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INVESTIGATIVE REPORT

Cutaneous Sensory Function is Not Related to Depression and Anxiety in Patients with Chronic Pruritus with Dysesthetic Subqualities

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The objective of this study was to examine the subgroup of patients with chronic pruritus with dysesthetic subqualities for the presence of psychiatric comorbidities and to evaluate whether anxiety and depression make a difference in perception of somatosensory stimuli in quantitative sensory testing (QST). Forty-nine patients underwent routine diagnostics, a standardised QST testing battery, a psychosomatic evaluation for psychic comorbidities and filled out 2 questionnaires: the Patient Health Questionnaire for the assessment of depressive mood and the State Trait Anxiety Inventory. Twenty-seven patients (55.1%) had at least one psychiatric comorbid diagnosis. QST parameters were not correlated to anxiety and depression levels. We conclude that psychosomatic evaluation should become part of routine diagnostics of these patients in order to detect and treat psychiatric comorbidity. However, research on somatosensory aspects in these patients seems not to be affected by the levels of anxiety and depression. ***Key words: chronic pruritus with dysesthetic subqualities; psychiatric comorbidity; anxiety; depression; quantitative sensory testing (QST).***

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Chronic pruritus (CP) is a frequent symptom in the general population and in dermatologic patients (1, 2). However, the aetiology as well as the clinical manifestation differs between affected patients. While some patients experience chronic itch as a pure itchy sensation, up to 60% of patients describe a mix of itch and dysesthetic subqualities such as pain, stinging and burning sensations (data obtained from local databank). Up to now there is little research on this subsample of patients with mixed sensory disturbances. It is generally assumed that a mix of itch and dysesthetic sensations refers to neuropathic origin (3) or psychogenic diseases (4). However, this has not been systematically investigated until now. As neurological causes are discussed, a more in-depth neurological examination like quantitative sensory testing (QST) seems appropriate to clarify this issue. QST is a certified method to determine the function of small unmyelinated C- and small myelinated Aδ-fibres, which are involved in the transmission of pruritus as well as pain (5) and is recommended as a clinical screening test for the assessment of sensory abnormalities as a consequence of small and large fibre neuropathies (6).

As chronic pruritus can be a very tormenting condition and can profoundly impair the quality of life, the development of psychiatric comorbidities is common and may worsen CP and the capability of coping with the symptoms (7, 8). In order to assess a possible psychiatric comorbidity in a patient with CP and its possible impact on the chronification process of the pruritus, each individual case requires a thorough examination and evaluation. However, psychosomatic evaluation is usually not part of the dermatologic management of pruritus, although psychic comorbidities are frequent in patients with CP (8, 9).

The objective of this study was to examine a specific subgroup of patients with CP that presents a mix of itch, pain, stinging and/or burning sensations (CP with dysesthetic subqualities) for the presence of psychiatric comorbidities and to evaluate whether anxiety and depression have an impact on the somatosensory profile assessed by using a standardised QST (6, 10).

METHODS

Sample

Forty-nine patients who attended the Chronic Pruritus Competence Center for diagnostics and/or treatment of CP with dysesthetic subqualities underwent routine diagnostics, a standardised QST protocol and a psychosomatic evaluation for psychic comorbidities. In addition they filled out 2 questionnaires: the Patient Health Questionnaire (PHQ-9) for the assessment of depressive mood and the State Trait Anxiety Inventory (STAI). The State-Anxiety subscale was filled out immediately prior to QST in order to evaluate the influence of anxiety as a state on sensory perception.

Measurement

Psychosomatic evaluation. In 1–3 clinical interviews of one hour duration at the Department of Psychosomatics and Psy-

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chotherapy of the University Hospital Münster, psychosomatic and psychiatric ICD-10 diagnoses (11) were evaluated as expert rating by trained psychotherapists. Psychic comorbidity includes so-called "psychogenic pruritus", which was classified as "somatoform disorder (ICD-10 F45.8)" or "psychosomatic aspects in multifactorial pruritus (ICD-10: F54)".

Depressive reactions to pruritus which were not severe enough to fulfill the criteria of a "depressive episode" according to ICD-10 were coded "adjustment disorder (F43.2)".

The Patient Health Questionnaire (PHQ) (12; German version in ref. 13) is the first self-report questionnaire designed for use in primary care that actually diagnoses specific disorders using criteria from the DSM-IV. Reliability and validity of the depression subscale PHQ-9 have been demonstrated for medical settings and community samples (14). Item scores are 0–3 and added to a sum score of 0 to 27. The cutoff for minor depression is a sum score of 5 points, for major depression 10 points (13).

The STAI (15) measures the underlying anxiety of a person as a personality trait and anxiety as a state in different situations. Therefore the patients filled out the State questionnaire directly before the QST examination. The 2 STAI subscales have 20 items each.

Quantitative Sensory Testing (QST)

QST was performed after clinical examination and before psychiatric assessment. The skin area affected most by CP (area of maximal itch) was chosen as testing area. A standardised testing protocol was used (10); testing stimuli, number of applications as well as order of stimulus application was the same as described by Rolke et al. (10). Furthermore, patients received standardised instructions on how to rate (thresholds and intensities) and respond to the testing stimuli. The examiner was the same in all patients. The following QST tests were performed:

Thermal detection and pain thresholds and the number of paradoxical heat sensations. A commercial available peltier device (TSA 2001-II, MEDOC, Israel, contact area of the probe 9 cm^2) was used to assess thermal sensory function. Cold and warm detection thresholds (CDT, WDT) were assessed with ramped thermal stimuli starting at 32°C and an increasing rate of 1°C/s. Cold and heat pain thresholds were assessed by starting at 32°C and an increasing rate of 5°C/s. Patients were instructed to press a button if they just felt a change to cold CDT or warm temperature WDT or if they experienced a change from non-painful to painful cold (cold pain threshold, CPT) or from warm to painful hot (heat pain threshold, HPT). By pressing the button, the stimulus was terminated and the last temperature (threshold) was recorded automatically; the cut-off temperature was 49°C. The mean threshold temperature of 3 consecutive measurements was calculated. In between testing of detection and pain thresholds, we assessed paradoxical heat sensations (PHS) by alternating warm and cold stimuli (thermal sensory limen, TSL).

Mechanical detection threshold (MDT). A standardised set of von Frey hairs (Optihair2-Set, Marstock Nervtest, Germany) with calibrated forces between 0.25 and 512 mN graded by a factor of 2 and a tip of 0.5 mm in diameter was applied with a contact time of 1–2 s to the affected skin. Five threshold determinations were made starting with the 0.25 filament and using a series of ascending and descending stimulus intensities depending on the response of the patient (''method of limits''). The final threshold was the geometric mean of these 5 series (10).

Mechanical pain threshold (MPT). We used a set of 7 custom-made weighted pinprick stimuli with a flat contact area of 0.2 mm that exerted forces of 8, 16, 32, 64, 128, 256, and 512 mN (10). Each pinprick stimulus was applied at a rate of 2 s on, 2 s off in an ascending order. If a perception of sharpness or pain was reached the next lower stimulus was applied ("Method of limits"). The final threshold was the geometric mean of 5 series of ascending and descending stimuli.

Mechanical pain sensitivity for pinprick stimuli and dynamic mechanical allodynia. The same set of 7 weighted pinprick stimuli used for mechanical pain threshold was used to obtain a stimulus–response function for pinprick-evoked pain (Mechanical pain sensitivity, MPS). In between pinprick-stimuli application, 3 light tactile stimulators were applied (a cotton wisp, a cotton wool tip and a standardised brush (Somedic, Hörby, Sweden)) with a single stroke of approximately 2 cm in length over the skin. Stimulus application (7 pinprick and 3 tactile stimuli) was performed in 5 runs; each run consisted of pseudorandom sequences of the 3 tactile and 7 pinprick stimuli with a total of 50 stimuli. Patients were instructed to give a pain rating for each stimulus on a '0–100' numerical rating scale ('0' indicating ''no pain'', and '100' indicating ''most intense pain imaginable'' (10)). Mechanical pain sensitivity and dynamic mechanical allodynia were calculated as the geometric mean of all numerical ratings for pinprick stimuli to obtain MPS and across all 3 different types of light touch stimulators to determine if mechanical allodynia was present.

Temporal pain summation (wind-up ratio). One pinprick stimulus with a force of 256 mN was applied 10 times at a 1/s rate within a small area of approximately 1 cm^2. The pain rated by the patient at the end was divided by the pain rated to the same stimulus applied once before the train. The pinprick stimulation was repeated 5 times and the mean of the 5 results was determined as the Wind-up ratio (WUR).

Pressure pain threshold. A blunt pressure device (FDN200, Wagner Instruments, USA) with a probe area of 1 cm^2 (probe diameter of 1.1 cm) was used to assess the pressure pain threshold. The probe was applied to a muscle close to or at the area of maximum itch; stimulus intensity was increased with a rate of approximately 50 kPa/s until the patient reported pain. The pressure required to induce pain was recorded from 3 consecutive tests and the mean calculated for determining the pressure pain threshold.

Statistics

Statistical analysis was performed employing the software SPSS (Statistical Package for Social Sciences; Chicago, IL, USA, release 21.0). For the comparison of 2 groups, we used *t*-tests for metric variables and Chi-square tests for nominal variables. Relations between the variables were assessed by Pearson's correlations. *p*-values of significance were to be interpreted in an explorative way and are regarded as significant in case $p < 0.05$. No adjustment for multiple testing was conducted.

Ethics

The study was approved by the local ethics committee (2007-135-f-S); all patients gave their written informed consent.

RESULTS

The sample

A consecutive sample of 49 patients (23 men and 26 women) with CP with dysesthetic subqualities was evaluated with the methods described above. Accor-

ding to the classification proposed by Ständer et al. (16), with regard to the underlying origins of pruritus, 34 (69.4%) had neuropathic pruritus, 5 (10.2%) had an underlying systemic disease, 9 (18.4%) had pruritus of mixed origin and in 1 patient the origin remained unknown. Twenty-six patients showed no scratch lesions of the skin, 19 had some scratch lesions and 4 had pruritus with multiple secondary scratch lesions. Table I shows clinical pruritus characteristics and the results of the psychometric scales PHQ and STAI.

The extensive psychiatric-psychosomatic evaluation revealed at least one psychiatric comorbid diagnosis in 27 (55.1%) of the sample. Twenty (40.8%) had one diagnosis, 5 (10.2%) had 2 and 2 (4.1%) had 3 psychiatric diagnoses. More specifically, according to ICD-10-criteria the following diagnoses were given: F54 (psychosomatic cofactors of chronic pruritus) $n=6$ (12.2%); F32/F33 (depression or recurrent depression) $n=8$ (26.3%); F43.2 (adjustment disorder with depressive symptoms) $n=10$ (20.5%); F10 (alcohol addiction) $n=3$ (6.1%); F43.1 (Posttraumatic Stress Disorder) $n=2$ (4.1%). F45.4 (somatoform pain disorder), F51.0 (bulimia nervosa), F17 (tobacco addiction), F48.9 (other neurotic disorder) were diagnosed each for one patient %. Twenty-two patients received no psychiatric diagnosis.

When applying the cutoff of the PHQ-9, 8 patients were classified as major and 15 patients as minor depressive.

Comparison between the two subsamples with and without depression

Patients with depression according to PHQ-9 ($n=23$) were compared to those without (Table II).

Patients with PHQ depression also had higher anxiety scores. There were no differences between those patients with depression and those without in age, pruritus intensity and duration. There was a tendency towards more scratch lesions in patients with depression: 56% of those without depression showed no and 44% some scratch lesions, but none of them multiple lesions. Of those patients with depression, 47.8% had no scratch lesions, while 34.8% of them had some and 17.4% multiple scratch lesions (χ^2 4.76, df 2, $p=0.093$). Regarding the composition of the mixed sensations (stinging, burning, crawling), there were no group differences. The same was true for the questions whether cooling or warmth alleviates or whether mechanic stimuli increase their itch (data not shown).

Table I. *Sample characteristics (n=49)*

	Min	Max	Mean	SD
Age, years	24	86	57.63	12.61
Mean pruritus intensity (VAS)	0.0	9.5	5.82	2.13
Maximum pruritus intensity (VAS)	5.0	10.0	8.53	1.65
Duration of pruritus, months	6	480	81.59	103.21
Depression – sum score (PHQ)	0.0	20.0	5.69	5.15
State anxiety (STAI)	21.0	64.0	42.88	11.77
Trait anxiety (STAI)	22.0	70.0	41.28	12.09

SD: Standard deviation; VAS: Visual Analog Scale; PHQ: Patient Health Questionnaire; STAI: State Trait Anxiety Inventory.

Table II. *Comparison of clinical features, psychometric scales, and Quantitative Sensory Testing (QST) results between patients with depression (*n *= 23) and those without (*n *= 26)*

	No depression	Depression		
	Mean (SD)	Mean (SD)	T	*p*
Demographics				
Age	58.4 (11.83)	56.1 (13.72)	0.57	0.573
Mean pruritus intensity (VAS)	5.7 (2.29)	5.9 (2.03)	–0.33	0.746
Maximum pruritus intensity (VAS)	8.6 (1.92)	8.6 (1.31)	–0.15	0.883
Pruritus duration (months)	71.8 (69.45)	95.3 (132.08)	–0.78	0.440
Questionnaires				
Depression sum score (PHQ)	1.8 (1.41)	9.9 (4.31)	–8.62	0.001
State anxiety (STAI)	37.2 (9.47)	48.8 (10.85)	–3.69	0.001
Trait anxiety (STAI)	35.2 (8.07)	46.5 (12.45)	–3.58	0.001
Quantitative Sensory Testing (QST)				
Cold detection threshold	–5.0 (8.36)	–4.7 (6.21)	–0.16	0.876
Warm detection threshold	5.4 (4.27)	6.0 (4.40)	–0.45	0.656
Thermal sensory limen	10.3 (11.18)	10.1 (9.13)	0.06	0.956
Paradoxical heat sensation	0.2 (0.71)	0.3 (0.91)	–0.56	0.580
Cold pain threshold	10.6 (11.26)	9.9 (9.40)	0.26	0.798
Heat pain threshold	45.3 (4.70)	46.1 (3.73)	–0.68	0.498
Mechanical detection threshold	29.0 (91.79)	6.6 (9.91)	1.21	0.238
Mechanical pain threshold	99.1 (154.78)	80.7 (137.03)	0.43	0.666
Mechanical pain sensitivity	2.8 (5.27)	2.6 (4.32)	0.09	0.927
Dynamic mechanical allodynia	0.01 (0.04)	0.0 (0.00)	0.96	0.343
Wind-up ratio	3.9 (6.77)	3.5 (3.06)	0.29	0.773
Vibration detection threshold	6.6 (2.19)	7.1 (0.95)	–1.06	0.293
Pressure pain threshold	360.3 (155.99)	409.9 (216.73)	–0.92	0.365

VAS: Visual Analog Scale; PHQ: Patient Health Questionnaire; STAI: State Trait Anxiety Inventory.

Quantitative Sensory Testing parameters

QST was performed on the skin area most affected by pruritus. This was the hand, the dorsal lower arm or upper arm for 13 patients without and for 14 patients with depression; the back of the foot, the lower or upper leg for 10 patients without and 2 patients with depression; the shoulders, back or abdomen for 2 patients without and 6 patients with depression (χ^2 8.3, df 3, $p=0.040$). Obviously in patients with depression, the shoulder, back or abdomen were more often the sites affected most by CP, while in patients without depression legs and feet were more often the most CP afflicted skin areas. In Table II QST parameters are presented for the group with and without depression. There were no significant differences between groups with regard to any of the parameters.

Table III shows the correlations between each QST parameter of pruritus-afflicted skin with depression and trait and state anxiety. On the whole, the correlations were low. Positive correlations above 0.20 were found only for state anxiety with paradoxical heat sensation

Table III. *Pearson correlations between psychometric scales and quantitative sensory testing results*

	Depression score (PHQ)	State anxiety (STAI)	Trait anxiety (STAI)
Cold detection threshold	–0.06	–0.08	–0.03
Warm detection threshold	0.13	0.05	0.11
Thermal sensory limen	0.14	0.12	0.11
Paradoxical heat sensation	0.15	0.22	–0.03
Cold pain threshold	–0.09	–0.09	–0.10
Heat pain threshold	0.10	–0.01	0.01
Mechanical detection threshold	–0.07	0.10	0.05
Mechanical pain threshold	–0.05	–0.12	0.02
Mechanical pain sensitivity	0.05	0.09	0.06
Dynamic mechanical allodynia	–0.13	0.24	0.24
Wind-up ratio	–0.06	–0.12	–0.01
Vibration detection threshold	0.04	–0.01	0.07
Pressure pain threshold	0.23	0.08	0.08

*$p \leq 0.05$; **$p \leq 0.01$; ***$p \leq 0.001$.
PHQ: Patient Health Questionnaire; STAI: State Trait Anxiety Inventory.

(0.22) and for state and trait anxiety with dynamic mechanical allodynia.

DISCUSSION

This is the first study on patients with CP with dysesthetic subqualities which focuses on anxiety, depression and QST and the potential relations between them. The major result of our study is that sensory function in CP patients with dysesthetic subqualities seems not to be altered by anxiety or depression. However, our results have to be interpreted in the light of the small sample size of 49 patients only.

More than half of our collective (55.1%) showed psychic comorbidities. The most common diagnoses were psychosomatic co-factors of multifactorial chronic pruritus, depression or recurrent depression and adjustment disorders with depressive symptoms. However, in a previous study in a consecutive sample with patients with CP (8) from the same institution, a psychiatric comorbidity of 71.6% was found. This indicates that patients with CP with dysesthetic subqualities might be somewhat less psychically affected than the whole sample of CP in-patients. The diagnosis of psychosomatic co-factors had been given in 46.8% of the previously described whole sample of CP patients but in only 12.2% of the sample with dysesthetic subqualities as reported here. This indicates that somatic factors might play a more important role in pruritus with dysesthetic subqualities. Accordingly, we cannot confirm that dysesthetic subqualities refer *per se* to psychiatric comorbidities. Depression (16.3% in our sample, 10.1% in the previous sample) and adjustment disorders (22.4 vs. 22.9% respectively), which often develop as a consequence or reaction to CP were comparable.

In this sample of CP with dysesthetic subqualities, patients with depression did not differ in itch intensity and duration from non-depressed patients. Obviously, in this sample duration and intensity of the symptoms did not predict the individual risk for the development of depression.

However, we show for the first time that responses to non-painful and painful stimuli did not correlate to anxiety and depression. This was surprising as we had expected that psychic factors might influence the somatosensory testing. There is for example some indication that positive and negative affect may influence pain perception and sensory function in patients with chronic osteoarthritis pain (17); depressed subjects also had a changed pain perception (18–20).

Although there are many parallels between chronic pain and chronic itch, only few studies compared both groups. As shown previously, patients with CP diagnosed with atopic dermatitis had significantly lower tolerance thresholds to pinprick and electrical stimulation compared to healthy controls (21). We suggest that itch associated with other sensory dysfunction like burning sensations may be at least in part a result of changes in sensory fibre function, however, this was not the goal of our study and is therefore still an unanswered question.

However, some recent QST studies performed in patients with neuropathic pain have indicated that sensory dysfunction is an important measure to understand the underlying mechanisms of pain in (individual) patients (e.g. in 22). For instance, this important paper demonstrates that a mechanism-based rather than a disease-related classification is important to understand mechanisms and – in the future – treat neuropathic pain (23). Our vision is that a similar approach applies to chronic itch. We hypothesise that assessment of the sensory profiles of individual patients can indicate the underlying mechanisms of itch and may guide us in the future for treatment options. Future research is, however, required and the present study may show how to deal with depression in future studies if patients with CP with dysesthetic subqualitites are investigated with QST.

From our results we have nothing to suggest that depression or anxiety as such could lead to sensitisation for different qualities in pruritus patients with dysesthetic subqualities.

Limitations

Although with 49 patients the sample size is small, it nevertheless is the biggest sample of pruritus patients examined with QST so far. We cannot rule out that the lack of significant differences between depressive and non-depressive patients could be due to the small sample size. As we only analysed patients and not healthy controls, we cannot compare our sample to healthy controls but only analyse for associations of QST with anxiety and depression within the sample. As an additional limitation to the study, our data were collected in an in-patient Dermatology Department;

the data are therefore not transferable to out-patients nor to the general population. Also the psychiatric assessment was made only after the patients had been admitted (cross-sectional design). Further research should investigate whether the depression and anxiety scores are stable over time or whether they change when the pruritus is successfully treated. Similarly, future studies should ask the question if the psychiatric disorders are a cause or a consequence of CP and try to replicate our results in larger samples.

Conclusion

Psychic comorbidities were numerous in this sample of patients with CP with dysesthetic subqualities, though our study design does not allow conclusions whether this is cause or consequence of CP. We therefore suggest including psychosomatic evaluation in the routine diagnostics of these patients in order to detect and treat psychiatric comorbidities adequately.

However, depression, anxiety states and anxiety as a personality trait does not seem to influence sensory detection or tolerance thresholds as measured by QST in patients with CP with dysesthetic sensations. This is of high importance for future research on somatosensory aspects of CP.

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REFERENCES

1. Ständer S, Schäfer I, Phan NQ, Blome C, Herberger K, Heigel H, Augustin M. Prevalence of chronic pruritus in Germany: results of a cross-sectional study in a sample working population of 11,730. Dermatology 2010; 221: 229–235.
2. Misery L, Rahhali N, Duhamel A, Taieb C. Epidemiology of pruritus in France. Acta Derm Venereol 2012; 92: 541–542.
3. Stumpf A, Ständer S. Neuropathic itch: diagnosis and management. Dermatol Ther 2013; 26: 104–109.
4. Tey HL, Wallengren J, Yosipovitch G. Psychosomatic factors in pruritus. Clin Dermatol 2013; 31: 31–40.
5. Lamotte RH, Dong X, Ringkamp M. Sensory neurons and circuits mediating itch. Nat Rev Neurosci 2013; 15: 19–31.
6. Backonja MM, Attal N, Baron R, Bouhassira D, Drangholt M, Dyck PJ, et al. Value of quantitative sensory testing in neurological and pain disorders: NeuPSIG consensus. Pain 2013; 154: 1807–1819.
7. Schneider G, Gieler U. Psychosomatische Dermatologie – aktueller Forschungsstand. Z Psychosom Med Psychother 2001; 47: 307–331.
8. Schneider G, Driesch G, Heuft G, Evers S, Luger TA, Ständer S. Psychosomatic cofactors and psychiatric comorbidity in patients with chronic itch. Clin Exp Dermatol 2006; 31: 762–767.
9. Picardi A, Abeni D, Melchi CF, Puddu P, Pasquini P. Psychiatric morbidity in dermatological outpatients: an issue to be recognized. Br J Dermatol 2000; 143: 983–991.
10. Rolke R, Magerl W, Campbell KA, Schalber C, Caspari S, Birklein F, Treede RD. Quantitative sensory testing: a comprehensive protocol for clinical trials. Eur J Pain 2006; 10: 77–88.
11. World Health Organisation. International classification of diseases and related health problems. Tenth revision. WHO, 1992.
12. Spitzer RL, Kroenke K, Williams JBW. Validation and utility of a self-report version of PRIME-MD: the PHQ primary care study. Primary care evaluation of mental disorders, Patient Health Questionnaire. J Am Med Acad 1999; 282: 1737–1744.
13. Löwe B, Spitzer RL, Zipfel S, Herzog W. Gesundheitsfragebogen für Patienten (PHQ-D), zweite Auflage. (Prime MD Patient Health Questionnaire (PHQ) – German version, 2. ed). Karlsruhe, Pfizer, 2002.
14. Löwe B, Spitzer RL, Gräfe K, Kroenke K, Quenter A, Zipfel S, et al. Comparative validity of three screening questionnaires for DSM-IV depressive disorders and physicians` diagnoses. J Affect Dis 2004; 78: 131–140.
15. Laux L, Glanzmann P, Schaffner P, Spielberger CD. Das State-Trait-Angst Inventar. Göttingen, Hogrefe 2006.
16. Ständer S, Weisshaar E, Mettang T, Szepietowski JC, Carstens E, Ikoma A, et al. Clinical classification of itch: a position paper of the International Forum for the Study of Itch. Acta Derm Venereol 2007; 87: 291–294.
17. Finan PH, Quartana PJ, Smith MT. Positive and negative affect dimensions in chronic knee osteoarthritis: effects on clinical and laboratory pain. Psychosom Med 2013; 75: 463–470.
18. Bär J, Brehm S, Boettger MK, Boettger S,Wagner G, Sauer H. Pain perception in major depression depends on pain modality. Pain 2005; 117: 97–103.
19. Uhl I, Krumova EK, Regeniter S, Bär KJ, Norra C, Richter H, et al. Association between wind-up ratio and central serotonergic function in healthy subjects and depressed patients. Neurosci Lett 2011; 504: 176–180.
20. Klauenberg S, Maier C, Assion HJ, Hoffmann A, Krumova EK, Magerl W, et al. Depression and changed pain perception: hints for a central disinhibition mechanism. Pain 2008; 140: 332–343.
21. Van Laarhoven AIM, Kraaimaat FW, Wilder-Smith OH, van de Kerkhof PCM, Cats H, van riel PLCM, Evers AWM. Generalized and symptom-specific sensitization of chronic itch and pain. J Eur Acad Derm Venereol 2007; 21: 1187–1192.
22. Maier C, Baron R, Tölle TR, Binder A, Birbaumer N, Birklein F, et al. Quantitative sensory testing in the German Research Network on Neuropathic Pain (DFNS): Somatosensory abnormalities in 1236 patients with different neuropathic pain syndromes. Pain 2010; 150: 439–450.
23. Serra J. Sensory profiles: the cliché and the challenge. Pain 2010; 150: 384–385.