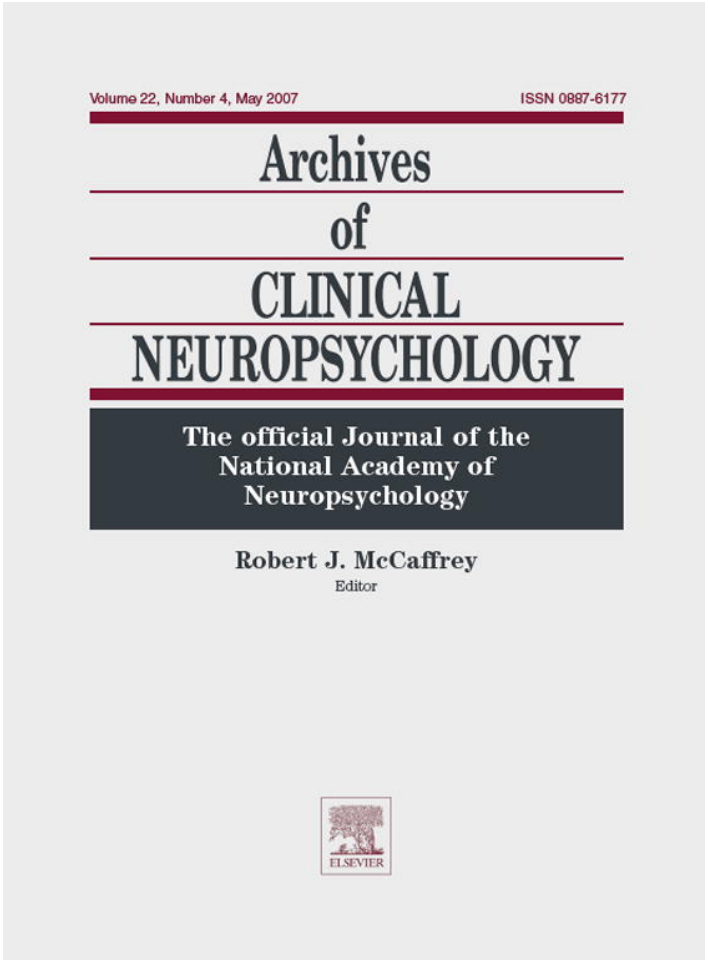

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Trail Making Test in traumatic brain injury, schizophrenia, and normal ageing: Sample comparisons and normative data

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Abstract

The Trail Making Test (TMT) has been a useful assessment tool to investigate executive function. Several studies have recently improved the existing TMT norms by mean of large samples of healthy individuals stratified by a number of demographic variables from different populations. In contrast, criticisms have been raised about the utility of norms from healthy samples to detect changes across time in clinical samples where TMT performance used to be altered. In addition, few studies have compared groups of patients with deficits in TMT performance, making it difficult to decide whether a single set of norms is sufficient to assess different clinical populations. We provide normative data from three large samples of patients with traumatic brain injury (TBI) ($n = 90$), schizophrenia spectrum disorders ($n = 127$), and healthy Spanish speakers ($n = 223$). Differences between healthy participants and patients in all TMT direct (TMT-A, TMT-B) and derived (B–A, B:A, B–A/A) scores were found. TMT performance was poorer in TBI patients than in schizophrenia patients except for the B:A and B–A/A scores, suggesting a similar underlying executive deficit. Normal ageing impaired both direct and derived TMT indices, as revealed by lower scores in the healthy elderly group (55–80 years old) as compared with young (16–24) and middle-aged (25–54) healthy participants. Three different sets of norms stratified by age, education, or both are presented for clinical use. Recommendations on TMT scores are made for future research.

Keywords: Attentional control; Brain damage; Clinical norms; Executive function; Neuropsychological assessment; Schizophrenia

1. Introduction

The Trail Making Test (TMT) is one of the most widely used instruments in neuropsychological assessment. It was originally designed as a part of the Army Individual Test Battery (1944), soon validated as a sensitive indicator of brain damage (Reitan, 1958), and subsequently incorporated into the Halstead–Reitan Battery (Reitan & Wolfson,

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1985). According to different authors, the purpose of the TMT is to test speed of processing, sequence alternation, cognitive flexibility, visual search, motor performance, and executive functioning (Arbuthnott & Frank, 2000; Crowe, 1998; Gaudino, Geisler, & Squires, 1995; Kizilbash, Warschausky, & Donders, 2000; Kortte, Horner, & Windham, 2002; Lezak, 1995; Miner & Ferraro, 1998; Ríos, Periáñez, & Munoz-Céspedes, 2004; Spreen & Strauss, 1998; Stuss et al., 2001; Szoke et al., 2005).

The test consists of two parts (A and B) that must be performed as quickly and accurately as possible. TMT-A requires subjects to draw lines sequentially connecting in ascending order 25 encircled numbers randomly distributed on a sheet of paper (i.e., 1–2–3–4, etc.). In TMT-B, the subject must alternate between numbers (1–13) and letters (A–L) while connecting them (i.e., 1–A–2–B–3–C, etc.). The score on each part represents the amount of time required to complete the task. Apart from these two direct scores, other authors have proposed additional indexes to better describe the cognitive skills required to complete the TMT. The difference score (B–A) is meant to remove the speed component from the test evaluation (Lezak, 1995). Arbuthnott and Frank (2000) reported that the B/A ratio score proposed by Lamberty, Putnam, and Chatel (1994) may provide an indicator of executive control function according to its correlation with task-switching ability. Third, the proportional score (B–A/A) presented by Stuss et al. (2001) seems to provide a sensitive index of prefrontal cortex functioning (for a critical review on derived scores, see Drane, Yuspeh, Huthwaite, & Klingler, 2002). In the last 10 years, many studies have improved TMT normative data increasing sample sizes and stratifying norms according to different demographic variables such as age, education, or gender (Mitrushina, Boone, Razani, & D'Elia, 2005; Strauss, Sherman, & Spreen, 2006). It has been done in different populations to avoid the risk of using neuropsychological normative data with a population that is culturally or sociodemographically different from the original under- or over-estimating cognitive functioning (Ardila, 1995, 2005; Kennepohl, 1999; Mitrushina, Boone, & D'Elia, 1999; Periáñez and Barceló, 2001; Soukup, Ingram, Grady, & Schiess, 1998). For instance, norms exist for North American (Drane et al., 2002; Salthouse et al., 2000; Steinberg, Bieliauskas, Smith, & Ivnik, 2005), Canadian (Tombaugh, 2004), Australian (Hester, Kinsella, Ong, & McGregor, 2005), Italian (Giovagnoli et al., 1996), Chinese (Lu & Bigler, 2002), Japanese (Hashimoto et al., 2006), or Korean healthy populations (Seo et al., 2006). But no specific set of norms exists for Spanish population, which in fact can be used for comparison purposes with North and South American Spanish-speaking Latino groups.

In the clinical context, using norms from healthy samples to assess groups of patients may allow to detect the presence or absence of specific cognitive impairments. In addition, comparing the scores of the patients with their own clinical population should be useful to set the level of severity and therefore the level of incapacity. This is also a relevant issue in terms of indexing patient's evolution, i.e., detecting clinical changes across time, which is a central concern in the assessment of the effectiveness of rehabilitation (Heaton et al., 2001; Woods et al., 2006). In spite of the clear linear relationship between clinical severity and TMT performance demonstrated in certain pathologies (Lange, Iverson, Zakrzewski, Ethel-King, & Franzen, 2005), most normative studies on the TMT have focused in non-clinical samples that do not allow a comprehensive classification of patients according to performance (Kizilbash et al., 2000). The elaboration of clinical norms would require between-samples comparisons in order to address the need of specific norms for different pathologies. But till date, there is a lack of both (1) studies comparing TMT performance in different clinical samples, and (2) specific norms for clinical groups where the test has shown to be sensitive. Cognitive and neuroimaging evidence has related frontal lobe involvement and executive dysfunction to schizophrenia (Crespo-Facorro, Kim, Andreasen, O'Leary, & Magnotta, 2000; Goldberg & Weinberger, 1988; Manoach, 2003; Rodríguez-Sánchez et al., 2005; Szoke et al., 2005; Weinberger, Berman, & Zec, 1986), to traumatic brain injury or TBI (Ciaramelli, Serino, Di Santantonio, & Ladavas, 2006; Rieger & Gauggel, 2002; Ríos & Muñoz-Céspedes, 2004; Serino et al., 2006; Stuss et al., 2001), and to normal ageing (Chao & Knight, 1997; Lowe & Rabbitt, 1997; West, 1996). Some authors have even suggested a common reticulo-frontal disconnection syndrome underlying the executive deficits in both TBI and schizophrenia patients (Goldberg, Bilder, Hughes, Antin, & Mattis, 1989).

On the one hand, these executive cognitive deficits in schizophrenia seem to be present from the very onset of the disorder as revealed by first episode studies (Bilder et al., 2000). Particularly, the TMT has been frequently used in neuropsychological research on schizophrenia, and abnormal performance has been frequently reported. For instance, a meta-analysis by Heinrich and Zakzanis (1998) found that TMT, especially part B, was among the tests that yielded the highest proportion of significant results on studies that compared schizophrenia patients versus healthy controls. The use of derived indices has also produced positive results. Brazo et al. (2005) reported that schizophrenia patients performed significantly worst than healthy controls on B–A index independently of their predominant symptoms, whereas Rodríguez-Sánchez et al. (2005) found an underperformance of patients with respect to healthy controls on

the B:A index. To our knowledge, the sensibility of other indices (i.e., B–A/A) to discriminate these patients has not been studied yet.

On the other hand, early TMT studies demonstrated its sensibility to brain damage (Reitan, 1958). More recent works, have suggested the presence of independent speed of processing and disexecutive deficits in TBI as revealed by poor performance in both direct scores, and B/A derived score, respectively (Ríos et al., 2004). The TMT has also showed a positive linear relation between brain-injury severity and TMT performance (Lange et al., 2005). There is also neuropsychological evidence supporting the relationship between frontal lobe damage after TBI and altered TMT performance, but conclusions are still open to discussion. For instance, the meta-analysis by Demakis (2004) demonstrated that patients with frontal lobe damage performed worse than non-frontal participants on Trails A but not in Trails B. Even more, a medium effect size for this comparison suggested that Trails A was not sufficient by itself to discriminate between frontal and non-frontal lesions. This apparent discrepancy with the long-held assumption that TMT-B is sensitive to frontal lobe damage (Lezak, 1995) was attributed in part to the lack of precision of many neuropsychological studies regarding the specific site of frontal lesions. Thus, the consideration of frontal lobes as a 'functional unit' neglects known functional subdivisions within this brain region (Demakis, 2004; Stuss & Alexander, 2000). It should be noted that the study by Demakis (2004) did not include derived indexes that have been proposed as more pure indicators of executive and prefrontal lobe functioning. For instance, Stuss et al. (2001) divided frontal-damaged patients into sub-groups in order to address specific brain–behavior relations within the frontal lobes during TMT performance. The authors found that patients with damage in dorsolateral frontal areas were most impaired in TMT-B performance, while those with inferior medial damage in the frontal lobes were not significantly affected. Particularly, the proportional score (B–A/A) was the most sensitive index to this kind of damage in prefrontal cortex. Contrasting this evidence, few TMT norms from healthy samples and no clinical norms include the proportional score and other derived indices as potentially useful clinical tools.

In addition, normal ageing is known to lead to a reduction of the cortical volume or thickness of the frontal lobes and particularly to volume decreases in the prefrontal cortex (Salat, Kaye, & Janowsky, 1999; Raz et al., 2004; Tisserand et al., 2002). This selective loss is taken to support the view that executive abilities decline faster with increasing age compared to other cognitive functions (Chao & Knight, 1997; Lowe & Rabbitt, 1997; West, 1996). Some authors have even suggested that this early executive decline may provide sensitive measures to detect preclinical changes in dementia (Albert, Moss, Tanzi, & Jones, 2001; Chen et al., 2000). It has been widely reported in the literature that time completion for TMT-A and -B increases with ageing (Salthouse & Fristoe, 1995; Salthouse et al., 2000; Amodio et al., 2002; Drane et al., 2002; Tombaugh, 2004; Hester et al., 2005). In contrast, conclusions regarding the influence of age on the TMT-derived indices have been inconsistent between studies. Thus, while some authors reported that both B–A and B:A derived indices are sensitive to the effects of ageing (Drane et al., 2002; Hashimoto et al., 2006), others have shown that they are relatively unaffected by this demographic variable (Hester et al., 2005).

The main purpose of the present study was to compare the performance and to provide normative data from two large samples of schizophrenia and TBI patients in the TMT-A and TMT-B direct scores and three derived indices (B–A; B:A; B–A/A). These norms will offer the clinician a comprehensive classification of groups of patients according to the severity of their scores. We also provide normative data from a large sample of healthy Spanish speakers which could be useful for comparison purposes with North and South American Latino groups. In addition, the use of a large healthy group in a wide age range (16–80 years) may help to address in a Spanish sample whether TMT direct and derived indices change across life span as showed in previous studies.

2. Method

2.1. Participants

A total of 440 participants took part in this study (242 male and 198 female; 15–80 years). They were all Spanish speakers and had normal or corrected-to-normal vision. This large group was conformed by three different samples: healthy controls, patients with diagnosis of schizophrenia spectrum disorders, and patients with TBI.

The first sample was constituted by healthy controls ($n = 223$) recruited as volunteers from undergraduate university classes, university staff, social organizations, government staff, hospitals, and health care centers from four different regions of Spain (Madrid, Bilbao, Santander, and Mallorca). A self-reported history of medical and psychiatric problems was obtained from each participant. Any person with a history of neurological disease, psychiatric illness, head injury,

Table 1
Statistical properties of the demographic and TMT variables for each sample

	Control[a]		Schizophrenia[b]		TBI[c]	
	Mean ± S.D.	Minimum–maximum	Mean ± S.D.	Minimum–maximum	Mean ± S.D.	Minimum–maximum
Education	13.3 ± 3.6	2–23	10.4 ± 3.2	5–19	12.9 ± 3.7	8–18
Age	38.9 ± 18.7	16–80	26.2 ± 7.2	15–48	34.6 ± 12.7	16–72
TMT-A	31.7 ± 13.7	12–120	40.9 ± 16.6	19–127	70.7 ± 53.1	21–320
TMT-B	68.1 ± 43.2	28–461	97.5 ± 49.6	43–307	172.8 ± 113.7	45–591
B–A	36.4 ± 35.1	0–348	56.5 ± 43.7	4–255	102.1 ± 80.1	14–475
B:A	2.2 ± 0.8	1–5	2.5 ± 0.9	1.1–5.9	2.7 ± 1.3	1.3–6.3
B–A/A	1.2 ± 0.8	0–4	1.5 ± 0.9	0.1–4.9	1.7 ± 1.3	0.3–5.3

[a] $n = 223$. Gender: male, 88; female, 135.
[b] $n = 127$. Gender: male, 82; female, 45.
[c] $n = 90$. Gender: male, 72; female, 18.

stroke, substance abuse (excluding nicotine), learning disabilities, or any other difficulty that may interfere with testing were criteria for exclusion in this sample. In addition, older subjects (48–80 years old) with scores lower than 24 on the Mini Mental State Examination (Folstein, Folstein, & McHugh, 1975) and higher than 14 on the Geriatric Depression Scale (Brink et al., 1982) were discarded for the analysis.

The second sample was constituted by patients with diagnosis of non-affective psychosis (schizophrenia, $n = 77$; schizophreniform disorder, $n = 34$; non-specified psychosis, $n = 9$; and brief psychotic disorder, $n = 7$) in their first episode ($n = 127$). All patients attended at a program for first-episode psychosis (PAFIP) carried out at the Hospital Marques de Valdecilla (Santander) (see a detailed description in Crespo-Facorro, Perez-Iglesias, Ramírez, Martinez, & Vazquez-Barquero, 2006). Diagnoses were confirmed by an experienced psychiatrist by means of the Structured Clinical Interview for DSM-IV (SCID-I) 6 months after the initial contact. The program was designed in a naturalistic manner and all patients with a first psychotic episode in the hospital catchment area aged between 15 and 50 were included. Any patient with a history of neurological disease, previous psychiatric illness, head injury, stroke, substance abuse (excluding nicotine), learning disabilities, or any other difficulty that may interfere with testing were also criteria for exclusion in this sample. None of the patients had received neuroleptic medication prior to contact with the program. However, they all were on neuroleptic medication and had reached clinical stabilization when neuropsychological assessment for the current study was done.

Patients within the TBI sample ($n = 90$) were recruited from the Brain Damage Unit at Beata Maria Ana Hospital (Madrid), and the Brain Damage Unit at Aita Menni Hospital (Bilbao). Mean Glasgow Coma Scale (GCS) (Teasdale & Jennett, 1974) was 6.7 ± 3.2 (65% severe, 8% moderate, 8% mild), with the exception of 19% of cases where GCS was not provided. The specific site of lesion was not considered for analyses. Post-traumatic amnesia duration assessed with the Galveston Orientation and Amnesia Test (GOAT) (Levin, O'Donnell, & Grossman, 1979) was also recorded in 67 patients: mean 42.4 ± 31 days. The mean time since injury was 12.5 ± 10 months. All patients were out of post-traumatic amnesia and were alerted and awake at the time of testing (see Table 1 for a description of demographic and dependent variables in the three samples). Any TBI patient with a history of psychiatric illness, substance abuse (excluding nicotine), learning disabilities, or any other difficulty that may interfere with testing (visual or motor difficulties, aphasia or apraxia) were also criteria for exclusion in this sample. Neuropsychological examination of these patients was part of the initial assessment protocol of the brain damage rehabilitation program and had no forensic value in terms of litigation or disability claims.

All participants signed a consent form according to the Declaration of Helsinki and were informed about the investigation prior to the neuropsychological evaluation session.

2.2. Procedure

Subjects were administered part A and part B of the TMT (Reitan, 1958, 1992) according to the guidelines presented by Spreen and Strauss (1998), as a part of a larger battery of neuropsychological tests. All tests were administered by staff psychologists who verbally instructed to complete each part of the TMT as quickly and accurately as possible. An example of each part was performed by all participants. When an error was made, subjects were instructed to return

to the point where the error originated and to continue until the test was finished. Total time (in seconds) for parts A and B respectively was recorded, representing the TMT-A and TMT-B direct scores. Then, three derived indices were calculated for all subjects: difference score (B–A), ratio score (B:A), and proportional score (B–A/A).

2.3. Data analysis

A series of analyses of covariance (ANCOVA) were used to explore the presence of differences in TMT direct and derived scores among the three samples. The confirmation of such differences will justify the need for different sets of norms for each sample. Age and education were used as covariates in these analyses in order to control between-group differences in TMT scores due to demographic differences. Second, separate correlation and regression analyses for each sample helped to decide which demographic variables could represent the best criteria for data stratification in norms. Univariate analyses of variance (ANOVA) were performed on the dependent measures in order to decide the number of useful set of norms to be considered within each sample. A significance level of 0.05 was set for all main contrasts. A Bonferroni-corrected significance level of $p < 0.05$ was adopted for all tests of simple effects involving multiple comparisons. Finally, direct and derived scores from the resulting groups were transformed into percentile scores. SPSS version 13.0 statistical software package was used for all the analyses.

3. Results

3.1. Between-group comparisons

A set of preliminary Student *t*-tests showed differences between the three groups in age and education ($ps < 0.01$ for all comparisons, except education between controls and TBI $p = 0.54$; see descriptive statistics in Table 1). Thus, univariate ANCOVAs were performed in order to address between-group differences in TMT using age and education as covariates to eliminate their influence in performance. There was a significant main effect of the group factor in both TMT-A ($F(2,435) = 71.7$; $p < 0.0001$) and TMT-B scores ($F(2,435) = 99.3$; $p < 0.0001$). Post-hoc analyses evidenced the presence of differences in the two direct scores between patients and controls (TMT-A: $p < 0.019$ control vs. schizophrenia patients; $p < 0.0001$ control vs. TBI patients; TMT-B: $p < 0.0001$ control vs. schizophrenia patients; $p < 0.0001$ control vs. TBI patients) as well as between the two patients groups, scores being worse in the TBI sample (TMT-A: $p < 0.0001$; TMT-B: $p < 0.0001$).

There were also a significant main group effect in both B–A ($F(2,435) = 66.2$; $p < 0.0001$), B:A ($F(2,435) = 11.7$; $p < 0.0001$), and B–A/A derived indices ($F(2,435) = 11.7$; $p < 0.0001$). Post-hoc analyses revealed differences between healthy controls and patients on B–A ($p < 0.002$ control vs. schizophrenia samples; $p < 0.0001$ control vs. TBI samples), B:A ($p < 0.034$ control vs. schizophrenia samples; $p < 0.0001$ control vs. TBI samples), and B–A/A derived indices ($p < 0.034$ control vs. schizophrenia samples; $p < 0.0001$ control vs. TBI samples). There were also differences between TBI and schizophrenia patients in B–A, difference score ($p < 0.0001$) being worst performance in the TBI group. In contrast, B:A and B–A/A scores did not differ between the two samples of patients ($ps = 0.198$).

3.2. Data stratification

Correlations among the demographic variables and scores on Trails A and B in the control sample ($N = 223$) provided an approach for selection of stratification variables (see Table 2).

3.2.1. Healthy controls

The results of analyses in the sample of healthy controls revealed that age and education were more highly correlated with TMT scores than was gender. The relative effects of these variables on TMT performance were further explored using regression analyses. Age, education, and gender accounted together for 27.4% and 23.3% of the variance of Trails A and B, respectively. These three variables also accounted for 16.5%, 5.2%, and 5.2% of variance for B–A, B:A, and B–A/A scores, respectively. Age taken alone accounted for 19.2% of variance of TMT-A, 20.5% of TMT-B, 15% of B–A, 5.2% of B:A, and 5.2% of B–A/A. Education considered alone accounted for 15.7% of variance of TMT-A, 10.0% of TMT-B, 5.6% of B–A, 0.4% of B:A, and 0.4% of B–A/A. Finally, gender alone accounted for 4% of variance of TMT-A, 2.4% of TMT-B, 1.3% of B–A, 0% of B:A, and 0% of B–A/A.

Table 2
Correlation matrixes

	Gender	Education	Age	TMT-A	TMT-B	B–A	B:A	B–A/A
Controls								
Gender								
Education	−0.207**							
Age	0.066	−0.355**						
TMT-A	0.201**	−0.396**	0.438**					
TMT-B	0.155*	−0.317**	0.453**	0.695**				
B–A	0.113	−0.236**	0.387**	0.467**	0.960**			
B:A	0.009	−0.067	0.228**	−0.062	0.594**	0.755**		
B–A/A	0.009	−0.067	0.228**	−0.062	0.594**	0.755**	1**	
Schizophrenia								
Gender								
Education	0.319**							
Age	0.373**	0.430**						
TMT-A	0.026	−0.119	0.117					
TMT-B	−0.052	−0.306**	0.128	0.503**				
B–A	−0.070	−0.302**	0.101	0.191*	0.944**			
B:A	−0.128	−0.252**	−0.002	−0.220*	0.678**	0.854**		
B–A/A	−0.128	−0.252**	−0.002	−0.220*	0.678**	0.854**	1**	
TBI								
Gender								
Education	0.046							
Age	−0.112	0.139						
TMT-A	0.010	−0.186	0.148					
TMT-B	−0.113	−0.290**	0.255*	0.768**				
B–A	−0.167	−0.286**	0.263*	0.419**	0.903**			
B:A	−0.177	−0.150	0.136	−0.260*	0.322**	0.631**		
B–A/A	−0.177	−0.150	0.136	−0.260*	0.322**	0.631**	1**	

* $p < 0.05$.
** $p < 0.01$.

Age and education were the two variables selected to stratify control participants, since most variables were affected by them in a higher degree than was gender. First, and following a series of exploratory ANOVAs and prior approaches to normative data for the TMT (Soukup et al., 1998), it was decided to create three age groups: (1) young group ($n = 69$; ages 16–24), (2) middle-aged adults ($n = 89$; ages 25–54), and (3) elderly adults ($n = 65$; ages 55–80). Analysis of variance were performed on these data for Trails A and B, and the derived scores B–A, B:A and B–A/A. As shown in Fig. 1, all scores tend to increase with age (TMT-A: $F(2,220) = 22.8$, $p < 0.0001$; TMT-B: $F(2,220) = 25.5$, $p < 0.0001$; B–A: $F(2,220) = 18.1$, $p < 0.0001$; B:A: $F(2,220) = 8$, $p < 0.0001$; B–A/A: $F(2,220) = 8$, $p < 0.0001$). Post-hoc analyses revealed differences between the elderly group and young, and middle-aged groups in all scores ($ps < 0.05$). No differences were found between young and middle-aged groups in any of the direct and derived TMT scores ($ps > 0.9$). This pattern of results was replicated when the influence of education was removed by mean of ANCOVA analysis except for a just marginal significant difference between the elderly group and the middle-aged group in both B:A and B–A/A scores ($ps = 0.07$). Second, a series of exploratory ANOVAs were performed to decide how to stratify each age group according to the number of years of education. In a first step, we used median scores of each group in order to split into high and low educational levels. No differences in TMT direct and derived scores were found between high and low education levels in young and elderly groups. In contrast, middle-aged group exhibits differences in TMT-A ($t = 3.736$; $df = 82.573$; $p < 0.001$), high educational level being outperformed. In a second step, an education quartile based division of each of the three age groups was performed in an attempt to further explore if differences could be found. Again, no differences in TMT direct and derived scores were found between quartile sub-groups from the young and elderly age groups. In contrast, middle-aged group exhibits differences in TMT-A ($F = 6.723$; $df = 3$; $p < 0.001$) when first versus third and when first versus fourth quartile sub-groups were compared, and in TMT-B ($F = 3.758$; $df = 3$; $p < 0.014$) when first versus second and when first versus third quartile sub-groups were compared, higher educational

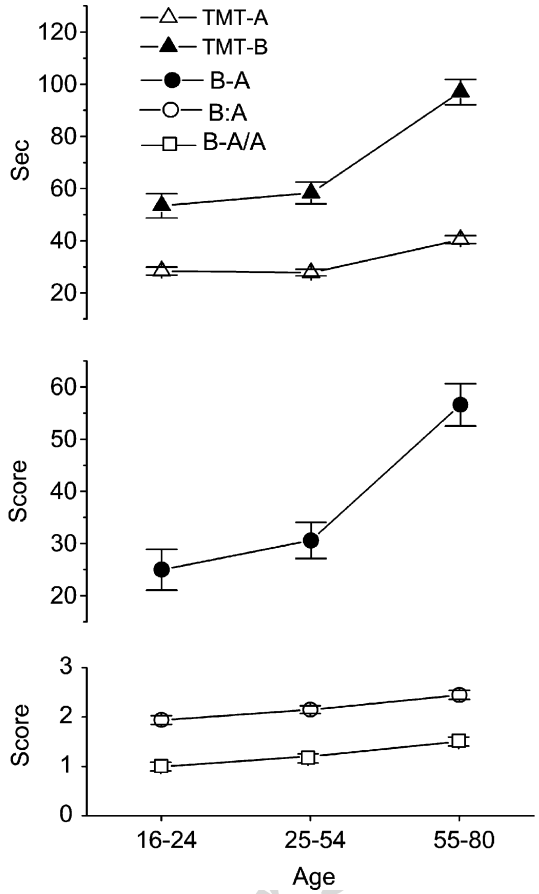

Fig. 1. Performance on Trails A, Trails B, B–A, B:A, and B–A/A of the sample of healthy controls as a function of age: young group (16–24 years old), middle-aged group (25–54 years old), and elderly group (55–80 years old).

levels being outperformed. Thirdly, in an attempt to increase statistical power for sub-groups comparisons in the middle-aged group, second, third, and fourth quartile groups were collapsed in a high-education sub-group ($n = 65$) compared with first quartile low-education sub-group ($n = 24$). Middle-aged subjects from the high-education sub-group were better than those from the low-education sub-group in TMT-A, TMT-B, and B–A scores ($t = 3.722$, $df = 87$, $p < 0.001$; $t = 2.672$, $df = 29.02$, $p = 0.012$; $t = 2.339$, $df = 87$, $p = 0.022$, respectively). The results of these analyses led to the decision to divide only the middle-aged group into two education levels for stratification of norms (0–12 and 13+ years).

3.2.2. Schizophrenia patients

In the schizophrenia sample, education was the variable with the largest correlations with TMT scores (see Table 2). Age, gender, and education together accounted for 4.9% of variance of TMT-A, 17.7% of TMT-B, 15.9% of B–A, 8.5% of B:A, and 8.5% of B–A/A. Education accounted for 1.4% of variance for TMT-A, 9.4% for TMT-B, 9.1% for B–A, 6.4% for B:A, and 6.4% for B–A/A. Age accounted for 1.4% of variance of TMT-A, 1.6% of TMT-B, 1% of B–A, 0% of B:A, and 0% of B–A/A. Gender accounted 0.1% of variance of TMT-A, 0.3% of TMT-B, 0.5% of B–A, 1.6% of B:A, and 1.6% of B–A/A.

Therefore, education was chosen as stratification variable on schizophrenia patients, and they were divided into two levels: low education (0–11 years) and high education (12+ years). ANOVA results revealed significant main effects for Trails B ($F(1,125) = 11.3$; $p < 0.001$), and the derived scores B–A ($F(1,125) = 14.1$; $p < 0.0001$), B:A ($F(1,125) = 11.9$; $p < 0.001$), and B–A/A ($F(1,125) = 11.9$; $p < 0.001$). There were no differences for Trails A ($F(1,125) = 0.07$; $p = 0.8$).

3.2.3. TBI patients

For brain-injury patients, gender, age, and education considered together accounted for 6.7% of variance for TMT-A, 17.7% for TMT-B, 18.9% for B–A, 7.1% for B:A, and 7.1% for B–A/A. Age considered alone could only explain 2.2%

Table 3
Statistical properties of the demographic and TMT variables for each normative group of healthy controls

	Mean	S.D.	Minimum	Maximum	Skewness	Kurtosis
Young group (16–24 years; $N = 69$: male = 24, female = 45)						
Age	20.35	2.29	16	24		
Education	13.35	2.2	8	19		
TMT-A	28.42	27	15	47	0.38	−0.82
TMT-B	53.41	51	28	95	0.76	−0.11
B–A	24.99	23	0	60	0.68	0.95
B:A	1.94	1.9	1	3.67	1.05	2.32
B–A/A	0.94	0.9	0	2.67	1.05	2.32
Middle-aged group (25–54 years; education: 0–12 years; $N = 24$: male = 10, female = 14)						
Age	37.29	10.79	25	54		
Education	10.25	1.8	7	12		
TMT-A	33.04	7.89	23	49	0.48	−0.92
TMT-B	71.5	31.07	35	164	1.83	3.5
B–A	38.46	27.1	8	123	1.93	4.26
B:A	2.16	0.67	1.22	4	1.12	1.38
B–A/A	1.16	0.67	0.22	3	1.12	1.38
Middle-aged group (25–54 years; education: 13+ years; $N = 65$: male = 32, female = 33)						
Age	34.23	9.18	25	54		
Education	16.83	1.73	14	23		
TMT-A	25.82	8.21	12	60	1.62	3.95
TMT-B	53.51	18.19	30	118	1.22	1.37
B–A	27.69	15.52	8	78	1.29	1.16
B:A	2.15	0.65	1.27	4	0.97	0.39
B–A/A	1.15	0.65	0.27	3	0.97	0.39
Elderly group (55–80 years; $N = 65$: male = 22, female =43)						
Age	64	6.44	55	80		
Education	10.72	3.5	2	19		
TMT-A	40.45	37	15	120	2.29	7
TMT-B	97.03	79	34	461	3.28	14.97
B–A	56.58	38	4	348	3.11	12.62
B:A	2.45	2.13	1.11	5	1.07	0.1
B–A/A	1.45	1.13	0.11	4	1.07	0.1

of variance for TMT-A, 6.5% for TMT-B, 6.9% for B–A, 1.8% for B:A, and 1.8% for B–A/A. Gender alone explained 0% of variance of TMT-A, 1.3% of TMT-B, 2.8% of B–A, 3.1% of B:A, and 3.1% of B–A/A. On the contrary, education could explain 3.5% of variance for TMT-A, 8.4% for TMT-B, 8.2% for B–A, 2.3% for B:A, and 2.3% for B–A/A. Thus, education was considered a more appropriate stratification variable than age for brain-injury patients. This gave two levels: low education (0–11 years of education) and high education (12+ years of education). The ANOVA results revealed main effects for Trails B ($F(1,88) = 9.5$; $p < 0.003$), and the derived scores B–A ($F(1,88) = 10.3$; $p < 0.002$), B:A ($F(1,88) = 3.8$; $p = 0.055$), and B–A/A ($F(1,88) = 3.8$; $p = 0.055$). No differences were found for Trails A ($F(1,88) = 2.8$; $p = 0.098$).

Tables 3–5 provide descriptive statistics (mean, standard deviation, maximum, minimum, skewness, and kurtosis) for age, education, and TMT variables for the different groups in the three samples. Tables 6–8 provide normative data for TMT variables, stratified by age or age and education in the case of controls, and education in the case of schizophrenia and TBI samples.

4. Discussion

The aim of this study was to present clinical (TBI and schizophrenia patients) and non-clinical norms (Spanish healthy subjects) for the TMT, one of the most widely used tests in neuropsychological assessment. These norms represent a useful tool for the clinical setting and provide Spanish norms from healthy controls useful for comparative

Table 4
Statistical properties of the demographic and TMT variables for each normative group of patients with schizophrenia

	Mean	S.D.	Minimum	Maximum	Skewness	Kurtosis
Education: 0–11 years ($N = 60$: male = 47, female = 13)						
Age	23.52	6.44	15	42		
Education	7.4	1.21	5	8		
TMT-A	41.37	40	23	81	0.85	0.44
TMT-B	112.47	97.5	47	307	1.7	2.71
B–A	71.1	57	4	255	1.66	2.84
B:A	2.76	2.39	1.05	5.9	0.95	0.63
B–A/A	1.76	1.39	0.05	4.9	0.95	0.63
Education: 12+ years ($N = 67$: male = 35, female = 32)						
Age	28.58	7.04	18	48		
Education	13	1.83	12	19		
TMT-A	40.61	35	19	127	2.12	6.16
TMT-B	84	73	43	235	1.88	4.76
B–A	43.39	37	14	181	2.73	9.96
B:A	2.2	2.06	1.2	4.73	1.48	2.78
B–A/A	1.2	1.06	0.2	3.73	1.48	2.78

purposes with already existing norms. In the last 10 years, there has been an increase in the number of studies providing norms from non-clinical samples that allow to better address the presence or absence of cognitive difficulties in TMT performance across different populations (Lu & Bigler, 2002; Mitrushina et al., 2005; Salthouse et al., 2000; Seo et al., 2006; Steinberg et al., 2005; Strauss et al., 2006; Tombaugh, 2004). But, to our knowledge, no clinical norms exist for populations in which TMT performance is altered (i.e., schizophrenia or TBI patients). One of the main advantages of using normative data from clinical samples is to improve the interpretation of cognitive deficits and clinical evolution of patients (Kizilbash et al., 2000).

Results from univariate ANCOVAs comparing TMT scores between the three samples, once the influence of age and education was controlled, confirmed the presence of differences between healthy controls and the two groups of patients in all direct and derived indices. Moreover, TBI patients' performance was poorer in Trails A, Trails B, and B–A than schizophrenia patients'. No differences were found in the B:A and B–A/A ratio scores between TBI and schizophrenia samples. As suggested in the literature, a possible explanation for these dissociations between direct and derived scores in the two groups of patients is that B:A and B–A/A derived scores may represent more reliable

Table 5
Statistical properties of the demographic and TMT variables for each normative group of patients with TBI

	Mean	S.D.	Minimum	Maximum	Skewness	Kurtosis
Education: 0–11 years ($n = 34$: male = 30, female = 4)						
Age	35.26	12.88	16	59		
Education	8.91	1.11	8	11		
TMT-A	82.76	51	24	320	1.89	3.42
TMT-B	218	155	78	591	513	1.34
B–A	135.24	106.5	36	96.58	475	1.79
B:A	3.03	2.62	1.51	6.33	1.42	1.14
B–A/A	2.03	1.62	0.51	5.33	1.42	1.14
Education: 12+ years ($n = 56$: male = 42, female = 14)						
Age	34.27	12.48	18	72		
Education	15.46	2.3	12	18		
TMT-A	63.41	53.5	21	247	2.97	10.76
TMT-B	145.36	120	45	379	0.99	0.41
B–A	81.95	58	14	240	1.11	0.32
B:A	2.49	2	1.28	6.33	1.61	1.89
B–A/A	1.49	1	0.28	5.33	1.61	1.89

Table 6
Percentile ranks for healthy subjects ($n = 223$)

Percentile	TMT-A	TMT-B	B–A	B:A	B–A/A
Young group (16–24 years; $n = 69$)					
5	42.5	82	48	2.8	1.8
10	40	78	39	2.52	1.52
15	39	73.5	36.5	2.4	1.4
20	36	68	35	2.22	1.22
25	35	61.5	32.5	2.18	1.18
30	33	60	30	2.05	1.05
35	32	56.5	27	2.03	1.03
40	30	54	26	2	1
45	29	52	24	1.96	0.96
50	27	51	23	1.9	0.9
55	25.5	48	21.5	1.86	0.86
60	25	47	21	1.82	0.82
65	23.5	45	20	1.75	0.75
70	22	44	20	1.68	0.68
75	21.5	41.5	18.5	1.63	0.63
80	21	40	17	1.54	0.54
85	20	38.5	15	1.5	0.5
90	18	37	11	1.36	0.36
95	17	34.5	7.5	1.27	0.27

Percentile	TMT-A		TMT-B		B–A		B:A		B–A/A	
	0–12[a] ($n = 24$)	13+[a] ($n = 65$)	0–12[a] ($n = 24$)	13+[a] ($n = 65$)	0–12[a] ($n = 24$)	13+[a] ($n = 65$)	0–12[a] ($n = 24$)	13+[a] ($n = 65$)	0–12[a] ($n = 24$)	13+[a] ($n = 65$)
Middle-aged group (25–54 years; $n = 89$)										
5	48.25	43.8	160.25	88.8	118.5	61.7	3.85	3.61	2.85	2.61
10	45	36.8	125.5	79.4	81	55	3.29	3.07	2.29	2.07
15	44	32.3	94.5	76.1	54	46.1	2.88	2.95	1.88	1.95
20	41	31	91	70.8	51	42.8	2.6	2.75	1.6	1.75
25	39.5	30	81.75	65	46.25	31	2.45	2.5	1.45	1.5
30	37.5	28	76.5	59.6	41	27.2	2.29	2.32	1.29	1.32
35	36.25	26	72.75	54.8	40.25	27	2.26	2.25	1.26	1.25
40	36	26	66	51.6	40	25.6	2.2	2.08	1.2	1.08
45	32.75	25	65	49.3	38.5	25	2.11	2.04	1.11	1.04
50	31	25	64.5	49	36.5	24	2.09	2	1.09	1
55	30	22.7	59.5	46.7	31.5	23	2	1.96	1	0.96
60	29	22	56	45	25	21.4	1.89	1.9	0.89	0.9
65	27.75	22	54.5	42	23	20	1.85	1.85	0.85	0.85
70	27	21	53	41	22.5	18.8	1.81	1.72	0.81	0.72
75	26.25	20	52.25	39.5	19.75	17.5	1.66	1.61	0.66	0.61
80	26	20	52	39	19	16	1.58	1.56	0.58	0.56
85	24.5	19	48.5	37	17.75	13.9	1.52	1.5	0.52	0.5
90	23	18	43	35	12	11.6	1.39	1.44	0.39	0.44
95	23	17	36.75	34	8.5	10	1.24	1.33	0.24	0.33

Percentile	TMT-A	TMT-B	B–A	B:A	B–A/A
Elderly group (55–80 years; $n = 65$)					
5	82.8	221.7	169.1	4.77	3.77
10	61.4	165.8	117.8	4.11	3.11
15	53	140.4	89.4	3.78	2.78
20	49.8	125.6	74.8	3.55	2.55
25	47.5	105.5	64	3	2
30	42.6	100.4	54.4	2.59	1.59
35	40	91	50	2.5	1.5
40	38.6	90	46.6	2.28	1.28
45	37.3	85.3	42	2.21	1.21

Table 6 (*Continued*)

Percentile	TMT-A	TMT-B	B–A	B:A	B–A/A
50	37	79	38	2.13	1.13
55	35.7	74.1	34.7	1.98	0.98
60	35	69	32.4	1.9	0.9
65	33.1	66.1	31.1	1.82	0.82
70	31.6	62.8	29.6	1.72	0.72
75	29	60	28	1.69	0.69
80	27	55.4	25.2	1.63	0.63
85	25	54	22.7	1.56	0.56
90	22	50	18	1.5	0.5
95	20	43.2	14.3	1.43	0.43

[a] Education (in years).

indicators of executive control, relatively free from the influence of speed of processing (Arbuthnott & Frank, 2000; Lamberty et al., 1994; Lezak, 1995; Stuss et al., 2001). The absence of differences in these scores between the two clinical groups may be explained by an analogous executive deficit in both TBI and schizophrenia patients even when TBI patients were significantly slower as revealed by those differences measured in direct scores. These results confirm and extend prior evidences about a specific executive control deficit in both TBI and schizophrenia patients, that should be dissociated from a deficit in speed of processing (Evans, Chua, McKenna, & Wilson, 1997; Krabbendam, de Vugt, Derix, & Jolles, 1999; Ríos et al., 2004; Rodríguez-Sánchez et al., 2005).

The analyses derived from the stratification of healthy controls according to age confirmed prior results from different populations that normal ageing had a significant impact on TMT performance in our Spanish sample as reflected by direct scores (Salthouse & Fristoe, 1995; Salthouse et al., 2000; Tombaugh, 2004) Thus, direct scores did not significantly change in the two groups comprised between 16 and 54 years of age. On the contrary, there was a significant increment in the time to complete both A and B parts in the elderly group (55–80 years) compared to both young and middle-aged groups. In addition, our results support prior findings that B–A, B:A, and B–A/A derived indices are also sensitive to the effects of ageing (Drane et al., 2002; Hashimoto et al., 2006). Specifically, derived indices were worst in the elderly group when compared to both young and middle-aged groups.

Table 7
Percentile ranks for the schizophrenia sample ($n = 127$) stratified by education

Percentile	TMT-A		TMT-B		B–A		B:A		B–A/A	
	0–11[a] ($n = 60$)	12+[a] ($n = 67$)	0–11[a] ($n = 60$)	12+[a] ($n = 67$)	0–11[a] ($n = 60$)	12+[a] ($n = 67$)	0–11[a] ($n = 60$)	12+[a] ($n = 67$)	0–11[a] ($n = 60$)	12+[a] ($n = 67$)
5	68.75	83.8	268.3	148	207.8	108	5.13	3.96	4.13	2.96
10	60	62.4	199.1	140	140.7	69.6	4.47	3.01	3.47	2.01
15	57	56	159.7	113.6	121.7	58.8	3.9	2.88	2.9	1.88
20	50.8	54	144.2	106.4	94.2	56	3.71	2.68	2.71	1.68
25	48.5	47	123.75	91	81.5	49	3.46	2.61	2.46	1.61
30	45.7	43.6	122	88	77	45	3.18	2.34	2.18	1.34
35	44.65	42	116.3	87	73.9	44	2.95	2.27	1.95	1.27
40	43	38.8	109.4	83.8	68.2	42.6	2.69	2.2	1.69	1.2
45	41.55	36.8	102	75.8	60.55	39	2.6	2.12	1.6	1.12
50	40	35	97.5	73	57	37	2.39	2.06	1.39	1.06
55	38	34	94	71.6	53.45	35	2.34	1.99	1.34	0.99
60	36	32	85.4	70	51.4	31.2	2.28	1.92	1.28	0.92
65	34.35	31	82.7	66	47.05	30.8	2.22	1.84	1.22	0.84
70	33	30	76	63	40.9	28.4	2.06	1.76	1.06	0.76
75	30.25	29	71.25	62	36.25	27	2.02	1.71	1.02	0.71
80	29.2	26.8	68	57.6	33	25	1.93	1.66	0.93	0.66
85	27.15	24.2	64.15	56	28.15	24	1.79	1.57	0.79	0.57
90	27	22.8	61.2	50.6	21.3	21	1.63	1.47	0.63	0.47
95	26	21	53.05	43	8.3	17.2	1.19	1.32	0.19	0.32

[a] Education (in years).

Table 8
Percentile ranks for TBI sample ($n = 90$) stratified by education

Percentile	TMT-A		TMT-B		B–A		B:A		B–A/A	
	0–11[a] ($n = 34$)	12+[a] ($n = 56$)	0–11[a] ($n = 34$)	12+[a] ($n = 56$)	0–11[a] ($n = 34$)	12+[a] ($n = 56$)	0–11[a] ($n = 34$)	12+[a] ($n = 56$)	0–11[a] ($n = 34$)	12+[a] ($n = 56$)
5	233.75	137.7	538.5	303.4	358.75	219.8	6.3	5.46	5.3	4.46
10	196.5	107.9	512	280.4	289.5	193.6	5.85	4.75	4.85	3.75
15	185	88.8	404	232.2	242.25	158.35	4.86	3.76	3.86	2.76
20	127	76.8	309	210	194	131.8	3.67	3.25	2.67	2.25
25	94.25	71.25	294.5	196.5	170.75	108.75	3.15	2.82	2.15	1.82
30	78.5	63.7	237	189.4	156.5	104.9	3.06	2.71	2.06	1.71
35	71.5	60	222.5	158.55	125	91.45	3.02	2.25	2.02	1.25
40	60	60	180	137.4	115	74.4	2.93	2.15	1.93	1.15
45	55.25	59	166.25	128.4	113.25	60.7	2.74	2.11	1.74	1.11
50	51	53.5	155	120	106.5	58	2.62	2	1.62	1
55	49	51	150	117.3	101	55.3	2.55	2	1.55	1
60	49	49.8	150	111.6	100	52.8	2.48	1.9	1.48	0.9
65	46.75	47.9	137.25	97.9	90.75	50.9	2.38	1.81	1.38	0.81
70	42	44	129.5	90.3	76	45.1	2.28	1.75	1.28	0.75
75	40	40.5	126	80.5	68	36.75	2.19	1.68	1.19	0.68
80	40	35.8	116	74.8	55	29.6	2.07	1.57	1.07	0.57
85	37.25	32.55	94.5	63.1	52.5	26	1.79	1.49	0.79	0.49
90	34.5	29.4	81	55.8	48.5	17.7	1.76	1.42	0.76	0.42
95	25.5	25.85	79.5	49.7	41.25	16.7	1.6	1.36	0.6	0.36

[a] Education (in years).

The norms presented here meet six of the criteria proposed by Mitrushina et al. (1999) when evaluating norms for the TMT. According to Criterion 1, sample sizes were of at least 50 subjects per grouping, except in the low-education TBI group with 34 subjects and in the middle-aged low-education healthy group with 24 subjects. In spite of this, sample size is not judged to be a particularly serious problem in these groups, since standard deviations in TMT scores from the TBI and middle-aged healthy subjects were generally analogous in the high and low-education groups (see Tables 3 and 5). According to Criterion 2, we provided the description of sample composition including exclusion criteria. Data were presented by age (Criterion 3), education (Criterion 5), or both when appropriate, reporting gender distribution (Criterion 6) and presenting means and standard deviations for total time (in seconds) for TMT-A and TMT–B (Criterion 7). However, some specifications need to be made in order to clarify the clinical utility of the present norms. First, TBI and schizophrenia samples were stratified by education on the basis of the results from correlation and regression analysis. It has to be noted that none of the subjects within the schizophrenia sample was older than 48 years (according to the inclusion criteria), and that only five patients from the TBI sample were older than 55 years. The fact that the clinical samples were younger compared to healthy controls may explain the low influence of age in these two samples. In fact, the two control groups in this same age range (16–55) did not differ in any of the TMT scores. Therefore, caution must be taken when using the present clinical norms in patients with TBI and schizophrenia that are out of this age range. Second, it should be noted that the TBI sample was constituted by a high proportion of severe patients (65% severe vs. 8% moderate vs. 8% mild vs. 19% where GCS was not reported). Prevalence studies in Europe have recently indicated that for every severely injured patient there are about 1.5 moderately injured and 22 mildly injured patients (Tagliaferri, Compagnone, Korsic, Servadei, & Kraus, 2006). In spite of this bias in severity level within the TBI sample, the appropriateness of using the present norms for clinical purposes is supported by the fact that the effect of moderate–severe TBI has been shown to be more than three times the effect of mild head injury on overall cognitive functioning (for a meta-analysis see Schretlen & Shapiro, 2003). Thus, severe TBI patients are those that most frequently need to be followed up to assess their rehabilitation demands (see Turner-Stokes, Disler, Nair, & Wade, 2005, for a systematic review). The present clinical norms for TBI did not intend to improve the detection of impairment and disability in TBI (as it could be done using norms from healthy samples), but to improve the assessment of clinical evolution (i.e., detecting clinical changes across time or during treatment), severe patients being those who most frequently demand this kind of neuropsychological evaluation. Consequently, caution must be taken when using the present set of norms to assess mild TBI patients.

Some additional comments and suggestions for clinical practice could be derived from the present set of data. First, the utility of cut-off indexes in derivate scores has been previously questioned in the literature. For instance, it has been suggested that the use of a cut-off of 3.0 or greater for B:A ratio score would result in an unacceptable rate of false positives detecting impairment (Drane et al., 2002). Our results showed that only around 2.9% of healthy controls from the young group, 12.4% of participants from the middle-aged group, and 26.2% of participants from the elderly group were above this cut-off (13.5% of the total sample of healthy controls). These results contrast with the 50% of false positives reported by Drane et al. However, a B:A cut-off of 3.0 may represent a more sensitive and specific index to detect cognitive impairment than the screening tests usually employed in neurological and neuropsychological examination (i.e., Mini-Mental State Examination). The fact that the B:A score surpassed the 3.0 cut-off in 28.9% and 22.1% of the TBI and schizophrenia patients, respectively, may be taken as an evidence of different profiles of cognitive impairment and different severity levels within these two samples (Goldberg et al., 1989). In the light of the present evidence, the use of a cut-off of 3.0 for B:A ratio could not be dismissed as a sensitive indicator of executive abilities involved in TMT performance. However, further research is needed to validate its clinical utility as a severity index. Second, correlation analyses showed a strong linear relationship between B–A and TMT-B scores (higher than 0.9 in the three samples), as well as a linear dependence between B:A and B–A/A scores ($r = 1$ in the three samples; where B–A/A equals B:A − 1). Therefore, the clinical use of B–A and B–A/A scores seems to be redundant with regard to TMT-B and B:A scores, respectively.

To summarize, the major value of the present study is to provide a new set of clinical and non-clinical norms for neuropsychologists to determine more precisely the extent to which scores on Trails A and B, and derived indices reflect the impaired performance. This issue has repercussions for research, forensic, and clinical settings that would benefit from both a more precise classification of the patients and the detection of small changes in performance. In addition, we provide norms from a large sample of Spanish healthy individuals that could be used for comparison purposes with North and South American Latino groups.

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