Modulation Effects of Baduanjin Exercise on Subjective Cognitive Decline (BDJ)

NCT04009382

02/6/2025

Background

Over the past decade, a string of disappointing clinical trial results have raised concerns about our strategy of preventing the development of AD. Currently, most studies are being performed on prodromal AD and MCI. At this stage, however, the progressive neurological loss and irreversible cognitive impairment may have already occurred. Thus, investigation of the early stage with only mild neuronal damage and still-sufficient functional compensation is crucial for the prevention of AD, MCI, and other age-related dementia.

SCD is receiving increasing attention from investigators. Mechanistic studies have provided evidence linking SCD with MCI and AD, suggesting that SCD is associated with a greater risk of dementia and biological markers of AD. These studies have also identified SCD as a precursor to MCI and potentially the earliest clinical sign of AD. Thus, SCD might be the optimal stage in which to intervene with preventative therapies, before irreversible neural impairment occurs.

Recently, mind-body interventions have demonstrated their potential in preventing cognitive decline in older adults. Baduanjin (BDJ) is a unique mind-body exercise that combines both mindfulness and physical exercise. It focuses on breathing, increases flexibility, and strengthens muscles and tendons. It consists of only eight postures, is very simple, and does not require a large amount of space. These characteristics make it a suitable option for older adults with cognitive decline.

This study aim to investigate if BDJ can modulate the cognitive function of SCD patients using the Alzheimer's Disease Cooperative Study-Preclinical Alzheimer Cognitive Composite (PACC), an assessment that is very sensitive to subtle changes in early cognitive decline overall. If successful, our findings will provide a new solution to AD and dementia prevention.

In this study we will recruit individuals with SCD. Subjects who pass the screening will be randomly assigned to one of two groups (60 per group): 1) Baduanjin group or 2) control group. All subjects will participate in the study for six months and will continue to be monitored for three months following participation. All individuals will be required to continue recording in their diaries during the study and follow-up stage. Patients will also be instructed to maintain their normal medications and lifestyle. Assessments will be taken at baseline, three months, six months, and nine months (follow-up).

Detailed experimental procedure

Session 1 is an in-person screening session. After a phone screening, all recruited subjects will be further screened by a trained research staff. Only subjects that pass the in-person screening will continue with the study. Session 1 may be done remotely via Zoom after consent is obtained.

Session 2 is an assessment session, including subjective and objective cognitive assessments.

When possible, session 1 and 2 can be combined.

Assessments

4.1 Objective cognitive assessment

All assessments will be administered by well-trained staff under the supervision of Dr. Wong.

Alzheimer's Disease Cooperative Study-Preclinical Alzheimer Cognitive Composite (PACC): The PACC is an assessment that is very sensitive to subtle changes in early cognitive decline. It combines four widely used cognitive tests: (1) the Total Recall score from the Free and Cued Selective Reminding Test (FCSRT), (2) the Delayed Recall score on the Logical Memory IIa subtest from the Wechsler Memory Scale (0–25 story units), (3) the Symbol Digit Modalities Test (SDMT), and (4) the MMSE total score (0–30 points). We substituted the Digit Symbol Substitution Test with the SDMT, which has comparable sensitivity to processing speed and attention while being more feasible for remote administration, an important consideration during the COVID-19 pandemic. As suggested by a previous study, the composite score was calculated from its components using an established normalization method, with each component's change score divided by its baseline standard deviation to form standardized z scores. These z scores were summed to form the composite, such that a 1-SD change on each component corresponded to a 4-point change on the composite.

Symbol Digit Modalities Test (SDMT): This is an oral version of the Digit Symbol Substitution Test.

The Stroop Color and Word Test (SCWT): This is a test to assess executive functions, the ability to inhibit cognitive interference, attention, processing speed, and cognitive flexibility.

Trail-making Test A and B: This is a test of speeded visual search, vigilance, and set-shifting.

Controlled Oral Word Association Test, Category Fluency and Category Switching: These are tests of rapid word retrieval, cognitive flexibility, and semantic access/semantic network integrity.

4.2 Subjective assessments We selected measures that have been used in previous studies of SCD [12]. Administration of self-report questionnaires will occur in a quiet testing room with several subjects simultaneously. Measures will be scored according to the test creators' guidelines, producing either mean or total scores for further analysis.

Everyday Cognition Report Form (ECog): the ECog was developed to 1) measure relatively mild functional changes that may predate loss of independence in major activities of daily living; and 2) assess functional abilities that are clearly linked to specific cognitive abilities.

Patient Reported Outcomes Measurement Information System® (PROMIS®) Cognition

Function and ability subset: The PROMIS Cognitive Function and Cognitive Function Abilities Subset item banks assess patient-perceived cognitive deficits. Facets include mental acuity, concentration, verbal and nonverbal memory, verbal fluency, and perceived changes in these cognitive functions.

Beck Depression Inventory-II (BDI-II): The BDI is widely used as a depression assessment tool by health care professionals and researchers in a variety of settings. BDI-II is designed for individuals 13 years and older and is composed of items relating to symptoms of depression.

Beck Anxiety Inventory (BAI): The BAI is a 21-question multiple-choice self-report inventory that is used for measuring the severity of anxiety in children and adults.

Patient Reported Outcomes Measurement Information System (PROMIS-29): PROMIS-29 is a system of reliable, flexible, precise, and responsive assessment tools that has been widely validated in numerous samples. The PROMIS-29 includes assessments of physical function, depression, anxiety, fatigue, sleep, social activity, and pain in the past 7 days.

International Physical Activity Questionnaire Short Form (IPAQ-SF): Regular physical activity (PA) is essential in the maintenance of health and can produce positive effects on cognitive functions. A previous study indicates that the modified version of IPAQ, the IPAQ-E, was well accepted by socially active elderly and provided acceptable estimates of physical activity, well in line with other questionnaires. The IPAQ-SF is low burden for participants with only nine items and a 7-day recall. Activity is recorded for four categories of intensity: vigorous PA, moderate PA, walking, and sitting.

PROMIS Short Form v2.0 – Physical Function 24a (PROMIS-PF): PROMIS-PF includes PROMIS items that are analogous to the Health Assessment Questionnaire Disability Index (HAQ-DI), it measures the physical function of the individuals in past week.

MRI data acquisition Data collection will be performed at the Martinos Center for Biomedical Imaging on the 3T Siemens whole-body system. Resting state fMRI data will be acquired using a gradient echo T2*-weighted sequence (TR/TE=2000/30 msec, flip angle=90º, slice thickness=3.5 mm) for 10 minutes. A high-resolution 3D MPRAGE sequence with 1 mm^3 isotropic resolution (TR/TE1= 2530/1.69, slice thickness = 1, FoV = 256) will be collected for brain morphometry analysis. In addition, although there is no specific hypothesis, we will also collect DTI data to explore the modulation effect of BDJ on brain white matter.

When possible, subject will also perform Behavioral Pattern Separation–Objects (BPSO) task during scan. BPSO is a test of memory that has been used extensively to assess individual differences in memory and hippocampal structure and function in individuals[42].

During scan, participants view novel (new), repeated (old) and lure (similar) stimuli. Stimuli are color photographs of common objects. Each participant completes five functional runs, each consisting of 96 similar pairs, 96 identical pairs and 346 unrelated novel items (foils), fully randomized throughout all five runs. Each stimulus is presented for 2000 ms with a 500-millisecond inter-stimulus-interval. The number of trials separating similar and identical pairs is randomly varied between 10 and 40 trials. Participants are instructed to make a judgment as to whether the object seen was new (i.e., novel items), old (i.e., repeated items) or similar but not identical (i.e., lure items). Of critical interest are the participants' responses on the lure items. A response of “old” to a lure (i.e., similar) item would suggest that the participant was more biased towards pattern completion, whereas an accurate response of “similar” to a lure would suggest a bias towards pattern separation instead. It may take about half hour for subject to complete the BPSO task.

Session 3 is the MRI data collection session.

Session 4 is the first Baduanjin or Cognitive Fitness Program session. All training/exercise will be held at the Charlestown Navy Yard (CNY) or online with a maximum of 12 individuals per session by a Baduanjin mentor team. Attendance data and logs of home practice will be collected weekly. Absent participants will receive a reminder phone call to attend subsequent sessions. Research staff will monitor home practice adherence through monthly phone calls and practice diaries during the follow-up.

Baduanjin exercise Subjects in the BDJ exercise group will receive 24 weeks of BDJ exercise training three times a week for the first three months and two times a week for the remaining three months. Similar to our previous study, each session will include: 1) 10 min of warm-up (i.e. arm swinging, gentle stretches of the neck) and a review of BDJ principles, 2) 30 min of BDJ exercises, 3) 10 min of breathing techniques, and 4) 10 min of relaxation.

Control condition - Cognitive Fitness Program We will use the Cognitive Fitness Program (CFP) as the control task in this study. CFP is an attention control condition matched to the amount of BDJ class time and home practice. The program uses paper puzzles (Sudoku, crosswords, word-search, etc.) to engage subjects, similar to what has been used previously .

Trained staff will lead the CFP program with an identical frequency as Baduanjin (three times a week for the first three months and two times a week for the remaining three months). Similar to BDJ, after the first training and with the approval of the instructor based on their performance, subjects will be allowed to participate in the “onsite” training remotely via Skype or Zoom with video to allow for instructor/staff feedback.

Mid-term and final assessments the mid-term and final assessments will be identical to the baseline assessment and will include cognitive measurements and MRI scans data collection. Our previous studies showed that three months of BDJ significantly enhanced memory function and resting state functional connectivity. We thus believe it is important to have the mid-term assessment. Also, multiple time points can increase the power of the experiment.

Follow-up Upon completion of the training programs, subjects will be encouraged to continue with BDJ practice at home and fill out weekly diary entries for an additional three months. At the end of this period, we will perform a follow-up assessment identical to the baseline assessment, excluding the MRI scan.