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Validation of a brief screening tool for alcohol-related neuropsychological impairments (BEARNI)

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Abstract:	<p>Background: Alcohol-related neuropsychological impairments mainly affect episodic memory, working memory and visuospatial abilities, as well as executive and motor functioning. These impairments can prevent alcoholic patients early in abstinence from benefiting fully from treatment, and reduce their ability to remain abstinent. A neuropsychological assessment at alcohol treatment entry therefore seems essential for making the relevant clinical decisions. However, very few alcohol treatment departments have the financial and human resources needed to conduct an extensive neuropsychological examination of each alcoholic patient. The goal of the present study was therefore to assess the validity and the psychometric properties of the Brief Evaluation of Alcohol-Related Neuropsychological Impairments (BEARNI), a new screening tool especially designed to assess patients at alcohol treatment entry.</p> <p>Methods: A total of 254 healthy controls completed the BEARNI, and 58 of them also performed an extensive neuropsychological battery. 73 alcoholic patients underwent both the BEARNI and the neuropsychological battery. This extensive neuropsychological battery of proven classification accuracy served as the reference (i.e., gold standard) for determining the alcoholic patients' cognitive status.</p> <p>Results: An exploratory factor analysis validated the BEARNI's underlying</p>

	<p>structure, highlighting five factors that reflected visuospatial abilities, executive functions, ataxia, verbal episodic memory and verbal working memory. The standardization of each BEARNI subtest and the two total scores revealed that this test has sufficient diagnostic accuracy for the detection of alcoholic patients with cognitive and motor impairments. Conclusion: The present study indicates that the BEARNI is a useful screening tool in clinical settings for detecting alcoholic patients' motor and cognitive impairments at treatment entry.</p>

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1 **Validation of a brief screening tool for alcohol-related neuropsychological impairments**

2 **(BEARNI)**

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1 **ABSTRACT**

2 **Background:** Alcohol-related neuropsychological impairments mainly affect episodic
3 memory, working memory and visuospatial abilities, as well as executive and motor
4 functioning. These impairments can prevent alcoholic patients (ALs) early in abstinence from
5 benefiting fully from treatment, and reduce their ability to remain abstinent. A
6 neuropsychological assessment seems essential for making the relevant clinical decisions.
7 However, very few alcohol treatment departments have the financial and human resources
8 needed to conduct an extensive neuropsychological examination of each alcoholic patient.
9 The goal of the present study was therefore to assess the validity and the psychometric
10 properties of the Brief Evaluation of Alcohol-Related Neuropsychological Impairments
11 (BEARNI), a new screening tool especially designed to assess alcohol-related
12 neuropsychological impairments.

13 **Methods:** A total of 254 healthy controls (HCs) completed the BEARNI, and 58 of them also
14 performed an extensive neuropsychological battery. 73 ALs underwent both the BEARNI and
15 the neuropsychological battery. This extensive neuropsychological battery of proven
16 classification accuracy served as the reference (i.e., gold standard) for determining the ALs'
17 cognitive status.

18 **Results:** An exploratory factor analysis validated the BEARNI's underlying structure,
19 highlighting five factors that reflected visuospatial abilities, executive functions, ataxia,
20 verbal episodic memory and verbal working memory. The standardization of each BEARNI
21 subtest and the two total scores revealed that this test has sufficient diagnostic accuracy for
22 the detection of ALs with cognitive and motor impairments.

23 **Conclusion:** The present study indicates that the BEARNI is a useful screening tool in
24 clinical settings for detecting ALs' motor and cognitive impairments.

25

- 1 **Keywords:** alcoholism, neuropsychological impairment, brief cognitive screening tool,
- 2 exploratory factor analysis, ROC curve

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1 INTRODUCTION

2 Chronic alcoholism results in brain damage and compromised motor and cognitive
3 functioning, even in alcoholic patients (ALs) with no severe neurological complications (i.e.
4 those without Korsakoff's syndrome (KS), or alcoholic dementia). The neuropsychological
5 impairments mainly encompass executive dysfunction (Ihara et al., 2000), working memory
6 deficits (Pitel et al., 2007; Uekermann et al., 2007) and visuospatial disabilities (Fama et al.,
7 2004). Genuine episodic memory impairments (i.e., not resulting solely from executive
8 dysfunctions) are also observed in ALs (Noël et al., 2012), but are generally less severe than
9 executive and visuospatial impairments (Sullivan et al., 2000). Deficits in motor functions
10 including ataxia of gait and balance (Fein and Greenstein, 2013) are just as severe as the
11 visuospatial deficits (Sullivan et al., 2000). These cognitive and motor impairments have been
12 estimated to affect more than two thirds of ALs (Ihara et al., 2000). The deficits range from
13 mild-to-moderate (Sullivan et al., 2000), that is, about one standard deviation from the mean
14 for non-alcoholic healthy controls (HCs) (Goldstein et al., 2004), to severe impairments
15 comparable to those observed in KS patients (Kopelman et al., 2009).

16 The treatment of alcohol-dependence includes several types of therapy such as Motivational
17 Enhancement Therapy, Twelve-Step Facilitation or cognitive behavioral therapy, which all
18 require attending to and receiving new information, and being able to integrate and translate it
19 into behavioral changes (Bates et al., 2006). To benefit from these therapies, ALs must
20 implement cognitive functions such as episodic memory, planning, inhibition and problem-
21 solving abilities, which have been repeatedly found as impaired. Episodic memory deficits
22 and executive dysfunction hinder complex learning, such as the learning of semantic
23 information and cognitive procedures (Pitel et al., 2007), affect readiness to change (Blume et
24 al., 2005), ability to elaborate alternative behavioral responses (Bates et al., 2006) and
25 decision making (Noël et al., 2007). These cognitive disabilities impact treatment compliance

1 and treatment outcomes (Bates et al., 2006). Thus, ALs with impaired cognitive functions
2 may be unable to benefit fully from therapy interventions. The detection of
3 neuropsychological impairments is therefore essential for making the appropriate clinical
4 decisions regarding the nature and timing of treatment.

5 Few alcohol departments and clinics have the financial and human resources needed to
6 administer an extensive neuropsychological examination to each ALs. Previous studies have
7 proposed a range of screening instruments for the detection of cognitive impairments in
8 patients with substance use disorders (SUDs), including the Neurobehavioral Cognitive Status
9 Examination (NCSE; (Kiernan et al., 1987), the Repeatable Battery for Assessment of
10 Neuropsychological Status (RBANS; (Randolph et al., 1998) and the Montreal Cognitive
11 Assessment (MOCA; (Nasreddine et al., 2005). According to (Shulman, 2000), an ideal
12 cognitive screening test should fulfill the following criteria: a) be readily administered; b) be
13 easy to score; c) have concurrent validity; and d) have high levels of sensitivity, specificity
14 and predictive validity. Despite the fact that existing screening tools can be administered
15 within 10-30 minutes and have satisfactory sensitivity to cognitive impairment in SUD
16 patients (Copersino et al., 2009; Fals-Stewart, 1997), they have several limitations. In addition
17 to poor specificity in detecting impaired patients (36% for NCSE and 69% for MOCA; Fals-
18 Stewart, 1997; Wester et al., 2013), these tools assess cognitive functions that are not usually
19 reported as impaired in ALs, including orientation, attention and concentration, language and
20 naming. Even though total MOCA and RBANS scores are lower for SUD patients than for
21 controls, analysis of individual subscores has shown that only memory, executive and
22 visuospatial abilities are impaired in patients compared with controls (Alarcon et al., 2015;
23 Green et al., 2010; Wester et al., 2013). More specifically, in a recent study (Alarcon et al.,
24 2015), performances of ALs with low (≤ 21), medium (22-25) and high (≥ 26) MOCA total
25 score were compared on each subscore of this test. The most affected domains concerned

1 abstraction and fluency. The authors raised a limitation to the MOCA that is the narrow range
2 of these subscores (respectively from 0 to 1 and 2) that can limit the assessment of the
3 severity of cognitive deficits and its improvement with abstinence and treatment.

4 Overall, these screening tools do not have a satisfactory level of content validity for chronic
5 alcoholism probably because they were initially designed to detect cognitive impairments
6 either in older individuals (Nasreddine et al., 2005; Randolph et al., 1998) or else in patients
7 receiving neurosurgical care for brain lesions (Kiernan et al., 1987). A screening tool must be
8 validated against a gold standard, in order to avoid misdiagnosis due to false negatives or
9 false positives. In the above-mentioned studies conducted in SUD patients, these patients'
10 cognitive profile was either not reported (Alarcon et al., 2015; Wester et al., 2013) or else
11 determined using the Neuropsychological Screening Battery (Heaton et al., 1990) or the
12 Neuropsychological Assessment Battery–Screening Module (White and Stern, 2003). These
13 short neuropsychological batteries both have poor specificity (Fals-Stewart, 1996) and have
14 been validated in SUD patients (Fals-Stewart, 1996; Grohman and Fals-Stewart, 2004) but not
15 specifically in alcoholic ones. Moreover, a main limitation of a previous study (Wester et al.,
16 2013) was that the MOCA was administered to patients at admission whereas the extensive
17 neuropsychological battery was conducted 6 to 8 weeks later. Since some of the cognitive
18 functions can recover, even after a short time of abstinence (from 3-5 weeks of abstinence;
19 (Mann et al., 1999)), the delay between the MOCA and the extensive battery substantially
20 limits the determination of the psychometric properties of the MOCA. Other brief screening
21 tools have been used in previous studies to describe the general cognitive status of alcoholic
22 patients, such as the MMSE (Folstein et al., 1975) and DRS Mattis (Mattis and Inc, 1988).
23 Results are discrepant since some of them reported impairments (Le Berre et al., 2010;
24 Rosenbloom et al., 2007) whereas other did not (Pitel et al., 2011). These tools are mainly

1 used as inclusion criteria in studies conducted in ALs and to exclude patients with low scores
2 that may be explained by dementia.

3 The goal of the present study was therefore to validate a new screening tool especially
4 designed for the rapid assessment of alcohol-related neuropsychological deficits. The Brief
5 Examination of Alcohol-Related Neuropsychological Impairment (BEARNI) is intended to be
6 short and easy to score, making it usable by non-psychologists. It is expected to enable
7 physicians or nurses to rapidly determine whether a patient can attend and gain from standard
8 alcohol treatment or whether some adjustments are required. More specifically, we sought to
9 assess the BEARNI's validity and its psychometric properties in order to determine whether it
10 is an appropriate tool for identifying cognitive and motor impairments in ALs. A value of
11 80% or above indicates high psychometric quality (Blazer and Hays, 1998), and we expected
12 the BEARNI's psychometric properties to meet this criterion.

13

14 **MATERIALS AND METHODS**

15 *Participants*

16 A total of 254 HCs completed the BEARNI, and 58 of them also performed an extensive
17 neuropsychological battery. We administered both the BEARNI and the extensive battery to
18 73 ALs. None of the participants had a history of neurological pathologies, endocrine or
19 infectious diseases, mental illness (psychiatric disorders assessed by the MINI 500;
20 (American Psychiatric Association, 2004), depression (Beck Depression Inventory, BDI-II;
21 (Beck et al., 1961), or other forms of substance misuse or dependence (except tobacco) over
22 the lifetime. None were under psychotropic medication that might have had an effect on their
23 cognitive functioning. All the participants were informed about the study (approved by the
24 local ethics committee) and provided their written informed consent before their inclusion.
25 Their demographic characteristics (age, sex ratio and education) with their scores on the Mini

1 Mental State Examination (MMSE; Folstein et al., 1975) and the Mattis Dementia Rating
2 Scale (DRS; Mattis and Inc, 1988) are reported in Table 1.

3 The ALs were recruited by clinicians while they were receiving withdrawal treatment as
4 inpatients at Caen University Hospital. All the patients met the DSM-IV criteria for alcohol-
5 dependence (American Psychiatric Association, 2004). None of them had severe, enduring
6 and global amnesia defining the Korsakoff's syndrome nor alcoholic dementia, Marchiafava-
7 Bignami or central pontine myelinolysis. Although the patients were early in abstinence, none
8 of them presented physical symptoms of alcohol withdrawal at inclusion. They were
9 interviewed with the Alcohol Use Disorders Identification Test (AUDIT; (Gache et al., 2005)
10 and a modified version of the semistructured Lifetime Drinking History questionnaire.
11 Measures included the duration of alcohol use (in years), alcohol misuse (in years), number of
12 withdrawals, and daily alcohol consumption prior to treatment (in standard drinks, a standard
13 drink corresponding to a beverage containing about 10 g of pure alcohol) (Table 1).

14 All the HCs were interviewed with the AUDIT (Gache et al., 2005) to ensure that they did not
15 meet the criteria for alcohol abuse or dependence over the lifetime (AUDIT <7 for men and
16 <6 for women) (Table 1). None of the HCs had a MMSE (Folstein et al., 1975) or a Mattis
17 DRS (Mattis and Inc, 1988) scores below the cut-off score of 24 and 127 respectively.

18

19 *Material*

20 Participants completed the BEARNI and the extensive battery of neuropsychological tests
21 over 2-3 days to minimize fatigue and interference. Only 58 of the HCs completed the
22 neuropsychological battery (demographic characteristics in Table 1) in addition to the
23 BEARNI. The latter was administered on the first day to avoid the possible influence of the
24 extensive battery on performances. The order of the test administration was fixed because
25 some of the BEARNI subtests were inspired by neuropsychological tests administered to

1 participants (see below the description of the BEARNI subtests). Thus, in administering the
2 BEARNI before the extensive neuropsychological battery, all the subjects in our study were
3 in the same situation than patients in clinical settings who would first undergo the BEARNI
4 and then, an extensive neuropsychological examination. Raw scores of the BEARNI and the
5 extensive neuropsychological battery are provided in Supporting Information B table 4.

6

7 **Brief Examination of Alcohol-Related Neuropsychological Impairments** 8 **(BEARNI)**

9 The BEARNI is designed to assess the cognitive and motor functions that are impaired in
10 ALs, namely episodic memory, working memory, executive functions, visuospatial abilities,
11 and ataxia (Table 2). It takes approximatively 15-20 minutes to administer the BEARNI. In
12 order to avoid errors, instructions for administration and scoring are provided in Supporting
13 Information A. Examples of the working memory, flexibility, visuospatial and ataxia subtests
14 are provided to participants prior to data collection. The BEARNI is provided in Supporting
15 Information A.

16 The *episodic memory* subtest was inspired by the California Verbal Learning Test (Delis et
17 al., 1988). It consists of two learning trials of a 12-word list (4 words x 3 semantic
18 categories). The list is read aloud by the examiner. After each trial, the patient is instructed to
19 freely recall as many words as possible, in any order (1 minute per trial, no points scored).
20 Once the remaining tests from the BEARNI have been administered, delayed free recall is
21 performed (one trial lasting 1 minute). The episodic measure is the number of correct
22 responses (0.5 point per response) minus the number of errors (intrusions and perseverations;
23 0.5 point per error) during the delayed free recall task (maximum score: 6 points).

24 *Working memory* is assessed with an alphabetical span subtest adapted from the alpha-span
25 task (Belleville et al., 1998). This task probes the ability to manipulate information stored in

1 verbal working memory. Increasingly long letter sequences are read out loud, and for each
2 sequence the patient has to repeat the letters in alphabetical order. Two trials are performed
3 for each sequence. The task ends when the participant fails both two trials of a sequence (0.5
4 point per trial; maximum score: 5 points).

5 **Flexibility abilities** are assessed with the alternating verbal fluency subtest. Patients are given
6 120 seconds to generate as many words as possible from two alternating categories (“color
7 name” and “city name”). Depending on the number of correct responses, points range from 0
8 to 6 (for scoring details, see Supporting Information A).

9 **Visuospatial abilities** are assessed with an adapted version of the Hidden Figures Test
10 (Corkin, 1979; Thurstone, 1944). This subtest includes five complex figures, each containing
11 two separate hidden figures that the patient has to find. An example is provided and explained
12 to the patient by the examiner. For each complex figure, one point is provided when the
13 patient finds both hidden figures within 1 minute (maximum score: 5 points).

14 Finally, the **ataxia** subtest, drawn from the Walk-a-Line Ataxia Battery (Fregly, 1971),
15 requires patients to stand on each foot in turn for 30 seconds, first with eyes open, then with
16 eyes closed. There are up to two trials per condition. For each condition, 2 points are awarded
17 when patients successfully perform the task at the first trial, 1 point when they successfully
18 perform the task at the second trial, and 0 point when they fail both trials (maximum score: 8
19 points).

20 The BEARNI yields seven scores: five subscores (one for each of the subtests), a total score
21 (maximum score: 30 points) and a total *cognitive* score (excluding the ataxia subtest;
22 maximum score: 22 points).

23

24 **Neuropsychological examination**

1 The extensive neuropsychological battery we administered targeted a broad range of cognitive
2 and motor functions: *verbal episodic memory* (French adaptation of the CVLT (Delis et al.,
3 1988)); *working memory* (verbal and visuospatial spans of the MEM-III (Wechsler, 2001a)
4 and the Letter-Number Sequencing subtest of the WAIS-III (Wechsler, 2001b)); *executive*
5 *functions* (the Trail Making Test (Reitan, 1955), the Ruff Figural Fluency Test (RFFT;
6 (Foster et al., 2005), the Stroop test (Stroop, 1935), and fluency tasks (Cardebat et al., 1990);
7 *visuospatial abilities* (the Rey-Osterrieth Complex Figure (ROCF; (Osterrieth, 1944)) and
8 *ataxia* (the Walk-a-Line Ataxia Battery). The data collected for each test are summarized in
9 Table 2.

10

11 ***Data analysis***

12 **Validation of the BEARNI's internal structure**

13 The first step consisted of an exploratory factor analysis (EFA) to determine the BEARNI's
14 factorial structure, the explained variance for each factor and the total variance. An orthogonal
15 rotation (normalized varimax rotation) was used because the latent factors were not correlated
16 with each other (data not shown). The number of factors was determined by three criteria: a)
17 eigenvalues above 1 (Kaiser criterion; (Kaiser, 1960); b) proportion of variance explained by
18 the factor above 5%; and c) number of theoretical variables in the integrated model. Given the
19 number of cognitive and motor functions targeted by the BEARNI (delayed verbal memory,
20 verbal working memory, flexibility, visuospatial abilities and ataxia), we expected to extract
21 five factors reflecting these five domains. A threshold ≥ 0.50 was used to determine the factors
22 on which each variable loaded. Any factor below the threshold of 0.50 was assigned to the
23 factor on which it most highly loaded. The EFA was conducted with the 58 HCs and 73 ALs
24 who had completed both the BEARNI and the extensive battery.

1 In addition, we compared the performance profiles of the ALs and HCs on each of the
2 BEARNI subtests. The objective was to determine whether the BEARNI's
3 neuropsychological profile was consistent with that described in the literature. To do so, we
4 carried out multivariate analyses of variance (MANOVAs; 2 groups x 5 subtests x 2 sexes;
5 age and education entered as covariates) and Tukey's tests for post-hoc comparisons.

6

7

Standardization of the BEARNI

8

Total scores

9 For the BEARNI's two total scores (total score and total cognitive score), the standardization
10 was performed for the 58 HCs who had completed the neuropsychological battery. We used
11 the method described in (Godefroy et al., 2014) and reported in Supporting Information B.

12

13

Psychometric properties of the BEARNI total scores

14 Sensitivity, specificity, positive and negative predictive values, diagnostic accuracy (% of
15 patients well classified; i.e., reliability of the screening test) and Yule's Q coefficient
16 (coefficient measuring the association between two attributes, ranging from 0 to 1, where a Q
17 coefficient of 0.70-1 is deemed to represent a very strong association) were computed using
18 the ALs' results on the BEARNI.

19

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BEARNI subtests

25 For each subtest, we determined cut-off scores using the data collected from the 254 HCs who
26 had completed the BEARNI with the method described in (Godefroy et al., 2014) and in
27 Supporting Information B. We then investigated the predictive value of these cut-off scores

1 for detecting ALs with impaired performances on the neuropsychological battery. Based on
2 the cut-off scores, patients were classified as either impaired or preserved on each BEARNI
3 subtest. Performances on the tasks in the extensive neuropsychological battery were thus
4 compared across three groups (HCs ($n=58$), ALs with impaired BEARNI performances, and
5 ALs with preserved BEARNI performances) using an ANOVA. Tukey's tests were then
6 carried out for post-hoc comparisons. For each subtest, we regarded the BEARNI cut-off
7 score as predictive when ALs classified as impaired on a specific BEARNI subtest performed
8 more poorly on the corresponding domain of the neuropsychological battery than ALs with
9 preserved results on that subtest and HCs.

10

11 Statistical analyses were performed using Statistica and MedCalc software and the probability
12 significance threshold was set at $p \leq 0.05$. Where necessary, Bonferroni corrections were
13 applied to prevent Type-I errors.

14

15 **RESULTS**

16 *Validation of the BEARNI's internal structure*

17 The results of the EFA analysis are reported in Table 3. All the factors met the criteria of an
18 eigenvalue above 1 (Kaiser, 1960) and more than 5% of variance explained by the factor.
19 Consistent with our hypothesis, five factors were extracted. Factor 1 was deemed to reflect
20 executive and visuospatial abilities, factor 2 was represented by ataxia, factor 3 included
21 variables related to verbal episodic memory, factor 4 was represented by fluency tasks and
22 factor 5 included variables related to verbal working memory. Taken together, these five
23 factors accounted for 60.08% of the total variance. When restricted to HCs ($n=58$), the EFA
24 yielded the same results.

1 The two (group: ALs vs. HCs) x two (sexes) x five (BEARNI subtests) MANOVA on
2 BEARNI performances revealed significant effects of group, $F_{(1, 324)} = 53.53, p < 0.001$, age,
3 $F_{(1, 327)} = 11.28, p < 0.001$, and education, $F_{(1, 327)} = 69.72, p < 0.001$, the Subtest x Group
4 interaction, $F_{(4, 1308)} = 16.02, p < 0.001$, and the Subtest x Education interaction, $F_{(4, 1308)} = 3.55,$
5 $p = 0.007$, but no other significant effects. Tukey's post-hoc tests revealed that ALs performed
6 more poorly than HCs (effect of group), and this effect was found for each of the BEARNI
7 subtests (Subtest x Group interaction) except for delayed verbal memory (Figure 1).

8

9 ***Standardization of the BEARNI***

10 Most of the raw scores (both for the BEARNI and for the extensive neuropsychological
11 battery) deviated from normality and were influenced by age, education, sex, or all three.

12

13 **Standardization of the BEARNI's total scores**

14 On the extensive neuropsychological battery, 86% of ALs were classified as having at least a
15 mild impairment, 53% as having a moderate-to-severe impairment, and 14% having no
16 impairment. Regarding the neuropsychological battery with only cognitive functions (i.e.,
17 excluding performances on the Walk-a-Line Ataxia Battery), 84% of ALs were classified as
18 having at least a mild impairment, 45% as having a moderate-to-severe impairment and 16%
19 as having no impairment.

20 The ROC curve analysis performed to standardize the total BEARNI score (cognitive
21 functions plus ataxia) showed that a cut-off score of ≤ 19 yielded the best balance between
22 sensitivity and specificity for detecting mild impairment in the neuropsychological battery
23 (Supporting Information B Table 2, Figure 2A). For moderate-to-severe impairment, a cut-off
24 score of ≤ 16 yielded the best balance between sensitivity and specificity (Supporting
25 Information B Table 2, Figure 2B).

1 Regarding the total cognitive score (excluding the ataxia BEARNI subtest), a cut-off score of
2 ≤ 15 yielded the best balance between sensitivity and specificity for detecting mild impairment
3 in the neuropsychological battery (Supporting Information B Table 2, Figure 2C). For
4 moderate-to-severe impairment, a cut-off score of ≤ 11.5 yielded the best balance between
5 sensitivity and specificity (Supporting Information B Table 2, Figure 2D).

6 Linear regression analysis (forward stepwise) conducted in HCs and ALs showed a significant
7 effect of education on these two total BEARNI scores, indicating that participants with more
8 than 12 years of schooling had better performances. Thus, in order to correct for this
9 education effect, we adjusted the cut-off scores for participants with more than 12 years of
10 schooling. This adjustment of the cut-off scores was determined by the best balance between
11 true positive and true negative on the extensive neuropsychological battery. All total cut-off
12 scores are summarized in Table 5.

13

14 ***Psychometric properties of the BEARNI***

15 The psychometric properties of the BEARNI total scores are reported in Table 5. The
16 sensitivity, positive and negative predictive values, Yule's Q coefficient and diagnostic
17 accuracy to identify ALs showing mild or moderate-to-severe impairments on the extensive
18 neuropsychological battery range from acceptable to excellent. However, the specificity of the
19 BEARNI total scores for identifying ALs with mild impairments was low.

20 Only 9.59% and 8.22% of alcoholic patients were impaired on the MMSE and Mattis DRS
21 respectively. Although the specificity and the positive predictive value were excellent for the
22 MMSE (Folstein et al., 1975) and the Mattis DRS (Mattis and Inc, 1988) in identifying
23 alcoholic patients with mild impairment, the positive predictive value for moderate-to-severe
24 impairment as well as the sensitivity, negative predictive value, Yule's Q coefficient and
25 diagnostic accuracy were poor for mild and moderate-to severe impairments (Table 5).

1

2

Standardization of the BEARNI subtests and predictability

3 Each of the subtest scores yielded sensitivity values of 100%, specificity values ranging from
4 75.21% to 99.59%, and AUC values ranging from 0.950 to 0.998 (Supporting Information B
5 Table 3). ROC analyses provided cut-off scores for the following BEARNI subtests: delayed
6 verbal memory ≤ 2 ; alphabetical span ≤ 2.5 ; alternating fluency ≤ 2 ; visuospatial ≤ 1 ; and ataxia
7 ≤ 3 .

8 These cut-off scores indicated that 16% of the ALs were impaired on the episodic memory
9 subtest, 32.91% on the alphabetical span subtest, 21.52% on the alternating fluency subtest,
10 45.57% on the visuospatial subtest, and 49.36% on the ataxia subtest.

11 We then compared the HCs, ALs with impaired BEARNI results, and patients with preserved
12 BEARNI results on cognitive performances. Using the cut-off scores of each BEARNI
13 subtest, we compared these three groups on the corresponding domain of the
14 neuropsychological battery. As the raw scores on the neuropsychological battery were
15 influenced by demographic factors, each comparison was conducted using standard residuals.

16 All ANOVA results are provided in Table 6. The cut-off score of ≤ 2 for the delayed verbal
17 memory BEARNI subtest was predictive of performances on CVLT. Regarding the
18 alphabetical span BEARNI subtest, the cut-off score of ≤ 2.5 was predictive of performances
19 on verbal forward span and Letter-Number Sequencing. The cut-off of ≤ 2 for the flexibility
20 subtest was predictive of performances on the verbal fluency tasks and the TMT (Part B
21 minus Part A; $F_{(1, 128)} = 9.25, p < 0.001$, Tukey's post-hoc: impaired ALs < (preserved ALs
22 =HCs)). Regarding the visuospatial BEARNI subtest, the cut-off score of ≤ 1 was predictive of
23 performances on visuospatial backward span, Stroop, TMT and RFFT (total design but not
24 total strategies). For the ROCF and visuospatial forward span, although impaired ALs had
25 lower performances than preserved ALs and HCs (who did not differ between each other), no

1 statistical differences were found between the two patient groups. Finally, the cut-off of ≤ 3
2 for the ataxia subtest was predictive of performances on the Walk-a-Line Ataxia Battery.

3

4 **DISCUSSION**

5 The goal of the present study was to assess the validity and psychometric properties of the
6 BEARNI, a new screening tool especially designed for the rapid assessment of alcohol-related
7 neuropsychological deficits. An extensive neuropsychological battery of proven classification
8 accuracy (Godefroy et al., 2014) served as the reference (i.e., gold standard) for determining
9 the ALs' cognitive status.

10 In agreement with our theoretical hypothesis, the EFA validated the BEARNI's underlying
11 structure, as it highlighted five factors that accounted for 60% of the total variance: a first
12 factor including visuospatial and visual executive abilities, a second one reflecting ataxia, a
13 third one verbal episodic memory, a fourth one spontaneous cognitive flexibility, and a fifth
14 one verbal working memory. Three of these factors involved executive functions and
15 visuospatial abilities, which are impaired in two thirds of ALs (Ihara et al., 2000), and more
16 severely so than other cognitive deficits (Sullivan et al., 2000). The second factor, which
17 pertained to ataxia, was in agreement with deficits in gait and balance described in previous
18 studies (Fein and Greenstein, 2013) as being just as severe as the visuospatial impairments
19 (Sullivan et al., 2000). The delayed verbal memory factor represented a smaller proportion of
20 the explained variance in the present study, in accordance with a less severe and consistent
21 impairment of this function in ALs compared with other deficits (Ihara et al., 2000; Sullivan
22 et al., 2000). Thus, these results suggest that the BEARNI has satisfactory content validity.

23 Even though the BEARNI includes most of the cognitive domains known to be impaired in
24 ALs, such a brief screening tool cannot allow for the assessment of all cognitive functions.
25 For example, there is no evaluation of inhibition abilities, even though inhibition deficits have

1 repeatedly been reported in alcoholism (Ihara et al., 2000; Lusher et al., 2004) and have been
2 linked to poorer delayed recall in episodic memory (Noël et al., 2012) and motivation to
3 change (Blume et al., 2005). The EFA revealed that inhibition abilities contributed to the
4 variability of the visuospatial BEARNI subtest, which requires participants to find two figures
5 hidden in a complex figure. Impaired visuospatial global-local processing in alcoholism has
6 also been found to reflect difficulty inhibiting local information (Müller-Oehring et al., 2009).
7 Thus, performances on the visuospatial BEARNI subtest seem to be cognitively multi-
8 determined and may also reflect inhibition abilities.

9 This interpretation is confirmed by the high concurrent validity we observed when we
10 standardized the BEARNI subtests. ALs classified as impaired on the BEARNI subtests using
11 the cut-off scores were also impaired on the corresponding cognitive and motor domains of
12 the extensive battery. Those classified as preserved did not differ from HCs. Performances on
13 the visuospatial BEARNI subtest were predictive of results for the visuospatial abilities
14 assessed by the extensive neuropsychological battery, as well as for visuospatial working
15 memory, inhibition and flexibility. The episodic memory, verbal working memory, flexibility
16 and ataxia subtests were similarly predictive. Thus, the cut-off scores computed for each
17 BEARNI subtest had high diagnostic efficiency in terms of accurately detecting the cognitive
18 impairments observed on the extensive neuropsychological battery. In addition, performances
19 on each BEARNI subtest were only predictive of results on the corresponding cognitive
20 domains, and not of all the domains evaluated by the extensive battery. Taken together, these
21 findings indicate that the BEARNI could be used in clinical settings to obtain a reliable
22 estimation of neuropsychological performances, including episodic memory, executive
23 functions, working memory, visuospatial abilities and ataxia. Compared to other screening
24 tools, such as the MOCA (Alarcon et al., 2015; Wester et al., 2013), the BEARNI provides

1 larger scales of cut-off score for each subtest, that may lead to a more accurate assessment of
2 the severity and the improvement of neuropsychological deficits with abstinence.

3 Analysis of the BEARNI's psychometric properties showed that the two total scores made it
4 possible to distinguish between ALs with no impairment, mild deficits or moderate-to-severe
5 impairments, with satisfactory sensitivity, predictive validity and diagnostic accuracy (Blazer
6 and Hays, 1998). This finding suggests that 1) even ALs with mild impairments can be
7 detected with the BEARNI, and 2) the BEARNI identifies alcohol-related cognitive and
8 motor impairments with a high degree of accuracy. Yule's Q coefficients highlighted a strong
9 association between the cognitive profiles identified by the extensive neuropsychological
10 battery and by the BEARNI, suggesting a high reliability of our screening tool. Whereas it
11 takes 20 minutes at most to administer the BEARNI, an extensive neuropsychological battery
12 takes at least 90, if not 120 minutes, to complete, hand-score and interpret. Moreover, the
13 latter is not accessible to non-psychologists, making its routine use impracticable in clinical
14 settings. When an extensive neuropsychological battery cannot be readily conducted, the
15 BEARNI is therefore a useful and reliable screening tool for detecting cognitive and motor
16 impairments in ALs.

17 Compared to the BEARNI, the MMSE and DRS Mattis were found in our study to have poor
18 sensitivity, negative predictive value and diagnostic accuracy. 50% and more of the alcoholic
19 patients were not well identified by these screening tools. This finding could be explained by
20 the fact that these screening tools were initially designed to detect cognitive decline
21 associated with dementia. They are therefore neither relevant nor sensitive to assess cognitive
22 functioning in alcoholic patients. However, the use of the MMSE, the DRS Mattis as well as
23 the MOCA should not be disregarded in older alcoholic patients and/or in a context of
24 differential diagnosis. Our findings do not aim at convincing the readers they should not use

1 these tools any more. We believe that BEARNI is more relevant to detect alcohol-related
2 neuropsychological deficits but that these tools would be useful, as a complement.

3 The main limitation of the BEARNI is its relatively low specificity, especially for detecting
4 patients with mild impairment. Between 7 and 14% of patients were classified as impaired on
5 the BEARNI, whereas they had preserved results on the extensive neuropsychological battery.

6 This result cannot be attributed to incorrect sampling, as the prevalence of no, mild, and
7 moderate-to-severe impairments among the patients included in the present investigation,
8 according to the neuropsychological battery, matched that reported in previous study (Ihara et
9 al., 2000). The BEARNI therefore tends to overestimate motor and cognitive impairments in
10 ALs. As this screening tool has been developed to identify patients who should be referred to
11 a psychologist for a more comprehensive neuropsychological evaluation, the BEARNI seems
12 unlikely to miss impaired patients, instead referring some who may actually have a preserved
13 cognitive profile. It is important to stress that the BEARNI is not intended as a substitute for
14 an extensive neuropsychological examination, as it does not cover all the cognitive domains
15 and does not assess specific processes within a given domain. An extensive
16 neuropsychological examination will still be crucial when a differential diagnosis is required
17 or when a detailed profile is needed to ensure adequate treatment in relation to cognitive
18 rehabilitation.

19 In the light of these findings, we can make several recommendations for the clinical use of the
20 BEARNI (Figure 3). In this study, all alcoholics underwent both the BEARNI and the
21 neuropsychological battery while they were inpatients at treatment entry immediately after
22 withdrawal from alcohol. In this clinical context, ALs diagnosed as having preserved abilities
23 on the BEARNI can attend and benefit from standard alcohol treatment. For patients
24 identified by the BEARNI as having mild impairments, several clinical and medical factors
25 need to be considered to determine whether the treatment needs to be adjusted. Alcohol

1 history, including repeated withdrawals (Duka et al., 2003), bouts of thiamine deficiency
2 (Thomson, 2000), liver complications (Arria et al., 2007) and level of motivation (Blume et
3 al., 2005) have all been reported to be related to neuropsychological impairments in ALs.
4 Finally, ALs identified by the BEARNI as having moderate-to-severe impairments are
5 unlikely to benefit fully from treatment and should be referred for an extensive
6 neuropsychological examination. As the neuropsychological impairments present at treatment
7 entry are partially reversible, even after a short time of abstinence (Mann et al., 1999), a safe
8 and enriched environment (withdrawal from alcohol and nutrition treatment) may prove
9 beneficial for these impaired patients before they undergo standard alcohol treatment. A re-
10 test after this recovery period would determine whether their cognitive abilities were
11 sufficient for them to benefit from the standard treatment. A parallel version of the BEARNI,
12 allowing for this second assessment, is therefore required. More generally, the BEARNI aims
13 at determining the neuropsychological profile of ALs and whether a patient is able to attend
14 and gain from standard alcohol treatment or whether some adjustments are required.
15 Depending on the clinical context or the time when the BEARNI is administered, it will
16 enable to adjust alcohol treatment to the neuropsychological profile or to assess the
17 modification of neuropsychological performance with abstinence, reduction of alcohol
18 consumption or relapse.

19 To conclude, the present study suggests that the BEARNI has high content validity, as it
20 assesses the cognitive functions known to be impaired in chronic alcoholism, and reliable
21 diagnostic accuracy in detecting ALs with cognitive and motor impairments. It provides a
22 cognitive and motor profile that can guide the adjustment of alcohol treatment and further
23 cognitive assessments. As such, the BEARNI seems to be a useful screening tool in clinical
24 settings for detecting motor and cognitive impairments present at alcohol treatment entry. An

- 1 English/US version is ongoing to make available the BEARNI to native English speaker
- 2 patients.

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1 **CONFLICT OF INTEREST**

2 Authors declare no conflict of interest.

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1 **TABLES**

2

Table 1: Participants' Demographic Characteristics

	Alcoholic patients	Control participants		p-values
Number	73	254	58 ¹	
Men/women	53/20	154/100	27/31	0.06; 0.002*
Age (years)	45.47 ± 8.85	43.22 ± 9.32	42.81 ± 10.86	0.07; 0.13
Range	26-67	20-66	31-60	
Education (years of schooling)	11.18 ± 1.69	12.83 ± 2.61	12.76 ± 2.47	<0.001*; <0.001
Range	8-15	6-21	5-18	
MMSE	27.90 ± 1.90	-	28.79 ± 1.13	0.002*
Range	21-30		26-30	
DRS Mattis	136.96 ± 6.07	-	141.76 ± 2.31	<0.001*
Range	115-144		134-144	
AUDIT	29.90 ± 6.33	3.07 ± 1.68	2.84 ± 1.68	<0.001*; <0.001
Range	9-40	0-6	0-6	
Days of sobriety before inclusion	13.17 ± 6.73	-	-	
Range	4-50			
Alcohol use (years)	30.25 ± 9.07	-	-	
Range	10-51			
Alcohol misuse (years)	17.49 ± 9.23	-	-	
Range	5-43			
Daily alcohol consumption (units)	23.48 ± 35.36	-	-	
Range	0-300			
Number of withdrawals	3.52 ± 6.05	-	-	
Range	0-52			

3 Data are shown as means ± standard deviation. Only 58 of the control participants underwent the extensive
 4 neuropsychological battery. AUDIT = Alcohol Use Disorders Identification Test.

5 * Significant difference between alcoholic patients and control participants (n=254 ; n=58) at p<0.05 (t-tests)

6

1 Table 2: Cognitive and Motor Domains Assessed by the Brief Evaluation of Alcohol-Related
 2 Neuropsychological Impairments (BEARNI) and the Extensive Neuropsychological Battery

Domains	BEARNI subtests	Neuropsychological battery tests
<i>Verbal episodic memory</i>	Learning	CVLT Learning (sum of correct responses across 5 trials)
	Delayed free recall	CVLT Delayed free recall (number of correct responses)
		CVLT Delayed free recall (number of errors)
<i>Working memory</i>	Alphabetical span	Verbal Span (forward span)
		Verbal Span (backward span)
		Letter-Number Sequencing (standard score)
		Visuospatial Span (forward span)
		Visuospatial Span (backward span)
<i>Executive function</i>	Alternating fluency	TMT Part B - Part A (time)
		Fluency task (letter <i>p</i> ; number of correct responses)
		Fluency task (animal category; number of correct responses)
		Stroop Interference-Naming (time)
		RFFT (total design)
		RFFT (total strategies)
<i>Visuospatial abilities</i>	Visuospatial	ROCF (copy accuracy /36)
	(hidden figures)	
<i>Ataxia</i>	Ataxia (balance)	Stand in Romberg position (one foot in front of the other placed heel to toe) (two 60-s trials; eyes open)
		Stand in Romberg position (one foot in front of the other placed heel to toe) (two 60-s trials; eyes closed)
		Walk heel-to-toe (two 10-step trials, eyes open)
		Walk heel-to-toe (two 10-step trials, eyes closed)

3 CVLT = California Verbal Learning Test; TMT B-A = Trail Making Test Part A minus Part B; RFFT = Ruff

4 Figural Fluency Test; ROCF = Rey Osterrieth Complex Figure.

5

1

Table 3 Results of the Exploratory Factor Analysis (EFA)

Variables	Factors				
	Factor 1	Factor 2	Factor 3	Factor 4	Factor 5
Eigenvalues	6.70	2.24	1.65	1.31	1.10
Explained variance	30.45%	10.18%	7.48%	5.97%	5.00%
BEARNI Delayed free recall			0.49*		
BEARNI Alphabetical span					0.69
BEARNI Fluency				0.57	
BEARNI Visuospatial	0.67				
BEARNI Ataxia		0.63			
Feet placed heel-to-toe (eyes open)		0.74			
Feet placed heel-to-toe (eyes closed)		0.77			
Walk heel-to-toe (eyes open)		0.78			
Walk heel-to-toe (eyes closed)		0.68			
CVLT Learning			0.85		
CVLT Delayed free recall (correct responses)			0.80		
CVLT Delayed free recall (errors)			-0.75		
Letter (<i>p</i>) fluency				0.67	
Categorical (animals) fluency				0.78	
Verbal forward span					0.69
Verbal backward span					0.73
Letter-Number Sequencing					0.77
ROCF (copy accuracy)	0.30*				
Visuospatial forward span	0.69				
Visuospatial backward span	0.72				
Stroop Interference-Naming (time)	-0.61				
TMT B-A (time)	-0.47*				
RFFT (total strategies)	0.59				
RFFT(total design)	0.62				

2 Marked factor loadings with significance threshold set at 0.5. * Variable not significant at established threshold of 0.5, but
3 assigned to the factor on which it most highly loaded. CVLT = California Verbal Learning Test; ROCF = Rey Osterrieth
4 Complex Figure; TMT B-A = Trail Making Test Part A minus Part B; RFFT = Ruff Figural Fluency Test.

5

1 Table 4: Summary of Total BEARNI Cut-Off Scores Adjusted for Education Level

BEARNI total score	Criteria	Education (years of schooling)	
		≤ 12	> 12
Total score /30 (cognitive functions plus ataxia)	Mild impairment	≤ 19	≤ 21
	Moderate-to-severe impairment	≤ 16	≤ 17
Total cognitive score /22 (excluding the Ataxia subtest)	Mild impairment	≤ 15	≤ 16
	Moderate-to-severe impairment	≤ 11.5	≤ 12.5

2

3

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1 Table 5: Psychometric properties of the BEARNI, MMSE (Folstein et al., 1975; Kalafat et al.,
 2 2003) and Mattis DRS (Lucas et al., 1998; Mattis and Inc, 1988)

Psychometric properties	BEARNI (total score)	BEARNI (total "cognitive" score)	MMSE	Mattis DRS
<i>Mild impairment</i>				
Sensitivity	98.41 %	93.44 %	9.52 %	7.94 %
Specificity	50.00 %	50.00 %	90.00 %	90.00 %
Positive predictive value	92.54 %	90.48 %	85.71 %	83.93 %
Negative predictive value	83.33 %	60.00 %	13.64 %	13.43 %
Yule's Q coefficient	0.97	0.87	0.03	0.13
Diagnostic accuracy	91.78 %	86.30 %	20.54 %	19.17 %
<i>Moderate-to-severe impairments</i>				
Sensitivity	94.87 %	81.82 %	7.69 %	7.69 %
Specificity	70.59 %	85.00 %	88.24 %	91.18 %
Positive predictive value	78.72 %	81.82 %	42.86 %	50.00 %
Negative predictive value	92.31 %	85.00 %	45.45 %	46.27 %
Yule's Q coefficient	0.96	0.92	0.23	0.07
Diagnostic accuracy	83.56 %	83.56 %	24.09	46.57 %

3

4

1 Table 6: Predictive Value of the Cut-Off Scores of Each BEARNI Subtest for Detecting the
 2 Neuropsychological Impairments Identified by the Extensive Battery

NP battery tasks	Alcoholic patients		Controls	Statistics	Tukey post hoc
	AL ⁻	AL ⁺	(n = 58) HC		
<i>Episodic memory (BEARNI cut-off score ≤ 2)</i>					
CVLT Learning	-1.41 ± 1.23	-0.24 ± 1.14	0.00 ± 1.00	$F_{(2,128)} = 9.02$; $p < 0.001^*$	AL ⁻ < AL ⁺ = NC
CVLT Delayed recall (correct response)	-1.64 ± 1.20	-0.55 ± 1.56	0.00 ± 0.98	$F_{(2,128)} = 9.12$; $p < 0.001^*$	AL ⁻ < AL ⁺ = NC
CVLT Delayed recall (error)	-1.36 ± 2.02	-0.24 ± 1.53	0.00 ± 0.99	$F_{(2,128)} = 5.15$; $p = 0.007^*$	AL ⁻ < AL ⁺ = NC
<i>Verbal working memory (BEARNI cut-off score ≤ 2.5)</i>					
Verbal forward span	-1.01 ± 0.94	-0.23 ± 0.88	0.00 ± 1.00	$F_{(2,128)} = 9.25$; $p < 0.001^*$	AL ⁻ < AL ⁺ = NC
Verbal backward span	-1.41 ± 0.64	-0.50 ± 0.90	0.00 ± 1.00	$F_{(2,128)} = 19.68$; $p < 0.001^*$	AL ⁻ < AL ⁺ < NC
Letter-Number Sequencing	-1.69 ± 0.78	-0.21 ± 0.80	0.00 ± 1.00	$F_{(2,128)} = 29.73$; $p < 0.001^*$	AL ⁻ < AL ⁺ = NC
<i>Flexibility (BEARNI cut-off score ≤ 2)</i>					
Letter (p) fluency	-0.66 ± 0.93	0.00 ± 0.93	0.00 ± 1.00	$F_{(2,128)} = 3.30$; $p = 0.04$	AL ⁻ < AL ⁺ = NC
Categorical (animals) fluency	-0.96 ± 1.20	-0.32 ± 1.20	0.00 ± 1.00	$F_{(2,128)} = 5.20$; $p = 0.007^*$	AL ⁻ < AL ⁺ = NC
<i>Visuospatial abilities (BEARNI cut-off score ≤ 1)</i>					
ROCF (copy accuracy)	-0.61 ± 1.11	-0.22 ± .092	0.00 ± 1.00	$F_{(2,128)} = 3.86$; $p = 0.02$	AL ⁻ < NC AL ⁺ = NC
Visuospatial forward	-0.83 ± 0.67	-0.38 ± 0.93	0.00 ± 1.00	$F_{(2,128)} = 9.12$;	AL ⁻ < AL ⁺

span				$p < 0.001^*$	$AL^+ = NC$
Visuospatial	-0.74 ± 0.80	-0.18 ± 0.79	0.00 ± 1.00	$F_{(2,128)} = 7.34;$	$AL^- < AL^+ = NC$
backward span				$p < 0.001^*$	
Stroop Interference-	-1.97 ± 3.10	-0.50 ± 1.94	0.00 ± 1.00	$F_{(2,128)} = 10.42;$	$AL^- < AL^+ = NC$
Naming (time)				$p < 0.001^*$	
TMT Part A-Part B	-2.77 ± 6.57	-0.45 ± 1.40	0.00 ± 1.00	$F_{(2,128)} = 7.20;$	$AL^- < AL^+ = NC$
(time)				$p = 0.001^*$	
RFFT	-0.73 ± 0.74	-0.44 ± 0.89	0.00 ± 1.00	$F_{(2,128)} = 2.59;$	<i>ns</i>
(total strategies)				$p = 0.07$	
RFFT(total design)	-1.10 ± 1.02	-0.18 ± 1.21	0.00 ± 1.00	$F_{(2,128)} = 11.64;$	$AL^- < AL^+ = NC$
				$p < 0.001^*$	
<i>Ataxia (BEARNI cut-off score ≤ 3)</i>					
Heel-to-toe	-1.68 ± 2.15	-0.06 ± 0.89	0.00 ± 1.00	$F_{(2,128)} = 18.68;$	$AL^- < AL^+ = NC$
(eyes open)				$p < 0.001^*$	
Heel-to-toe	-0.92 ± 0.94	-0.37 ± 0.92	0.00 ± 1.00	$F_{(2,128)} = 10.19;$	$AL^- < AL^+ < NC$
(eyes closed)				$p < 0.001^*$	
Walk heel-to-toe	-1.56 ± 2.05	-0.21 ± 1.21	0.00 ± 1.00	$F_{(2,128)} = 14.57;$	$AL^- < AL^+ = NC$
(eyes open)				$p < 0.001^*$	
Walk heel-to-toe	-0.92 ± 0.82	0.01 ± 1.12	0.00 ± 1.00	$F_{(2,128)} = 11.61;$	$AL^- < AL^+ = NC$
(eyes closed)				$p < 0.001^*$	

- 1 Data are shown as standard residuals (i.e., *z* scores) mean \pm standard deviation.
- 2 NP = neuropsychological; CVLT = California Verbal Learning Test; ROCF = Rey Osterrieth Complex Figure;
- 3 TMT B-A = Trail Making Test Part A minus Part B; RFFT = Ruff Figural Fluency Test;
- 4 AL^+ = preserved alcoholic patients; AL^- = impaired alcoholic patients; HC = healthy controls.
- 5 * still significant after Bonferroni correction.
- 6 *ns* = not significant ($p > 0.05$).
- 7

1 **FIGURE LEGENDS**

2 Figure 1: Results of the comparison between ALs (in red) and HCs (in black) on each
3 BEARNI subtest. Data are shown as mean \pm standard error of mean, taking the significant
4 effects of age and education into account.
5 (*ns*: nonsignificant).

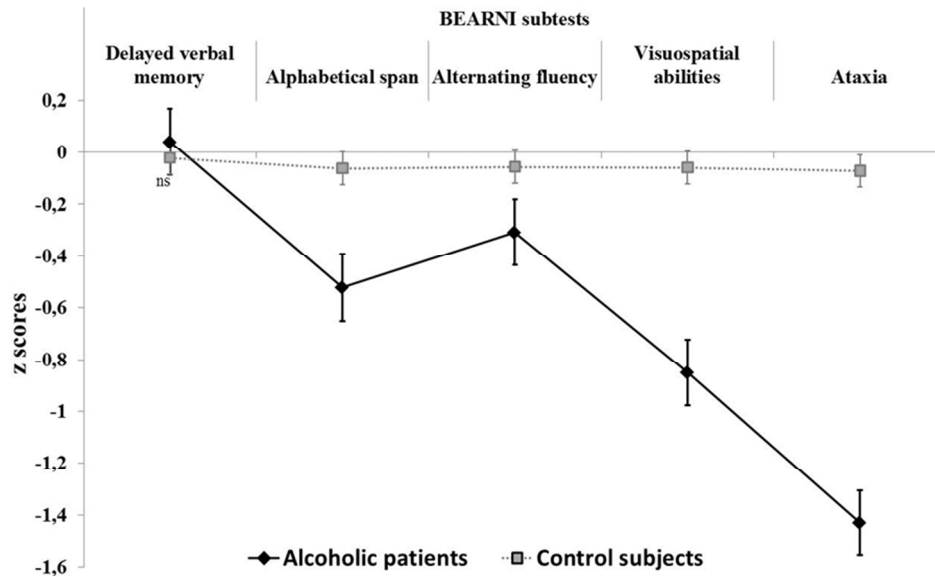
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7 Figure 2: ROC curve analyses for determining the total BEARNI (A and B) and total
8 cognitive BEARNI (C and D) cut-off scores reflecting mild impairment (A and C) and
9 moderate-to-severe impairment (B and D).

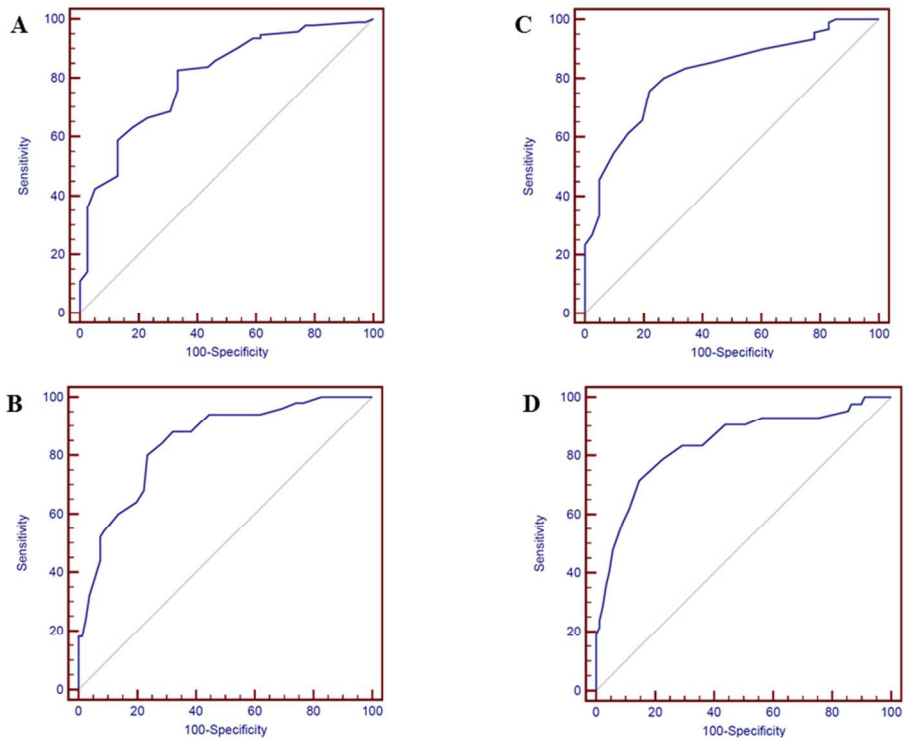
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11 Figure 3: Clinical recommendations according to the cognitive status of alcoholic patients at
12 treatment entry as diagnosed by the BEARNI.

13

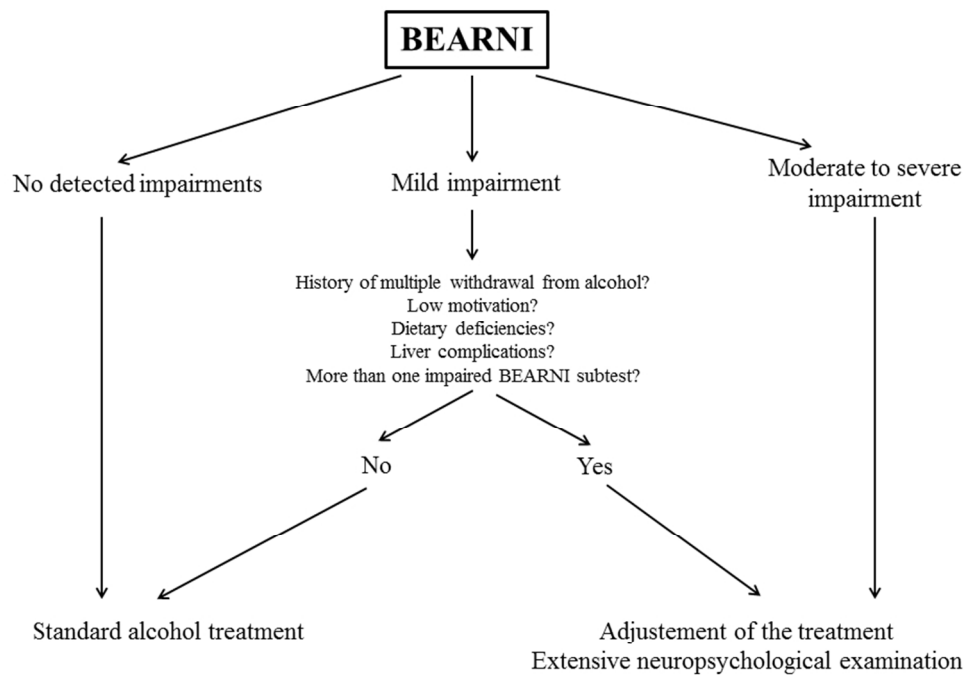


Results of the comparison between alcoholic patients (in black) and controls (in grey) on each BEARNI subtest. Data are shown as mean \pm standard error of mean, taking the significant effects of age and education into account. Alcoholic patients were impaired on all the BEARNI subtests except for episodic delayed free recall (ns: nonsignificant).
254x190mm (96 x 96 DPI)



ROC curve analyses for determining the total BEARNI (A and B) and total cognitive BEARNI (C and D) cut-off scores reflecting mild impairment (A and C) and moderate-to-severe impairment (B and D).
254x190mm (96 x 96 DPI)

Only



Clinical recommendations according to the cognitive status of alcoholic patients at treatment entry as diagnosed by the BEARNI.
254x190mm (96 x 96 DPI)

Only

BEARNI**Brief Evaluation of Alcohol Related Neuropsychological Impairment**

NOM : _____ **Prénom :** _____
Date de naissance (âge) : _____ **Années de scolarité :** _____
Date de l'examen : _____

I. Mémoire verbale

	Liste de mots	Rappel libre 1	Rappel libre 2
1.	Plage		
2.	Tenaille		
3.	Blouson		
4.	Fleuve		
5.	Pioche		
6.	Jupe		
7.	Râteau		
8.	Montagne		
9.	Chapeau		
10.	Bêche		
11.	Jungle		
12.	Ceinture		
Pas de points			

II. Ataxie en équilibre

<i>Yeux ouverts</i>	
Jambe droite au sol	Jambe gauche au sol
Essai 1	Essai 1
Essai 2	Essai 2
<i>Yeux fermés</i>	
Jambe droite au sol	Jambe gauche au sol
Essai 1	Essai 1
Essai 2	Essai 2
Score total (score max 8) :	

III. Fluences alternées

Maximum de mots en alternant catégories des « couleurs » et « noms de ville » en 2 minutes

Score total (score max 6):

IV. Ordination alphabétique

Items/essai	(Bonnes réponses)	Note
1/ Essai 1 : V-K (K-V) Essai 2 : U-T (T-U)		
2/ Essai 1 : R-H-L (H-L-R) Essai 2 : I-F-B (B-F-I)		
3/ Essai 1 : A-X-T-H (A-H-T-X) Essai 2 : L-G-R-U (G-L-R-U)		
4/ Essai 1 : P-N-I-G-V (G-I-N-P-V) Essai 2 : Q-O-J-D-E (D-E-J-O-Q)		
5/ Essai 1 : C-T-H-E-V-S (C-E-H-S-T-V) Essai 2 : L-T-A-D-R-I (A-D-I-L-R-T)		
Score total (score max 5):		

V. Capacités visuo-spatiales

Score total (score max 5):

VI. Mémoire verbale différée

	Liste de mots	Rappel différé
1.	Plage	
2.	Tenaille	
3.	Blouson	
4.	Fleuve	
5.	Pioche	
6.	Jupe	
7.	Râteau	
8.	Montagne	
9.	Chapeau	
10.	Bêche	
11.	Jungle	
12.	Ceinture	
Score total (score max 6):		

Figure d'exemple

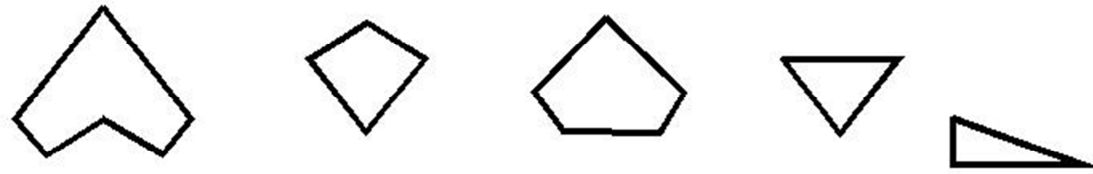
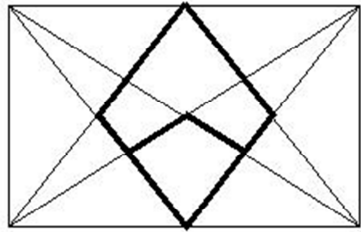


Figure 1

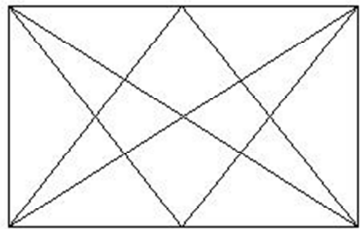


Figure 2

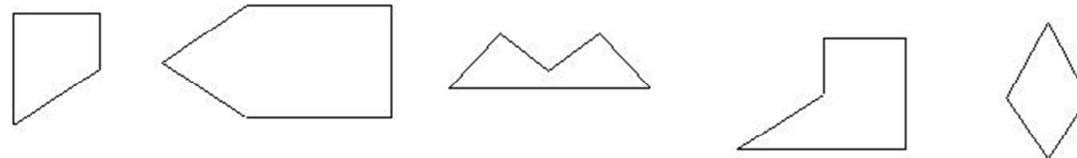
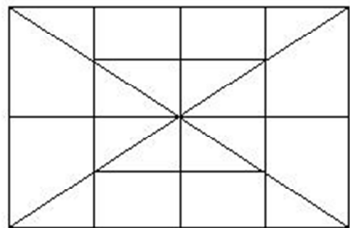


Figure 3

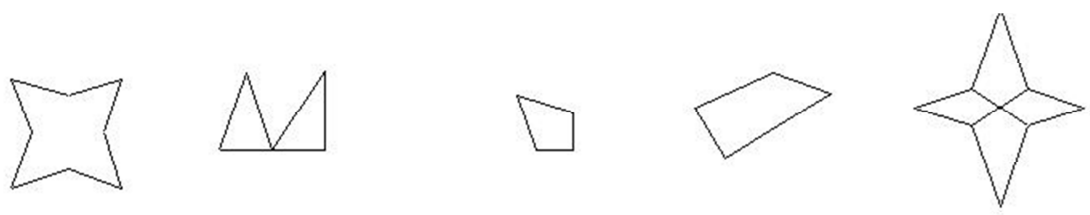
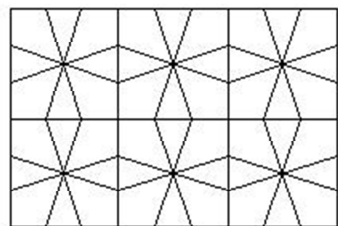


Figure 4

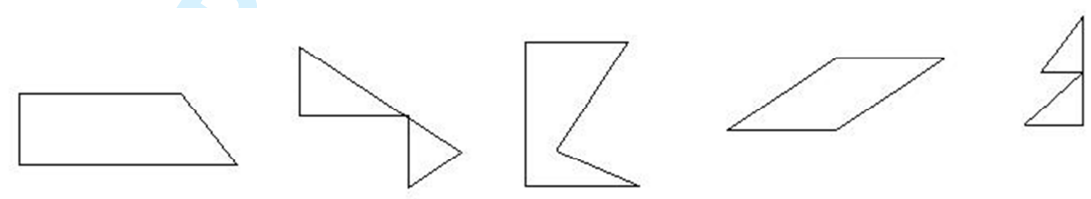
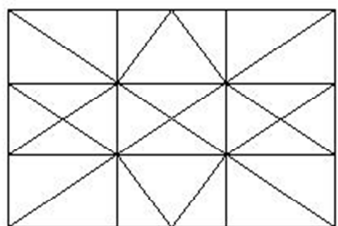
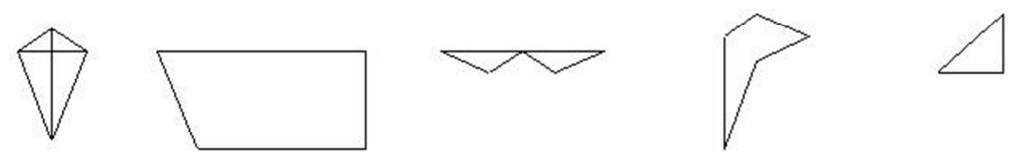
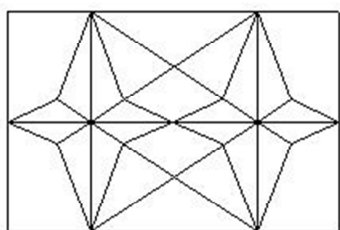


Figure 5



BEARNI**Brief Evaluation of Alcohol Related Neuropsychological Impairment****Instructions pour l'administration et la cotation****I- Mémoire verbale****Consigne**

1^{er} rappel : Je vais vous lire une liste de mots que vous aurez à retenir. Ecoutez attentivement et quand j'aurais terminé, je veux que vous me redonniez le plus de mots possible dont vous vous rappelez, et dans l'ordre que vous voulez.

2^{ème} rappel : Maintenant je vais vous relire la même liste de mots. Essayez de vous rappeler du plus grand nombre de mots possible y compris ceux que vous avez déjà énoncés.

(Temps maximum pour chaque rappel : 1 minute. Relire la liste complète avant chaque rappel. Au dernier rappel, ne pas préciser au patient que la liste lui sera à nouveau demandée à la fin du test)

Cotation

Score total : pas de points

II- ATAXIE En équilibre**Consigne**

Maintenant nous allons tester votre équilibre sur une jambe. Dans un premier temps, aidez-vous du mur si besoin. Ensuite, croisez les bras et levez la jambe comme ceci (à hauteur du genou), sans vous appuyer sur votre genou. Si à un moment vous sentez que vous risquez de tomber, posez votre pied par terre et appuyez-vous contre le mur.

Durée maximum : 30 secondes par essai. Indiquer le temps pendant lequel le sujet réussit à maintenir la position.

Préciser si le sujet réussit dès le premier essai ou au second.

Cotation

2 points par condition si le sujet réussit dès le premier essai à tenir en équilibre pendant 30 secondes.

1 point par condition si le sujet ne réussit qu'au second essai à tenir en équilibre pendant 30 secondes.

0 point en cas d'échec aux deux essais.

Score total : maximum 8 points

III- Fluences alternées**Consigne**

Je vous demande de me donner le plus de noms que vous connaissez dans les catégories des couleurs et des noms de ville, pendant 2 minutes sans vous répéter. Vous devrez alterner les deux catégories, vous me donnerez d'abord une couleur, puis un nom de ville, une couleur, un nom de ville, etc... Je ne vous demande pas de faire un lien entre les villes et les couleurs.

(Noter toutes les réponses du sujet, y compris celles qui ont déjà été données et les erreurs). Arrêt de l'épreuve au bout de deux minutes.

Cotation

0 point si entre 0 et 4 mots (alternance et catégorie respectées)

1 point si entre 5 et 9

2 points si entre 10 et 14

3 points si entre 15 et 19

4 points si entre 20 et 24

5 points si entre 25 et 29

6 points si ≥ 30

Score total : maximum 6 points

Les erreurs de catégorie correspondent à tous les mots fournis n'étant ni des couleurs, ni des noms de villes.

Les erreurs d'alternance correspondent à la production de deux mots dans la même catégorie (lorsque le sujet fournit deux noms de villes ou deux couleurs à la suite).

Exemple de cotation : si le patient fournit les mots « Paris ; vert ; Angers ; Caen ; bleu ; Rouen ; orange », 7 mots sont fournis mais il y a une erreur d'alternance (deux noms de ville à la suite : Angers ; Caen). Ainsi, 6 mots corrects sont fournis car Caen ; bleu sont considérés comme des mots correctement fournis car catégorie et alternance respectée.

IV- Ordination alphabétique

Consigne

Je vais vous lire des séries de lettres et je vous demanderai de me les rappeler dans l'ordre alphabétique. Par exemple si je vous donne « C-B », vous devrez me dire « B-C » car la lettre B se situe avant la lettre C dans l'alphabet.

(Les séries de lettres ne doivent être lues qu'une seule fois. Arrêter l'épreuve si le patient échoue aux deux essais d'un même item. Les deux essais d'une même longueur doivent être administrés, même si le premier essai est correctement réussi.)

Cotation

0,5 point par essai correctement rappelé

Score total : maximum 5 points

V- Capacités visuo-spatiales



Consigne

A l'intérieur de chacune des figures complexes sont cachées deux figures simples. Je vous demande d'essayer de retrouver, parmi les 5 figures de droite, quelles sont les deux figures cachées. *(Préciser au sujet que les formes à découvrir sont de même taille et de même forme/orientation)*

(Montrer un exemple avec la figure d'exemple.) Vous voyez ici par exemple dans cette figure, on peut retrouver celle-ci (1^{ère} figure) ici et celle-ci ici (2^{ème} figure).

Durée maximum : 1 minute par figure.

Pour chacune des figures, l'épreuve s'arrête après 1 minute même si le patient n'a pas retrouvé les deux éléments de la figure complexe.

Cotation

1 point si le sujet trouve les deux figures cachées.

0 point si le sujet ne trouve qu'une figure ou aucune sur les deux.

Score total : maximum 5 points

Bonnes réponses :

Figure complexe 1 : figures 1 et 3

Figure complexe 2 : figures 1 et 4

Figure complexe 3 : figures 1 et 3

Figure complexe 4 : figures 2 et 4

Figure complexe 5 : figure 3 et 4

VI- Mémoire verbale différée



Consigne

Au début du test, vous avez appris une liste de mots. Je vous demande à présent de me redonner le plus possible de mots dont vous vous souvenez, dans l'ordre que vous voulez.

Ne pas relire la liste de mots au participant.

(rappel : 1 minute)

Cotation

Nombre de réponse correcte	0,5 point par réponse correcte
Nombre d'erreur (intrusion)	Retirer 0,5 point par erreur
Total	Réponses correctes - erreurs

Score total : maximum 6 points

Les erreurs d'intrusions correspondent à tous les mots produits qui n'étaient pas dans la liste de mots. Par exemple : manteau, outils, robe ...

Les répétitions ne sont pas considérées comme des erreurs.

SCORES TOTAUX

Additionnez les points de chacun des subtests. Le score total est de 30 points.

Il est possible de calculer un score cognitif, ne comprenant pas la cotation du subtest d'ataxie, lorsque les patients ne peuvent pas réaliser la tâche. Ce score total est de 22 points.

Subtests	Note maximum	Cut-off score
Mémoire : <ul style="list-style-type: none"> • Mémoire verbale • Mémoire verbale différée 	Pas de points 6	≤ 2
Ataxie en équilibre	8	≤ 3
Fluence alternée	6	≤ 2
Ordination alphabétique	5	$\leq 2,5$
Capacités visuospatiales	5	≤ 1
SCORE TOTAL	30	
SCORE COGNITIF	22	

Cut-off scores des scores totaux

Etant donné que les scores totaux du BEARNI sont influencés par le nombre d'années de scolarité, les cut-offs ont été adaptés.

Le baccalauréat correspond à 12 années d'études (ne pas compter les redoublements ni la maternelle).

		SCORE TOTAL	SCORE COGNITIF
\leq BAC	Trouble léger	≤ 19	≤ 15
	Trouble modéré	≤ 16	$\leq 11,5$
$>$ BAC	Trouble léger	≤ 21	≤ 16
	Trouble modéré	≤ 17	$\leq 12,5$

Supplementary B: Standardization of the BEARNI total scores

First of all, we examined the normality of the distribution of all scores of the neuropsychological battery in HCs, using kurtosis, skewness and Shapiro-Wilk tests. Scores deviating from normality were transformed using the Box-Cox transformation. The potential effects of age, education and sex were then tested with linear regression analysis (forward stepwise) and only significant factors were retained. Standardized residuals (i.e., z -scores; poor performance corresponding to a negative z -score) were computed, and cut-off scores for each scores of the battery were then determined using the 5th percentile, in order to maintain a false-positive rate (i.e., percentage of HCs classified as impaired) equal to or below 5%. The 5th percentile was found to provide the most appropriate cut-off score (compared with the commonly used -1.50 or -1.65 standard deviation), as it was not influenced by variation from the normal distribution (Godefroy et al., 2014). The participants' performances were dichotomized (normal = 0; impaired = 1) and based on these cut-offs, we determined the cognitive profile of each participant (HCs and ALs) on the neuropsychological battery according to the following criteria:

- Mild impairment: one affected domain (i.e., one impaired score for episodic memory, working memory or visuospatial abilities, or two impaired scores for ataxia or executive functions (Godefroy and GREFEX, 2008; Pitel et al., 2011; Sullivan et al., 2000a);
- Moderate-to-severe impairment: at least two affected domains.

As the BEARNI's total cognitive score does not include the ataxia subtest, we did not consider the profile for the Walk-a-Line Ataxia Battery (Fregly, 1971) in its standardization.

We ran ROC curve analyses on the BEARNI's two total scores to determine their cut-off scores (one for mild impairment, the other for moderate-to-severe impairment). These scores

were determined by the best balance between sensitivity and specificity, based on the ALs' and HCs' profiles on the battery.

For Review Only

Supplementary B: Standardization of the BEARNI subtests

Based on the dichotomized participants' performances (normal = 0; impaired = 1), cut-off scores for each subtest were determined using receiver operating characteristic (ROC) curve analysis (sensitivity, specificity and area under the curve, AUC). The cut-off score was determined with this method in order to provide only one cut-off score for each BEARNI subtest that considers the effects of demographic factors. This choice was made to simplify the scoring of the BEARNI and the determination of impaired performance as reported in (Godefroy et al., 2014). This method also enabled us to have more statistical power for the determination of the cut-off score on each BEARNI subtest based on the 254 healthy controls rather than the 58 ones.

Supplementary B Table 1: Cut-off scores for the Mini Mental State Examination (Folstein et al., 1995; Kalafat et al., 2003) taking into account of education (years of schooling)

	Education (years of schooling)			
	<9	9-10	11	≥12
MMSE cut-off score	22	23	25	26

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Supplementary B Table 2

Results of the ROC curve analysis: the Sensitivity, Specificity, Area Under the Curve (AUC) and 95% Confidence Interval (CI) for Determining the Cut-Off Scores for the Total BEARNI Scores

Cut-off scores	Sensitivity	95% CI	Specificity	95% CI	AUC	95% CI
<i>Total BEARNI score</i>						
Mild impairment	82.61	73.30-89.70	66.67	49.80-80.90	0.802	0.724-0.867
Moderate-to-severe impairment	80.00	66.30-90.00	76.54	65.80-85.20	0.842	0.769-0.900
<i>Total cognitive BEARNI score</i>						
Mild impairment	82.76	73.20-90.00	61.36	45.50-75.60	0.796	0.716-0.861
Moderate-to-severe impairment	71.43	55.40-84.30	85.39	76.30-92.90	0.839	0.765-0.898

Supplementary B Table 3

Results of the ROC curve analysis: the Sensitivity, Specificity, Area Under the Curve (AUC) and 95% Confidence Interval (CI) for Determining the Cut-Off Scores for Each BEARNI

Subtest

BEARNI subtests	Sensitivity	95% CI	Specificity	95% CI	AUC	95% CI
Delayed verbal memory	100	73.50-100	90.08	85.60-93.50	0.990	0.968-0.998
Alphabetical span	100	73.50-100	75.21	69.30-80.50	0.950	0.915-0.973
Alternated fluency	100	73.50-100	99.59	97.70-100	0.998	0.983-1.000
Visuospatial	100	73.50-100	89.26	84.70-92.90	0.980	0.955-0.994
Ataxia	100	73.50-100	96.69	93.60-98.60	0.997	0.981-1.000

Supplementary B Table 4: Raw scores for Cognitive and Motor Domains Assessed by the Brief Evaluation of Alcohol-Related Neuropsychological Impairments (BEARNI) and the Extensive Neuropsychological Battery

Cognitive and motor domains	Alcoholic patients	Healthy controls	
	(N=73)	(N=58)	(N=254)
<i>Episodic memory</i>			
BEARNI Learning	6.62 ± 1.65	7.47 ± 1.75	7.43 ± 1.75
BEARNI Delayed free recall	3.49 ± 1.27	4.10 ± 1.04	3.62 ± 1.27
CVLT Learning	54.92 ± 9.62	6.57 ± 8.50	na
CVLT Delayed free recall (number of correct responses)	11.81 ± 3.19	13.67 ± 2.02	na
CVLT Delayed free recall (number of errors)	1.14 ± 1.50	0.67 ± 0.92	na
<i>Working memory</i>			
BEARNI alphabetical span	2.60 ± 1.13	3.45 ± 0.83	3.27 ± 0.87
Verbal span (forward span)	6.05 ± 1.29	6.69 ± 1.50	na
Verbal span (backward span)	4.33 ± 1.27	5.40 ± 1.41	na
Letter-Number Sequencing (standard score)	9.07 ± 3.01	10.96 ± 2.89	na
Visuospatial span (forward span)	5.78 ± 1.28	6.62 ± 1.45	na
Visuospatial span (backward span)	5.29 ± 1.33	6.00 ± 1.61	na
<i>Executive functions</i>			
BEARNI alternating fluency	4.24 ± 1.09	4.69 ± 1.10	4.67 ± 1.05
TMT part B- part A (time)	77.52 ± 108.90	37.33 ± 24.53	na
Fluency task (letter <i>p</i> ; number of correct responses)	22.11 ± 7.24	23.22 ± 7.52	na
Fluency task (animal category; number of correct responses)	29.90 ± 9.39	33.64 ± 8.14	na
Stroop Interference-Naming (time)	64.24 ± 41.28	44.83 ± 15.91	na
RFFT (total design)	80.40 ± 22.62	91.57 ± 18.69	na
RFFT (total strategies)	18.18 ± 19.21	31.36 ± 22.99	na
<i>Visuospatial abilities</i>			

BEARNI visuospatial	1.77 ± 1.36	3.00 ± 1.18	2.92 ± 1.34
ROCF (copy accuracy /36)	33.55 ± 2.73	34.61 ± 2.67	na
<i>Ataxia</i>			
BEARNI ataxia	2.63 ± 1.76	4.43 ± 2.10	5.65 ± 1.99
Stand in Romberg position (one foot in front of the other placed heel to toe) (two 60-s trials; eyes open) ¹	-0.86 ± 1.82	0.00 ± 1.00	na
Stand in Romberg position (one foot in front of the other placed heel to toe) (two 60-s trials; eyes closed) ¹	-0.64 ± 0.97	0.00 ± 1.00	na
Walk heel-to-toe (two 10-step trials, eyes open) ¹	-0.88 ± 1.80	0.00 ± 1.00	na
Walk heel-to-toe (two 10-step trials, eyes closed) ¹	-0.45 ± 1.08	0.00 ± 1.00	na

CVLT = California Verbal Learning Test; TMT B-A = Trail Making Test Part A minus Part B; RFFT = Ruff

Figural Fluency Test; ROCF = Rey Osterrieth Complex Figure.

Na: not applicable

¹ data are shown as z-score

BEARNI***Brief Evaluation of Alcohol Related Neuropsychological Impairment*****Administration and scoring instructions****I- Verbal memory****Instruction**

First free recall: I am going to read a list of words. Listen carefully because your job is to remember as many of these words as possible. *Say the list of words in 13 to 15 seconds.*

Ok, now, tell me as many words as you can remember in any order.

Second free recall: I am going to read the list of words again. As before, try to remember as many words as possible. You will be asked to recall them afterwards.

Maximum time for each recall: 1 minute. DO NOT tell the participant that she/he will be asked to recall the words at the end of the test.

Scoring

Total score : no point

II- ATAXIA of balance**Instruction**

Now, we are going to test your balance. First, you will stand on one leg. Use the wall to support yourself. Then, put one foot on the line, cross your arms, and lift your other leg like this (*up to knee*). Be sure not to press your leg on your standing leg. If at any time you feel as if you're going to fall, open your eyes, put your foot down and use the wall for support.

2 trials for each condition

30 seconds maximum for each trial. Record the time reached for each trial in that position.

Specify whether the participant successfully performs the task at first trial or at second trial.

Scoring

2 points for each condition when the participant successfully performs the task on the first trial.

1 point for each condition when the participant successfully performs the task on the second trial.

0 point when the participant fails two trials.

Total score: max 8 points

III- Alternating fluency**Instruction**

For this task, you will have **2 minutes** to list as many different colors and cities. You must alternate between these two categories: start with one color, then one city, then a different color, and a different city, etc. The cities and the colors do not have to be related.

(Report all the responses of the participant, including perseverations and errors).

Stop the task after 2 minutes

Scoring

0 point for 0-4 words (alternating and category respected)

1 point for 5-9 words

2 points for 10-14 words

3 points for 15-19

4 points for 20-24

5 points for 25-29 words

6 points \geq 30 words

Total score: maximum 6 points

Error of category refers to the words produced that are not colors nor cities.

Error of alternating refers to the production of two words consecutively in the same category (for example when the subject produces two cities or two colors consecutively).

Exemple of scoring : if the patient produces the words : « Paris, green, New-York, Amsterdam ; blue ; San Francisco ; orange », 7 words are produced but there is one alternating error (two cities consecutively: “New-York; Amsterdam”). So, 6 words are correct because “Amsterdam ; blue” are considered as word well produced (category and alternating respected).

IV- Alphabetical span**Instructions**

I am going to read aloud a series of letters. Your job is to say those letters in alphabetical order. For example, if I say « C-B », you must say « B-C » because the letter B comes before C in the alphabet.

(The series of letters must be read only once. Stop the subtest if the participant fails both trials of the same item.)

Scoring

0.5 point for each successful trial

Total score : maximum 5 points

V- Visuospatial abilities**Instruction**

I am going to show you some figures. Each complex figure contains 2 separate figures. Your job is to find those two hidden figures. The hidden figures and those on the right side are exactly the same size (*Show the example of the first figure*). See, for example, in this figure, you can find this hidden figure (1st one) and this other one (2nd one).

Duration: 1 minute maximum per figure.

Scoring

1 point when the participant finds the two hidden figures

0 point when the participant finds one or none of the hidden figures

Total score : maximum 5 points

Correct answers :

Complexe figure 1 : figures 1 et 3

Complexe figure 2 : figures 1 et 4

Complexe figure 3 : figures 1 et 3

Complexe figure 4 : figures 2 et 4

Complexe figure : figures 3 et 4

VI- Delayed verbal memory



Instructions

At the beginning of this test, you learned a list of words. Now, I would like you to recall as many of those words as possible in any order.

DO NOT read the list of word.

(recall : **1 minute**)

Scoring

Number of correct response	0,5 point for each correct answer
Number of error (intrusion)	Remove 0,5 point per error
Total	-Correct answer - error

Total score : maximum 6 points

An error of intrusion refers to the production of a word that was not in the list. For example: dress, tools...

Repetitions are not scored as errors.

TOTAL SCORES

Add-up the points of each subtest. The total score is /30 points.

It is possible to compute a total « cognitive » score (excluding the ataxia subtest; maximum score: 22 points).

Subtests	Maximum score	Cut-off score
Memory : <ul style="list-style-type: none"> • Verbal memory • Delayed verbal memory 	No point 6	≤ 2
Ataxia of balance	8	≤ 3
Alternating fluency	6	≤ 2
Alphabetical span	5	$\leq 2,5$
Visuospatial abilities	5	≤ 1

Total score cut-

Since the BEARNI total scores were influenced by education (years of schooling), cut-off score were adjusted.

Years of schooling		TOTAL SCORE (30 max.)	TOTAL COGNITIVE SCORE (22 max.)
$\leq 12^*$	Mild impairment	≤ 19	≤ 15
	Moderate-to-severe impairment	≤ 16	$\leq 11,5$
> 12	Mild impairment	≤ 21	≤ 16
	Moderate-to-severe impairment	≤ 17	$\leq 12,5$

* corresponding approximately to high school diploma

1 **Validation of a brief screening tool for alcohol-related neuropsychological impairments**

2 **(BEARNI)**

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1 **ABSTRACT**

2 **Background:** Alcohol-related neuropsychological impairments mainly affect episodic
3 memory, working memory and visuospatial abilities, as well as executive and motor
4 functioning. These impairments can prevent alcoholic patients (ALs) early in abstinence from
5 benefiting fully from treatment, and reduce their ability to remain abstinent. A
6 neuropsychological assessment seems essential for making the relevant clinical decisions.
7 However, very few alcohol treatment departments have the financial and human resources
8 needed to conduct an extensive neuropsychological examination of each alcoholic patient.
9 The goal of the present study was therefore to assess the validity and the psychometric
10 properties of the Brief Evaluation of Alcohol-Related Neuropsychological Impairments
11 (BEARNI), a new screening tool especially designed to assess alcohol-related
12 neuropsychological impairments.

13 **Methods:** A total of 254 healthy controls (HCs) completed the BEARNI, and 58 of them also
14 performed an extensive neuropsychological battery. 73 ALs underwent both the BEARNI and
15 the neuropsychological battery. This extensive neuropsychological battery of proven
16 classification accuracy served as the reference (i.e., gold standard) for determining the ALs'
17 cognitive status.

18 **Results:** An exploratory factor analysis validated the BEARNI's underlying structure,
19 highlighting five factors that reflected visuospatial abilities, executive functions, ataxia,
20 verbal episodic memory and verbal working memory. The standardization of each BEARNI
21 subtest and the two total scores revealed that this test has sufficient diagnostic accuracy for
22 the detection of ALs with cognitive and motor impairments.

23 **Conclusion:** The present study indicates that the BEARNI is a useful screening tool in
24 clinical settings for detecting ALs' motor and cognitive impairments.

25

- 1 **Keywords:** alcoholism, neuropsychological impairment, brief cognitive screening tool,
- 2 exploratory factor analysis, ROC curve

For Review Only

1 INTRODUCTION

2 Chronic alcoholism results in brain damage and compromised motor and cognitive
3 functioning, even in alcoholic patients (ALs) with no severe neurological complications (i.e.
4 those without Korsakoff's syndrome (KS), or alcoholic dementia). The neuropsychological
5 impairments mainly encompass executive dysfunction (Ihara et al., 2000), working memory
6 deficits (Pitel et al., 2007; Uekermann et al., 2007) and visuospatial disabilities (Fama et al.,
7 2004). Genuine episodic memory impairments (i.e., not resulting solely from executive
8 dysfunctions) are also observed in ALs (Noël et al., 2012), but are generally less severe than
9 executive and visuospatial impairments (Sullivan et al., 2000). Deficits in motor functions
10 including ataxia of gait and balance (Fein and Greenstein, 2013) are just as severe as the
11 visuospatial deficits (Sullivan et al., 2000). These cognitive and motor impairments have been
12 estimated to affect more than two thirds of ALs (Ihara et al., 2000). The deficits range from
13 mild-to-moderate (Sullivan et al., 2000), that is, about one standard deviation from the mean
14 for **non-alcoholic** healthy controls (HCs) (Goldstein et al., 2004), to severe impairments
15 comparable to those observed in KS patients (Kopelman et al., 2009).

16 The treatment of alcohol-dependence includes several types of therapy such as Motivational
17 Enhancement Therapy, Twelve-Step Facilitation or cognitive behavioral therapy, which all
18 require attending to and receiving new information, and being able to integrate and translate it
19 into behavioral changes (Bates et al., 2006). To benefit from these therapies, ALs must
20 implement cognitive functions such as episodic memory, planning, inhibition and problem-
21 solving abilities, which have been repeatedly found as impaired. Episodic memory deficits
22 and executive dysfunction hinder complex learning, such as the learning of semantic
23 information and cognitive procedures (Pitel et al., 2007), affect readiness to change (Blume et
24 al., 2005), ability to elaborate alternative behavioral responses (Bates et al., 2006) and
25 decision making (Noël et al., 2007). These cognitive disabilities impact treatment compliance

1 and treatment outcomes (Bates et al., 2006). Thus, ALs with impaired cognitive functions
2 may be unable to benefit fully from therapy interventions. The detection of
3 neuropsychological impairments is therefore essential for making the appropriate clinical
4 decisions regarding the nature and timing of treatment.

5 Few alcohol departments and clinics have the financial and human resources needed to
6 administer an extensive neuropsychological examination to each ALs. Previous studies have
7 proposed a range of screening instruments for the detection of cognitive impairments in
8 patients with substance use disorders (SUDs), including the Neurobehavioral Cognitive Status
9 Examination (NCSE; (Kiernan et al., 1987), the Repeatable Battery for Assessment of
10 Neuropsychological Status (RBANS; (Randolph et al., 1998) and the Montreal Cognitive
11 Assessment (MOCA; (Nasreddine et al., 2005). According to (Shulman, 2000), an ideal
12 cognitive screening test should fulfill the following criteria: a) be readily administered; b) be
13 easy to score; c) have concurrent validity; and d) have high levels of sensitivity, specificity
14 and predictive validity. Despite the fact that existing screening tools can be administered
15 within 10-30 minutes and have satisfactory sensitivity to cognitive impairment in SUD
16 patients (Copersino et al., 2009; Fals-Stewart, 1997), they have several limitations. In addition
17 to poor specificity in detecting impaired patients (36% for NCSE and 69% for MOCA; Fals-
18 Stewart, 1997; Wester et al., 2013), these tools assess cognitive functions that are not usually
19 reported as impaired in ALs, including orientation, attention and concentration, language and
20 naming. Even though total MOCA and RBANS scores are lower for SUD patients than for
21 controls, analysis of individual subscores has shown that only memory, executive and
22 visuospatial abilities are impaired in patients compared with controls (Alarcon et al., 2015;
23 Green et al., 2010; Wester et al., 2013). More specifically, in a recent study (Alarcon et al.,
24 2015), performances of ALs with low (≤ 21), medium (22-25) and high (≥ 26) MOCA total
25 score were compared on each subscore of this test. The most affected domains concerned

1 abstraction and fluency. The authors raised a limitation to the MOCA that is the narrow range
2 of these subscores (respectively from 0 to 1 and 2) that can limit the assessment of the
3 severity of cognitive deficits and its improvement with abstinence and treatment.

4 Overall, these screening tools do not have a satisfactory level of content validity for chronic
5 alcoholism probably because they were initially designed to detect cognitive impairments
6 either in older individuals (Nasreddine et al., 2005; Randolph et al., 1998) or else in patients
7 receiving neurosurgical care for brain lesions (Kiernan et al., 1987). A screening tool must be
8 validated against a gold standard, in order to avoid misdiagnosis due to false negatives or
9 false positives. In the above-mentioned studies conducted in SUD patients, these patients'
10 cognitive profile was either not reported (Alarcon et al., 2015; Wester et al., 2013) or else
11 determined using the Neuropsychological Screening Battery (Heaton et al., 1990) or the
12 Neuropsychological Assessment Battery–Screening Module (White and Stern, 2003). These
13 short neuropsychological batteries both have poor specificity (Fals-Stewart, 1996) and have
14 been validated in SUD patients (Fals-Stewart, 1996; Grohman and Fals-Stewart, 2004) but not
15 specifically in alcoholic ones. Moreover, a main limitation of a previous study (Wester et al.,
16 2013) was that the MOCA was administered to patients at admission whereas the extensive
17 neuropsychological battery was conducted 6 to 8 weeks later. Since some of the cognitive
18 functions can recover, even after a short time of abstinence (from 3-5 weeks of abstinence;
19 (Mann et al., 1999)), the delay between the MOCA and the extensive battery substantially
20 limits the determination of the psychometric properties of the MOCA. Other brief screening
21 tools have been used in previous studies to describe the general cognitive status of alcoholic
22 patients, such as the MMSE (Folstein et al., 1975) and DRS Mattis (Mattis and Inc, 1988).
23 Results are discrepant since some of them reported impairments (Le Berre et al., 2010;
24 Rosenbloom et al., 2007) whereas other did not (Pitel et al., 2011). These tools are mainly

1 used as inclusion criteria in studies conducted in ALs and to exclude patients with low scores
2 that may be explained by dementia.

3 The goal of the present study was therefore to validate a new screening tool especially
4 designed for the rapid assessment of alcohol-related neuropsychological deficits. The Brief
5 Examination of Alcohol-Related Neuropsychological Impairment (BEARNI) is intended to be
6 short and easy to score, making it usable by non-psychologists. It is expected to enable
7 physicians or nurses to rapidly determine whether a patient can attend and gain from standard
8 alcohol treatment or whether some adjustments are required. More specifically, we sought to
9 assess the BEARNI's validity and its psychometric properties in order to determine whether it
10 is an appropriate tool for identifying cognitive and motor impairments in ALs. A value of
11 80% or above indicates high psychometric quality (Blazer and Hays, 1998), and we expected
12 the BEARNI's psychometric properties to meet this criterion.

13

14 **MATERIALS AND METHODS**

15 *Participants*

16 A total of 254 HCs completed the BEARNI, and 58 of them also performed an extensive
17 neuropsychological battery. We administered both the BEARNI and the extensive battery to
18 73 ALs. None of the participants had a history of neurological pathologies, endocrine or
19 infectious diseases, mental illness (psychiatric disorders assessed by the MINI 500;
20 (American Psychiatric Association, 2004), depression (Beck Depression Inventory, BDI-II;
21 (Beck et al., 1961), or other forms of substance misuse or dependence (except tobacco) over
22 the lifetime. None were under psychotropic medication that might have had an effect on their
23 cognitive functioning. All the participants were informed about the study (approved by the
24 local ethics committee) and provided their written informed consent before their inclusion.
25 Their demographic characteristics (age, sex ratio and education) with their scores on the Mini

1 Mental State Examination (MMSE; Folstein et al., 1975) and the Mattis Dementia Rating
2 Scale (DRS; Mattis and Inc, 1988) are reported in Table 1.

3 The ALs were recruited by clinicians while they were receiving withdrawal treatment as
4 inpatients at Caen University Hospital. All the patients met the DSM-IV criteria for alcohol-
5 dependence (American Psychiatric Association, 2004). None of them had severe, enduring
6 and global amnesia defining the Korsakoff's syndrome nor alcoholic dementia, **Marchiafava-**
7 **Bignami** or **central pontine myelinolysis**. Although the patients were early in abstinence, none
8 of them presented physical symptoms of alcohol withdrawal at inclusion. They were
9 interviewed with the Alcohol Use Disorders Identification Test (AUDIT; (Gache et al., 2005)
10 and a modified version of the semistructured Lifetime Drinking History questionnaire.
11 Measures included the duration of alcohol use (in years), alcohol misuse (in years), number of
12 withdrawals, and daily alcohol consumption prior to treatment (in standard drinks, a standard
13 drink corresponding to a beverage containing about 10 g of pure alcohol) (Table 1).

14 All the HCs were interviewed with the AUDIT (Gache et al., 2005) to ensure that they did not
15 meet the criteria for alcohol abuse or dependence over the lifetime (AUDIT <7 for men and
16 <6 for women) (Table 1). None of the HCs had a MMSE (Folstein et al., 1975) or a Mattis
17 DRS (Mattis and Inc, 1988) scores below the cut-off score of 24 and 127 respectively.

18

19 ***Material***

20 Participants completed the BEARNI and the extensive battery of neuropsychological tests
21 over 2-3 days to minimize fatigue and interference. Only 58 of the HCs completed the
22 neuropsychological battery (demographic characteristics in Table 1) in addition to the
23 BEARNI. The latter was administered on the first day to avoid the possible influence of the
24 extensive battery on performances. The order of the test administration was fixed because
25 some of the BEARNI subtests were inspired by neuropsychological tests administered to

1 participants (see below the description of the BEARNI subtests). Thus, in administering the
2 BEARNI before the extensive neuropsychological battery, all the subjects in our study were
3 in the same situation than patients in clinical settings who would first undergo the BEARNI
4 and then, an extensive neuropsychological examination. Raw scores of the BEARNI and the
5 extensive neuropsychological battery are provided in Supporting Information B table 4.

6

7 **Brief Examination of Alcohol-Related Neuropsychological Impairments** 8 **(BEARNI)**

9 The BEARNI is designed to assess the cognitive and motor functions that are impaired in
10 ALs, namely episodic memory, working memory, executive functions, visuospatial abilities,
11 and ataxia (Table 2). It takes approximatively 15-20 minutes to administer the BEARNI. In
12 order to avoid errors, instructions for administration and scoring are provided in Supporting
13 Information A. Examples of the working memory, flexibility, visuospatial and ataxia subtests
14 are provided to participants prior to data collection. The BEARNI is provided in Supporting
15 Information A.

16 The *episodic memory* subtest was inspired by the California Verbal Learning Test (Delis et
17 al., 1988). It consists of two learning trials of a 12-word list (4 words x 3 semantic
18 categories). The list is read aloud by the examiner. After each trial, the patient is instructed to
19 freely recall as many words as possible, in any order (1 minute per trial, no points scored).

20 **Once the remaining tests from the BEARNI have been administered**, delayed free recall is
21 performed (one trial lasting 1 minute). The episodic measure is the number of correct
22 responses (0.5 point per response) minus the number of errors (intrusions and perseverations;
23 0.5 point per error) during the delayed free recall task (maximum score: 6 points).

24 *Working memory* is assessed with an alphabetical span subtest adapted from the alpha-span
25 task (Belleville et al., 1998). This task probes the ability to manipulate information stored in

1 verbal working memory. Increasingly long letter sequences are read out loud, and for each
2 sequence the patient has to repeat the letters in alphabetical order. Two trials are performed
3 for each sequence. The task ends when the participant fails both two trials of a sequence (0.5
4 point per trial; maximum score: 5 points).

5 **Flexibility abilities** are assessed with the alternating verbal fluency subtest. Patients are given
6 120 seconds to generate as many words as possible from two alternating categories (“color
7 name” and “city name”). Depending on the number of correct responses, points range from 0
8 to 6 (for scoring details, see Supporting Information A).

9 **Visuospatial abilities** are assessed with an adapted version of the Hidden Figures Test
10 (Corkin, 1979; Thurstone, 1944). This subtest includes five complex figures, each containing
11 two separate hidden figures that the patient has to find. An example is provided and explained
12 to the patient by the examiner. For each complex figure, one point is provided when the
13 patient finds both hidden figures within 1 minute (maximum score: 5 points).

14 Finally, the **ataxia** subtest, drawn from the Walk-a-Line Ataxia Battery (Fregly, 1971),
15 requires patients to stand on each foot in turn for 30 seconds, first with eyes open, then with
16 eyes closed. There are up to two trials per condition. For each condition, 2 points are awarded
17 when patients successfully perform the task at the first trial, 1 point when they successfully
18 perform the task at the second trial, and 0 point when they fail both trials (maximum score: 8
19 points).

20 The BEARNI yields seven scores: five subscores (one for each of the subtests), a total score
21 (maximum score: 30 points) and a total *cognitive* score (excluding the ataxia subtest;
22 maximum score: 22 points).

23

24 **Neuropsychological examination**

1 The extensive neuropsychological battery we administered targeted a broad range of cognitive
2 and motor functions: *verbal episodic memory* (French adaptation of the CVLT (Delis et al.,
3 1988)); *working memory* (verbal and visuospatial spans of the MEM-III (Wechsler, 2001a)
4 and the Letter-Number Sequencing subtest of the WAIS-III (Wechsler, 2001b)); *executive*
5 *functions* (the Trail Making Test (Reitan, 1955), the Ruff Figural Fluency Test (RFFT;
6 (Foster et al., 2005), the Stroop test (Stroop, 1935), and fluency tasks (Cardebat et al., 1990);
7 *visuospatial abilities* (the Rey-Osterrieth Complex Figure (ROCF; (Osterrieth, 1944)) and
8 *ataxia* (the Walk-a-Line Ataxia Battery). The data collected for each test are summarized in
9 Table 2.

10

11 *Data analysis*

12 **Validation of the BEARNI's internal structure**

13 The first step consisted of an exploratory factor analysis (EFA) to determine the BEARNI's
14 factorial structure, the explained variance for each factor and the total variance. An orthogonal
15 rotation (normalized varimax rotation) was used because the latent factors were not correlated
16 with each other (data not shown). The number of factors was determined by three criteria: a)
17 eigenvalues above 1 (Kaiser criterion; (Kaiser, 1960); b) proportion of variance explained by
18 the factor above 5%; and c) number of theoretical variables in the integrated model. Given the
19 number of cognitive and motor functions targeted by the BEARNI (delayed verbal memory,
20 verbal working memory, flexibility, visuospatial abilities and ataxia), we expected to extract
21 five factors reflecting these five domains. A threshold ≥ 0.50 was used to determine the factors
22 on which each variable loaded. Any factor below the threshold of 0.50 was assigned to the
23 factor on which it most highly loaded. The EFA was conducted with the 58 HCs and 73 ALs
24 who had completed both the BEARNI and the extensive battery.

1 In addition, we compared the performance profiles of the ALs and HCs on each of the
2 BEARNI subtests. The objective was to determine whether the BEARNI's
3 neuropsychological profile was consistent with that described in the literature. To do so, we
4 carried out multivariate analyses of variance (MANOVAs; 2 groups x 5 subtests x 2 sexes;
5 age and education entered as covariates) and Tukey's tests for post-hoc comparisons.

6

7 **Standardization of the BEARNI**

8 ***Total scores***

9 For the BEARNI's two total scores (total score and total cognitive score), the standardization
10 was performed for the 58 HCs who had completed the neuropsychological battery. We used
11 the method described in (Godefroy et al., 2014) and reported in Supporting Information B.

12

13 ***Psychometric properties of the BEARNI total scores***

14 Sensitivity, specificity, positive and negative predictive values, diagnostic accuracy (% of
15 patients well classified; i.e., reliability of the screening test) and Yule's Q coefficient
16 (coefficient measuring the association between two attributes, ranging from 0 to 1, where a Q
17 coefficient of 0.70-1 is deemed to represent a very strong association) were computed using
18 the ALs' results on the BEARNI.

19 The psychometric properties of the BEARNI were then compared with those of the MMSE
20 (Folstein et al., 1975; Kalafat et al., 2003; cut-off scores in Supporting Information B Table 1)
21 and the Mattis DRS (cut-off score for persons aged under 69 years ≤ 127 ; Lucas et al., 1998;
22 Mattis and Inc, 1988).

23

24 ***BEARNI subtests***

25 For each subtest, we determined cut-off scores using the data collected from the 254 HCs who
26 had completed the BEARNI with the method described in (Godefroy et al., 2014) and in
27 Supporting Information B. We then investigated the predictive value of these cut-off scores

1 for detecting ALs with impaired performances on the neuropsychological battery. Based on
2 the cut-off scores, patients were classified as either impaired or preserved on each BEARNI
3 subtest. Performances on the tasks in the extensive neuropsychological battery were thus
4 compared across three groups (HCs ($n=58$), ALs with impaired BEARNI performances, and
5 ALs with preserved BEARNI performances) using an ANOVA. Tukey's tests were then
6 carried out for post-hoc comparisons. For each subtest, we regarded the BEARNI cut-off
7 score as predictive when ALs classified as impaired on a specific BEARNI subtest performed
8 more poorly on the corresponding domain of the neuropsychological battery than ALs with
9 preserved results on that subtest and HCs.

10

11 Statistical analyses were performed using Statistica and MedCalc software and the probability
12 significance threshold was set at $p \leq 0.05$. Where necessary, Bonferroni corrections were
13 applied to prevent Type-I errors.

14

15 **RESULTS**

16 *Validation of the BEARNI's internal structure*

17 The results of the EFA analysis are reported in Table 3. All the factors met the criteria of an
18 eigenvalue above 1 (Kaiser, 1960) and more than 5% of variance explained by the factor.
19 Consistent with our hypothesis, five factors were extracted. Factor 1 was deemed to reflect
20 executive and visuospatial abilities, factor 2 was represented by ataxia, factor 3 included
21 variables related to verbal episodic memory, factor 4 was represented by fluency tasks and
22 factor 5 included variables related to verbal working memory. Taken together, these five
23 factors accounted for 60.08% of the total variance. When restricted to HCs ($n=58$), the EFA
24 yielded the same results.

1 The two (group: ALs vs. HCs) x two (sexes) x five (BEARNI subtests) MANOVA on
2 BEARNI performances revealed significant effects of group, $F_{(1, 324)} = 53.53, p < 0.001$, age,
3 $F_{(1, 327)} = 11.28, p < 0.001$, and education, $F_{(1, 327)} = 69.72, p < 0.001$, the Subtest x Group
4 interaction, $F_{(4, 1308)} = 16.02, p < 0.001$, and the Subtest x Education interaction, $F_{(4, 1308)} = 3.55,$
5 $p = 0.007$, but no other significant effects. Tukey's post-hoc tests revealed that ALs performed
6 more poorly than HCs (effect of group), and this effect was found for each of the BEARNI
7 subtests (Subtest x Group interaction) except for delayed verbal memory (Figure 1).

8

9 ***Standardization of the BEARNI***

10 Most of the raw scores (both for the BEARNI and for the extensive neuropsychological
11 battery) deviated from normality and were influenced by age, education, sex, or all three.

12

13 **Standardization of the BEARNI's total scores**

14 On the extensive neuropsychological battery, 86% of ALs were classified as having at least a
15 mild impairment, 53% as having a moderate-to-severe impairment, and 14% having no
16 impairment. Regarding the neuropsychological battery with only cognitive functions (i.e.,
17 excluding performances on the Walk-a-Line Ataxia Battery), 84% of ALs were classified as
18 having at least a mild impairment, 45% as having a moderate-to-severe impairment and 16%
19 as having no impairment.

20 The ROC curve analysis performed to standardize the total BEARNI score (cognitive
21 functions plus ataxia) showed that a cut-off score of ≤ 19 yielded the best balance between
22 sensitivity and specificity for detecting mild impairment in the neuropsychological battery
23 (Supporting Information B Table 2, Figure 2A). For moderate-to-severe impairment, a cut-off
24 score of ≤ 16 yielded the best balance between sensitivity and specificity (Supporting
25 Information B Table 2, Figure 2B).

1 Regarding the total cognitive score (excluding the ataxia BEARNI subtest), a cut-off score of
2 ≤ 15 yielded the best balance between sensitivity and specificity for detecting mild impairment
3 in the neuropsychological battery (Supporting Information B Table 2, Figure 2C). For
4 moderate-to-severe impairment, a cut-off score of ≤ 11.5 yielded the best balance between
5 sensitivity and specificity (Supporting Information B Table 2, Figure 2D).

6 Linear regression analysis (forward stepwise) conducted in HCs and ALs showed a significant
7 effect of education on these two total BEARNI scores, indicating that participants with more
8 than 12 years of schooling had better performances. Thus, in order to correct for this
9 education effect, we adjusted the cut-off scores for participants with more than 12 years of
10 schooling. This adjustment of the cut-off scores was determined by the best balance between
11 true positive and true negative on the extensive neuropsychological battery. All total cut-off
12 scores are summarized in **Table 5**.

13

14 ***Psychometric properties of the BEARNI***

15 The psychometric properties of the BEARNI total scores are reported in Table 5. The
16 sensitivity, positive and negative predictive values, Yule's Q coefficient and diagnostic
17 accuracy to identify ALs showing mild or moderate-to-severe impairments on the extensive
18 neuropsychological battery range from acceptable to excellent. However, the specificity of the
19 BEARNI total scores for identifying ALs with mild impairments was low.

20 Only 9.59% and 8.22% of alcoholic patients were impaired on the MMSE and Mattis DRS
21 respectively. Although the specificity and the positive predictive value were excellent for the
22 MMSE (Folstein et al., 1975) and the Mattis DRS (Mattis and Inc, 1988) in identifying
23 alcoholic patients with mild impairment, the positive predictive value for moderate-to-severe
24 impairment as well as the sensitivity, negative predictive value, Yule's Q coefficient and
25 diagnostic accuracy were poor for mild and moderate-to severe impairments (Table 5).

1

2

Standardization of the BEARNI subtests and predictability

3 Each of the subtest scores yielded sensitivity values of 100%, specificity values ranging from
4 75.21% to 99.59%, and AUC values ranging from 0.950 to 0.998 (Supporting Information B
5 Table 3). ROC analyses provided cut-off scores for the following BEARNI subtests: delayed
6 verbal memory ≤ 2 ; alphabetical span ≤ 2.5 ; alternating fluency ≤ 2 ; visuospatial ≤ 1 ; and ataxia
7 ≤ 3 .

8 These cut-off scores indicated that 16% of the ALs were impaired on the episodic memory
9 subtest, 32.91% on the alphabetical span subtest, 21.52% on the alternating fluency subtest,
10 45.57% on the visuospatial subtest, and 49.36% on the ataxia subtest.

11 We then compared the HCs, ALs with impaired BEARNI results, and patients with preserved
12 BEARNI results on cognitive performances. Using the cut-off scores of each BEARNI
13 subtest, we compared these three groups on the corresponding domain of the
14 neuropsychological battery. As the raw scores on the neuropsychological battery were
15 influenced by demographic factors, each comparison was conducted using standard residuals.

16 All ANOVA results are provided in Table 6. The cut-off score of ≤ 2 for the delayed verbal
17 memory BEARNI subtest was predictive of performances on CVLT. Regarding the
18 alphabetical span BEARNI subtest, the cut-off score of ≤ 2.5 was predictive of performances
19 on verbal forward span and Letter-Number Sequencing. The cut-off of ≤ 2 for the flexibility
20 subtest was predictive of performances on the verbal fluency tasks and the TMT (Part B
21 minus Part A; $F_{(1, 128)} = 9.25, p < 0.001$, Tukey's post-hoc: impaired ALs < (preserved ALs
22 =HCs)). Regarding the visuospatial BEARNI subtest, the cut-off score of ≤ 1 was predictive of
23 performances on visuospatial backward span, Stroop, TMT and RFFT (total design but not
24 total strategies). For the ROCF and visuospatial forward span, although impaired ALs had
25 lower performances than preserved ALs and HCs (who did not differ between each other), no

1 statistical differences were found between the two patient groups. Finally, the cut-off of ≤ 3
2 for the ataxia subtest was predictive of performances on the Walk-a-Line Ataxia Battery.

3

4 **DISCUSSION**

5 The goal of the present study was to assess the validity and psychometric properties of the
6 BEARNI, a new screening tool especially designed for the rapid assessment of alcohol-related
7 neuropsychological deficits. An extensive neuropsychological battery of proven classification
8 accuracy (Godefroy et al., 2014) served as the reference (i.e., gold standard) for determining
9 the ALs' cognitive status.

10 In agreement with our theoretical hypothesis, the EFA validated the BEARNI's underlying
11 structure, as it highlighted five factors that accounted for 60% of the total variance: a first
12 factor including visuospatial and visual executive abilities, a second one reflecting ataxia, a
13 third one verbal episodic memory, a fourth one spontaneous cognitive flexibility, and a fifth
14 one verbal working memory. Three of these factors involved executive functions and
15 visuospatial abilities, which are impaired in two thirds of ALs (Ihara et al., 2000), and more
16 severely so than other cognitive deficits (Sullivan et al., 2000). The second factor, which
17 pertained to ataxia, was in agreement with deficits in gait and balance described in previous
18 studies (Fein and Greenstein, 2013) as being just as severe as the visuospatial impairments
19 (Sullivan et al., 2000). The delayed verbal memory factor represented a smaller proportion of
20 the explained variance in the present study, in accordance with a less severe and consistent
21 impairment of this function in ALs compared with other deficits (Ihara et al., 2000; Sullivan
22 et al., 2000). Thus, these results suggest that the BEARNI has satisfactory content validity.

23 Even though the BEARNI includes most of the cognitive domains known to be impaired in
24 ALs, such a brief screening tool cannot allow for the assessment of all cognitive functions.
25 For example, there is no evaluation of inhibition abilities, even though inhibition deficits have

1 repeatedly been reported in alcoholism (Ihara et al., 2000; Lusher et al., 2004) and have been
2 linked to poorer delayed recall in episodic memory (Noël et al., 2012) and motivation to
3 change (Blume et al., 2005). The EFA revealed that inhibition abilities contributed to the
4 variability of the visuospatial BEARNI subtest, which requires participants to find two figures
5 hidden in a complex figure. Impaired visuospatial global-local processing in alcoholism has
6 also been found to reflect difficulty inhibiting local information (Müller-Oehring et al., 2009).
7 Thus, performances on the visuospatial BEARNI subtest seem to be cognitively multi-
8 determined and may also reflect inhibition abilities.

9 This interpretation is confirmed by the high concurrent validity we observed when we
10 standardized the BEARNI subtests. ALs classified as impaired on the BEARNI subtests using
11 the cut-off scores were also impaired on the corresponding cognitive and motor domains of
12 the extensive battery. Those classified as preserved did not differ from HCs. Performances on
13 the visuospatial BEARNI subtest were predictive of results for the visuospatial abilities
14 assessed by the extensive neuropsychological battery, as well as for visuospatial working
15 memory, inhibition and flexibility. The episodic memory, verbal working memory, flexibility
16 and ataxia subtests were similarly predictive. Thus, the cut-off scores computed for each
17 BEARNI subtest had high diagnostic efficiency in terms of accurately detecting the cognitive
18 impairments observed on the extensive neuropsychological battery. In addition, performances
19 on each BEARNI subtest were only predictive of results on the corresponding cognitive
20 domains, and not of all the domains evaluated by the extensive battery. Taken together, these
21 findings indicate that the BEARNI could be used in clinical settings to obtain a reliable
22 estimation of neuropsychological performances, including episodic memory, executive
23 functions, working memory, visuospatial abilities and ataxia. Compared to other screening
24 tools, such as the MOCA (Alarcon et al., 2015; Wester et al., 2013), the BEARNI provides

1 larger scales of cut-off score for each subtest, that may lead to a more accurate assessment of
2 the severity and the improvement of neuropsychological deficits with abstinence.

3 Analysis of the BEARNI's psychometric properties showed that the two total scores made it
4 possible to distinguish between ALs with no impairment, mild deficits or moderate-to-severe
5 impairments, with satisfactory sensitivity, predictive validity and diagnostic accuracy (Blazer
6 and Hays, 1998). This finding suggests that 1) even ALs with mild impairments can be
7 detected with the BEARNI, and 2) the BEARNI identifies alcohol-related cognitive and
8 motor impairments with a high degree of accuracy. Yule's Q coefficients highlighted a strong
9 association between the cognitive profiles identified by the extensive neuropsychological
10 battery and by the BEARNI, suggesting a high reliability of our screening tool. Whereas it
11 takes 20 minutes at most to administer the BEARNI, an extensive neuropsychological battery
12 takes at least 90, if not 120 minutes, to complete, hand-score and interpret. Moreover, the
13 latter is not accessible to non-psychologists, making its routine use impracticable in clinical
14 settings. When an extensive neuropsychological battery cannot be readily conducted, the
15 BEARNI is therefore a useful and reliable screening tool for detecting cognitive and motor
16 impairments in ALs.

17 Compared to the BEARNI, the MMSE and DRS Mattis were found in our study to have poor
18 sensitivity, negative predictive value and diagnostic accuracy. 50% and more of the alcoholic
19 patients were not well identified by these screening tools. This finding could be explained by
20 the fact that these screening tools were initially designed to detect cognitive decline
21 associated with dementia. They are therefore neither relevant nor sensitive to assess cognitive
22 functioning in alcoholic patients. However, the use of the MMSE, the DRS Mattis as well as
23 the MOCA should not be disregarded in older alcoholic patients and/or in a context of
24 differential diagnosis. Our findings do not aim at convincing the readers they should not use

1 these tools any more. We believe that BEARNI is more relevant to detect alcohol-related
2 neuropsychological deficits but that these tools would be useful, as a complement.

3 The main limitation of the BEARNI is its relatively low specificity, especially for detecting
4 patients with mild impairment. Between 7 and 14% of patients were classified as impaired on
5 the BEARNI, whereas they had preserved results on the extensive neuropsychological battery.
6 This result cannot be attributed to incorrect sampling, as the prevalence of no, mild, and
7 moderate-to-severe impairments among the patients included in the present investigation,
8 according to the neuropsychological battery, matched that reported in previous study (Ihara et
9 al., 2000). The BEARNI therefore tends to overestimate motor and cognitive impairments in
10 ALs. As this screening tool has been developed to identify patients who should be referred to
11 a psychologist for a more comprehensive neuropsychological evaluation, the BEARNI seems
12 unlikely to miss impaired patients, instead referring some who may actually have a preserved
13 cognitive profile. It is important to stress that the BEARNI is not intended as a substitute for
14 an extensive neuropsychological examination, as it does not cover all the cognitive domains
15 and does not assess specific processes within a given domain. An extensive
16 neuropsychological examination will still be crucial when a differential diagnosis is required
17 or when a detailed profile is needed to ensure adequate treatment in relation to cognitive
18 rehabilitation.

19 In the light of these findings, we can make several recommendations for the clinical use of the
20 BEARNI (Figure 3). In this study, all alcoholics underwent both the BEARNI and the
21 neuropsychological battery while they were inpatients at treatment entry immediately after
22 withdrawal from alcohol. In this clinical context, ALs diagnosed as having preserved abilities
23 on the BEARNI can attend and benefit from standard alcohol treatment. For patients
24 identified by the BEARNI as having mild impairments, several clinical and medical factors
25 need to be considered to determine whether the treatment needs to be adjusted. Alcohol

1 history, including repeated withdrawals (Duka et al., 2003), bouts of thiamine deficiency
2 (Thomson, 2000), liver complications (Arria et al., 2007) and level of motivation (Blume et
3 al., 2005) have all been reported to be related to neuropsychological impairments in ALs.
4 Finally, ALs identified by the BEARNI as having moderate-to-severe impairments are
5 unlikely to benefit fully from treatment and should be referred for an extensive
6 neuropsychological examination. As the neuropsychological impairments present at treatment
7 entry are partially reversible, even after a short time of abstinence (Mann et al., 1999), a safe
8 and enriched environment (withdrawal from alcohol and nutrition treatment) may prove
9 beneficial for these impaired patients before they undergo standard alcohol treatment. A re-
10 test after this recovery period would determine whether their cognitive abilities were
11 sufficient for them to benefit from the standard treatment. A parallel version of the BEARNI,
12 allowing for this second assessment, is therefore required. More generally, the BEARNI aims
13 at determining the neuropsychological profile of ALs and whether a patient is able to attend
14 and gain from standard alcohol treatment or whether some adjustments are required.
15 Depending on the clinical context or the time when the BEARNI is administered, it will
16 enable to adjust alcohol treatment to the neuropsychological profile or to assess the
17 modification of neuropsychological performance with abstinence, reduction of alcohol
18 consumption or relapse.

19 To conclude, the present study suggests that the BEARNI has high content validity, as it
20 assesses the cognitive functions known to be impaired in chronic alcoholism, and reliable
21 diagnostic accuracy in detecting ALs with cognitive and motor impairments. It provides a
22 cognitive and motor profile that can guide the adjustment of alcohol treatment and further
23 cognitive assessments. As such, the BEARNI seems to be a useful screening tool in clinical
24 settings for detecting motor and cognitive impairments present at alcohol treatment entry. An

- 1 English/US version is ongoing to make available the BEARNI to native English speaker
- 2 patients.

For Review Only

1 **CONFLICT OF INTEREST**

2 Authors declare no conflict of interest.

For Review Only

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1 **TABLES**

2

Table 1: Participants' Demographic Characteristics

	Alcoholic patients	Control participants		p-values
Number	73	254	58 ¹	
Men/women	53/20	154/100	27/31	0.06; 0.002*
Age (years)	45.47 ± 8.85	43.22 ± 9.32	42.81 ± 10.86	0.07; 0.13
Range	26-67	20-66	31-60	
Education (years of schooling)	11.18 ± 1.69	12.83 ± 2.61	12.76 ± 2.47	<0.001*; <0.001
Range	8-15	6-21	5-18	
MMSE	27.90 ± 1.90	-	28.79 ± 1.13	0.002*
Range	21-30		26-30	
DRS Mattis	136.96 ± 6.07	-	141.76 ± 2.31	<0.001*
Range	115-144		134-144	
AUDIT	29.90 ± 6.33	3.07 ± 1.68	2.84 ± 1.68	<0.001*; <0.001
Range	9-40	0-6	0-6	
Days of sobriety before inclusion	13.17 ± 6.73	-	-	
Range	4-50			
Alcohol use (years)	30.25 ± 9.07	-	-	
Range	10-51			
Alcohol misuse (years)	17.49 ± 9.23	-	-	
Range	5-43			
Daily alcohol consumption (units)	23.48 ± 35.36	-	-	
Range	0-300			
Number of withdrawals	3.52 ± 6.05	-	-	
Range	0-52			

3 Data are shown as means ± standard deviation. Only 58 of the control participants underwent the extensive
 4 neuropsychological battery. AUDIT = Alcohol Use Disorders Identification Test.

5 * Significant difference between alcoholic patients and control participants (n=254 ; n=58) at p<0.05 (t-tests)

6

1 Table 2: Cognitive and Motor Domains Assessed by the Brief Evaluation of Alcohol-Related
 2 Neuropsychological Impairments (BEARNI) and the Extensive Neuropsychological Battery

Domains	BEARNI subtests	Neuropsychological battery tests
<i>Verbal episodic memory</i>	Learning	CVLT Learning (sum of correct responses across 5 trials)
	Delayed free recall	CVLT Delayed free recall (number of correct responses)
		CVLT Delayed free recall (number of errors)
<i>Working memory</i>	Alphabetical span	Verbal Span (forward span)
		Verbal Span (backward span)
		Letter-Number Sequencing (standard score)
		Visuospatial Span (forward span)
		Visuospatial Span (backward span)
<i>Executive function</i>	Alternating fluency	TMT Part B - Part A (time)
		Fluency task (letter <i>p</i> ; number of correct responses)
		Fluency task (animal category; number of correct responses)
		Stroop Interference-Naming (time)
		RFFT (total design)
		RFFT (total strategies)
<i>Visuospatial abilities</i>	Visuospatial	ROCF (copy accuracy /36)
	(hidden figures)	
<i>Ataxia</i>	Ataxia (balance)	Stand in Romberg position (one foot in front of the other placed heel to toe) (two 60-s trials; eyes open)
		Stand in Romberg position (one foot in front of the other placed heel to toe) (two 60-s trials; eyes closed)
		Walk heel-to-toe (two 10-step trials, eyes open)
		Walk heel-to-toe (two 10-step trials, eyes closed)

3 CVLT = California Verbal Learning Test; TMT B-A = Trail Making Test Part A minus Part B; RFFT = Ruff
 4 Figural Fluency Test; ROCF = Rey Osterrieth Complex Figure.

5

1

Table 3 Results of the Exploratory Factor Analysis (EFA)

Variables	Factors				
	Factor 1	Factor 2	Factor 3	Factor 4	Factor 5
Eigenvalues	6.70	2.24	1.65	1.31	1.10
Explained variance	30.45%	10.18%	7.48%	5.97%	5.00%
BEARNI Delayed free recall			0.49*		
BEARNI Alphabetical span					0.69
BEARNI Fluency				0.57	
BEARNI Visuospatial	0.67				
BEARNI Ataxia		0.63			
Feet placed heel-to-toe (eyes open)		0.74			
Feet placed heel-to-toe (eyes closed)		0.77			
Walk heel-to-toe (eyes open)		0.78			
Walk heel-to-toe (eyes closed)		0.68			
CVLT Learning			0.85		
CVLT Delayed free recall (correct responses)			0.80		
CVLT Delayed free recall (errors)			-0.75		
Letter (<i>p</i>) fluency				0.67	
Categorical (animals) fluency				0.78	
Verbal forward span					0.69
Verbal backward span					0.73
Letter-Number Sequencing					0.77
ROCF (copy accuracy)	0.30*				
Visuospatial forward span	0.69				
Visuospatial backward span	0.72				
Stroop Interference-Naming (time)	-0.61				
TMT B-A (time)	-0.47*				
RFFT (total strategies)	0.59				
RFFT(total design)	0.62				

2 Marked factor loadings with significance threshold set at 0.5. * Variable not significant at established threshold of 0.5, but
3 assigned to the factor on which it most highly loaded. CVLT = California Verbal Learning Test; ROCF = Rey Osterrieth
4 Complex Figure; TMT B-A = Trail Making Test Part A minus Part B; RFFT = Ruff Figural Fluency Test.

5

1 Table 4: Summary of Total BEARNI Cut-Off Scores Adjusted for Education Level

BEARNI total score	Criteria	Education (years of schooling)	
		≤ 12	> 12
Total score /30 (cognitive functions plus ataxia)	Mild impairment	≤ 19	≤ 21
	Moderate-to-severe impairment	≤ 16	≤ 17
Total cognitive score /22 (excluding the Ataxia subtest)	Mild impairment	≤ 15	≤ 16
	Moderate-to-severe impairment	≤ 11.5	≤ 12.5

2

3

For Review Only

1 Table 5: Psychometric properties of the BEARNI, MMSE (Folstein et al., 1975; Kalafat et al.,
 2 2003) and Mattis DRS (Lucas et al., 1998; Mattis and Inc, 1988)

Psychometric properties	BEARNI (total score)	BEARNI (total "cognitive" score)	MMSE	Mattis DRS
<i>Mild impairment</i>				
Sensitivity	98.41 %	93.44 %	9.52 %	7.94 %
Specificity	50.00 %	50.00 %	90.00 %	90.00 %
Positive predictive value	92.54 %	90.48 %	85.71 %	83.93 %
Negative predictive value	83.33 %	60.00 %	13.64 %	13.43 %
Yule's Q coefficient	0.97	0.87	0.03	0.13
Diagnostic accuracy	91.78 %	86.30 %	20.54 %	19.17 %
<i>Moderate-to-severe impairments</i>				
Sensitivity	94.87 %	81.82 %	7.69 %	7.69 %
Specificity	70.59 %	85.00 %	88.24 %	91.18 %
Positive predictive value	78.72 %	81.82 %	42.86 %	50.00 %
Negative predictive value	92.31 %	85.00 %	45.45 %	46.27 %
Yule's Q coefficient	0.96	0.92	0.23	0.07
Diagnostic accuracy	83.56 %	83.56 %	24.09	46.57 %

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4

1 Table 6: Predictive Value of the Cut-Off Scores of Each BEARNI Subtest for Detecting the
 2 Neuropsychological Impairments Identified by the Extensive Battery

NP battery tasks	Alcoholic patients		Controls	Statistics	Tukey post hoc
	AL ⁻	AL ⁺	(n = 58) HC		
<i>Episodic memory (BEARNI cut-off score ≤ 2)</i>					
CVLT Learning	-1.41 ± 1.23	-0.24 ± 1.14	0.00 ± 1.00	$F_{(2,128)} = 9.02$; $p < 0.001^*$	AL ⁻ < AL ⁺ = NC
CVLT Delayed recall (correct response)	-1.64 ± 1.20	-0.55 ± 1.56	0.00 ± 0.98	$F_{(2,128)} = 9.12$; $p < 0.001^*$	AL ⁻ < AL ⁺ = NC
CVLT Delayed recall (error)	-1.36 ± 2.02	-0.24 ± 1.53	0.00 ± 0.99	$F_{(2,128)} = 5.15$; $p = 0.007^*$	AL ⁻ < AL ⁺ = NC
<i>Verbal working memory (BEARNI cut-off score ≤ 2.5)</i>					
Verbal forward span	-1.01 ± 0.94	-0.23 ± 0.88	0.00 ± 1.00	$F_{(2,128)} = 9.25$; $p < 0.001^*$	AL ⁻ < AL ⁺ = NC
Verbal backward span	-1.41 ± 0.64	-0.50 ± 0.90	0.00 ± 1.00	$F_{(2,128)} = 19.68$; $p < 0.001^*$	AL ⁻ < AL ⁺ < NC
Letter-Number Sequencing	-1.69 ± 0.78	-0.21 ± 0.80	0.00 ± 1.00	$F_{(2,128)} = 29.73$; $p < 0.001^*$	AL ⁻ < AL ⁺ = NC
<i>Flexibility (BEARNI cut-off score ≤ 2)</i>					
Letter (p) fluency	-0.66 ± 0.93	0.00 ± 0.93	0.00 ± 1.00	$F_{(2,128)} = 3.30$; $p = 0.04$	AL ⁻ < AL ⁺ = NC
Categorical (animals) fluency	-0.96 ± 1.20	-0.32 ± 1.20	0.00 ± 1.00	$F_{(2,128)} = 5.20$; $p = 0.007^*$	AL ⁻ < AL ⁺ = NC
<i>Visuospatial abilities (BEARNI cut-off score ≤ 1)</i>					
ROCF (copy accuracy)	-0.61 ± 1.11	-0.22 ± .092	0.00 ± 1.00	$F_{(2,128)} = 3.86$; $p = 0.02$	AL ⁻ < NC AL ⁺ = NC
Visuospatial forward	-0.83 ± 0.67	-0.38 ± 0.93	0.00 ± 1.00	$F_{(2,128)} = 9.12$;	AL ⁻ < AL ⁺

span				$p < 0.001^*$	$AL^+ = NC$
Visuospatial	-0.74 ± 0.80	-0.18 ± 0.79	0.00 ± 1.00	$F_{(2,128)} = 7.34;$	$AL^- < AL^+ = NC$
backward span				$p < 0.001^*$	
Stroop Interference-	-1.97 ± 3.10	-0.50 ± 1.94	0.00 ± 1.00	$F_{(2,128)} = 10.42;$	$AL^- < AL^+ = NC$
Naming (time)				$p < 0.001^*$	
TMT Part A-Part B	-2.77 ± 6.57	-0.45 ± 1.40	0.00 ± 1.00	$F_{(2,128)} = 7.20;$	$AL^- < AL^+ = NC$
(time)				$p = 0.001^*$	
RFFT	-0.73 ± 0.74	-0.44 ± 0.89	0.00 ± 1.00	$F_{(2,128)} = 2.59;$	<i>ns</i>
(total strategies)				$p = 0.07$	
RFFT(total design)	-1.10 ± 1.02	-0.18 ± 1.21	0.00 ± 1.00	$F_{(2,128)} = 11.64;$	$AL^- < AL^+ = NC$
				$p < 0.001^*$	
<i>Ataxia (BEARNI cut-off score ≤ 3)</i>					
Heel-to-toe	-1.68 ± 2.15	-0.06 ± 0.89	0.00 ± 1.00	$F_{(2,128)} = 18.68;$	$AL^- < AL^+ = NC$
(eyes open)				$p < 0.001^*$	
Heel-to-toe	-0.92 ± 0.94	-0.37 ± 0.92	0.00 ± 1.00	$F_{(2,128)} = 10.19;$	$AL^- < AL^+ < NC$
(eyes closed)				$p < 0.001^*$	
Walk heel-to-toe	-1.56 ± 2.05	-0.21 ± 1.21	0.00 ± 1.00	$F_{(2,128)} = 14.57;$	$AL^- < AL^+ = NC$
(eyes open)				$p < 0.001^*$	
Walk heel-to-toe	-0.92 ± 0.82	0.01 ± 1.12	0.00 ± 1.00	$F_{(2,128)} = 11.61;$	$AL^- < AL^+ = NC$
(eyes closed)				$p < 0.001^*$	

- 1 Data are shown as standard residuals (i.e., *z* scores) mean \pm standard deviation.
- 2 NP = neuropsychological; CVLT = California Verbal Learning Test; ROCF = Rey Osterrieth Complex Figure;
- 3 TMT B-A = Trail Making Test Part A minus Part B; RFFT = Ruff Figural Fluency Test;
- 4 AL^+ = preserved alcoholic patients; AL^- = impaired alcoholic patients; HC = healthy controls.
- 5 * still significant after Bonferroni correction.
- 6 *ns* = not significant ($p > 0.05$).
- 7

1 **FIGURE LEGENDS**

2 Figure 1: Results of the comparison between ALs (in red) and HCs (in black) on each
3 BEARNI subtest. Data are shown as mean \pm standard error of mean, taking the significant
4 effects of age and education into account.
5 (*ns*: nonsignificant).

6

7 Figure 2: ROC curve analyses for determining the total BEARNI (A and B) and total
8 cognitive BEARNI (C and D) cut-off scores reflecting mild impairment (A and C) and
9 moderate-to-severe impairment (B and D).

10

11 Figure 3: Clinical recommendations according to the cognitive status of alcoholic patients at
12 treatment entry as diagnosed by the BEARNI.

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