## **RESEARCH ARTICLE**



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# Cognitive deficits in schizophrenia: an updated metanalysis of the scientific evidence

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### Abstract

Background: This is an update of a previous meta-analysis published in 2005.

**Methods:** It includes the data published up to march 2010 for a total of 247 papers and 18,300 cases. Cognitive deficits are examined in 5 different domains: Memory functioning (128 studies), Global cognitive functioning (131 studies), Language (70 studies), Executive function (67 studies), Attention (76 studies). Only controlled studies were included: patients vs. normal subjects.

**Results:** Results evidence that in all domains and in all different analyses performed within each domain, patients show a significant reduction of cognitive efficiency with respect to normal subjects. The between studies heterogeneity is very high in almost all domains. There are various sources of this heterogeneity (age, sex, sample size, type of patients, and type of measurement) which contribute to the high degree of not-overlapping information offered by the single studies.

**Conclusions:** Our results, based on the current scientific evidence, confirm the previous findings that there is a generalized impairment of various cognitive functions in patients with schizophrenia when compared to normal cases. The modalities with which these results are obtained have not changed over the years and the more recent studies do not modify the high heterogeneity previously found between the studies. This reduces the methodological quality of the results. In order to improve the methodological quality of the studies performed in the field of cognitive deficits of patients with schizophrenia, various factors should be taken into account and better managed in designing future studies.

Keywords: Schizophrenia, Cognitive deficits, Memory, Attention, Executive function, Language, IQ, Meta-analysis

#### Background

There is a vast scientific evidence, accumulated in several years of research, that the cognitive functioning of patients with schizophrenia is characterized by deficits [1]. An early hypothesis was that these cognitive deficits might have a progression over time and depend on the length of disease [2].

More recent evidence indicates that the severity of cognitive deficits of patients with schizophrenia is related to age of onset (deficits of patients with early onset are more severe than those of patients with a late onset) while, the subsequent length of disease does not add further deterioration to the deficits already present at the early stages [3,4].

Many other studies have made a link between the functional disability of these patients and their cognitive impairment [5] but, at the same time, they have put in evidence the heterogeneous distribution of cognitive deterioration in this population of patients [6].

As a whole, the scientific production concerning the cognitive problems linked to schizophrenia is very large and prolonged across many decades. Our search, performed 5 years ago on this topic, found 1,275 papers published up to that time on schizophrenia and cognitive deficits [7] and even more papers were published in the following 5 years.

There are many problematic hypotheses and uncertainties about the meaning and the origins of the cognitive problems associated with schizophrenia, and these are still waiting for an answer despite the high and still growing trend of the scientific production in this area. It



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is unclear if there are specific cognitive problems due to schizophrenia or if they may be linked to intervening and concomitant factors during the chronic development of the disease. These factors could be age, differences between clinical forms, concomitant treatments, or severity and length of disease [4].

A common conclusion offered by the different studies concerning the various aspects of schizophrenia and cognitive deficits, is the presence of high heterogeneity of results. Partially, this heterogeneity is due to methodological problems such as the relative small number of cases of most of the studies, the often unclear characterization of patients and their clinical history, and the systematic unbalance between the number of patients and that of the control groups [7].

Another component of heterogeneity is due to the clinical diversity of patients included in the different studies where groups are composed of inpatients in some instances and of outpatients in other instances, while the majority of studies present results obtained from an unspecified mixture of both types of patients. In some other studies groups of patients with different length of disease or with different types of therapies are indiscriminately put together.

The third component of heterogeneity is the statistical heterogeneity which includes the chance component of variance plus the other components due to possible specific sources. This part of heterogeneity should be the one which with appropriate procedures could be explored, but this possibility will be real only after the offsetting of the obscuring interference of the methodological and clinical heterogeneity.

The previous meta-analysis that we performed in 2005 was based on distinct cognitive areas of which deficits were analyzed in separate tables: memory deficits, IQ deterioration, language deficits, executive functioning deficits, and attention deficits. The presence of a cognitive impairment was found in all cognitive areas, but it was not possible to overcome the prevalent component of the methodological and clinical heterogeneity which emerged from the results.

The present work is an update, after five years, of the previous meta-analysis and incorporates all the data produced after the previous review up to March 2010. The more recent data-sources were identified with the same criteria used in the previous systematic review.

This meta-analysis principally aims to evaluate the presence of cognitive differences between patients with schizophrenia and normal cases. No specific cognitive area is addressed or excluded and those described in this metaanalysis are empirically defined according to the prevalent themes of the current scientific literature. The secondary aim in updating the previous work was to control for the stability of results in comparison to the results obtained in the previous meta-analysis and the methodological quality of the studies.

#### Methods

In order to perform the update of the previous review the following databases were searched, PubMed, PsycInfo, PsycArticles by these keywords: 'cognitive deficit\*' AND 'schizophrenia patients'; 'controlled study'. Only data obtained by human subjects and identifiable until March 2010 were included. No restrictive language selection criteria were applied.

A total of 1,219 works were identified including 700 papers from PubMed, and 654 from PsychInfo and PsycArticles. The 135 papers found from multiple sources were considered only once.

All papers examined for inclusion concerned controlled studies with human subjects where patients with schizophrenia were compared to normal subjects in terms of cognitive functioning. The decision for inclusion was taken by consensus between two of the authors. In case of disagreement, a third author was called in to give his judgment.

After this search, 270 papers were eligible to be added to the 117 already included to the previous systematic review (see Figure 1).

Some of the excluded studies were found lacking of results expressed in numerical form and their data could not be retrieved even when the authors were contacted for this reason (a curious example of this lack of numerical data is constituted by several papers published by the same Journal of which the editorial guidelines required by the authors to avoid to put numerical tables in their papers); other papers were excluded because they did not conform to the inclusion criteria for this meta-analysis. In particular, we excluded all the studies where the inclusion of patients was done by selecting the cases on the basis of a specific stratification by IQ level.

In the following phase, consisting of the data extraction, more papers were excluded from the 270 already found compliant with the inclusion criteria, when they were found part of a series of partial data publications all concerned with the same study. In these cases, in order to avoid an unsuitable redundancy of the data included, we accepted only the data which were found in the most recent of the publications or which indicated the largest number of cases among the other papers of the same series.

In conclusion of the data extraction process, 123 new papers were added to the 117 ones already present in the previous systematic review for a total of 240 papers. Each study may have offered data to one (111 papers) or more than one (129 papers) domains examined in the review.

The analysis of data is articulated on different cognitive domains. This organization is maintained the same as in the previous meta-analysis, since it still represents the most inclusive way of ordering the different types of measurement prevalently used in this field. As a confirmation of this, we have found a still growing number of papers which were carried out in the last years with



modalities of cognitive assessment compatible with this organization of cognitive domains.

The distribution of the included papers in the various tables concerning the areas of cognitive functioning is:

- 1. Memory functioning (128 studies),
- 2. Global cognitive functioning (131 studies),
- 3. Language (70 studies),
- 4. Executive function (67 studies),
- 5. Attention (76 studies).

The different areas of cognitive functioning are articulated in different analyses as follows (see Table 1):

#### Memory Functioning

Measures of Memory Efficiency (47 studies). This analysis includes all data from papers where there wasn't a more specific distinction between types of memory characteristic to be examined (see Additional file 1: Table S1 and Figure 2).

Measures of Memory Functioning (inpatients only) (17 studies). This analysis includes only those studies from Additional file 1: Table S1 which were specified to be

performed with inpatients (see Additional file 1: Table S1 and Figure 3).

Measures of Memory Functioning (outpatients only) (16 studies). This analysis includes only those studies from the Additional file 1: Table S1 which were specified to be performed with outpatients (see Additional file 1: Table S1 and Figure 4).

Digit Span (31 studies). This analysis includes only those studies which were performed by the Digit Span as a measure of immediate memory (see Additional file 1: Table S1 and Figure 5).

LTM (45 studies). This analysis includes only those studies which were specified to be performed with measures of long term memory (see Additional file 1: Table S1 and Figure 6).

STM (56 studies). This analysis includes only those studies which were specified to be performed with measures of short term memory (see Additional file 1: Table S1 and Figure 7).

#### Global cognitive functioning

Measures of IQ (102 studies). This analysis includes only those studies which were specified to be performed with measures of IQ or with measures

#### Table 1 Distribution of the included studies in the different cognitive domains

#### Measures of Memory Efficiency

Altshuler (2004)<sup>b</sup>; Baldeweg (2004); Bora (2008)<sup>b</sup>; Braff (1991)<sup>b</sup>; Braw (2005)<sup>a,b</sup>; Brebion (2001)<sup>a</sup>; Broerse (2001); Buckley (1994); Cadenhead (1999); Cantor-Graae (1995); Cavézian (2007); Clare (1993); Crespo-Facorro (1999)<sup>a</sup>; Egan (2001)<sup>b</sup>; Frith (1991); Goldberg (1990); Gras-Vincendon (1994); Hartman (2003)<sup>a</sup>; Henry (2007)<sup>b</sup>; Hill (2004)<sup>a</sup>; Hoff (1998); Holthausen (2003)<sup>a</sup>; Joyce (2002)<sup>b</sup>; Katz (2007); Kiefer (2002)<sup>a</sup>, Kopelowicz (2005)<sup>a,b</sup>; Kravariti (2003)<sup>a</sup>; Lanser (2002)<sup>a</sup>; Nechel (1998); Minzenberg (2003)<sup>b</sup>; Mulholland (2008)<sup>a</sup>; Nestor (1998)<sup>a</sup>; Neufeld (1995)<sup>a</sup>; Niekawa (2007); Park S (1995)<sup>b</sup>; Perlstein (2001)<sup>b</sup>; Rodriguez-Sànchez (2007); Roesch-Ely (2009)<sup>a</sup>; Tek (2002)<sup>b</sup>; Van Erp (2008)<sup>b</sup>; Weiss (2002)<sup>b</sup>; Woonings (2002)<sup>a</sup>.

#### STM

Achim (2007); Arango (1999); Barch (2008); Barrantes-Vidal (2007); Birkett (2006); Brebion (2004); Brissos (2008); Cellard (2010); Chey (2002); Cosman (2009); Danion (2001); Dickinson (2004); Dragovic (2005); Fucetola (2000); Goldberg (1998); Gonzàlez-Blanch (2008); Gooding (2002); Gras-Vincendon (1994); Gur (2001); Harvey (1990); Hazlett (2000); Hill (2004); Hoff (1992); Hoff (1998); Hoff (2005); Huddy (2009); Huges (2002); Keefe (2004); Kerns (2007); Kiang (2007); Kim (2003); Kopelowicz (2005); Landro (1993); Leeson (2005); Leonard (2008); MacDonald (2003); Manning (2009); Midorikawa (2008); Muller (2004); Nestor (1998); Ohrmann (2008); Palmer (2010); Pino (2008); Riley (2000); Schuepbach (2004); Seidman (2003); Skelley (2008); Snyder (2008); Weickert (2000); Wexler (1998); Wilk (2002); Wood (2006).

#### Premorbid IQ

Altshuler (2004); Baas (2008); Badcock (2005); Badcock (2008); Baldeweg (2004); Birkett (2006); Brebion (2004); D' Argembeau (2008); Doughty (2008) <sup>a</sup>; Egan (2001)<sup>b</sup>; Elvevag (2000)<sup>a</sup>; Elvevag (2000)<sup>a</sup>; Elvevag (2001)<sup>a</sup>; Elvevag (2003); Frith (1991); Goldberg (1998); Henry (2007) <sup>b</sup>; Hill (2004); Hoff (1992); Horan (2009); Huddy (2009); Hughes (2002)<sup>b</sup>; Joyce (2002); Kiehl (2005) <sup>b</sup>; Kircher (2001); Kuperberg (1998); Leeson (2009); Majoreck (2009); Manning (2009) <sup>a</sup>; Menzies (2007); Moritz (2005); Moritz (2008); Phillips (2000); Roesch-Ely (2009); Roiser (2009); Rossell (1999); Rossell (2008); Schmand (1992); Smith (1998); Snyeder (2008); Stirling (2001)<sup>a</sup>; Stirling (2006); Sullivan (1994)<sup>a</sup>; Sullivan (2004); Surguladze (2002); Tsoi (2008); Waters (2006); Wood (2006).

#### Language

Alptekin (2005); Altshuler (2004); Al-Uzri (2004); Arango (1999)<sup>b</sup>; Baldeweg (2004); Barrantes-Vidal (2007); Bora (2008); Braff (1991)<sup>b</sup>; Brazo (2005); Brissos (2008); Broerse (2001); Burbridge (2007); Cantor-Graae (1995); Chino (2006); Cuesta (2007); D' Argembeau (2008); Danion (2001); Deep (2007); Docherty (1996); Docherty (1999); Dragovic (2005); Earle Boyer (1991); Egan (2001)<sup>b</sup>; Frith (1991); Giovannetti (2003)<sup>a</sup>; Glahn (2000); Goldberg (1990); Goldberg (1998)<sup>a</sup>; Green (1985); Gur (2001); Harvey (1990); Haskins (1995); Heinrichs (2008); Hoff (2005); Hoff (1992); Hoffmann (1999); Keefe (2004); Kiefer (2002)<sup>a</sup>; Kim (2003); Kopelowicz (2005); Kosmidis (2005); Kuperberg (1998); Leeson (2005); Leonard (2008); Manning (2009); Matsui (2008); Menzies (2007); Miller (1995); Minzenberger (2003); Mirsky (1995); Morice (1990); Muller (2004); Myles-Worsley (1991); Ojeda (2002)<sup>a</sup>; Paulsen (1994); Pino (2008); Riley (2000); Rossell (1999); Rossell (2008); Sarfati (1999); Stirling (2006); Stone (1998)<sup>a</sup>; Szoke (2009); Tendolkar (2002); Van Beilen (2004); Verdoux (1995); Vinogradov (2002)<sup>b</sup>; Wang (2008); Weickert (2000); Wilk (2002).

#### Attention

Achim (2007); Altshuler (2004) <sup>b</sup>; Babin (2007) <sup>a</sup>; Barch (2003); Bertrand (2007); Besche (1997)<sup>a</sup>; Birkett (2006); Birkett (2007); Braw (2008) <sup>a</sup>; <sup>b</sup>; Brazo (2002)<sup>b</sup>; Brazo (2005) <sup>b</sup>; Brisson (2008); Broerse (2001); Cantor-Graae (1995); Carter (1992)<sup>b</sup>; Chey (2002); Cuesta (2007); Deep (2007) <sup>b</sup>; Dragovic (2005) <sup>a</sup>; Elvevag (2000b); Fucetola (study 1) (1999); Fucetola (study 2) (1999); Fucetola (2000) <sup>b</sup>; Giovannetti (2003)<sup>a</sup>; Glahn (2000); Goldberg (1990); Gooding (2002)<sup>b</sup>; Grillon C (1990); Grillon ML (2010);

#### **Digit Span**

Achim (2007); Alptekin (2005); Baldeweg (2004); Bertrand (2007); Birkett (2006); Brébion (2001)<sup>a</sup>; Brissos (2008); Buckley (1994); Burbridge (2007); Cohen (1999); Conklin (2002); Deep (2007); Fucetola (2000); Javitt (1997); Kiefer (2002)<sup>a</sup>; Kircker (2001); Kurachi (1994); Leonard (2008); Matsui (2008); Minzenberg (2003)<sup>b</sup>; Papageorgiou (2003); Rodriguez-Sànchez (2007); Roiser (2009); Schuepbach (2004); Silver (2003); Stirling (2006); Stone (1998)<sup>a</sup>; Thomas (1996); Waters (2006); Weiler (2009); Wood (2006).

#### LTM

Barrantes-Vidal (2007); Birkett (2006); Brazo (2002); Buckley (1994); Conklin (2002); Davidson (1996); Deep (2007); Dickinson (2004); Dragovic (2005); Evans (2003); Fucetola (2000); Gonzàlez-Blanch (2008); Green (1985); Gur (2001); Harvey (1988); Harvey (2000); Heinrichs (2008); Hill (2004b); Hoff (2005); Huges (2002); Kerns (2007); Kiang (2007); Kim (2003); Kravariti (2003); Leeson (2005); Leonard (2008); MacDonald (2003); Manning (2009); Menzies (2007); Michel (1998); Midorikawa (2008); Müller (2004); Nestor (1998); Ohrmann (2008); Pino (2008); Riley (2000); Schmand (1992); Schuepbach (2004); Seidman (2003); Skelley (2008); Tendolkar (2002); Van Beilen (2004); Wang (2008); Wilk (2002); Wood (2006).

#### **Global Cognitive Functioning**

Achim (2007); Aloia (1998)  $^{\rm a}$ ; Baas (2008); Badcock (2005); Badcock (2008); Barch (2008)  $^{\rm b}$ ; Barrantes-Vidal (2007)  $^{\rm b}$ ; Bell (2009); Bertrand (2007); Besche (1997)<sup>a</sup>; Bora (2008)<sup>b</sup>; Braff (1991)<sup>b</sup>; Brazo (2002)<sup>b</sup>; Brazo (2005) <sup>b</sup>; Brisson (2008); Burbridge (2007) <sup>b</sup>; Cadenhead (1999); Cellard (2007)<sup>a; b</sup>; Cellard (2010); Chen (2008) <sup>b</sup>; Conklin (2002) <sup>a</sup>; Conklin (2005); Cuesta (2007); Danion (2001)<sup>b</sup>; Deep (2007) <sup>b</sup>; Dickinson (2004) <sup>b</sup>; Doughty (2008) <sup>a</sup>; Edell (1987) <sup>a</sup>; Egan (2001)<sup>b</sup>; Elvevag (2000)<sup>a</sup>; Elvevag (2000b)<sup>a</sup>; Elvevag (2001)<sup>a</sup>; Elvevag (2003); Frith (1991); Fucetola (2000) <sup>a</sup>; Giovannetti (2003)<sup>a</sup>; Glahn (2000); Gold (2000) <sup>b</sup> Goldberg (1990); Goldstein (1998)<sup>b</sup>; Gooding (2002)<sup>b</sup>; Granholm (1991)<sup>b</sup>; Granholm (1999); Gras-Vincendon (1994); Grillon ML (2010); Heaton (1994); Heinrichs (2008) <sup>b</sup>; Henquet (2005) <sup>a</sup>; Henry (2007) <sup>b</sup>; Hoff (1992); Hoff (1998); Hoff (2005); Huddy (2009); Hughes (2002)<sup>b</sup>; Javitt (1995); Javitt (1997) <sup>a</sup>; Keefe (2004); Kiehl (2005) <sup>b</sup>; Krabbendam (2000)<sup>b</sup>; Kravariti (2003)<sup>a; b</sup>; Kurachi (1994); Langdon (2002); Lanser (2002)<sup>a</sup>; Leeson (2009); Leitman (2006); Leonard (2008); Luck (2008) <sup>b</sup>; Macdonald (2003); Manning (2009) <sup>a</sup>; Martin (2008); McNealy (2003) <sup>b</sup>; Michel (1998) <sup>b</sup>; Midorikawa (2008); Minzenberg (2003) <sup>b</sup>; Morice (1990); Morrison-Stewart (1991); Mulholland (2008) <sup>a</sup>; Nestor (2008); Neufeld (1978) <sup>a</sup>; O' Carroll (1999); Ohrmann (2008)<sup>a</sup>; Okada (2002)<sup>a</sup>; Park IH (2008)<sup>b</sup>; Penn (1993)<sup>a</sup>; Perry (Study 1) (2001)<sup>a</sup>; Perry (Study 3) (2001); Premkumar (2008)<sup>b</sup>; Rodriguez-Sànchez (2007); Ross (2000)<sup>b</sup>; Rund (2004)<sup>a</sup>; Sayers (1995)<sup>a</sup>; Schreiber (1995); Seidman (2003); Silver (2003); Skelley (2008); Stirling (2001)<sup>a</sup>; Stirling (2006); Sullivan (1994)<sup>a</sup>; Vinogradov (2002)<sup>b</sup>; Wang (2008)<sup>a</sup>; Weikert (2000); Zuffante (2001).

#### **Executive Function**

Altshuler (2004); Arango C. (1999)<sup>b</sup>; Bertrand (2007); Bersche-Richard (1999); Braff (1991)<sup>b</sup>; Brankovic (1999); Braw (2008); Brazo (2002)<sup>b</sup>; Brazo (2005); Cadenhead (1999); Cantor-Graae (1995); Cavèzian (2007); Corrigan (1991); Egan (2001)<sup>b</sup>; Fucetola (2000); Glahn (2000); Goldberg (1990); Goldberg (1998)<sup>a</sup>; Gooding (2002)<sup>b</sup>; Gur (2001); Henry (2007)<sup>b</sup>; Hill (2004); Hoff (1992); Hoff (1998); Hoff (2005); Hughes (2002)<sup>b</sup>; Keefe (2004); Kesserl (2007); Kiang (2007); Kim (2003); Kopelowicz (2005); Lanser (2002)<sup>a</sup>; Lee (2007); Leeson (2009); Manning (2009)<sup>a</sup>; Michel (1998); Midorikawa (2008); Minzenberg (2003); Mirsky (1995); Morice (1990); Moritz (2008); Nestor (2008); Ohrmann (2008); Ojeda (2002)<sup>a</sup>; Parellada (1994); Paulsen (1994); Perlstein (1998)<sup>a</sup>; Perry (Study 3) (2001); Perry (Study 4) (2001); Rile (1991); Riley (2000); Saoud (2000); Sarfati (1999); Schwartz (1991); Shelley (1996); Silver (2003); Smith (1998); Stirling (2006); Stratta (2001); Torres (2007); Verdoux (1995); Wang (2008); Weickert (2000); Woonings (2002)<sup>a</sup>; Yogev (2004).

#### Table 1 Distribution of the included studies in the different cognitive domains (Continued)

Gur (2001); Hartman (2003)<sup>a</sup>; Hirt (1991)<sup>a</sup>; Hoff (1992); Hoff (1998); Holthausen (2003) <sup>a</sup>; Hughes (2002)<sup>b</sup>; Javitt (1995); Karch (2009); Kerns (2007); Kim (2003); Kim (2004) <sup>b</sup>; Kurachi (1994)<sup>b</sup>; Laplante (1992)<sup>a</sup>; Luck (2008)<sup>b</sup>; MacDonald (2003); Mathews (2004) <sup>b</sup>; McNealy (2003) <sup>b</sup>; Mirsky (1995); Moritz (2001)<sup>a</sup>; Muller (2004) <sup>a</sup>; Ober (1995)<sup>b</sup>; Ojeda (2002)<sup>a</sup>; Park S (1995)<sup>b</sup>; Penn (1993)<sup>a</sup>; Perlstein (1998)<sup>a</sup>; Perlstein (2001)<sup>b</sup>; Perry (Study 4) (2001)<sup>a</sup>; Rabinowicz (1996); Riley (2000); Roesch-Ely (2009) <sup>a</sup>; Roiser (2009); Schreiber (1995); Sereno (1996); Smid (2009); Smith (1998) <sup>b</sup>; Stirling (2001)<sup>a</sup>; Stirling (2006); Stratta (1999)<sup>a</sup>; Strik (1993); Surguladze (2002); Symond (2002) <sup>b</sup>; Tek (2002)<sup>b</sup>; Ueno (2004); Van Den Bosh (1992); Vinogradov (2002)<sup>b</sup>; Weiss (1992)<sup>a</sup>; Zuffante (2001).

<sup>a</sup> : studies with cases as inpatients; <sup>b</sup> : studies with cases as outpatients.

	California									Chil Mana Difference
Church and Carb array	Schizop	hrenia g	roup	Healthy	individu	als	184-1-1-4	Std. Mean Difference		Std. Mean Difference
Study or Subgroup	Mean	SD	lotal	Mean	SD	lotal	weight	IV, Random, 95% CI	Year	IV, Random, 95% Cl
1.1.1 measures of memory	Eniciency					-				
Goldberg 1990	81.4	16.3	16	112.7	16.8	7	1.6%	-1.83 [-2.90, -0.77]	1990	
Braff 1991	6.33	1.86	40	8.03	1.23	40	2.3%	-1.07 [-1.54, -0.60]	1991	
Frith 1991	2.05	1	283	2.07	0.75	35	2.5%	-0.02 [-0.37, 0.33]	1991	T
Clare 1993	39.8	7.6	12	45.7	4.6	12	1.9%	-0.91 [-1.75, -0.06]	1993	
Gras-Vincendon 1994	95.9	8.9	24	109.7	7.8	24	2.1%	-1.62 [-2.28, -0.96]	1994	
Buckley 1994	84.1	20.8	27	112	14.2	20	2.1%	-1.50 [-2.16, -0.84]	1994	
Neuteld 1995	10.67	2.12	15	13.44	2.5	16	2.0%	-1.16 [-1.93, -0.39]	1995	
Park S 1995	71.4	16	18	95.2	4.8	18	1.9%	-1.97 [-2.78, -1.16]	1995	
Cantor-Graae 1995	21.4	5.9	14	28.1	2.5	14	1.9%	-1.44 [-2.28, -0.59]	1995	
Michel 1998	85.96	16.47	26	100.6	12.7	26	2.2%	-0.98 [-1.56, -0.40]	1998	
Nestor 1998	37	13.5	18	47	15.7	21	2.1%	-0.67 [-1.31, -0.02]	1998	
Stone 1998	77.55	13.42	18	87.5	8.18	15	2.0%	-0.85 [-1.57, -0.14]	1998	
Hoff 1998	11.24	4.71	132	16.95	3.5	74	2.5%	-1.32 [-1.63, -1.01]	1998	~
Stratta 1999	84.75	12.55	25	98.33	2.33	25	2.2%	-1.48 [-2.11, -0.85]	1999	
Cadenhead 1999	45.6	6.2	20	48.6	1.7	20	2.1%	-0.65 [-1.28, -0.01]	1999	~
Crespo-Facorro 1999	5.4	1.9	14	6.6	1.5	13	2.0%	-0.68 [-1.46, 0.10]	1999	
Ross 2000	72.9	5.1	10	85.1	5.7	10	1.5%	-2.16 [-3.31, -1.01]	2000	
Peristein 2001	3.12	0.83	17	3.32	0.36	16	2.1%	-0.30 [-0.99, 0.39]	2001	-†
Brébion 2001	14.7	7.3	50	25.6	7.8	40	2.4%	-1.44 [-1.90, -0.97]	2001	-
Broerse 2001	31.47	4.35	24	32.98	2.2	20	2.2%	-0.42 [-1.02, 0.18]	2001	
Egan 2001	31.8	19.2	120	54.6	10	43	2.4%	-1.31 [-1.69, -0.94]	2001	~
Lanser 2002	19.02	3.87	39	23.44	3.2	36	2.3%	-1.23 [-1.72, -0.73]	2002	
Kiefer 2002	4.42	1.06	24	4.92	1.18	24	2.2%	-0.44 [-1.01, 0.13]	2002	
Tek 2002	76.2	1.1	30	86.1	1.3	20	0.9%	-8.24 [-10.01, -6.46]	2002	
Woonings 2002	36.5	10.7	44	47.2	10.4	79	2.4%	-1.01 [-1.40, -0.62]	2002	~
Weiss A.P. 2002	0.45	0.23	40	0.61	0.19	32	2.3%	-0.74 [-1.22, -0.26]	2002	~
Hartman 2002	10.6	1.9	16	11.6	0.9	16	2.0%	-0.66 [-1.37, 0.06]	2002	
Joyce 2002	5.62	1.37	136	6.58	1.3	81	2.5%	-0.71 [-0.99, -0.43]	2002	~
Minzenberg 2003	-1.25	1.29	57	0.36	0.85	20	2.3%	-1.33 [-1.89, -0.78]	2003	
Kravariti 2003	82.8	20.7	18	108.5	8.1	17	2.0%	-1.58 [-2.35, -0.81]	2003	
Silver 2003	5.33	3.37	27	6.25	1.69	38	2.3%	-0.36 [-0.86, 0.14]	2003	-
Holthausen 2003	45.69	9.21	118	56.38	8.52	45	2.5%	-1.18 [-1.55, -0.81]	2003	~
Baldeweg 2004	18.3	5.7	28	22.9	1.6	20	2.2%	-1.01 [-1.62, -0.40]	2004	
Altshuler, 2004	36.6	10.8	20	50.9	6.2	22	2.1%	-1.61 [-2.32, -0.91]	2004	
Hill 2004	-0.73	1.17	86	-0.01	0.85	81	2.5%	-0.70 [-1.010.38]	2004	~
Kopelowicz 2005	46	9	28	43.2	9	26	2.3%	0.31 [-0.23, 0.84]	2005	+-
Katz 2007	7	2.13	31	9.48	2.66	29	2.3%	-1.02 [-1.560.48]	2007	
Rodriguez-Sanchez 2007	-0.76	1	124	0	0.9	28	2.4%	-0.77 [-1.19, -0.35]	2007	
Niekawa 2007	7.76	2.37	25	9.95	0.21	22	2.2%	-1.24 [-1.87, -0.61]	2007	
Henry 2007	41	10.18	30	51.5	6.78	29	2.2%	-1.19[-1.75 -0.64]	2007	
Cavézian 2007	0.3	0.48	10	12	0.02	10	1 7%	-1 17 [-2 14 -0 21]	2007	
Mulholland 2008	18	2.36	30	22.2	0.02	15	1 9%	-2 69 [-3 53 -1 9/1	2007	
van Ern 2008	68 68	10.4	35	76.68	7 36	36	23%	-0.88 [-1.37 -0.30]	2000	
Bora 2008	30.1	43	30	36.3	4.1	30	2.5%	-1 46 [-2 03 -0 88]	2000	
Braw 2000	77.52	1.6/	37	86.5	1 20	44	1.6%	-6.00[-2.03,-0.00]	2000	
Poech-Ely 2000	6.4	2.09	50	7 02	1.20	44	2.4%	-0.03 [-7.14, -0.03]	2000	4
Soriano 2000	46.00	2.00	20	69.06	1.08	40	2.470	-0.33 [-0.73, 0.08]	2009	
Subtotal (95% Cl)	40.55	3.07	2066	00.00	4.74	1366	100.0%	-3.00 [-3.92, -2.19] -1.22 [-1.44 -1.04]	2009	•
	Chi2 - 220	61 46-	46/0 - 0	000043	8 - 0.00V	1500	100.070	- 1.22 [- 1.44, - 1.01]		•
Test for succell offect: 7 = 44	CHF= 326	.04, 01 =	40 (P < U	.00001);1	r≓80%					
rest for overall effect: Z = 11	i.ii (P < 0.	00001)								
										worse than controls better than controls

Figure 2 Measures of Memory Efficiency.

	Schizo	ohrenia g	roup	Healthy	, individu	lals		Std. Mean Difference		Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% Cl	Year	IV, Random, 95% CI
1.1.2 Measures of Memory	y Functioni	ng (inpat	ients only	()						
Neufeld 1995	10.67	2.12	15	13.44	2.5	16	5.5%	-1.16 [-1.93, -0.39]	1995	
Stone 1998	77.5	13.42	18	87.5	8.18	15	5.6%	-0.86 [-1.58, -0.14]	1998	
Nestor 1998	37	13.5	18	47	15.4	21	5.8%	-0.67 [-1.32, -0.02]	1998	
Stratta 1999	84.75	12.55	25	98.33	2.33	25	5.9%	-1.48 [-2.11, -0.85]	1999	
Crespo-Facorro 1999	5.4	1.9	14	6.6	1.5	13	5.5%	-0.68 [-1.46, 0.10]	1999	
Brébion 2001	14.7	7.3	50	25.6	7.8	40	6.3%	-1.44 [-1.90, -0.97]	2001	+
Lanser 2002	19.02	3.87	39	23.44	3.2	36	6.2%	-1.23 [-1.72, -0.73]	2002	+
Woonings 2002	36.5	10.7	44	47.2	10.4	79	6.4%	-1.01 [-1.40, -0.62]	2002	+
Hartman 2002	10.6	1.9	16	11.6	0.9	16	5.7%	-0.66 [-1.37, 0.06]	2002	
Kiefer 2002	4.42	1.06	24	4.92	1.18	24	6.0%	-0.44 [-1.01, 0.13]	2002	
Kravariti 2003	82.8	20.7	18	108.5	8.1	17	5.5%	-1.58 [-2.35, -0.81]	2003	
Holthausen 2003	45.69	9.21	118	56.38	8.52	45	6.5%	-1.18 [-1.55, -0.81]	2003	+
Hill 2004	-0.73	1.17	86	-0.01	0.85	81	6.6%	-0.70 [-1.01, -0.38]	2004	+
Kopelowicz 2005	46	9	28	43.2	9	26	6.1%	0.31 [-0.23, 0.84]	2005	+-
Mulholland 2008	18	2.36	30	23.3	0.1	15	5.3%	-2.69 [-3.53, -1.84]	2008	
Braw 2008	77.53	1.64	37	86.5	1.29	44	4.7%	-6.09 [-7.14, -5.03]	2008	
Roesch-Ely 2009	6.4	2.08	50	7.02	1.59	40	6.4%	-0.33 [-0.75, 0.09]	2009	-
Subtotal (95% CI)			630			553	100.0%	-1.21 [-1.63, -0.80]		◆
Heterogeneity: Tau <sup>2</sup> = 0.65;	; Chi <sup>2</sup> = 158	6.34, df =	16 (P < 0	.00001); I	²= 90%					
Test for overall effect: Z = 5	.74 (P < 0.0	00001)								
										+
										-10 -5 0 5 1
										worse than controls better than controls

Figure 3 Measures of memory functioning (inpatients only).

of general intelligence (see Additional file 1: Table S1 and Figure 8).

Measures of IQ (inpatients only) (27 studies). This analysis includes only those studies from Additional file 1: Table S1.1 which were specified to be performed with inpatients (see Additional file 1: Table S1 and Figure 9). Measures of IQ (outpatients only) (27 studies). This analysis includes only those studies from Additional file 1: Table S1.1 which were specified to be performed with outpatients (see Additional file 1: Table S1 and Figure 10). Premorbid IQ (48 studies). This analysis includes only those studies which were specified to be performed with measures of premorbid IQ as described by the authors (see Additional file 1: Table S1 and Figure 11).

#### Language

Verbal functioning (70 studies). This analysis includes measures of fluency, naming tasks, etc. (see Additional file 1: Table S1 and Figure 12).

	Schizon	bronia a	roup	Health	rindividu	iale		Std. Mean Difference		Std Mean Difference
Study or Subaroun	Mean	SD	Total	Mean	SD	Total	Weight	IV Random 95% Cl	Year	M Random 95% Cl
Study of Subgroup	mean	50	Total	mean	50	Total	Treight	10, runuoni, 55% cr	Teur	
1.1.3 Measures of Mem	ory Functionii	ng (outpa	tients o	ıly)						
Braff 1991	6.33	1.86	40	8.03	1.23	40	6.8%	-1.07 [-1.54, -0.60]	1991	+
Park S 1995	71.4	16	18	95.2	4.8	18	6.1%	-1.97 [-2.78, -1.16]	1995	
Ross 2000	72.9	5.1	10	85.1	5.7	10	5.3%	-2.16 [-3.31, -1.01]	2000	
Egan 2001	31.8	19.2	120	54.6	10	43	6.9%	-1.31 [-1.69, -0.94]	2001	+
Perlstein 2001	3.12	0.83	17	3.32	0.36	16	6.4%	-0.30 [-0.99, 0.39]	2001	
Joyce 2002	5.62	1.37	136	6.58	1.3	81	7.0%	-0.71 [-0.99, -0.43]	2002	+
Weiss A.P. 2002	0.45	0.23	40	0.61	0.19	32	6.7%	-0.74 [-1.22, -0.26]	2002	+
Tek 2002	76.2	1.1	30	86.1	1.3	20	3.9%	-8.24 [-10.01, -6.46]	2002	
Minzenberg 2003	-1.25	1.29	57	0.36	0.85	20	6.6%	-1.33 [-1.89, -0.78]	2003	-
Altshuler, 2004	36.6	10.8	20	50.9	6.2	22	6.3%	-1.61 [-2.32, -0.91]	2004	
Kopelowicz 2005	36.2	8.3	28	43.2	9	26	6.6%	-0.80 [-1.35, -0.24]	2005	
Henry 2007	41	10.18	30	51.5	6.78	29	6.6%	-1.19 [-1.75, -0.64]	2007	
Braw 2008	77.53	1.64	37	86.5	1.29	44	5.5%	-6.09 [-7.14, -5.03]	2008	
Bora 2008	30.1	4.3	30	36.3	4.1	30	6.6%	-1.46 [-2.03, -0.88]	2008	-
van Erp 2008	68.68	10.4	35	76.68	7.36	35	6.7%	-0.88 [-1.37, -0.39]	2008	-
Soriano 2009	45.33	3.67	30	58.05	4.74	18	6.0%	-3.05 [-3.92, -2.19]	2009	
Subtotal (95% CI)			678			484	100.0%	-1.83 [-2.35, -1.31]		•
Heterogeneity: Tau <sup>2</sup> = 0.9	97; Chi <sup>2</sup> = 194	.51, df = 1	15 (P < 0	.00001);1	l² = 92%					
Test for overall effect: Z =	6.95 (P < 0.0	0001)								
										worse than controls better than control
										Norde and Control Deller and Control
gure 4 Measures of	memory fu	unctioni	ing (ou	tpatient	ts only)	).				

	Schizor	ohrenia a	roup	Health	v individu	lais		Std. Mean Difference		Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% Cl	Year	IV, Random, 95% Cl
1.1.4 Digit Span										
Buckley 1994	16	4 1	27	19.3	3.1	20	2.9%	-0.87 [-1.48, -0.27]	1994	
Kurachi 1994	9.6	2.8	39	9.8	2.4	20	3.3%	-0.07 [-0.61, 0.47]	1994	
Thomas 1996	15.2	6.5	38	18.4	5.3	16	3.0%	-0.51 [-1.10, 0.08]	1996	
Javitt 1997	10.7	0.2	18	10.9	0.15	17	2.4%	-1.10 [-1.82, -0.38]	1997	
Stone 1998	4.07	1.28	18	5.13	1.55	15	2.4%	-0.73 [-1.45, -0.02]	1998	
Cohen 1999	5.7	1	33	6	1.5	31	3.6%	-0.23 [-0.73, 0.26]	1999	
Fucetola 2000	9.13	2.48	87	11.1	2.36	94	5.1%	-0.81 [-1.11, -0.51]	2000	
Brébion 2001	5.9	2.25	50	7.25	2.85	40	4.1%	-0.53 [-0.95, -0.11]	2001	
Kircher 2001	6	2	12	7.7	1.9	7	1.5%	-0.83 [-1.80, 0.15]	2001	
Kiefer 2002	5.48	1.08	24	5.52	1.13	20	3.0%	-0.04 [-0.63, 0.56]	2002	
Schuepbach 2002	15.03	4.01	29	18.71	4.35	24	3.1%	-0.87 [-1.44, -0.30]	2002	
Minzenberg 2003	-1.02	1.05	57	0.02	0.92	20	3.3%	-1.01 [-1.55, -0.48]	2003	
Papageorgiou 2003	54.4	7.2	9	68	4.5	11	1.1%	-2.22 [-3.39, -1.05]	2003	
Silver 2003	5.53	1.67	27	8.03	2.58	39	3.4%	-1.10 [-1.62, -0.57]	2003	
Baldeweg 2004	6.25	2.15	28	8.9	2.25	20	2.8%	-1.19 [-1.81, -0.56]	2004	
Conklin 2005	6.3	2.45	39	8.6	2.45	56	4.1%	-0.93 [-1.36, -0.50]	2005	
Alptekin 2005	10.97	3.25	38	11.81	4.7	31	3.7%	-0.21 [-0.69, 0.27]	2005	
Birkett 2006	4.9	0.8	15	5.3	0.96	15	2.3%	-0.44 [-1.17, 0.29]	2006	+
Stirling 2006	19.33	2.175	30	19	1.675	18	3.0%	0.16 [-0.42, 0.75]	2006	
Waters 2006	5.54	1.65	43	6.7	1.65	24	3.5%	-0.69 [-1.21, -0.18]	2006	
Wood 2006	10	0.91	20	11.2	0.96	20	2.5%	-1.26 [-1.94, -0.57]	2006	
Burbridge 2007	6.4	2.3	49	7.5	2.3	47	4.3%	-0.47 [-0.88, -0.07]	2007	
Depp 2007	7.8	2.5	150	9.8	2.7	85	5.4%	-0.77 [-1.05, -0.50]	2007	
Rodriguez-Sanchez 2007	4.36	1.2	118	5.4	1.5	22	3.8%	-0.83 [-1.29, -0.36]	2007	
Bertrand 2007	16.29	3.96	36	17.24	4.1	27	3.6%	-0.23 [-0.73, 0.27]	2007	
Achim 2007	16.7	4	26	17.2	4.1	20	3.0%	-0.12 [-0.71, 0.46]	2007	
Brissos 2008	8.83	1.77	23	9.48	1.88	23	3.1%	-0.35 [-0.93, 0.23]	2008	
Leonard 2008	98	26	34	123	24	34	3.5%	-0.99 [-1.49, -0.48]	2008	
Matsui 2008	7.5	1.94	53	9.4	2.6	31	3.8%	-0.85 [-1.32, -0.39]	2008	
Roiser 2009	12.9	2	20	14.2	2.35	17	2.6%	-0.59 [-1.25, 0.07]	2009	
Weiler 2009	16.1	1.95	19	18.8	1.95	19	2.4%	-1.36 [-2.07, -0.64]	2009	<u> </u>
Subtotal (95% CI)			1209			883	100.0%	-0.67 [-0.81, -0.53]		•
Heterogeneity: Tau <sup>2</sup> = 0.07;	Chi² = 60.1	66, df = 3	0 (P = 0.0	)008); I² =	= 51%					
Test for overall effect: Z = 9.9	59 (P < 0.0	00001)								
										+ + + + + + + + + + + + + + + + + + + +
										-4 -2 0 2 4
										worse than controls better than controls
Figure 5 Digit span.										

**Executive Function** 

Measures of cognitive flexibility (67 studies). This analysis includes tasks principally obtained from the Wisconsin Card Sorting Test (see Additional file 1: Table S1 and Figure 13).

#### Attention

Reaction Time (76 studies). This analysis includes the reaction time registered with various techniques and in various types of tasks (see Additional file 1: Table S1 and Figure 14).

Attention (inpatients only) (19 studies). This analysis includes only those studies where it was specified that the cases were inpatients (see Additional file 1: Table S1 and Figure 15).

Attention (outpatients only) (21 studies). This table includes only those studies where it was specified that the cases were outpatients (see Additional file 1: Table S1 and Figure 16).

In general, since there isn't any substantial change with respect to the measures utilized in the previous review, the same detailed descriptive table of the measures found in the previous review is valid also for this updated version [7].

#### Description of the studies

The clinical criteria to individuate and select the patients of the studies added to this review are the same as those of the previous version (in general they were defined according to DSM III, DSM III R, DSM IV, DSM IV-TR, ICD 9, ICD 10, and RCD the Research Diagnostic Criteria). Only in few instances there was a distinction of patients according to different types of diagnosis, but since this information is present in very few papers, it has not been utilized for this review. The total number of cases of this updated version of the review is 18,049: 10,120 patients of the Schizophrenia Group (SG) and 7,929 normal cases of the Control Group (CG).

As shown in Table 2, the unbalance between the number of patients and that of the normal cases is persistent and generalized in all analyses but one. It ranges between a maximum of 38% of patient surplus with respect to the normal cases to a minimum of 12%. Only the

Study or Subaroup		nin onnu gi	oup	пеаш	y maivia	lais		sta. Mean Difference		Std. Mean Difference
study of Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	Year	IV, Random, 95% Cl
1151TM										
Croop 1005	24.22	4.76		27.26	1.00	10	1.00	4 44 5 2 40 0 7 21	1005	
5reen 1985	21.23	4.70	44	27.30	1.30	12	1.9%	-1.41 [-2.10, -0.72]	1985	
Harvey 1988	0.74	0.25	20	0.96	0.07	25	2.1%	-1.17 [-1.77, -0.57]	1988	
Schmand 1992	8.1	3.3	67	9.09	3.7	19	2.2%	-0.29 [-0.80, 0.22]	1992	
Buckley 1994	86.8	21.4	27	109.9	15.6	20	2.0%	-1.19 [-1.82, -0.55]	1994	
Javidson 1996	1.4	1.7	66	6.9	1.8	66	2.2%	-3.12 [-3.64, -2.61]	1996	
dichel 1998	85.6	15.96	26	106.5	10.8	26	2.0%	-1.51 [-2.13, -0.89]	1998	
Fucetola 2000	29.28	17.55	87	51.21	12.17	94	2.5%	-1.46 [-1.78, -1.13]	2000	
Harvey 2000	2.34	2.82	165	6.91	2.43	165	2.6%	-1.73 [-1.99, -1.48]	2000	
Riley 2000	31.6	8.33	40	37.14	2.57	22	2.2%	-0.79 [-1.33, -0.25]	2000	
3ur 2001	16.4	8.4	53	25.1	7.5	71	2.4%	-1.10 [-1.48, -0.71]	2001	
//ilk 2002	74	18.72	181	105.38	13.93	99	2.5%	-1.82 [-2.11, -1.53]	2002	
Fendolkar 2002	9.71	2.9	14	12.58	1.8	14	1.7%	-1.15 [-1.96, -0.35]	2002	
Brazo 2002	8.5	2.8	35	10.8	2.9	35	2.2%	-0.80 [-1.29, -0.31]	2002	
Conklin 2002	12.2	2.7	37	14.4	0.9	56	2.3%	-1.19 [-1.64, -0.74]	2002	
Hughes 2002	7.35	6.2	65	17.18	5.83	25	2.2%	-1.60 [-2.12, -1.08]	2002	
Seidman 2003	15.98	8.02	88	25	6.4	48	2.4%	-1.20 [-1.58, -0.82]	2003	
Evans 2003	7.9	2.8	93	9.9	1.7	73	2.5%	-0.84 [-1.16, -0.52]	2003	
≺ravariti 2003	85.6	20.8	20	107.1	10.1	21	1.9%	-1.30 [-1.98, -0.62]	2003	
≺im 2003	12.3	5.49	22	21.5	5.49	21	1.9%	-1.64 [-2.35, -0.94]	2003	
MacDonald 2003	1.96	1.12	24	3.32	0.68	36	2.1%	-1.52 [-2.11, -0.93]	2003	
/an Beilen 2004	7.54	3.05	50	10.44	2.57	25	2.2%	-0.99 [-1.50, -0.48]	2004	
3chuepbach 2004	11.48	3.46	32	13	2.51	21	2.1%	-0.48 [-1.04, 0.08]	2004	
Dickinson 2004	8.1	3.5	97	11.2	2.9	87	2.5%	-0.96 [-1.26, -0.65]	2004	
Hill 2004b	10.32	3.75	62	12.09	2.57	67	2.4%	-0.55 (-0.90, -0.20)	2004	
Muller 2004	12.87	7.1	100	26.16	6.3	62	2.4%	-1.94 [-2.33, -1.56]	2004	
Dragovic 2005	5.7	3.06	157	9.58	3.1	77	2.5%	-1.26 [-1.55, -0.96]	2005	
Hoff 2005	0.3	0.2	51	0.54	0.1	74	2.4%	-1.60[-2.01, -1.19]	2005	
Mond 2006	25.96	10.79	20	31.6	8.64	20	2.0%	-0.57 [-1.20 0.07]	2006	
Rirkett 2006	57	4.6	15	11.8	71	15	1.8%	-0.99 [-1.76 -0.23]	2000	
Barrantes-Vidal 2007	13.2	61	68	25.1	8.2	63	2 4 %	-1 65 [-2 04 -1 25]	2000	
Denn 2007	6.8	3.0	150	10	3.6	85	2.4%	-0.84 [-1.12] -0.56]	2007	
kiang 2007	0.0 8.0	27	19	12.2	21	19	1 0%	-1 03 [-1 72 -0 22]	2007	
Korne 2007	0.0 A Ø Ø	124.2	10	53.2	54.7	20	7 204	0.16 [.0.30 0.62]	2007	
Monties 2007	10.0	24.2	47	22.4	1 /	11	2.370	-1 00 [-0.30, 0.02]	2007	
Menzies 2007 Alana 2009	7.00	0.0	50	20.1	1.4	62	7.470	-1.00 [-2.03, -0.70]	2007	
Prang 2006 Pikelley 2000	7.98	4.03	162	11.00	4.94 11 E	205	2.470	-0.07 [-1.07, -0.28]	2008	
Shelley 2000 Contolog Blonch 2000	07.1	J8.4 2	102	93.0 5.65	11.5	205	2.0%	-0.24 [-0.45, -0.03]	2008	
Jonzalez-Blanch 2008	4.04	11 22	51	5.05	2.0	34	2.5%	-0.57 [-1.05, -0.10]	2008	
Heinrichs 2008	40.46	11.32	151	50.74	11.08	12	2.5%	-0.91 [-1.20, -0.62]	2008	
Leonard 2008	85	19	34	98	15	34	2.2%	-0.75 [-1.24, -0.26]	2008	
Midorikawa 2008	72.1	19.2	27	110.8	12	49	2.0%	-2.57 [-3.19, -1.94]	2008	
2008	4.56	2.25	124	6.59	1.93	39	2.4%	-0.93 [-1.30, -0.55]	2008	
Jhrmann 2008	10.1	2.6	43	11	2.6	37	2.3%	-0.34 [-0.79, 0.10]	2008	
Vestor 2008	88.77	12.74	25	105.07	14.79	28	2.1%	-1.16 [-1.74, -0.57]	2008	
√anning 2009	2.7	2.3	30	5.9	2	30	2.1%	-1.47 [-2.04, -0.89]	2009	
Leeson 2009	7.43	2.85	60	10.09	2.96	60	2.4%	-0.91 [-1.29, -0.53]	2009	
subtotal (95% CI)			2801			2244	100.0%	-1.14 [-1.32, -0.96]		▼
Heterogeneity: Tau <sup>2</sup> = 0.30;	Chi <sup>2</sup> = 337	7.12, df = 4	44 (P < 0	).00001);	l² = 87%					
Fest for overall effect: Z = 1	2.61 (P < 0	.00001)								
										+ + + +
										-4 -2 0 2

Figure 6 Long term memory.

analysis concerning the IQ measures has a balanced number of patients and normal cases. The systematic unbalance between the groups was already identified in the previous review and it has remained unchanged in the more recent papers. This unbalanced design is not due to few big studies where there was a an asymmetrical recruitment of patients and controls, but it is due to a generalized and persistent modality of recruitment of the great majority of studies.

The mean age of cases described in the single studies ranges between a minimum of 16.5 years for patients of the SG and of 16.2 years of the CG to a maximum of 73.3 years in both groups.

Not all the studies describe the composition of their cases and patients by sex. When this information is available, the mean percentage of males is 70.60% in the SG and 60.81% in the CG with a range from a minimum of 0% (all females) to a maximum of 100% (all males). The average number of male cases of the CG is 87% of the average number of male patients of the SG.

In general, most of the patients were examined while taking antipsychotic drugs but it is very rare to

	Schizop	hrenia g	roup	Health	/ individu	als		Std. Mean Difference		Std. Mean	Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% Cl	Year	IV, Rando	m, 95% Cl
1.1.6 STM											
Harvey 1990	0.34	0.26	26	0.7	0.11	25	1.5%	-1.76 [-2.42, -1.11]	1990		
Van Den Bosch 1992	67.4	11.5	30	75.4	11.3	21	1.7%	-0.69 [-1.26, -0.12]	1992		
Hoff 1992	13.2	7.2	26	20.9	5	25	1.6%	-1.22 [-1.82, -0.62]	1992		
Landro 1993	18	8.9	30	25.3	3.4	18	1.6%	-0.98 [-1.59, -0.36]	1993		
Gras-Vincendon 1994	6.3	3.2	24	9.4	3	24	1.6%	-0.98 [-1.58, -0.38]	1994		
Coldborg 1994	15.73	0.71	17	22.53	5.3 2.5	22	1.4%	-1.10[-1.83,-0.37]	1994		
Meyler 1998	5.63	2.27	25 36	10.7	2.5	20	1.3%	-1.05[-1.57]-0.53]	1990		
Hoff 1998	9.35	5.2	58	17.67	5 4 2	74	2.0%	-1.55 [-1.95, -1.16]	1998		
Arango 1999	17	9.4	85	29.1	7	36	1.9%	-1.37 [-1.80, -0.94]	1999		
Hazlett 2000	7.8	3.7	20	12.1	3.3	32	1.6%	-1.22 [-1.83, -0.61]	2000		
Fucetola 2000	38.16	19	87	58.95	10.05	94	2.1%	-1.38 [-1.70, -1.05]	2000		
Weickert 2000	15.24	8.91	117	23.63	6.93	24	1.9%	-0.97 [-1.42, -0.51]	2000		
Riley 2000	33.62	6.07	40	37.18	2.44	22	1.7%	-0.69 [-1.22, -0.15]	2000		
Gur 2001	20.1	8.1	53	28.2	6.5	71	2.0%	-1.11 [-1.50, -0.73]	2001		
Danion 2001	23.2	7.8	48	27.5	8.5	24	1.8%	-0.53 [-1.03, -0.03]	2001		
Wilk 2002 Gooding 2002	12.17	18.04	181	105.75	12.04	99	2.2%	-2.00 [-2.30, -1.70]	2002		
Chev 2002	25	27.93	34 15	97.09 4.63	00.0	16	1.770	-1.42[-1.90,-0.07]	2002		
Tendolkar 2002	11 79	2.8	14	4.55	0.50	14	1.2%	-0.91 [-1.69 -0.12]	2002		
Hughes 2002	11.97	6.61	62	20.96	5.02	25	1.8%	-1.44 [-1.95, -0.92]	2002		
Seidman 2003	20.51	7.83	88	28.4	5.7	48	2.0%	-1.10 [-1.47, -0.72]	2003		
MacDonald 2003	3	0.91	24	3.87	0.29	36	1.6%	-1.39 [-1.97, -0.82]	2003		
Kim 2003	12.43	5.04	22	21.21	5.6	21	1.4%	-1.62 [-2.32, -0.92]	2003		
Hill 2004b	9.53	3.87	62	11.48	2.79	67	2.1%	-0.58 [-0.93, -0.23]	2004		
Dickinson 2004	8.6	3.3	97	11.1	3.1	87	2.2%	-0.78 [-1.08, -0.48]	2004		
Brebion 2004	5.51	2.19	39	8.21	2.98	39	1.8%	-1.02 [-1.50, -0.55]	2004		
Schuepbach 2004	11.14	3.71	32	12.24	3.06	21	1.7%	-0.31 [-0.87, 0.24]	2004		-
Muller 2004	17.46	7.1	100	29.79	6.7	62	2.0%	-1.77 [-2.14, -1.39]	2004		
Reete 2004	7.79	3.94	148	12.9	3.85 5.07	50	2.1%	-1.30 [-1.65, -0.95]	2004		
Vonelowicz 2005	20.0	2C.0 88.8	107	28.7	0.97 Q	26	2.2%	-1.27 [-1.57, -0.98]	2005		-
Hoff 2005	0.4	0.00	51	0.5	01	74	21%	-0.67 [-1.03 -0.30]	2005		
Wood 2006	28.65	10.65	20	34.45	7.43	20	1.5%	-0.62 [-1.26, 0.02]	2006		
Birkett 2006	8.1	5.2	15	13.3	6.5	15	1.3%	-0.86 [-1.61, -0.11]	2006		
Barrantes-Vidal 2007	18.1	6.9	68	28.5	6.4	63	2.0%	-1.55 [-1.94, -1.16]	2007		
Achim 2007	56.2	20.5	26	79.5	19.3	20	1.5%	-1.15 [-1.78, -0.51]	2007		
Kiang 2007	42.4	15.3	18	53.8	10.3	18	1.4%	-0.85 [-1.54, -0.17]	2007		
Kerns 2007	1.12	0.7	47	2.92	1.18	30	1.7%	-1.95 [-2.50, -1.39]	2007		
Gonzalez-Blanch 2008	5.12	2.97	37	7.06	2.75	34	1.8%	-0.67 [-1.15, -0.19]	2008		
BillSSUS 2000 Barch 2008	0.9	2.04	20	0.05	2.00	23	7.0%	-1.29[-1.95, -0.00]	2000		_
Wang 2008	0.54	4.67	53	12.55	4.26	53	2.0%	-0.62 [-1.01 -0.23]	2000		
Skellev 2008	66	27.9	162	84.3	14	205	2.3%	-0.86 [-1.07, -0.64]	2008		
Snyeder 2008	35.1	12.1	38	39.8	11.2	20	1.7%	-0.39 [-0.94, 0.15]	2008		-
Pino 2008	18.46	3.81	124	22	3.55	39	2.0%	-0.94 [-1.31, -0.57]	2008		
Nestor 2008	84.68	15.12	25	102.32	15.72	28	1.6%	-1.13 [-1.71, -0.54]	2008		
Ohrmann 2008	48.6	9.9	43	54	8	37	1.9%	-0.59 [-1.04, -0.14]	2008		
Leonard 2008	100	19	34	105	13	34	1.8%	-0.30 [-0.78, 0.17]	2008		-
Midorikawa 2008 Ceemen 2009	76.6	19.5	27	110.2	12.9	49	1.6%	-2.14 [-2.73, -1.55]	2008		
Cosman 2009 Monning 2000	42.65	12.87	40	51.8	14.31	30	1.8%	-0.67 [-1.16, -0.18]	2009		
Manning 2009	9.9 6.69	0.4	30 60	20.2	1.96	00 60	7.1%	-1.40 [-2.03, -0.00]	2009		
Huddy 2009	5.50	1.70	33	64	11	24	1.7%	-0.85 [-1 40 -0.30]	2009		
Cellard 2010	0.68	0.22	25	0.86	0.13	25	1.6%	-0.98 [-1.570.39]	2010		
Palmer 2010 Subtotal (95% CI)	79.3	15.8	127	100.3	13.8	127	2.2%	-1.41 [-1.69, -1.14]	2010	_	
Heterogeneity: Tau <sup>2</sup> = 0.17; 0	Chi² = 240	.02, df=	55 (P < 0	.00001);	l² = 77%	2313	100.070	- 1.05 [- 1.10, -0.92]		•	
Test for overall effect: Z = 16	.00 (P < 0.	.00001)									
										-4 -2 (	
Figure 7 Short torm man	nony									worse than controls	better than controls
rigure / Short term men	nory.										

find specified the length of the therapeutic treatment or the eventual suspension of it in occasion of the cognitive evaluation. In few instances, it is indicated that therapies different from antipsychotic drugs were also administered to the patients such as BZD, antidepressants, etc.

Many studies do not specify if patients were examined in an acute, chronic, or remission phase.

	Study or Subgroup	Schizop Mean	hrenia g SD	oup Total	Healthy cor Mean S	rols Total	Weight	Std. Mean Difference IV, Random, 95% Cl	Year	Std. Mean Difference IV, Random, 95% CI
	1.2.1 Measures of IQ Neufeld 1978	104 9	10.02	26	111 00	20	0.9%	-0.60 [-1 20 -0.041	1979	
	Edell 1987	98.3	14.4	30	112.6 11	5 20	0.9%	-1.06 [-1.66, -0.45]	1987	
Inter 190       6:01       6:01       6:02       6:01       6:02       6:01       6:02       6:01       0:01	Goldberg 1990 Morice 1990	89.7 84.5	14.2 11.9	16 60	108.6 21.	1 7 3 34	0.7%	-1.10 [-2.05, -0.14] -1.50 [-1.98, -1.03]	1990 1990	
Description       0.0	Braff 1991	95.18	14.91	40	104.6 14.5	2 40	1.1%	-0.63 [-1.08, -0.18]	1991	
Materia Decent 190         0.04 <td>Frith 1991</td> <td>9.1</td> <td>1.9</td> <td>283</td> <td>105.5 12</td> <td>35</td> <td>1.1%</td> <td>-0.75 [-1.10, -0.39]</td> <td>1991</td> <td></td>	Frith 1991	9.1	1.9	283	105.5 12	35	1.1%	-0.75 [-1.10, -0.39]	1991	
Prime         Prim         Prime         Prime	Morrison-Stewart 1991	104.8	18.49	20	110.2 13.7	30	1.0%	-0.34 [-0.91, 0.23]	1991	
Halen 1994         100         102         10         100         1	Penn 1993	113	13	31	130 7	5 25 5 31	1.0%	-1.58 [-2.15, -1.00]	1993	
Nameri 1990 Separet 1996 Separet 1996 Separet 1996 Separet 1996 Separet 1996 Separet 1996 Separet 1996 Separet 1996 Separet 1996 Separet 1997 Separet 1997 Sep	Heaton 1994 Gras-Vincendon 1994	96.3	13.2	35	113.9 10	5 38 7 24	1.0%	-1.46 [-1.98, -0.94]	1994	
Barent 1000         101         1444         27         101         201         101 <td< td=""><td>Kurachi 1994</td><td>91.6</td><td>12.2</td><td>39</td><td>96.3 8</td><td>3 30</td><td>1.0%</td><td>-0.43 [-0.91, 0.05]</td><td>1994</td><td></td></td<>	Kurachi 1994	91.6	12.2	39	96.3 8	3 30	1.0%	-0.43 [-0.91, 0.05]	1994	
Serves 1998 9 117 2 2 116 9 13 2 2 2 2 10 9 19 10 2 2 2 2 2 10 19 10 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1	Sayers 1995 Javitt 1995	83.7 98.1	14.64 12.9	27 31	97.5 23 110.8 8	5 19 9 11	0.9%	-0.72 [-1.33, -0.12] -1.04 [-1.76, -0.31]	1995 1995	
Display       43       9       9       4       9       9       9       11       12	Schreiber 1995	91	11.7	21	108.5 9	22	0.9%	-1.62 [-2.32, -0.93]	1995	
Adds 1980       99.5       11.33       20       11.65       6.5       21       99.4       -1.414       43.04.07       1980	Besche 1997 Javitt 1997	24.6 96.3	5.1	24	25.2 2 99.6 1	3 20 3 17	0.9%	-0.14 [-0.73, 0.46] -1.65 [-2.43, -0.87]	1997	
Declamine 1999 07 12 13 14 10 10 23 11 25 12 10 14 11 27 23 1999 14 14 15 15 23 10 109 14 14 15 15 12 14 15 45 15 10 109 14 14 15 15 12 15	Aloia 1998	99.51	11.83	20	110.5 6	5 21	0.9%	-1.14 [-1.80, -0.47]	1998	
Market 1998 9 9 9 9 9 9 9 9 9 9 9 9 9 9 9 9 9 9	Goldstein 1998	97.71	13.11	31	109.39 11.6	5 27	1.0%	-0.93 [-1.47, -0.38]	1998	
Oranio 1990 0 Carlon 1990 1 65 6 1 27 0 Carlon 1990 1 65 6 1 27 0 Carlon 1990 1 65 6 1 27 0 Carlon 1990 1 65 6 1 27 1 6 7 1 7 10 2 2 1 7 10 1 2 1 1 7 1 2 2 1 7 10 1 2 1 1 7 1 2 2 1 7 10 1 2 1 1 7 1 2 2 1 7 10 1 2 1 1 7 1 2 2 1 7 10 1 2 1 1 7 1 1 2 1 1 1 1 1 1 1 1 1 1 1 1	Michel 1998 Cadenhead 1999	91.81 8.7	18.86	26	99.2 12 11.5	3 26	1.0%	-0.46 [-1.01, 0.09]	1998	
O'Amra 1999 165.00 17.7 4.1 10.2 7.9 20 10% 0.16 14.0.7 1999 1.4 14.1 14.1 14.1 14.1 14.1 14.1	Granholm 1999	7.6	2.2	22	11.4 2	20	0.9%	-1.43 [-2.06, -0.80]	1999	
Kabebenima 2000 99.5 14.1 27 1152 11.5 19 0.9% -121 143, 0.57 2000	O'Carroll 1999 Glahn 2000	105.56 44.6	13.75 15.5	41 62	103.2 7. 58.6 7	3 20 2 62	1.0%	0.19 [-0.34, 0.73]	1999 2000	1-
Sang Joung, P. 33, 13, 43, 93, 101, 6, 76, 20, 108, 40, 112, 104, 200, 40, 40, 40, 40, 40, 40, 40, 40, 40,	Krabbendam 2000	99.5	14.1	27	115.6 11	5 19	0.9%	-1.21 [-1.85, -0.57]	2000	
Elemej 2000b 90.8 12.28 20 110.7 12.35 30 0.9% -1.65 12.31.001 2000 Res 2000 101 3 0 110 101 12 10 0.7% -0.0511.44.027 2000 Res 2000 101 3 0 110 101 12 12 0 0.7% -0.0511.44.027 2000 Res 2000 10 4.7 23 22 12.5 12.5 12.5 44 1.0% -1.65 12.33.104 2001 Subhar 2001 9.7 4 0.25 22 15 12.1 12.9 20 9.9 - Subhar 2001 9.7 12.2 25 10 27.5 12.9 20 9.9 - Elemej 2001 8.0 12 6 44 9.4 14.4 21 0.9% -0.55 12.51.52 0.201 Elemej 2001 8.0 12.5 24 0.112 9.4 13.0 - Elemej 2001 9.0 2 55 40 112 9.4 13.0 - Subhar 2001 9.4 12.5 22 10 12.5 14.5 13.0 - Subhar 2001 9.4 14.6 14.4 25 10.8 30 0.9% -1.55 12.51.50 2001 Elemej 2001 9.4 12.5 24 0.112 9.4 38 10.9 - Elemej 2001 9.4 12.5 24 0.112 9.4 48 10.9 - Elemej 2001 9.4 44 6.4 25 15 3.3 20 0.9% -1.55 12.51.50 2001 Elemej 2001 9.4 14.6 14.6 14.7 15 0.00 1.0.4 (Ad.4 2001 Elemej 2002 9.4 21 15.2 20 10.2 5 10.2 5 10.2 5 10.2 5 10.7 5 10.8 0.0 1.0.4 (Ad.4 2001 Elemej 2002 9.4 21 14.9 3 10.12 10.7 5 10.98 - 1.34 F1.86.000 2002 Hughes 2002 9.4 21 15.2 20 10.0 5 11.2 44 25 10.9 - 1.34 F1.86.000 2002 Hughes 2002 9.4 21 14.9 3 10.12 11.7 35 11.8 40 11.6 - 0.008 2002 Hughes 2002 9.4 21 14.9 3 10.12 10.7 55 10.8 00 1.9% -1.34 F1.86.000 2002 Hughes 2002 9.4 22 14.2 17 16.7 13 13 48 11.5 - 0.48 [1.10, 0.	Gold 2000 Elvevag 2000	91.53 86	13.34 14	37 28	101.1 7.	5 20 5 48	1.0%	-0.81 [-1.37, -0.24] -1.35 [-1.87, -0.84]	2000 2000	
Latenta Jobi Latenta Jobi Weisent 2001 9874 9875 1975	Elvevag 2000b	90.8	12.86	20	110.7 12.3	5 30	0.9%	-1.56 [-2.21, -0.91]	2000	
Weikels 2000         98.7         117         119.12         13.85         20         11.8         -1.12         15.5         20         -1.5           Summa 2001         9.1         23         23         12.5	Ross 2000	96.18	14.57	87	106.47 13.7	3 94 2 10	0.7%	-0.72 [-1.02, -0.42] -0.63 [-1.54, 0.27]	2000	
Administriction         Bit is         Dist is <thdist is<="" th="">         Dist is         <thdist is<="" th=""></thdist></thdist>	Weickert 2000	89.63	9.57	117	101.32 13.5	3 26	1.1%	-1.12 [-1.56, -0.67]	2000	
Eleverg 2011 92 128 24 112 129 29 09% - 153 (2.15, 0.91 2001	Sullivan 2001	94.74	2.3	23	12.9 2	5 84	1.0%	-1.54 [-2.03, -1.04]	2001	
Emer 2001 Perry 2001 bit 12 05 23 25 01 27.5 117 43 1156 - 116 153 - 081 2001 Perry 2001 bit 2 55 40 112 984 85 1.05 - 126 1.75, 0.76 2001 Langebon 2002 444 64 25 518 38 20 0.95 - 0.314 2.00, 0.66 2002 Langebon 2002 444 64 25 518 38 20 0.95 - 0.314 2.00, 0.66 2002 Hughes 2002 9 51 113 12 0.22 0 10.5 113 14 00 0.95 - 0.017 150, 0.65 2002 Hughes 2002 9 422 15.32 0.2 10.25 10.7 35 10.8 - 0.314 2.00, 0.68 2002 Hughes 2002 9 422 15.32 0.2 10.2 45 11.7 35 10.8 - 0.38 10.47, 0.21 2002 9 412 114 9 31 1012 10.7 35 10.8 - 0.38 10.47, 0.22 2002 Hughes 2002 9 422 15.32 0.2 10.2 28 12.1 21 22 0.95 - 0.38 10.47, 0.21 2002 9 422 15.32 0.2 10.2 28 146 34 110.9 7 488 30 1.05 - 0.134 16.06, 0.60 2002 9 412 1138 128 22 12.2 12.1 21 22 0.95 - 0.38 10.47, 0.22 0.03 Hughes 2002 9 422 15.32 12.1 22 12.2 10.95 - 0.38 10.47, 0.22 0.03 Hughes 2002 9 422 15.3 12 12 22 0.106.4 14.3 21 0.95 - 0.38 10.47, 0.22 0.03 Hughes 2003 9 124 14.2 11 0.21 10.7 35 130 - 0.38 10.47, 0.23 2003 9 124 14.2 11 0.21 10.7 35 130 - 0.48 11.0.04 2003 9 124 14.2 11 0.21 10.01 11.1 11.0 10 - 0.06 2003 9 124 14.2 11 0.21 10.01 11.1 11.1 10.8 - 0.48 10.50.24 2003 	Elvevag 2001	92	12.8	24	112 12	29	0.9%	-1.53 [-2.15, -0.91]	2001	
Perry 2001 shuhy1 20:5 3.82 50 27.5 4.05 50 11% - 181 12.22, 1.34 2001	Egan 2001	92.6	13.5	120	107.9 11	43	1.1%	-1.18 [-1.55, -0.81]	2001	
Perry 2007 study 3 86 228 40 96 23 40 115 000 1044, 044 2001 Minogradov 2002 97 11 40 104 12 16 0.95 -0.86 17.20, 0.06 2002	Perry 2001 study 1 Stirling 2001	20.5	3.62	50 40	27.5 4.0	5 50 L 36	1.1%	-1.81 [-2.28, -1.34] -1.26 [-1.75, -0.76]	2001	
Langdon 2002 44.4 6.4 6.4 25 5.18 38 20 0.9% -1.34 1.240.0.68 2002	Perry 2001 study 3	9.6	2.8	40	9.6 2	3 40	1.1%	0.00 [-0.44, 0.44]	2001	+
Condim 2002. 938 134 39 1115 154 66 11% -1201165.078 2002	Langdon 2002 Vinogradov 2002	44.4 97	6.4 11	25 40	51.8 3. 104 1	3 20 2 16	0.9%	-1.34 [-2.00, -0.69] -0.61 [-1.20, -0.02]	2002 2002	
Highes 2002 942 15.22 62 10.30 12.4 25 10.8 1.10 12.10 13 10.10 13 10.8 1.31 14.10.40.082 2002	Conklin 2002	93.8	13.4	39	111.5 15	56	1.1%	-1.20 [-1.65, -0.76]	2002	
Gooding 2002         102.26         0.4.8         34         110.97         4.6.8         30         1.0.8        1.31-1660.601         2002            Lamser 2002         97.8         12.8         32         92.6         11.1         3         11.8        0.816.95.0.33         2002            Silver 2003         11.27         2.4.1         22         0.9.8        1.8        0.816.95.0.23         2003            Silver 2003         11.27         2.4.1         27         10.6.7         10.85         38         10.8        1.841.20.023            Givernmeth 2003         84.24         12.7         7.1         10.4         84.3         10.8        0.916.14.3         2003            Givernmeth 2003         46.2         10.4         57.1         10.5         11.4.8         97         12.8        0.951.12.5.0.641         2003            Rind 2004         12.5         11.4         11.8         10.6         7.31         0.8         11.94.9.0.92         2003            Rind 2004         12.5         11.4         11.8         10.2         12.4         0.0.8         10.2	Hugnes 2002 Brazo 2002	92.42 84.22	15.32 14.19	62 35	108.36 13.2	25	1.0%	-1.07 [-1.56, -0.58] -1.34 [-1.86, -0.82]	2002	
Dimension         Dimension         Disk         Disk <thdisk< th="">         Disk         Disk</thdisk<>	Gooding 2002	102.26	9.46	34	110.97 4.6	30	1.0%	-1.13 [-1.66, -0.60]	2002	
Seldman 2003 97.05 18.11 88 112.9 13 48 1.1% - 1.0.4F.142.0.671 2003	Okada 2002	87.8	12.9	22	92.6 12	22	0.9%	-0.38 [-0.97, 0.22]	2002	
Cravaiti 2003         92.6         162.2         20         106.4         14.3         21         0.9%         -0.98         1.53.         0.24         2003	Seidman 2003 Silver 2003	97.05 11.27	16.11	88 27	112.9 1	3 48 5 38	1.1%	-1.04 [-1.42, -0.67] -1.48 [-2.04, -0.92]	2003	
Elverag 2003 91.24 18.87 19 118.23 20.81 23 0.9% -1.33 12.0006.9 2003	Kravariti 2003	92.6	16.2	20	106.4 14	3 21	0.9%	-0.89 [-1.53, -0.24]	2003	
Mac Donaid 2003         47         7.3         24         48         36         10%         -0.48         101         0.04         2003	Elvevag 2003 Giovannetti 2003	91.24 84.94	18.87 12.51	19 47	118.23 20.8	23	0.9%	-1.33 [-2.00, -0.65] -1.99 [-2.54, -1.43]	2003	
Min2ebrerg 2003 96.2 10.4 57 104.5 12.5 20 10.% -0.79 12.7.0.23 2003 - Min2ebrerg 2003 11.2 32 13 11.7 15 13 0.8% -0.91 4.0.8,0.58 2003 - Rund 2004 12.61 553 14.2 18.02 7.3 50 12.% -0.56 10.8.0.23 2004 - Conkin 2005 83.3 13.4 33 11.6 15.4 56 11.% -1.21 14.8.0.70 2005 - Braco 2005 88.7.8 362 10.0 108.4 9 149 12.% -1.21 14.8.0.70 2005 - Braco 2005 88.7.8 362 10.0 108.4 9 149 12.% -1.21 14.8.0.70 2005 - Henquet 2005 86.7.8 362 10.0 108.4 9 149 12.% -1.21 14.24.0.01 2005 - Henquet 2005 86.1 10.2 15 11.3 15 12.5 18.0 .9% -0.74 14.24.26.0 2005 - Henquet 2005 86.1 10.2 11.5 11.3 15 12.5 18.0 .9% -0.74 14.24.26.1 2005 - Henquet 2005 86.1 10.2 11.5 10.4 17 0.8% -0.74 14.24.26.1 2005 - Henquet 2005 86.1 10.2 12.0 4 51 11.1 15 1.7 4 1.1% -0.55 16.9.1, 0.18 2005 - Henquet 2005 83.1 10.1 30 102 13.46 18 0.9% -0.72 11.32.0.12 2006 - Henquet 2005 83.1 10.1 30 102 13.46 19.2% 1.44 12.25.02 2005 - Henquet 2005 83.1 10.1 30 102 13.46 19.2% 1.44 12.25.02 2007 - Henquet 2005 83.1 10.1 30 102 13.46 19.2% 1.44 12.25.02 2007 - Henquet 2007 92.71 15.2 0.4 10.0 11.6 2.9 11.0 .9% -0.74 15.20.21 2007 - Henquet 2007 10.5.74 11.22 12 12.2 12.7 11.5 10.4 17 0.8% -0.74 15.20.25 2007 - Henquet 2007 10.5.74 11.22 12 12.2 12.7 11.5 10.4 12.2 12.0 .97 10.% -0.54 15.56 .0.01 2007 - Henquet 2007 10.5.74 11.22 12.0 11.0 2.0 10.2 7 11.0% -0.54 15.56 .0.01 2007 - Henquet 2007 10.5.74 11.20 40 10.57 17 9 10.0% -0.74 15.20.25 2007 - Henquet 2007 10.5.74 11.20 40 10.57 17 9 10.0% -0.74 15.20.25 2007 - Henquet 2007 10.5.74 12.0 10.10 77 77 15 10.0 40 10.27 10.75 -0.46 10.07 10.7 Henquet 2007 10.5.7 11.5 10.4 12.2 23 11.1% -1.41 14.78.0.20 10.00 - Henquet 2007 10.5.7 11.1 10.5 15 0.9% -0.64 14.20.70 2008 - Henquet 2007 10.5 17.4 0.00 10.77 17 10.0 40.10 2007 - Henquet 2008 8.5 37 55 10.4 36 37 11.1% -0.54 16.04, 2.72 12.08 - Henquet 2008 8.5 37 55 10.4 36 37 11.1% -0.54 16.04, 2.77 2.00 - Henquet 2008 11.6 2.1 30 11.9 2.3 30 10.% -0.24 16.74 .0.00 2008 - Henquet 2008 9.74 11.9 10.15 15 15.9 75 12.5 1	MacDonald 2003	47	7.3	24	49.9 4	3 36	1.0%	-0.48 [-1.01, 0.04]	2003	
Dickinson 2004 90.6 16.2 97 105.4 14.8 87 1.2% -0.95 [+1.25, 0.64] 2004	Minzenberg 2003 McNeely 2003	96.2	3.2	13	104.5 12	5 20 5 13	0.8%	-0.19 [-0.96, 0.58]	2003	
Acting 2004 1201 1201 533 142 1002 731 50 123 120 123 120 1203 0.03 0.03 0.04 0.04 0.02 1200 1200 1200 1200 1200 1200 1200	Dickinson 2004	90.6	16.2	97	105.4 14	8 87	1.2%	-0.95 [-1.25, -0.64]	2004	
Conklin 2005 93.8 13.4 39 111.6 15.4 56 1.1% - 1.21 [-1.65, 0.78] 2005 Badcock 2005 85.78 9.62 109 108.4 9 149 1.2% - 2.11 [-2.42, -1.68] 2005 Henquel 2005 10.5 9.9 118 106.6 5.73 18 0.9% -0.74 [-1.42, -0.66] 2005 Henquel 2005 10.2 15 113.5 13.2 15 0.8% -1.44 [-2.25, 0.62] 2005 Henquel 2005 10.2 204 51 111.6 15.1 74 11.1% -0.55 [-0.16] 2005 Leltman 2006 96 10.7 22 111.5 10.4 17 0.8% -1.44 [-2.15, 0.73] 2006 Consta 2007 10.9 74 11.22 23 121 997 23 0.9% -1.04 [-0.6, 0.24] 2007 Cuesta 2007 10.9 74 11.22 23 121 997 23 0.9% -1.04 [-0.6, 0.24] 2007 Cuesta 2007 12.24 [-4.52 169 12.07 1.62 26 11.% -0.56 [-0.90, 0.08] 2007 Burbridge 2007 92.31 15.94 38 106.31 10.9 27 10% -0.98 [-1.22, 0.46] 2007 Burbridge 2007 97.4 12.2 49 103.2 10.9 47 11.% -0.56 [-0.90, 0.08] 2007 Burbridge 2007 97.4 12.2 49 103.2 10.9 47 11.% -0.56 [-0.90, 0.08] 2007 Redrigue2Sanchez 2007 91.6 3.1 126 10.44 2.5 28 1.1% -0.46 [-0.87, 0.04] 2007 Redrigue2Sanchez 2007 91.2 8 61 09.4 10.37 29 10.% -0.78 [-1.32, 0.25] 2007 Redrigue2Sanchez 2007 92.1 15.94 30 10.84 10.77 29 10.% -0.78 [-1.32, 0.25] 2007 Redrigue2Sanchez 2007 91.2 8 61 09.4 10.37 29 10.% -0.78 [-1.32, 0.25] 2007 Redrigue2Sanchez 2007 91.2 8 61 09.4 10.37 20 10.8 Redrigue2Sanchez 2007 91.2 8 61 09.4 10.37 20 10.8 Redrigue2Sanchez 2007 91.2 9 61 09.4 10.37 2008 Burbridge 2008 8.5 15 17.4 20 107.87 17.25 15 0.8% -1.28 [-2.0, 0.49] 2007 Redrigue2Sanchez 2008 10.65 6.2 1 27 17.87 507 23 10.0%0.21 [-0.037] 2008 Bachez 2008 10.65 5 10.1 10.38 10.3 8 0.7% 0.118 [-0.61, 0.37] 2008 Bachez 2008 10.65 13 17.4 12.0 11.9 12.0 12.0 12.0 0.04 (-0.097) 2008 Park H 2008 92.2 45 14.3 11.1 7.2 14 0.7% -0.51 [-2.8, 0.50] 2008 Park H 2008 91.2 45 11.2 5 10.2 18 0.7% -0.018 [-0.61, 0.37] 2008 Park H 2008 92.2 45 11.2 5 11.	Rund 2004	92.5	11.4	51	105 7.	3 47	1.1%	-1.26 [-1.69, -0.82]	2004	
Badcoxiz 2005         68 79         96 2         109         108 4         0         16         1.2%         -211 1 2 4 2 - 180         2005            Wein 2005         161 1         102         15         113 5         132         15         0.8%         -1.44 1 2 25, 0.62         2005            Hernquel 2005         161 1         102         15         113 5         132         15         0.8%         -1.44 1 2 25, 0.62         2005            Letiman 2006         36         10.11         30         102         13.46         18         0.9%         -0.721 1.32, 0.12         2006            Cellard 2007         9.6         3         150         11         2.5         85         1.2%         0.491 1.68, 0.42         2007            Celesta 2007         12.4         452         180         10.81         10.9         27         1.0%         -0.991 1.52, 0.46         2007            Berrands 2007         9.4.6         15.44         30         16.4         10.77         29         1.0%         -0.791 1.32, 0.25         2007            Henry 2007         9.4.6         15.34         30         <	Conklin 2005 Brazo 2005	93.8 85.39	13.4	39 56	111.6 15	56	1.1%	-1.21 [-1.65, -0.76]	2005	
Kishi 2005 110.5 9.9 18 116.6 5.73 18 0.9% -0.74 [1.42_0.06 2005	Badcock 2005	88.78	9.62	109	108.4	9 149	1.2%	-2.11 [-2.42, -1.80]	2005	
Hort 2005       102       20.4       51       111       5       7       4       1.1%       -0.45       6.01       7.1%       20.05	Kiehl 2005 Henguet 2005	110.5 96.1	9.9 10.2	18 15	116.6 5.7	3 18 2 15	0.9%	-0.74 [-1.42, -0.06] -1.44 [-2.25, -0.62]	2005	
Leitman 2006 96 10.7 22 111.5 10.4 17 0.8% -1.44 [2.15.0.72] 2006 - Depp 2007 9.6 3 150 11 2.5 85 1.2% -0.49 [0.76, 22] 2007 - Cuesta 2007 19.74 11.22 23 121 997 23 0.9% -1.04 [1.66, 0.42] 2007 - Destrand 2007 92.31 15.94 86 106.31 10.9 27 1.0% -0.98 [1.52, 0.46] 2007 - Burbridge 2007 97.4 12.2 49 103.2 10.9 47 1.1% -0.50 [0.40] 2007 - Henry 2007 94.4 15.24 49 103.2 10.9 47 1.1% -0.50 [0.40] 2007 - Burbridge 2007 97.4 12.2 49 103.2 10.9 47 1.1% -0.50 [0.40] 2007 - Barantes-Vidal 2007 96 31 12.8 10.44 12.2 63 1.1% -0.46 [0.67, 0.04] 2007 - Achim 2007 94.3 15.3 26 108.4 9.2 20 0.9% -1.04 [1.47, 9.1.02] 2007 - Achim 2007 94.3 15.3 26 108.4 9.2 20 0.9% -1.06 [1.69, -0.44] 2007 - Achim 2007 94.3 15.3 26 108.4 9.2 20 0.9% -1.06 [1.69, -0.44] 2007 - Achim 2007 94.3 15.3 26 108.4 9.2 20 0.9% -1.06 [1.69, -0.44] 2007 - Achim 2007 94.3 15.3 26 108.4 9.2 20 0.9% -1.06 [1.69, -0.44] 2007 - Achim 2008 85.5 17.49 0.0 107.87 17.25 15 0.8% -1.28 [1.67, 1.11] 2008 - Brissos 2008 116.5 8.3 10 103.8 10.3 8 0.7% 0.18 [1.67, 5.11] 2008 - Brissos 2008 116.5 8.3 10 103.9 10.3 8 0.7% 0.18 [1.67, 5.11] 2008 - Brissos 2008 11.6 2.1 30 11.9 2.3 30 1.0% -0.31 [1.64, 0.37] 2008 - Brissos 2008 11.6 2.1 30 11.9 2.3 30 1.0% -0.31 [1.64, 0.37] 2008 - Brissos 2008 11.6 2.1 30 11.9 2.3 30 1.0% -0.15 [1.024, 0.69] 2008 - Brissos 2008 11.6 2.1 30 11.9 2.3 30 1.0% -0.15 [1.024, 0.09] 2008 - Brissos 2008 11.6 2.1 30 11.9 2.3 30 1.0% -0.15 [1.024, 0.40] 2008 - Derra 2008 11.4 2.1 10.24 10.55 15 0.9% -0.00 [1.21, 0.00] 2008 - Derra 2008 11.4 3.1 25 109.25 13.79 28 0.9% -0.00 [1.21, 0.00] 2008 - Derra 2008 11.4 3.1 25 109.25 13.79 28 0.9% -0.00 [1.21, 0.00] 2008 - Derra 2008 10.1 3 19 11.25 12.2 19 0.9% -1.19 [1.17, 1.69, 0.65] 2008 - Derra 2008 10.2 2.45 11 11.25 11.25 11.2% -0.57 [1.00, 0.40] 2008 - Derra 2008 10.1 3 3 19 11.25 12.2 10.9% -1.08 [1.03, 1.02] 2008 - Derra 2008 10.1 4 3.1 19 94.05 2.2 11.9% -0.38 [1.03, 1.02] 2008 - Derra 2008 10.1 4 33 19 12.5 2.2 19 0.9% -0.38 [1.03, 1.02] 2008 - Derra 2008 10.1 4 33 19 12	Hoff 2005	102	20.4	51	111.6 15	74	1.1%	-0.55 [-0.91, -0.18]	2005	
Depp 2007 9.6 3 150 11 2.5 85 1.2% -0.49[0.76,022 2007	Leitman 2006 Stirling 2006	96 93.6	10.7	22	111.5 10	17 5 18	0.8%	-1.44 [-2.15, -0.72] -0.72 [-1.32, -0.12]	2006	
Central 2007 109.14 11.22 23 121 9.37 23 0.93% -1.04 P1.05.04.22 0.061 2007 Bertrand 2007 92.31 15.94 36 106.31 10.9 27 1.0% -0.99 P1.52.0461 2007 Henny 2007 97.4 12.2 49 10.52 10.9 47 11.% -0.50 P0.09. 0.09 2007 Henny 2007 97.4 12.2 49 10.52 10.9 47 11.% -0.50 P0.09. 0.09 2007 Henny 2007 90.6 3.1 126 10.44 2.5 28 1.1% -0.46 P0.87.032 2007 Charlan 2007 90.6 3.1 126 10.44 2.5 28 1.1% -0.46 P0.87.032 2007 Henny 2008 85.15 17.49 20 107.87 17.25 15 0.8% -1.28 P2.02.054 2008 Charlan 2008 16.5 8.3 10 10.88 10.3 8 0.7% 0.18 P0.73 2008 Henny 2008 85.15 17.49 20 107.87 17.25 15 0.8% -1.28 P2.02.054 2008 Henny 2008 16.5 8.3 10 10.88 10.3 8 0.7% 0.18 P0.73 2008 Charlan 2008 11.6 2.1 30 11.9 2.3 30 1.0% -0.31 P0.42 0.007 - Basco 2008 11.6 2.1 30 11.9 2.3 30 1.0% -0.31 P0.43 2007 2008 Henny 2008 9.75 15.1 14 10.65 48 0.7% 0.18 P0.73 2008 Henny 2008 9.62 2.45 151 11.25 1.99 72 1.2% -0.01 P0.90 2008 - Henny 2008 9.62 2.45 151 11.25 1.99 72 1.2% -0.01 P0.90 2008 - Henny 2008 9.62 2.45 151 11.25 1.99 72 1.2% -0.01 P0.90 2008 - Henny 2008 9.62 2.45 151 11.25 1.99 72 1.2% -0.01 P0.90 2008 - Henny 2008 9.62 2.45 151 11.25 1.99 72 1.2% -0.01 P0.90 2008 - Henny 2008 9.62 2.45 151 11.25 1.99 72 1.2% -0.01 P0.90 2008 - Henny 2008 9.62 2.45 151 11.25 1.99 72 1.2% -0.01 P0.90 2008 - Henny 2008 9.62 2.45 151 11.25 1.99 72 1.2% -0.01 P0.90 2008 - Henny 2008 9.62 2.45 151 11.25 1.99 72 1.2% -0.01 P0.90 2008 - Henny 2008 9.74 11.9 30 111.2 10.5 15 0.8% -1.68 P2.40.097 2008 - Henny 2008 9.154 11.9 30 111.2 10.5 10 8.0% -1.18 P2.40.079 2008 - Henny 2008 10.137 20.32 2.15 5 10.9 4.14 92 5.22 19 0.5% -4.00 P2.05 2008 - Hudy 2008 10.137 20.32 2.14 10.54 11.4 92 10.2% -1.56 P1.73.4.20 2008 - Hudy 2008 10.137 20.32 2.14 10.54 11.4 92 10.2% -1.56 P1.73.4.20 2008 - Hudy 2008 10.137 20.32 2.14 10.54 11.9 2.22 10.9% -0.38 P1.03 0.20 200 - Hudy 2009 10.77 4 10.97 2.20 2.44 10.84 2.20 0.9% - Hudy 2009 10.77 4 10.97 2.20 14.41 11.4 10.5% -0.09 P2.67.151 2008 - Hudy 2009 10.77 4 10.97 2.20 2.44 10.44 200 - Hudy 2009 10.74 10	Depp 2007	9.6	3	150	11 2	5 85	1.2%	-0.49 [-0.76, -0.22]	2007	
Bertrand 2007 92.31 15.4 36 106.31 10.9 27 1.0% -0.99[+15.2.048] 2007	Cuesta 2007	12.91	4.52	23 169	121 9.9	2 26	0.9%	0.20 [-0.22, 0.61]	2007	+-
Construction         61.7         1.2         1.6         1.18         1.000         0.0000         0.000         0.000         <	Bertrand 2007 Burbridge 2007	92.31	15.94	36	106.31 10	27	1.0%	-0.99 [-1.52, -0.46]	2007	
Barrantes-Vidal 2007 90.9 12.9 68 109.4 12.2 63 1.1% -1.41 [-17.9, -1.02 2007	Henry 2007	97.4 94.6	15.84	49	105.4 10.7	29	1.0%	-0.78 [-1.32, -0.25]	2007	
Annumber         Construction	Barrantes-Vidal 2007 Rodriguez-Sanchez 2007	9.09 an e	12.9	68 126	109.4 13	2 63	1.1%	-1.41 [-1.79, -1.03]	2007	
Doughty 2009 85.15 17.49 20 107.87 17.25 15 0.8% -1.28 [2.02, 0.54] 2008	Achim 2007	94.3	15.3	26	108.4 9	2 20	0.9%	-1.06 [-1.69, -0.44]	2007	
Chen 2008 105.5 8.3 10 10.8 10.3 5 0.7% 0.18 (10.7%, 1.11 2008 10.5 10.4 3.6 37 1.1% 0.51 (0.34, 1.00 2008 10.5 10.4 3.6 37 1.1% 0.51 (0.34, 1.00 2008 10.5 10.4 3.6 51 11.5 10.4 3.6 51 11.5 10.4 3.6 51 11.5 10.4 3.6 51 11.5 10.4 3.6 51 11.5 10.4 3.6 51 11.5 10.4 3.6 51 11.5 10.4 3.6 51 11.5 10.4 3.6 51 11.5 10.4 3.6 51 11.5 10.4 3.6 51 11.5 10.4 3.6 51 11.5 10.4 1.5 10.	Doughty 2008 Brissos 2008	85.15 16.65	17.49 6.21	20 23	107.87 17.2	5 15 7 23	0.8%	-1.28 [-2.02, -0.54] -0.21 [-0.79 0 37]	2008 2008	
Barch 2008 8:5 3,7 55 10.4 3.6 37 1.1% -0.51 [0.04, -0.09] 2008	Chen 2008	105.5	8.3	10	103.8 10	3 8	0.7%	0.18 [-0.76, 1.11]	2008	
Bora 2008 11.6 2.1 30 11.9 2.3 30 1.0% -0.13 [0.64, 0.37] 2008 + Heinrichs 2008 97.7 15.71 18 10.66 13.65 28 0.9% -0.66 [1 + 21, 0.00] 2008 + Park H2 2009 96.2 2.45 151 11.25 1.98 72 1.2% -0.70 [-0.99, -0.41] 2008 - Park H2 2009 96.2 2.45 151 11.2 5 1.98 72 1.2% -0.70 [-0.99, -0.41] 2008 - Park H2 2009 96.2 2.5 43 22.5 5 37 1.1% -0.09 [-0.53, 0.35] 2008 - Nestor 2008 92.36 14.31 25 109.25 13.79 28 0.9% -1.19 [-1.77, -0.60] 2008 - Premkumar 2008 91.2 2.1 75 119.3 14.9 25 1.1% -0.87 [+1.34, -0.40] 2008 - Premkumar 2008 102 2.1 75 119.3 14.9 25 1.1% -0.87 [+1.34, -0.40] 2008 - Premkumar 2008 102 2.1 75 119.3 14.9 25 1.1% -0.87 [+1.34, -0.40] 2008 - Leonard 2008 93 3.11 19 94.05 2.23 19 0.9% -0.17 [+1.34, -0.40] 2008 - Martin 2008 11.4 31 19 94.05 2.23 19 0.9% -0.38 [+1.03, 0.25] 2008 - Martin 2008 10.1 7 2.032 54 105.43 11.4 9 1.3 34 1.0% -1.17 [+1.69, 0.65] 2008 - Martin 2008 10.1,7 2.032 54 105.43 11.4 19 - 0.3% +1.09 [+2.67, -1.51] 2008 - Huddy 2008 10.1,7 2.032 54 105.43 11.44 10.9% -2.09 [+2.67, -1.51] 2008 - Huddy 2009 10.77 4 10.97 2.2 104.84 11.81 15 0.9% 0.22 [+2.64, 0.88] 2008 - Huddy 2009 10.77 4 10.97 2.2 104.84 11.81 15 0.9% 0.22 [+2.64, 0.88] 2008 - Huddy 2009 10.77 4 10.97 2.2 104.84 11.81 1.1% -0.21 [+2.94, 0.48] 2008 - Huddy 2009 10.78 11.02 12 10.69.7 12.2 0.09% -1.22 [+1.79, 0.64 2008 - Huddy 2009 19.3.6 13.3 39.9.7 12.7 2.4 1.0% -1.22 [+1.79, 0.64 2009 - Huddy 2009 19.3.6 10.2 92 11.27 12.9 30 1.0% -0.78 [+1.31, -0.28] 2009 - Huddy 2009 19.3.4 10.4 30 10.27 12.9 30 1.0% -0.78 [+1.31, -0.28] 2009 - Huddy 2019 19.8 15.38 60 102.99 11.27 12.9 0.10 % -0.78 [+1.31, -0.28] 2009 - Huddy 2019 19.3.4 10.4 30 10.27 12.9 30 1.0% -0.78 [+1.31, -0.28] 2009 - Huddy 2019 19.3.4 10.4 30 10.27 12.9 30 1.0% -0.78 [+1.31, -0.28] 2009 - Huddy 2019 19.3.4 10.4 30 10.27 12.9 30 1.0% -0.78 [+1.31, -0.28] 2009 - Huddy 2019 19.3.4 10.4 30 10.27 12.9 30 1.0% -0.78 [+1.21, -0.07] 200 - Huddy 2019 19.3.4 10.4 30 10.27 12.9 30 1.0% -0.78 [+1.21, -0.07] 201 - Heterogenetik C31 - 0.74 (-0.90001);	Barch 2008 Badcock 2008	8.5 87.74	3.7 12.21	55 42	10.4 3.	5 37 5 48	1.1%	-0.51 [-0.94, -0.09] -2.31 [-2.85, -1.77]	2008 2008	
Balas 2008 97.7 15.71 18 106.6 13.05 28 0.9% -0.00[+12.7].000] 2008 — Heinrichs 2008 9.62 2.45 151 11.25 13.99 72 1.2% -0.70 (-0.990.41] 2008 — Park IH 2008 98.2 9.3 14 111.1 7.2 14 0.7% -1.51 [+2.360.68] 2008 — Nestor 2008 92.2 6.5 43 22.5 5 37 1.1% -0.09 (-0.53, 0.35] 2008 — Mutholland 2008 91.24 11.9 01 111.2 10.5 15 0.8% -1.68 [+2.400.97] 2008 — Premkumar 2008 102 2.1 75 119.3 14.9 25 1.1% -0.87 [+1.34, -0.40] 2008 — Premkumar 2008 102 2.1 75 119.3 14.9 25 1.1% -0.87 [+1.34, -0.40] 2008 — Luck 2008 89 3 1.1 19 94.05 2.23 19 0.5% -4.00 [>5.44, -2.86] 2008 — Martin 2008 11.4 34 109 13 34 1.0% -1.17 [+1.69, -0.65] 2008 — Martin 2008 101.7 20.32 64 105.41 11.4 90 10% -2.09 [+2.67, -1.51] 2008 — Martin 2008 101.7 20.32 64 105.41 11.4 90 10% -2.09 [+2.67, -1.51] 2008 — Martin 2008 101.37 20.32 64 105.41 15.8 15 0.9% 0.22 [2.06 4.08] 2008 — Huddy 2009 107.74 10.97 2.21 164.81 154 11 15 0.9% 0.22 [1.05.40, 0.17] 2008 — Huddy 2009 10.74 10.97 2.124 16.18 15 0.9% 0.22 [1.2% -1.65 [+1.79, -1.32] 2008 — Huddy 2009 93.4 10.4 30 102.7 12.7 24 10.9% -1.22 [+1.79, -0.64] 2009 — Huddy 2009 93.4 10.4 30 102.7 12.7 24 10.9% 0.75 [+1.0, -0.48] 2009 — Huddy 2009 93.4 10.4 30 102.7 12.9 30 1.0% -0.76 [+1.31, -0.29] 2008 — Huddy 2009 93.4 10.4 30 102.7 12.9 30 1.0% -0.76 [+1.31, -0.20] 2009 — Huddy 2009 93.4 10.4 30 102.7 12.9 30 1.0% -0.76 [+1.31, -0.20] 2009 — Huddy 2009 93.4 10.4 30 102.7 12.9 30 1.0% -0.76 [+1.31, -0.20] 2009 — Huddy 2009 93.4 10.0 10.7 12.9 10.0% -0.76 [+1.31, -0.20] 2009 — Huddy 2009 93.4 10.0 10.0 19.1 12.5 12.7 1.1 25 10.9% -0.38 [+1.07, -0.35] H Huddy 2009 93.4 10.0 10.0 19.1 12.5 12.7 1.1 2.5 10.2 200 — Huddy 2009 93.4 10.0 10.0 19.1 12.5 12.7 1.2 5 10.0 % -0.76 [+1.31, -0.20] 2009 — Huddy 2009 93.4 10.0 (7 < 0.0001); I* = 80% T Testfor overall effect Z = 17.15 (P < 0.00001); I* = 80% T Testfor overall effect Z = 17.15 (P < 0.00001); I* = 80% T Testfor overall effect Z = 17.15 (P < 0.00001); I* = 80% T Testfor overall effect Z = 17.15 (P < 0.00001); I* = 80% T Huddy 2	Bora 2008	11.6	2.1	30	11.9 2	3 30	1.0%	-0.13 [-0.64, 0.37]	2008	
Park IH 2008 98.2 9.3 14 11.1 7.2 14 0.7% -1.51 E 2.8 0.051 2008	Baas 2008 Heinrichs 2008	97.7	15.71	18	106.6 13.6	) 28 ) 72	0.9%	-0.60 [-1.21, 0.00] -0.70 [-0.99, -0.41]	2008	
Ontmain 2008       22       5.3       4.3       22.3       5.3       1.1%       -0.09 (PU.5), 0.33       2006         Mulholland 2008       91.54       11.9       30       11.1%       -0.09 (PU.5), 0.33       2006	Park IH 2008	98.2	9.3	14	111.1 7.	2 14	0.7%	-1.51 [-2.36, -0.65]	2008	
Mulholiand 2008       91:54       11.9       30       111.2       10.5       15       0.8%       -1.68 [2:400.97] 2008	Nestor 2008	92.36	5.5 14.31	43 25	22.5 109.25 13.7	) 37 3 28	0.9%	-0.09 [-0.53, 0.35] -1.19 [-1.77, -0.60]	2008	T
Lemnania 2000       102       21       15       1123       11200       1120 <td>Mulholland 2008 Premkumar 2008</td> <td>91.54</td> <td>11.9</td> <td>30</td> <td>111.2 10</td> <td>5 15</td> <td>0.8%</td> <td>-1.68 [-2.40, -0.97]</td> <td>2008</td> <td></td>	Mulholland 2008 Premkumar 2008	91.54	11.9	30	111.2 10	5 15	0.8%	-1.68 [-2.40, -0.97]	2008	
$ \begin{array}{c} \text{Leonard 2008} & 93 & 14 & 34 & 109 & 13 & 34 & 1.0\% & -1.17 [1.69, -0.69] 2008 & \\ \text{Martin 2008} & 11.4 & 33 & 19 & 12.5 & 2.2 & 19 & 0.9\% & -0.38 [-1.03, 0.29] 2008 & \\ \text{Martin 2008} & 101.37 & 20.32 & 64 & 105.43 & 18.34 & 54 & 11.1\% & -0.21 [-0.59, 0.17] & 2008 & \\ \text{Skelley 2008} & 90.78 & 11.02 & 162 & 106.97 & 9.82 & 205 & 1.2\% & -1.66 [+1.79, -1.32] 2008 & \\ \text{Hudsy 2009} & 107.74 & 10.97 & 2.104.84 & 15.18 & 15 & 0.9\% & 0.22 (-0.44, 0.88] 2009 & \\ \text{Hudsy 2009} & 83.6 & 13.3 & 33 & 99.7 & 12.7 & 24 & 10.\% & -1.25 (-1.40, 0.40] 2009 & \\ \text{Hudsy 2009} & 93.6 & 13.3 & 39.97 & 12.7 & 24 & 10.\% & -0.78 [+1.31, -0.28] 2008 & \\ \text{Hudsy 2009} & 93.4 & 10.4 & 30 & 10.27 & 12.9 & 30 & 1.2\% & -0.76 [+1.31, -0.28] 2009 & \\ \text{Hudsy 2019} & 93.4 & 10.4 & 30 & 10.27 & 12.9 & 30 & 1.0\% & -0.78 [+1.31, -0.28] 2009 & \\ \text{Hudsy 2019} & 93.4 & 10.4 & 30 & 10.27 & 12.9 & 30 & 1.0\% & -0.78 [+1.31, -0.28] 2009 & \\ \text{Hudsy 2019} & 93.4 & 10.4 & 30 & 10.27 & 12.9 & 10.5\% & -0.78 [+1.21, -0.07] 2010 & \\ \text{Heterogeneity: Tau" = 0.24; Chi" = 498.11, df = 101 (f < 0.0001); I" = 80\% \\ \text{Test for overall effect Z = 17.15 (P < 0.00001)} \end{array}$	Luck 2008	83	3.11	19	94.05 2.2	3 19	0.5%	-4.00 [-5.14, -2.86]	2008	
$\begin{array}{c c c c c c c c c c c c c c c c c c c $	Leonard 2008 Midorikawa 2008	93 79.3	14 18 9	34	109 1	3 34	1.0%	-1.17 [-1.69, -0.65]	2008	
$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	Martin 2008	11.4	3.3	19	12.5 2	19	0.9%	-0.38 [-1.03, 0.26]	2008	-+
Dell 2009         10.7         10.8         1.2         10.6         10.9         10.6	Wang 2008 Skelley 2008	101.37 90.78	20.32	54 162	105.43 18.3	54	1.1%	-0.21 [-0.59, 0.17] -1.56 [-1 79 -1 32]	2008	- 1
Huddy 2009       83.6       13.3       33       99.7       12.7       24       1.0%       -1.22 {1.79,0.64}       2009          Lesson 2009       91.98       15.38       60       102.99       14.02       80       1.2%       -0.75 {1.10,0.40}       2009          Manning 2009       93.4       10.4       30       102.7       12.9       30       1.0%       -0.78 {1.31,0.20}       2009          Grillon ML 2010       100.9       19.1       25       112.7       12.2       10%       -0.64 {1.21,-0.071}       2010          Grillon ML 2010       100.9       19.1       25       112.7       17.1       25       10%       -0.64 {1.21,-0.071}       2010          Subtrati (95% CI)       466       3656       100.0%       -0.96 [-1.07,-0.85]       +       +         Heterogenetic, Tau*= 0.24; Chi*= 498.11, df = 101 (P < 0.00001); P = 80%	Bell 2009	107.74	10.97	22	104.84 15.1	3 15	0.9%	0.22 [-0.44, 0.88]	2009	
Manning 2009         93.4         10.4         30         102.7         12.9         30         1.0%         -0.78 [1.31, -0.26]         2009            Cellard 2010         108.6         15.57         25         121.56         6.22         25         0.9%         -1.02 [1.62, -0.43]         2010	Huddy 2009 Leeson 2009	83.6 91.98	13.3 15.38	33 60	99.7 12 102.99 14 0	24	1.0%	-1.22 [-1.79, -0.64] -0.75 [-1 10 -0 40]	2009	
veniaro 2010 1085 15.57 25 127.58 8.22 25 0.9% -1.02 [-1.62,-0.43] 2010	Manning 2009	93.4	10.4	30	102.7 12	30	1.0%	-0.78 [-1.31, -0.26]	2009	
Subtotal (95% CI) 4760 3656 100.0% -0.96 [-1.07, -0.85] Heterogeneity. Tau" = 0.24; Chi" = 498.11, df = 101 (P < 0.00001); I" = 80%. Test for overall effect Z = 17.15 (P < 0.00001) - 4 - 2 0 2 4 worse than controls better than control	Cellard 2010 Grillon ML 2010	108.6 100.9	15.57 19.1	25 25	121.56 8.2	25	0.9% 1.0%	-1.02 [-1.62, -0.43] -0.64 [-1.21, -0.07]	2010 2010	
Test for overall effect Z = 17.15 (P < 0.00001) $\frac{1}{-4}$ $\frac{1}{-2}$ $\frac{1}{2}$ $\frac{1}{4}$ worse than controls better than controls	Subtotal (95% CI)	Chiz- 400	11 df-	4760	0.000043-17-	3656	100.0%	-0.96 [-1.07, -0.85]		•
→ ↓ ↓ ↓ ↓ worse than controls better than controls	meterogeneity. Tau* = 0.24;	, Unr = 498 7.15 (P < 0.	.00001)	01 (P <	0.00001); P=	10.10				
-4 -2 0 2 4 worse than controls better than controls	Test for overall effect: $Z = 1$									1
	Test for overall effect: $Z = 1$									<u> </u>

Figure 8 Measures of IQ.

	Schizop	ohrenia gr	roup	Health	y contr	ols		Std. Mean Difference		Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% Cl	Year	IV, Random, 95% Cl
1.2.2 Measures of IQ (in	patients only	)								
Neufeld 1978	104.9	10.02	26	111	9.81	20	3.6%	-0.60 [-1.20, -0.01]	1978	
Edell 1987	98.3	14.4	30	112.6	11.5	20	3.6%	-1.06 [-1.66, -0.45]	1987	
Penn 1993	113	13	31	130	7.6	31	3.7%	-1.58 [-2.15, -1.00]	1993	
Sullivan 1994	9.4	2.4	34	12.4	2.6	67	4.1%	-1.17 [-1.62, -0.73]	1994	
Savers 1995	83.7	14.64	27	97.5	23.5	19	3.6%	-0.72 [-1.33, -0.12]	1995	
Javitt 1997	96.3	2	18	99.6	1.9	17	3.0%	-1.65 [-2.43, -0.87]	1997	
Besche 1997	24.6	5.1	24	25.2	2.9	20	3.6%	-0.14 [-0.73, 0.46]	1997	
Aloia 1998	99.51	11.83	20	110.5	6.5	21	3.4%	-1.14 [-1.80, -0.47]	1998	
Fucetola 2000	96.18	14.57	87	106.47	13.78	94	4.5%	-0.72 [-1.02, -0.42]	2000	+
Elvevag 2000	86	14	28	106	15	48	3.9%	-1.35 [-1.87, -0.84]	2000	
Elvevag 2000b	90.8	12.86	20	110.7	12.35	30	3.4%	-1.56 [-2.21, -0.91]	2000	
Stirling 2001	102	5.5	40	112	9.84	36	3.9%	-1.26 [-1.75, -0.76]	2001	
Perry 2001 study 1	20.5	3.62	50	27.5	4.05	50	4.0%	-1.81 [-2.28, -1.34]	2001	
Elvevag 2001	92	12.8	24	112	12.9	29	3.5%	-1.53 [-2.15, -0.91]	2001	
Okada 2002	87.8	12.9	22	92.6	12.1	22	3.6%	-0.38 [-0.97, 0.22]	2002	
Lanser 2002	54.42	13.86	39	55.4	11.77	36	4.1%	-0.08 [-0.53, 0.38]	2002	
Conklin 2002	93.8	13.4	39	111.5	15.4	56	4.1%	-1.20 [-1.65, -0.76]	2002	
Giovannetti 2003	84.94	12.51	47	109.3	11.51	31	3.7%	-1.99 [-2.54, -1.43]	2003	
Kravariti 2003	92.6	16.2	20	106.4	14.3	21	3.4%	-0.89 [-1.53, -0.24]	2003	
Rund 2004	92.5	11.4	51	105	7.9	47	4.1%	-1.26 [-1.69, -0.82]	2004	
Henquet 2005	96.1	10.2	15	113.5	13.2	15	2.9%	-1.44 [-2.25, -0.62]	2005	
Wang 2008	101.37	20.32	54	105.43	18.34	54	4.3%	-0.21 [-0.59, 0.17]	2008	
Ohrmann 2008	22	5.5	43	22.5	5	37	4.1%	-0.09 [-0.53, 0.35]	2008	
Mulholland 2008	91.54	11.9	30	111.2	10.5	15	3.2%	-1.68 [-2.40, -0.97]	2008	<u> </u>
Doughty 2008	85.15	17.49	20	107.87	17.25	15	3.1%	-1.28 [-2.02, -0.54]	2008	
Manning 2009	93.4	10.4	30	102.7	12.9	30	3.8%	-0.78 [-1.31, -0.26]	2009	
Cellard 2010	108.6	15.57	25	121.56	8.22	25	3.6%	-1.02 [-1.62, -0.43]	2010	
Subtotal (95% CI)			894			906	100.0%	-1.04 [-1.25, -0.82]		•
Heterogeneity: Tau <sup>2</sup> = 0.2 Test for overall effect: Z =	24; Chi <sup>2</sup> = 114 9.44 (P < 0.0	1.12, df = 2 00001)	26 (P < 0	).00001);	I <sup>2</sup> = 779	6				
										worse than controls better than controls
igure 9 Measures of	IQ.									

The inclusion of data in specific analyses was decided according to the description offered by the authors of the single papers.

#### Data analysis

All analyses are performed comparing patients with schizophrenia to normal cases using Review Manager (RevMan) Version 5.1., Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration, 2011. All variables used are continuous measures which are analyzed by the Standardized Mean Difference, Random Effect Models, due to diversity of methods of measurement used in each analysis, to the randomness of patients sampling empirically done in each of the included studies, and to the high level of heterogeneity of their variance. The heterogeneity is also quantified by the index  $I^2$  [8] which indicates the part of variance due to the presence of specific causes different from chance but not equally distributed in all the studies considered. In those instances where the original data were presented as different subgroups of patients, these data were recomputed in order to be inserted as a single group of patients.

The type of studies included in this meta-analysis does not require a quality assessment of the randomization procedure of allocation of cases. It has other quality assurance requirements, mostly devoted to warrant a sound methodological quality of results. The quality analysis was carried out adopting the method proposed by Egger et al. [9] which evaluates the presence of interfering factors on the results by the method of meta-regression. The meta-regression was used to investigate the relationship of sex, age, and number of participants with the magnitude of the effect size of the single cognitive areas.

Finally, the effect size of each cognitive function was transformed according to the method proposed by Grissom [10] to the probability of superiority estimate (PS index) which allows for the quantification of the probability [11] that a case from the schizophrenia group will present a score different from that obtained by a case from the control group for each of the cognitive areas examined.

## **Results and discussion**

#### Memory functioning

In this cognitive area concerning the measures of memory functioning, the comparison between 2,066 patients with schizophrenia and 1,366 normal subjects (47 studies for a total of 3,432 cases) produces an ES = -1.22[-1.44, -1.01] with an I<sup>2</sup> = 86% and a PS = 81%. These

	Schizop	ohrenia g	roup	Health	y contr	ols		Std. Mean Difference		Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% Cl	Year	IV, Random, 95% Cl
1.2.3 Measures of IQ (out	patients on	IV)								
Granholm 1991	9.1	1.9	15	10.7	2.7	15	2.8%	-0.67 [-1.41, 0.07]	1991	
Braff 1991	95.18	14.91	40	104.6	14.52	40	4.1%	-0.63 [-1.08, -0.18]	1991	
Michel 1998	91.81	18.86	26	99.2	12.3	26	3.6%	-0.46 [-1.01, 0.09]	1998	
Gold 2000	91.53	13.34	37	101.1	7.5	20	3.6%	-0.81 [-1.37, -0.24]	2000	
Krabbendam 2000	99.5	14.1	27	115.6	11.5	19	3.2%	-1.21 [-1.85, -0.57]	2000	<u> </u>
Ross 2000	101	9	10	108	12	10	2.2%	-0.63 [-1.54, 0.27]	2000	
Egan 2001	92.6	13.5	120	107.9	11.1	43	4.6%	-1.18 [-1.55, -0.81]	2001	-
Danion 2001	88.1	16	48	94	16.4	24	3.9%	-0.36 [-0.86, 0.13]	2001	
Gooding 2002	102.26	9.46	34	110.97	4.68	30	3.7%	-1.13 [-1.66, -0.60]	2002	
Hughes 2002	92.42	15.32	62	108.36	13.24	25	3.9%	-1.07 [-1.56, -0.58]	2002	
Brazo 2002	84.22	14.19	35	101.2	10.7	35	3.8%	-1.34 [-1.86, -0.82]	2002	
Minzenberg 2003	96.2	10.4	57	104.5	12.5	20	3.8%	-0.75 [-1.27, -0.23]	2003	
McNeely 2003	11.2	3.2	13	11.7	1.5	13	2.7%	-0.19 [-0.96, 0.58]	2003	
Dickinson 2004	90.6	16.2	97	105.4	14.8	87	4.9%	-0.95 [-1.25, -0.64]	2004	-
Kiehl 2005	110.5	9.9	18	116.6	5.73	18	3.0%	-0.74 [-1.42, -0.06]	2005	
Brazo 2005	85.39	15.4	56	101.3	10.8	56	4.4%	-1.19 [-1.59, -0.79]	2005	
Depp 2007	9.6	3	150	11	2.5	85	5.1%	-0.49 [-0.76, -0.22]	2007	+
Henry 2007	94.6	15.84	30	105.4	10.77	29	3.7%	-0.78 [-1.32, -0.25]	2007	
Barrantes-Vidal 2007	90.9	12.9	68	109.4	13.2	63	4.5%	-1.41 [-1.79, -1.03]	2007	-
Cellard 2007	109.74	11.22	23	121	9.97	23	3.3%	-1.04 [-1.66, -0.42]	2007	
Burbridge 2007	97.4	12.2	49	103.2	10.9	47	4.4%	-0.50 [-0.90, -0.09]	2007	
Heinrichs 2008	9.62	2.45	151	11.25	1.99	72	5.0%	-0.70 [-0.99, -0.41]	2008	-
Luck 2008	83	3.11	19	94.05	2.23	19	1.6%	-4.00 [-5.14, -2.86]	2008	
Barch 2008	8.5	3.7	55	10.4	3.6	37	4.3%	-0.51 [-0.94, -0.09]	2008	
Bora 2008	11.6	2.1	30	11.9	2.3	30	3.8%	-0.13 [-0.64, 0.37]	2008	
Chen 2008	105.5	8.3	10	103.8	10.3	8	2.1%	0.18 [-0.76, 1.11]	2008	_ <del>_</del> _
Premkumar 2008 <b>Subtotal (95% CI)</b>	102	21	75 1355	119.3	14.9	25 919	4.0% 100.0%	-0.87 [-1.34, -0.40] - <b>0.83 [-1.00, -0.66]</b>	2008	•
Heterogeneity: Tau <sup>2</sup> = 0.13	; Chi <sup>2</sup> = 84.9	99, df = 2	6 (P < 0.	00001); P	²= 69%					
Test for overall effect: Z = 9	9.55 (P < 0.0	00001)								
										-4 -2 0 2 4 worse than controls better than controls
Figure 10 Measures of	IQ (outpa	tients o	only).							

results demonstrate that there is a significant decline of memory functioning among the patients with schizophrenia confirmed by the high probability (81%) to find a patient with a memory impairment vs. a 19% of probability to find a patient with scores similar to those of a normal case. The high heterogeneity of these studies limits the usefulness of these findings, since it is not possible to exclude that factors other than the diagnosis could contribute, at least partially, to determine the difference between patients and normal subjects (see Table 2).

The results obtained for the same area, separating inpatients from outpatients, apparently show that outpatients have a larger difference from normal subjects but also maintain a very large amount of heterogeneity between studies (respectively: inpatients, ES = -1.21 [-1.63, -0.80],  $I^2 = 90\%$ , PS = 80%; outpatients, ES = -1.83 [-2.35, -1.31],  $I^2 = 92\%$ , PS = 90%). The number of studies was similar in both instances. In this analysis, the difference of ES magnitude between in and out-patients is only apparent. In fact, their confidence intervals overlap in a way that let us exclude that the two ES's can be considered different.

An example of the influence of the methodological heterogeneity on the ES is offered by the results concerning data obtained by the systematic use of a single type of measure in all studies on memory functioning; in this case the Digit Span. In a total of 2,092 cases from 31 works, there is an ES = -0.67 [-0.81, -0.53] with an I<sup>2</sup> 51%. These results show that when a source of variance due to the differences between measurement methods employed in the different studies is eliminated, there is a consistent reduction of the effect size (which is still demonstrative of a statistically significant difference between groups) accompanied by a reduction to almost half of the heterogeneity.

Analysis of data in function of the type of memory model adopted in the studies was carried out in order to control for a likely source of heterogeneity. The data allowed us to separate results concerning short term memory (STM) vs. those concerning long term memory (LTM). Other models of memory were not suited for this type of analysis since specific data were only sporadically available.

When only LTM data are included in the analysis, from 45 studies for a total of 5,045 cases, ES is -1.14 [-1.32, -0.96], I<sup>2</sup> 87%, and PS 79%. Similar but slightly less intense results are obtained for STM data, obtained from 56 studies for a total of 5,405 cases, where ES = -1.05 [-1.18, -0.92], I<sup>2</sup> 77%, PS 77%.

These results show that the separation of the type of memory model reduces the heterogeneity, while the use

Roiser 2009

Subtotal (95% CI)

	Schizo	phrenia g	roup	Health	y contro	ols		Std. Mean Difference		Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% Cl	Year	IV, Random, 95% Cl
1.2.4 premorbid IQ										
Frith 1991	109	10.1	283	108.1	9.9	35	2.6%	0.09 [-0.26, 0.44]	1991	+-
Hoff 1992	97.6	14.8	26	111.5	17.1	25	2.0%	-0.86 [-1.43, -0.28]	1992	
Schmand 1992	105	17	30	105	15	19	2.0%	0.00 [-0.57, 0.57]	1992	
Sullivan 1994	106.5	9.3	34	112	7.1	67	2.4%	-0.69 [-1.11, -0.27]	1994	
Goldberg 1998	99.1	12.1	23	109	14.6	23	1.9%	-0.73 [-1.32, -0.13]	1998	
Kuperberg 1998	110.9	9.3	27	113	8	10	1.6%	-0.23 [-0.96, 0.50]	1998	
Smith 1998	111.44	9.02	24	110.37	8.45	24	2.0%	0.12 [-0.45, 0.69]	1998	
Rossell 1999	112.6	10.4	74	115.7	9.2	31	2.4%	-0.31 [-0.73, 0.12]	1999	
Phillips 2000	107.65	2.88	27	116	1.9	18	1.3%	-3.23 [-4.15, -2.31]	2000	
Elvevag 2000	115	6	28	120	5	48	2.2%	-0.92 [-1.41, -0.43]	2000	
Elvevag 2000b	96	15	24	109	11.1	29	2.0%	-0.98 [-1.56, -0.41]	2000	
Kircher 2001	101	9.32	12	107.6	9,6	7	1.2%	-0.67 [-1.63, 0.29]	2001	
Elvevag 2001	93.3	14.18	20	110,7	12.35	30	1.9%	-1.31 [-1.93, -0.68]	2001	
Stirling 2001	112	2.56	40	114	1.88	36	2.3%	-0.87 [-1.35, -0.40]	2001	
Sullivan 2001	106.7	8.4	25	113.2	6.9	84	2.3%	-0.89 [-1.35 -0.43]	2001	
Egan 2001	101.6	11.9	120	104.5	11.6	43	2.6%	-0.24 [-0.59, 0.11]	2001	-+
Joyce 2002	99.67	10.37	110	104.64	9.54	73	2.7%	-0.49[-0.79]-0.19]	2002	
Hughes 2002	102.48	14.98	62	109.4	9.09	25	2.3%	-0.51 [-0.98 -0.03]	2002	
Surguladze 2002	101.40	10.9	20	100.4	0.00 Q	26	1 9%	-0.80[-1.40]-0.19]	2002	
Elvevan 2003	102.63	13.28	19	112 48	932	23	1 9%	-0.86[-1.49]-0.22]	2002	
Hill 2004	99.87	14.23	86	104 74	10.56	81	2.7%	-0.39[-0.690.08]	2000	
Altshuler 2004	24.4	11.2	20	153	11.2	22	1 9%	0.80 (0.17 1.43)	2004	
Baldewen 2004	106.3	14.6	20	120.1	9.5	20	1 9%	-1 07 [-1 68 -0 45]	2004	
Brehion 2004	100.0	13	30	106.4	11.7	20	2 3 96	-0.37 [-0.82 0.08]	2004	
Kiehl 2005	109.2	11.4	18	116.4	635	18	1.8%	-0.76[-1.440.08]	2004	
Leeson 2005	101.4	13.55	56	107.3	10.33	24	7.7%	-0.46[-0.94_0.02]	2005	
Moritz 2005	102.01	9.03	30	110.64	679	15	1.8%	-1 01 [-1 67 -0 36]	2005	
Radcock 2005	97.43	8.56	100	106.4	8.5	100	2.8%	-1.05 [-1.33 -0.76]	2005	
Matere 2005	100.21	0.00	103	103.62	4 75	24	2.0%	-0.42 [-0.03, -0.70]	2005	
Wood 2006	102.6	11.53	20	107 2	9.05	24	1 9%	-0.43 [-1.06_0.20]	2000	
Birkett 2006	33.1	8.5	15	37.6	96.5 9 P	15	1.6%	-0.48 [-1.21 0.24]	2000	
Stirling 2006	102.7	7 84	30	103.17	11 69	18	2.0%	-0.05[-0.63_0.54]	2006	
Henny 2007	102.7	12.35	30	102.0	12.37	20	2.0%	-0.14 [-0.65_0.39]	2000	
Menzies 2007	105	7.6	11	102.3	11	11	1 4 %	-0.31 [-1.15 0.54]	2007	
Teni 2008	106	11	30	110	11	30	2.2%	-0.36[-0.87_0.16]	2008	+
Moritz 2008	100	1.4	00 89	116	15	26	2.2.20	-0.30 [-0.07, 0.15]	2000	
Baas 2008	105	13 21	19	106.9	983	2J 29	2.3%	-0.42 [0.00, 0.00]	2000	
Rossell 2009	107	13.51	22	116	10.00	20	2.0%	-0.10[0.75, 0.44]	2000	
Radrock 2000	0102	10.4	32	100.04	8.01 93.3	3Z 40	2.270	-0.03 [-1.10, -0.14]	2000	
Daulock 2000	94.0Z 100	10.71 6.2	42	103.04	60.00	40 10	2.270	-1.75[-2.28,-1.30]	2000	
Chigembeau 2008 Chuodor 2009	108	11.2	10	101.2	0.3	10	1.770	-0.01[-1.21, 0.20]	2000	
Doughty 2000	96.4 100 5	24.76	34	101.3	21 62	20	2.170	-0.20[-0.01, 0.30]	2000	
Doughly 2008	100.5	24.70	20	102.38	31.03	10	1.8%	-0.07 [-0.74, 0.60]	2008	
Huuuy 2009 Monning 2000	91.2	13.3	33	98.9	1.4	24	2.1%	-0.08 [-1.22, -0.14]	2009	
Manfillig 2009	99.5	9.3	30	101	9.4	3U 44	2.2%	-0.10[-0.07, 0.35]	2009	
Molecek 2009	30.4	9.8	55	35.4	8.7	44	2.5%	-0.53 [-0.94, -0.13]	2009	
Majorek 2009 Decesh Elu 2000	102.5	13.3	38	111.1	13.4	29	2.2%	-0.64 [-1.13, -0.14]	2009	
RUESCH-EIV 2009	109.07	12.11	50	120.92	12.91	40	Z.4%	-0.92 [-1.35, -0.48]	2009	

1.8%

17

1519 100.0%

Figure 11 Premorbid IQ.

Test for overall effect: Z = 8.23 (P < 0.00001)

of only a specific memory measure cuts the heterogeneity to a much less amount (from around 90% when put together to about 80% when separated by memory model and to 50% when using a single type of measure). In synthesis, these results show that, without a question, there is a reduction in memory functioning among the patients with schizophrenia, whatever the method of examination. They also demonstrate that, at least for memory functioning, it would be preferable, in the future research activity, to identify a specific method of measurement to be adopted on the basis of research

92.7

Heterogeneity: Tau<sup>2</sup> = 0.15; Chi<sup>2</sup> = 154.72, df = 47 (P < 0.00001); l<sup>2</sup> = 70%

12.1

20

2049

97.8 10.3

hypotheses and feasibility of use in this clinical area, with respect to the current practice of evaluating memory functioning with whatever task is occasionally available at the moment. The heterogeneity would be greatly reduced and the results would be much more informative.

. 4

-2

Ó worse than controls better than controls

#### Global cognitive functioning

-0.44 [-1.10, 0.21] 2009

-0.57 [-0.70, -0.43]

This area was evaluated in general, by IQ measures (102 works, 8,416 total cases). The ES is -0.96 [-1.07, -0.85] with  $I^2 = 80\%$  and PS = 75%. When outpatients' and inpatients' results are separated and analyzed, the former

	Schizor	phrenia a	roup	Health	v contr	ols		Std. Mean Difference		Std. Mean Difference
Study or Subgrou	o Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% Cl	Year	IV, Random, 95% Cl
1.3.1 Verbal Tasks	6									
Green 1985	90.28	4.11	44	95.36	1	12	1.2%	-1.36 [-2.04, -0.67]	1985	
Goldberg 1990	9.4	2.8	16	12.5	3.5	7	0.9%	-0.99 [-1.93, -0.05]	1990	
Morice 1990	7.8	3.4	60 4 7	10.4	3.3	34	1.6%	-0.77 [-1.20, -0.33]	1990	
Earle Boyer 1991 Frith 1991	18.29	1.9	283	12.23	0.01	19	1.1%	-1.28 [-2.01, -0.56]	1991	
Braff 1991	95.18	14.91	203	104.6	14.52	40	1.6%	-0.63[-1.080.18]	1991	
Myles-Worsley 19	0.37	0.22	20	0.42	0.2	20	1.3%	-0.23 [-0.86, 0.39]	1991	
Hoff 1992	51.5	5.2	26	54.8	3.7	25	1.4%	-0.72 [-1.29, -0.15]	1992	
Verdoux 1994	10.25	2.63	16	12.87	3.22	16	1.1%	-0.87 [-1.60, -0.14]	1994	
Paulsen 1994	0.49	0.65	20	0.94	0.19	30	1.3%	-1.02 [-1.62, -0.42]	1994	
Haskins 1995	11.64	3.5	47	13.04	2.4	51	1.7%	-0.47 [-0.87, -0.06]	1995	
Cantor-Graae 199	5 31	12.6	14	40.9	6.9	14	1.0%	-0.95 [-1.73, -0.16]	1995	
Miller 1995	22	16	30	36	25	27	1.4%	-0.67 [-1.20, -0.13]	1995	
Mirsky 1995	7.1	3.4	22	10	2.1	42	1.4%	-1.10[-1.65, -0.54]	1995	
Goldberg 1998	-0.07	1.73	40	1122	1.43	23	1.470	-1.01 [-1.55, -0.46]	1990	
Kunerberg 1998	12.74	3	23	112.2	10.5	10	1.0%	-1 42 [-2 22 -0.62]	1998	
Stone 1998	1.67	0.91	18	3.27	1.1	15	1.0%	-1.56 [-2.35, -0.77]	1998	
Hoffman 1999	81.7	16.5	21	95.6	5.5	26	1.3%	-1.16 [-1.79, -0.54]	1999	
Docherty 1999	97.71	1.94	43	99.41	0.28	23	1.4%	-1.06 [-1.60, -0.52]	1999	
Arango 1999	33.2	11.2	85	41.6	11.1	36	1.7%	-0.75 [-1.15, -0.35]	1999	
Sarfati 1999	21.65	4.3	26	25.9	1.4	13	1.1%	-1.15 [-1.87, -0.43]	1999	
Rossell 1999	48.16	13.46	74	64.7	18.5	31	1.6%	-1.09 [-1.53, -0.64]	1999	
Harvey 2000	7.42	5.03	165	16.67	5.09	165	1.9%	-1.82 [-2.08, -1.57]	2000	
Glann 2000	34.1	12.7	62	47.8	8.7	62	1.7%	-1.25 [-1.64, -0.86]	2000	
Riley 2000	30.03	11.02	40	43.7	10.58	24	1.0%	-0.00[-1.10,-0.21]	2000	
Gur 2000	37.3	12.4	53	45.55	10.20 N 4	71	1.4%	-1.45 [-2.04, -0.07]	2000	
Danion 2001	48.7	11.6	48	62.1	9.6	24	1 4 %	-1 21 [-1 74 -0 68]	2001	
Egan 2001	34.4	11.8	120	45.2	10	43	1.7%	-0.95 [-1.31, -0.58]	2001	
Broerse 2001	17.22	3.08	24	22.05	6.38	20	1.3%	-0.98 [-1.61, -0.35]	2001	
Kiefer 2002	17.62	5.34	24	24.63	6.32	24	1.3%	-1.18 [-1.80, -0.56]	2002	
Tendolkar 2002	16.86	4.3	14	30.25	6.6	14	0.8%	-2.33 [-3.33, -1.34]	2002	
Vinogradov 2002	-0.52	1.2	40	0.12	1.1	16	1.3%	-0.54 [-1.13, 0.05]	2002	
Wilk 2002	84.73	14.85	181	105.69	14.23	99	1.9%	-1.43 [-1.70, -1.16]	2002	
Ojeda 2002 Minzenhera 2002	32.1	10.08	11	50.2	9.93	10	0.8%	-1.74 [-2.77, -0.70]	2002	
Minzenberg 2003	-0.33	0.98	57	0.23	0.87	20	1.5%	-0.58 [-1.10, -0.06]	2003	
Giovannetti 2003	45.7	9.13	47	41.02	0.70	21	1.2.70	-1.70[-2.40,-0.99]	2003	
Keefe 2004	10.53	4.16	137	14.4	4.88	50	1.8%	-0.88 [-1.22, -0.55]	2004	
Al-Uzri 2004	15.83	4.41	12	20.83	6.44	12	1.0%	-0.87 [-1.72, -0.03]	2004	
Altshuler, 2004	30.2	7.7	20	52.2	9.8	22	1.0%	-2.43 [-3.25, -1.62]	2004	
Baldeweg 2004	30.5	18.1	28	43.4	13.3	20	1.3%	-0.78 [-1.38, -0.18]	2004	
van Beilen 2004	18.58	4.12	50	26.24	6.76	25	1.4%	-1.47 [-2.01, -0.94]	2004	
Muller 2004	28.81	11.2	100	34.9	9.3	62	1.8%	-0.58 [-0.90, -0.25]	2004	
Dragovic 2005	29.02	9.97	157	38.98	10.42	11	1.9%	-0.98 [-1.27, -0.69]	2005	
Alptekin 2005	29.4	14.27	38 51	30.05	14.92	31	1.5%	-0.49 [-0.97, -0.01]	2005	
Leeson 2005	65.96	15 55	56	89.46	16 32	24	1.7%	-1 47 [-2 01 -0.94]	2005	
Kopelowicz 2005	34.15	11.36	56	38.5	7.7	26	1.5%	-0.42 [-0.89, 0.05]	2005	
Kosmidis 2005	23.55	10.18	42	42.55	8.55	42	1.4%	-2.00 [-2.53, -1.47]	2005	
Brazo 2005	22.8	5.7	56	26.2	4.1	56	1.7%	-0.68 [-1.06, -0.30]	2005	
Chino 2006	22.7	7.8	36	28	8.6	25	1.5%	-0.64 [-1.17, -0.12]	2006	
Stirling 2006	22.97	7.54	30	41.33	4.54	18	1.0%	-2.74 [-3.56, -1.92]	2006	
Menzies 2007	12.1	4.2	11	17.3	5.8	11	0.9%	-0.99 [-1.88, -0.09]	2007	
Burbridge 2007	1.1	3	49	11.6	3.2	47	1.6%	-1.25 [-1.69, -0.81]	2007	
Cuesta 2007 Parrantee-Vidal 20	10.4	4.07	601	21.09	0.05	62	1.0%	-1.00[-1.49,-0.04]	2007	
Denn 2007	29.2	4.7	150	39.2	4.5	85	1.0%	-0.83 [-1.11 -0.55]	2007	
Heinrichs 2008	17.84	5.37	151	20.01	5.33	72	1.9%	-0.40[-0.69]-0.12]	2008	
D'Argembeau 200	8 19.6	4.1	16	24.5	6	16	1.1%	-0.93 [-1.66, -0.20]	2008	
Bora 2008	39.2	9.2	30	41.2	14	30	1.5%	-0.17 [-0.67, 0.34]	2008	-+
Brissos 2008	15.48	3.58	23	17.17	3.54	23	1.3%	-0.47 [-1.05, 0.12]	2008	
Wang 2008	19.59	5.36	54	20.08	5.53	54	1.7%	-0.09 [-0.47, 0.29]	2008	-+
Leonard 2008	92	16	34	110	16	34	1.5%	-1.11 [-1.63, -0.60]	2008	
Matsui 2008	27.9	8	53	38.9	5.9	31	1.5%	-1.49 [-1.99, -0.99]	2008	
Pino 2008 Boocoll 2008	14.34	5.4	124	20.44	5.22	39	1.7%	-1.13[-1.51,-0.75]	2008	
RUSSEII 2008	49.7	20.4	3Z 54	22.0	10.77	3Z //1	1.4%	-1.20[-1.80,-0.72]	2008	
Manning 2009	20.00	4.2	30	20.2	52	30	1.5%	-0.75 [-1.28 -0.23]	2003	
Subtotal (95% CI)	10.0	7.2	3962	20.2	5.2	2434	100.0%	-0.99 [-1.10, -0.87]	2000	•
Heterogeneity: Tau	1 <sup>2</sup> = 0.16; Chi <sup>2</sup> =	262.53,	df = 69 (F	o < 0.000	01); I² =	74%				
Test for overall effe	ect: Z = 16.99 (F	• < 0.0000	01)							
										-4 -2 0 2 4
										worse than controls better than controls
Figure 12 Verbal func	tioning.									

	Schizop	ohrenia g	roup	Health	y contro	ls		Std. Mean Difference		Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% Cl	Year	IV, Random, 95% Cl
1.4.1 Measures of Flexil	bility					10.5	N 1000000		600070752	
Morice 1990	7.2	3	60	10.4	3.2	34	1.6%	-1.03 [-1.48, -0.59]	1990	~
Goldberg 1990	2.8	2.5	16	7.7	1.4	7	1.0%	-2.11 [-3.22, -1.00]	1990	
Rief 1991	78.3	25.4	24	95.9	4.5	24	1.5%	-0.95 [-1.55, -0.35]	1991	-
Schwartz 1991	3.8	2	16	5.5	1.3	16	1.4%	-0.98 [-1.72, -0.24]	1991	
Braff 1991	4.8	1.92	40	5.58	1.2	40	1.6%	-0.48 [-0.93, -0.04]	1991	~
Hoff 1992	4	2.5	26	5.8	8	25	1.5%	-0.30 [-0.85, 0.25]	1992	-
Corrigan 1992	0.66	0.26	30	0.93	0.09	15	1.4%	-1.21 [-1.88, -0.54]	1992	~
Verdoux 1994	4 61	1.6	13	5.76	0.59	13	1.3%	-0.92[-1.740.11]	1994	
Parellada 1994	4 33	3.2	6	8.67	2.8	6	0.9%	-1 33 [-2 64 -0 03]	1994	
Paulcan 1004	0.2	0.2	20	0.96	0.31	30	1 5%	-1 31 [-1 93 -0 69]	1004	
Mirely 1005	27.1	120	16	60.6	15.4	41	1 / 06	-1.51[-1.33,-0.00]	1005	
Mirsky 1990	37.1	12.0	10	39.5	10.4	41	1.4%	-1.50 [-2.14, -0.65]	1995	
Cantor-Graae 1995	28.4	8.0	14	32	8.3	14	1.4%	-0.41 [-1.16, 0.34]	1995	
Shelley 1996	65.6	9.7	11	82.2	7.5	13	1.1%	-1.87 [-2.86, -0.88]	1996	
Smith 1998	-3.49	5.59	24	1.84	7.11	24	1.5%	-0.82 [-1.41, -0.23]	1998	-
Perlstein 1998	29	9	55	49	11	24	1.5%	-2.05 [-2.64, -1.47]	1998	-
Michel 1998	5.45	0.89	26	5.7	0.7	26	1.5%	-0.31 [-0.85, 0.24]	1998	-1
Hoff 1998	2.85	2.03	132	5.65	0.86	74	1.7%	-1.64 [-1.96, -1.31]	1998	~
Goldberg 1998	4.79	3.27	23	8	2.7	23	1.5%	-1.05 [-1.67, -0.43]	1998	-
Brankovic 1999	2.09	2.35	29	3.04	1.49	35	1.6%	-0.49 [-0.99, 0.01]	1999	~
Sarfati 1999	18.65	6.11	26	24.4	2.3	13	1.4%	-1.09 [-1.80, -0.37]	1999	~
Arango 1999	42.6	14.1	85	62.8	13.7	36	1.6%	-1.44 [-1.871.00]	1999	-
Cadenhead 1999	47	22	20	5.6	n q	20	1 4 %	-0.82 [-1 46 -0 17]	1999	
Resche-Richard 1000	11.4	2.4 g a	20	16	9.J	19	1.6%	-0.18[-0.62 0.24]	1900	4
Weickert 2000	1 20	200	117	0	0.4	90	1.0.70	-1.21 [4.77 -0.94]	2000	~
Dilau 2000	4.20	2.09	117	0 5 0 5	4.07	24	1.0 %	-1.31 [-1.77, -0.04]	2000	
Riney 2000	2.9	1.97	40	5.05	1.27	22	1.5%	-1.21 [-1.77, -0.64]	2000	
Saoud 2000	5	2	18	б	0.0001	15	1.4%	-0.66 [-1.36, 0.05]	2000	
Gold 2000	22.32	10.52	37	33.45	5.43	20	1.5%	-1.21 [-1.80, -0.62]	2000	-
Glahn 2000	3.9	2.2	62	5.29	1.5	62	1.7%	-0.73 [-1.10, -0.37]	2000	~
Fucetola 2000	2.69	2.22	87	5.35	1.45	94	1.7%	-1.42 [-1.75, -1.10]	2000	~
Perry 2001 study 3	4.4	1.8	40	5.2	1.6	40	1.6%	-0.47 [-0.91, -0.02]	2001	~
Gur 2001	3.8	2.9	53	6	2.2	71	1.7%	-0.87 [-1.24, -0.49]	2001	~
Stratta 2001	3.82	2.42	25	4.94	1.76	35	1.5%	-0.54 [-1.06, -0.01]	2001	~
Egan 2001	40.2	11.1	120	54.7	9.5	43	1.7%	-1.35 [-1.73, -0.97]	2001	~
Perry 2001 study 4	1.6	12	37	33	14	34	1.6%	-1 29 [-1 81 -0 78]	2001	-
Gooding 2002	2.56	2	34	5.23	1.6	30	1.5%	-1 45 [-2 00 -0 89]	2007	
Longor 2002	2.50	- 0.66	20	3.23	0.00	26	1.570	1143[-2.00,-0.03]	2002	-
Lanser 2002	0.76	0.00	- 39 60	2.39	0.00	30	1.0 %	-1.14 [-1.03, -0.00]	2002	
Hugnes 2002	3.70	2.24	02	4.95	1.89	25	1.0%	-0.55 [-1.02, -0.08]	2002	
Brazo 2002	3.92	1.45	35	5.4	1.1	35	1.6%	-1.14 [-1.64, -0.63]	2002	-
Woonings 2002	3.4	1.4	44	4.2	1	79	1.7%	-0.69 [-1.07, -0.31]	2002	~
Ojeda 2002	4.22	2.22	11	5.5	0.76	10	1.2%	-0.73 [-1.62, 0.16]	2002	-1
Kim 2003	3.55	2.34	22	5.33	1.68	21	1.5%	-0.85 [-1.48, -0.23]	2003	
Evans 2003	6.5	2.4	93	8.6	1.9	73	1.7%	-0.95 [-1.28, -0.63]	2003	-
Silver 2003	20.91	4	27	24.14	1.46	38	1.5%	-1.14 [-1.67, -0.61]	2003	-
Minzenberg 2003	-0.2	1.07	57	0.4	0.16	20	1.5%	-0.64 [-1.16, -0.12]	2003	~
Yogev 2004	11.75	3.84	41	14.3	0.98	24	1.5%	-0.81 [-1.33, -0.28]	2004	~
Hill 2004	-1 2	0.07	86	-0.04	0.72	81	1 7%	-1 35 [-1 68 -1 01]	2004	-
Veefe 2004	2.02	1.50	117	3.03	1.65	50	1 7 %	-0.62 [-0.06 -0.28]	2004	~
Altobulor 2004	2.00	1.00	20	5.05	1.00	20	1 4 04	1 07 [ 2 61 1 1 4]	2004	
Altshuler, 2004	2.4	2.2	20	0.0	0.0	22	1.470	-1.07 [-2.01, -1.14]	2004	
H011 2005	30.5	15.5	51	43.5	9.8	74	1.7%	-0.56 [-0.92, -0.20]	2005	
Kopelowicz 2005	2.8	1.36	56	3.6	1.5	26	1.6%	-0.56 [-1.04, -0.09]	2005	1
Brazo 2005	4.4	1.4	56	5.3	1.1	56	1.7%	-0.71 [-1.09, -0.33]	2005	~
Stirling 2006	50	13.98	30	68.67	8.87	18	1.4%	-1.49 [-2.15, -0.83]	2006	~
Torres 2007	8.357	4.923	50	15.447	4.594	40	1.6%	-1.47 [-1.94, -1.00]	2007	~
Henry 2007	35.1	10.85	30	42.3	13.37	29	1.5%	-0.58 [-1.11, -0.06]	2007	-
Lee 2007	1.9	0.3	68	6	0.3	95	0.8%	-13.60 [-15.13, -12.08]	2007	
Kessler 2007	14.42	2.36	20	17.29	1.24	28	1.4%	-1.58 [-2.24, -0.92]	2007	
Kiang 2007	2.6	1.5	18	3.1	1.5	18	1.4%	-0.33 [-0.98, 0.33]	2007	-+
Cavézian 2007	0.5	0.85	10	4 1	3.38	10	1.1%	-1.40 [-2.40 -0.40]	2007	
Bertrand 2007	-81 57	37 69	36	-63.6	14.6	27	1.6%	-0.59 [-1.10 -0.08]	2007	-
Wong 2009	4.26	51.05	54	4 70	1 00	54	1 706	-0.27 [-0.65 0.11]	2007	
Nector 2000	4.20	24	24	6 4 3	1.03	204	1.0	-0.27 [0.00, 0.11]	2000	4
Ohmone 2000	4.08	2.1	20	3.12	1.01	28	1.0%	-0.00 [-1.10, -0.00]	2008	
Onrmann 2008	42.9	9.8	43	48.8	1.2	37	1.6%	-0.67 [-1.12, -0.22]	2008	
Midorikawa 2008	2.1	2.17	27	4.1	1.98	49	1.6%	-0.97 [-1.46, -0.47]	2008	~
Moritz 2008	4.56	1.82	68	5.36	1.47	25	1.6%	-0.46 [-0.92, 0.01]	2008	7
Braw 2008	7.11	0.31	38	8.62	0.26	44	1.2%	-5.26 [-6.20, -4.33]	2008	
Leeson 2009	7.2	2.56	97	8.64	1.78	97	1.7%	-0.65 [-0.94, -0.36]	2009	~
Manning 2009	5.8	2.3	30	7.3	2.3	30	1.5%	-0.64 [-1.16, -0.12]	2009	-
Subtotal (95% CI)			2867			2390	100.0%	-1.10 [-1.27, -0.92]		1
Heterogeneity: Tau <sup>2</sup> = 0.4	45: Chi <sup>2</sup> =	530.31. d	f = 66 (P	< 0.0000	1): <b>I<sup>2</sup> = 8</b>	8%				
Test for overall effect: 7 =	12.18 (P	< 0.0000	1)	2.0000						
. cottor overall ellett. Z =	. 2.10 ()*	0.0000	.,							
										-10 -5 0 5 10
										-10 -5 0 5 10 worse than controls better than controls

Study or Subaroun	Schizop Mean	hrenia gr sn	oup Total	Healthy	control:	S Total	Weight	Std. Mean Difference	Year	Std. Mean Difference M. Random, 95% Cl
1.5.1 Reaction Time	wean	50	Total	wean	30	rotal	weight	iv, ranuom, 95% Cl	real	
Goldberg 1990	62.3	173	16	38.6	7.9	7	0.0%	0.97 60 06 1 90	1000	
Grillon C 1990	525.3	73.2	15	132.0	73.6	15	1 1 96	1 36 10 55 2 161	1000	
Uid 1001	000.0	104	10	432.8	13.0	10	0.00	1.30 [0.33, 2.10]	1004	
HILLISSI Van Dan Daash 4000	000	184	10	303	90	10	0.8%	2.06 [0.93, 3.16]	1991	
Van Den Bosch 1992	498	83	30	458	12	21	1.4%	0.50 [-0.07, 1.07]	1992	
Carter 1992	890	260.7	13	692.7	83.3	11	1.0%	0.95 (0.09, 1.80)	1992	
Hoff 1992	202.6	86.5	26	139.4	51.9	25	1.4%	0.87 [0.29, 1.44]	1992	
Weiss K.M. 1992	100	41.1	18	62.7	15.1	13	1.1%	1.10 [0.33, 1.87]	1992	
Laplante 1992	1,810	389	10	1,021	224	35	0.9%	2.90 [1.96, 3.84]	1992	
Strik 1993	363.8	45	22	334.9	37.2	22	1.3%	0.69 [0.08, 1.30]	1993	
Penn 1993	343.5	87.1	31	263.4	21.9	31	1.4%	1.25 [0.70, 1.79]	1993	
Kurachi 1994	10	3.6	12	9.6	2.3	12	1.1%	0.13 [-0.67, 0.93]	1994	
Cantor-Graae 1995	28.8	6.05	14	21.8	2.4	14	1.0%	1.48 [0.63, 2.33]	1995	
Park S 1995	1,210	695	18	683	234	18	1.2%	0.99 [0.30, 1.69]	1995	
Schreiber 1995	1.276	563.4	21	822	268.7	22	1.3%	1.02 (0.38, 1.66)	1995	
Ober 1995	711	105	19	644	113	22	1.3%	0.60 (-0.03, 1.23)	1995	
Mirsky 1995	523.5	76.1	23	4421	46.1	43	1 4 %	1 38 [0 82 1 94]	1995	
Javitt 1995	556	77 95	31	430	26.53	11	1 1 96	1 80 [1 00 2 59]	1995	
Sereno 1006	504	110.57	17	264	27.42	1.4	1 1 96	1.60 [1.00, 2.00]	1006	
Dehinowicz 1006	067.67	471.10	24	664.74	226.7	20	1 406	0.77 [0.24 1.20]	1006	
Rabinowitz 1990	257.0	971.12	24	550.0	323.7	30	1.470	4.04 [0.24, 1.30]	1990	
Comith 1000	101.9	243.2	24	009.0	14.04	20	1.3%	1.04 [0.40, 1.67]	1997	
Omili 1998 Devictoria 4000	50.03	20.95	24	29.41	14.81	24	1.3%	1.24 [0.62, 1.86]	1998	
reristein 1998	1,049	201	55	815	180	24	1.4%	1.19 (0.67, 1.70)	1998	
ноп 1998	189.98	110.02	132	59.31	28.23	74	1.7%	1.45 [1.13, 1.77]	1998	~
Fucetola 1999 study 2	563	66.3	20	472	57.9	20	1.2%	1.43 [0.73, 2.14]	1999	
Fucetola 1999 study 1	510	32.6	20	483	38.2	20	1.3%	0.75 [0.10, 1.39]	1999	<u> </u>
Stratta 1999	1,770.3	647	25	1,023.4	175.6	25	1.3%	1.55 [0.91, 2.19]	1999	
Glahn 2000	102.9	85.6	62	48.6	10.2	62	1.6%	0.89 [0.52, 1.25]	2000	
Fucetola 2000	52.8	29.53	87	28.49	11.68	94	1.7%	1.09 [0.78, 1.41]	2000	
Elvevag 2000b	379	107	20	323	52	30	1.3%	0.70 [0.12, 1.29]	2000	<u>├</u> ~
Riley 2000	45.31	19.41	40	28.82	8.69	22	1.4%	0.99 [0.44, 1.54]	2000	
Broerse 2001	516 58	93.77	24	441.85	65 94	20	1.3%	0.89 (0.27, 1.52)	2001	
Zuffante 2001	1 172 65	407.65	23	1 016 7	265 52	23	1 3 %	0 45 [-0 14 1 03]	2001	
Stirling 2001	477	128.04	40	411	65 76	36	1.5%	0.63 (0.17, 1.00)	2001	
Dorry 2001 study 4	224.0	62.6	27	1727	202.70	37	1.570	1 10 [0 60 1 60]	2001	
Perly 2001 Study 4	234.9	4444	37	570	102.3	37	1.0 %	0.76 (0.05, 1.00)	2001	
Peristein 2001	007.4	114.4	17	3/2	103.2	10	1.2%	0.76 [0.05, 1.47]	2001	
Montz 2001	813.7	184.1	20	763.9	114.3	20	1.3%	0.32 [-0.31, 0.94]	2001	-
Gur 2001	104.8	71.1	53	53.5	17.5	71	1.6%	1.06 [0.68, 1.44]	2001	~
Chey 2002	1,296	411	15	897	240	16	1.1%	1.16 [0.39, 1.93]	2002	
Brazo 2002	98.12	64.89	35	31.8	17	35	1.4%	1.38 [0.86, 1.91]	2002	
Vinogradov 2002	651	145	40	579	82	16	1.3%	0.54 [-0.05, 1.13]	2002	-
Hartman 2002	2,163	457	16	421	473	16	0.7%	3.65 [2.47, 4.83]	2002	
Surguladze 2002	1,120	387.5	20	639.5	113.9	26	1.2%	1.76 [1.06, 2.45]	2002	
Oieda 2002	428.75	84.4	11	420.81	65.4	10	1.0%	0.10 (-0.76, 0.96)	2002	
Hughes 2002	454.66	107.21	62	396.45	68.69	25	1.5%	0.59 (0.12, 1.06)	2002	
Gooding 2002	633.04	160.61	34	581 56	157.7	30	1.5%	0.32 -0.17 0.811	2002	<u>+</u> -
Tek 2002	602	1 083	30	100	130	20	1 3 96	0.68 (0.10, 1.26)	2002	
MacDonald 2002	546	07	24	/10	02	20	1 206	1 42 [0 94 2 00]	2002	
MeNooly 2002	067	245	10	670	00	12	1.0%	1.42 [0.04, 2.00]	2003	
Kime 2002	5000	240	13	27.05	24.04	13	1.0%	1.00 [0.07, 2.40]	2003	
Nini 2003	03.82	22.30	22	37.95	24.04	21	1.3%	0.67 [0.06, 1.29]	2003	Ľ
Hoimausen 2003	38.13	38.88	118	20.71	25.13	45	1.0%	0.32 [-0.03, 0.66]	2003	
Giovannetti 2003	108.9	59.6	47	61.4	29.6	30	1.5%	0.94 [0.45, 1.42]	2003	
Barch 2003	510	130	42	418	88	72	1.6%	0.87 [0.47, 1.26]	2003	
Ueno 2004	433.6	78.8	32	436.5	68.67	32	1.5%	-0.04 [-0.53, 0.45]	2004	+
Kim 2004	1,022.3	183.5	16	977.8	179.3	16	1.2%	0.24 [-0.46, 0.93]	2004	+-
Altshuler, 2004	53.9	23.3	20	34.5	12.6	22	1.3%	1.03 [0.38, 1.68]	2004	
Muller 2004	51.18	33.7	100	28.75	10.23	62	1.6%	0.82 [0.49, 1.15]	2004	~
Mathews 2004	1,140	419	27	1,066	285	28	1.4%	0.20 [-0.33, 0.73]	2004	+
Dragovic 2005	40.51	15.54	157	37.14	13.28	77	1.7%	0.23 [-0.05, 0.50]	2005	t-
Brazo 2005	101.6	67.5	56	40	17.2	56	1.6%	1.24 [0.84, 1.65]	2005	
Symond 2005	384.6	106 2	40	309.6	41.4	40	1.5%	0.92 [0.46.1.38]	2005	
Birkett 2006	575.5	293.8	15	302.7	43.6	15	1 1 94	1.26 (0.47 2.06)	2006	
Stirling 2006	100.0	62.60	20	59.12	11 260	10	1 204	1.20 [0.47, 2.00]	2000	
Cupeto 2007	62.62	20 72	100	37.32	12.04	10	1.370	0.0210.64 4.351	2000	
Achim 2007	03.03	20.72	109	37.23	13.01	20	1.0%	0.00 [0.01, 1.00]	2007	1
Dopp 2007	54.5	10.7	20	32.9	9.8	20	1.3%	0.13 [-0.45, 0.72]	2007	
Depp 2007	54.7	31	150	33.8	13.1	85	1.7%	0.80 [0.53, 1.08]	2007	
Babin 2007	950.88	227.18	20	677.29	88.55	20	1.2%	1.56 [0.84, 2.27]	2007	
Birkett 2007	397	115	61	314	59	47	1.6%	0.87 [0.47, 1.27]	2007	
Kerns 2007	286.6	145.8	47	182.3	50.9	30	1.5%	0.87 [0.39, 1.35]	2007	
Bertrand 2007	36.09	11.64	36	32.92	9.13	27	1.4%	0.29 [-0.21, 0.80]	2007	<u>+-</u>
Luck 2008	1,891.85	419.41	19	1,534.18	303.6	19	1.2%	0.96 [0.28, 1.63]	2008	
Braw 2008	1,011.74	57.89	39	707.38	13.75	44	0.7%	7.37 [6.15, 8.60]	2008	
Brissos 2008	49.39	23.61	23	34.78	11.82	23	1.3%	0.77 [0.17, 1.37]	2008	
Smid 2009	857	101	16	690	126	16	11%	1.43 [0.64 2.21]	2009	
Roiser 2009	201 A	07	20	247	120 E	224	1 504	1 46 10 00 1 041	2003	
1101361 2003	447.0	56.0	20	1241	21 62	40	1.0%	0.55 (0.33, 1.34)	2009	L
Rosech-Ely 2000	447.9	120.04	00	421.70	0744	40	1.0%	0.00 [0.12, 0.97]	2009	
Roesch-Ely 2009	/	1.511114	61	526	97.14	61	1.0%	0.55 [0.19, 0.91]	2009	
Roesch-Ely 2009 Karch 2009 Subtotal (95% CI)	589.7	100.01	2952			2/04	100 007	0 00 10 06 4 4 31		
Roesch-Ely 2009 Karch 2009 Subtotal (95% CI)	589.7		2852			2481	100.0%	0.99 [0.86, 1.12]		•
Roesch-Ely 2009 Karch 2009 Subtotal (95% CI) Heterogeneity: Tau <sup>2</sup> = 0.2	589.7 4; Chi <sup>2</sup> = 3	23.63, df=	<b>2852</b> = 75 (P <	0.00001);1	l² = 77%	2481	100.0%	0.99 [0.86, 1.12]		,
Roesch-Ely 2009 Karch 2009 <b>Subtotal (95% CI)</b> Heterogeneity: Tau <sup>2</sup> = 0.2 Test for overall effect: Z =	589.7 4; Chi² = 3 14.90 (P <	23.63, df=	2852 = 75 (P <	0.00001);1	l²= 77%	2481	100.0%	0.99 [0.86, 1.12]		,

Figure 14 Reaction time.

	Healthy	/ control	s	:	Std. Mean Difference					
Study or Subgroup	pup Mean SD Total Mean SD Total Weight IV, Random,		IV, Random, 95% Cl	Year	IV, Random, 95% Cl					
1.5.2 Attention (inpatiens only)										
Hirt 1991	668	184	10	353	96	10	4.2%	2.06 [0.93, 3.18]	1991	
Weiss K.M. 1992	100	41.1	18	62.7	15.1	13	5.1%	1.10 [0.33, 1.87]	1992	
Laplante 1992	1,810	389	10	1,021	224	35	4.7%	2.90 [1.96, 3.84]	1992	
Penn 1993	343.5	87.1	31	263.4	21.9	31	5.6%	1.25 [0.70, 1.79]	1993	-
Besche 1997	757.9	243.2	24	559.6	80.7	20	5.4%	1.04 [0.40, 1.67]	1997	
Perlstein 1998	1,049	201	55	815	180	24	5.6%	1.19 [0.67, 1.70]	1998	-
Stratta 1999	1,770.3	647	25	1,023.4	175.6	25	5.4%	1.55 [0.91, 2.19]	1999	
Elvevag 2000b	379	107	20	323	52	30	5.5%	0.70 [0.12, 1.29]	2000	
Stirling 2001	477	128.94	40	411	65.76	36	5.7%	0.63 [0.17, 1.09]	2001	
Moritz 2001	813.7	184.1	20	763.9	114.3	20	5.4%	0.32 [-0.31, 0.94]	2001	+
Ojeda 2002	428.75	84.4	11	420.81	65.4	10	4.9%	0.10 [-0.76, 0.96]	2002	+
Hartman 2002	2,163	457	16	421	473	16	4.1%	3.65 [2.47, 4.83]	2002	
Holthausen 2003	38.13	38.88	118	26.71	25.13	45	5.9%	0.32 [-0.03, 0.66]	2003	-
Giovannetti 2003	108.9	59.6	47	61.4	29.6	30	5.7%	0.94 [0.45, 1.42]	2003	
Muller 2004	51.18	33.7	100	28.75	10.23	62	5.9%	0.82 [0.49, 1.15]	2004	*
Dragovic 2005	40.51	15.54	157	37.14	13.28	77	6.0%	0.23 [-0.05, 0.50]	2005	-
Babin 2007	950.88	227.18	20	677.29	88.55	20	5.2%	1.56 [0.84, 2.27]	2007	
Braw 2008	1,011.74	57.89	39	707.38	13.75	44	4.0%	7.37 [6.15, 8.60]	2008	
Roesch-Ely 2009	447.9	56.9	50	421.75	31.63	40	5.8%	0.55 [0.12, 0.97]	2009	
Subtotal (95% CI)			811			588	100.0%	1.34 [0.93, 1.76]		•
Heterogeneity: Tau <sup>2</sup> = 0	1.74; Chi <sup>2</sup> = 2	03.32, df=	= 18 (P <	0.00001);	l² = 91%					
Test for overall effect: Z	= 6.29 (P < I	0.00001)								
										-4 -2 0 2 4
										better than controls worse than control

group has an ES = -0.83 [-1.00, -0.66] I<sup>2</sup> 69%, PS 72% while the latter group has an ES = -1.04 [-1.25, -0.82], I<sup>2</sup> 77%, PS 77%. These results show how the cognitive impairment is generic and diffuse among the patients with schizophrenia, in at least 3 patients out of 4, and it is

not dependent on the severity of the disease (inpatients and outpatients do not differ very much in their results concerning the IQ).

The data concerning the premorbid IQ, are in general measured by NART or WRAT or using specific subtests

Schizophrenia			oup	Healthy	Healthy controls			Std. Mean Difference		Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% Cl	Year	IV, Random, 95% Cl
1.5.3 Attention (outpat	ients only)									
Carter 1992	890	260.7	13	692.7	83.3	11	4.1%	0.95 (0.09, 1.80)	1992	
<urachi 1994<="" td=""><td>10</td><td>3.6</td><td>12</td><td>9.6</td><td>2.3</td><td>12</td><td>4.3%</td><td>0.13 [-0.67, 0.93]</td><td>1994</td><td>+</td></urachi>	10	3.6	12	9.6	2.3	12	4.3%	0.13 [-0.67, 0.93]	1994	+
Park S 1995	1,210	695	18	683	234	18	4.6%	0.99 [0.30, 1.69]	1995	
Ober 1995	711	105	19	644	113	22	4.8%	0.60 [-0.03, 1.23]	1995	
Smith 1998	56.03	25.95	24	29.41	14.81	24	4.8%	1.24 [0.62, 1.86]	1998	-
ucetola 2000	52.8	29.53	87	28.49	11.68	94	5.5%	1.09 [0.78, 1.41]	2000	+
Perlstein 2001	657.4	114.4	17	572	103.2	16	4.5%	0.76 [0.05, 1.47]	2001	
razo 2002	98.12	64.89	35	31.8	17	35	5.1%	1.38 [0.86, 1.91]	2002	-
lughes 2002	454.66	107.21	62	396.45	68.69	25	5.2%	0.59 [0.12, 1.06]	2002	-
Fooding 2002	633.04	160.61	34	581.56	157.7	30	5.1%	0.32 [-0.17, 0.81]	2002	+-
ek 2002	692	1,083	30	109	130	20	4.9%	0.68 [0.10, 1.26]	2002	
inogradov 2002	651	145	40	579	82	16	4.9%	0.54 [-0.05, 1.13]	2002	-
IcNeely 2003	967	245	13	672	83	13	4.0%	1.56 [0.67, 2.46]	2003	
1athews 2004	1,140	419	27	1,066	285	28	5.0%	0.20 [-0.33, 0.73]	2004	+
(im 2004	1,022.3	183.5	16	977.8	179.3	16	4.6%	0.24 [-0.46, 0.93]	2004	+
ltshuler, 2004	53.9	23.3	20	34.5	12.6	22	4.7%	1.03 [0.38, 1.68]	2004	
Brazo 2005	101.6	67.5	56	40	17.2	56	5.3%	1.24 [0.84, 1.65]	2005	-
ymond 2005	384.6	106.2	40	309.6	41.4	40	5.2%	0.92 [0.46, 1.38]	2005	+
Depp 2007	54.7	31	150	33.8	13.1	85	5.6%	0.80 [0.53, 1.08]	2007	+
3raw 2008	1,011.74	57.89	39	707.38	13.75	44	3.1%	7.37 [6.15, 8.60]	2008	
_uck 2008	1,891.85	419.41	19	1,534.18	303.6	19	4.6%	0.96 [0.28, 1.63]	2008	
Subtotal (95% CI)			771			646	100.0%	1.02 [0.70, 1.34]		♦
leterogeneity: Tau <sup>2</sup> = (	0.45; Chi <sup>2</sup> = 1	41.88, df=	= 20 (P <	0.00001);	I² = 86%					
'est for overall effect: Z	(= 6.26 (P < 1	0.00001)								
										<u>_</u>
										-4 -2 0 2 4
										better than controls worse than control

#### **Table 2 Summary of results**

Outcome	N Studies	N Total cases	N SG	N CG	CG/SG*100	Effect Size C.I. 95%	PS	l <sup>2</sup>
1 Memory functioning	128							
1.1 Measures of Memory Efficiency	47	3,432	2,066	1,366	66.12	-1.22 [-1.44, -1.01]*	0.81	86%*
1.2 Measures of Memory Functioning (inpatients only)	17	1,183	630	553	87.78	-1.21 [-1.63, -0.80]*	0.80	90%*
1.3 Measures of Memory Functioning (outpatients only)	16	1,162	678	484	71.39	-1.83 [-2.35, -1.31]*	0.90	92%*
1.4 Digit Span	31	2,092	1,209	883	73.04	-0.67 [-0.81, -0.53]*	0.68	51% **
1.5 LTM	45	5,045	2,801	2,244	80.11	-1.14 [-1.32, -0.96]*	0.79	87%*
1.6 STM	56	5,405	3,032	2,373	78.26	-1.05 [-1.18, -0.92]*	0.77	77%*
2 Global cognitive functioning	131							
2.1 Measures of IQ	102	8,416	4,760	3,656	76.81	-0.96 [-1.07, -0.85]*	0.75	80%*
2.2 Measures of IQ (inpatients only)	27	1,800	894	906	101.34	-1.04 [-1.25, -0.82]*	0.77	77%*
2.3 Measures of IQ (outpatients only)	27	2,274	1,355	919	67.82	-0.83 [-1.00, -0.66]*	0.72	69%*
2.4 premorbid IQ	48	3,568	2,049	1,519	74.13	-0.57 [-0.70, -0.43]*	0.65	70%*
3 Language	70							
3.1 Verbal Tasks	70	6,396	3,962	2,434	61.43	-0.99 [-1.10, -0.87]*	0.76	74%*
4 Executive function	67							
4.1 Measures of Flexibility	67	5,257	2,867	2,390	83.36	-1.10 [-1.27, -0.92]*	0.78	88%*
5 Attention	76							
5.1 Reaction Time	76	5,333	2,852	2,481	86.99	0.99 [0.86, 1.12]*	0.76	77%*
5.2 Attention (inpatients only)	19	1,399	811	588	72.50	1.34 [0.93, 1.76]*	0.83	91%*
5.3 Attention (outpatients only)	21	1,417	771	646	83.79	1.02 [0.70, 1.34]*	0.76	86%*

SG = Patients with Schizophrenia Group; CG normal control cases group.

CG/SG\*100: percentage of control cases with respect of patients.

PS = probability of superiority;  $I^2 = percentage$  of heterogeneity.

\* p < .00001; \*\* p < .00008.

of the WAIS considered stable over-time. These data are based on 48 works for a total number of 3,568 cases and show an ES = -0.57 [-0.70, -0.43], I<sup>2</sup> = 70%, PS 65 = %. The hypothesis based on the premorbid IQ, that some cognitive discrepancies are already present in the patients population years ahead of an explicit expression of the clinical features of this disease, might be confirmed by these results, at least in 2 cases every 3. Naturally, since the largest part of these pre-morbid data are retroactively reconstructed when the disease is already diagnosed, it seems necessary a further confirmation of this hypothesis by the longitudinal proactive method of study where the pre-morbid IQ data are obtained before the diagnosis.

In general, IQ data confirm the findings already seen for the memory functioning both in terms of ES and of a large heterogeneity. It must be noted that the heterogeneity is around 80% when an homogeneous function is evaluated, such as the IQ or specific models of memory functioning,

#### Language

The language functioning was evaluated in 70 works for a total of 6,396 cases (3,962 SG and 2,434 CG). The ES is -0.99 [-1.10, -0.87] with I<sup>2</sup> = 74% and PS = 76%.

#### **Executive function**

Data concerning this cognitive area were studied in 67 works for a total of 5,257 cases (2,867 SG and 2,390 CG). The ES is -1.10 [-1.27, -0.92] with I<sup>2</sup> = 88% and PS = 78%.

Both measures of language functioning and executive function show that SG patients obtain significantly worse results than those obtained by the normal controls. The magnitude of differences is similar to that of the other areas already examined and the same happens for the heterogeneity.

#### Attention

Data in this cognitive area are measures of reaction time, obtained in a variety of techniques and tasks from 76 studies for a total of 5,333 cases (2,852 SG and 2,481 CG). The ES is 0.99 [0.86, 1.12] with  $I^2 = 77\%$  and PS = 76%. When inpatients are separately analyzed from outpatients, the inpatients' ES is 1.34 [0.93, 1.76] with  $I^2 = 91\%$  and PS = 83%, while the outpatients' ES is 1.02 [0.70, 1.34] with  $I^2 = 86\%$  and PS = 76%. Patients with schizophrenia have a slower reactivity to stimuli than normal cases and in particular there is a slight stronger tendency of this to happen among the inpatients (4 out

of 5 inpatients are probably found slower in their RT's with respect to 3 out of 4 outpatients).

#### **Meta-regression**

The ES for every type of analysis was correlated with number of cases, sex distribution, and age of participants of each group in order to identify the role of these structural variables in the identification of the between group differences expressed in terms of ES.

- The number of cases has a significant effect on the between group differences for the pre-morbid IQ, the memory functioning (outpatients only), and the attention measures (expressed in terms of reaction time). We must remind that there is a wide and generalized imbalance between group composition for all cognitive variables examined in this meta-analysis (Table 2).
- The composition by sex of the groups has a significant effect on the between group difference for the IQ measures, the memory functioning, the language functioning, the executive function, and the attention measures. In general, there is an unbalance of sex composition between the SG and CG groups (Table 2).
- The age of participants has a significant effect on between group differences for the executive function and the attention measures.

In particular, the between group difference on measures of pre-morbid IQ seems to be partially related to the unbalance of number of cases in the two groups (respectively increasing the number of SG patients decreases the ES, p < .04, while increasing the number of CG cases increases it, p < .04). The magnitude of the ES concerning the IQ measures seems to be related to the differences in sex distribution, in particular for the SG group (p < .003) where increasing the number of females reduces the difference between SG and CG groups. The memory functioning measures (outpatients only) show that increasing the number of patients of the SG group and the number of male cases of the CG decreases the between group difference. For the language functioning measures the increment of males in the CG increases the between group difference (p < .05). For the executive function measures the increasing of age of the CG (p < .03) and the number of females patients of the SG (p < .04) decreases the between group difference. The measure of RT's of inpatients shows that increasing the number of the SG patients decreases the between group difference (p < .04). The measures of RT's in general show that an increase of number of males of the CG (p < .001) and the age of SG patients (p < .001) increases the between group difference.

All these results show that the reduction of the discrepancies and the unbalance of composition of the groups, together with the reduction of the heterogeneity, could produce a parallel reduction of the magnitude of the ES. For what is possible to see from our analysis, despite this attenuation of effects, the present differences would remain significant in most domains.

#### Conclusions

This updated version of the meta-analysis on cognitive deficits of patients with schizophrenia evidenced by the comparison with normal control cases, has confirmed the stability of the results found in the previous work [7]. These findings show a generalized presence of cognitive impairment among the patients with schizophrenia. These results cannot be considered free of the potential bias that only controlled studies with positive results are available in the published evidence, while all those with negative results are not traceable. The real possibility of such a bias, should make us consider that the results obtained in this meta-analysis might be, in some degree, inflated by an underrepresentation of negative results.

Another problem is evidenced by the quality analysis of the included studies. The methodological characteristics of the studies on this cognitive impairment, could be improved with a better control on the balance of number of cases, sex composition of the two groups, and, at a less extent, age of participants. The balance of these factors will take care of some of the structural dysfunctional characteristics evidenced in this meta-analysis.

The identification of precise and replicable measurement procedures is another of the requirements that have demonstrated to be useful in reducing the methodological heterogeneity of the present results. By means of the standardization of methodology, the studies on cognitive deficits of patients with schizophrenia might move, from the current situation where they are mostly descriptive, to the level where they could be of help in refining and confirming explanatory hypotheses concerning the characteristics and the nature of the cognitive impairment.

In the course of the updating process of this metaanalysis, various characteristics of the available data have come to attention. It is of general knowledge that there is a reduction of cognitive efficiency in patients with schizophrenia, but it is important to consider that the intensity of this reduction (evidenced by comparing patients' results to those of normal cases) is not sufficient to classify most of the patients' level of functioning below the normal limits. As an example, the range of mean IQ level, found in the studies concerning patients is 84–107 which indicates that in general, the average intellectual abilities of the groups of patients studied are not below the medium-low level of classification. Analogous considerations could be made about the memory efficiency and the other cognitive areas explored, based on the magnitude of the effect sizes obtained in the analyses.

All the elements evidenced in the discussion, converge on the high heterogeneity found among the studies. A heterogeneity so high as that found in our results, shows that there are diffuse and structural problems in considering all the studies performed in this area of research as belonging to the same class of studies. It is necessary to reduce the heterogeneity to the only acceptable source in this area of research, the clinical heterogeneity, dependent on clinical and functional differences among patients classified in the same diagnostic area. In order to obtain this simplification of heterogeneity, it is necessary to eliminate or control for the other unwanted sources of heterogeneity, principally the methodological heterogeneity. This could be obtained by developing and adopting a standardized and consensus-based set of measurement procedures and criteria for identification and selection of cases for the groups to be studied. It is possible to foresee from our results, that improving the methodological models adopted for each study, there will be a reduction of the heterogeneity and an attenuation of the differences commonly found between patients and normal subjects in most of the cognitive domains. It seems likely from our results that even if attenuated, in most cases, these differences will remain statistically significant.

#### **Additional file**

Additional file 1: Table S1. Summary of included papers.

#### **Competing interests**

The authors declare that they have no competing interests.

#### Authors' contributions

MF monitored the data base search and papers selection. Executed the statistical analyses and contributed to the preparation of the manuscript. VB carried out the data base search and the initial selection of the to be included papers. Contributed to the data extraction from the single papers. MEC carried out the data base search and the phases of selection of the to be included papers. Executed the data extraction and input process. Contributed to the preparation of the manuscript. All authors read and approved the final manuscript.

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#### Received: 23 February 2011 Accepted: 13 April 2012 Published: 20 June 2012

#### References

- Heinrichs RW, Zakzanis KK: Neurocognitive deficit in schizophrenia, a quantitative review of the evidence. *Neuropsychol* 1998, 12(Suppl 3): 426–445.
- Bilder RM, Lipschutz-Broch L, Reiter G, Geisler S, Mayerhoff D, Lieberman JA: Neuropsychological deficits in the early course of first episode schizophrenia. Schizophr Res 1991, 5:198–199.

- Raji TK, Mulsant BH: Nature and course of cognitive function in late-life schizophrenia: a systematic review. Schizophr Res 2008, 102:122–140.
- Mesholam-Gately RI, Giuliano AJ, Goff KP, Faraone SV, Seidman L: Neurocognition in first-episode schizophrenia: a meta-analytic review. Neuropsychol 2009, 23:315–336.
- 5. Green MF: What are the functional consequences of neurocognitive deficit in schizophrenia? *Am J Psych* 1996, **153**:32–330.
- Kremen WS, Seidman LS, Faraone SV, Toomey R, Lyons MJ, Tsuang MT: Heterogeneity of schizophrenia: a study of individual neuropsychological profiles. Schizophr Res 2004, 71:307–314.
- Fioravanti M, Carlone O, Vitale B, Cinti ME, Clare L: A meta-analysis of cognitive deficits in adults with a diagnosis of schizophrenia. *Neuropsychol Rev* 2005, 15(Suppl 2):73–95.
- Higgins JPT, Thompson SG: Quantifying heterogeneity in a meta-analysis. Stat Med 2002, 21:1539–1558.
- Egger M: Davey Smith G, Altman DG: Systematic reviews in health care: metaanalysis in context. 2nd edition. London: BMJ Publishing Group; 2001.
- Grissom RJ: Probability of the superior outcome of one treatment over another. J Appl Psychol 1994, 79:314–316.
- Grissom RJ: The Magical Number .7 ± .2: Meta-meta-analysis of the probability of superior outcome in comparisons involving therapy, placebo, and control. J Consult Clin Psychol 1996, 64:973–982.

#### doi:10.1186/1471-244X-12-64

**Cite this article as:** Fioravanti *et al.*: **Cognitive deficits in schizophrenia:** an updated metanalysis of the scientific evidence. *BMC Psychiatry* 2012 **12**:64.

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