RESEARCH PROTOCOL: Brain connections, self-care and blood pressure in Black and African Americans with problems with memory Version: 02/19/2019

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I. Objectives

The purpose of this pilot randomized controlled study is to adapt a previously tested intervention to improve resting state network and blood pressure in 120 (n=40 intervention; n=40 attention control; n = 40 control) Black and AA older adults with early Alzheimer's disease and related dementia disorders and HTN.
The study aims are to:

A.1. Establish the feasibility and acceptability of the intervention in Black and AAs with Alzheimer's disease and related dementia disorders and HTN.

H1: The intervention will be feasible and acceptable to Black and AAs with Alzheimer's disease and related dementia disorders. Feasibility will be measured by recruitment, attendance, and attrition. Acceptability will be measured by a garnering feedback in a debriefing after each session.

A.2. Determine the effect size of the difference between the intervention, attention control, and control groups in resting state network connectivity and working memory and blood pressure to inform the sample size for the R01 trial.

H2: We hypothesize that compared to both control groups; the intervention group will have greater improvement in process measures of self-management mechanisms (self-efficacy, self-regulation, and emotion regulation), chronic stress, diet, and physical activity. The fMRIs and blood pressure will be obtained at baseline and 3 months. The intervention group (Mindfulness + DASH) will have improved resting state network connectivity and blood pressure as compared to the attention control (2-hour group social time and brief lecture on a non-diet/mindfulness topic such as personal safety, fire safety, and disaster preparedness) and the control group (care as usual with no intervention). The Center for Cognitive and Behavioral Brain Imaging, Arts & Sciences co-investigators will analyze imaging data using their newly published statistical network model to quantify the subnetwork structures of the resting state network and evaluate changes of their topological properties.

II. Background and Rationale

African Americans (AA) are **twice as likely** to develop Alzheimer's disease and related dementia disorders and develop hypertension (HTN) at an earlier age as compared to European-Americans (EA).[1,2] The health behavior recommendations to improve cognition and decrease blood pressure share similar self-management strategies: healthy eating, physical activity and stress management.[3,4] While other healthy diet and physical activity interventions (e.g., Dietary Approaches to Stop Hypertension[5] [DASH]) are delivered to self-manage blood pressure, we have not determined the effects of combining DASH with self-management interventions like mindfulness based stress reduction[5] (Mindfulness) on brain functional connectivity and blood pressure in AA older adults.

Functional connectivity is the statistical correlation between spatially remote sensory networks in the brain (e.g., ventral-medial prefrontal cortex and adjacent regions of sub-genual anterior cingulate and nucleus accumbens).[6,7] The resting state network is part of the "emotional brain" and is the opposite of the analytic brain; as one activates, the other de-activates. Functional connectivity in the brain at rest, also known as the *resting state network or empathy network*, is responsible for retrieving memories, introspective thought and daydreaming.[7] Dysregulation of the resting state network has been associated with Alzheimer's disease.[7] From our preliminary work, the ability to efficiently task differentiate between the emotional brain (the brain at rest) and analytic brain were associated with self-management mechanisms (self-efficacy, self-regulation, emotion regulation). Chronic stress, which is amenable to mindfulness interventions, acts to suppress cognitive

performance.[8] Mindfulness training improves the resting state network function in older adults with cognitive impairment and depression.[8]

In our initial work, our group tested a culturally informed intervention that combined mindfulness with DASH to improve blood pressure, diet and quality of life in prehypertensive AAs. This 8-week trial compared mindfulness + DASH and controls on blood pressure and resting state network function.[10] The combined intervention group showed greater positive changes in diet, resting state network function and blood pressure as compared to controls.[10] We will extend this work to those with Alzheimer's disease and hypertension in AAs. To compensate for memory impairment, we will simplify diet education materials; incorporate repetition; use mnemonics; change the pace of the delivery; use easy to understand graphics; modify homework assignments; provide audio/video recordings for smartphone or CD player; and reminder calls between sessions to deliver the intervention in African American older adults with Alzheimer's disease and related dementia disorders. Findings from this pilot RCT will inform an R01 parent application to the National Institutes on Aging for primary funding; the National Heart Lung and Blood and the National Institute of Nursing Research for secondary funding.

RATIONALE. Interventions such as the DASH diet, lack **cultural appropriateness** (attention to the value of oneness in mind, body and spirit) and the appreciation of the social significance of food within the community and family unit.[11-14] Therefore, they do not target the self-management of the mind and body in AAs with Alzheimer's disease and HTN. In African Americans, socioeconomic disadvantage, such as low income, low education, and neighborhood safety, increases the cumulative stressors experienced and contributes to acute and chronic stress responses influence engagement in healthy self-management behaviors.[15] The cognitive performance of older adults is impaired by stress so that learning new information is suppressed.[15,16] Mindfulness is a mechanism by which older adults can regulate emotions that produce excess mental stress.[17] Providing older adults with chronic conditions the opportunity to learn self-management skills in a group setting increases self-efficacy, self-regulation and emotion regulation resulting in the adoption of healthy behaviors.[18]Our rationale for combing two self-management interventions, mindfulness + DASH is to maximize the benefits of a simultaneously delivered intervention on neural network function. Alzheimer's disease is a neural network connectivity disease.[7] The scientific premise for mindfulness is that the practice of mindfulness increases attention and awareness by suppressing over activation of the resting state mode in the ventromedial prefrontal cortex and posterior cingulate cortex region of the brain.[7] This in turn reduces distractive, ruminative thought and stress that impairs cognitive performance.[7] Whereas practicing DASH recommendations (physical activity, stress management, low-fat, low sodium, and high in fish, fruits, fiber and vegetables) is proposed to prevent cognitive decline by decreasing glycemic spikes, triglycerides, cholesterol and neuroinflammation.[19] Both interventions have been found to reduce blood pressure in older adults.[19,20] In our preliminary study of prehypertensive AAs, suppression of the resting state network was observed in the intervention group. We are now translating what we learned to adapt the intervention to target resting state network function and blood pressure in AA older adults with Alzheimer's disease and related dementia disorders.

Separately, the use of mindfulness or DASH are not new. However, our project is unique in the combination of mindfulness + DASH and translation to community-dwelling AA older adults that are at risk of the deleterious effects of cognitive impairment and HTN on health outcomes. The proposed project is innovative in several ways. First, this study is unique because we implore a culturally informed intervention that is designed to affect two of the greatest threats to the health and well-being of older AAs: Alzheimer's disease and related dementia disorders and hypertension related cardiovascular disease. Our study fills in the gaps in self-management research through the exploration of the effects of this mindfulness + DASH intervention to improve the resting state network and blood pressure in this vulnerable population. Moreover, a novel feature of this study is the use of the first ever approach to imaging analysis; the breakdown that reveal the subnetworks in

resting state. We use a novel statistical network model to capture topological and exogenous properties of the subnetworks in the brain. The benefit of using this method is that we can quantify, in a non-dichotomized threshold technique, the operating principles of the subnetworks associated with higher-order cognitive functions, including working memory, emotion and cognitive control. Findings of this study are expected to contribute to the dearth of science on neural network processing in Black and AA older adults.

III. Procedures

A. Research Design

Approach. We will conduct a three-group RCT to describe the effect of the mindfulness + DASH diet on resting state network function (fMRI) and blood pressure (sphygmomanometer). The intervention involves eight weekly sessions for mindfulness +DASH education. The attention control group will participate in an 8-week social group on non-health related topics. The control group will not receive attention or intervention. Sample. A sample of 120 (n=40 mindfulness + DASH; n=40 attention control group, n=40 control group) community dwelling Black and African Americans adults aged 65 and older who meet study inclusion criteria will be recruited. Inclusion criteria are: (1) diagnosis of hypertension with or without medication use; (2) diagnosis of Alzheimer's disease or related dementia disorders; (3) if no formal diagnosis of Alzheimer's disease, then a SAGE score 17-10 or a MoCA 25-19.[21,22] *Rationale*. These criteria were chosen to avoid persons with early-onset Alzheimer's disease; age ≤64.[21] The cut point scores for the SAGE and MoCA are representative of persons with dementia and Alzheimer's disease.[21,22] Exclusion criteria are: (1) unable to understand spoken English; (2) expect to move out of the area within six months (3) fMRI imaging contraindicated (history of shrapnel, metal in the body, heart pacemaker, heart defibrillator, metal in the eye, gunshot wound, or some types of metal elsewhere within the body such as certain surgical clips for aneurysms in the head, heart valve prostheses, electrodes, and some other implanted devices) or claustrophobia; (4) Visible signs of a previous, major stroke such as extreme weakness in one side of the body (5) <6 on the Brief Assessment of Understanding of the Study.[23] *Rationale.* To avoid recruitment of persons that are unable to engage in the intervention.[23]

B. Sample

Community-dwelling African Americans aged 65 and older in Columbus and surrounding areas with hypertension and early-stage Alzheimer's disease and related dementia disorders.

C. Measurement / Instrumentation

Table 1 displays all study measures. We have carefully chosen measures based on their appropriateness for this population, validity, reliability and level of burden. The study team has experience with all measures. Instruments either have been used by the study team in prior work or have been pilot tested for the purpose of the proposed application. In addition to the study visits for survey completion and fMRI, Most of the questionnaires use Likert-type scales and consist of 1-30 items averaging 10 items or less. **Participant burden** for participants was a major consideration in the selection of the study measures and thus, we chose measures used with older people that are short and easy to administer. Study staff offer breaks to participants to use facilities as needed. In our previous experiences, it takes no longer than 90 minutes to complete the visit. The fMRI lasts 30 minutes. From our experiences, it is best to do the fMRI at a separate visit to reduce participant burden. However, we will give participants the option to complete study visits one and two (fMRI) on the same day.

Prescreen Measures

Brief Assessment of Understanding the Study[23] has eight questions (3 open-ended and 5 yes/no). The questions include describing the study and risks associated and benefits. The participant must get 6 out of 8 questions to provide consent.

Table 1

ITEMS	MEASUREMENTS	RATIONALE	TIMEFRAME	RELIABILITY / VALIDITY
Informed consent	Brief Assessment of Understanding of the Study	Participant comprehension of study	Baseline	Rasch analysis and the inter-rater reliability (r =.81)
Mental status screen	Self-Administered Gerocognitive Examination (SAGE) and Montreal Cognitive Assessment Screen	One self-administered (SAGE) One delivered by researcher	Baseline, 3months	SAGE-Spearman rank correlation between SAGE and neuropsychiatric battery =.84 MoCA- dected 100% of Alzheimer's dementia with a specificity of 87%.
Demographic data and baseline functional status	NINR Demographics Katz Activities of Daily Living Lawton Instrumental Activities of Daily Living	Potential characteristics that could further describe feasibility	Pre-rand Pre-rand, post-intervention, 3mo	Katz-Cronbach's α=0.838 Lawton-Interrater reliability= .85
Process measures				
Self-regulation	Fleury survey	Self-management mechanism	Pre-rand, post-intervention, 3mo	Cronbach's α= .87
Self-efficacy	Stanford Chronic Disease Self-management Survey	Self-management mechanism	Pre-rand, post-intervention, 3mo	Internal consistency= .91
Emotion-regulation	Cognitive and affective mindfulness scale SF-36 QOL (mental composite score for emotions of anxiety and depression) PROMIS Anxiety and Depression Subscale	Self-management mechanism and Potential characteristics that could further describe feasibility	Pre-rand, post-intervention, 3mo	Cronbach's α =0.77 Cronbach's α =0.72–0.94
Chronic stress	Perceived stress scale) Hair cortisol concentration analysis Everyday Discrimination Stress in the Healthcare Setting	Self-report measure of stress Objective measure of long-term cortisol exposure as a proxy for chronic stress	Pre-rand, post-intervention, 3mo Pre rand and3 mo.	Perceived stress scale-Cronbach α = 0.83 Hair cortisol- Within <3% and between (including extraction with each assay) <15% assays for pooled hair control. Everyday Discrimination Cronbach α = 0.83
Healthy eating	DASH diet survey	Receipt of treatment	Pre-rand, post-intervention, 3mo	Internal consistency (α = .77-.83).
DASH questionnaire	Twenty-one questions. Multiple choice and open-ended questions that are given to the mindfulness plus DASH intervention participants. The responses are reviewed as a group and it is used as a teaching tool.	Receipt of treatment Investigator generated pre-post test questions to survey the intervention participant's knowledge about the DASH eating plan and to also use a teaching tool.	Mindfulness plus DASH participants only Session one and Session eight.	Investigator generated used as a teaching tool.
Mindfulness	Cognitive and affective mindfulness scale	Receipt of treatment	Pre-rand, post-intervention, 3mo	Cronbach α=.77
Physical activity	Physical Activity Scale for the Elderly (PASE)	Receipt of treatment	Pre-rand, post-intervention, 3mo	Spearman correlation coefficient of 0.43 (p<0.01) between Actigraph data and total PASE score.
Outcomes				
Resting state network	fMRI scanner and investigator generated audiovisual delivered by EPrime.	Primary outcome	Pre-rand, post-intervention, 3mo	To be determined with preliminary data this pilot study
Pain Scale	Brief Pain Inventory Short Form (BPI-SF)	A strong internal consistency reliability tool to measure clinical pain	Pre-rand, post-intervention, 3mo	α =0.86-0.96

BP	Omron HEM-907XL SBP333 and DBP	Primary outcome	Pre-rand, post-intervention, 3mo	ICC 0.94 and 0.92, SBP and DBP respectively
Covariate				
AntiHTN medication use	Medication labels on bottles	Control for medication use	Pre-rand, post-intervention, 3mo	Not available

Mental and Functional Status and Demographic Data

Self-Administered Gerocognitive Examination[21] is a battery of 12 self-administered questions and drawings include naming pictures, similarities, calculation, memory, clock drawing and verbal fluency. Montreal Cognitive Assessment Screen[22] is 13 questions that include visuospatial, memory, attention, abstraction and delayed recall. National Institutes of Nursing Research common data elements demographic[24] that includes gender, age, race, ethnicity, education, caregiver primary type, employment, marital status and number of household member and income in U.S. dollars per month. Katz Activities of Daily Living[25] has six questions to function of basic activities such as bathing, dressing toileting, transferring, and continence and feeding. Instrumental activities of daily living[26] are eight question that cover ability to use the phone, shopping, transportation, laundry food preparation, housing keeping and handling finances.

Process Measures

Self-regulation survey[27] of nine questions on a Likert scale to determine health behavior practice. Self-efficacy[18] scale is for the participant to rates how confident they are in managing their chronic condition on a scale of 1-10 for each of the six questions. SF-36 survey questions and PROMIS Anxiety and Depression Subscale that includes subscales for anxiety and depression symptoms.[29] Perceived Stress Scale[30] is a 10-item Likert scale questionnaire regarding stress over the past month. Every day Discrimination in the Healthcare Setting is 7 questions on a Likert scale to measure the stress of discrimination in the healthcare setting as a result of age in ethnicity.[37] The Brief Pain Scale will be administered prior to obtaining the imaging data since pain can contribute to chronic stress and difficulties regulation emotions.[41,42] Scalp hair cortisol[31] is an emerging measure of chronic stress without the limitations of other biological specimens (saliva, urine, blood) used to assess cortisol regulation.[30] Hair cortisol is a proxy measure to the total retrospective activity of stress exposure over the preceding 3 months, much like hemoglobin A1c is a proxy measure of glucose control over the past three months. The reconstituted sample can be assayed immediately or frozen at -20 °C for later analysis. The lyophilized samples can also be stored frozen until reconstitution. Because cortisol ELISA kits are designed to measure cortisol values in liquid samples such as saliva or plasma, the output of the microplate reader software must be converted to amount of cortisol per unit weight of powdered hair. The following formula converts assay output in µg/dl to pg cortisol per mg hair:

(A/B) * (C/D) * E * 10,000 = F where A = µg/dl from assay output; B = weight (in mg) of hair subjected to extraction; C = vol. (in ml) of methanol added to the powdered hair; D = vol. (in ml) of methanol recovered from the extract and subsequently dried down; E = vol. (in ml) of assay buffer used to reconstitute the dried extract; and F = final value of hair cortisol concentration in pg/mg. DASH Q[32] is an 11-item self-report survey of foods recommended on the DASH diet (e.g., fruits, nuts, vegetable) that are eaten from 0-7 days in a week. Cognitive and affective mindfulness scale[28,33] has 12 questions on a Likert scale regarding daily experiences such as " I rush through activities without being really attentive to them. "Physical Activity Scale for the Elderly (PASE)[34] is a brief (5 minutes) and easily scored survey designed specifically to assess physical activity in epidemiological studies of persons age 65 years and older (10 questions).

DASH questionnaire. They will take an investigator-generated survey regarding their knowledge of the DASH diet during the first and last intervention, session eight.This will be used as a teaching tool to facilitate discussion and increase knowledge.

Outcomes

Resting state network.[9,10] Prior to entering the scanner, participants will be scanned for metals in the body. Participants will be scanned using FDA approved Siemens 3T Wide Bore Scanner (60-70 cm diameter). A 2-minute structural run following by a 7 minute resting scan (no task) will be done. A 1-minute flare will be followed by a 6 minute DTI scan. Working memory. Working memory data will be obtained from the mental status examination (SAGE, MoCA).

Systolic and diastolic blood pressure[35] will be collected using an Omron automatic blood pressure machine. Small and large cuff sizes will be used.

Covariate

The diagnosis of hypertension duration and number of chronic conditions will be obtained by self-report. The number of chronic conditions will be limited to the 17 Medicare chronic conditions. Names of medications will be copied from prescription bottles or medication list[36] depending upon participant preference.

D. Detailed study procedures

Recruitment. We will recruit participants from area clinics and the local African American Churches, The Charitable Pharmacy of Central Ohio. Additionally, participants will be recruited from the CON Total Health and Wellness Center, local senior centers that service the African American community.

Participant ID: Participant *ID*: Participants will be assigned a 5-digit ID number which will identify them at all data collection points.

Retention Plans.

In studies involving older adult (aged 65 and older), a threat to internal validity is selection bias or selection threat. This can occur due to study drop out. To decrease the risk of participants dropping out of the study, we have employed several strategies.

1. Participant preferred location to collect baseline and3-month survey data.
2. Participant may have significant other/family member/friend present throughout the process of enrollment an, study participation excluding entering the area where the MRI is housed.
3. Holding intervention sessions and control session in a location with free parking.
4. Providing cab transfers for participant to OSU and intervention/control sessions per participant's preference.
5. Frequent rest breaks and nutritious snacks during data collection and intervention/control sessions.
6. Reminder calls to participants for study visits and sessions.
7. In case we cannot contact a participant directly, we will also obtain contact information for family and friends who would know how to contact the participant. This frequent contact will also enable us to keep updated contact information for participants.
8. For imaging data collection, the participant and the significant other/family member/friend that accompanies the participant for the fMRI will receive an incentive for their time.
9. Booster calls will be made to remind participants to practice what they've learned and to provide an opportunity to ask questions between sessions.

10. Participants will be remunerated for their assessment time according to the following schedule:

Visit Type	Remuneration
Baseline surveys fMRI	$30 $75 participant and $30 for support person that accompanies participant
If there is a gap of 4 or more months between the initial data collection and the start of the intervention, Baseline surveys will be recollected. If a participant refers a friend or family member	$30 $5
3 Month surveys fMRI	$30 $75 participant and $30 for support person that accompanies participant

The reason for any participant's discontinuation and the date of withdrawal will be recorded in the participant's case file. The participant's case file, which will be completed up to the point of withdrawal, will be retained for three years. The study report will include reasons for participants' withdrawals as well as details relevant to the Withdrawal. Each participant will be encouraged to complete the full course of the intervention assignment and study assessments. However, it is understood that the participant may discontinue study participation at any time for any reason. The reason for early withdrawal must be documented in the participant's case file and in the participant tracking document.
Reasons for Withdrawal. Participants are free to withdraw from the study at any time for any reason.
a. Participants should normally be withdrawn from the trial if a serious adverse event (SAE) occurs.
b. Participants must be withdrawn from the trial if:
c. They withdraw their consent;
d. The investigator considers it in the best interest of the participant that he or she is withdrawn;
e. participants' withdrawals. Any participant withdrawn from the trial prior to completion will undergo all procedures indicated in this protocol as being scheduled to occur at discharge or upon early withdrawal. The Principal Investigator or a monitor, and recommendation for follow up with health care provider will evaluate any participant withdrawn due to an adverse event (whether serious or non-serious).
f. Relevant post-study procedures will be performed, wherever possible, on participants who elect to withdraw.

Handling of withdrawal. If a participant is withdrawn from participation in the study at any time at his or her request, at the IRB or Principal Investigator's discretion, the reason(s) for discontinuation shall be documented thoroughly in the source documents and participant's case file. All participants who are withdrawn prematurely will undergo the procedures outlined in the Discharge visit

Procedures overview. Using an IRB approved script, we will recruit, screen and enroll participants until we have 120 qualified participants. This script will include hypertension status, presence of metals in the body, and self-report of problems with memory. An initial visit will be scheduled to consent, screen, obtain baseline survey data (approximately 90 minutes), and complete the baseline fMRI (75 minutes, this includes getting the participant comfortable on the scanner table). If the participant expresses apprehension about entering the scanner, a mock scanner will be used to prepare the participant for study. Participants will be randomized by group after completion of baseline data collection (refer to table 1). If a gap of 4 or more months between the initial data collection and the start of the intervention exists, then data will be

recollected. A second visit will be done to collect post-intervention surveys and complete the final fMRI.

Procedures. Potential participants will be pre-screened by phone or in person at a location that is convenient for the participant and in a private area using an IRB approved script. The IRB phone script will include a verbal consent so that we may ask pre-screening questions that include the following: self-reported diagnosis of hypertension; self-identified as having memory concerns. If the participant matches the inclusion criteria, then we will schedule a time and place that is **convenient for the participant** to complete the MoCA and SAGE. Potential convenient locations for the participant include, The OSU Department of Psychology, OSU East, home visit, or The Charitable Pharmacy Clinic.

*Informed consent***.** Consenting will occur in a quiet private area. It will be the participants' choice to have family or significant other present during the consenting process and subsequent data collection. Participants will be given a copy of the consent form to follow along as the researcher reviews the consent form. Following the review of the consent form, the participant will be asked question from the Brief Assessment of Understanding of the Study.[23] If the participant scores less than 6, we will thank the participant for their time and recommend that they contact their health provider if they have any questions or concerns.

If the participant has a score 6 or greater on the Brief Assessment of Understanding of the Study and signs the consent form, we will begin with the SAGE and MOCA cognitive surveys. If the participant does not meet inclusion criteria based upon the results of the SAGE or MOCA, then we will thank the participant for their time. A copy of the consent form will be retained by the PI in a locked office in a locked file cabinet for 3 years.

If the participant meets the inclusion criteria, the researcher will proceed with baseline blood pressure, surveys and hair collection. The first baseline visit should take approximately 90 minutes and will be held at the location of the participant's preference. The second baseline visit will be held in the OSU Department of Psychology to gather imaging data.

The following will be collected during at baseline and 3 months (refer to table 1) at two separate visits:

1. Brief Assessment of Understanding of the Study survey
2. Self-Administered Gerocognitive Examination (SAGE)
3. Montreal Cognitive Assessment Screen
4. NINR Demographics form and self-reported list of chronic conditions
5. Omron HEM-907XL SBP and DBP
6. Katz Activities of Daily Living
7. Medication labels on bottles
8. Lawton Instrumental Activities of Daily Living
9. Fleury of self-regulation
10. Lorig Chronic Disease Self-Management Efficacy scale
11. SF-36 QOL (mental composite score for emotions of anxiety and depression)
12. PROMIS Anxiety and Depression Subscale
13. Perceived stress scale
14. Everyday Discrimination Scale in the Healthcare Setting
15. Hair cortisol concentration analysis at baseline and 6 months
16. DASH diet survey

17. Cognitive and Affective Mindfulness Scale
18. Physical activity survey
19. Scalp hair cortisol analysis is the HPA system's response and responds to a variety of chronic stressors.
20. Brief Pain Scale

To promote participant comfort, frequent breaks for will be taken during data collection. Healthy snacks of water, fruit, and or granola bars will be available for participants. On hand will be an external assistive listening device should the participant request one for communication.

We will begin with measuring blood pressure using an automatic blood pressure cuff (include brand). The left arm is preferred for blood pressure measurements. We will collect 3 blood pressure readings. The arm will be raised passively for 15 seconds between measures.

The questions to surveys will be read to the participant and answers recorded in RedCap under the participant's study ID number. Response cards will be given to participants to follow along with the interviewer.

Cortisol will be measured as from hair samples collected from the posterior vertex region of the scalp using thinning shears leaving no noticeable change in appearance. A 3 cm sample is taken from the posterior vertex of the scalp because this area has been shown to have less variation in cortisol levels than other areas of the scalp. The hair samples will be wrapped in aluminum foil, labeled with a coded participant identifier, and stored. Processing of hair samples will be completed in The Ohio State University College of Nursing Stress Lab.

Randomization. Using a computer-generated random number sequence, we will randomly allocate the 120 recruited participants with a ratio of 1:1:1 to intervention (mindfulness + DASH) or attention control or control. For retention purposes, incentives are provided for completion of data collection.

Intervention Protocol: PowerPoints and other computer aided strategies for delivery of the intervention. Repetition of key concepts will be embedded throughout the presentations and handouts. Changes will be made based upon their feedback. The mindfulness training will be delivered in the first hour and will include practice meditations, reflective thinking, and self-monitoring of thoughts. Following a 10-minute break, the dietitian will deliver the 60-minute DASH intervention. Each will include didactic content, an experiential skills oriented portion (bringing in canned food, reading labels, and adapting favorite "soul food "recipe to low sodium guidelines), behavior change goal-setting and problem-solving. A time for review and homework will be provided at the end of each session (20-minutes).

Mindfulness is the mental ability to enhance self-awareness of present internal and external experiences in a non-judgmental way. Mindfulness encourages a state of mind in which one distances from one's own mental noise.[5] It allows for a new awareness of mind that permits focused attention on releasing stressful constructions and a more relaxed moment-to-moment awareness and movement. MBSR is a participatory educational approach, exposing the power of internal resources in framing what a person experiences as stressful. Lifestyle change in MBSR refers to a change in one's interior disposition toward awareness. The goal in MBSR is to habitually participate in meditation, without evaluating one's meditation performance. In 2004, Bishop produced an operational definition of mindfulness for research investigations concerning

the mediating role and mechanism of the action of mindfulness.[38]. The two critical components were determined to be (1) self-regulation of attention and (2) the adoption of an orientation toward one's experiences in the present moment. MIM was developed to retain the construct of mindfulness, as originally conceived and taught by Kabat-Zinn, while adapting it for working adults. Mindfulness in Motion (MIM) is comparable to traditional MBSR programs concerning the operational definition, differing only in the amount of time committed to the intervention.

Summary of Intervention:

- Duration: 8 weeks
- Weekly group sessions of 1 hr. include a didactic presentation on stress and work-related stress, theoretical material related to mindfulness, the somatic mind/body connection, relaxation, yoga, meditation, self-awareness, and bodily cues relating to emotional reactivity. Practices will include the body scan, gentle yoga movement, walking meditation, breathing, relaxation, and sitting meditation.
- Additionally, daily 20 min individual practices are done at least 5 times a week delivered via a CD or on a preloaded device. The 20 minute practices are an abbreviated version of the weekly hour instruction. Each participant is asked to track his/her daily meditation practice (adherence with the study protocol). A diary for adherence records will be given to participants.
- MIM will be provided by Dr. Klatt or an MIM trained teacher who has Mindfulness training, and has been trained by Dr. Klatt in the adaptations necessary to successfully implement MIM.
- The location of the intervention will be in a room in the OSU East, allowing for a convenient, calm intervention environment.

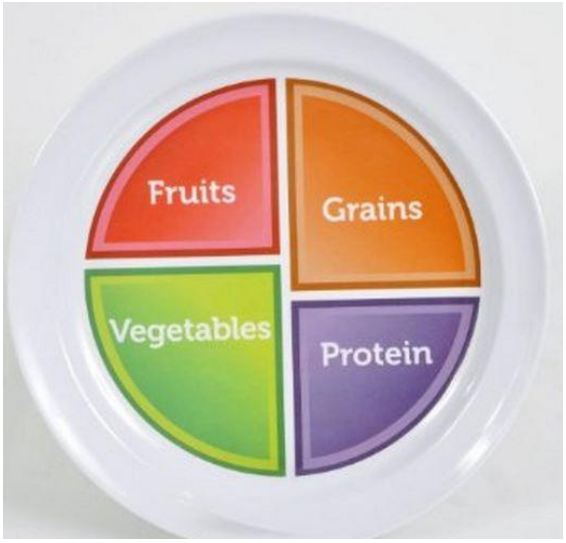
The on-site MIM intervention sessions were designed by, and will be conducted or supervised by Maryanna Klatt, PhD.[39,40] Each week, the group meeting consists of material related to mindfulness, e.g., the somatic mind/body connection, relaxation, yoga, meditation, self-awareness, and bodily cues relating to emotional reactivity. Group interaction centers on sharing ideas towards effective practice and practical daily challenges to being mindful. All instruction is conducted with the participants in chairs, or standing behind the chair. Loose fitting professional clothing is recommended to allow for movement. Each class begins with a prompt for contemplation during the next hour. The prompts directly relate to each weekly theme. Participants will receive a workbook, similar to the weekly handouts with space to reflect on these prompts, as the prompt serves as the focus of that week's meditation. Participant's response to the prompt is personal and silent. Some participants may then choose to share their thoughts, but there is no pressure to verbalize personal reflections. The workbook also provides assigned additional mindfulness exercises and brief readings. The participants will bring the workbook to each class.

Each weekly meeting employs the use of breathing techniques, progressive relaxation, body scans, pre-meditation movement, various yoga poses, and formal meditation practice. The intent of the didactic/experiential sessions is to encourage the explicitly defined objective of the study: stress reduction. The MBSR protocol calls for the MBSR curriculum to be employed in a way sensitive to the unique local conditions but the fundaments of MBSR are invariant.[37] This program will be geared towards the local stresses commonly experienced by healthy working adults in SICU departments. The pre-meditation stretching brings the focus to the breath and body, enabling meditative awareness, while the background music is

standardized to be the background music in each session, and in the background of each meditation practice contained on the downloads. After introduction of the weekly theme/prompt the participants are led through a body scan, gentle stretching, yoga, progressive relaxation, and/or an eating meditation, and then into formal meditation. During the weekly session, participants can discuss if they wish thoughts and emotional responses experienced during meditation but this is not a requirement.

The DASH[3] eating plan is endorsed by the National Health, Lung, and Blood Institute and consists of a flexible and balanced eating plan. The emphasis of the DASH eating plan is on increasing intake of fruits and vegetables, eating fat-free or low-fat dairy products, whole grains, fish, poultry, beans, nuts, and vegetables oils. The DASH diet recommendations stress limiting sodium, sweets, sugary beverages, and red meats. Overall, the DASH diet is low in saturated and trans fats, and rich in potassium, calcium, magnesium, fiber, and protein. In addition, participants will be provided with ethnic recipes that are adapted to meet the DASH dietary guidelines. A combination of didactic, experiential, and "hands on" activities will be done to deliver the DASH diet guidelines. Participants will be encouraged to complete a weekly homework assignment to practice application of the DASH diet in daily life. They will received a plastic plate that displays serving sizes and food groups for a balance meal. (Figure 1)

Figure 1. Nutrition Plate



Reminders. A research assistant will contact participants prior to each session to answer questions and remind participants of the following session.

The attention control group will attend eight, 2.5 hours sessions on non-health topics such as personal safety, fire prevention, cold weather protection, disaster preparation, internet safety, aging in place, how to know when it's time to move and managing your money. The format will include lecture, break, educational video on the topic and question/answer time. The attention control and the mindfulness + DASH groups will have healthy snacks (i.e., fresh fruit, nuts, cheese, crackers, granola bars) and water during each meeting. Transportation will be provided or gas cards for those who drive/driven by others to the sessions. All sessions will be held at an easy to access location in the community with free parking (i.e., the CON Total Health and Wellness Clinic). Table of the lesson plan for the intervention and control groups can be found in attachments.

The control group, will not receive any form of intervention or attention. This will provide true and reliable insight of the impacts of mindfulness + DASH intervention on brain activity, in comparison to that of non-health related intervention given to the attention control group. The benefit of having a pure control group is that, the information collected can then be used to guide future comparison groups for the R01.

Fidelity Monitoring. Each session of the Mindfulness + DASH will be audiotaped and an investigator generated fidelity check-list. The checklist is composed of the key elements needed to deliver Mindfulness and DASH education that was used in a previous study. Fidelity of the intervention "dose" will be monitored by tracking session attendance and time spent on each booster phone call. Interventionists will track the homework completion each week to assess treatment enactment fidelity.

*Incidental findings: Blood pressure***.** The following guidelines will be used to triage unanticipated blood pressure findings: If average systolic BP is >150 or diastolic BP is >110, we will instruct the participant to follow up with health provider or an urgent care center if the participant does not have a health provider. If blood pressure is 200/120 or greater refer to ED for immediate care.

Incidental findings and interpretations of scans. Under no circumstances may an investigator, research staff, or the imaging center staff interpret scans as normal or abnormal. All scans performed at the Center for Cognitive and Behavioral Brain Imaging are for research purposes only and are NOT intended for clinical diagnoses or therapeutic purposes. However, in recognition of the fact that, on occasion, incidental findings may need to be investigated medically, and in a best faith effort to inform research participants of that possibility, the policy of having all scans of normal research participants by a neroradiologist has been implemented. Every normal participant studied at the Center for Cognitive and Behavioral Brain Imaging will have, in addition to the structural MRI performed as part of the study, a brief T2 weighted sequence (2 minutes). This data will be sent for expert neuroradiological review, which will be provided, by contractual agreement between Center for Cognitive and Behavioral Brain Imaging and Nationwide Children's Hospital at Columbus, Ohio, by neuroradiologists at Nationwide Children's Hospital Columbus. This policy will be included in the Consent Form. The language in the consent form allows the participant to choose if she/he wants the neuroradiologist to contact her/him or a physician of her/his choice in the event of an incidental finding. The scans will be provided to the neuroradiologists by Deborah Hardesty without identifying data. Scans will solely contain the CCBBI identifying number, gender and age of the participant. In the unlikely event that the team of neuroradiologists identifies an incidental finding, Deborah Hardesty will be asked to provide the participant's name and contact, as well as his/her physician's name and contact. The neuroradiologists will, at that time, inform us that the participant is not appropriate for research and will take it upon himself to contact the participant/physician and discuss the finding and any further action to be taken, if necessary. The Center for Cognitive and Behavioral Brain Imaging will not be involved in any medical interaction with the participant and will not be informed of any medical diagnosis. Deborah Hardesty will simply inform the respective PI/investigator identified on the forms signed prior to scanning, as soon as neuroradiologists report that a participant is not appropriate for research. There are two exceptions to the above mentioned policy:

1. Participants who are part of repeated scanning for multiple studies, will have their scans reviewed after their first scanning session. If their participation continues for over one year,

the first scan performed one year after the previously reviewed scan will be sent for review. We need your cooperation in identifying such participants.

2. Participants with known brain diseases who are part of structural/functional MR protocols will not have their scans sent to neuroradiologists for review and should therefore not sign the attached document.

Per The Center for Cognitive and Behavioral Brain Imaging Investigators who will use brain damaged participants in research protocols should follow the policy of providing the structural scan to the participants' physician. CDs with the structural images are offered to the participants so that, those who wish can consult directly with their own medical practitioner.

Data Validity/Integrity

It is the responsibility of the Principal Investigator to ensure that all team members handle data and related documentation appropriately. All participant information, including source documents must be reviewed by the PI and clinical team and entered into the RedCAP database. To maintain up-to-date information, data will be entered directly into RedCap data entry forms. There will be ongoing processing of data and quality checks by the study statistician and or PI.

Recruitment:
Participant recruitment will be tracked and reviewed in the weekly meetings of the research team. In order to maintain confidentiality, the list, which includes the names of all potential participants, will be kept separately from the documentation and tracking spreadsheet in Redcap. Basic demographic information, as well as reasons for refusal will be noted for eligible individuals who decline participation. Tracking will be carried out to determine which and how many individuals are interested in study participation, are eligible for study participation, enroll in the study, and complete the first assessments. We will also track retention past random assignment. Enrolled participants will be given code numbers and their study participation will continue to be tracked via spreadsheet in Redcap, which will include documenting the occurrence and date of completion of data collection at each time point and their participation in the intervention and attention control sessions.

Consistency of Data Collection:
Data collection will follow study procedures. Data collection will be tracked as specified above and will be monitored in the bi-weekly meetings of key members of the research team. Any issues that arise can therefore be dealt with in a timely manner. Weekly meetings will also include review of upcoming data collection so questionnaires can be prepared in a timely manner.
Imaging data will be uploaded to the PACS server automatically.
To access the data, the PI will go to http://pacs.psy.ohio-state.edu/ from any computer. The PI will have a user name and password to access the data.

Quality Assurance:
Dr. Wright will work closely with the statistician to design forms and a database that maximize accurate data entry using Redcap. To minimize data-entry error and data-management miscoding, data will be either be entered directly into the study database in REDCap by the study staff or if collected via paper, will be will be double-entered by study staff into REDCap and verified by the PI. PI Wright will review the data collected and all related documentations monthly. Summary results will be entered into the larger

REDCap database. Source documents and electronic data will be checked for accuracy and adherence to study protocols.

Data Storage:
Consent forms and participant lists will be stored in locked file cabinets separate from participant data. The PI and designated study staff will have access to data. All participant data will be labeled only with a code number. These coded data will be kept separate from the master list that links participants and their code numbers. Only the PI and research coordinator will have access to the master list. Research staff data collectors will have access to REDCap survey to collect participant data under their unique ID number.

This study will utilize REDCap (Research Electronic Data Capture), a software toolset and workflow methodology for electronic collection and management of clinical and research data, to collect and store data. The OSU Center for Clinical and Translational Science (CCTS) Research Informatics Services will be used as a central location for data processing and management. REDCap provides a secure, web-based application that provides an intuitive data manipulation interface, custom reporting capabilities, audit trail functionality, real-time data monitoring/querying of participant records, and variations of data exporting/importing. REDCap is hosted by OSUWMC IT in the Ackerman Datacenter (640 Ackerman Road; Room 345)

REDCap instance is located on internal OSUWMC network. Remote access to this network can be obtained over an encrypted VPN tunnel (AnyConnect) This VPN uses Protocol: DTLS and Cipher: RSA_AES_128_SHA1. Background checks are performed on all staff that are on the network or obtaining VPN access.

Protocol Compliance:
Mindfulness plus DASH diet education Intervention Integrity and Consistency. The interventionists (mindfulness trainer and dietitian) will follow the program outline. With permission, the sessions will be digitally recorded. To ensure fidelity, Dr. Kathy Wright will review and rate digital recordings for acceptable interventionist communication for checking-in regarding participant comfort, and skills training. Dr. Kathy Wright will communicate regularly with the interventionists on the project to provide feedback and continued training as necessary. Problems with implementation will be documented in writing and a plan developed to correct any discrepancies between the protocol and implementation practice.

Termination for Significant Risk:
Although the study is deemed low risk and adverse events are not anticipated, diligent monitoring will occur as specified above under Adverse Events Protocols. A participant that expresses concern about his or her participation or reports distress associated with receiving the mindfulness and DASH education or attention control group may be asked to discontinue participation in the study if there is concern about participant safety and wellbeing or about the safety and wellbeing of others. Likewise, if one of the research assistants, interventionists or supervising members of the Research Team expresses a concern about a participant's safety or wellbeing, the Adverse Events Protocol would be used and it is possible that the participant could be asked to discontinue participation if there were concern about his or her, or others, safety and wellbeing.

E. Internal Validity

To reduce the threats to internal validity we will do the following: data collectors will be blinded to the hypothesis of the study after randomization is completed; the PI will participate in baseline data collection only to train data collectors and we will use an intent to treat analysis.

F. Data analysis

We will use descriptive statistics to examine variable distribution, check for outliers and summarize sample characteristics. Bivariate tests (T-test and Chi-square) will be used to compare sample characteristics between the two study arms. Congruent with a RCT nature of the design, we will conduct intent-to-treat analysis.

For Aim 1, we will use descriptive statistics to quantify the rates of recruitment, attendance, and attrition for feasibility. Using a semi-structured list of open-ended questions, we will elicit participant feedback regarding the acceptability of the intervention. A debriefing will be conducted following each session to identify any areas for improvements.

For Aim 2, we will first use descriptive statistics and trend plots to examine the primary outcomes (resting state network connectivity and BP) and secondary outcomes (process measures, including self-management mechanisms [self-efficacy, self-regulation, and emotion regulation], diet, and physical activity) (see Table 1), among intervention, attention control group, control group over time (baseline and 3 months). Next, the mixed-effects linear modeling will be used to estimate the between-group difference in each outcome. From the mixed-effects modeling, we will 1) derive estimates of the between-group difference overall and at each time point, 2) adjust for within-participant clustering from repeated measures and 3) control for covariates (e.g., baseline measure, use of antihypertension medications). Based on our previous study, we expect small-to-medium intervention effect on the primary outcomes (resting state network connectivity and BP). Sample size from this pilot study (40 per arm after accounting for 20% attrition) will not have sufficient power to detect small-to-medium effect sizes for between-group difference (e.g., 34% power to detect a Cohen'd of 0.5 with a two-sided significance level of 0.05). Therefore, we will not rely on statistical significance. Instead, we will estimate point estimates, 95% confidence intervals and effect sizes for between-group differences using mixed-effect linear modeling. These estimates along with clinical significance will guide our results interpretation and inform the sample size determination for a future R01 full-scale trial.

Table 2. Project timeline.

Activity	**1-2 months**	**3-4 months**	**5-6 months**	**7-8 months**	**9-10 months**	**11-12 months**
IRB application	**X**	**X**				
Recruitment and randomization		**X**				
Adaptation of intervention for ADRD	**X**					
Data collection (baseline and Time 1)		**X**	**XT1**		**XT2**	
Delivery of Intervention		**X**	**X**			
Preliminary data analysis of baseline data for R01 submission in June 2018		**X**	**X**			
Final data analysis					**X**	**X**
Dissemination						**X**

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