Development and validation of the Neuropathic Pain Symptom Inventory

Didier Bouhassira, Nadine Attal, Jacques Fermanian, Haiel Alchaar, Michele Gautron, Etienne Masquelier, Sylvie Rostaing, Michel Lanteri-Minet, Elisabeth Collin, Jacques Grisart, Francois Boureau

INSERM E-332, Centre d’Evaluation et de Traitement de la Douleur, Hôpital Ambroise Paré, Boulogne-Billancourt, France
Université Versailles Saint-Quentin, Versailles, France
Service de Bistatistique, Hôpital Necker, Paris, France
Hôpital Pasteur, Nice, France
Cliniques Universitaires Saint-Luc, Brussels, Belgium
Hôpital Saint-Antoine, Paris, France
Hôpital Pitié-Salpêtrière, Paris, France

Received 8 September 2003; received in revised form 15 December 2003; accepted 22 December 2003

Abstract

This study describes the development and validation of the Neuropathic Pain Symptom Inventory (NPSI), a new self-questionnaire specifically designed to evaluate the different symptoms of neuropathic pain. Following a development phase and a pilot study, we generated a list of descriptors reflecting spontaneous ongoing or paroxysmal pain, evoked pain (i.e. mechanical and thermal allodynia/hyperalgesia) and dysesthesia/paresthesia. Each of these items was quantified on a (0–10) numerical scale. The validation procedure was performed in 176 consecutive patients with neuropathic pain of peripheral (n = 120) or central (n = 56) origin, recruited in five pain centers in France and Belgium. It included: (i) assessment of the test–retest reliability of each item, (ii) determination of the factorial structure of the questionnaire and analysis of convergent and divergent validities (i.e. construct validity), and (iii) evaluation of the ability of the NPSI to detect the effects of treatment (i.e. sensitivity to change). The final version of the NPSI includes 10 descriptors (plus two temporal items) that allow discrimination and quantification of five distinct clinically relevant dimensions of neuropathic pain syndromes and that are sensitive to treatment. The psychometric properties of the NPSI suggest that it might be used to characterize subgroups of neuropathic pain patients and verify whether they respond differentially to various pharmacological agents or other therapeutic interventions.

Keywords: Neuropathic pain; Evaluation; Psychometric validation; Self-questionnaire

1. Introduction

Neuropathic pain syndromes represent highly heterogeneous clinical conditions. Such a heterogeneity is apparent from the clinical examination of the patients who may present with various painful symptoms including spontaneous continuous or paroxysmal pain and evoked pain (i.e. allodynia and/or hyperalgesia). Due to poor understanding of their pathophysiological mechanisms, neuropathic pain syndromes are often grouped together and treated in a uniform fashion. This empirical approach might represent a major cause of therapeutic failures in these patients.

The development of novel treatment strategies might well depend on the identification of relevant criteria, allowing classification of neuropathic pain patients into several subgroups who would respond differentially to treatments. In this respect, an optimal therapeutic approach would rely on identification of the mechanisms presumably responsible for the various neuropathic pain symptoms in order to select treatments targeting these mechanisms (Baron, 2000; Sindrup and Jensen, 1999; Woolf and Decosterd, 1999; Woolf and Mannion, 1999; Woolf and Max, 2001; Woolf et al., 1998). Such a rational approach is
attractive but does not yet seem to be attainable, mainly because of the difficulty of translating in the clinic the mechanisms identified in animal studies (Hansson, 2003; Jensen and Baron, 2003; Max, 2000). A more clinically oriented approach seems to be more realistic and rapidly applicable. It may contribute in determining whether the different neuropathic pain symptoms—spontaneous ongoing pain, paroxysmal pain and evoked pain—respond differently to the treatments.

Such a clinical approach needs adequate methods for evaluating the neuropathic pain symptoms. Current pain questionnaires, such as the McGill Pain Questionnaire (MPQ; Melzack, 1975) or Brief Pain Inventory (BPI; Cleeland and Ryan, 1994) are not specific enough for this purpose, although the diagnostic value of MPQ descriptors for neuropathic pain has been suggested (Boureau et al., 1990; Masson et al., 1989). Quantitative sensory testing (QST) appears to be particularly suitable for the assessment of evoked pain (Fruhstorfer et al., 1976; Hansson and Lindblom, 1992). However, QST presents some limitations due to long duration, variability of the test–retest, and the fact that it must be conducted by trained investigators (Yarnitsky, 1997; Zaslansky and Yarnitsky, 1998). In 1997, the Neuropathic Pain Scale was developed for the assessment of symptoms (Galer and Jensen, 1997) but its validation was only preliminary. In particular, although it has demonstrated some sensitivity to treatment (Galer et al., 2002), it is not clear whether its structure is adapted to detect differential effects on the neuropathic pain symptoms. More recently, the LANSS Pain Scale (Bennett, 2001) and the Neuropathic Pain Questionnaire (Krause and Backonja, 2003) have been developed for the diagnosis of neuropathic pain rather than for their evaluation.

In this context, we thought it would be of interest to develop and validate a specific self-questionnaire for the assessment of the different symptoms of neuropathic pain. Ideally, such a questionnaire could represent a useful and exploitable tool for large cohorts of patients in multicenter studies and give information comparable to that provided by quantitative evaluation, as regards the nature and intensity of the various painful symptoms.

2. Methods

Following an initial development phase, the validation of the Neuropathic Pain Symptom Inventory (NPSI) was performed in consecutive patients recruited in five pain clinics from January 2001 to December 2002. The study was approved by the Local Ethical Committee and the patients gave informed written consent.

2.1. Patients

The inclusion criteria were: men or women with pain of at least moderate severity (≥ 30 on a 100 mm visual analog scale) which could be clearly attributed to a peripheral or central nervous system injury. Diagnoses of nervous lesion were based on medical history, physical examination and electromyography, laboratory tests and/or imaging when indicated.

The exclusion criteria were: association with any painful symptoms other than those due to the lesion of the nervous system, nerve injury not clearly identified (e.g. complex regional pain syndrome type I), pain presumably of mixed origin (e.g. lumbo-radicular and cancer pain), severe depression, chronic alcoholism or substance abuse, any reason preventing an accurate understanding of the questionnaire.

2.2. Study design

The patients were scheduled for two visits with an interval of 1 month ± 1 week. During each visit, the patients were asked: (i) to rate the mean intensity of their pain during the last 24 h on an 11-point (0–10) numerical scale; (ii) to complete the NPSI; (iii) to complete the French version of the Hospital Anxiety and Depression Scale (HADS), including two seven-item subscales for anxiety and depression. After the first visit, usual treatments of neuropathic pain (mostly antidepressants and/or antiepileptics, more rarely opioids) were prescribed in a non-controlled manner.

During the second visit, evolution of pain during the 1-month treatment was self-evaluated by Patient Global Impression of Change (PGIC). This scale included seven categorical responses to measure improvement or aggravation of pain: ‘Since your last visit do you feel that your pain is ____’: (1) very much improved, (2) moderately improved, (3) slightly improved, (4) unchanged, (5) slightly aggravated, (6) moderately aggravated, (7) very much aggravated. A similar scale was used by the examiners to rate their Clinical Global Impression of Change (CGIC).

2.3. Construction of the NPSI

2.3.1. Initial version of the NPSI

A first list of items was generated on the basis of our experience and analysis of the literature. Following discussions and approval of content validity by a panel of seven French and Belgian experts, we selected 18 descriptors included in the initial version of the questionnaire, which could reflect four distinct dimensions of neuropathic pain: spontaneous ongoing pain, spontaneous paroxysmal pain, evoked pain and paresthesia/dyesthesias.

Six items were selected to evaluate spontaneous ongoing pain: ‘Does your pain feel like ____’: (1) burning (brûlure), (2) painful cold (froid douloureux), (3) pressure (compression), (4) squeezing (étou), (5) cramp (crampe), (6) dullness (lourdeur).

Four items were selected to evaluate spontaneous paroxysmal pain: ‘Does your pain feel like ____’: (7) electric...
shock (décharges électriques), (8) shooting (éclairs), (9) stabbing (coupes de couteau), (10) lancinating pain (éclancements).

Four items were selected to evaluate evoked pain: ‘Is your pain provoked or increased by ___ on the painful area’; (11) brushing (frottement), (12) pressure (pression), (13) contact with something cold (contact avec le froid), (14) contact with something warm (contact avec le chaud).

Four items were selected to evaluate paresthesia/dysesthesia: ‘Do you feel ___ in the painful area’; (15) pins and needles (picotements), (16) tingling, (fourmillements), (17) numbness (engourdissement), (18) itching ( démangeaisons).

The mean intensity of each of these items during the last 24 h had to be reported on a 0–10 numerical scale in which 0 was ‘no pain’ and 10 was ‘the most intense pain imaginable’.

Two additional categorical items evaluated the temporal sequence of spontaneous ongoing pain (i.e. number of hours during the last 24 h) and paroxysmal pain (i.e. number of paroxysms during the last 24 h).

2.3.2. Pilot study
A pilot study was performed in 39 patients presenting with neuropathic pain in order to verify the face validity of the questionnaire. The patients were asked to complete the first version and to rate each item for clarity in wording, understanding and relevance to their painful symptoms. After the pilot study item 6 ‘dullness’ ( ‘lourdeur’) was excluded because it was considered irrelevant by a majority of patients.

2.3.3. Final version of the NPSI
This provisional 17-item scale was administered in 176 patients. The number of items was further reduced on the basis of the assessment of reliability (Intraclass Correlation Coefficient, ICC, measurement) and factor analysis performed according to the statistical methods described below. Several items (i.e. items 2, ‘painful cold’; 5, ‘cramp’; 10, ‘lancinating pain’; 17, ‘numbness’; and 18, ‘itching’), showed a poor reliability. In addition, these items did not fit in the five-factor solution identified by the factor analysis. Items 2 (painful cold), 6 (lancinating pain) and 18 (itching) had similar loadings on more than one factor, while item 5 (cramp) had no loading on any of the five factors. Two other items were excluded in the final version. Item 8 (shooting) was excluded because it was inter-correlated with item 7 (electric shock) suggesting that these two items measured the same quality. Item 14 (pain evoked or aggravated by contact with something warm) was excluded because of very low ‘prevalence’ (i.e. <20% of the patients reported a score >0) as compared to other items. Exclusion of these seven items did not change the five-factor structure of the questionnaire.

Thus, the final version of the NPSI includes 12 items: 10 descriptors of the different symptoms and 2 items for assessing the duration of spontaneous ongoing and paroxysmal pain. A total intensity score can be calculated as the sum of the scores of the 10 descriptors. In addition, we propose to derive five subscores corresponding to the mean scores of the items belonging to each of the five factors identified in the factor analysis.

The French version of the NPSI is presented in Appendix A and an English translation is proposed in Appendix B. This translation was performed using the iterative forward–backward translation sequence but has not yet been formally validated in English-speaking patients.

2.4. Assessment of the psychometric properties of the NPSI

2.4.1. Test–retest reliability
The test–retest reliability of each item and total score of the NPSI was assessed using the ICC under the random-effect model. ICC were calculated in the usual manner after estimation of the components of total variance by analysis of variance (Shrout and Fleiss, 1979). As a measure of ‘short-term’ reliability, we compared the responses to each item in a subgroup of 40 patients who were asked to fill out the questionnaire for a second time during visit 1 after a delay of 3 h. In addition, the ‘long-term’ test–retest reliability of the instrument was assessed by comparing the responses to each item at visits 1 and 2 in those patients who reported on the PGIC scale that their pain had not been modified between the two visits.

2.4.2. Factor analysis
An exploratory factor analysis was performed to determine whether the 10 items of the scale related to the description of painful symptoms could be combined into independent factors representing different dimensions of neuropathic pain. Factor analysis was performed using the principal component analysis as the method of extraction. The Catell screen test was used for determining the number of factors extracted. Independent factors were obtained using the Varimax rotation method.

2.4.3. Convergent and divergent validities
The relationship between global pain intensity measured on a numerical scale, HADS scores and both the total intensity score and subscores of the NPSI was assessed by the Spearman correlation coefficient.

2.4.4. Criterion-related validity
Criterion validity was assessed for the three items related to evoked pain. After each visit the investigators (two per center), blind to the responses to the questionnaire, had to fill out a separate sheet including three questions based on clinical examination to evaluate the intensity of pain evoked by brushing, pressure, cold or warm stimuli in the painful area on four-point categorical scales (absent, mild, moderate, severe). Clinical examination of evoked pain was standardized: tactile allostynia was evaluated with a soft
brush (three movements), pressure allodynia was evoked by blunt pressure with a finger at a pressure that does not provoke pain in a normal area and glass tubes filled with hot (38–40 °C) or cold (22–24 °C) water were used to evaluate thermal allodynia. Allodynia was considered to be present if these stimulations evoked a clear sensation of pain in comparison with a normal non-painful side. Spearman’s rank correlation coefficient was measured to analyze the correlation between the scores of the items of the NPSI related to evoked pain and the clinical evaluation performed by the examinators and considered as gold standard.

2.4.5. Analysis of sensitivity to change between the two visits

Spearman’s rank correlation coefficient was performed to determine whether there was a relationship between changes (i.e. difference) in the total score of the NPSI and both the subjective evaluation made by the patients (PGIC) and the clinical estimation made by the examinators (CGIC).

3. Results

One hundred and seventy-six patients with neuropathic pain due to peripheral or central injury participated in this study. Clinical and demographic details are provided in Table 1. A second visit with an interval of 1 month ± 1 week was performed in 111 patients.

Table 1

<table>
<thead>
<tr>
<th>Clinical and demographic data</th>
<th>N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age (range)</td>
<td>55 (20–85)</td>
</tr>
<tr>
<td>Sex (men/women)</td>
<td>97/79</td>
</tr>
<tr>
<td>Mean duration of pain (months) (range)</td>
<td>70 (6–420)</td>
</tr>
<tr>
<td>Mean pain intensity (VAS) (range)</td>
<td>65 (30–100)</td>
</tr>
<tr>
<td>Site of injury</td>
<td>N (%)</td>
</tr>
<tr>
<td>Peripheral</td>
<td>120 (68)</td>
</tr>
<tr>
<td>Central</td>
<td>56 (32)</td>
</tr>
<tr>
<td>Aetiology of neuropathic pain</td>
<td>N (%)</td>
</tr>
<tr>
<td>Nerve trauma</td>
<td>39 (22)</td>
</tr>
<tr>
<td>Postherpetic neuralgia</td>
<td>20 (11)</td>
</tr>
<tr>
<td>Non-diabetic polyneuropathy</td>
<td>20 (11)</td>
</tr>
<tr>
<td>Diabetic polyneuropathy</td>
<td>15 (9)</td>
</tr>
<tr>
<td>Post-stroke pain</td>
<td>15 (9)</td>
</tr>
<tr>
<td>Spinal cord trauma</td>
<td>14 (8)</td>
</tr>
<tr>
<td>Nerve entrapment</td>
<td>13 (7)</td>
</tr>
<tr>
<td>Syringomyelia</td>
<td>11 (6)</td>
</tr>
<tr>
<td>Plexus avulsion</td>
<td>10 (6)</td>
</tr>
<tr>
<td>Multiple sclerosis</td>
<td>7 (4)</td>
</tr>
<tr>
<td>Benign intraspinal tumor</td>
<td>4 (2)</td>
</tr>
<tr>
<td>Spinal cord ischemia/haematoma</td>
<td>3 (2)</td>
</tr>
<tr>
<td>Radiation induced plexopathy</td>
<td>3 (2)</td>
</tr>
<tr>
<td>Myelitis</td>
<td>2 (1)</td>
</tr>
</tbody>
</table>

3.1. Face validity

The NPSI was completed accurately and appeared to be fully understood, notably by elderly subjects. The mean duration for filling out the questionnaire was <7 min in a large majority of patients (i.e. approximately 85%). The ‘prevalence’ (i.e. percentage of patients reporting a score >0) of the majority of the items was >60% (see Table 2).

3.2. Test–retest reliability

Forty patients filled out the questionnaire twice during the first visit with an interval of 3 h. ICC was very high (i.e. >0.90) for all the items (see Table 3). The reliability of the NPSI was confirmed by the evaluation of the ‘long-term’ reliability in 41 out of 111 patients who estimated that their symptomatology had not been changed after the 1-month period between the two visits (see Table 3).

3.3. Factor analysis

The factor analysis identified a five-factor solution which accounted for 76% of the total variance. All the items had high loadings on only one factor (see Table 4). Each of the five factors corresponds to a relevant clinical component of neuropathic pain. Factor 1 includes the three items related to evoked pain (i.e. pain evoked by brushing, pressure or contact with cold). Factor 2 includes two items (i.e. pressure and squeezing) which might correspond to the pressive (or deep) component of spontaneous ongoing pain. Factor 3 includes two items (i.e. electric shock and stabbing) clearly related to paroxysmal pain. Factor 4 includes two items (i.e. tingling and pins and needles) corresponding to the abnormal sensations (i.e. paresthesia/dysesthesia) frequently observed in neuropathic pain syndromes. Finally, factor 5, which includes only one item (i.e. burning), corresponds to the superficial component of spontaneous ongoing pain.

The strength of the NPSI structure was further reinforced by the factorial analysis performed with the results of
the 111 patients who completed the questionnaire on the second visit and which identified a similar five-factor solution.

3.4. Convergent and divergent validities

The total score of the questionnaire, but not the five subscores derived from the factor analysis, was correlated with the rating of global pain intensity with a numerical scale ($r = 0.60, P < 0.001$).

In contrast, there was no relationship between the total score (and subscores) of the NPSI and the anxiety ($r = 0.27$) and depression ($r = 0.32$) scores measured by the HADS. In addition, no correlation was observed between the changes of NPSI and HADS scores between the two visits.

3.5. Criterion-related validity

Criterion validity was evaluated for the three items of the NPSI related to evoked pain. The scores (0–10) of these items were compared (Spearman rank correlation test) to the magnitude of mechanical and/or thermal evoked pain estimated on a four-point categorical scale (i.e. absent, light, moderate, severe) by the investigator, on the basis of their clinical examination. A correlation was evidenced between the scores of the three items of the NPSI and the estimations performed by the investigators ($r = 0.70, 0.66$ and $0.73$ for pain evoked by brushing, pressure and cold, respectively).

3.6. Sensitivity to change

The global impression of change of the patient and examiner after one month of treatment (i.e. PGIC and CGIC scores) was correlated ($r = 0.67$ and $0.58$, respectively) with changes of NPSI total score between visits 1 and 2 (i.e. total score at visit 1 − total score at visit 2; see Fig. 1). In contrast, changes in the subscores were not related to PGIC or CGIC.

4. Discussion

This study describes the development and validation of a novel instrument, the NPSI, for evaluating the different symptoms of neuropathic pain. Analysis of the psychometric properties of NPSI indicates that this self-questionnaire: (i) allows discrimination and quantification of five distinct clinically relevant dimensions of neuropathic pain; (ii) is valid and reliable; and (iii) is sensitive to the effects of treatment.

Over the last few years, three instruments have been developed for the assessment of neuropathic pain. Two of them, the LANSS pain scale (Bennett, 2001) and the Neuropathic Pain Questionnaire (Krause and Backonja, 2003), were designed to discriminate between neuropathic and non-neuropathic pain. Consequently, the validation studies were mainly oriented towards analysis of the sensitivity, specificity and discriminant properties of the items included in these questionnaires. The third one, the Neuropathic Pain Scale developed by Galer and Jensen (1997), was designed for evaluating the different symptoms of neuropathic pain. The validation of this

### Table 3

<table>
<thead>
<tr>
<th>Test–retest reliability</th>
<th>ICC1 (during the same visit)</th>
<th>ICC2 (between the two visits)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Burning</td>
<td>0.95</td>
<td>0.89</td>
</tr>
<tr>
<td>Pressure</td>
<td>0.98</td>
<td>0.82</td>
</tr>
<tr>
<td>Squeezing</td>
<td>0.91</td>
<td>0.88</td>
</tr>
<tr>
<td>Electric shocks</td>
<td>0.90</td>
<td>0.78</td>
</tr>
<tr>
<td>Stabbing</td>
<td>0.92</td>
<td>0.98</td>
</tr>
<tr>
<td>Evoked by brushing</td>
<td>0.97</td>
<td>0.87</td>
</tr>
<tr>
<td>Evoked by pressure</td>
<td>0.95</td>
<td>0.95</td>
</tr>
<tr>
<td>Evoked by cold stimuli</td>
<td>0.88</td>
<td>0.81</td>
</tr>
<tr>
<td>Pins and needles</td>
<td>0.98</td>
<td>0.96</td>
</tr>
<tr>
<td>Tingling</td>
<td>0.87</td>
<td>0.87</td>
</tr>
<tr>
<td>Total score</td>
<td>0.94</td>
<td>0.89</td>
</tr>
</tbody>
</table>

### Table 4

<table>
<thead>
<tr>
<th>Percentage of variance explained</th>
<th>Factor 1</th>
<th>Factor 2</th>
<th>Factor 3</th>
<th>Factor 4</th>
<th>Factor 5</th>
</tr>
</thead>
<tbody>
<tr>
<td>Burning</td>
<td>26.9</td>
<td>14.8</td>
<td>12.5</td>
<td>11.5</td>
<td>10.3</td>
</tr>
<tr>
<td>Pins and needles</td>
<td>0.07</td>
<td>0.04</td>
<td>0.10</td>
<td>0.09</td>
<td>0.95</td>
</tr>
<tr>
<td>Tingling</td>
<td>0.08</td>
<td>0.08</td>
<td>0.82</td>
<td>0.11</td>
<td>0.16</td>
</tr>
<tr>
<td>Electric shocks</td>
<td>0.11</td>
<td>0.05</td>
<td>0.23</td>
<td>0.05</td>
<td>0.01</td>
</tr>
<tr>
<td>Stabbing</td>
<td>0.09</td>
<td>0.02</td>
<td>−0.03</td>
<td>0.88</td>
<td>0.04</td>
</tr>
<tr>
<td>Pressure</td>
<td>0.03</td>
<td>0.87</td>
<td>0.20</td>
<td>−0.07</td>
<td>0.01</td>
</tr>
<tr>
<td>Squeezing</td>
<td>0.08</td>
<td>0.88</td>
<td>−0.02</td>
<td>0.16</td>
<td>0.04</td>
</tr>
<tr>
<td>Evoked by brushing</td>
<td>0.80</td>
<td>−0.04</td>
<td>0.06</td>
<td>0.16</td>
<td>0.28</td>
</tr>
<tr>
<td>Evoked by pressure</td>
<td>0.85</td>
<td>0.14</td>
<td>−0.01</td>
<td>−0.01</td>
<td>−0.01</td>
</tr>
<tr>
<td>Evoked by cold stimuli</td>
<td>0.62</td>
<td>0.029</td>
<td>0.13</td>
<td>0.14</td>
<td>−0.12</td>
</tr>
</tbody>
</table>

One important feature of the NPSI was its sensitivity to treatment. Increases or decreases of the NPSI total score were related to the subjective improvement or alteration of pain as assessed by the global impression of changes of both the patients and examinators, after 1 month of treatment. Not surprisingly, such a sensitivity to change was only evidenced for the total score, but not for the five subscores. Indeed, the treatments were not standardized and due to the variety of drugs, combinations of drugs, and the different dosages used in our patients, we did not expect to demonstrate any selective or preferential therapeutical effects. This property would have to be confirmed in controlled studies. Application of the NPSI in future pharmacological trials should be of help in analyzing the effects of different compounds on the different symptoms of neuropathic pain. A major facet of such studies would be to evidence selective or preferential effects of pharmacological agents on some dimensions or symptoms of neuropathic pain syndromes and the identification of subgroups of responders. In accordance with this hypothesis, several studies have shown that current treatments of neuropathic pain do not induce global and uniform analgesic effects but rather act preferentially or selectively on some of their components (Attal et al., 2000, 2002, 2004; Eide et al., 1994, 1995; Leung et al., 2001; Vestergaard et al., 2001; Wallace et al., 2000a,b). In this respect, it remains to be confirmed in controlled studies that the subscores of the NPSI defined below are more sensitive to treatment than the individual score of each item.

Another major and complementary application of the NPSI would be the identification of specific clusters of symptoms in large population of patients. Such observational studies might provide new criteria for the classification of neuropathic pain patients. In particular, they might help to identify selective combinations of symptoms and allow the definition of new syndromes which might represent the basis for a new classification of neuropathic pain. There is a general agreement to consider that the large and heterogeneous category of neuropathic pain refers, in fact, to several subsets of patients. However, the criteria for defining such subgroups have not yet been identified. An optimal classification of neuropathic pain would rely on self-questionnaire was mainly based on analysis of the discriminant validity and predictive values of its 10 descriptors. It was shown that all the items but one were sensitive to treatment suggesting that this scale might be used in pharmacological trials. Although the objectives of the Neuropathic Pain Scale and NPSI were similar, the items retained in these two self-questionnaires are completely different. Only two items, related to ‘burning pain’ and ‘pain provoked by touch’, are common to the Neuropathic Pain Scale and NPSI, although they are termed differently. Three items of the Neuropathic Pain Scale, that is to say dullness, cold and itching, which were included in the preliminary version of the NPSI, have not been retained in its final version because they were not judged reliable enough and/or were not loaded to a specific factor in the principal component analysis. Several items of the NPSI (i.e. those related to pressure pain, paroxysmal pain, cold allodynia, paresthesia/dysesthesia) were not included in the Neuropathic Pain Scale. Thus, although the factorial structure of the Neuropathic Pain Scale has not been verified statistically, it is unlikely that the same dimensions of neuropathic pain are evaluated by these two instruments. In this respect, it would be of interest to compare the responses to the two questionnaires in the same patients.

Our main objective was to provide a simple and easy-to-use instrument for daily practice and clinical studies. Thus, we deliberately chose to reduce the number of items to the minimum necessary for evaluating the different components of neuropathic pain syndromes. The descriptors which were not clearly loaded to a definite factor in the factor analysis and/or were not reliable enough in the test–retest analysis were eliminated in the final version of the questionnaire. We kept the two ‘temporal’ items related to the duration of spontaneous and paroxysmal pain since this represents another important aspect of the evaluation of neuropathic pain patients. Our working hypothesis was that neuropathic pain syndromes comprised four distinct dimensions, that is to say spontaneous ongoing pain, spontaneous paroxysmal pain, evoked pain (i.e. allodynia/hyperalgesia to mechanical and/or thermal stimuli) and paresthesia/dysesthesia. The present results suggest that neuropathic pain syndromes include five dimensions with a dichotomy of spontaneous ongoing pain. In our opinion, such a subcategorization is clinically relevant since ‘burning’ could correspond to the classical superficial component of ongoing pain, while the two items ‘pressure’ and ‘squeezing’ might reflect the deep component of spontaneous ongoing pain which is often reported by the patients (Otto et al., 2003). In any case, our data tend to confirm that neuropathic pain is a heterogeneous category which includes several independent dimensions. Interestingly, the fact that the NPSI total score, but not the subscores, was correlated with the global rating of pain intensity made with a Likert scale suggests that the latter is a composite of several components.

Fig. 1. Relationship between Patient Global Impression of Change and changes in the NPSI total score.
identification of the mechanisms presumably responsible for the pain (ultimately in individual patients) in order to select treatments targeting these mechanisms. Although most authors consider that such a rational approach is theoretically interesting, there is still little data confirming its feasibility and its real benefit in patients with neuropathic pain (Hansson, 2003; Jensen and Baron, 2003). Moreover, due to the limitations of animal studies, it appears necessary to address these questions in the clinical setting. Future clinical studies should notably aim to clarify the relationships between symptoms or combinations of symptoms (i.e. syndromes) and etiological factors or the topography of the nervous lesion. Such information should greatly facilitate the interpretation of animal data and their translation in the clinic. The present data suggest that the NPSI would be helpful for carrying out such studies.

In conclusion, the psychometric properties of the NPSI renders it suitable for the evaluation of the different dimensions of neuropathic pain syndromes. The reliability of the different descriptors appears to be sufficient and its sensitivity to change indicates that the NPSI could be used in future pharmacological studies to characterize subgroups of patients who might respond differentially to the treatments.

Acknowledgements

The authors thank Pr David Bowsher for his help in the translation of the NPSI. The authors also thank Drs Patrice Baud (†), Bruno Brochet, Jean-François Doubre, Bernard Laurent, Gérard Mick, Roland Peyron, Léon Plaghki, for providing expert advice in the design of the preliminary version of the questionnaire. This study was supported by a grant from ‘la Fondation Caisse Nationale de Prévoyance (CNP).

Appendix A. Questionnaire d’évaluation des douleurs neuropathiques

Date: __________________________
Prénom: __________________________
Nom: __________________________
Sexe: __________________________
Age: __________________________

Vous souffrez de douleurs secondaires à une lésion du système nerveux. Ces douleurs peuvent être de plusieurs types. Il existe des douleurs spontanées, c’est-à-dire des douleurs présentes en l’absence de toute stimulation, qui peuvent être durables ou apparaître sous forme de crises douloureuses brèves. Il existe également des douleurs provoquées par diverses stimulations (frottement, pression, contact avec le froid). Vous pouvez ressentir un ou plusieurs types de douleur. Le questionnaire que vous allez remplir a été conçu pour permettre à votre médecin de mieux connaître les différents types de douleurs dont vous souffrez, afin de mieux adapter votre traitement.

Nous voudrions savoir si vous avez des douleurs spontanées, c’est-à-dire des douleurs en l’absence de toute stimulation. Pour chacune des questions suivantes, entourez le chiffre qui correspond le mieux à l’intensité de vos douleurs spontanées en moyenne au cours des 24 dernières heures. Entourez le chiffre 0 si vous n’avez pas ressenti ce type de douleur (Veuillez n’entourer qu’un seul chiffre).

Q1. Votre douleur est-elle comme une brûlure?

Aucune brûlure 0 1 2 3 4 5 6 7 8 9 10 Brûlure maximale imaginable

Q2. Votre douleur est-elle comme un étau?

Aucun étau 0 1 2 3 4 5 6 7 8 9 10 Étau maximal imaginable

Q3. Votre douleur est-elle comme une compression?

Aucune compression 0 1 2 3 4 5 6 7 8 9 10 Compression maximale imaginable

Q4. Au cours des dernières 24 heures, vos douleurs spontanées ont été présentes: Veuillez cocher la réponse qui correspond le mieux à votre état

En permanence /_/
Entre 8 et 12 heures /_/
Entre 4 et 7 heures /_/
Entre 1 et 3 heures /_/
Moins d’1 heure /_

Nous voudrions savoir si vous avez des crises douloureuses brèves. Pour chacune des questions suivantes, entourez le chiffre qui correspond le mieux à l’intensité de vos crises douloureuses en moyenne au cours des 24 dernières heures. Entourez le chiffre 0 si vous n’avez pas ressenti ce type de douleur (Veuillez n’entourer qu’un seul chiffre).

Q5. Avez-vous des crises douloureuses comme des décharges électriques?

Aucune décharge électrique 0 1 2 3 4 5 6 7 8 9 10 Décharge électrique maximale imaginable
Q6. Avez-vous des crises douloureuses comme des coups de couteau?

Aucun coup de couteau

Q7. Au cours des dernières 24 heures, combien de ces crises douloureuses avez-vous présenté?

Veuillez cocher la réponse qui correspond le mieux à votre état

Plus de 20 /_/
Entre 11 et 20 /_/
Entre 6 et 10 /_/
Entre 1 et 5 /_/
Pas de crise douloureuse /_/

Nous voudrions savoir si vous avez des douleurs provoquées ou augmentées par le frottement, la pression, le contact d’objets froids sur la zone douloureuse. Pour chacune des questions suivantes, entourez le chiffre qui correspond le mieux à l’intensité de vos douleurs provoquées en moyenne au cours des 24 dernières heures. Entourez le chiffre 0 si vous n’avez pas ressenti ce type de douleur (Veuillez n’entourer qu’un seul chiffre).

Q8. Avez-vous des douleurs provoquées ou augmentées par le frottement sur la zone douloureuse?

Aucune douleur

Q9. Avez-vous des douleurs provoquées ou augmentées par la pression sur la zone douloureuse?

Aucune douleur

Q10. Avez-vous des douleurs provoquées ou augmentées par le contact avec un objet froid sur la zone douloureuse?

Aucune douleur

Nous voudrions savoir si vous avez des sensations anormales dans la zone douloureuse. Pour chacune des questions suivantes, entourez le chiffre qui correspond le mieux à l’intensité de vos sensations anormales en moyenne au cours des 24 dernières heures. Entourez le chiffre 0 si vous n’avez pas ressenti ce type de sensation (Veuillez n’entourer qu’un seul chiffre).

Q11. Avez-vous des picotements?

Aucun picotement

Q12. Avez-vous des fourmillements?

Aucun fourmillement

RESULTATS

Score total

Sous-scores

Brûlures (douleurs spontanées superficielles):

1. \( Q1 = \)

Constriction (douleurs spontanées profondes):

2. \( (Q2 + Q3) = \)

Douleurs paroxystiques:

3. \( (Q5 + Q6) = \)

Douleurs évoquées:

4. \( (Q8 + Q9 + Q10) = \)

Paresthésies/dysthésies:

5. \( (Q11 + Q12) = \)

\((1 + 2 + 3 + 4 + 5) = /100\)

Appendix B. Neuropathic Pain Symptom Inventory

Date:  
First name:  
Last name:  
Sex:  
Age:  

You are suffering from pain due to injury or disease of the nervous system. This pain may be of several types. You may have spontaneous pain, i.e. pain in the absence of any stimulation, which may be long-lasting or occur as brief attacks. You may also have pain provoked or increased by brushing, pressure, or contact with cold in the painful area. You may feel one or several types of pain. This questionnaire has been developed to help your doctor to better evaluate and treat various types of pain you feel.

We wish to know if you feel spontaneous pain, that is pain without any stimulation. For each of the following questions, please select the number that best describes your average spontaneous pain severity during the past 24 h. Select the number 0 if you have not felt such pain (circle one number only).
Q1. Does your pain feel like burning?

| No burning | 0 1 2 3 4 5 6 7 8 9 10 | Worst burning imaginable |

Q2. Does your pain feel like squeezing?

| No squeezing | 0 1 2 3 4 5 6 7 8 9 10 | Worst squeezing imaginable |

Q3. Does your pain feel like pressure?

| No pressure | 0 1 2 3 4 5 6 7 8 9 10 | Worst pressure imaginable |

Q4. During the past 24 h, your spontaneous pain has been present:

Select the response that best describes your case

| Permanently | // |
| Between 8 and 12 h | // |
| Between 4 and 7 h | // |
| Between 1 and 3 h | // |
| Less than 1 h | // |

We wish to know if you have brief attacks of pain. For each of the following questions, please select the number that best describes the average severity of your painful attacks during the past 24 h. Select the number 0 if you have not felt such pain (circle one number only).

Q5. Does your pain feel like electric shocks?

| No electric shocks | 0 1 2 3 4 5 6 7 8 9 10 | Worst electric shocks imaginable |

Q6. Does your pain feel like stabbing?

| No stabbing | 0 1 2 3 4 5 6 7 8 9 10 | Worst stabbing imaginable |

Q7. During the past 24 h, how many of these pain attacks have you had?

Select the response that best describes your case

| More than 20 | // |
| Between 11 and 20 | // |
| Between 6 and 10 | // |
| Between 1 and 5 | // |
| No pain attack | // |

We wish to know if you feel abnormal sensations in the painful area. For each of the following questions, please select the number that best describes the average severity of your abnormal sensations during the past 24 h. Select the number 0 if you have not felt such sensation (circle one number only).

Q8. Is your pain provoked or increased by brushing on the painful area?

| No pain | 0 1 2 3 4 5 6 7 8 9 10 | Worst pain imaginable |

Q9. Is your pain provoked or increased by pressure on the painful area?

| No pain | 0 1 2 3 4 5 6 7 8 9 10 | Worst pain imaginable |

Q10. Is your pain provoked or increased by contact with something cold on the painful area?

| No pain | 0 1 2 3 4 5 6 7 8 9 10 | Worst pain imaginable |

We wish to know if you feel abnormal sensations in the painful area. For each of the following questions, please select the number that best describes the average severity of your abnormal sensations during the past 24 h. Select the number 0 if you have not felt such sensation (circle one number only).

Q11. Do you feel pins and needles?

| No pins and needles | 0 1 2 3 4 5 6 7 8 9 10 | Worst pins and needles imaginable |

Q12. Do you feel tingling?

| No tingling | 0 1 2 3 4 5 6 7 8 9 10 | Worst tingling imaginable |

RESULTS

<table>
<thead>
<tr>
<th>Total intensity score</th>
<th>Subscores</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Q1 = Burning (superficial) spontaneous pain: Q1 = /10</td>
<td></td>
</tr>
<tr>
<td>2. (Q2 + Q3) = Pressing (deep) spontaneous pain: (Q2 + Q3)/2 = /10</td>
<td></td>
</tr>
<tr>
<td>3. (Q5 + Q6) = Paroxysmal pain: (Q5 + Q6)/2 = /10</td>
<td></td>
</tr>
<tr>
<td>4. (Q8 + Q9 + Q10) = Evoked pain: (Q8 + Q9 + Q10)/3 = /10</td>
<td></td>
</tr>
<tr>
<td>5. (Q11 + Q12) = Paresthesia/dysesthesia: (Q11 + Q12)/2 = /10</td>
<td></td>
</tr>
<tr>
<td>(1 + 2 + 3 + 4 + 5) = /100</td>
<td></td>
</tr>
</tbody>
</table>

References


