

The Brief Assessment of Cognition in Schizophrenia. Normative data for the Italian population

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Abstract *Objective* To provide normative values for the Italian population for the Brief Assessment of Cognition in Schizophrenia (BACS), a recent brief neuropsychological instrument for the assessment of cognition in patients with schizophrenia. *Participants* Data were collected from 204 healthy adult Italian subjects, stratified by gender, education and age. *Measurements and results* Tests included in the BACS are the following: list learning, digit sequencing, verbal fluency, token motor task, symbol-coding and Tower of London. Normative values were established using the Equivalent Scores method in order to enable comparison with other neuropsychological tasks commonly used in the assessment of the Italian population. Performance on the BACS was influenced by the commonest demographic variables such as age and educa-

tion. *Conclusions* The availability of normative data for the Italian population will increase the usefulness of this test for both clinical and experimental purposes.

Keywords Cognitive functioning · Schizophrenia · BACS · Equivalent Scores

Introduction

Cognitive deficits are a core characteristic of schizophrenia, affecting 75% of patients [1]. Patients with chronic schizophrenia are impaired in a wide range of cognitive functions, which include verbal memory, working memory, motor speed, attention, executive functions and verbal fluency [2–4]. These impairments should be carefully taken into account, as they have a striking impact on functional outcome [5, 6], including personal, social and professional abilities [7].

It is not yet clear if the new generation of antipsychotic medications has a real impact on these dysfunctions. Contradictory data may result from the lack of an adequate measurement instrument aimed at assessing cognitive dysfunction in schizophrenia. Current test batteries differ widely in content, duration and procedures. Most of those used in schizophrenia are long and complex, as they assess the entire profile of neuropsychological strengths and weaknesses in individuals. The excessive length of this form of neuropsychological evaluation may represent a limiting factor, for example in clinical trials that compare groups of patients, especially when repeated assessment is required [8]. A further problem is the test–retest effect due to the lack of alternative formulations.

The administration of short screening tests, such as the Mini Mental State Examination [9], even though solving the problem of the excessive length and duration of the assessments, results in decreased sensitivity to the impair-

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ments typically observed in schizophrenia, and in an underestimation of the degree of deficit.

The availability of a quick and efficient tool for measuring cognitive abilities in patients with schizophrenia could be an extremely useful guide for clinicians making decisions about potential rehabilitation and antipsychotic drug treatments, as well as for researchers implementing clinical trials to assess cognitive changes. The application of computerised batteries, for example the Cambridge Neuropsychological Test Automated Battery [10] or the Cogtest Battery [11], has been limited by practical obstacles, such as cost, portability, regular software and hardware version changes, etc.

Another option is the Repeatable Battery for the Assessment of Neuropsychological Status (RBANS) [12, 13]. Even though this battery is capable of providing reliable and valid assessments of patients with schizophrenia for a wide variety of cognitive functions, it was originally developed as a screening measure for elderly subjects. Therefore, it favours the evaluation of cognitive domains more severely impaired in patients with dementing illnesses, such as memory or visual-perceptual abilities, and it leaves out important measures such as motor, executive and working memory tasks, which are important targets for cognitive enhancement in schizophrenia.

The Brief Assessment of Cognition in Schizophrenia (BACS) [14] preserves the desirable features of the RBANS, but it overcomes its limits, as it was specifically designed for use in schizophrenia clinical trials and it meets all the required criteria: brief administration and scoring time, portability, repeatability and availability of alternate forms. The domains assessed by this recent pen-and-paper battery of neurocognitive tests are those found to be consistently impaired and closely related to outcome in schizophrenia: verbal memory, working memory, motor speed, attention, executive functions and verbal fluency. To test its reliability and sensitivity, Keefe et al. [14] compared all the performances obtained by administering the BACS, A and B versions, and a standard neurocognitive battery, both to patients and to healthy controls. Results suggest a high test–retest reliability of the same version and of the two

alternate forms of the BACS, both in schizophrenic patients and healthy controls. The primary measures from the subtests without alternate versions, including tests of motor speed, working memory, verbal fluency and information processing speed, were highly reliable, with ICCs equal to or greater than 0.79. The practice effects of these tests were minimal, with none of the improvements exceeding 0.25 standard deviations. Test–retest reliability for measures with alternative forms (the Verbal memory and the Tower of London subtests) was measured with intra-class correlations (ICC) in the patient and control groups separately. The ICCs for the Verbal memory subtest were high, ranging from 0.78 to 0.93 in patients and from 0.40 to 0.90 in controls. The ICCs for the Tower of London subtest ranged from 0.66 to 0.89 in patients and from 0.73 to 0.96 in controls.

Moreover the composite scores from the BACS and the standard battery were highly correlated in patients and in controls and the magnitude of the deficits found in patients with schizophrenia was about one and a half standard deviations below the healthy controls, which is consistent with the range of magnitude reported in meta-analyses of studies of neurocognitive impairment in schizophrenia [15]. These data suggest that the BACS is a valid, sensitive and repeatable instrument for testing cognitive functioning in schizophrenia.

The aim of this study was to establish normative values for the BACS in the Italian population. Norms were computed with the Equivalent Scores method [16], in order to enable the comparison with other neuropsychological tasks commonly used in Italy [17–19].

Methods

Subjects

Two hundred and four healthy subjects (87 males and 117 females) without any history of neurological or psychiatric symptoms were recruited to participate in this study. The participants were between 18 and 69 years of age, with a mean age of 32.99 (SD 12.7). Years of education

Table 1 Demographic characteristics of the sample

Years of education	Age					Total
	18–29	30–39	40–49	50–59	60–69	
5–8 years						
Females	13	4	6	6	0	29
Males	6	3	1	1	2	13
9–13 years						
Females	26	15	3	8	0	52
Males	20	6	8	5	0	39
14–18 years						
Females	19	4	6	7	0	36
Males	25	2	2	5	1	35
Total						
Females	58	23	15	21	0	117
Males	51	11	11	11	3	87

ranged from 5 to 22 years with a mean of 13.35 (SD 3.7). The distribution across the different age/education level combinations is shown in Table 1.

Procedures

Subjects were randomly recruited from the general population. A clinical interview that included the Structured Clinical Interview for DSM-IV Axis I Disorders, Clinical Version [20] suitable for selection and screening of individuals was administered by a trained psychiatrist (R.C.). Exclusion criteria were the presence of an Axis I disorder according to DSM-IV criteria, any relevant neurologic illness, such as a history of brain trauma, or a past history of substance abuse.

The constructs measured with the BACS, including the tests, procedures and measures are listed in the order administered as follows.

Verbal memory – list learning

Subjects were presented with 15 words and then asked to recall as many words as possible. This procedure was repeated five times. There were two alternate forms. Performance was measured as number of words recalled per trial, in any order (range: 0–75).

Working memory – digit sequencing task

Subjects were presented with clusters of numbers of increasing length. They were asked to tell the experimenter the numbers in order, from lowest to highest. Performance was measured as number of correct responses (range: 0–28).

Motor speed – token motor task

Subjects were given 100 plastic tokens and asked to place them two at a time into a container as quickly as possible. A 60-s time limit was imposed. Performance was measured in terms of the number of tokens correctly placed into the container for the first half-minute, second half-minute and the 1-min total (final outcome, range: 0–100).

Verbal fluency

Category instances. Subjects were given 60 s to name as many words as possible within a given category (supermarket items).

Controlled oral words association test. In two separate trials, subjects were given 60 s to generate as many words as possible that began with a given letter: T, R. The measure of performance was the total number of words generated in the verbal fluency trials.

Attention and speed information processing – symbol coding

In this subtest patients were required to write as quickly as possible the numerals 1–9 as matches to symbols on a

response sheet for 90 s. The measure of performance consisted in the number of correct numerals (0–110).

Executive functions – Tower of London

Subjects were shown two pictures simultaneously. Each picture showed three balls of different colours arranged on three pegs, with the balls in a unique arrangement in each picture. Subjects were asked to give the total number of times the balls in one picture needed to be moved in order to make the arrangement of balls identical to that of the other, opposing picture. There were 20 trials. The items were of variable difficulty, with a general tendency for later items to be more difficult. If patients responded correctly to all 20 trials, two additional trials of greater difficulty were administered. There were two alternate forms. The measure of performance consisted in the number of correct responses (range: 0–22).

Translation of the original English version into Italian

The presence of verbal tasks required a thorough translation of the original English version into Italian. For the verbal memory subtest, words were matched with the original English ones, for the number of syllables, the frequency of usage and the level of concreteness/abstraction [21]. Moreover the Italian version was re-translated into English by a mother tongue speaker and it was approved by the author (R.K.).

Data analyses

The BACS scores were analysed by means of simultaneous multiple regression, in order to assess the influence of age, education (years of schooling) and gender. For each score, a linear regression model was applied to adjust the original score for age, education and gender. The effect of each variable was evaluated within the complete model by partialling out the effect held in common with the other variables.

On the basis of the corresponding regression model, an adjusted score was calculated for each subject by adding or subtracting the contribution of the concomitant variable from the original score as necessary to account for the influence of those factors which showed a significant effect, and correction grids were generated to provide pre-calculated correction factors to adjust the score of any new individual performing the task.

To establish the score at which an individual falls within the normal range, cut-off scores were obtained by calculating tolerance limits. The cut-off score indicates the score at or below which the probability that an individual belongs to the normal population is less than 0.05 with a confidence level of 0.95. Adjusted scores

were then fitted into a 5-point interval scale to obtain equivalent scores, in which 0 sets the limit for pathological performance and 4 is equal or better than the median value. Equivalent score 1 could be considered as a borderline value while equivalent scores 2 and 3 are intermediate.

Results

Verbal memory

Table 2a shows the results of the analysis of the verbal memory task. Overall adjusted mean number of correctly recalled word was 48.95 (SD=8.71). Range was 28.55–72.43.

Multiple regression analysis showed that age and education play a significant role (respectively $t=-5.99$, $p=0.000$ and $t=3.21$, $p=0.001$). Gender did not influence the performance ($t=1.05$, ns).

To adjust the performance of each individual in terms of education and age, correction grids were computed for the combined effect of these variables (Table 2a1). Cut-

off and equivalent scores are shown in Table 2a2.

In order to evaluate the parallel-forms reliability we collected data on an additional 50 controls not included in the original sample, who were assessed with the two different forms of verbal memory task. In this separate sample the word lists were not significantly different in difficulty (A list: mean=49.45, SD=9.51; B list mean=50.58, SD=10.65; $R=0.59$, $p=0.000$).

Working memory

Table 2b shows the results for the analysis of the working memory task. The overall adjusted mean number of correct responses was 22.32 (SD=4.04). Range was 7.62–28. Multiple regression analysis showed that age ($t=-4.21$, $p<0.000$) and gender ($t=-3.58$, $p<0.000$) play a significant role. Education did not influence the performance ($t=-0.24$, ns).

To adjust the performance of each individual in terms of gender and age, correction grids were computed for combined effect of these variables (Table 2b1). Cut-off and equivalent scores are shown in Table 2b2.

Table 2 Correction grids and equivalent scores for the BACS subtests. The formula at the bottom of each grid contains the model that permits the calculation of the correction factor for individuals who do not fit the age/education combinations for which pre-calculated correction factors are provided

a Verbal memory

a1 Correction grid

Education	Age									
	20	25	30	35	40	45	50	55	60	65
5 years	-3.25	-1.25	0.5	1.75	4.5	6.25	8.25	10	12	14
8 years	-3.75	-2	0	2.5	3.75	5.75	7.5	9.5	11.5	13.25
13 years	-4.75	-3	-1	1.75	2.75	4.75	6.5	8.5	10.25	12.25
17 years	-5.75	-3.75	-2	0	2	3.75	5.75	7.75	9.5	11.5

Corrected score=raw score-[-0.381x(age'-32.99)]-[-0.206x(scol-13.36)]

a2 Equivalent scores

Equivalent scores	
0	≤33.01
1	33.02–38.35
2	38.36–43.70
3	43.71–49.04
4	≥49.05

b Working memory

b1 Correction grid

Gender	Age									
	20	25	30	35	40	45	50	55	60	65
M	-0.5	-0.25	-0.25	0	0	0.25	0.25	0.25	0.5	0.5
F	-0.25	0	0	0.25	0.25	0.5	0.5	0.5	0.75	0.75

Corrected score=raw score-[-0.387x(√age-5.643)]-[-0.240x(0.42 if F/-0.57 if M)]

Cont. Table 2 →

Table 2**b2** Equivalent scores

Equivalent scores

0	≤14.93
1	14.94–17.65
2	17.66–20.37
3	20.38–23.08
4	≥23.09

c Token task**c1** Correction grid

Education	Age									
	20	25	30	35	40	45	50	55	60	65
5 years	-4.5	-3.5	-2.5	-1.75	-0.75	0	1	2	3	4
8 years	-3.75	-2.75	-2	-1	0	0.75	1.75	2.75	3.5	4.5
13 years	-2.75	-1.75	-0.75	0	1	2	2.75	3.75	4.75	5.5
17 years	-1.75	-1	0	1	1.75	2.75	3.75	4.5	5.5	6.5

Corrected score=raw score-[-0.185x(age-34.14)]-[-0.215x(education-13.36)]

c2 Equivalent scores

Equivalent scores

0	≤68.77
1	68.78–76.02
2	76.03–83.27
3	83.28–90.52
4	≥90.53

d Verbal fluency**d1** Correction grid

	5 years	8 years	13 years	17 years
Education	3.75	2.50	0.25	-1.75

Corrected score=raw score-[0.457x(education-13.36)]

d2 Equivalent scores

Equivalent scores

0	≤31.68
1	31.69–39.17
2	39.18–46.66
3	46.67–54.15
4	≥54.16

e Symbol-coding task**e1** Correction grid

	20	25	30	35	40	45	50	55	60	65
Age	-4.5	-2.75	-1	0.75	2.5	4.25	6	7.75	9.5	11.25

Corrected score=raw score-[-0.185x(age-32.99)]

e2 Equivalent scores

Equivalent scores

0	≤40.49
1	40.5–46.34
2	46.35–52.19
3	52.2–58.04
4	≥58.05

Cont. Table 2 →

f Tower of London**f1** Correction grid

Education	Age									
	20	25	30	35	40	45	50	55	60	65
5 years	0	0	0.25	0.5	0.5	0.75	0.75	0.75	1	1
8 years	-0.25	0	0	0.25	0.5	0.5	0.5	0.75	0.75	1
13 years	-0.25	-0.25	0	0	0.25	0.25	0.5	0.5	0.75	0.75
17 years	-0.5	-0.25	-0.25	0	0	0.25	0.25	0.5	0.5	0.75

Corrected score=raw score-[-0.313x(√age-5.64)]-[0.222x(√education-3.62)]

f2 Equivalent scores

Equivalent scores

0	≤12.37
1	12.38–14.23
2	14.24–16.09
3	16.1–17.97
4	≥17.96

Token task

Table 2c shows the results of the analysis of the token task. The overall adjusted mean number of tokens was 89.00 (SD=10.93). Range was 44.05–100. Multiple regression analysis showed that age ($t=-2.43$, $p=0.016$) and education ($t=-2.81$, $p=0.005$) played a significant role. Gender did not influence the performance ($t=-0.68$, $p=ns$). To adjust the performance of each individual in terms of education and age, correction grids were computed for the combined effect of these variables (Table 2c1). Cut-off and equivalent scores are shown in Table 2c2.

Verbal fluency

Table 2d shows the results of the analysis of the verbal fluency tasks. The overall adjusted mean number of words generated was 55.07 (SD=12.79). The range was 26.16–126.24. Multiple regression analysis showed that only education played a significant role ($t=7.19$, $p<0.000$). Age ($t=0.63$, ns) and gender ($t=0.06$, ns) had no significant effect on performance. To adjust the performance of each individual in terms of education, correction grids were computed for the effect of this variable (Table 2d1). Cut-off and equivalent scores are shown in Table 2d2.

Symbol-coding task

Table 2e shows the results of the analysis of the symbol-coding task. The overall adjusted mean number of correct responses was 58.20 (SD=9.68). The range was 23.16–85.26. Multiple regression analysis showed that only age ($t=-5.35$, $p<0.000$) played a significant role.

Gender ($t=0.92$, ns) and education ($t=1.83$, ns) did not influence the performance. To adjust the performance of each individual in terms of age, correction grids were computed for the effect of this variable (Table 2e1). Cut-off and equivalent scores are shown in Table 2e2.

Tower of London

Table 2f shows the results of the analysis of the Tower of London task. The overall adjusted mean number of correct responses was 17.62 (SD=2.86). Range was 8.33–22.00. Multiple regression analysis showed that age ($t=-4.83$, $p<0.000$) and education ($t=3.39$, $p<0.000$) played a significant role. Gender did not influence the performance ($t=-1.67$, ns). To adjust the performance of each individual in terms of education and age, correction grids were computed for the combined effect of these variables (Table 2f1). Cut-off and equivalent scores are shown in Table 2f2.

Discussion

The aim of this study was to provide normative values for the Italian version of a battery widely used in clinical practice to assess neuropsychological deficits in patients with schizophrenia. The BACS is an easily administered pen-and-paper battery of neurocognitive tests, which has demonstrated high reliability and concurrent validity with a standard battery of tests in schizophrenia patients. This short battery assesses the major constructs of cognition that have been found to be most impaired and correlated with functional outcome in patients with schizophrenia. All these aspects make this battery a useful tool for both clinical and experimental purposes, as it allows the

assessment of cognitive functions repeatedly in patients with schizophrenia, especially in clinical trials of drugs enhancing cognitive performance. The establishment of normative data is important to better define a clinical sample based upon comparison to the general healthy population, to understand the magnitude of change during the course of treatment and to adjust for the effects of age, education and gender in the healthy population. The Equivalent Scores standardisation method we adopted is the most widely used method of standardisation in Italy, and allows a direct comparison among different tests.

The collection of normative data in a healthy sample may sometimes have the limit of an age-class distribution that does not match the general population. In this study we attempted to collect data from a broad sample of controls stratified across different age, gender and education classes. The regression model of each test showed a significant effect of education on almost all variables, in agreement with previous normative studies [22]. Age also played a significant role on performance on almost all subtests, in agreement with previous studies that have shown a considerable decrement of cognitive performance with increasing age [23]. The only exception was the verbal fluency subtest. Performance on this subtest was significantly affected only by education and this finding is inconsistent with previous studies that have shown a significant influence of age and gender [22]. The absence of influence of age could be explained by the upper limit age range, which was limited to a small number of subjects over 60. This choice was made to have a sample more readily comparable to schizophrenic samples, who are unlikely to include people older than 60.

Moreover, the high test–retest reliability properties of this battery are important for assessing change over time, such as in clinical trials.

This study has some limitations when applied to a schizophrenia sample, due to the more subtle and heterogeneous impairments that patients with schizophrenia show compared to neurological populations [24, 25]. Normative data allow the assessment of an individual patient's performance with reference to inferential cut-off scores, which are population-based and determine the level of "pathological" performance. It may be useful for clinical practice and for experimental design not only to know if the performance of a person with schizophrenia is within the "pathological" range, but also to assess whether performance falls within the lower end of the normal distribution, even after correction for the effects of demographic variables. This latter assessment is particularly useful to clarify whether, overall, schizophrenic people show cognitive skills which are of a lower level with reference to the mean of the healthy population [25, 26]. Further studies in clinical populations are required to evaluate the prevalence of cognitive impairment in schizophrenia when assessed with an instrument standardised

with the Equivalent Scores method. Finally, it may be worthwhile to attempt to implement and replicate in an Italian sample some studies to verify whether there is a correlation between performance on the BACS and that on other standard batteries as reported in the case of the original US version.

Sommario *Non esistono ad oggi batterie specifiche brevi e facilmente fruibili in lingua italiana per la valutazione del deficit cognitivo dei pazienti con schizofrenia. Lo scopo di questo studio è di tradurre e tarare sulla popolazione italiana la batteria BACS (Brief Assessment of Cognition in Schizophrenia), un breve strumento di screening creato per indagare in modo specifico gli ambiti cognitivi riconosciuti come quelli con le maggiori disfunzioni e correlati ai sintomi della schizofrenia (memoria verbale, velocità e coordinazione psico-motoria, attenzione, funzioni esecutive e fluency verbale) e che ha mostrato nella validazione in lingua americana una buona correlazione con batterie neuropsicologiche standard e una buona affidabilità test-retest. Il campione è costituito da 204 soggetti italiani stratificati per sesso, età e scolarità. I test inclusi nella BACS sono i seguenti: memoria di lista di parole, riordinamento di cifre, fluency verbale, compito motorio dei gettoni, associazione simboli-numeri e Torre di Londra. I dati normativi sono stati calcolati con il metodo statistico dei Punteggi Equivalenti, con l'obiettivo di rendere possibile il confronto con altri test neuropsicologici usati comunemente in lingua italiana. Le prestazioni alla BACS sono risultate influenzate da variabili demografiche come età e scolarità, confermando i dati presenti in letteratura. La disponibilità di dati normativi per la popolazione italiana ha la potenzialità di aumentare l'utilità di questo test per scopi sia clinici che di ricerca.*

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