce as well as the intensification of work, improving our
71 understanding of work related non-specific conditions is imperative for improving
72 intervention selection and outcomes.

73

74 Quantitative sensory testing (QST) is a non-invasive means of assessing sensory and pain
75 perception, which potentially provides insights into underlying pathophysiological
76 mechanisms of a condition,⁴ and has seen growing use in the investigation of patient
77 populations such as complex regional pain syndrome, whiplash and neuropathic pain.⁵⁻¹⁰ In
78 studies of NSAP, the presence of hypoesthesia to vibration has previously been recorded,¹¹⁻
79 ¹³ which may suggest the presence of a minor neuropathy^{11 12} and/or altered central
80 processing,¹³ possibly secondary to pain.¹⁴ Furthermore, we recently reported the presence of
81 sensory hypersensitivity to pressure, cold and heat as characteristic of NSAP, while
82 hypoesthesia to vibration explained a small percentage of the variance (11%).¹⁵ In addition,
83 in comparison to people with cervical radiculopathy and healthy controls, people with NSAP
84 had normal thermal detection thresholds, whereas sensory hypoesthesia, to both thermal and
85 vibration stimuli, was evident in people with cervical radiculopathy.¹⁵

86

87 The German Research Network on Neuropathic Pain has suggested that detailed analyses of
88 sensory profiles may yield information regarding the underlying sensory phenotype in
89 individuals and within patient populations and that this may help to direct clinical decision
90 making.¹⁶ They presented data from a large group of people with various neuropathy and
91 neuropathic pain conditions with key sensory phenotypes identified i.e. sensory loss, sensory
92 hypersensitivity, both sensory hypersensitivity + sensory loss and no abnormality.⁶ Each of
93 the phenotypes was represented both within each patient population and across the different
94 conditions studied.⁶ A further study by Gierthmühlen et al.⁵ identified the presence of
95 different sensory phenotypes in people with complex regional pain syndrome, with some
96 people exhibiting increased sensitivity while others demonstrated decreased sensitivity to

97 thermal and mechanical stimuli; thus, comparison of mean values may not thoroughly
98 represent sensory findings in patient groups. Therefore, while results from between group
99 comparisons identified the presence of sensory hypersensitivity as well as hypoaesthesia to
100 vibration in NSAP, the presence of various sensory phenotypes or indeed a dominant sensory
101 phenotype is not yet known in this group.

102

103 The use of QST in clinical practice has limitations in that equipment is not widely available
104 and as such, understanding the relationship between QST findings and clinical features of
105 pain and clinical signs of sensory loss or sensory hypersensitivity is important. Previous
106 reports suggest that pain and disability ratings are poorly correlated with QST findings;¹⁷
107 however, data on the relationship between clinical features of pain in study populations sub-
108 grouped according to sensory phenotype is lacking and warrants further investigation.

109

110 The primary research question under review in this study was whether distinct phenotypes are
111 identifiable in NSAP and if they differ to cervical radiculopathy, a known neuropathic
112 disorder. A secondary question considered whether the frequency of features of neuropathic
113 pain, kinesiophobia, high pain ratings, hyperalgesia and allodynia differed according to sub-
114 groups of sensory phenotypes. We hypothesised that individuals with NSAP would present
115 with a spectrum of sensory phenotypes within the group and that group sensory phenotypes
116 would differ between NSAP and cervical radiculopathy. We also hypothesized that people
117 with sensory hypersensitivity on QST would present with higher pain ratings, clinical
118 features of hyperalgesia and higher scores on kinesiophobia and neuropathic pain screening
119 scales.

120

121 **METHODS**

122 **Design**

123 A cross-sectional observational study investigating sensory profiles in participants with
124 NSAP, cervical radiculopathy and healthy controls was undertaken. Volunteers were
125 screened for inclusion criteria for each particular group, the criteria for which have been
126 previously reported.¹⁵ Subsequently, participants underwent a physical examination and QST
127 and were asked to complete a series of questionnaires for self-reported pain features and
128 kinesiophobia. All aspects of group allocation and data collection were performed by one
129 investigator (NM). The order of QST testing was randomized. The study was approved by the
130 Human Research Ethics Committee for Life Sciences in University College Dublin and the

131 involved hospitals. All participants were unpaid volunteers and all provided written informed
132 consent before inclusion.

133

134 **Participants**

135 In relation to NSAP, volunteers with arm pain, aged between 18-65 years old that were
136 recruited from metropolitan hospitals, medical and physiotherapy practices and via a multi-
137 media campaign were screened for inclusion in this study (through a medical history and
138 physical examination). Participants were assigned to the NSAP group if they had pain in the
139 arm in the absence of a specific diagnosis,¹⁸ were office workers who had significant upper
140 limb pain as defined by a numerical pain rating of $\geq 3/10$,^{19,20} for longer than 3 months, who
141 spent more than 40% of their working week using desktop equipment,¹² and who had been
142 employed using desk-top equipment for at least two years.²¹

143 Participants with possible cervical radiculopathy were recruited from metropolitan hospitals
144 as well as medical and physiotherapy practices. They were assigned to the cervical
145 radiculopathy group if they had *all* of the following: radicular pain in the upper limb
146 ($\geq 3/10$),^{19,20} a positive upper limb neurodynamic test, a positive Spurling's test, MRI
147 confirmation of nerve compression,²²⁻²⁴ as well as at least one concordant clinical sign of
148 conduction loss²⁵ (i.e. one of diminished/absent reflexes, myotomal weakness or sensory loss
149 in a dermatomal pattern).

150 Control participants were included if they did not have a history of significant neck, scapular
151 or shoulder pain over the previous 12 months and did not use desktop equipment for more
152 than 40% of their working week.¹² As participants from the cervical radiculopathy group
153 were older than the non-specific arm pain group, control participants were age- and gender-
154 matched to each group.

155 Volunteers were excluded from the study if they had any of the following: generalized
156 neurological disorders, generalized musculoskeletal/inflammatory disorders, a history of low
157 back pain and/or low back related leg pain over the previous six months, a history of
158 migraine over the previous six months, previous trauma to the upper quadrant, diabetes,
159 endocrine disorders, epilepsy or if they had been diagnosed with any mental health /
160 psychiatric disorders.

161

162

163

164 **Measurements**

165 ***Sensory assessment***

166 A previously published QST protocol was undertaken²⁶ measuring the following parameters:
167 cold, warm and vibration detection thresholds; cold, heat and pressure pain thresholds. All
168 measures were recorded on three sites on each upper limb. Thermal and vibration tests were
169 performed using a NeuroSensory Analyser (TSA 2001 II Medoc, Israel). For thermal testing,
170 a Peltier thermode (16 x 16mm) was attached directly over sites in the hand innervated by
171 C6, C7 and C8. A Vibrometer (VSA 3000 II 2001 Medoc, Israel) was used to measure
172 vibration thresholds with readings taken over sites of the hand innervated by C6, C7 and C8.
173 Pressure pain thresholds were determined using a hand held pressure algometer with a probe
174 size of 1cm² (Somedic AB, Farsta, Sweden) and an application rate of 40 kPa/s over the
175 median nerve (cubital fossa), ulnar nerve (between olecranon and medial epicondyle of the
176 humerus) and radial nerve (mid-lower third of the humerus). Triplicate recordings were taken
177 at each site for all QST parameters and the mean values used for analyses. In order to assess
178 the presence of widespread sensitivity, thermal testing and pressure pain thresholds were
179 recorded at a site remote from the upper quadrant, in this case, unilaterally over Tibialis
180 anterior muscle. All aspects of QST have been found to have acceptable reliability.²⁷⁻²⁹

181

182 Hyperalgesia to pin prick was assessed by recording pain responses to a pin-prick stimulus
183 applied in the affected area compared to an unaffected area i.e. the contralateral limb where
184 possible, otherwise the nearest pain-free area was used. The presence of hyperalgesia was
185 determined if the response in the affected area was more painful than in the unaffected area.³⁰
186 Allodynia was assessed by moving a brush over the affected area and comparing the response
187 to that in an unaffected area. The stimulus was applied with a single light stroke of at least
188 2cm in length. Brush stroke allodynia was considered present if the participant reported the
189 stimulus as painful.³⁰

190

191 ***Self-reported measures of pain and fear avoidance***

192 All participants in the patient groups completed the following questionnaires: the Leeds
193 Assessment for Neuropathic Symptoms and Signs (LANSS) questionnaire with a score of
194 ≥ 12 (out of 24) indicating the possible presence of neuropathic pain;³¹ the Tampa Scale of
195 Kinesiophobia³² with a score of ≥ 37 (out of 68) considered to indicate the presence of
196 significant fear-avoidant pain beliefs,³³ and all provided an average numerical pain rating
197 (NPRS) for the previous 24 hours.

198

199 **Data Analysis**

200 Data were analysed using SPSS software, version 19.0 (SPSS, USA).

201 ***Preliminary data management***

202 QST data were log-transformed before statistical analyses in order to achieve normal
203 distribution of the data,⁴ which subsequent analysis revealed was successful. Friedman's tests
204 were used to assess the effect of test site between upper limb sites (C6, C7 & C8 dermatomes
205 or median, ulnar & radial nerves) for QST parameters. As no significant differences were
206 identified for QST parameters between these sites, data were averaged and the resultant value
207 used for subsequent analyses.

208 ***Z-transformation***

209 To compare sensory phenotypes of individuals with NSAP or cervical radiculopathy with
210 age-matched healthy controls, QST data were z-transformed to generate z-scores, which
211 allows scores from individuals with a condition to be directly compared to 'normals' in order
212 to identify any abnormality in that individual, as has been previously advocated for
213 assessment of individual sensory profiles.^{6 16} QST data were z-transformed using the mean
214 (SD) of their respective control group as reference data i.e. control participants were divided
215 into two groups; one group of 40 participants matched, according to age and gender, to the 40
216 participants with NSAP and a further group of 14 participants matched to the cervical
217 radiculopathy group. The formula used for z-transformation was: $Z\text{-score} = (X \text{ single}$
218 $\text{participant} - \text{Mean controls}) / \text{SD controls}$.⁴ For clarity of data presentation, the algebraic sign
219 of the resulting z-score was adjusted appropriately so that it reflected patients' sensitivity for
220 each parameter i.e. values above zero indicated increased sensitivity to the tested stimuli;
221 values below zero indicated reduced sensitivity to the tested stimuli.

222

223 Sensory phenotypes for each participant were assessed by generating sensory phenotype
224 graphs using resultant z-scores. Z-scores of > 1.96 was considered indicative of increased
225 sensitivity to the tested stimuli compared with controls (hyperalgesia/allodynia), while z-
226 scores of < -1.96 was considered indicative of sensory loss.⁶ Each individual was classified
227 according to their sensory phenotype into one of six possible phenotypes: (1) sensory loss_{small}
228 i.e. small fibre sensory loss as determined in this study by the presence of cold and/or warm
229 hypoaesthesia; (2) sensory loss_{large} i.e. large fibre sensory loss as determined by the presence
230 of vibration hypoaesthesia; (3) sensory loss_{mixed} i.e. a combination of small and large fibre
231 sensory loss; (4) sensory hypersensitivity as determined by the presence of hyperalgesia in
232 response to cold pain, and/or heat pain and/or pressure pain thresholds; (5) a combination of

233 sensory hypersensitivity + sensory loss, and (6) no abnormality.⁶ When sensory
234 hypersensitivity was recorded, data were inspected to see if hypersensitivity was localised to
235 upper limb sites or if it was widespread i.e. included sensory hypersensitivity at the Tibialis
236 Anterior site.

237 The frequencies of different sensory phenotypes in each patient group were recorded and
238 between-group comparisons of sensory phenotypes were conducted using percentage risk
239 difference with 95% confidence intervals.

240

241 *Sample size:*

242 The sample size was calculated based on mean and standard error vibration threshold data
243 from a study by Greening et al., (2003). A sample of size of 40 participants with NSAP, 40
244 participants with cervical radiculopathy and 40 matched control subjects was required to
245 detect a medium effect size (0.5) with 0.8 power and 0.05 two tailed significance level.

246

247 **RESULTS**

248 **Characteristics of NSAP and cervical radiculopathy groups**

249 The baseline characteristics of participants are presented in Table 1. The groups were similar
250 with regards to pain duration; however, the cervical radiculopathy group were older
251 ($p<0.001$) and more disabled ($p=0.002$) than the NSAP group. The cervical radiculopathy
252 sample was smaller than anticipated ($n=17$), primarily due to the strict inclusion criteria. The
253 control group for the NSAP group comprised of 40 age- and gender- matched healthy people,
254 while the control group for the cervical radiculopathy group comprised of 14 age- and
255 gender- matched healthy people.

256 Individual sensory phenotypes are presented in Table 2. Overall, both groups presented with
257 divergent sensory phenotypes; 45% of the NSAP group and 35% of the cervical
258 radiculopathy group presented with the phenotypes 'sensory hypersensitivity' and 'sensory
259 hypersensitivity + sensory loss'. A further 30% of both groups had evidence of 'sensory
260 loss'. No sensory abnormality was evident in 25% ($n=10$) of the NSAP group and 35% ($n=6$)
261 of the cervical radiculopathy group.

262 Results from risk difference analyses revealed no significant differences between the groups
263 with respect to the frequency of sensory phenotype. Equal numbers of participants presented
264 with localised and widespread sensory hypersensitivity in both groups.

265

266 **Clinical features and questionnaire results across sensory phenotypes**

267 The frequency of LANSS scores ≥ 12 , Tampa scale of kinesiophobia scores ≥ 37 , pain
268 $> / < 5 / 10$, hyperalgesia and allodynia across each sensory phenotype in both patient groups is
269 depicted in Table 3. No distinct pattern was evident with respect to the representation of
270 questionnaire results, high pain levels or clinical measures of hypersensitivity across sensory
271 phenotypes in either patient group. Those with widespread sensory hypersensitivity did not
272 present with higher scores on any clinical measure than those with localised or no sensory
273 hypersensitivity.

274

275 **DISCUSSION**

276 *Sensory phenotypes in NSAP and cervical radiculopathy*

277 The results of this study provide evidence of bi-directional sensory abnormalities in
278 individuals with NSAP with evidence that a distinct sensory phenotype is not evident in these
279 individuals. While bi-directional sensory abnormalities were also evident in individuals with
280 cervical radiculopathy, it was notable that 35% of the cervical radiculopathy group presented
281 with no sensory abnormality using QST. The presence of bi-directional sensory abnormalities
282 in both groups in this study is consistent with data from a similar cohort of people with neck
283 and arm pain,³⁴ as well as other cohorts with neuropathies and complex regional pain
284 syndrome.^{5 6} This further supports the argument for assessment of sensory phenotypes in
285 patient populations on the basis that heterogeneity with respect to sensory phenotypes exists
286 within patient cohorts; hence, people with the same condition could warrant different
287 approaches to assessment and treatment.^{6 35}

288

289 The identification of different sensory phenotypes within NSAP is an important finding.
290 Whilst we previously reported group data indicating that sensory hypersensitivity was a key
291 characteristic in this group,¹⁵ the current findings indicate that just over 50% of the NSAP
292 group did not have signs of sensory hypersensitivity and presented with either sensory
293 hypoaesthesia or no sensory abnormality. The identification of the absence or presence of
294 sensory hypersensitivity is important as the presence of sensory hypersensitivity has been
295 shown to be a predictor of poor prognosis and poor treatment response in other
296 musculoskeletal populations,^{7 38 39} and thus, may be an important consideration in NSAP and
297 cervical radiculopathy. Further, the presence of sensory hypersensitivity is important
298 clinically in considering appropriate interventions in order to prevent acute exacerbations of
299 symptoms. For example, people with sensory hypersensitivity have previously been shown to
300 have less effective descending pain modulation in response to exercise,⁴⁰ therefore, selected

301 exercise dosages would need careful consideration in a patient with a dominance of sensory
302 hypersensitivity. However, for those identified with sensory hypoaesthesia or no sensory
303 abnormality, it is possible that their prognosis is more favourable, although prospective
304 studies are required to elucidate this further.

305

306 Almost half of the NSAP group and 35% of the cervical radiculopathy group in this study
307 presented with sensory hypersensitivity, which likely reflects mechanisms of peripheral and
308 central sensitisation. In addition, 27% of the NSAP group presented ‘sensory loss + sensory
309 hypersensitivity’. This may reflect the interplay between the mechanisms of hypoaesthesia
310 and hypersensitivity. The presence of pain has been shown to cause an increase in detection
311 thresholds;¹⁴ in contrast, the presence of neuronal insult, as has been suggested in NSAP³⁶
312 may lead to sensitisation of peripheral and central pathways.³⁷ Both scenarios could explain
313 the presentation of sensory hypersensitivity in addition to sensory loss.

314 .

315

316 *Clinical features and sensory phenotypes*

317 How to identify sensory hypersensitivity in clinical practice is an important consideration.
318 Currently, there are neither established guidelines nor validated measures to do this and
319 whether QST could fill this void is hampered by the limited availability of equipment in
320 clinical practice, as well as the large variability in normative data and lack of established cut-
321 off values. Recent guidelines for the assessment of neuropathic pain recommend that if QST
322 is used in clinical practice, it should only form part of an overall clinical assessment.⁴² This
323 raises the question whether self-reports of pain intensity and features of bedside examination
324 are valid means of assessing sensory hypersensitivity. Previous meta-analysis indicated that
325 QST measures of sensory hypersensitivity and self-reported pain and disability were poorly
326 correlated;⁴¹ however, it was highlighted in that study that many of the study participants
327 included in the analysis may not have been sensitised, in which case a strong relationship
328 between QST and self-reports of pain and disability would not be expected.⁴¹ In the current
329 study, we aimed to investigate whether particular clinical features would be more frequent
330 among sub-groups of sensory phenotypes. Specifically, we hypothesized that higher levels of
331 pain, higher scores on neuropathic pain and kinesiophobia questionnaires and clinical features
332 of hypersensitivity (pin-prick hyperalgesia and allodynia) would be more evident in those
333 with the phenotype ‘sensory hypersensitivity’; however, we did not find a distinct pattern in

334 either the NSAP or cervical radiculopathy groups, even when comparing those with a sensory
335 abnormality to those without a sensory abnormality.

336 Relatively few people with NSAP in this study (28%) presented with kinesiophobia with no
337 demonstrable pattern noted across different phenotypes. The cervical radiculopathy group
338 presented with kinesiophobia more frequently (59% of participants), with 24% of those with
339 kinesiophobia demonstrating sensory hypersensitivity as their dominant sensory phenotype.
340 Both groups had over 60% of participants presenting pain rating ≥ 5 , but no discernible
341 pattern was evident regarding which sensory phenotypes presented with higher pain ratings.
342 Indeed, nine of the 13 people with no sensory abnormality in the NSAP group had a pain
343 rating of ≥ 5 . In considering these findings, it is important to note that the small sample size
344 and particularly the small numbers in each subgroup, mean these data should be considered
345 preliminary and as such, further studies on larger sample sizes are warranted.

346

347 Nonetheless, the challenge of how to assess the presence of sensory hypersensitivity in
348 clinical practice without using QST remains. One reason for the poor relationship between
349 QST and clinical measures may be that the clinical measures tested to date against QST are
350 not measuring the same construct. Two clinical measures that may be useful are pin-prick
351 hyperalgesia and brush stroke allodynia⁴³ but these measures were rarely positive in this
352 study, despite the frequent presence of sensory hypersensitivity to other measures e.g. heat
353 and cold. Recently, stronger correlations were identified between pain ratings on application
354 of ice versus cold pain thresholds;⁴⁴ therefore, this may be a better clinical measure of cold
355 sensitivity. A final consideration is that, QST, which quantifies responses to experimentally
356 induced pain may evoke different central nervous system responses than spontaneous pain,
357 normally experienced by patients, as has been demonstrated by brain imaging studies.⁴⁵
358 Therefore, the development of better clinical tools for the assessment of sensory
359 hypersensitivity is needed. The recommendation that assessment of descending pain
360 modulation and pain magnitude rating for a suprathreshold stimulus might facilitate a better
361 understanding of a sensitized nociceptive system rather than threshold measures may also
362 hold validity.⁴⁶

363

364 **Study Limitations**

365 Due to the relatively small sample size of this study, particularly for cervical radiculopathy,
366 and the small numbers in each sensory phenotype group, these results should be considered
367 as preliminary findings.

368
369
370
371
372
373
374
375
376
377
378
379

Conclusion

The results of this study demonstrate divergent sensory phenotypes in NSAP as well as in cervical radiculopathy with implications for clinical decision making. NSAP and cervical radiculopathy should not be considered homogenous groups and individuals may warrant different intervention approaches according to their sensory phenotype. Researchers should also consider this when stratifying people for intervention studies. Identifying the presence of sensory hypersensitivity is difficult in clinical practice and while some studies have reported criteria for classifying pain;⁴⁷⁻⁴⁹ validated tools are still lacking with further research needed in this regard.

380 **REFERENCES**

381

- 382 1. Eurostat work and health in the European Union: A statistical portrait, office for official
383 publications of the European communities Luxemburg, 2004.
- 384 2. Walker-Bone K, Palmer KT, Reading I, Coggon D, Cooper C. Prevalence and impact of
385 musculoskeletal disorders of the upper limb in the general population. *Arthritis and*
386 *Rheumatism* 2004;51(4):642-51.
- 387 3. van Eijsden-Besseling MDF, van der Bergh KA, Staal JB, De Bie RA, van der Heuvel WJ.
388 The course of non-specific work-related upper limb disorders and the influence of
389 demographic factors, psychologic factors and physical fitness on clinical status and
390 disability. *Arch Phys Med Rehabil* 2010;91:862-67.
- 391 4. Rolke R, Magel W, Campbell, Andrews K, et al. Quantitative Sensory testing: A
392 comprehensive protocol for clinical trials. *European Journal of Pain* 2006;10:77-88.
- 393 5. Gierthmühlen J, Maier C, Baron R, Tolle T, Treede R-D, Birbaumer N, et al. Sensory
394 signs in complex regional pain syndrome and peripheral nerve injury. *Pain*
395 2012;153:765-74.
- 396 6. Maier C, Baron R, Tölle TR, Binder A, Birbaumer N, Birklein F, et al. Quantitative
397 sensory testing in the German Research Network on Neurophatic Pain (DFNS):
398 Somatosensory abnormalities in 1236 patients with difference neuropathic pain
399 syndromes. *Pain* 2010;150(3):439-50.
- 400 7. Sterling M, Jull G, Vicenzino B, Kenardy J. Sensory hypersensitivity occurs soon after
401 whiplash injury and is associated with poor recovery. *Pain* 2003;104:509-17.
- 402 8. Kamper SJ, Maher CG, Hush JM, Pedler A, Sterling M. Relationship between pressure
403 pain thresholds and pain ratings in patients with whiplash associated disorder. *Clinical*
404 *Journal of Pain* 2011;27(6):495-501.
- 405 9. Chien A, Eliav E, Sterling M. Hypoaesthesia occurs with sensory hypersensitivity in
406 chronic whiplash - Further evidence of a neuropathic condition. *Manual Therapy*
407 2009;14(2):138-46.
- 408 10. Chien A, Sterling M. Sensory hypoaesthesia is a feature of chronic whiplash but not
409 chronic idiopathic neck pain. *Manual Therapy* 2010;15:48-53.
- 410 11. Greening J, Lynn B. Vibration sense in the upper limbs of patients with RSI and at risk
411 workers. *International Archives of Occupational and Environmental Health*
412 1998;71:29-34.
- 413 12. Greening J, Lynn B, Leary R. Sensory and autonomic function in the hands of patients
414 with non-specific arm pain (NSAP) and asymptomatic office workers. *Pain*
415 2003;104:275-81.
- 416 13. Tucker AT, White PD, Kosek E, Pearson RM, Henderson M, Coldrick AR, et al.
417 Comparison of vibration perception thresholds in individuals with diffuse upper limb
418 pain and carpal tunnel syndrome. *Pain* 2007;127:263-69.
- 419 14. Apkarian A, Stea R, Bolanowski S. Heat-induced pain diminishes vibrotactile perception:
420 a touch gate. *Somatosensory Motor Research* 1994;11(3):259-67.
- 421 15. Moloney NA, Hall TM, Doody CM. Sensory hyperalgesia is characteristic of non-specific
422 arm pain. *Clinical Journal of Pain* 2013;29:948-56.
- 423 16. Rolke R, Baron R, Maier C, Tolle TR, Treede R-D, Beyer A, et al. Quantitative sensory
424 testing in the german research network on neuropathic pain (DFNS): standardized
425 protocol and reference values. *Pain* 2006;123(3):231-43.
- 426 17. Hübscher M, Moloney N, Leaver A, Rebbeck T, McAuley JH, Refshauge KM.
427 Relationship between quantitative sensory testing and pain or disability in people with
428 spinal pain—A systematic review and meta-analysis. *Pain* 2013;154(9):1497-504.

- 429 18. Boocock MG, Collier JM, McNair PJ, Simmonds M, Larmer PJ, Armstrong B. A
430 Framework for the Classification and Diagnosis of Work- Related Upper Extremity
431 Conditions: Systematic Review. *Seminars in Arthritis and Rheumatism* 2009;38:296-
432 311.
- 433 19. Agostinho CMS, Scherens A, Richter H, Schaub C, Rolke R, Treede R-D, et al.
434 Habituation and short-term repeatability of thermal testing in healthy human subjects
435 and patients with chronic non-neuropathic pain. *European Journal of Pain*
436 2009;13:779-85.
- 437 20. Madeleine P, Lundager B, Voigt M, Arendt-Nielsen L. Sensory manifestations in
438 experimental and work-related chronic neck-shoulder pain. *European Journal of Pain*
439 1998;2:251-60.
- 440 21. Johnston V, Jimmieson NL, Jull G, Souvlis T. Quantitative sensory measures distinguish
441 office workers with varying levels of neck pain and disability. *Pain* 2008;137:257-65.
- 442 22. Radhakrishnan K, Litchy W, O'Fallon W, Kurland L. Epidemiology of cervical
443 radiculopathy. A population- based study from Rochester, Minnesota, 1976 through
444 1990. *Brain* 1994;117(Pt 2): 325-35.
- 445 23. Rubinstein SM, Pool JJM, van Tulder MW, Riphagen II, de Vet HCW. A systematic
446 review of the diagnostic accuracy of provocative tests of the neck for diagnosing
447 cervical radiculopathy. *Eur Spine J* 2007;16:307-19.
- 448 24. Wainner LR, Fritz JM, Irrgang JJ, Boninger ML, Delitto A, Allison CS. Reliability and
449 diagnostic accuracy of the clinical examination and patient self-report measures for
450 cervical radiculopathy. *Spine* 2003;28(1):52-62.
- 451 25. Bono CM, Ghiselli G, Gilbert TJ, Kreiner DS, Reitman C, Summers JT, et al. An
452 evidence-based clinical guideline for the diagnosis and treatment of cervical
453 radiculopathy from degenerative disorders. *THE Spine Journal* 2011;11:64-72.
- 454 26. Moloney N, Hall T, Doody C. An investigation of somatosensory profiles in work related
455 upper limb disorders: a case-control observational study protocol. *BMC*
456 *Musculoskeletal Disorders* 2010;11(1):22.
- 457 27. Moloney N, Hall T, Doody C. Reliability of thermal quantitative sensory testing: A
458 systematic review. *Journal of Rehabilitation, Research and Development*
459 2012;49(2):191-208.
- 460 28. Moloney N, O'Sullivan T, Hall T, Doody C. Reliability in thermal quantitative sensory
461 testing of the hand in a cohort of young healthy adults. *Muscle and Nerve*
462 2011;44(4):547-52.
- 463 29. Geber CK, T, Azad S, Birklein F, Gierthmühlen J, Hüge V, Lauchart M, et al. Test-retest
464 and interobserver reliability of quantitative sensory testing according to the protocol
465 of the German Research Network on Neuropathic Pain (DFNS): a multi-centre study.
466 *Pain* 2011;152(3):548-56.
- 467 30. Leffler A-S, Hansson P. Painful traumatic peripheral partial nerve injury - sensory
468 dysfunction profiles comparing outcomes of bedside examination and quantitative
469 sensory testing. *European Journal of Pain* 2008;6 (Suppl A):47-50.
- 470 31. Bennett M. The LANSS Pain Scale: the Leeds assessment of neuropathic symptoms and
471 signs. *Pain* 2001;92(1-2):147-57.
- 472 32. Kori S, Miller R, Todd D. Kinesophobia: a new view of chronic pain behaviour. *Pain*
473 *Management* 1990;3(35-43).
- 474 33. Vlaeyen JWS, Kole-Snijders AMJ, Boeren RGB, van Eek H. Fear of movement/(re)
475 injury in chronic low back pain and its relation to behavioral performance. *Pain*
476 1995;62:363-72.

- 477 34. Tampin B, Slater H, Hall T, Lee G, Briffa NK. Quantitative sensory testing
478 somatosensory profiles in patients with cervical radiculopathy are distinct from those
479 in patients with nonspecific neck-arm pain. *Pain* 2012;153(12):2403-14.
- 480 35. Cruz-Almeida Y, Fillingim RB. Can quantitative sensory testing move us closer to
481 mechanism-based pain management? *Pain Med* 2014;15(1):61-72.
- 482 36. Greening J. How inflammation and minor nerve injury contribute to pain in nerve root
483 and peripheral neuropathies. In: Boyling JD, Jull GA, editors. *Grieve's Modern*
484 *Manual Therapy: The Vertebral Column*. Third ed. London: Churchill Livingstone,
485 2004.
- 486 37. Woolf CJ. Dissecting out mechanisms responsible for peripheral neuropathic pain:
487 Implications for diagnosis and therapy. *Life Sciences* 2004;74:2605-10.
- 488 38. Schafer A, Hall T, Muller G, Briffa K. Outcomes differ between subgroups of patients
489 with low back and leg pain following neural manual therapy: a prospective cohort
490 study. *European Spine Journal* 2011;20(3):482-90.
- 491 39. Jull G, Sterling M, Kenardy J, Beller E. Does the presence of sensory hypersensitivity
492 influence outcomes of physical rehabilitation for chronic whiplash?--A preliminary
493 RCT. *Pain* 2007;129(1-2):28-34.
- 494 40. Nijs J, Kosek E, Van Oosterwijck J, Meeus M. Dysfunctional endogenous analgesia
495 during exercise in patients with chronic pain: to exercise or not to exercise? *Pain*
496 *Physician* 2012;15(3Suppl):ES205-13.
- 497 41. Hübscher M, Moloney N, Leaver A, Rebbeck T, McAuley J, Refshauge K. Relationship
498 between quantitative sensory testing and pain or disability in people with spinal pain -
499 a systematic review and meta-analysis. *Pain* 2013;154:1497-504.
- 500 42. Backonja MM, Attal N, Baron R, Bouhassira D, Drangholt M, Dyck PJ, et al. Value of
501 quantitative sensory testing in neurological and pain disorders: NeuPSIG consensus.
502 *Pain* 2013;154(9):1807-19.
- 503 43. Woolf CJ. Central sensitization: Implications for the diagnosis and treatment of pain.
504 *Pain* 2011;15(3):S2-15.
- 505 44. Maxwell S, Sterling M. An investigation of the use of a numeric pain rating scale with ice
506 application to the neck to determine cold hyperalgesia. *Manual Therapy*
507 2013;18(2):172-74.
- 508 45. Parks EL, Geha PY, Baliki M, Katz JN, Schnitzer TJ, Apkarian VA. Brain activity for
509 chronic knee osteoarthritis: Dissociating evoked pain from spontaneous pain.
510 *European Journal of Pain* 2011;15:843e1-43e14.
- 511 46. Arendt-Nielsen L, Yarnitsky D. Experimental and clinical applications of quantitative
512 sensory testing applied to skin, muscles and viscera. *J Pain* 2009;10(6):556-72.
- 513 47. Haanpää M, Attal N, Backonja M, Baron R, Bennett M, Bouhassira D, et al. NeuPSIG
514 guidelines on neuropathic pain assessment. *Pain* 2011;152(1):14-27.
- 515 48. Nijs J, Van Houdenhove B, Oostendorp RAB. Recognition of central sensitization in
516 patients with musculoskeletal pain: Application of pain neurophysiology in manual
517 therapy practice. *Manual Therapy* 2010;15(3):135-41.
- 518 49. Smart KM, Blake C, Staines A, Doody CM. The discriminative validity of "nociceptive",
519 "peripheral neuropathic" and "central sensitisation" as mechanism-based
520 classifications of musculoskeletal pain. *Clinical Journal of Pain* 2012;28(9):655-63.
- 521
522
523