Pain Medicine 2016; 17: 1465–1489
doi: 10.1093/pm/pnv077

OXFORD

*Review Article*

# Methods and Instruments to Evaluate Cognitive Function in Chronic Pain Patients: A Systematic Review

**Begoña Ojeda, MSc,* Inmaculada Failde, MD, PhD,* María Dueñas, PhD,† Alejandro Salazar, MSc,* and Christopher Eccleston, PhD‡**

*Preventive Medicine and Public Health Area, The Observatory of Pain (External Chair of Pain), University of Cádiz, Cádiz, Spain; †Salus Infirmorum Faculty of Nursing, University of Cádiz, Spain; ‡Centre for Pain Research, the University of Bath, Bath, UK

*Correspondence to:* Begoña Ojeda, Preventive Medicine and Public Health Area, The Observatory of Pain (External Chair of Pain), University of Cádiz, Ave Ana of Viya 52, 11009 Cádiz, Spain. Tel: (+34)956019086; Fax: (+34) 956-252-426; E-mail: begona.ojeda@uca.es.

Funding sources: This research was generously supported by a grant from the Spanish Pain Foundation and the External Chair of Pain (Grünenthal Foundation-University of Cádiz) and was carried out in collaboration with the Centre for Pain Research at the University of Bath.

Disclosure and conflicts of interest: The Grünenthal Foundation is a private nonprofit organization that promotes the dissemination of scientific knowledge and supports research. We wish to confirm that there are no known conflicts of interest associated with this publication and there has been no significant financial support for this work that could have influenced its outcome.

## Abstract

**Objective. We aimed to systematically review the methods and instruments used to evaluate cognitive function in chronic pain (CP) patients.**

**Methods. A sensitive search strategy was designed using five databases. Based on the objectives and methodology, we selected cross-sectional studies on adults with chronic non-cancer pain in which cognitive function was assessed using validated instruments. The characteristics of the subjects, control groups, and other variables that might affect cognitive function, and the instruments used, were extracted from each article.**

**Results. In the 42 articles identified, 53 instruments were used to assess cognitive function. Chronic pain criteria were defined in 83.3% of the articles and more than half (57.1%) included single diagnosis samples, with fibromyalgia being the most frequent studied (75%). Patients with prior cognitive impairment were excluded in 61.9% of the studies, and a control group was included in 64.3% of the studies. In most cases potential confounding variables were evaluated. More than 14% of the studies used self-report measures, and 73.8% used neuropsychological instruments, particularly for assessing attention (30%) and memory (27.5%). None of the instruments were specifically validated for pain patients and only five studies analyzed the psychometric properties of the instruments.**

**Conclusions. Various instruments and methods were used to assess cognitive function in CP patients, particularly fibromyalgia patients, but also other cohorts with well-defined CP. The instruments used had been validated, but not for pain populations, thus they require specific adaptation and validation to be used in CP patients. Certain recommendations are made in order to improve the evaluation of cognitive function in these patients.**

**Key Words. Assessment; Chronic Pain; Cognitive Function; Neuropsychological Testing; Self-Report Questionnaire**

## Introduction

Chronic pain patients frequently report memory impairment and poor concentration, characteristics that disturb their normal functioning, impair their ability to cope with everyday life, and affect the way they relate to their

immediate social environment [1]. Indeed, to ensure the adequate management of patients with chronic pain, it has been suggested that an assessment of cognitive function should be considered one of the priorities for medical professionals [2].

There are different reasons why cognitive function should be evaluated in chronic pain patients, including the negative influence of cognitive impairment on anxiety, depression, and a restriction of activities, which further diminish the already compromised quality of life of patients with chronic pain [3]. Given that cognitive complaints are common in these patients and that they represent an additional source of suffering, especially when such symptoms cannot be clearly explained, informing a patient and evaluating such changes should be part of the initial assessment. In this way, a significant part of the distress associated with impaired memory and concentration will be alleviated [4]. Cognitive function is also relevant to the evaluation and handling of pain by professionals, especially when cognitive status is limited and hinders oral communication between the doctor and the patient. Likewise, the selection of effective therapeutic strategies for the treatment of pain could be compromised. For example, patients may blame their cognitive problems on their medication and refuse to comply with the appropriate prescriptions [5]. Alternatively, they might be incapable of responding to psychological cognitive-behavioural pain therapies in which the patient must rely on cognitive function in order to pay attention and concentrate, as well as to process, memorize, and perform different tasks.

Apart from the complaints and cognitive impairment, there is also physical evidence supporting this relationship. Structural magnetic resonance imaging studies involving multiple types of chronic pain patients show that the brains of these individuals differ from those of matched healthy control subjects. Some studies have found alterations in gray matter volume or white matter integrity, and even epigenetic changes in regions of the brain implicated in pain processing, mood regulation, and cognition [6].

In light of the above, it is worth highlighting the importance of exploring the cognitive impact of pain in order to acquire more information about the brain mechanisms that mediate both pain and cognition, which would point the way towards new treatment strategies [7,8].

To date, the relationship between chronic pain and diminished or impaired cognitive function has been demonstrated in several studies [9–12], including those involved in attention, memory, executive function, or psychomotor speed and information processing [13]. Likewise, most of these patients score below average compared to the standardized data for the general population when instruments assessing cognitive function are employed [12,14–16]. However, the diversity of methods and instruments used to assess cognitive function in patients with pain makes it difficult to compare the results between studies [13] and to reach a consensus about the potential relationship between pain and cognitive function.

Given the importance of evaluating cognitive function, and bearing in mind the heterogeneous landscape associated with evaluation, we set out to perform a systematic review of the literature in order to identify and describe the methodological approaches and instruments used to assess cognitive function in chronic pain patients.

## Methods

This review is divided into two phases that were guided by the methodology from the Cochrane Handbook for Systematic Reviews [17]. Phase 1 involved a systematic search of the literature based on a specific selection strategy and with a subsequent combination of keywords for the data search. Phase 2 involved the screening of titles, abstracts, and full articles, with data being extracted by three independent reviewers (BO, MD, and AS) in accordance with specific inclusion criteria.

### *PHASE 1: Selection and Search Strategy*

Following the advice of a medical librarian, systematic searches of the following electronic databases were undertaken for articles published between 1995 and 2013: Medline, Scopus, PsycINFO, ScienceDirect, and the Cochrane Database of Systematic Reviews. The searches were not restricted to the English language, and Spanish references were also included. The strategy for selecting articles was based on pre-specified eligibility criteria, including the aim of the study and the methodology used (design, subjects, and instruments). Thus, an article was eligible only when the main aim of the study was to assess cognitive function in chronic pain patients, hence, studies in which cognitive function was used to evaluate the result of a therapeutic intervention or as part of a neurophysiological study were excluded. Furthermore, only studies using a cross-sectional design were included, excluding clinical trials and studies in animal models. In terms of the subjects, studies carried out on chronic pain patients suffering non-malignant chronic pain of any cause were included (except migraine, chronic daily headache, and visceral pain). The definition of chronic pain used in each study was not considered as a criterion for inclusion or exclusion, although this information was collected as a variable in the review in order to evaluate the risk of introducing bias. In addition, the use of instruments that had been previously validated in papers published elsewhere was established as a quality control criterion for the articles.

According to these criteria, the keywords used in the search were general terms referring to chronic illnesses associated with pain, as well as more specific terms that sought to gather information on complaints that have specific features related to pain (e.g., fibromyalgia, low back pain, or complex regional syndromes) and in

**Table 1** Keywords and key topic areas in the search strategy

| Pain | | Evaluation | | Cognition |
|---|---|---|---|---|
| "chronic pain" OR "persistent pain" OR "continuous pain" OR fibromyalgia OR "complex regional pain syndrome" OR "back pain" OR arthritis OR "widespread chronic pain" OR "neuropathic pain" | AND | evaluation OR assessment* | AND | "cognitive function" OR "cognitive performance" OR "cognitive disruption" OR "cognitive impairment" OR "cognitive interference" OR "cognitive complaint" OR neuropsychol* OR memory OR attention OR "executive function" |

which chronic pain is common. We also used additional keywords associated with the assessment or evaluation of cognitive function. Thus, the keywords shown in Table 1 were combined in different search strategies depending on the architecture of the different search engines.

*PHASE 2: Screening of Literature and Data Extraction*

Three of the authors (BO, MD, and AS) independently reviewed the titles and abstracts of the papers to identify the studies that best fulfilled the selection criteria. All duplicated items were removed using the bibliographic tool Refworks. The references of all the studies retrieved were checked to identify whether any had not been detected by the computerized search, a procedure that led to the inclusion of several more studies that fulfilled the selection criteria. When a consensus did not exist between these three reviewers, the senior authors (IF and CE) were consulted to make a final decision on the inclusion or exclusion of the papers.

To classify the results, we extracted the following information: the aim of each study, the type of pain and number of patients, the inclusion criteria used to define chronic pain, and the exclusion criteria; information related to the control groups (if used) and their characteristics (healthy control subjects or other patients, matched for sex, age, or education level); and other variables related to pain and cognitive functions, such as affective status, sleep disorders, and the consumption of medication. The instruments were classified into two groups according to the type of evaluation: self-report (SR) and neuropsychological tests (NT). Neuropsychological assessment was defined as a measure of the ability to perform mental functions [18], while self-report measures were not based on the performance of subjects but on their own reported opinion, i.e., the patients' perception of their own cognitive state [19]. Finally, information on the instruments used to assess cognitive function in each study was collected, such as the version of the instrument used and what the authors aimed to measure with the tool.

## Results

Of the 1,135 articles initially identified in the five databases searched, 42 were ultimately selected and included in our analysis (Figure 1). From these studies, we identified 53 instruments that were used to assess cognitive function.

*Study Characteristics*

Table 2 summarizes the information of each study included in the review (42 papers). The table includes information on the type of cognitive assessment conducted in each study, whether classified as self-report (SR), neuropsychological (NT), or both (SR+NT), and the name of the specific instrument(s) used in each assessment (one or more, depending on the paper). Then the information concerning pain patients who have participated in each study is shown, including the type of pain patients and the sample size of each study, the inclusion criteria for selecting such patients, the criteria for selecting pain or chronic pain (if used), and the exclusion criteria. Finally, the last two columns of the table describe the control group (if applicable) and other variables considered in each study, which were related to cognitive function in selected papers.

The aims of all of the articles included were in accordance with the inclusion criteria of the review. Most of the studies (57.1%) described patients with specific chronic pain syndromes: neuropathic pain (NP), rheumatoid arthritis (RA), chronic back pain (CBP), complex regional pain syndrome (CRPs), and fibromyalgia (FM) [15,16,20–41]. The latter group of patients was studied most often (in 75% of the articles selected for this review).

Of the 42 articles included, 83.3% used specific criteria to define chronic pain. Of these, 21 used disease diagnosis, especially in cases of FM [15,16,20–26,28–35,38–42], whereas 19 used the duration of pain (over 3 months, 6 months, or 1 year) [12,16,25–27,29,32,36,37,42–51] and 3 used pain intensity [32,48,50]. We also identified several studies (n = 7) in which no criteria were used to define chronic pain [1,5,14,52–55].

An analysis of the exclusion criteria revealed that in 26 of the 42 studies, patients with current or prior traumatic brain injury, impaired cognitive function, or nervous system diseases were excluded [5,12,14,21,22,24,26,29,32–

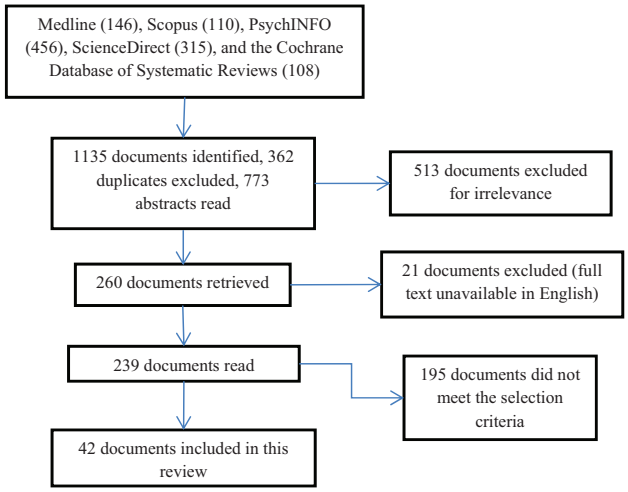


**Figure 1** Flow diagram of the articles accepted and rejected during the search and selection process.

35,37,39,44–46,48,49,51–54]. Indeed, two studies used the patients' results in neuropsychological evaluations as exclusion criteria. In one case the Auditory Verbal Learning test was used as a measure of effort, so patients scoring ≥3 were excluded from further analysis [22]. In the other, the threshold score of 24 in the MMSE was used to exclude participants with severe cognitive impairment (Table 2: [51]). Likewise, 16 studies excluded patients with psychopathological disturbances (major depression or psychiatric illness meeting DSM-IV criteria) [26,30,32–34,38,39,41,44–46,49,51,54,55], and 9 excluded individuals with a history of alcohol abuse or other neurotoxic substance abuse [12,21,24–26,30,34,51,55]. Other exclusion criteria were related to being under litigation, having cardiovascular or renal diseases, and being pregnant. Finally, 10 articles did not specify any exclusion criteria in their methodology [20,23,27,28,31,36,42,43,47,50].

Most studies (64.3%) used a control group [12,15,16,20,22–27,29–34,36–38,44,49,55]; in over 85% of the studies they were healthy subjects. An age-, sex-, and/or education level–matched control group was used in 14 studies, whereas in 4 studies a pain-free population with cognitive impairment was used as the control group (Table 2).

In addition to cognitive function, all studies (n = 42) analyzed variables closely linked to pain and cognitive function, including age and/or education level (54.8%) [5,14,16,20–26,34,37,38,40,43–47,52–55]; medication (35.7%) [1,5,12,14,16,27,29,39,41,45–47,49,54,55]; pain intensity measures, often analyzed using numerical scales (71.4%) [5,12,15,16,21–23,27–29,32,35,37,42–50,53,55]; sleep quantity and/or quality (16.7%); and affective/emotional parameters, most commonly depression and anxiety (90%: Table 2).

Of the articles reviewed, 6 used a SR questionnaire (14.3%) [5,27,38,47,52,54], 31 used NP evaluation (73.8%) [12,14–16,20,23,25,26,29–37,39–46,48–51,53,55] and the remaining 5 used a combination of both assessment strategies [1,21,22,24,28] (11.9%: Table 2).

The studies used original versions, later versions, or transcultural adaptations of the questionnaires and assessment strategies, although they were not specifically validated on chronic pain patients. Of the 42 studies, 4 of them based the choice of instruments on previous studies in which the sensitivity of the questionnaires in patients with non-specific chronic pain [42,44] and FM [30,38] was demonstrated. In addition, and given the need to apply the test on several occasions, 4 studies chose the instruments based on their ability to be replicated [23,29,48,55]. The use of the Test of Everyday Attention (TEA) was justified, given the important benefits associated with its multiple forms [29,48]: version A and B, and the Iowa Gambling Task (IGT) was used twice to determine the effects of the intensity of pain on performance [23]. The Paced Auditory Serial Addition Test (PASAT), Cognitive Reflection Test (CRT), and Finger Tapping Test (FTT) display high reliability in a study in which they were used on two different occasions [55]. Finally, only 5 studies [27,45–47,55] analyzed the reliability of the instruments used to assess patients with pain without properly validating them.

### *Instruments*

The data pertaining to the instruments used in each study was recorded in Table 2. In addition, in Tables 3 and 4 the information summarized includes the name of the instrument (NT in Table 3 and SR in Table 4), the reference to the published study in which it was used, that to the article describing the instrument and what

**Table 2** Summary of the main characteristics from studies selected

| Ref. Type of evaluation | Instrument | Participants (chronic pain) | | | | Controls [N] | Other variables related to cognition |
|---|---|---|---|---|---|---|---|
| | | Patients [N] | Inclusion criteria | Pain criteria | Exclusion criteria | | |
| [42] **NT** | Numerical Interference Task (N-task & V-task) | CP [46] | Chronic pain of a persistent and continuous nature | D | No | No | Intensity of pain, somatic complaints, affective distress |
| [20] **NT** | Randt Memory Test<br>Code Memory Test<br>Word Fluency task<br>Kimura Recurring Recognition Figures Test<br>Wechsler Intelligence Scale for Adults (WIS-A) | FM [25] | Criteria of ACR | ✓ | No | Healthy controls [18] and major depression [22] | Age and education; pain intensity; fatigue and depression |
| [52] **SR** | Sickness Impact Profile, Alertness subscale (SIP) | CP [170] | No | No | Head injuries, involved in a litigation claim | No | Age and education; depression and somatic complaints |
| [43] **NT** | Numerical Interference Task (N-task & V-task) | CP [40] | Chronic pain of a persistent and continuous nature | D | No | No | Age and education; pain intensity; pain related fear; emotional distress; negative affect |
| [21] **NT + SR** | Memory Observation Questionnaire (MOQ)<br>Rey Auditory Verbal Learning Test (RAVLT)<br>Paced Auditory Serial Additions Test (PASAT)<br>Symbol Digit Modalities Test (SDMT), written version<br>Wechsler Memory Scale (WMS) | FM [30] | Criteria of ACR | ✓ | Neurological disorders, cognitive dysfunction, substance abuse, or head trauma | Healthy controls matched for age and sex [30] | Age and education; intellectual level; sleep quality; pain severity scale; anxiety; depression |
| [44] **NT** | Stroop tests | CP [33] | >1 year | D | Severe psychopathological disturbances, cerebral disease, or head injury and colour blindness | Healthy controls [20] | Age and socio-cultural level; pain intensity; anxiety; depression |
| [45]***NT** | | CP [73] | | D | | No | |

(continued)

**Table 2** Continued

| Ref. | Type of evaluation | Instrument | Participants (chronic pain) | | | | Controls [N] | Other variables related to cognition |
|---|---|---|---|---|---|---|---|---|
| | | | Patients [N] | Inclusion criteria | Pain criteria | Exclusion criteria | | |
| | | Paced Auditory Serial Additions Test (PASAT)<br>Stroop tests<br>Complex Figure Test (CFT)<br>Wisconsin Card Sorting Test (WCST)<br>Trail Making Test (TMT)<br>Design Fluency Test<br>Controlled Oral Word Association (COWA)<br>Grooved Pegboard Test<br>Wechsler Intelligence Scale for Adults (WIS-A)<br>Wechsler Memory Scale (WMS) | | Pain reported daily, ≥6 months. | | Psychosis, major depression, neuropathic pain syndrome, headache or migraine, and documented changes in cognitive function | | Age; education; medication; emotional distress; pain intensity |
| [55] | ***NT** | Paced Auditory Serial Additions Test (PASAT)<br>Continuous Reaction Time (CRT)<br>Finger Tapping Test (FTT) | CP [40] | Non-malignant pain patients. | No | Taking other psychotropic drugs, metabolic disturbances or drinking alcoholic beverages, physical or neurological dysfunction | Healthy controls matched for age and sex [40] | Age and medication; pain intensity; anxiety and depression; physical functioning |
| [5] | **SR** | Sickness Impact Profile (SIP), alertness subscale | CP [275] | No | No | Head trauma or stroke and dementing illness | No | Age, education and medication; pain severity; depression, anxiety, and sleep quality |
| [53] | **NT** | Wechsler Intelligence Scale for Adults (WIS-A) | CP [736] | No | No | Traumatic brain injury or other neurologic disease | No | Age; pain intensity; unpleasantness and suffering; pain behaviour |
| [22] | **SR+NT** | Meta Memory Questionnaire (MMQ)<br>Wechsler Intelligence Scale for Adults (WIS-A)<br>Rey Auditory Verbal Learning Test (RAVLT)<br>Paced Auditory Serial | FM [28], CP [27] | Criteria of ACR-10 | ✓ | Poor effort on cognitive tasks (<3), significant head injury, or other neurological condition | Healthy controls [21] | Age and intelligence; depression; pain intensity; fatigue; effort |

(continued)

**Table 2** Continued

| Ref. | Type of evaluation | Instrument | Participants (chronic pain) | | | | Controls [N] | Other variables related to cognition |
|---|---|---|---|---|---|---|---|---|
| | | | Patients [N] | Inclusion criteria | Pain criteria | Exclusion criteria | | |
| | | Additions Test (PASAT)<br>Stroop testsComplex Figure Test (CFT)<br>Wisconsin Card Sorting Test (WCST)<br>Trail Making Test (TMT)<br>Controlled Oral Word Association (COWA)<br>Iowa Gambling Task (IGT) | | | | | | |
| [(23] | **NT** | Wechsler Memory Scale (WMS)<br>Stroop tests<br>Wisconsin Card Sorting Test (WCST)<br>Wechsler Intelligence Scale for Adults (WIS-A) | CBP [26] and CRP [12] | IASP criteria | ✓ | No | Healthy controls matched for age, sex and education [26] | Age and education; pain, anxiety, and depression |
| [46] | ***NT** | Stroop tests<br>Complex Figure Test (CFT)<br>Wisconsin Card Sorting Test (WCST)<br>Trail Making Test (TMT)<br>Wechsler Intelligence Scale for Adults (WIS-A)<br>Wechsler Memory Scale (WMS) | CP [73] | Pain reported daily, ≥6 months | D | Psychosis, major depression, neuropathic pain syndrome, headache or migraine, and documented changes in cognitive function | No | Age, education and medication; pain severity; psychological distress |
| [47] | ***SR** | Brief Symptom Inventory (BSI) | CP [222] | Continuous pain ≥3 months | D | No | No | Age; sex; education; opioid use; pain intensity, depression, posttraumatic stress, pain catastrophizing |
| [24] | **SR + NT** | Metamemory in Adulthood (MIA) questionnaire<br>Free recall | FM [23] | Criteria of ACR | ✓ | Regular use of tobacco and recreational drugs, central nervous system disease or brain injury, education <10th grade, psychiatric illness, other rheumatic | Healthy controls matched for aged [23] and older controls [22] | Age; DSM disorders |

(continued)

**Table 2** Continued

| Ref. | Type of evaluation | Instrument | Participants (chronic pain) | | | | Controls [N] | Other variables related to cognition |
|---|---|---|---|---|---|---|---|---|
| | | | Patients [N] | Inclusion criteria | Pain criteria | Exclusion criteria | | |
| | | | | | | diseases or significant health conditions | | |
| [12] | **NT** | Paced Auditory Serial Additions Test (PASAT)<br>Continuous Reaction Time (CRT)<br>Finger Tapping Test (FTT)<br>Mini-Mental State Examination (MMSE) | CP [91] | >6 months | D | Head injury, depression, alcohol consumption, use of benzodiazepine, metabolic disturbances, physical and/or neuropsychological disturbances interfering with the test | Healthy controls matched for age and sex [64] | Medication; pain intensity |
| [54] | **SR** | Cuestionario de Olvidos Cotidianos (COC) | CP [149] | No | No | Severe psychopathologic disturbances, previous and present cerebral disease, or head injury | No | Age and medication; anxiety and depression, catastrophizing |
| [25] | **NT** | Paced Auditory Serial Additions Test (PASAT)<br>Auditory Consonant Trigram (ACT)<br>Wechsler Intelligence Scale for Adults (WIS-A)<br>Wechsler Memory Scale (WMS) | FM [35] | Criteria of ACR & persistent memory loss (>6 months) | D✓ | Drug or alcohol abuse, auditory impairment | Healthy controls matched for age, sex, and memory complaints [35] | Age and education; depression; general intelligence |
| [26] | **NT** | Stroop tests<br>Complex Figure Test (CFT)<br>The 10/36 Spatial Recall test (10/36 SRT)<br>Shape recognition and line orientation<br>tests of Benton<br>Road Map Test<br>Wechsler Intelligence Scale for Adults (WIS-A)<br>Wechsler Memory Scale (WMS) | FM [15], RA [15] | Diagnostic criteria for FM and RA, duration illness 0–5 years | D✓ | Neurological problems, brain damage, psychiatric illness, or medical conditions that could affect cognition | Healthy controls [15] | Cerebral reserve (intelligence) |
| [15] | **NT** | | | | ✓ | | Normative data | |

(continued)

**Table 2** Continued

| Ref. Type of evaluation | Instrument | Participants (chronic pain) | | | | Controls [N] | Other variables related to cognition |
|---|---|---|---|---|---|---|---|
| | | Patients [N] | Inclusion criteria | Pain criteria | Exclusion criteria | | |
| | Mini-Mental State Examination (MMSE) | NP [856], MP [603] | Clinical diagnosis of NP or MP | | Hypersensitivity to gabapentin, pregnant or nursing women, patients receiving other analgesic drug | | Age, sex and body mass; pain intensity; anxiety and depression |
| [48] **NT** | The Test of Everyday Attention (TEA)<br>Reading Span Test (RST)<br>Spatial Span Test (SST) | CP [24] | Baseline pain intensity ≥4/10 on a numerical pain rating scale (NRS) and pain for ≥6 months | D, I | Significant head injury, neurological disorder, or disease known to impair attentional functioning | No | Pain, catastrophizing, mental health, and sleep |
| [27]***SR** | Prospective Memory Questionnaire (PMQ) | CBP [50] | Diagnosis of mechanical low back pain, >3 months | D | – | Healthy controls matched for age, sex, and socio-economic status [50] | Analgesic use; pain intensity; depression |
| [49] **NT** | The Remember/Know (R/K) procedure | CP [30] | >1 year | D | Severe psychopathological disturbances, cerebral disease, or head injury meeting DSM IV-R criteria diagnosed | Healthy controls [30] | Psychotropic medication; pain intensity; anxiety and depression |
| [28] **SR + NT** | Everyday Memory Failures Questionnaire (EMF)<br>Stroop tests<br>Test de Aprendizaje Verbal España-Complutense (TAVEC)<br>Test Toulouse-Piéron | FM [68], CP [42] | Criteria of ACR and CIE-9 | ✓ | No | No | Pain intensity; anxiety; depression |
| [29] **NT** | Auditory Consonant Trigram (ACT)<br>Test of Everyday Attention (TEA)<br>Reading Span Test (RST) | FM [30] | Criteria of ACR, >6 months | D, ✓ | Significant head injury, neurological disorder, or disease known to impair attentional function | Healthy control group matched for age and sex [30] | Opioids use; pain intensity; quality of life; anxiety and depression; sleep |
| [50] **NT** | Stroop tests<br>Mini-Mental State Examination (MMSE)<br>Wechsler Intelligence Scale | CP [21] | Postlaminectomy syndrome, >6 months with subjective | D, I | No | No | Depression; pain intensity |

(continued)

**Table 2** Continued

| Ref. | Type of evaluation | Instrument | Participants (chronic pain) | | | | Controls [N] | Other variables related to cognition |
|---|---|---|---|---|---|---|---|---|
| | | | Patients [N] | Inclusion criteria | Pain criteria | Exclusion criteria | | |
| | | for Adults (WIS-A)<br>Wechsler Memory Scale (WMS) | | complaints of memory loss. VAS 7–10 | | | | |
| [30] | **NT** | Rey Auditory Verbal Learning Test (RAVLT)<br>Paced Auditory Serial Additions Test (PASAT)<br>Trail Making Test (TMT)<br>Controlled Oral Word Association (COWA)<br>Test Barcelona | FM [81] | Criteria of ACR | ✓ | Drug or alcohol abuse, neurological and/or psychiatric disorder, and other immune rheumatic conditions | Healthy control group matched for age, education, and working situation [35] | Psychiatry conditions; anxiety; threshold of pain |
| [16] | **NT** | Mini-Mental State Examination (MMSE) | FM [46] | Criteria of ACR >2 years; clinical diagnosis of neuropathic or mixed pain | D, ✓ | Hypersensitivity to gabapentin or its ingredients, pregnant or nursing women, and patients receiving other analgesic drugs indicated for neuropathic pain | Mixed pain [92] and neuropathic pain [92] | Age; sex; education; analgesic drugs; pain intensity; anxiety; depression |
| [31] | **NT** | Stroop tests<br>Complex Figure Test (CFT)<br>Wisconsin Card Sorting Test (WCST)<br>London Tower<br>Test Barcelona<br>Wechsler Intelligence Scale for Adults (WIS-A)<br>Wechsler Memory Scale (WMS) | FM (32) | Women with FM and cognitive complaints | ✓ | No | Patients with MCI [86] | Psychiatric disorders |
| [32] | **NT** | Wechsler Memory Scale (WMS) | CBP [21] and RA [23] | >6 months, VAS >4, criteria of ACR | D, I, ✓ | Psychiatric illness (other than depression and anxiety), head injury, neurological disorders, learning disability, | Normative data | Pain and disability; coping; fear avoidance; pain severity; anxiety; depression |

(continued)

**Table 2** Continued

| Ref. | Type of evaluation | Instrument | Participants (chronic pain) | | | | Controls [N] | Other variables related to cognition |
|---|---|---|---|---|---|---|---|---|
| | | | Patients [N] | Inclusion criteria | Pain criteria | Exclusion criteria | | |
| | | | | | | cancer, and metabolic or bone diseases | | |
| [33] | **NT** | Wisconsin Card Sorting Test (WCST)<br>Iowa Gambling Task (IGT) | FM [36] | Criteria of ACR | ✓ | Co-morbid neurological or neuropsychiatric disorders | Healthy control group matched for age, education, and socio-economic status [36] | Personality; pain experience |
| [34] | **NT** | Rey Auditory Verbal Learning Test (RAVLT)<br>Auditory Consonant Trigram (ACT)<br>Wechsler Intelligence Scale for Adults (WIS-A)<br>Wechsler Memory Scale (WMS) | FM [91] | Criteria of ACR and memory problems | ✓ | Drug or alcohol abuse, psychiatric treatment in the past 3 years, auditory impairment that might interfere with cognitive testing | Control group with memory problems but no FM [43] | Age and education; general intelligence; depression |
| [35] | **NT** | Stroop tests<br>Wechsler Intelligence Scale for Adults (WIS-A) | RA [157] | ACR criteria for RA | ✓ | Dementia or psychotic disorder | No | Pain intensity; negative and positive affect; f atigue; depressed mood |
| [36] | **NT** | Stroop tests<br>Iowa Gambling Task (IGT)<br>Conditional Associative Learning Task (CALT)<br>Wechsler Intelligence Scale for Adults (WIS-A) | FM [15] | FM diagnosis >6 months | D | No | Healthy controls matched for age, sex and education [20] | Anxiety; depression |
| [37] | **NT** | Stroop tests<br>Complex Figure Test (CFT)<br>Wisconsin Card Sorting Test (WCST)<br>Digit Symbol Substitution Test<br>Verbal Associations Test<br>12-word memorization and reproduction test<br>Number sequence repetition test | MSK [64] | >3 months | D | Neurological and somatic diseases that can be accompanied by cognitive function impairments | Healthy controls [20] | Age; pain intensity, disability; pain behavior; catastrophizing; anxiety; depression; psychological distress |

(continued)

**Table 2** Continued

| Ref. | Type of evaluation | Instrument | Participants (chronic pain) | | | | Controls [N] | Other variables related to cognition |
|---|---|---|---|---|---|---|---|---|
| | | | Patients [N] | Inclusion criteria | Pain criteria | Exclusion criteria | | |
| | | Wechsler Intelligence Scale for Adults (WIS-A) | | | | | | |
| [38] | **SR** | Multiple Abilities Self-Report Questionnaire (MASQ) | FM [72] | ACR criteria, under standard medical care | ✓ | Severe physical impairment, co-morbid medical illnesses, psychiatric disorders, status associated with disability or receipt of disability compensation | Healthy controls matched for age [24] | Age; body mass index; pain intensity; fatigue; sleep; anxiety; anger; depression; curiosity; illness burden |
| [14] | **NT** | Trail Making Test (TMT)<br>Continuous Reaction Time (CRT)<br>Finger Tapping Test (FTT)<br>Mini-Mental State Examination (MMSE)<br>Wechsler Intelligence Scale for Adults (WIS-A) | CP [49] | Chronic non-cancer pain | No | Poor general health, dementia or encephalopathy, brain trauma, liver/renal insufficiency, pregnancy, metabolic disturbances, residence, participation in other studies | No | Sex; age; cohabitation; education; work; annual income; opioid treatment; pain; anxiety; depression; hours of sleep |
| [39] | **NT** | Uchida-Kraepelin Test | FM [35] | Criteria of ACR | ✓ | Cardiovascular diseases, metabolic abnormalities, inflammatory cause of pain, neurological disorders, and severe somatic (e.g., cancer) or psychiatric diseases | Healthy controls matched for body mass, age, sex and education [29] | Medication; pain intensity; mental disorders; depression; anxiety; sleep quality; blood pressure |
| [51] | **NT** | Stroop tests<br>Trail Making Test (TMT)<br>Bourdon-Vos TestZoo Map Test | CP [34] | Persistent pain >6 months | D | Neurodegenerative disorders, severe cognitive decline (MMSE<24), stroke, major depression disorders, and alcohol or other substance abuse | Healthy controls matched for age and IQ [32] | Pain intensity; premorbid IQ; catastrophizing; depression; exclude participants (MMSE) |
| [40] | **NT** | Stroop testsControlled Oral Word Association (COWA)<br>Wechsler Intelligence Scale for Adults (WIS-A) | FM [104] | Criteria of ACR, tender points ≥11, evaluated for memory complaints | ✓ | Auditory impairment that might interfere with cognitive testing | Non-FMS medical patients with memory complaints [48] | Age and education; depression |
| [41] | **NT** | Word-Stem Completion Task | FM [18] | Criteria of ACR | ✓ | | Healthy controls [25] | |

(continued)

**Table 2** Continued

| Ref. | Type of evaluation | Instrument | Participants (chronic pain) | | | | Controls [N] | Other variables related to cognition |
|---|---|---|---|---|---|---|---|---|
| | | | Patients [N] | Inclusion criteria | Pain criteria | Exclusion criteria | | |
| | | | | | | Inflammatory causes of pain, neurological disorders, metabolic abnormalities, and severe somatic or psychiatric diseases | | Medication; pain severity; emotion disorders; co-morbid psychiatric disorders |
| [1] | **SR+NT** | Everyday Memory Failures Questionnaire (EMF)<br>California Verbal Learning Test, Second edition (CVLT-II)<br>Paced Auditory Serial Additions Test (PASAT)<br>Stroop tests<br>Wechsler Intelligence Scale for Adults (WIS-A) | CP [72] | Non-malignant pain | No | Acute pain and pain due to known organic brain dysfunction | No | Medication; depression; pain intensity |

*Note*. *Articles that have made any kind of psychometric testing to the instrument(s) used in the chronic pain population. CP = Chronic pain; FM = Fibromyalgia; CBP = Chronic back pain; CRP = Complex regional pain; RA = Rheumatoid arthritis; ACR = American College of Rheumatology; D = Duration; I = Intensity; ✓ = Diagnostic; SR = Self-report; NT = Neuropsychological testing; IQ = Intelligence quotient; VAS = Visual analogue scale.

**Table 3** Self-report instruments and versions used: Studies (n = 11) in the review that used each instrument and the measurement target in each case.

| Self-report instrument | Instrument version (Ref.) | Ref.* | What did they want to measure? (target/goal) |
|---|---|---|---|
| Sickness Impact Profile (SIP), alertness subscale | [65] | [52]<br>[5] | Cognitive complaints |
| Brief Symptom Inventory (BSI) | [66] | [47] | Cognitive impairment complaints |
| Metamemory in Adulthood (MIA) Questionnaire | [67] | [24] | Ability to self-reflect on one's own memory function |
| Cuestionario de Olvidos Cotidianos (COC) | [68) | [54] | Memory complaints |
| Prospective Memory Questionnaire (PMQ) | [69] | [27] | Prospective memory |
| Multiple Abilities Self-Report Questionnaire (MASQ) | [70] | [38] | Perceived cognitive difficulties |
| Everyday Memory Failures Questionnaire (EMF) | [71] | [28] | Perception of the degree of memory impairment |
| | [72] | [1] | Cognitive complaints |
| Metamemory Questionnaire (MMQ) | [73] | [22] | Subjective cognitive complaints |
| Memory Observation Questionnaire (MOQ) | [74] | [21] | Subjective self-perceptions of memory and concentration |

*Reference to articles included in the review.

the authors intended to measure with the instrument (target/goal).

*Self-Report Measures*

Among the articles that used SR assessment, we identified nine different instruments used for evaluation (Table 3): 1) self-perceived memory (the Everyday Memory Failures Questionnaire, the Memory Observation Questionnaire I and II, the Metamemory Questionnaire, and the Multiple Abilities Self-Report Questionnaire: n = 4); 2) memory complaints or memory beliefs (the Everyday Memory Questionnaire [EMQ], the Metamemory in Adulthood Questionnaire [MIAQ], and the Prospective Memory Questionnaire: n = 3); 3) cognitive problems or difficulties in daily life (the Sickness Impact Profile [SIP] Alertness subscale and the Brief Symptom Inventory [BSI]: n = 2). These instruments consisted of complete scales of 28 (EMQ) to 108 items (MIAQ), or subscales of instruments that assessed cognitive function as part of a multidimensional questionnaire (SIP and BSI).

*Neuropsychological Measures*

From the articles selected, we identified 44 neuropsychological instruments that were used to objectively evaluate patient performance. In Table 2 it is evident that in 35.7% of the articles, the objective was to evaluate individual cognitive elements, such as attention, memory, verbal fluency, and executive function [20,23,24,28,32,34–36,40,43,44,49,50,53].
Nevertheless, the majority of studies chose a combination of instruments to assess a variety of neuropsychological capacities or skills (Table 4).

The evaluation of memory was the capacity that appeared most often in the objectives of the studies, and was most frequently evaluated with instruments that focused on the mode of information acquisition (e.g., visual or verbal memory), including: the Kimura Recurring Recognition Figures Test, the Complex Figure Test, the Rey Auditory Verbal Learning Test, the California Verbal Learning Inventory, and the 10/36 Spatial Recall Test. Specific instruments that assess different forms of memory storage (e.g., long-term memory, immediate memory, or recognition) were also detected, such as the 12-word memorization and reproduction test, the Code Memory Test, the Randt Memory Test, the Free Recall Test, the Recognition/Known Test, and the Word-Stem Completion (Table 4). Some studies used instruments that assessed learning, storage, and information retrieval abilities as elements of the memory capacity set (Table 4).

Attention was the second most frequently evaluated capacity, using the largest number of instruments (n = 12). We identified a group of instruments used to assess sustained attention, which is usually assessed by measuring reaction time and the number of correct responses: the Symbol Digit Modalities Test, Continuous Reaction Time, the Toulouse-Pieron Test, the Bourdon-Vos Test, and the TEA (Table 4). Several studies also assessed divided or selective attention, which involves evaluating the discriminative ability of the patient while changing his or her attentional focus or discriminating irrelevant information: the Paced Auditory Serial Addition Test, the Stroop Test, the Trail Making Test, and the Numerical Interference Task (Table 4). Attentional skills combined with memory function (Auditory Consonant Trigram) and working memory (the Spatial Span Test and the Reading Span Test) were

**Table 4** Neuropsychological instruments and versions used: Studies (n = 36) in the review that used each instrument and the measurement target in each case.

| Instrument | Instrument version (Ref.) | Ref.* | What did they want to measure? (target/goal) |
|---|---|---|---|
| Numerical Interference Task (N-task & V-task) | [75] | [42] | Attention |
| | | [43] | |
| Randt Memory Test | [76] | [20] | Long term memory; acquisition and recall |
| Code Memory Test | [77] | [20] | Long term memory |
| Word Fluency Task | [78] | [20] | Semantic memory |
| Kimura Recurring Recognition Figures Test | [79] | [20] | Visual memory with free recall |
| Rey Auditory Verbal Learning Test (RAVLT) | [80] | [21] | Verbal learning |
| | | [30] | Verbal episodic memory |
| | [81] | [22] | Visual and verbal memory |
| | [82] | [34] | Learning and recall |
| California Verbal Learning Test, Second edition (CVLT-II) | [83] | [1] | Verbal learning and memory |
| Paced Auditory Serial Additions Test (PASAT) | [84] | [21] | Sustained auditory concentration sensitive to information-processing deficits |
| | [85] | [45] | Information processing and sustained attention |
| | | [55] | Working memory |
| | | [12] | |
| | [86] | [22] | Attention/working memory |
| | [87] | [25] | Sustained and divided attention, auditory information processing speed, and stimulus competition filtering skill |
| | | [30] | Working memory and speed of information processing |
| | [88] | [1] | Working memory |
| Symbol Digit Modalities Test (SDMT), written version | [89] | [21] | Attention |
| Stroop tests | [90] | [44] | Capacity to focus on relevant cues and the concomitant ability to ignore irrelevant (even conflicting) material |
| | [91] | [45] | Mental flexibility; ability to shift set and focus concentration |
| | | [22] | Executive function |
| | | [46] | Reasoning ability |
| | | [36] | Cognitive flexibility and resistance to interference |
| | | [40] | Naming speed and inhibitory control |
| | [92] | [23] | Ability to inhibit a response |
| | | [35] | Inhibitory control or selective attention |
| | [93] | [26] | Attention; effect of interference |
| | [94] | [28] | Attentional processes |
| | | [50] | Attention and executive function |
| | [95] | [31] | Executive function |
| | [96] | [1] | Psychomotor speed and attention |
| | [88] | [37] | Attention-switching ability and left frontal lobe function |
| | [97] | [51] | Inhibition |
| Complex Figure Test (CFT) | [98] | [45] | Visuospatial/constructional ability and visual memory |
| | | [46] | |

(continued)

**Table 4** Continued

| Instrument | Instrument version (Ref.) | Ref.* | What did they want to measure? (target/goal) |
|---|---|---|---|
| | [81] | [22] | Visual and verbal memory |
| | [99] | [26] | Visuoconstructive capacity |
| | [95] | [31] | |
| | [88] | [37] | Memory |
| Wisconsin Card Sorting Test (WCST) | [100] | [45] | Concept formation and shifting and maintaining set |
| | | [46] | Reasoning ability |
| | [101] | [22] | Executive function |
| | | [23] | Ability to solve problems in response to changing stimuli, to shift and maintain set, and utilize feedback |
| | [95] | [31] | Abstraction-comprehension |
| | [102] | [33] | Executive function |
| | [88] | [37] | Ability to switch and maintain a defined program using feedback |
| Trail Making Test (TMT) | [103] | [45] | Speed of visual search, attention, |
| | | [46] | mental flexibility, and motor functions |
| | [104] | [22] | Complex psychomotor speed |
| | [105] | [30] | Attention and executive function |
| | [95] | [46] | Visuomotor function |
| | [106] | [14] | Visual scanning speed, motor function, attention, and mental flexibility |
| | [107] | [51] | Mental flexibility |
| Design Fluency Test | [108] | [45] | Nonverbal fluency |
| Controlled Oral Word Association (COWA) | [109] | [45] | Remembering and following rules, and using strategies |
| | [110] | [22] | Complex psychomotor speed |
| | [105] | [30] | Verbal fluency |
| | [88] | [40] | |
| Grooved Pegboard Test | [111] | [45] | Manual dexterity and coordination |
| Continuous Reaction Time (CRT) | [112] | [55] | Attention/concentration |
| | | [12] | |
| | | [14] | Sustained attention or vigilance |
| Finger Tapping Test (FTT) | [113] | [55] | Psychomotor speed |
| | | [12] | |
| | | [14] | |
| Iowa Gambling Task (IGT) | [114] | [22] | Emotional decision-making ability |
| | | [33] | Decision-making |
| | | [36) | Executive functioning |
| Free recall | [115] | [24] | Long-term memory |
| Auditory Consonant Trigram (ACT) | [116] | [25] | Working memory encoded under |
| | | [34] | conditions of stimulus competition |
| | | [29] | Attentional functioning |
| 10/36 Spatial Recall Test (10/36 SRT) | [117] | [26] | Spatial learning and long-term memory |
| Shape recognition and line orientation tests of Benton | [118] | [26] | Visuospatial, visuoperceptive, and visuoconstructive function |
| Road Map Test | [119] | [26] | Spatial orientation |
| Test of Everyday Attention (TEA) | [120] | [48] | Attentional functioning: sustained |
| | | [29] | and selective attention |
| Reading Span Test (RST) | [121] | [48] | Verbal working memory |
| | | [29] | Attentional/working memory capacity |
| Spatial Span Test (SST) | [122] | [48] | Spatial working memory |

(continued)

**Table 4** Continued

| Instrument | Instrument version (Ref.) | Ref.* | What did they want to measure? (target/goal) |
|---|---|---|---|
| The Remember/Know (R/K) procedure | [123] | [49] | Memory |
| Test de Aprendizaje Verbal España-Complutense (TAVEC) | [124] | [28] | Verbal memory and learning ability |
| Test Toulouse-Piéron | [125] | [28] | Perceptual skills and continued attention |
| London Tower | [95] | [31] | Visuoperceptive capacity |
| Conditional Associative Learning Task (CALT) | [126] | [36] | Executive functioning |
| Digit Symbol Substitution Test | [81] | [37] | Information processing speed, visuomotor coordination, and selective attention |
| Verbal Associations Test | [88] | [37] | Verbal fluency and semantic memory |
| 12-word memorization and reproduction test | [88] | [37] | Memory: immediate and delayed reproduction |
| Number sequence repetition test | [81] | [37] | Short-term memory and attention |
| Uchida-Kraepelin Test | [127] | [39] | Mental calculation |
| Bourdon-Vos Test | [128] | [51] | Sustained attention |
| Zoo Map Test | [129] | [51] | Planning ability |
| Word-Stem Completion Task | [130] | [41] | Implicit memory |
| **Batteries of Instruments** | | | |
| Test Barcelona | [95] | [31] | Orientation, language, lecture, writing, visual recognition, memory and abstraction, attention, and executive function |
| | [131] | [30] | Attention and working memory |
| Mini-Mental State Examination (MMSE) | [60] | [12] | Cognitive impairment |
| | [132] | [15] | Mental aspects of cognitive function |
| | | [16] | |
| | [60] | [50] | General cognitive level |
| | [133] | [14] | Disease-related cognitive impairment |
| Wechsler Intelligence Scales for Adults (WIS-A) | [134] | [20] | Short term memory, verbal intelligence, visouconstructive ability, working memory |
| | | [23] | Memory, learning, concept and language development |
| | [135] | [45] | Overall intellectual functioning |
| | | [53] | Attention, working memory |
| | | [46] | Attention, concentration, constructional ability, memory, and reasoning ability |
| | | [14] | Attention/concentration, recent and working memory |
| | [136] | [26] | Attention and visuomotor processing |
| | [137] | [34] | General intelligence |
| | | [35] | Working memory |
| | | [22] | General intelligence, attention/working memory, complex psychomotor speed |
| | | [25] | Working memory, general intelligence, attention and concentration |
| | | [40] | Vocabulary knowledge |
| | [138] | [50] | Working and short-term memory |
| | [95] | [31] | Intelligence, attention, memory |
| | [137] | [36] | Expressive word knowledge, concept formation, social awareness, immediate auditory recall, visual attention |
| | [88] | [37] | Visuomotor coordination and mental flexibility |
| | [139] | [1] | General intelligence and working memory |
| Wechsler Memory Scales (WMS-R, WMS-III, WMS-IV) | [140] | [23] | Short-term memory |
| | [141] | [46] | |

(continued)

**Table 4** Continued

| Instrument | Instrument version (Ref.) | Ref.* | What did they want to measure? (target/goal) |
|---|---|---|---|
| | | | Attention and concentration, constructional ability, memory, and reasoning ability |
| | | [21] | Short-term memory (verbal, visual, immediate, delayed), attention, and concentration |
| | | [45] | Memory: namely the registration and retrieval of auditory, verbal material, and immediate and delayed reproduction of visuospatial material |
| | [142] | [25] | Memory performance free of stimulus |
| | | [34] | competition at encoding |
| | [143] | [32] | Memory |
| | [144] | [26] | Immediate and long-term visual memory |
| | | [50] | Executive function, short-term memory, and visual learning |
| | [95] | [31] | Memory |

*Reference to articles included in the review.

also commonly measured using this group of instruments (Table 4).

A number of articles used instruments that assess executive functions, defined as a group of higher-order tasks that mediate the coordination of all cognitive functions. The instrument most frequently used to assess these in chronic pain patients was the Wisconsin Card Sorting Test, which is used to evaluate abstraction, concept formation, and cognitive flexibility (Table 4). Verbal and non-verbal fluency (the Controlled Oral Word Association Test and the Design Fluency Test), emotional decision-making (the IGT), associative learning (the Conditioning Associative Learning Task), and planning (the Zoo Map) were also evaluated in these studies (Table 4).

Psychomotor performance, perception or concept formation, and reasoning were the abilities least frequently evaluated. These capacities were evaluated by assessing psychomotor speed (the Finger Tapping Test and the Grooved Pegboard Test); visuospatial, visuoperceptive, and visuoconstructive function (the Shape Recognition, Line Orientation, and Tower of London Tests); arithmetic capacity (the Uchida Kraepelin Test); and spatial orientation (the Money Road Map Test) (Table 4).

We found that 57.1% (24/42) of the studies used batteries of instruments to assess multiple neuropsychological functions, and two of the most commonly used tests were the Wechsler Adult Intelligence Scale and the Wechsler Memory Scale. These tests have been validated in patients with pathologies other than chronic pain and they use standardized scores that are normalized against the general population for specific cases of brain damage and different types of dementia (Table 4). The Barcelona Test, which was designed and validated in Spain, was used in two articles (Table 4). In this group, we also found five articles that used the MMSE to identify patients with and without cognitive impairment (Table 4), and one article [51] in which the MMSE was used to exclude cases of cognitive impairment (MMSE <24) rather than for cognitive evaluation.

## Discussion

This systematic review identified 42 articles in which cognitive function was assessed in adult patients suffering non–cancer-related chronic pain of different origins. Among the results obtained, it should be highlighted that more than half the studies specified at least one diagnostic criterion for the cause of pain, especially FM, and that neuropsychological assessment was the most frequent characteristic tested. Nevertheless, both the instruments used and the definition of chronic pain varied widely among the different studies analyzed, potentially adding a systematic bias to the measures of cognitive function. It is important that studies apply strict inclusion criteria to precisely define the sample to be assessed, such that cognitive function can be more accurately assessed and to be able to detect differences in the specific group of chronic pain patients [11,15,23].

It should also be noted that the majority of studies reviewed included a reference group whose results were compared with the results obtained for the chronic pain patients, and over 60% of studies excluded patients with known cognitive deficits. Likewise, most of the studies assessed additional variables that can negatively affect cognitive function, such as those associated with the affective sphere. However, only 54.8% of the studies included demographic variables as potential confounding factors, such as age and education-related data, despite the recognized influence of these parameters on cognitive processes [18]. Moreover, few studies evaluated the consumption of drugs that affect cognitive

function or the presence of sleep disorders, even though both these parameters can negatively affect cognitive function [3,7,53].

*Characteristics of the Instruments Used*

We observed a clear predominance of NT over SR assessments in the studies selected (85.7 vs 26.2%). This may be because the validity of the assessments based on self-reported symptoms are often questioned by clinicians, and self-perception may be biased by the individual's affective-emotional state [5,38]. Indeed, perceived cognitive function does not always correspond to performance in NT [22,28], suggesting that perceived impairment in cognition is more strongly associated with fatigue and mood than with pain itself. Nonetheless, the self-perception of memory, cognitive problems, or difficulties in daily life are important, since this is the only source of such information in daily clinical practice. Furthermore, it has been suggested that the weak correlation between perception and execution may sometimes be due to the type of questionnaire used. It should be noted that none of the SR questionnaires used in the articles reviewed were developed or validated specifically for use in patients with chronic pain. This is a failing, given that it has been shown that when SR instruments are specific to the population under study, the results obtained are better than when general questions about memory function and associated complaints are used [56]. Hence, there would appear to be a need for further research to develop SR tools that are specifically validated for patients with chronic pain and that can be used to gather more accurate information on the problems these patients experience. In the search performed here, we only found one article that used an instrument that had been adapted to populations with chronic pain [57], although this study was not included in the review because it was still in the preliminary stages of validation.

In the studies that included a neuropsychological evaluation, researchers assessed cognitive function in attention, memory, and executive function. Despite the difficulties associated with understanding cognitive deficits, due to their dependence on many different aspects [58], these measures may facilitate the study of functional cognitive domains and advance our understanding of the effects of pain [8,13]. However, like the SR instruments, none had been previously validated for use with chronic pain patients.

Among the instruments used there are advantages to some tests, such as the TMT, the IGT, and the TEA, that are highlighted, given that their flexible format enables skills to be retested without the potential confounding influence of test-retest effects [23,29,33,48]. However, test-retest effects have been reported for the TMT, even when the authors used alternate test forms [59]. Along other lines, the MMSE, a test originally developed and validated for patients with Alzheimer's disease [60], is a commonly used instrument in the clinic and in chronic pain evaluation. The items in the MMSE that measure language ability (repetition, comprehension, naming, reading, and writing) and constructional apraxia are rarely altered in patients with chronic pain. Thus, these patients often perform within the normal range of the MMSE, so this test is likely to be less discriminative in chronic pain and indeed, its use has been criticized [15].

In addition to adapting instruments to specific populations, it is important that the characteristics of a given instrument are fully understood before its application. While pain patients sometimes exert little effort in NT, this may not be due to cognitive dysfunction; rather, it may be an attempt to avoid "thinking too hard and causing pain," a concept known as cogniphobia [61,61,62]. Moreover, one may speculate that underperformance may be due to malingering [63] or little effort [22]. As noted in this review, some NT requires patients to accomplish a task as quickly or as accurately as possible, whereas others do not include performance-related instructions, with the advantage that the patient can be assessed without becoming aware of his or her achievements. It has been noted that patients referred to some parts of the PASAT as very stressful and humiliating [55]. Therefore, the two more straightforward versions of the PASAT were used in that study in order to avoid the individual experiencing a sense of frustration that might interfere with the results.

Another important aspect of the instrument used is its ecological validity (relevance to everyday tasks), focused on predicting what a patient can do in a real-world setting and less on diagnosing or localizing brain impairment. Therefore, an ecologically valid assessment measure should have characteristics similar to naturally occurring behaviour and value in predicting everyday functioning. For example, FM patients appear to be quite sensitive to distractions, although most NT takes place in a distraction-free environment that differs considerably from everyday life. Given that pain is the main distracting factor for this population [64], a distracting stimulus can be introduced during the NT to make the instrument more faithfully reflect reality. Likewise, the use of instruments with strong ecological validity, such as the TEA, has been justified [29,48]. However, pain specialists must confront the problem of the validity and reliability of these tests in patients with chronic pain. Indeed, the TEA seem to be unsuitable to evaluate chronic pain patients with cogniphobia due to the difficulty of the tasks and their demands on attentional resources. Although it is difficult to draw any conclusions concerning the utility of these tests in chronic pain patients, future studies with large sample sizes might investigate the ecological validity of tests in this specific group.

Some limitations of this review should be pointed out. First, we did not include studies that analyzed cognitive function in patients with headache, migraine, visceral pain, or cancer-related pain. Given the complexity of the different groups of pain patients and the broad extent of

the literature, we considered that it was more important to focus on a smaller group of patients and use a less complex methodology in order to achieve a more accurate analysis. Second, the information collected regarding the quality of the studies incorporated into this review was limited and centered on the subjects included, and on the instruments used in the distinct studies, rather than on the results obtained. Therefore, it did not appear to be necessary to analyze aspects that could affect the results of the cognitive evaluation. Third, we also assume that limiting the search to articles published in English or Spanish is a weakness of the study. However, most of the quality scientific literature is published in English, and as the native language of the authors is Spanish, they could adequately review papers written in this language.

Despite these limitations, a strength of this review was that it followed a rigorous method that included information based on validated instruments and addresses a complicated issue that has not previously been evaluated. It highlights the variability between the studies and the need for further research to develop and validate instruments to assess cognitive function in chronic pain patients.

## Conclusion

This review focuses on the challenge associated with the evaluation of cognitive function in patients with chronic pain. We found that the data retrieved from the literature were very heterogeneous, due to the assessment of patients in whom pain was poorly defined (except FM) and the high degree of variability in the evaluation measures used. We observed a notable lack of information pertaining to groups with specific types of pain, such as neuropathic or musculoskeletal pain, and of instruments developed and/or adapted for this specific population.

In order to improve the information obtained by evaluating cognitive function in chronic pain, and to ensure such data are homogeneous and comparable between studies, it might be necessary to implement the following recommendations:

- It is important to define the type of pain that is to be evaluated in the studies and to define the presence of pain based on well established diagnostic criteria.
- The information collected from the patients must be considered, especially those factors known to influence cognitive function, such as age, sex, and educational level, as well as factors related to the intensity, duration, and localization of the pain.
- It is also important to collect information related to comorbidities and the pharmacological treatment of these patients, which means taking into account the affective state of the patient: whether or not the patient has anxiety and depression, as well as the quality and quantity of sleep.
- A control group should be included, and the inclusion and exclusion criteria well defined for both the control group and for the subjects with pain. This serves to better define the methodology.
- Finally, instruments should be specifically designed and validated in patients with chronic pain, considering both SR and NT at the same time in order to obtain more complete information.

This review may provide clinicians and researchers with a methodological context for cognitive assessment associated with chronic pain, and could help them identify areas in which future research should focus.

## References

1 Landrø NI, Fors EA, Våpenstad LL, et al. The extent of neurocognitive dysfunction in a multidisciplinary pain centre population. Is there a relation between reported and tested neuropsychological functioning? Pain 2013;154(7):972–77.

2 Kreitler S, Niv D. Cognitive impairment in chronic pain. Pain: Clinical Updates 2007;XV(4):1–4.

3 Hart RP, Wade JB, Martelli MF. Cognitive impairment in patients with chronic pain: The significance of stress. Curr Pain Headache Rep 2003;7(2):116–26.

4 Esteve MR, Ramírez C, López-Martínez AE. Memory disorders in patients with chronic pain. Rev Soc Esp Dolor 2001;8(2):119–27.

5 McCracken LM, Iverson GL. Predicting complaints of impaired cognitive functioning in patients with chronic pain. J Pain Symptom Manage 2001;21 (5):392–96.

6 Bushnell MC, Case LK, Ceko M, et al. Effect of environment on the long-term consequences of chronic pain. Pain 2015;156(suppl 1): S42–49.

7 Simons LE, Elman I, Borsook D. Psychological processing in chronic pain: A neural systems approach. Neurosci Biobehav Rev 2014;39:61–78.

8 Kuchinad A, Schweinhardt P, Seminowicz DA, et al. Accelerated brain gray matter loss in fibromyalgia patients: Premature aging of the brain? J Neurosci 2007;27(15):4004–7.

9 Berryman C, Stanton TR, Jane Bowering K, et al. Evidence for working memory deficits in chronic pain: A systematic review and meta-analysis. Pain 2013;154(8):1181–96.

10 Lorenz J. Pain—Not just a feeling, but a working brain. Pain 2010;149(1):3–4.

11 Moriarty O, McGuire BE, Finn DP. The effect of pain on cognitive function: A review of clinical and preclinical research. Prog Neurobiol 2011;93(3):385–404.

12 Sjøgren P, Christrup LL, Petersen MA, Højsted J. Neuropsychological assessment of chronic non-malignant pain patients treated in a multidisciplinary pain centre. Eur J Pain 2005;9(4):453–62.

13 Hart RP, Martelli MF, Zasler ND. Chronic pain and neuropsychological functioning. Neuropsychol Rev 2000;10(3):131–49.

14 Kurita GP, De Mattos Pimenta CA, Braga PE, et al. Cognitive function in patients with chronic pain treated with opioids: Characteristics and associated factors. Acta Anaesthesiol Scand 2012;56(10):1257–66.

15 Povedano M, Gascón J, Gálvez R, Ruiz M, Rejas J. Cognitive function impairment in patients with neuropathic pain under standard conditions of care. J Pain Symptom Manage 2007;33(1):78–89.

16 Rodriguez-Andreu J, Ibanez-Bosch R, Portero-Vazquez A, et al. Cognitive impairment in patients with fibromyalgia syndrome as assessed by the mini-mental state examination. BMC Musculoskelet Disord 2009;10:162

17 Higgins JP, Green S. Cochrane handbook for systematic reviews of interventions. Wiley Online Library, 2008.

18 Lezak MD, Howieson DB, Bigler ED, Tranel D. Neuropsychological Assessment, 5th edition. Oxford: Oxford University Press; 2012.

19 Flavell JH, Wellman HM. Metamemory. In: RK Kail, JW Hagen, eds. Perspectives on the Development of Memory and Cognition. Hillsdale: Lawrence Erlbaum Associations; 1997:3–33.

20 Landrø NI, Stiles TC, Sletvold H. Memory functioning in patients with primary fibromyalgia and major depression and healthy controls. J Psychosom Res 1997;42(3):297–306.

21 Grace GM, Nielson WR, Hopkins M, Berg MA. Concentration and memory deficits in patients with Fibromyalgia Syndrome. J Clin Exp Neuropsychol 1999;21(4):477–87.

22 Suhr JA. Neuropsychological impairment in fibromyalgia: Relation to depression, fatigue, and pain. J Psychosom Res 2003;55(4):321–29.

23 Apkarian AV, Sosa Y, Krauss BR, et al. Chronic pain patients are impaired on an emotional decision-making task. Pain 2004;108(1):129–36.

24 Glass JM, Park DC, Minear M, Crofford LJ. Memory beliefs and function in fibromyalgia patients. J Psychosom Res 2005;58(3):263–69.

25 Leavitt F, Katz RS. Distraction as a key determinant of impaired memory in patients with fibromyalgia. J Rheumatol 2006;33(1):127–32.

26 Roldán-Tapia L, Cánovas-López R, Cimadevilla J, Valverde M. Cognition and perception deficits in fibromyalgia and rheumatoid arthritis. Reumatol Clin 2007;3(3):101–9.

27 Ling J, Campbell C, Heffernan TM, Greenough CG. Short-term prospective memory deficits in chronic back pain patients. Psychosom Med 2007;69 (2):144–48.

28 Castel A, Cascón R, Salvat M, et al. Cognitive performance and memory complaints in chronic patients: with fibromyalgia versus without fibromyalgia. Rev Soc Esp Dolor 2008;15(6):358–70.

29 Dick BD, Verrier MJ, Harker KT, Rashiq S. Disruption of cognitive function in Fibromyalgia Syndrome. Pain 2008;139(3):610–16.

30 Munguía-Izquierdo D, Legaz-Arrese A, Moliner-Urdiales D, Reverter-Masía J. Neuropsychological performance in patients with fibromyalgia syndrome: Relation to pain and anxiety. Psicothema 2008;20 (3):427–31.

31 Pericot-Nierga I, Hernández-Ferrándiz M, Lozano-Gallego M, et al. Cognitive profile in fibromyalgia. Comparison with a mild cognitive impairment group. Med Clin 2009;133(3):91–94.

32 Lourenco Jorge L, Gerard C, Revel M. Evidences of memory dysfunction and maladaptive coping in chronic low back pain and rheumatoid arthritis patients: Challenges for rehabilitation. Eur J Phys Rehabil Med 2009;45(4):469–77.

33 Verdejo-García A, López-Torrecillas F, Calandre EP, Delgado-Rodríguez A, Bechara A. Executive function and decision-making in women with fibromyalgia. Arch Clin Neuropsychol 2009;24(1):113–22.

34 Leavitt F, Katz RS. Normalizing memory recall in fibromyalgia with rehearsal: A distraction-counteracting effect. Arthritis Care Res 2009;61(6):740–44.

35 Abeare CA, Cohen JL, Axelrod BN, et al. Pain, executive functioning, and affect in patients with rheumatoid arthritis. Clin J Pain 2010;26(8):683–89.

36 Walteros C, Sánchez-Navarro JP, Muñoz MA, et al. Altered associative learning and emotional decision

making in fibromyalgia. J Psychosom Res 2011;70 (3):294–301.

37 Melkumova KA, Podchufarova EV, Yakhno NN. Characteristics of cognitive functions in patients with chronic spinal pain. Neurosci Behav Physiol 2011; 41(1):42–46.

38 Williams DA, Clauw DJ, Glass JM. Perceived cognitive dysfunction in fibromyalgia syndrome. J Musculoskelet Pain 2011;19(2):66–75.

39 Reyes Del Paso GA, Pulgar A, Duschek S, Garrido S. Cognitive impairment in fibromyalgia syndrome: The impact of cardiovascular regulation, pain, emotional disorders and medication. Eur J Pain 2012;16(3):421–29.

40 Leavitt F, Katz RS. Lexical memory deficit in fibromyalgia syndrome. J Musculoskelet Pain 2012;20 (2):82–86.

41 Duschek S, Werner NS, Winkelmann A, Wankner S. Implicit memory function in fibromyalgia syndrome. Behav Med 2013;39(1):11–16.

42 Eccleston C, Crombez G, Aldrich S, Stannard C. Attention and somatic awareness in chronic pain. Pain 1997;72(1–2):209–15.

43 Crombez G, Eccleston C, Baeyens F, Van Houdenhove B, Van Den Broeck A. Attention to chronic pain is dependent upon pain-related fear. J Psychosom Res 1999;47(5):403–10.

44 Grisart JM, Plaghki LH. Impaired selective attention in chronic pain patients. Eur J Pain 1999;3(4):325–33.

45 Iezzi T, Archibald Y, Barnett P, Klinck A, Duckworth M. Neurocognitive performance and emotional status in chronic pain patients. J Behav Med 1999;22 (3):205–16.

46 Iezzi T, Duckworth MP, Vuong LN, Archibald YM, Klinck A. Predictors of neurocognitive performance in chronic pain patients. Int J Behav Med 2004;11 (1):56–61.

47 Roth RS, Geisser ME, Theisen-Goodvich M, Dixon PJ. Cognitive complaints are associated with depression, fatigue, female sex, and pain catastrophizing in patients with chronic pain. Arch Phys Med Rehabil 2005;86(6):1147–54.

48 Dick BD, Rashiq S. Disruption of attention and working memory traces in individuals with chronic pain. Anesth Analg 2007;104(5):1223–29.

49 Grisart J, Van der Linden M, Bastin C. The contribution of recollection and familiarity to recognition memory performance in chronic pain patients. Behav Res Ther 2007;45(5):1077–84.

50 García-Nieto R, Ortega-Ladrón D, Cegama E, et al. Memory impairment in a sample of patients with chronic pain. Rev Soc Esp Dolor 2008;15(1):5–12.

51 Oosterman JM, Derksen LC, Van Wijck AJM, Kessels RPC, Veldhuijzen DS. Executive and attentional functions in chronic pain: Does performance decrease with increasing task load? Pain Res Manage 2012;17(3):159–65.

52 Iverson GL, McCracken LM. 'Postconcussive' symptoms in persons with chronic pain. Brain Inj 1997;11(11):783–90.

53 Wade JB, Hart RP. Attention and the stages of pain processing. Pain Med 2002;3(1):30–38.

54 Muñoz M, Esteve R. Reports of memory functioning by patients with chronic pain. Clin J Pain 2005;21 (4):287–91.

55 Sjøgren P, Thomsen AB, Olsen AK. Impaired neuropsychological performance in chronic nonmalignant pain patients receiving long-term oral opioid therapy. J Pain Symptom Manage 2000;19(2):100–108.

56 Hertzog C, Park DC, Morrell RW, Martin M. Ask and Ye Shall Receive: Behavioural specificity in the accuracy of subjective memory complaints. Appl Cognit Psychol 2000;14(3):257–75.

57 Schnurr RF, MacDonald MR. Memory complaints in chronic pain. Clin J Pain 1995;11(2):103–11.

58 Strauss ME. Demonstrating specific cognitive deficits: A psychometric perspective. J Abnorm Psychol 2001;110(1):6–14.

59 Fastenau PS, Hankins WT, McGinnis CM, Moy T, Richard M. Effects of alternate forms on retest effects in clinical testing. J Int Neuropsychol Soc 2002;7 (2):151–61.

60 Folstein MF, Folstein SE, McHugh PR. "Mini-mental state". A practical method for grading the cognitive state of patients for the clinician. J Psychiatr Res 1975;12(3):189–98.

61 Martelli MF. Assessment of avoidance conditioned pain related disability (ACPRD): Kinesiophobia and Cogniphobia. HeadsUp: RSS Newsletter 1999;2.

62 Suhr J, Spickard B. Pain-related fear is associated with cognitive task avoidance: Exploration of the cogniphobia construct in a recurrent headache sample. Clin Neuropsychol 2012;26(7):1128–41.

63 Etherton J, Bianchini K, Heinly M, Greve K. Pain, malingering, and performance on the WAIS-III processing speed index. J Clin Exp Neuropsychol 2006; 28(7):1218–37.

64 Glass JM. Cognitive dysfunction in fibromyalgia and chronic fatigue syndrome: New trends and future directions. Curr Rheumatol Rep 2006;8(6):425–29.

65 Bergner M, Bobbitt RA. The sickness impact profile: Development and final revision of a health status measure. Med Care 1981;19(8):787–805.

66 Derogatis LR, Spencer PM. Administration and Procedures: BSI Manual-I. Baltimore: Clinical Psychometric Research; 1982.

67 Dixon RA, Hultsch DF, Hertzog C. The Metamemory in Adulthood (MIA) Questionnaire. Psychopharmacol Bull 1988;24(4):671–88.

68 Benedet MJ, Seisdedos N. Evaluación Clínica de las Quejas de Memoria en la Vida Cotidiana. Madrid: Médica Panamericana; 1996.

69 Hannon R, Adams P, Harrington S, Fries-Dias C, Gipson MT. Effects of brain injury and age on prospective memory self-rating and performance. Rehabil Psychol 1995;40(4):289–98.

70 Seidenberg M, Haltiner A, Taylor MA, Hermann BB, Wyler A. Development and validation of a Multiple Ability Self-Report Questionnaire. J Clin Exp Neuropsychol 1994;16(1):93–104.

71 García MJ, Sánchez CJ. Adaptatión del cuestionario de fallos de memoria en la vida cotidiana (MFE). Bol Psicol 1994;43:89–107.

72 Sunderland A, Harris JE, Baddeley AD. Do laboratory tests predict everyday memory? A neuropsychological study. J Verb Learn Verb Behav 1983;22(3):341–57.

73 Zelinski EM, Gilewski MJ, Thompson LW. Do laboratory tests relate to self-assessment of memory ability in the young and old? In: LW Poon, J Fozard, LS Cermak, D Arenberg, and LW Thompson, eds. New Directions in Memory and Aging (PLE: Memory): Proceedings of the George A. Talland Memorial Conference London & New York: Psychology Press, 1980;519–44.

74 Humphrey D, McGlone J, Evans D, Gupta S. Manual for the MOQ and MOQ-2, The University of Western Ontario: London, Ontario: King's College; 1991.

75 Windes JD. Reaction time for numerical coding and naming of numerals. J Exp Psychol 1968;78(2 Part 1):318–22.

76 Randt C, Brown E. Randt Memory Test. Administration Manual. New York: Life Science Associates; 1983.

77 Levander S, Elithorn A. An automated psychological test system. The Automated Psychological Test System Trondheim. Trondheim, Norway: Department of Psychiatry and Behavioral Medicine, University of Trondheim; 1987.

78 Spreen O, Benton AL. Neurosensory Center Comprehensive Examination for Aphasia: Manual of instructions (NCCEA), Canada. Victoria, British Columbia: Neuropsychology Laboratory, University of Victoria; 1969.

79 Kimura D. Right temporal-lobe damage. Perception of unfamiliar stimuli after damage. Arch Neurol 1963;8:264–71.

80 Rey A. L'examen Clinique En Psychologie. París: Presses Universitaires de France; 1958.

81 Lezak MD. Neuropsychological Assessment. 2nd edition. New York: Oxford University Press; 1983.

82 Rey A. L'examen Clinique En Psychologie. Paris: Presses Universitaires de France; 1964.

83 Delis D, Kaplan E, Kramer JH, Ober BA. California Verbal Learning Test (CVLT-II). 2nd edition. San Antonio, TX: Psychological Corporation; 2000.

84 Gronwall DMA. Paced auditory serial addition task: A measure of recovery from concussion. Percept Mot Skills 1977;44(2):367–73.

85 Gronwall DMA, Sampson H. The Psychological Effects of Concussion. Auckland, NZ: Auckland University Press/Oxford University Press; 1974.

86 Gronwall D, Wrightson P. Memory and information processing capacity after closed head injury. J Neurol Neurosurg Psychiatry 1981;44(10):889–95.

87 Brittain JL, La Marche JA, Reeder KP, Roth DL, Boll TJ. Effects of age and IQ on paced auditory serial addition task (PASAT) performance. Clin Neuropsychol 1991;5(2):163–75.

88 Strauss E, Sherman EMS, Spreen O. A Compendium of Neuropsychological Tests. Administration, Norms and Commentary. Oxford: Oxford University Press; 2006.

89 Smith A. Manual for the Symbol Digit Modalities Test (Rev. edition.). Los Angeles, CA: Western Psychological Services; 1982.

90 Bohnen N, Jolles J, Twijnstra A. Modification of the Stroop Color Word Test improves differentiation between patients with mild head injury and matched controls. Clin Neuropsychol 1992;6 (2):178–84.

91 Golden CJ. Stroop Color and Word Test: A manual for clinical and experimental uses. Wood Dale, IL: Stoelting Co.; 1978.

92 Trenerry MR, Crosson B, DeBoe J, Leber WR. Stroop Neurological Screening Test. Odessa, FL: Psychological Assessment Resources; 1989.

93 Golden CJ. Test de Colores y Palabras (Stroop). Madrid: TEA; 1994.

94 Golden CJ. Stroop: Test de Colores y Palabras. Madrid: TEA; 2001.

95 Peña-Casanova J, Gramunt N, Gich J. Test neuropsicológicos. Fundamentos para una neuropsicología clínica basada en evidencias. Barcelona: Masson; 2004.

96 Delis D, Kaplan E, Kramer J. Delis-Kaplan executive functions scale. San Antonio, TX: Psychological Corporation; 2001.

97 Mead LA, Mayer AR, Bobholz JA, et al. Neural basis of the Stroop interference task: Response competition or selective attention? J Int Neuropsychol Soc 2002;8(6):735–42.

98 Osterrieth PA. Le test de copie d'une figure complexe. Arch Psychol 1944;30:206–356.

99 Rey A. Test de Copia y Reproducción de Memoria de Figuras Geométricas Complejas. Madrid: TEA; 1997.

100 Heaton RK. Wisconsin Card Sorting Test Manual. Odessa, FL: Psychological Assessment Resources; 1981.

101 Heaton RK, Chelune GJ, Talley JL, Kay GG, Curtis G. Wisconsin Card Sorting Test (WCST) Manual Revised and Expanded. Odessa, FL: Psychological Assessment Resources; 1993.

102 Grant DA, Berg EA. Wisconsin Card Sorting Test. Los Angeles, CA: Western Psychological Services; 1993.

103 Spreen O, Benton AL. Comparative Studies of Some Psychological Tests for Cerebral Damage. J Nerv Ment Dis 1965;140:323–33.

104 Reitan RM. Trail making test results for normal and brain-damaged children. Percept Mot Skills 1971; 33(2):575–81.

105 Reitan RM, Wolfson D. The Halstead-Reitan neuropsychological test battery: Theory and interpretation. Tucson: Neuropsychology Press; 1985.

106 Reitan RM. Validity of the Trail Making Test as an indicator of organic brain damage. Percept Mot Skills 1958;8:271–76.

107 Bowie CR, Harvey PD. Administration and interpretation of the Trail Making Test. Nat Protoc 2006;1 (5):2277–81.

108 Jones Gotman M, Milner B. Design fluency: The invention of nonsense drawings after focal cortical lesions. Neuropsychologia 1977;15(4–5):653–74.

109 Benton AL, Hamsher K. Multilingual Aphasia Examination: Manual of Instruction. Iowa City, IA: AJA Associates; 1978.

110 Benton AL, Hamsher K. Multilingual Aphasia Examination. Iowa City (IA): AJA Associates; 1994.

111 Matthews CG, Klove H. Instruction Manual for the Adult Neuropsychology Test Battery. Madison, WI: University of Wisconsin Medical School; 1964.

112 Elsass P. Continuous reaction times in cerebral dysfunction. Acta Neurol Scand 1986;73(3):225–46.

113 Peters M. Prolonged practice of a simple motor task by preferred and nonpreferred hands. Percept Mot Skills 1976;42(43):447–50.

114 Bechara A, Damasio AR, Damasio H, Anderson SW. Insensitivity to future consequences following damage to human prefrontal cortex. Cognition 1994;50(1–3):7–15.

115 Park DC, Lautenschlager G, Smith AD, et al. Mediators of long-term memory performance across the life span. Psychol Aging 1996;11 (4):621–37.

116 Stuss D, Stethem L, Pelchat G. Three tests of attention and rapid information processing: An extension. Clin Neuropsychol 1988;2(3):246–50.

117 Achiron A, Polliack M, Rao SM, et al. Cognitive patterns and progression in multiple sclerosis: Construction and validation of percentile curves. J Neurol Neurosurg Psychiatr 2005;76(5):744–49.

118 Benton AL, Sivan AB, Hamsher KD, Varney NR, Otfried S. Contributions to Neuropsychological Assessment, 2nd edition. New York: Oxford University Press; 1994.

119 Lezak MD. Neuropsychological Assessment, 3rd edition. New York: Oxford University Press; 1995.

120 Robertson IH, Ward T, Ridgeway V, Nimmo-Smith I. The Test of Everyday Attention. Suffolk: Thames Valley Test Company; 1994.

121 Daneman M, Carpenter PA. Individual differences in working memory and reading. J Verb Learn Verb Behav 1980;19(4):450–66.

122 Shah P, Miyake A. The separability of working memory resources for spatial thinking and language processing: An individual differences approach. J Exp Psychol: Gen 1996; 125(1):4–27.

123 Tulving E. Memory and consciousness. Can Psychol 1985;26:1–12.

124 Benedet MJ, Alejandre MA. Test de AprendizajeVerbal España-Complutense. Madrid: TEA; 1998.

125 Toulouse E, Piéron H. T-P, Prueba Perceptiva y de Atención. Madrid: TEA; 1998.

126 Blay N, Barcelo F, Montoya P, Yagüez L. Age-related differences in executive control: Introducing the Canavan Conditional Associative Learning Task (C-CALT). In: I Reinvang, MW Greenlee, M Herrmann, eds. The Cognitive Neuroscience of Individual Differences. Oldenburg: bis-Publishers; 2003:267–78.

127 Uchida Y. A Manual of the Uchida-Kraepelin Psychodiagnostic Test. Tokyo: Psychotechnological Institute; 1951.

128 Vos PG. Bourdon Vos Test Handleiding (Bourdon Vos Test Manual). Lisse: Swets & Zeitlinger BV; 1998.

129 Wilson BA, Alderman N, Burgess PW, Emslie H, Evans JJ. Behavioural Assessment of the Dysexecutive Syndrome. Bury St Edmunds: Thames Valley Test Company; 1996.

130 Werner NS, Peres I, Duschek S, Schandry R. Implicit memory for emotional words is modulated by cardiac perception. Biol Psychol 2010;85 (3):370–76.

131 Peña-Casanova J, Guardia J, Bertran-Serra I, Manero RM, Jarne A. Shortened version of the Barcelona test (I): Subtests and normal profiles. Neurologia 1997;12(3):99–111.

132 Blesa R, Pujol M, Aguilar M, et al. Clinical validity of the 'mini-mental state' for Spanish speaking communities. Neuropsychologia 2001;39(11): 1150–57.

133 Kørner EA, Lauritzen L, Nilsson FM, et al. Mini mental state examination—Validation of new Danish version. Ugeskr Laeg 2008;170(9):745–49.

134 Wechsler D. WAIS Manual. The Wechsler Adult Intelligence Scale. New York: The Psychological Corporation; 1955.

135 Wechsler D. Wechsler Adult Intelligence Scale. Revised manual. New York: Psychological Corporation; 1981.

136 Wechsler D. Escala de Inteligencia de Wechsler para Adultos. Madrid: TEA; 1993.

137 Wechsler D. Wechsler Adult Intelligence Scale III. San Antonio, TX: Psychological Corporation; 1997.

138 Wechsler D. Escala de Inteligencia de Wechsler para Adultos. Madrid: TEA; 1999.

139 Wechsler D. Wechsler Adult Intelligence Scale, 3rd edition [manual, Norwegian version]. New York: The Psychological Corporation; 2003.

140 Wechsler D. A standardized memory scale for clinical use. J Psychol 1945;19:87–95.

141 Wechsler D. Wechsler Memory Scale. Revised Manual. San Antonio, TX: The Psychological Corporation; 1987.

142 Wechsler D. Wechsler Memory Scale III. Administration and Scoring Manual. San Antonio, TX: The Psychological Corporation; 1997.

143 Wechsler D. Echelle Clinique de Mémoire de Wechsler MEM III (WMS-III). Paris: Editions du Centre de Psychologie appliquée; 2001.

144 Wechsler D. Escala de Memoria de Wechsler-III (WMS-III). Madrid: TEA; 2004.