

Neurocognition in schizophrenia: A study of the productivity and visibility of Spanish authors

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This paper provides a map of the scientific productivity of authors affiliated to a Spanish institution and who have addressed one of the most important current topics in schizophrenia: The study of cognitive performance. A search of the Web of Science yielded 125 articles that met the inclusion criteria. In order to provide a comprehensive overview of scientific productivity, we examine several bibliometric indicators, concerning both productivity and impact or visibility. The analysis also focuses on qualitative aspects of key theoretical importance, such as the kinds of cognitive functions that are most often assessed and the tests most widely used to evaluate them in clinical practice. The study shows that interest in the subject of cognitive function in schizophrenia has increased considerably in Spain since the beginning of this century. The results also highlight the need to standardize the type of tests to be used in the cognitive assessment of patients with schizophrenia.

Neurocognición en la esquizofrenia: estudio de la productividad y visibilidad de los autores españoles. Este trabajo se centra en ofrecer un mapa de la productividad científica de los autores adscritos a una institución española que se han interesado por uno de los tópicos actuales más relevantes en la esquizofrenia: el estudio del rendimiento cognoscitivo. Se localizaron los estudios en la Web of Science y cumplieron criterios de inclusión 125 artículos. Con la finalidad de ofrecer una visión completa de la productividad científica se analizan diversos indicadores bibliométricos, tanto de productividad como de impacto o visibilidad. Además, se analizaron aspectos cualitativos de gran relevancia teórica actual, como son el tipo de funciones cognoscitivas que más se evalúan, así como los test más utilizados en el campo de la clínica para evaluarlas. Este estudio evidencia que el interés en España por el tema de la función cognitiva en la esquizofrenia ha aumentado considerablemente con la entrada al siglo XXI, teniendo expertos en nuestras instituciones con impacto elevado a nivel internacional. También se constata la necesidad de estandarizar y normalizar el tipo de pruebas que se deben utilizar en la evaluación cognoscitiva de los pacientes con esquizofrenia.

It is now recognized that psychotic disorders are complex brain diseases or syndromes with a genetic component in their aetiopathogenesis. However, despite being considered, to all intents and purposes, as brain diseases, symptoms in the form of cognitive deficits are not included in current definitions or diagnostic classifications. Indeed, in line with classical psychopathology the definition of psychosis is mainly based on the identification of psychotic or affective symptoms.

Although the cognitive deficits associated with schizophrenia were first described by Kraepelin, interest in the neuropsychological examination of psychiatric patients did not really develop until the 1950s and the 1970s. The initial findings showed that the cognitive alterations of patients diagnosed with chronic schizophrenia were similar to those observed in patients with organic brain disorders

(Heaton, Baade, & Johnson, 1978), although Kolb and Wishaw (1983) subsequently identified distinct profiles and types of deficits between these two groups. At all events, these cognitive deficits were initially considered to be an epiphenomenon that was secondary to the positive symptoms presented by patients. However, in the mid-1990s, Green (1996) related these deficits to measures of patients' everyday psychosocial functioning, highlighting that these neurocognitive aspects showed a stronger correlation than did the positive or negative symptoms. This review led to renewed interest in the cognitive deficits associated with psychosis, to the extent that it is now one of the most important areas of research in the field of schizophrenia, not to mention the increasing weight it is being given in the context of bipolar affective disorders.

A large number of studies have described different types of neuropsychological deficits in patients with psychosis, and they may appear to different degrees (see Table 1). This has led to debate as regards their heterogeneity and specificity, which directly affects the types of cognitive tests that should be used and how these are interpreted. This heterogeneity derives not only from the different patterns of deficits among patients, but also has to do with the

fact that the disorders in question affect the life cycle of sufferers, which means that the cognitive performance of patients is different in the initial stages compared to later, more chronic ones (Saykin, Shtasel, Gur, Kester, Mozley, & Stafinaiak, 1994).

As a result of the above, numerous studies have sought to relate the deficits presented by patients with the findings from other areas of neuroscientific research, such as neuropathology (Arnold, 2000), structural neuroimaging (Kindermann, Karimi, Symonds, Brown, & Jeste, 1997; Wexler, Zhu, Bell, Nicholls, Fulbright, Gore et al., 2009), cognitive psychology (Rubio Gómez, Hernández Bellido, Ruiz Beguilla, Ferrín Erdozaín, Pereda Baños, & Gómez Millán, 2010), functional neuroimaging (Goldman-Rakic & Selemon, 1997), personality studies (Fonseca-Pedrero, Paño, Lemos-Giráldez, García-Cueto, Campillo-Álvarez, Villazón-García et al., 2008; Jiménez, Muela, García, & Garrancho, 2004), neurophysiology (Kasai, Iwanami, Yamasue, Kuroki, Nakagome, & Fukuda, 2002) and even endophenotypes and genetics (Burdick, Goldberg, Funke, Bates, Lencz, Kucherlapati et al., 2007; Tabarés-Seisdedos, Mata, Escámez, Vieta, López-Ilundain, Salazar et al., 2008; Moreno Samaniego, Valero Oyarzábal, Gaviria Gómez, Hernández Fernández, Gutiérrez-Zotes, & Labad Alquézar, 2011). This has led to cognitive deficits being commonly assumed to be the expression of brain malfunctioning. More specifically, this new knowledge is producing a paradigm shift in our understanding of these types of disease and the therapeutic approach they require. Thus, the view of classical psychopathology, with its diagnosis centred on the positive and negative symptoms and which postulated a psychological or traumatic aetiology, is giving way to a more functionalist perspective in which cognitive deficits play a mediating role alongside the positive and negative symptoms. In this new perspective, aetiopathogenesis is based on neuroscience, and these diseases are beginning to be grouped together as functional psychoses, including bipolar disorders, schizophrenia and schizoaffective disorder (Jakobsen, Hansen, & Werge, 2007).

In sum, numerous studies conducted in recent decades have led to cognitive assessment being increasingly incorporated into the clinical practice of psychiatrists, and some authors have even proposed that it become one of the diagnostic criteria on which DSM-V is based (Barch & Keefe, 2010; Keefe & Fenton, 2007; Lewis, 2004). It is clear, therefore, that considerable efforts have been made within the psychiatric context to study cognitive function, and it is now an emerging field in which the number of international scientific publications has increased notably over the last decade. The present study focuses on the contributions made by Spanish institutions to this international context, providing a map of the scientific productivity of those Spanish authors who have sought to study cognitive performance in schizophrenia.

Methods

Identification of documents

Documents were located through the Web of Science (SCI-EXPANDED, SSCI and A&HCI) using the following search strategy: schizophren* and (cognit* or neuropsychol* or "neurobehavioral manifestati*"). The limits of the search were defined according to: a) the year of publication, selecting those studies published up until 2010, inclusive; b) the type of document, including only those articles published in scientific journals; and c) the country corresponding to the institutions to which the authors were affiliated, which in line with the study objective was limited to Spain.

This search strategy yielded a total of 348 documents.

Inclusion criteria

In line with the aim of the study we selected those scientific articles whose authors were affiliated to a Spanish institution and which addressed the topic of cognitive function in adult patients with schizophrenia-spectrum disorders (schizophrenia, schizoaffective disorder and schizophreniform disorder). Analysis of the abstracts of the 348 articles revealed that 140 were studies about cognitive function in schizophrenia. After eliminating 13 narrative or systematic reviews and two studies that focused exclusively on children and adolescents we were left with 125 articles that met the inclusion criteria, and which therefore formed the sample for the bibliometric study.

Data coding

In addition to the indicators offered directly by the Web of Science (WoS) and which were of interest here (year of publication, author names, institution and country of origin of the authors, journal, impact factor in the Journal Citation Reports 2008, language of publication, and category of the journal in 2008), the following variables were also coded:

1. Type of study. This referred to the nature of the study, i.e. if its purpose was solely the cognitive assessment of patients or whether it also included other aspects such as the recording of brain activity during performance of a given cognitive task, the study of genetic factors, or an interest in the psychometric properties of a neuropsychological instrument. We also noted whether any treatment intervention was applied, and, if so, this was coded. Studies were also classified as *cross-sectional*, if the assessment was performed at a single point in time, or *longitudinal*, if there were at least two test administration points. In the latter case the number of months that elapsed between the first and final assessment was specified. Finally, we took into account whether patients were recruited from one or more than one centre (single vs. multicentre study). When this was not made explicit in the article we assumed that patients were assessed in the same centre if all the authors came from that institution, whereas this aspect was coded as *not specified* if the authors were affiliated to various institutions.
2. Patients with schizophrenia-spectrum disorders. We coded the criterion used in the clinical diagnosis of patients with

Table 1

Types and degrees of neurocognitive deficit (adapted from Harvey & Sharma, 2002)

Mild	Moderate	Severe
Perceptual skills	Distractibility	Verbal learning
Recognition memory	Recall memory	Executive functions
Verbal naming	Visuo-spatial skills	Attention/Vigilance
	Working memory	Motor speed
		Verbal fluency

a schizophrenia-spectrum disorder. For these patients we specified the number of participants included in the study and the age range (either the range observed in the study sample or that specified in the study's inclusion criteria).

3. Assessment of cognitive function. Here we considered the neuropsychological tests used to assess patients, as well as the cognitive domains explored in each study.

Data control

The data provided by the WoS were obtained directly through automatic retrieval. A common problem with this approach, especially as regards Spanish scientific output, is that the same author or institution can often appear in a different form, whether for language reasons (for example, University of Valencia or Universidad de Valencia, which appear in the Web of Science as Univ of Valencia and Univ Valencia, respectively) or due to differences in the way a given author or reference is cited (for example, Cuesta MJ, Cuesta Zorita MJ or Zorita CMJ). Therefore, it is very important, when conducting a bibliometric study, to ensure that different authors are correctly identified and, in general, to sift all the data so that their productivity can be properly assessed.

Given the above, all the variables considered in this study were revised in order to standardize the format used for author names. Various errors of this kind were subsequently found, and typographical errors in the names of two authors were also corrected (Bernardo M was changed to Bernardo M, and Berrios GE to Berrios GE). We also corrected the language of publication of the study by Cuesta, Pelegrin, Peralta, Juan, Villaverde, and Fernández (1993), which was listed as being in French when in fact it was written in Spanish.

Bibliometric indicators

In order to provide a comprehensive overview of the scientific productivity of Spanish authors we ensured that the assignment of countries and journal categories was complete, i.e. each article was assigned to each of the participating countries and to the various categories that characterized the publication. It must therefore be taken into account that some articles are duplicated in the participation list, such that the sum may be greater than the total number of articles.

We then analysed various bibliometric indicators concerning both productivity and impact or visibility, thereby enabling a macro-analysis of the productivity of Spanish authors in the field of schizophrenia and cognition.

Results

As regards the temporal evolution of scientific productivity among Spanish authors the first study retrieved was published towards the end of the 1980s (Obiols, Marcos, & Salamero, 1987). Its subject matter was the relationship between cognitive function and the size of brain ventricles in two groups: patients with schizophrenia and controls. Following this publication, the contribution made by authors affiliated to a Spanish institution has risen progressively, especially since the turn of the century (see Figure 1).

The year with the highest productivity was 2007, with the publication of twenty articles about cognitive function and

schizophrenia. This was followed by the years 2009, 2008 and 2010, with 18, 17 and 16 papers, respectively.

In order to explain the evolution of productivity we performed a linear and an exponential regression for the trend in publication (see Figure 2), comparing the fit between the two models. Both showed a good fit, although the exponential model was better ($R^2=0.85$ vs $R^2=0.67$).

In terms of the names of contributors the analysis revealed a total of 361 authors. The mean number of authors per article was 6.76 (range 2-20). Table 2 shows the number of authors with respect to the different numbers of published articles.

It can be seen that 204 (56.51%) authors contributed to just one paper, whereas 16 (4.43%) made an intensive contribution to the study of cognition in patients with schizophrenia. This latter group, who are noteworthy for their high productivity (ten or more publications), comprised the following authors: Balanzá-Martínez V, Bernardo M, Crespo-Facorro B, Cuesta MJ, González-Blanch C, Martínez-Arán A, Penadés R, Peralta V, Pérez-Iglesias R, Rodríguez-Sánchez JM, Salamero M, Salazar-Fraile J, Selva-Vera

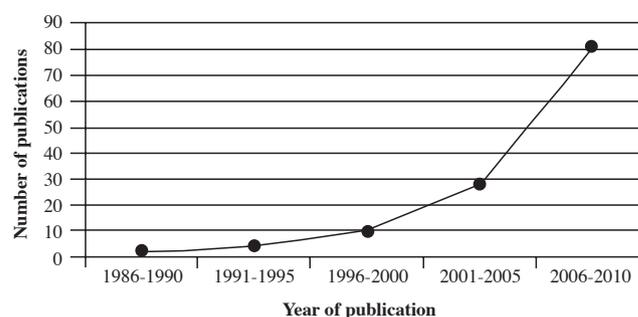


Figure 1. Temporal evolution of the number of publications

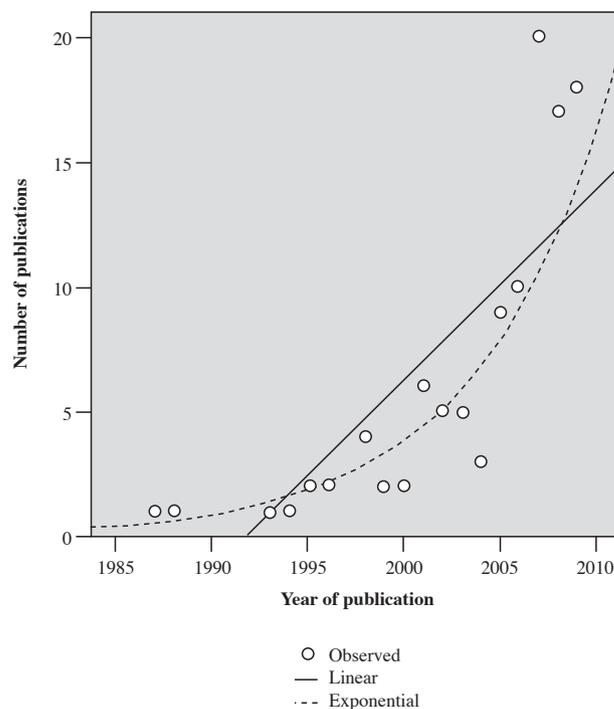


Figure 2. Linear and exponential regressions for the temporal evolution of productivity

G, Tabarés-Seidedos R, Vázquez-Barquero JL, and Vieta E (see Table 3).

As regards collaboration between countries, 93 of the retrieved articles were authored solely by researchers affiliated to a Spanish institution, whereas the remaining 32 (25.60%) involved international collaboration. The latter featured a total of 19 countries, with key contributions from the UK, the USA and the Netherlands (involvement in fifteen, seven and five articles, respectively). Relating the number of authors to the number of countries yielded a correlation coefficient of 0.45, which indicates a moderate relationship between the two variables (the trend being the greater the number of authors, the greater the number of countries involved).

The articles were published in three different languages, namely English (89.60%), Spanish (9.60%) and French (0.80%),

Number of authors	Number of articles	Percentage of authors
204	1	56,51
91	2	25,21
25	3	6,93
9	4	2,49
5	5	1,39
2	6	0,55
3	7	0,83
5	8	1,39
1	9	0,28
16	≥10	4,43

Author	Number of articles
Crespo-Facorro, B.	22
Rodríguez-Sánchez, J.M.	19
Vázquez-Barquero, J.L.	18
Cuesta, M.J.	17
Pérez-Iglesias, R.	16
Tabarés-Seisedos, R.	16
Bernardo, M.	15
González-Blanch, C.	15
Peralta, V.	15
Martínez-Arán, A.	13
Salamero, M.	13
Vieta, E.	12
Balanzá-Martínez, V.	11
Penadés, R.	11
Salazar-Fraile, J.	11
Selva-Vera, G.	11

in 46 different journals, although the journal most widely chosen by Spanish authors was *Schizophrenia Research*, which featured twenty-three (18.40%) of the articles retrieved. As regards WoS subject areas the articles corresponded to a total of twelve areas, the most noteworthy being *Psychiatry* (74.40%), *Neurosciences* (20.80%) and *Clinical Neurology* (12.80%); the remaining eight areas contributed to fewer than ten articles. Finally, the mean impact factor for the featured journals was 3.58 (range 0.446-10.545). Although the impact factor refers to the journal rather than a specific article, this figure suggests that the articles retrieved have a notable repercussion, since they should receive a mean of three citations during the two years following their publication.

In addition to assessing patients' performance by means of neuropsychological tests, 26 of the articles also described the study of brain activity (20.80%), eight studied genetic factors associated with cognition (76.40%), and three explored the psychometric properties of the tests used (2.40%).

Most of the articles (95; 76.00%) presented data referring to a single test administration, while the remaining 30 assessed patients at two or more time points. In the latter case the mean number of months that elapsed between the baseline and final assessments was 10.43, with almost all these articles stating that this type of design was used with the aim of testing the effectiveness of treatment. Among possible treatments the most widely studied was some kind of antipsychotic drug (50.00%), followed by cognitive rehabilitation (26.92%) and electroconvulsive therapy (15.38%).

In most of the studies (76.80%) patients were recruited in a single centre, although it should be noted that eleven articles did not specify this aspect.

The mean number of participants with a diagnosis of a schizophrenia-spectrum disorder was 62 subjects per article (range 2-498 patients). Given that in elderly subjects the cognitive deterioration associated with the disorder can be confounded by the patient's age, it is important to exclude those over 65 years of age from any study. When analysing this aspect it was surprising to discover that almost half the articles retrieved (45.60%) failed to specify the age range of subjects, whether in the inclusion criteria or in the description of the sample. However, in those which did specify it, the majority of them included patients younger than 65 years (79.41%), a further twelve articles (17.65%) studied patients up to 65 years of age, and only two papers (2.94%) presented the results derived from older subjects.

As regards the diagnosis of schizophrenia, 109 of the articles (87.20%) used the criteria of the *Diagnostic and Statistical Manual*, six studies (4.80%) applied the criteria of the *International Classification of Diseases-10*, two papers used both sets of diagnostic criteria, two used the *Research Diagnostic Criteria*, and the remaining six failed to specify this information. It should be noted that, at present, none of these classification systems includes cognitive deficit as a diagnostic criterion for schizophrenia. Figure 3 shows the temporal evolution of the criteria used in diagnosing patients.

The studies retrieved explored a total of fourteen cognitive domains (agnosias, verbal learning/memory, visual learning/memory, procedural learning, attention/vigilance, social cognition, global general intelligence, language/verbal comprehension, working memory, perception, praxis, psychomotor behaviour, reasoning/problem solving, and information processing speed), although those which were studied in more than fifty articles were attention/vigilance (75.20%), information processing speed

(68.00%), verbal learning/memory (61.60%), reasoning/problem solving (56.00%) and working memory (47.20%).

In order to assess these and the other cognitive domains the different articles used over 100 neuropsychological tests, the most common being subtests of the Wechsler Adult Intelligence Scale (WAIS; Wechsler, 1999) and the Wechsler Memory Scale (WMS; Wechsler, 2004), two batteries that are widely used in the neuropsychological exploration of psychiatric patients. However, the most widely used tests for the assessment of specific domains were as follows: for attention/vigilance, the Trail Making Test-Part B (TMT-B; Army Individual Test Battery, 1944); for information processing speed, the Trail Making Test-Part A; for verbal learning/memory, the Rey Auditory Verbal Learning Test (RAVLT; Rey, 1964); for reasoning/problem solving, the Wisconsin Card Sorting Test (WCST; Heaton, Chelune, Talley, Kay, & Curtiss, 1993); and for working memory, the Digits subtest of the WAIS-III (Wechsler, 1999).

Conclusions

This study has presented an extensive bibliometric analysis of the scientific activity of Spanish authors in an area of growing interest, namely cognitive function in schizophrenia. One of the first points to be made is that interest in the study of cognitive function has been slow to develop in Spain. Whereas the first international studies in this field were conducted in the 1950s, it was not until the 1980s that Spanish authors began to publish on this topic, with the number of articles increasing considerably after the turn of the century, especially since 2005. This finding is consistent with Price's law, which states that the growth of scientific literature is exponential rather than linear (Price, 1963). In practice, this means that as the research line of an investigator

or team becomes consolidated, the relevance and dissemination of their published studies increases and new researchers join the team; in turn, the research becomes more specialized and intensified, more financial resources are acquired, and greater international prestige is achieved. This pattern seems to be reflected among the Spanish research groups in the present analysis, suggesting that they are becoming more structured and increasingly able to obtain the resources needed to conduct progressively more studies in this field of knowledge.

As regards the productivity of Spanish authors the results identify 16 professionals with a notable output in this subject area, and they can consequently be considered as experts or specialists in this area.

With respect to the visibility of the published studies it should be noted that the journal most often chosen by Spanish authors is *Schizophrenia Research*, a journal of reference in the field of psychiatry and one which is indexed in a large number of databases, it being ranked within the first quartile for this knowledge area in the year 2008. Also noteworthy is the fact that most of the studies published by Spanish authors were in English, thereby implying high visibility; furthermore, 25.60% of the articles were conducted in conjunction with international authors and institutions.

In terms of the focus of the studies, the majority (76.00%) were dedicated to describing the cognitive function of patients at a single point in time. The remainders were longitudinal and explored the change in neuropsychological performance after administration of a psychotropic drug, after participation in a cognitive rehabilitation programme, or after a course of electroconvulsive therapy.

In most of the studies (76.80%) patients were recruited in a single centre (eleven did not specify this aspect), with the overall mean number of participants being 62 (range 2-498). Given the difficulty of recruiting clinical samples this is a considerable

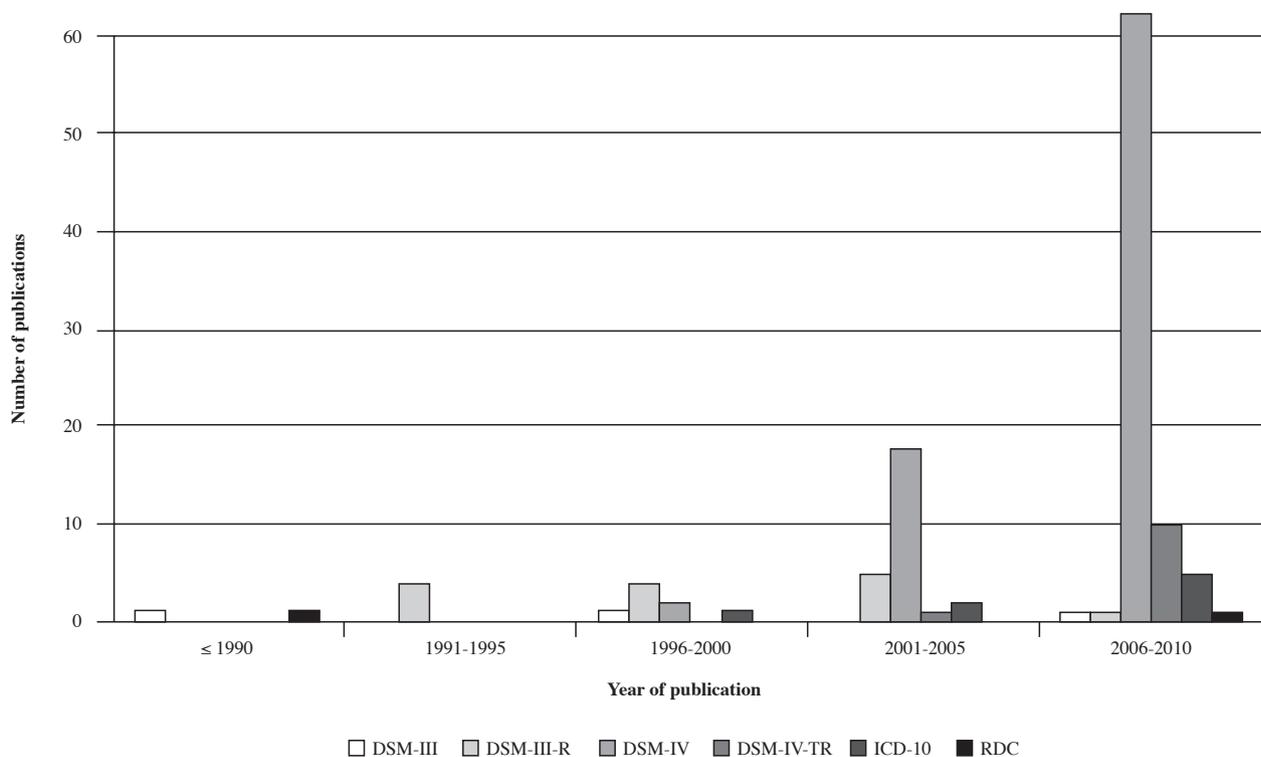


Figure 3. Temporal evolution of the diagnostic systems used

inclusion rate. However, it should also be noted that a large number of studies did not include age as an inclusion criterion. Although the mean age of subjects in the studies analysed does fall within accepted parameters it is nonetheless necessary in research of this kind or to exclude patients over the age of 65 or to control the effects of its inclusion. Strictly speaking, no patient over the age of 55 should be included, the purpose of this being to avoid potential performance bias due to the inclusion of subjects with early-onset dementia. It is important to take this aspect into account, since the ageing process is accompanied by a series of cortical changes that lead to decreased cerebral volume (Brans, Kahn, Schnack, van Baal, Posthuma, van Haren et al., 2010; van Haren, Hulshoff Pol, Schnack, Cahn, Brans, Carati et al., 2008), which in turn is associated with poorer cognitive performance in the general population (Hohmann, Beason-Held, Lamar, & Resnick, 2010; Schofield, Marder, Dooneief, Jacobs, Sano, & Stern, 1997).

In recent years this area of knowledge has witnessed a theoretical debate about the type of cognitive functions that should be assessed and which are altered in this group of patients, this being the result of the considerable heterogeneity of functions that have been reported to show a deficit. The analysis here revealed that 14 cognitive domains were assessed, corresponding to almost all of those which have been described from a theoretical point of view (Lezak, 2004). The most notable domains were attention, working memory, executive functions, verbal memory and information processing speed.

Another important aspect has to do with the lack of consensus regarding which tests should be used to assess the different cognitive

domains. In a little over twenty years of research in this area, more than 100 neuropsychological tests have been applied for this purpose. Recently, the MATRICS (Measurement and Treatment Research to Improve Cognition in Schizophrenia) initiative of the National Institute of Mental Health (Green & Nuechterlein, 2004; Kern, Green, Nuechterlin, & Deng, 2004) has sought to unify and standardize the type of deficits that should be measured and their corresponding tests, the ultimate aim being to develop new and effective treatments for the neurocognitive deficits presented by these patients. However, this project is still under development and a clear consensus has yet to be reached.

Finally, it should be noted that the overall scientific output of authors affiliated to Spanish institutions is actually much greater than that described here, since their work is usually disseminated through a wide variety of channels and is not restricted to journals indexed in the Web of Science. Nevertheless, the present study offers a comprehensive overview of the scientific productivity of these authors, as well as of the international visibility of their publications.

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