Atrial Fibrillation Follow-up Investigation to Recover Memory and Learning Trial (AFFIRMING): Rationale and Design of a Multi-center, Double-blind, Randomized Controlled Trial

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Abstract

Background: People with atrial fibrillation (AF) have elevated risk of developing cognitive impairment. At present, there is a dearth of randomized controlled trials investigating cognitive impairment management in patients with AF. The Atrial Fibrillation Follow-up Investigation to Recover Memory and Learning (AFFIRMING) study is aimed at evaluating the potential for computerized cognitive training to improve cognitive function in patients with AF.

Methods: The study is a multi-center, double-blind, randomized controlled study using a 1:1 parallel design. A total of 200 patients with AF and mild cognitive decline without dementia are planned to be recruited. The intervention group will use the adaptive training software with changes in difficulty, whereas the positive control group will use basic training software with minimal or no variation in difficulty level. At the end of 12 weeks, the participants will be unblinded, and the positive control group will stop training. The intervention group will be rerandomized 1:1 to stop training or continue training. All participants will be followed up until 24 weeks. The primary endpoint is the proportion of the improvement of the global cognitive function at week 12 compared with baseline, using the Basic Cognitive Ability Test (BCAT).

Keywords: atrial fibrillation; cognitive decline; cognitive training

Trial registry: NCT05374642 Registered 2022 May 16th
https://classic.clinicaltrials.gov/ct2/show/NCT05374642
Introduction

Background and Rationale

Mild cognitive impairment (MCI) refers to a decline in memory or other cognitive function without impairment in daily living skills. Epidemiological studies have indicated that the prevalence of dementia among people older than 65 years in China is 5.14% [1], and the prevalence of MCI is as high as 20.8% [2]. The annual transition rate of MCI to dementia is 10–15% [3]. Hypertension, heart failure, and diabetes are the three main cardiovascular risk factors for cognitive impairment [4–7]. Atrial fibrillation (AF) is one of the most common types of arrhythmias, and its prevalence gradually increases with age [8, 9]. The risk of cognitive decline and dementia in people with AF is significantly higher than that of people of the same age without AF [10]. People with AF have a significantly elevated risk of dementia, regardless of the presence of stroke [11]. Studies have suggested that, in addition to stroke, the mechanism of cognitive impairment caused by AF may be associated with systemic inflammation, decreased cerebral perfusion, and clinically insignificant brain lesions [12, 13].

To prevent cognitive dysfunction in patients with AF, a comprehensive management strategy should be followed, and common risk factors, such as hypertension, diabetes, sleep apnea, and cardiovascular factors, should be controlled [14]. However, current evidence has not clearly indicated whether anticoagulation strategies prevent cognitive impairment in patients with AF [15]. Regarding rhythm and rate control, in a sub-study of the Atrial Fibrillation Follow-up Investigation of Rhythm Management (AFFRIM) involving 245 patients with an average follow-up of 3.5 years, no significant difference in Mini-Mental State Examination Scale (MMSE) scores has been observed between the rhythm control group and the rate control group [16]. AF ablation is associated with a lower risk of dementia than drug treatment [17]. However, attention should be paid to post-operative neurocognitive dysfunction, which has a prevalence of 13–20% in patients with AF after ablation [18].

Non-drug therapy, particularly cognitive training, has the potential to improve cognitive function in various cognitive domains. Cognitive training can be performed for one or more cognitive domains such as memory, attention, and execution processing. Written or computerized training methods can be used. Randomized controlled trials and meta-analyses have shown that cognitive training significantly improves global cognitive function in patients with cognitive impairment [19, 20]. To date, few studies have investigated computerized-based cognitive training. In patients with diabetes, family-based multi-dimensional computerized cognitive training has been found to improve global cognitive function and disease management ability [21]. A 7-week cognitive training has also been reported to increase global cognitive function in patients with vascular cognitive impairment without dementia [22]. Another trial investigating the efficacy of cognitive training in patients with amnestic MCI is ongoing [23].

However, in patients with AF and cognitive impairment, randomized controlled studies on cognitive training are lacking. Therefore, this study was aimed at evaluating the effectiveness of computerized cognitive training in patients with AF and cognitive impairment.

Study Objective

The study objective is to determine the efficacy of computerized cognitive training on global cognitive function in patients with AF and cognitive impairment without dementia, compared with positive controls, over a 12-week training period.

Trial Design

The AFFIRMING study is a multicenter, double-blind, 1:1 parallel randomized controlled trial. A total of 200 eligible patients will be recruited from study centers and randomized to either the intervention group or the positive control group for a 12-week...
The randomization will be stratified by age and educational level. After the 12-week intervention, participants will be unblinded. The participants in the intervention group will then be rerandomized into two groups (stopping training vs continuing training) in a 1:1 ratio. All participants will be followed up for 24 weeks. The flowchart is shown in Figure 1.

**Methods**

**Study Setting**

The study was launched in June 2022 at Beijing Anzhen Hospital. Patients were planned to be recruited from multiple participating centers over 18 months. Medical teams in the Anzhen Hospital will evaluate the centers to ensure their adherence to proper management systems, including adequate facilities, staff, and potential participants.

**Eligibility Criteria**

Participants in this study were recruited among patients over 18 years of age at study centers. Participants were required to have documented AF and self-reported cognitive decline within 1 year. Eligibility will be determined through several cognitive function assessment tools.

Participants must meet all of the following criteria to be included in the study:
1) Age over 18 years  
2) Education of at least junior school or equivalent  
3) Documented AF  
4) Complaints of memory decline in the past 1 year  
5) Decline in cognitive function, defined by a Montreal Cognitive Assessment Scale score ≤ 25  
6) Consent to participate in this study

The exclusion criteria will include factors potentially affecting cognitive function, or conditions affecting the completion of computer training. Patients will not be included in this study if they meet any of the following criteria:

1) Inability to complete the cognitive function examination because of vision, hearing, or other problems  
2) Previously diagnosed dementia, or MMSE score ≤20  
3) Use of alcohol or drugs that affect cognitive function (for example, antihistamines or antipsychotics)  
4) Failure to master the use of the cognitive training software after two 1-hour training sessions  
5) Planned AF catheter ablation within 3 months  
6) AF catheter ablation in the past 3 months  
7) General anesthesia in the past 3 months  
8) History of stroke and head injury in the past 6 months  
9) History of Parkinson’s disease, schizophrenia, or epilepsy  
10) Prior neurosurgery or history of brain tumors

**Intervention Description**

The 200 patients will be randomly assigned to the intervention group or control group. The randomization will be stratified by age (≥70 years old or <70 years old) and education level (completion of junior high school or below, or completion of education above junior high school). Both groups will receive equal amounts of training.

**Intervention Group: Computerized Cognitive Training Group**

Patients in the intervention group will undergo comprehensive and targeted multidimensional cognitive function training, including attention, memory, executive function, thinking, processing speed, and perception. The system dynamically adjusts the training difficulty and plan according to the patient’s current performance and progress, to effectively enhance their weaker cognitive abilities. After 12 weeks of training, patients in the intervention group will be rerandomized into either the continuing training group, which will continue training for an additional 12 weeks, or the stopping training group, which will stop training immediately.

**Control Group: Positive Control Group**

The training content of the positive control group will comprise cognitive training tasks with weak difficulty or no difficulty changes. Patients in this group will undergo a standardized cognitive function training program consisting of 15 fixed training items, with the difficulty of each item remaining constant.

**Criteria for Discontinuing or Modifying Allocated Interventions**

The routine treatment of patients during and after the study will not be affected by this study. The study will not result in any foreseeable harm to patients, and any need to stop the intervention is unlikely to arise. The patients will be informed that they may request a pause in training or withdrawal from the study at any time for any reason, and that this decision will not affect their medical treatment.

No intentions are planned to modify the assigned intervention groups. If any adverse events occur, the investigators will evaluate whether continued intervention is harmful to the participants’ safety or health, and decisions will be made accordingly.

**Strategies to Monitor and Improve Adherence to Interventions**

After enrollment, patients will be provided with a tablet computer for cognitive training and will participate in one or two 1-hour sessions. These sessions will involve the use of cognitive training tablets, completion of weekly training tasks, and resolution of any technical issues. To ensure the quality of training, patients who do not complete the training independently after two sessions will be excluded.
After the training sessions, formal cognitive training will continue at home. Effective training will be defined as completion of at least five training sessions per week and successful completion of the assigned tasks within 30–60 minutes. During the training process, if patients are unable to complete their training on time, investigators or clinical associates will communicate with them to address potential technical difficulties and provide guidance via telephone or online communication channels, to ensure training quality.

To further enhance the quality of training, investigators and clinical assistants will collaborate in providing baseline visit trainings for both patients and their family members whenever possible. In the patients’ home training process, family members can assist patients by helping them understand how to perform various training processes and providing encouragement. As an incentive to comply with the study, patients will receive rewards after successful completion of each cognitive task; additionally, after study completion, participants will be offered free access to the cognitive software for 1 year.

Concomitant Care

Cardiovascular diseases, including hypertension, diabetes mellitus, and AF, significantly affect cognitive function. Therefore, careful management of cardiovascular disease in all enrolled participants will be performed to minimize the effects of confounders. For all patients diagnosed with AF, we recommend the use of oral anticoagulants (non-vitamin K antagonist oral anticoagulants or warfarin) in men with CHA2DS2-VASc scores $\geq 2$ and women with CHA2DS2-VASc scores $\geq 3$. For patients with renal dysfunction, the clinicians will recommend adjusting the dosage of non-vitamin K antagonist oral anticoagulants according to renal function. For patients with other cardiovascular diseases, management of those diseases according to the corresponding guidelines is recommended.

Outcomes

Primary Outcomes

The primary endpoint will be the proportion of patients with improved global cognitive function at week 12. The assessment of improved global cognitive function will be conducted using the Basic Cognitive Ability Test (BCAT), a test tool introduced by Li Deming’s research group at the Institute of Psychology of the Chinese Academy of Sciences [24]. The basic cognitive ability tests used in this study will include four cognitive functions: processing speed, working memory, situational memory, and visual-spatial processing. These functions correspond to the four tests included in the BCAT software: symbol search, portrait memory, operation span, and paper folding. The assessment will be conducted with the web-based version on a computer browser. Further details regarding the specific tasks used are provided in Appendix 1.

The Z-value for each cognitive domain can be obtained from the Z-value table according to the scale score obtained for each item in the test (Appendix 2, Table 1). The global cognitive function score will be calculated as the average of scores across each cognitive domain. Previous studies have defined cognitive function improvement as an increase of 1 standard deviation (SD) and 0.5 SD [25]. In the AFFIRMING study, improvement in cognitive function was defined as a Z-value of the global BCAT score 0.67 SD higher than the baseline Z-value after training.

Secondary Outcomes

1) The proportion of improvement in global cognitive function at week 24
2) The proportion of improvement in cognitive function for each cognitive domain at week 12 and week 24
3) Changes in scores of global cognitive function at week 12 and week 24
4) Changes in patients’ self-efficacy scores at week 12 and week 24
   (Self-efficacy scores will be measured with the Chinese version of the General self-efficacy Scale-Schwarzer (GSES) proposed by Schwarzer et al. The GSES consists of ten items scored on a four-point Likert scale [26]. The score ranges from 10–40, with higher scores indicating better self-efficacy.)
5) Changes in patients’ quality of life scores at week 12 and week 24
   (Quality of life scores will be measured with the European Five-Dimensional Health Scale)
(EQ-5D-3L), a self-rated scale including five dimensions: mobility, ability to take care of oneself, ability to perform daily activities, pain or discomfort, and depression [27].)

6) Changes in patients' anxiety and depression scores at week 12 and week 24 (Anxiety-depression status will be measured with the Patient Health Questionnaire Depression Scale (PHQ-9) [28] and the Generalized Anxiety Scale (GAD-7) [29].)

**Exploratory Outcomes**

1) Changes in structural and functional characteristics of brain MRI. The brain MRI will be evaluated at baseline, week 12, and week 24 in a subset of patients.

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### Table 1 Schedule of the Study.

<table>
<thead>
<tr>
<th>No. visiting</th>
<th>V1</th>
<th>V2</th>
<th>V3</th>
<th>V4</th>
<th>V5</th>
<th>V6</th>
</tr>
</thead>
<tbody>
<tr>
<td>Case report form</td>
<td>A Screening</td>
<td>B Baseline/randomization</td>
<td>C</td>
<td>D</td>
<td>E</td>
<td>F</td>
</tr>
<tr>
<td>Time from randomization</td>
<td>−12–0 weeks</td>
<td>0 weeks</td>
<td>4 weeks</td>
<td>8 weeks</td>
<td>12 weeks</td>
<td>24 weeks</td>
</tr>
<tr>
<td>Visiting window</td>
<td>-</td>
<td>-</td>
<td>±7 days</td>
<td>±7 days</td>
<td>−3−7 days</td>
<td>±14 days</td>
</tr>
<tr>
<td>Informed consent</td>
<td>×</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Face to face visit</td>
<td>×</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Questionnaires**

- FAQ score
- MMSE
- MoCA
- Self-efficacy score
- EQ-5D
- PHQ-9
- GAD-7
- SAE/AE

MRI: magnetic resonance imaging; BCAT: Basic Cognitive Ability Test; FAQ: Functional Activities Questionnaire; MMSE: Minimal Mental State Examination; MoCA: Montreal Cognitive Assessment; PHQ-9: Patient Health Questionnaire-9; GAD-7: General Anxiety Disorder-7; SAE: serious adverse event; AE: adverse event.

*The brain MRI will be evaluated in a subset of patients.

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### Sample Size

The sample size was calculated on the basis of previous studies and the following assumptions:

1. After 12 weeks of intervention, the global cognitive function in 30% of the patients in the intervention group will be improved.
2. After 12 weeks of intervention, global cognitive function will be improved in 10% of the patients in the control group.
Each group will have a sample size of 65 participants to provide 90% power at a significance level of 5%. Expecting a dropout rate of 20% over 12 weeks, we decided on a sample size of 200 participants.

**Recruitment**

Patients will be recruited from medical centers in the study. Clinicians will recommend and screen patients on the basis of the inclusion and exclusion criteria, and examination of patients’ electronic medical records. Additionally, a central advertising approach including social media and physician outreach will be used as an important recruitment strategy. To enhance patient willingness to participate, material incentives such as free medical examinations and reimbursement of transportation expenses for follow-up visits will be provided.

**Methods: Assignment of Interventions**

**Allocation: Sequence Generation**

A randomization network service system will be used to allocate interventions for study patients. After 12 weeks of training, patients in the control group will discontinue intervention, whereas those in the intervention group will be rerandomized to the continuing training group or stopping training group in a 1:1 ratio through the same randomization network system. Follow-up will continue until 24 weeks.

**Allocation: Concealment Mechanism**

Baseline randomization will be concealed from patients, investigators, and clinical associates to ensure blinding. A randomization code will be generated by the sponsor-managed network service system to maintain the concealment of baseline randomization. The corresponding randomization outcomes for each code will be securely stored on a server, and will remain inaccessible to participants and investigators. However, due to rerandomization at week 12, participants and investigators need to be unblinded to the results of the first randomization.

**Allocation: Implementation**

A separate system used by the cognitive training software will automatically generate individual patient accounts based on randomized codes. Patients can log into these accounts to use the cognitive training software to which they are assigned (intervention group or control group). This process will occur in the background of the system and will be invisible to the participants and investigators.

**Blinding**

Double-blind conditions will apply to the baseline groups in this study. The randomization results will be securely stored on the network server and will remain unrevealed to patients, researchers, and research assistants. The re-randomization at 12 weeks will be open label.

**Emergency Unblinding**

No emergency blinding is expected to occur in this study.

**Methods: Data Collection, Management, and Analysis**

**Data Collection Plan**

At baseline, patients will undergo laboratory tests and blood sampling for liver and kidney function, lipids, and blood glucose at the medical center. Electrocardiography and echocardiography will be performed at the same site. If these tests have been conducted within the past 6 months, repetition will be unnecessary. Demographic data such as age, sex, race, and education will also be collected during this initial visit. The schedule of the study is shown in Table 1.

**Data Management: Process to Promote Data Quality**

All the investigators will be required to undergo comprehensive training in data collection and reporting. Quality control meetings will be conducted regularly. To ensure investigator compliance with clinical trial quality management practices and fulfillment of their obligations, regular inspections will
be performed. The quality of the execution, including the integrity of study records and the diligent execution of investigators’ duties, will be monitored.

**Statistics: Outcomes**

The intention-to-treat analysis (ITT) will be used for data analysis, and patients will be categorized on the basis of their initial randomization. Continuous variables will be presented as means (and SDs) and assessed with P-P plots. Data with skewed distributions will be represented by medians (and interquartile ranges) and transformed to normal distribution. If transformation does not achieve an approximate normal distribution, Mann-Whitney U test can be performed. Statistical analysis will be conducted according to a pre-designed and published complete Statistical Analysis Plan. The differences in the primary endpoint will be evaluated with the chi-square test.

**Monitoring**

**Data Monitoring: Formal Committee**

The Data and Safety Monitoring Board (DSMB) will supervise the study. The DSMB members for this study consist of experts in cardiology, neurology, clinical trials, biostatistics, and other relevant fields. The DSMB is independent of the sponsor, thus ensuring the absence of any conflicts of interest.

**Ethics and Dissemination**

**Research Ethics Approval**

The protocol will be reviewed and approved by the Ethics Committee of Beijing Anzhen Hospital and other study centers. The study protocol was designed, conducted, and reported in compliance with International Conference on Harmonization Good Clinical Practice Guidelines, applicable local regulations, and the World Medical Association Declaration of Helsinki Ethics.

**Protocol Revision**

Any revisions to the study protocol must be approved by the sponsor, the regulatory authorities (if necessary), and the Ethics Committees. For the purpose of ensuring the safety of the participants, study protocol revision may be implemented before approval by the Ethics Committee.

**Confidentiality**

A series of measures will be taken to protect the privacy of participants throughout the course of the study. Before entry of data into the database, identifiable information pertaining to patients’ medical treatment will be removed to ensure privacy protection. When reporting study data and findings, all identifiable information will be concealed to protect individual privacy.

**Ancillary and Post-trial Care**

This study does not involve changes in clinical routine treatment, and the routine treatment of patients during and after the study will not be affected by this study.

**Discussion**

As a risk factor for cognitive decline [12, 13], the prevalence of AF in older people increases gradually with age [30]. Given the changing demographic structures in developing countries, the management of AF with cognitive impairment must increasingly be prioritized. Computerized cognitive training has shown potential as an intervention for vascular cognitive impairment [21]. However, randomized controlled studies on cognitive impairment in AF, particularly on cognitive training, are currently lacking. This study provides a unique opportunity to explore computerized training for the clinical management of cognitive impairment in patients with AF through a multicenter, large-sample randomized controlled trial.

One strength of this study is the high adaptability of the cognitive training used. AF has different effects on cognitive function in different domains, and processing speed is particularly affected [31]. The cognitive training software used in this study is highly adaptable and internet-based, thus enabling the training content to be adjusted according to individual patients’ performance. The Internet-based training design allows patients to complete the training at home while enabling physicians to manage and monitor the process remotely. Additionally, the study design includes a comprehensive suite of...
psychological assessments. Selected patients are also recommended for high-resolution MRI scanning as an exploratory endpoint, thereby increasing the sensitivity of detecting both the efficacy of cognitive training and structural brain changes.

Declaration

Data Availability Statement

The raw data are currently unavailable. Data are entered into a secure, password-protected electronic data capture system. All the documents mandated by the coordinating center and relevant regulatory authorities will be preserved at the coordination center for 15 years.

Competing Interests

Jianzeng Dong is the Co-Editor-in-Chief of CVIA, Xin Du is a board member of CVIA. Neither Jianzeng Dong nor Xin Du is involved in the peer review or decision-making process of the manuscript. The other authors have no competing interests to disclose.

Authors’ Contributions

Zhiyan Wang and Yiqun Zhang are the joint first authors and contributed equally to this article. Changsheng Ma and Xin Du are the corresponding authors of this article. Chao Jiang, Rong Hu, Wenli Dai, Yu Kong, Liling Sun, Litoao Wu, Hongxu Geng, Chunqi Ren, Xiangyang Zhang, Jia Wang, Hong Jiang, and Jianzeng Dong reviewed the article. The authors listed in this and subsequent articles will be in line with the authorship eligibility guidelines. No professional writers or artificial intelligence will be used in drafting articles.

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Appendix 1

BCAT Introduction

1) Symbol Search (Processing Speed)
This test is adapted from the same name subtest of the Wechsler Intelligence Scale [32]. A horizontal line is present in the middle of the screen, with two designed symbols above the horizontal line and five symbols below it. The participant’s task is to indicate whether one of the two symbols above the horizontal line is identical to the five symbols below the horizontal line. Participants are required to complete as many tasks as possible within this prescribed timeframe, and the total time is 120 seconds. Scoring is based on the number of correct responses achieved within this time limit.

2) Portrait Memory (Episodic Memory)
This test is adapted from the subtest of the clinical memory scale [33]. During the test, a series of six portraits are presented in a random sequence, accompanied by corresponding information such as the individual’s surname, occupation, and hobbies. Participants are instructed to memorize the associated details for each portrait. After the display of six sets of portraits and information, participants are required to recall the specific details associated with each displayed portrait. The entire assessment comprises two rounds of tasks that present identical information in different orders. Scoring is based on accurate responses.

3) Operation Span (Working Memory)
This test is self-designed. The test comprises two tasks: a calculation task and a memory task. The calculation task involves mentally solving mixed arithmetic problems, followed by an immediate judgment of the correctness of the given answer. Subsequently, a Chinese zodiac sign (e.g., rat or tiger) is displayed after each equation, and participants are required to remember the order of the signs presented. After several sets of calculations and zodiac signs, participants are asked to recall the sequence of the displayed zodiac signs. The difficulty level of equations and the frequency of zodiac sign appearances progressively increase until participants misjudge numerous equations or provide an incorrect sequence twice
Figure 1  Symbol Search Task Example.

Figure 2  Portrait Memory Task Example.

Figure 3  Operation Span Task Example.
consecutively. The final score for this study corresponds to the difficulty level at which participants experience failure.

4) Paper Folding (Visuospatial Ability)
This test is adapted from the identical subtest of the intelligence test suite developed by Ekstrom et al. (1976). During the test, participants are instructed to mentally simulate puncturing a hole with a pencil on a folded squared paper. Because the paper is folded, multiple holes will be present in the unrolled paper. Participants are required to identify the shapes of these holes on the unfolded paper. Each step of the folding process and the location of each puncture are visually presented. The participants are asked to choose the only correct answer from five possible answers. The difficulty level of questions increases progressively, and scoring is based on accurate responses.

Appendix 2

Table 1 Correspondence Between Cognitive Ability Scale Scores and Z-scores.

<table>
<thead>
<tr>
<th>Task score</th>
<th>Z score</th>
</tr>
</thead>
<tbody>
<tr>
<td>19</td>
<td>3.00 (2.83–3.17)</td>
</tr>
<tr>
<td>18</td>
<td>2.67 (2.50–2.83)</td>
</tr>
<tr>
<td>17</td>
<td>2.33 (2.17–2.50)</td>
</tr>
<tr>
<td>16</td>
<td>2.00 (1.83–2.17)</td>
</tr>
<tr>
<td>15</td>
<td>1.67 (1.50–1.83)</td>
</tr>
<tr>
<td>14</td>
<td>1.33 (1.17–1.50)</td>
</tr>
<tr>
<td>13</td>
<td>1.00 (0.83–1.17)</td>
</tr>
<tr>
<td>12</td>
<td>0.67 (0.50–0.83)</td>
</tr>
<tr>
<td>11</td>
<td>0.33 (0.17–0.50)</td>
</tr>
<tr>
<td>10</td>
<td>0.00 (−0.17–0.17)</td>
</tr>
<tr>
<td>9</td>
<td>−0.33 (−0.50–−0.17)</td>
</tr>
<tr>
<td>8</td>
<td>−0.67 (−0.83–−0.5)</td>
</tr>
<tr>
<td>7</td>
<td>−1.00 (−1.17–−0.83)</td>
</tr>
<tr>
<td>6</td>
<td>−1.33 (−1.50–−1.17)</td>
</tr>
<tr>
<td>5</td>
<td>−1.67 (−1.83–−1.50)</td>
</tr>
<tr>
<td>4</td>
<td>−2.00 (−2.17–−1.83)</td>
</tr>
<tr>
<td>3</td>
<td>−2.33 (−2.50–−2.17)</td>
</tr>
<tr>
<td>2</td>
<td>−2.67 (−2.83–−2.50)</td>
</tr>
<tr>
<td>1</td>
<td>−3.00 (−3.17–−2.83)</td>
</tr>
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</table>
Table 2  Cognitive Impairment Criteria in Different Age Groups, According to BCAT Measurements.

<table>
<thead>
<tr>
<th>Age</th>
<th>18–29</th>
<th>30–39</th>
<th>40–49</th>
<th>50–59</th>
<th>60–69</th>
<th>70+</th>
</tr>
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<tbody>
<tr>
<td>Domain</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Processing speed</td>
<td>−0.16</td>
<td>−0.43</td>
<td>−0.69</td>
<td>−1.09</td>
<td>−1.39</td>
<td>−1.71</td>
</tr>
<tr>
<td>Working memory</td>
<td>−0.25</td>
<td>−0.45</td>
<td>−0.74</td>
<td>−1.01</td>
<td>−1.26</td>
<td>−1.43</td>
</tr>
<tr>
<td>Episodic memory</td>
<td>−0.34</td>
<td>−0.52</td>
<td>−0.80</td>
<td>−1.07</td>
<td>−1.20</td>
<td>−1.47</td>
</tr>
<tr>
<td>Visuospatial ability</td>
<td>−0.53</td>
<td>−0.69</td>
<td>−0.76</td>
<td>−0.90</td>
<td>−1.05</td>
<td>−1.22</td>
</tr>
</tbody>
</table>

REFERENCES

21. Hill NT, Mowszowski L, Naismith SL, Chadwick VL, Valenzuela M,


