



Introduction

Patients with haemophilia (PwH) suffer from an enhanced pain sensitivity, depending on the severity of the joint status [1]. A comprehensive, quantitative examination of the somatosensory system has not been performed in this population to date.

Material and Methods

All 30 Patients with moderate or severe haemophilia A or B (severe A=23, B=3; moderate A=3, B=1; mean age 49 years) and 30 healthy controls (mean age 50 years) were examined by means of Quantitative Sensory Testing (QST), which is a validated instrument to assess the function of the somatosensory system by applying various thermal and mechanical stimuli [2]. Detection (DT) and pain thresholds (PT) were determined amounting to a total of 13 measurement parameters. Both knee joints as well as the hand, as a reference, were examined in order to assess both joint specific and general changes in the somatosensory profile. In addition, using the Physical Joint Examination instrument, which is described by Gilbert [3] and recommended by the World Federation of Haemophilia (WFH), the joint status of both cohorts were assessed. Grading of severity of chronic pain was gathered by means of von Korff et al. [4].

Table 1: WFH knee joint status and grading of severity of chronic pain in patients with haemophilia (n=30) and controls (n=30).

parameters	patients with haemophilia	controls	p-value
WFH score right knee (0-12)	3.2 ± 2.8 (0-10)	0.9 ± 0.7 (0-2)	0.001
WFH score left knee (0-12)	2.4 ± 1.9 (0-7)	1.1 ± 0.8 (0-3)	0.000
severity of chronic pain (0-4)	1.5 ± 1.0 (0-4)	0.3 ± 0.4 (0-1)	0.000

Data presented as mean ± standard deviation (min-max). Mann-Whitney U test.

Results

The knee joint status was more impaired in PwH when compared to controls. Also high gradings of chronic pain were determined in the patients group (Tab. 1). By using an ANOVA with the factors group (PwH; control group), region (both knees; hand) and all QST parameters, a significant main effect was found for the factor group*stimulus ($p \leq 0.001$). Post-hoc tests revealed significant differences in both DT and PT across the knees as well as the hand between PwH and controls for cold and

References

- Hilberg T, Czepa D, Freialdenhoven D, Boettger MK. Joint pain in people with hemophilia depends on joint status. *Pain* 2011; 152: 2029-2035.
- Rolke R, Magerl W, Campbell KA *et al*. Quantitative sensory testing: a comprehensive protocol for clinical trials. *European journal of pain* 2006; 10(1): 77-88.
- Gilbert MS. Prophylaxis: musculoskeletal evaluation. *Semin Hematol* 1993; 30(Suppl. 2): 3-6.
- von Korff M, Ormel J, Keefe FJ, Dworkin SF. Grading the severity of chronic pain. *Pain* 1992; 50: 133-49.

warm stimuli across both knees as well as the hand (e.g. mean cold DT in °C: PwH/controls; right knee: 28.4/30.3; left knee: 28.0/29.7; hand: 29.7/30.7). Mechanical DT was also decreased in PwH at both knee joints (left knee: $p \leq 0.05$; right knee: $p \leq 0.01$). Thermal PT at the knees was significantly altered for heat PT ($p \leq 0.05$), but not for cold PT. Further, pressure PT was decreased in PwH at both knees ($p \leq 0.001$). For further analyses of clinical abnormalities (data beyond the 95% confidence interval), raw data of PwH were compared with the data of control subjects by means of z-transformation as recommended [2]. By doing so, a haemophilia specific QST profile became apparent (Fig. 1).

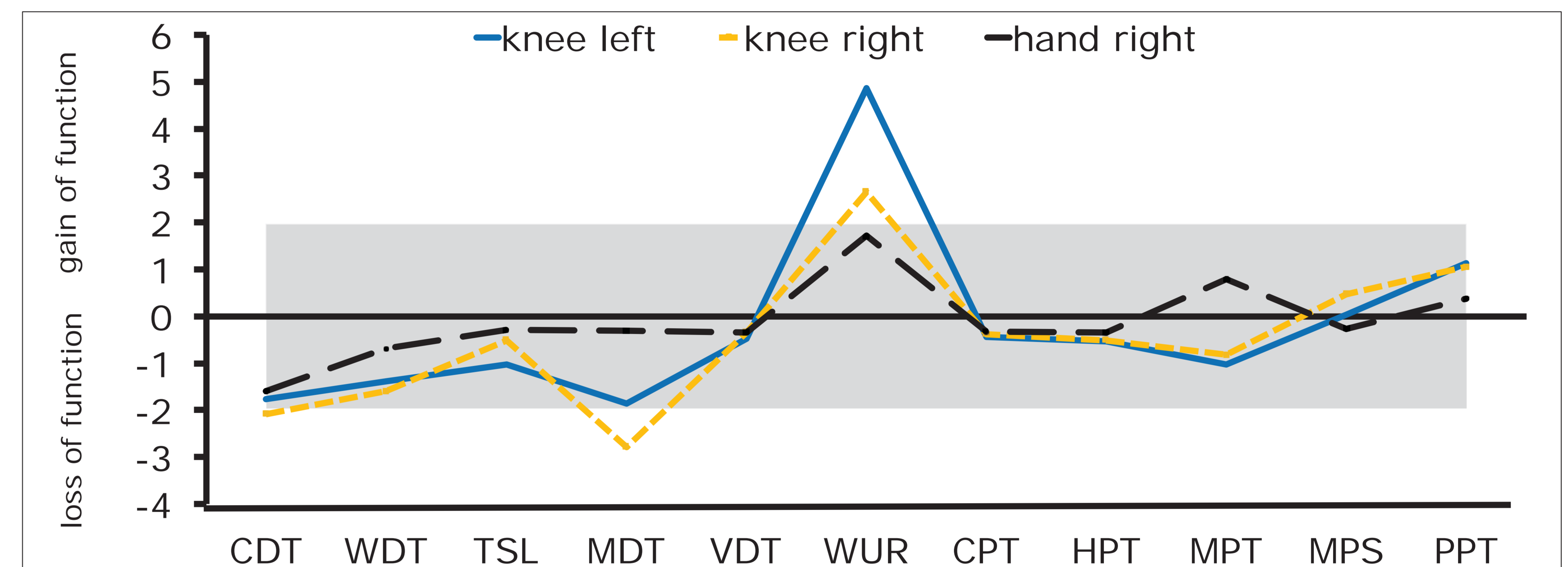


Figure 1: z-values of the QST-parameters in persons with haemophilia (n=30) for both knees and the right hand. CDT=cold detection threshold, WDT=warmth detection threshold, TSL=thermal sensory limen, MDT=mechanical detection threshold, VDT=vibration detection threshold, WUR=wind-up ratio, CPT=cold pain threshold, HPT=heat pain threshold, MPT=mechanical pain threshold, MPS=mechanical pain sensitivity, PPT=pressure pain threshold. Zero-axis value=mean value of the controls. grey zone=95% confidence interval.

Conclusion

Haemophilic arthropathy leads to significant alterations of the somatosensory profile in PwH. Our results reveal initial evidence for a combination of peripheral sensitization, indicated by decreased pressure PT and mechanical DT at the knee joints, as well as general changes in the somatosensory system, shown by reduced thermal DT at affected sites and remote from these. Based on this differentiated pain profile a detailed pain assessment is warranted to potentially improve individualised pain treatment in PwH.

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