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The Effect of an HIV Self-Management Intervention on Neurocognitive Behavioral Processing

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Abstract

People living with HIV (PLHIV) are increasingly diagnosed with comorbidities which requires increasing self-management. We examined the effect of a self-management intervention on neurocognitive behavioral processing. Twenty-nine PLHIV completed a two- group, three-month randomized clinical trial testing a self-management intervention to improve physical activity and dietary intake. At baseline and 3 months later everyone completed validated assessments of physical, diet, neurocognitive processing (fMRI-derived network analyses). We used linear mixed effects modelling with a random intercept to examine the effect of the intervention. The intervention improved healthy eating ($p=0.08$) and but did not improve other self-management behaviors. There was a significant effect of the intervention on several aspects of neurocognitive processing including in the task positive network (TPN) differentiation ($p=0.047$) and an increase in the default mode network (DMN) differentiation ($p=0.10$). Self-management interventions may influence neurocognitive processing in PLHIV, but those changes were not associated with positive changes in self-management behavior.

Keywords

HIV; Exercise; fMRI; Behavioral Interventions

There are approximately 1.1 million people in the United States living with HIV and almost half of this population is over the age of 50 years (Centers for Disease Control and Prevention, 2018). Both HIV disease and aging, necessitate increased self-management skills to live and age well. In the beginning of the HIV epidemic, self-management interventions were focused on palliative care and as HIV treatment transformed the self-

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management interventions increasingly focused on HIV medication adherence, symptom management, and engagement with HIV care providers (Webel, Prince-Paul, et al., 2018). Today, self-management for persons living with HIV has expanded to include traditional healthy living behaviors, such as eating a healthy diet and engaging in regular, moderate-to-vigorous physical activity (Foster, Hillsdon, & Thorogood, 2005; Grinspoon et al., 2008; O'Brien, Nixon, Tynan, & Glazier, 2010). While we have seen self-management interventions successfully improve HIV medication adherence and symptom management, (Kanters et al., 2017) there has been less success improving physical activity and healthy eating among people living with HIV (PLHIV; Cutrono et al., 2016; Jaggars et al., 2016; Webel, Moore, et al., 2018). Further, responses even among successful self-management interventions for HIV medication adherence and symptom management, have been varied; suggesting that better tailoring may improve the effectiveness of self-management interventions (Tufts et al., 2015).

Self-management and Neurocognitive Behavioral Processing

One way to improve tailoring of self-management interventions is by modifying them to the individual PLHIV's existing neurocognitive processes. Neurocognitive processes such as analytical reasoning, decision-making, and attention can influence how one receives and understands self-management information, and recalls and acts on this information. Self-management interventions can be tailored to an individual and their family based on their neurocognitive processes, however a better understanding of the relationship between neurocognitive constructs and self-management behaviors is necessary before this tailoring can occur.

Recent progress in neuroimaging now allows us to investigate the relationships among neurocognitive process, brain activity, and self-management behaviors. Functional magnetic resonance imaging (fMRI) couples a specific task with changes in blood flow in the brain. These quantifiable changes in blood flow, indicate changes in cortical brain activity and cognition, and now allow an examination of the neurocognitive mechanisms underpinning changes in the neurocognitive behavioral processes associated with changes in self-management behaviors.

Prior work indicates that changes in self-management behaviors may be associated with analytic (Task Positive Network [TPN]) and empathetic (Default Mode Network [DMN]) neural network activation (Jack et al., 2013). Specifically, our previous work identified the TPN as an important network in processing and acting upon analytic information while the DMN assists in processing and acting on empathetic information; Jack et al., 2013) – suggesting that an individual's ability to differentiate the activation of TPN and DMN in response to analytic or empathetic information is associated with better [self]-management skills. This work informed the guiding *a priori* hypothesis of our neural network differentiation task, that greater TPN and DMN task differentiation would be associated with better self-management behaviors

Purpose

The purpose of this paper is twofold, to: describe the effect of a self-management intervention on neurocognitive behavioral processing variables and to describe the association between changes in these neural markers in relation to changes in self-management behavior (i.e., physical activity, diet, HIV medication adherence, and retention in care) in PLHIV. We hypothesized that that better cognitive neural network task differentiation would be associated with improved self-management behaviors over time (Jones et al., 2018).

Method

Design

These data derive from a pre-planned, nested pilot study of a larger two-group randomized clinical trial testing the effect of the SystemCHANGE self-management intervention (Boosting health By Changing AcTivity hereafter referred to as BOBCAT study) to improve physical activity and cardiometabolic outcomes in sedentary PLHIV (NCT02553291; Webel, Moore, et al., 2018).

Recruitment

Potential participants were recruited using recruitment letters sent to an HIV Research Registry in Northeast Ohio and flyers distributed at local HIV clinics and service organizations. The letters and flyers indicated the study's purpose, time involvement, general inclusion criteria, and a phone number to call if someone was interested. Prospective participants responding to these advertisements were screened by a Research Assistant, using a standardized screening form, to ensure that they met study eligibility criteria. We consecutively enrolled all willing BOBCAT study participants meeting eligibility criteria for this nested study, until our we reached our *a priori* sample size of 30 participants. We selected a sample size of 30 participants based on financial constraints for pilot studies in the SMART Center (SMART Center, 2018).

Population

To be included in the BOBCAT clinical trial, potential participants had to 1) be diagnosed with HIV, 2) be 18 years of age, 3) be taking HIV anti-retroviral therapy, 4) had a recent HIV Viral Load less than 400 copies/mL, 5) be at high risk for developing cardiovascular disease (CVD; Framingham 30-year CVD risk score >20% for females and >30% for males), and 6) if taking a statin medication, be on it for at least 6 months. Potential participants were excluded if they 1) had a medical contraindication for exercise, 2) met the Department of Health and Human Service's recommendations for weekly exercise (assessed with the 7-day physical activity recall), 3) were unable to understand spoken English, 4) were expecting to move out of the immediate area in the next six months, 5) had planned surgery in the next six months, 6) were pregnant or planned on becoming pregnant, or 7) were enrolled in a formal weight loss program. Additionally, to undergo an fMRI procedure participants had to have a Montreal Cognitive Assessment (MOCA) score of 22 or greater, indicating intact cognitive functioning, 2) be willing and able sit in the MRI scanner for 45 minutes, and 3)

not have a medical contraindication for an MRI (e.g., aneurysm clips, MRI-incompatible devices, infusion pumps, chronic liver disease, metal or shrapnel in his or her body). Medical eligibility criteria (e.g., HIV status, medications, HIV viral load values) were confirmed, with the potential subject's consent, using his or her electronic medical record.

Procedures

Participants meeting inclusion criteria were scheduled for an in-person baseline appointment during which participants completed a written informed consent. They then completed assessments of self-management behavior and neurocognitive processing, as described below. After completing all assessments, participants were randomized 1:1, stratified by gender and race, to either a self-management intervention or a control condition. The intervention condition was a six-session, in-person, group intervention teaching behavior change techniques and healthy lifestyle education. Participants randomized to the intervention completed six group sessions where they completed a standardized lifestyle education session led by a health educator. Approximately 90% of participants randomized to the intervention attended 50% of the sessions and 60% of the participants attended at least five intervention sessions (Webel, Moore, et al., 2018). The health educator provided evidence-based information on the diet and exercise components of a healthy lifestyle (e.g., DASH and Mediterranean diets; types, frequency and intensity of physical activity). She also led them through a series of exercises (e.g., self-monitoring, cause and effect diagrams) to identify how to incorporate these behaviors into participants' daily routines. The intervention primarily taught analytical self-management skills (e.g., self-monitoring and tracking) but also contains social/empathic features (e.g., social support activities). The control condition was a one-on-one session in which a research assistant provided information on healthy eating and physical activity using an American Heart Association pamphlet. A full description of the intervention and control condition components can be found in a previous publication (Webel, Moore, et al., 2018).

As previously reported, participants in the intervention did not increase their physical activity or improve their overall diet quality, but did reduce their daily carbohydrate intake which led to more weight loss over time than those in the control group ($p < 0.05$; Webel, Moore, et al., 2018). All procedures for this nested pilot study, including a \$100 incentive to complete the pilot study measures, were approved by the Institutional Review Board at University Hospitals Cleveland Medical Center and occurred between June 2015 and April 2016.

Measures

To examine the effect of the self-management intervention on neurocognitive behavioral processing variables and the association between changes in self-management behaviors and neurocognitive behavioral processing all participants completed assessments of self-management behavior and neurocognitive processing at baseline and three months later (immediately post-intervention).

Demographics and Health Characteristics.—All participants completed a self-reported demographic survey assessing gender, race, education and monthly income using

REDCAP (Research Electronic Data Capture; Harris et al., 2009). Participants also consented to medical chart abstraction from which study staff abstracted detailed descriptive medical data including years living with HIV, current CD4+ T cell count, CD4+ T cell nadir, current medications, and current comorbid health conditions.

Self-management behaviors (physical activity and diet intake).

Physical Activity.: After completing the surveys, participants were given an ActiGraph accelerometer (Actigraph, LLC, Fort Walton Beach, FL) and a research assistant explained how to wear it for the next 7 consecutive days (Anastasopoulou et al., 2014; Berntsen et al., 2010; Strath et al., 2013). Among adults, the ActiGraph accelerometer has been found to have high reliability ($r = 0.90\text{--}0.99$) and valid (Aadland & Ylvisåker, 2015). Upon returning the accelerometer, we checked to ensure that data were recorded for at least 4 days and at least 8 hours per day (a valid wear day; Hamilton et al., 2011; Haskell et al., 2012; Hitz, Conway, Palcher, & McCarty, 2014). We defined moderate to vigorous physical activity as activity ≥ 2690 counts per minute for a minimum of 10 consecutive minutes (Caspersen, Powell, & Christenson, 1985). We used the ActiLife software to calculate the amount of physical activity per valid wear day using the Sasaki, John, and Freedson (2011) adult cutpoints for tri-axial accelerometers (Sasaki, John, & Freedson, 2011).

Diet Intake.: After receiving the Actigraph, participants completed an in-person 24-hour dietary recall with a trained dietician I. During this interview, each participant recalled what he or she consumed and the amount of each item in the previous 24 hours. Responses were simultaneously entered into the Nutrient Data System for Research (NDSR) software, (Buzzard & Feskanich, 1987; Dennis, Ernst, Hjortland, Tillotson, & Grambsch, 1980; Sievert, Schakel, & Buzzard, 1989) which calculated nutrients consumed and converted quantities to gram weight and corresponding nutrient values (Thompson & Subar, 2008). We used this software to calculate the Healthy Eating Index, a validated composite measure of diet quality assessing conformance to dietary guidelines and the preferred dietary outcome in the U.S. (Buzzard & Feskanich, 1987; Dennis et al., 1980; Freedman, Guenther, Krebs-Smith, & Kott, 2008; Guenther, Reedy, & Krebs-Smith, 2008; Guenther, Reedy, Krebs-Smith, & Reeve, 2008; Sievert et al., 1989).

Neurocognitive processing variables (fMRI-derived neural network differentiation and self-reported self-efficacy, patient activation, attention, and decision making).

Neural Network Differentiation.—To examine the neurocognitive behavioral processes associated with changes in self-management behaviors between the intervention and control groups, we designed an fMRI task to provoke our a priori regions of interest: the analytic (Task Positive Network) and empathetic (Default Mode Network) neural activation. To test our hypothesis, we developed an fMRI task that has been described in detail elsewhere (Jones et al., 2018). In brief, we designed four, seven minute and 40 second (total 30 minutes and 40 seconds) video conditions. These four conditions each contained 12 video clips emphasizing an analytic issue (e.g., an overview of HIV infects a CD4+ T cell), a social/empathy issue (e.g., someone telling a story about how they found out they were diagnosed with HIV), and health information interspersed with a rest condition (i.e., a red cross on a

black background with no sound). All video clips were presented using Eprime software (v 2.0.10) to standardize the task in the scanner.

The fMRI images were acquired using a Siemens 3T Skyra scanner. To establish an anatomical baseline, participants first completed a T1-weighted structural MRI sequence. Participants then completed four T2-weighted fMRI sequences using the task described above. Participants were in the fMRI scanner for approximately 60 minutes at each time point.

Prior to analyzing the fMRI images, all data were preprocessed using the procedure described by Power et al. (2014). Then a target atlas was made to align our participant's anatomy with the 711–2B space representing 3-D Talairach Space, which allowed us to locate and analyze the TPN and DMN. The specific coordinates used are presented in previous work.(Jack et al., 2013) As described by Boynton, Engel, Glover, and Heeger (1996) we used a general linear model with assumed hemodynamic response functions to estimate participants' average response to the video conditions at baseline and over time. The rest condition was not explicitly modeled and was implicitly captured by the baseline estimate (Boynton et al., 1996). To analyze neural network differentiation, TPN differential activation was defined as the contrast of analytic - empathetic video conditions and the DMN was defined as the contrast of empathetic – analytic video conditions.

In addition to the mechanistic data provided by the fMRI images, we also assessed self-efficacy, patient activation, attention, and decision making. The six-item *Chronic Disease Self-Efficacy Scale* asks participants to self-report their confidence completing various self-management tasks (e.g., taking medications, managing symptoms; Lorig, Sobel, Ritter, Laurent, & Hobbs, 2001). Each item is scored from 0–10 and then summed to create an overall score. Higher scores indicate more self-efficacy.

The 10-item, psychometrically sound *Patient Activation Measure* (PAM-10) assesses one's knowledge, skill, and confidence in managing his or her chronic health condition (Hibbard, Stockard, Mahoney, & Tusler, 2004). The items are scored on a 0–100 scale where higher scored indicated more patient activation. The PAM-10 had a Cronbach's α of 0.91.

The *Erikson Flanker Task* (Eriksen & Eriksen, 1974) was used to assess participants' selective attention, an important in skill in self-management (Hall & Marteau, 2014). This computer-administered task required that participants focus on five letters (s or h) despite sometimes being flanked by the incongruent letters, and to select the correct central letter. The endpoints for this task include the percent of time a respondent correctly identified the letter when the flankers were congruent and incongruent. A higher proportion of correct responses indicates more selective attention.

The *Iowa Gambling Test* was used to assess participant's decision-making. In this computer-administered task, participants are presented with four virtual card decks which will either award or deduct money. The “good” decks tend to award money and the “bad” decks tend to deduct it. The endpoint of this task is a demographically-adjusted T score in which higher scores indicate better decision making. All data collectors were trained in administering the Erikson Flanker Test and the Iowa Gambling Tests using a standardized guide.

Analysis

We summarized important demographic and medical characteristics, neurocognitive processing, and self-management variables using means, standard deviations, medians, interquartile ranges, counts, and percentages of participants in each arm of the study. We examined variability and distributions of all neurocognitive processing measures using standard deviations, skewness, kurtosis, and box plots. To examine the effect of the intervention on our *a priori* defined neurocognitive processing variables we then created a change score (three months –baseline). We then created box plots of the variables at baseline, 3 months and the change score by intervention group. The difference in the changes in neurocognitive processing was assessed using a Wilcoxon rank-sum test. We also used a linear mixed effects model with a random intercept to examine the effect of the self-management intervention on neurocognitive behavioral processing. A time by group interaction term was created to model the effect of the intervention over time. Given the exploratory, pilot nature of this study and because we did not want to miss an effect, we selected *a priori*, a significance level of 10% for all hypothesis tests. This decision is consistent with the 2016 *American Statistical Association* Statement on Statistical Significance and p-values, with an emphasis on cautiously interpreting findings within the overall context. (Wasserstein & Lazar, 2016). All analyses were conducted using Stata 14 and R.

Results

We enrolled 32 participants. Two did not complete time 2 measures and were replaced with additional participants and one did not have a valid baseline fMRI. A total of 29 participants completed all measures, including the fMRI, at baseline and 3 months later. The average age of the participants was approximately 53 (± 8.3) years, most were African-American (96%), had a high school degree or less (57%), and two (7%) were currently working. They had been living with HIV for an average of 14 years, were on HIV antiretroviral medications for 12.5 years and all had additional physical comorbidities (e.g., hypertension, hepatitis C). The intervention group had a higher body mass index (32.6 vs 27.1, $p=0.10$), but otherwise there were no differences in baseline characteristics between the two groups ($p>0.10$; Table 1). Participants engaged in a median of 31.9 (IQR: 0, 64.2) minutes of physical activity per week, well below the recommended average of 75–150 minutes per week. The median Healthy Eating Index score was 45.0 (IQR: 29,58), indicating low compliance with the U.S. recommended daily diet. Additional details can be found in Table 2.

Analysis of the effect of the intervention on self-management and neuroprocessing variables showed several significant relationships. Participants in the intervention group improved the quality of their overall diet intake over time ($\beta= 10.02$, $p=0.08$), however we did not see an effect of the intervention on physical activity (Table 3). We observed a decline in TPN task differentiation in patients receiving the control intervention as compared to patients receiving the SystemCHANGE intervention (z-value= -1.97 , $p=0.047$) and an increase in DMN task differentiation in the control group (z-value = 1.65 , $p=0.10$; Figure 1). General mixed modelling confirmed a group by time interaction on TPN task differentiation ($\beta= 0.14$, $p=0.05$ (Table 4). There were no differences between the intervention and control

groups over time on self-efficacy, patient activation, selective attention and decision making over 3 months ($p>0.10$; data not shown). In analyzing how changes in self-management variables were related to changes in our fMRI-derived neuroprocessing variables we conducted a linear mixed effects model. We found that changes in self-management variables were not associated with changes in either the TPN or the DMN (group by time interactions $p>0.10$, data not shown).

Discussion

This is the first longitudinal study to examine associations between fMRI-derived neurocognitive processing variables and self-management behaviors (i.e. physical activity and diet intake) in PLHIV. In this nested pilot study, we found that, as expected, our self-management intervention improved diet intake and TPN task differentiation. However, these improvements were not associated with each other, suggesting that changes in neural network activation did not lead to the observed improvements in diet intake. This was surprising and in contrast to our center's overarching hypothesis, that better cognitive neural network task differentiation would be associated with improved self-management behaviors over time (Jack et al., 2013). This novel hypothesis was built on promising literature in non-HIV populations, focusing on other behavioral outcomes. For example, studies in healthy college students found that those who balance these two neural networks tend to exhibit better leadership skills including, balancing creative thinking with analytic reasoning, avoiding ethical dangers, and properly motivating and incentivizing employees (Boyatzis, Rochford, & Jack, 2014; Friedman, Jack, Rochford., & Boyatzis, 2015). Others have reported that mindfulness training can reduce emotional reactivity (Default Mode Network) and increase attention in adolescents, (Sanger & Dorjee, 2015, 2016) thereby improving their mental health. While these studies suggest that improvements in neural network task differentiation would be associated with better health behaviors, none of these studies investigated this question, so it is challenging to contextualize our findings in this literature. However, as a nascent field of research, we need additional rigorous research to best understand if and how to use neuroimaging techniques to clarify the neurocognitive basis of chronic disease self-management; some of this research is ongoing (Jones et al., 2018).

Further, while fMRI analyses can provide a multitude of variables to investigate, as a pilot study it was important to investigate those that were pre-specified in our hypothesis. Our hypotheses was based on our prior work, (Boyatzis et al., 2014; Friedman et al., 2015) but this work was not conducted with PLHIV. HIV enters the brain early in HIV infection and remains there even when HIV medications suppress the HIV virus (Saylor et al., 2016). This leads to chronic inflammation and vascular dysfunction in the brain which may lead to the increased neurocognitive impairments experienced by PLHIV (Clifford, 2017). Up to 50% of PLHIV have neurocognitive impairments often impacting the frontostriatal neural systems diminishing important tasks needed for self-management including working memory, problem solving, and decision making (Casaletto, Weber, Iudicello, & Woods, 2017). We attempted to control for this in our eligibility criteria by using the MOCA brief screening tool and excluding those with a score indicating impaired cognition. However, the MOCA is not a diagnostic tool and without a full neuropsychiatric exam, it is hard to know if we enrolled anyone with mild cognitive impairment (Koenig, Fujiwara, Gill, & Power, 2016).

Further, the elevated prevalence of neurocognitive dysfunction of PLHIV underscore a continued need to test and refine existing, successful self-management interventions and to continue tailoring them to the target population, including to their neurocognitive function. Future neuroimaging research could expedite this tailoring and should seek to describe neurological and cognitive correlates of known self-management mediators including self-efficacy, patient activation and self-regulation, (Moore et al., 2016) as well as self-management behavioral outcomes.

In addition to examining cognitive hypotheses to identify the neurocognitive mechanisms underpinning changes in the neurocognitive behavioral processes of self-management behavior, it may be helpful to employ paradigms that combine structural and cognitive hypotheses. Such studies would also require repeated functional and structural images longitudinally, with careful attention to the immunological and vascular effects of HIV. Further, the neurological consequences of HIV infection using contemporary HIV treatment are only starting to be characterized (Behrman-Lay et al., 2016; Su et al., 2016). As such, future research should consider enrolling homogenous samples to best describe the neurological and cognitive effects of HIV and examine their relationship to self-management behavior and responsiveness to self-management interventions. Imaging techniques such as Diffusion Tensor MRI might be particularly helpful in evaluating the integrity of white matter of PLHIV (Leite et al., 2013; Su et al., 2016) and can be integrated with functional and structural imaging protocols.

This nested pilot study was designed to help discover associations between the neurocognitive mechanisms underpinning changes in the neurocognitive behavioral processes and self-management behaviors of PLHIV. Though we found limited support for our hypothesis, using a rigorous, longitudinal study design with a high retention rate, we demonstrated that fMRI studies are acceptable to this population, indicating that future research using these techniques should be encouraged. Given the intense resources needed to conduct fMRI assessments, it is advisable to consider nesting his methodology into larger existing studies, and pooling data across populations to better understand these neurocognitive mechanisms.

While this study has several strengths, as a pilot, this work is limited by a small sample size, a single data collection site, and the inclusion of PLHIV who are virally suppressed; all of which limit generalizability of our findings. We also did not include a well-matched sero-negative comparison group, which limits our ability to examine HIV-related effects on our neurocognitive endpoints. If feasible, future studies should consider enrolling well-matched sero-negative participants to help understand the role of HIV on the neurocognitive mechanisms underpinning self-management behavior. Finally, we were guided by a novel *a priori* hypothesis to help us examine these mechanisms, yet failed to find support for this hypothesis. This may be related to our small, heterogenous sample or that this hypothesis may not be applicable to this population. Future work should consider additional neurocognitive approaches, additional imaging techniques to augment the functional imaging findings, larger and perhaps, more homogenous and better-characterized participants.

In conclusion, despite demonstrating that our self-management intervention improved an important behavioral outcome- diet intake, the neural activity in our pre-hypothesized regions cannot account for that improvement. However, the novel neuroimaging and cognitive assessment techniques used in this study are a promising way to help us identify the neurocognitive processes underpinning chronic disease self-management behavior. Future research using these techniques to better understand how to improve self-management behavior is warranted.

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References

- Aadland E, & Ylvisåker E (2015). Reliability of the Actigraph GT3X+ accelerometer in adults under free-living conditions. *PLoS One*, 10(8), e0134606. doi:10.1371/journal.pone.0134606 [PubMed: 26274586]
- Anastasopoulou P, Tubic M, Schmidt S, Neumann R, Woll A, & Hartel S (2014). Validation and comparison of two methods to assess human energy expenditure during free-living activities. *PLoS One*, 9(2), e90606. doi:10.1371/journal.pone.0090606 [PubMed: 24587401]
- Behrman-Lay AM, Paul RH, Heaps-Woodruff J, Baker LM, Usher C, & Ances BM (2016). Human immunodeficiency virus has similar effects on brain volumetrics and cognition in males and females. *Journal of NeuroVirology*, 22(1), 93–103. doi:10.1007/s13365-015-0373-8 [PubMed: 26306688]
- Berntsen S, Hageberg R, Aandstad A, Mowinckel P, Anderssen SA, Carlsen KH, & Andersen LB (2010). Validity of physical activity monitors in adults participating in free-living activities. *British Journal of Sports Medicine*, 44(9), 657–664. doi:10.1136/bjsm.2008.048868 [PubMed: 18628358]
- Boytatzis RE, Rochford K, & Jack AI (2014). Antagonistic neural networks underlying differentiated leadership roles. *Frontiers in Human Neuroscience*, 8, 114. doi:10.3389/fnhum.2014.00114 [PubMed: 24624074]
- Boynton GM, Engel SA, Glover GH, & Heeger DJ (1996). Linear systems analysis of functional magnetic resonance imaging in human V1. *Journal of Neuroscience*, 16(13), 4207–4221. [PubMed: 8753882]
- Buzzard M, & Feskanich D (1987). Maintaining a food composition data base for multiple research studies: The NCC food table In Rand CWW, Wyse B, & Y. V (Ed.), *Food composition data: A user's perspective*. Tokyo, Japan: The United Nations University.
- Casaletto KB, Weber E, Iudicello JE, & Woods SP (2017). Real-world impact of HIV-associated neurocognitive impairment *Changes in the Brain* (pp. 211–245): Springer.
- Caspersen CJ, Powell KE, & Christenson GM (1985). Physical activity, exercise, and physical fitness: Definitions and distinctions for health-related research. *Public Health Reports*, 100(2), 126–131. [PubMed: 3920711]
- Centers for Disease Control and Prevention. (2018). HIV among people aged 55 and older. Retrieved from <https://www.cdc.gov/hiv/group/age/olderamericans/index.html>
- Clifford DB (2017). HIV-associated neurocognitive disorder. *Current Opinion in Infectious Diseases*, 30(1), 117–122. [PubMed: 27798498]
- Cutrono SE, Lewis JE, Perry A, Signorelli J, Tiozzo E, & Jacobs KA (2016). The Effect of a community-based exercise program on inflammation, metabolic risk, and fitness levels among persons living with HIV/AIDS. *AIDS and Behavior*, 20(5), 1123–1131. doi:10.1007/s10461-015-1245-1 [PubMed: 26607928]

- Dennis B, Ernst N, Hjortland M, Tillotson J, & Grambsch V (1980). The NHLBI nutrition data system. *Journal of the American Dietetic Association*, 77(6), 641–647. [PubMed: 6893713]
- Eriksen BA, & Eriksen CW (1974). Effects of noise letters upon the identification of a target letter in a nonsearch task. *Perception & Psychophysics*, 16(1), 143–149. doi:10.3758/bf03203267
- Foster C, Hillsdon M, & Thorogood M (2005). Interventions for promoting physical activity. *Cochrane Database of Systematic Reviews*, 1, CD003180.
- Freedman LS, Guenther PM, Krebs-Smith SM, & Kott PS (2008). A population's mean Healthy Eating Index-2005 scores are best estimated by the score of the population ratio when one 24-hour recall is available. *Journal of Nutrition*, 138(9), 1725–1729. [PubMed: 18716176]
- Friedman J, Jack AI, Rochford K, & Boyatzis R. (2015). Antagonistic neural networks underlying organizational behavior. *Organizational Neuroscience (Monographs in Leadership and Management)*, 7, 115–141.
- Grinspoon SK, Grunfeld C, Kotler DP, Currier JS, Lundgren JD, Dubé MP, . . . Eckel RH. (2008). State of the science conference: Initiative to decrease cardiovascular risk and increase quality of care for patients living with HIV/AIDS: Executive summary. *Circulation*, 118(2), 198–210. doi:10.1161/circulationaha.107.189622 [PubMed: 18566320]
- Guenther PM, Reedy J, & Krebs-Smith SM (2008). Development of the Healthy Eating Index-2005. *Journal of the American Dietetics Association*, 108(11), 1896–1901.
- Guenther PM, Reedy J, Krebs-Smith SM, & Reeve BB (2008). Evaluation of the Healthy Eating Index-2005 *Journal of the American Dietetics Association*, 108(11), 1854–1864.
- Hall PA, & Marteau TM (2014). Executive function in the context of chronic disease prevention: Theory, research and practice. *Preventative Medicine*, 68, 44–50. doi:10.1016/j.ypmed.2014.07.008
- Hamilton CM, Strader LC, Pratt JG, Maiese D, Hendershot T, Kwok RK, . . . Haines J. (2011). The PhenX Toolkit: Get the most from your measures. *American Journal of Epidemiology*, 174(3), 253–260. doi:10.1093/aje/kwr193 [PubMed: 21749974]
- Harris PA, Taylor R, Thielke R, Payne J, Gonzalez N, & Conde JG (2009). Research electronic data capture (REDCap)--A metadata-driven methodology and workflow process for providing translational research informatics support. *Journal of Biomedical Informatics*, 42(2), 377–381. doi:10.1016/j.jbi.2008.08.010 [PubMed: 18929686]
- Haskell WL, Troiano RP, Hammond JA, Phillips MJ, Strader LC, Marquez DX, . . . Ramos E. (2012). Physical activity and physical fitness: Standardizing assessment with the PhenX Toolkit. *American Journal of Preventative Medicine*, 42(5), 486–492. doi:10.1016/j.amepre.2011.11.017
- Hibbard JH, Stockard J, Mahoney ER, & Tusler M (2004). Development of the Patient Activation Measure (PAM): conceptualizing and measuring activation in patients and consumers. *Health Services Research*, 39(4 Pt. 1), 1005–1026. doi:10.1111/j.1475-6773.2004.00269.x [PubMed: 15230939]
- Hitz MM, Conway PG, Palcher JA, & McCarty CA (2014). Using PhenX toolkit measures and other tools to assess urban/rural differences in health behaviors: Recruitment methods and outcomes. *BMC Research Notes*, 7(1), 847. [PubMed: 25425113]
- Jack AI, Dawson AJ, Begany KL, Leckie RL, Barry KP, Ciccio AH, & Snyder AZ (2013). fMRI reveals reciprocal inhibition between social and physical cognitive domains. *Neuroimage*, 66, 385–401. doi:10.1016/j.neuroimage.2012.10.061 [PubMed: 23110882]
- Jaggers JR, Sneed JM, Lobelo RLF, Hand GA, Dudgeon WD, Prasad VK, . . . Blair, S. N. (2016). Results of a nine month home-based physical activity intervention for people living with HIV, 3(3), 14. doi:10.18203/2349-3259.ijct20162793
- Jones LM, Wright KD, Jack AI, Friedman JP, Fresco DM, Veinot T, . . . Moore SM. (2018). The relationships between health information behavior and neural processing in African-Americans with prehypertension. *Journal of the Association for Information Science and Technology*. Advance online publication. 10.1002/asi.24098
- Kanters S, Park JJ, Chan K, Socias ME, Ford N, Forrest JI, . . . Mills EJ. (2017). Interventions to improve adherence to antiretroviral therapy: A systematic review and network meta-analysis. *The Lancet HIV*, 4(1), e31–e40. [PubMed: 27863996]

- Koenig N, Fujiwara E, Gill MJ, & Power C (2016). Montreal cognitive assessment performance in HIV/AIDS: Impact of systemic factors. *Canadian Journal of Neurological Sciences/Journal Canadien des Sciences Neurologiques*, 43(01), 157–162. [PubMed: 26635008]
- Leite SCB, Corrêa DG, Doring TM, Kubo TTA, Netto TM, Ferracini R, . . . Gasparetto EL. (2013). Diffusion tensor MRI evaluation of the corona radiata, cingulate gyri, and corpus callosum in HIV patients. *Journal of Magnetic Resonance Imaging*, 38(6), 1488–1493. doi:10.1002/jmri.24129 [PubMed: 23559497]
- Lorig KR, Sobel DS, Ritter PL, Laurent D, & Hobbs M (2001). Effect of a self-management program for patients with chronic disease *Effective Clinical Practice*, 4(6), 256–262. [PubMed: 11769298]
- Moore SM, Schiffman R, Waldrop-Valverde D, Redeker NS, McCloskey DJ, Kim MT, . . . Grady P. (2016). Recommendations of common data elements to advance the science of self-management of chronic conditions. *Journal of Nursing Scholarship*, 48(5), 437–447. doi:10.1111/jnu.12233 [PubMed: 27486851]
- O'Brien K, Nixon S, Tynan A-M, & Glazier R (2010). Aerobic exercise interventions for adults living with HIV/AIDS. *Cochrane Database of Systematic Reviews*, 8, CD001796. doi: 10.1002/14651858.CD001796.pub3
- Power JD, Mitra A, Laumann TO, Snyder AZ, Schlaggar BL, & Petersen SE (2014). Methods to detect, characterize, and remove motion artifact in resting state fMRI. *Neuroimage*, 84, 320–334. [PubMed: 23994314]
- Sanger KL, & Dorjee D (2015). Mindfulness training for adolescents: A neurodevelopmental perspective on investigating modifications in attention and emotion regulation using event-related brain potentials. *Cognitive, Affective, & Behavioral Neuroscience*, 15(3), 696–711. doi:10.3758/s13415-015-0354-7
- Sanger KL, & Dorjee D (2016). Mindfulness training with adolescents enhances metacognition and the inhibition of irrelevant stimuli: Evidence from event-related brain potentials. *Trends in Neuroscience and Education*, 5(1), 1–11. 10.1016/j.tine.2016.01.001
- Sasaki JE, John D, & Freedson PS (2011). Validation and comparison of ActiGraph activity monitors. *Journal of Science and Medicine in Sport*, 14(5), 411–416. [PubMed: 21616714]
- Saylor D, Dickens AM, Sacktor N, Haughey N, Slusher B, Pletnikov M, . . . McArthur JC (2016). HIV-associated neurocognitive disorder [mdash] pathogenesis and prospects for treatment. *Nature Reviews Neurology*, 12(4), 234–248. [PubMed: 26965674]
- Sievert YA, Schakel SF, & Buzzard IM (1989). Maintenance of a nutrient database for clinical trials. *Controlled Clinical Trials*, 10, 416–425. [PubMed: 2605960]
- SMART Center. (2018). SMART center. Retrieved from <https://case.edu/nursing/research/centers-of-excellence/smart-center>
- Strath SJ, Kaminsky LA, Ainsworth BE, Ekelund U, Freedson PS, Gary RA, . . . Swartz AM. (2013). Guide to the assessment of physical activity: Clinical and research applications: a scientific statement from the american heart association. *Circulation*, 128(20), 2259–2279. doi: 10.1161/01.cir.0000435708.67487.da [PubMed: 24126387]
- Su T, Caan MW, Wit FW, Schouten J, Geurtsen GJ, Cole JH, . . . AGEHIV Cohort Study.. (2016). White matter structure alterations in HIV-1-infected men with sustained suppression of viraemia on treatment. *AIDS*, 30(2), 311–322. doi:10.1097/qad.0000000000000945 [PubMed: 26691551]
- Thompson FE, & Subar AF (2008). Dietary assessment methodology, Chapter 1 In Coulston A & Boushey C (Eds.), *Nutrition in the prevention and treatment of disease* (pp. 5–48). San Diego, CA: Academic Press.
- Tufts KA, Johnson KF, Shepherd JG, Lee J-Y, Ajzoon MSB, Mahan LB, & Kim MT (2015). Novel interventions for HIV self-management in African American women: A systematic review of mHealth interventions. *Journal of the Association of Nurses in AIDS Care*, 26(2), 139–150. [PubMed: 25283352]
- Wasserstein RL, & Lazar NA (2016). The ASA's statement on p-values: Context, process, and purpose. *The American Statistician*, 70(2), 129–133.
- Webel A, Prince-Paul M, Ganocy S, DiFranco E, Wellman C, Avery A, . . . Slomka J (2018). Randomized clinical trial of a community navigation intervention to improve well-being in persons

living with HIV and other co-morbidities. *AIDS Care*. Advance online publication. doi: 10.1080/09540121.2018.1546819

Webel A, Moore SM, Longenecker CT, Currie J, Horvat Davey C., Perazzo J, . . . Josephson RA. (2018). Randomized controlled trial of the SystemCHANGE intervention on behaviors related to cardiovascular risk in HIV+ adults. *Journal of Acquired Immune Deficiency Syndromes*, 78(1), 23–33. doi:10.1097/QAI.0000000000001635 [PubMed: 29373392]

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Figure1: Differentiation in Neural Network Activation Over Three Months, by Intervention Group

Table 1:Baseline Demographic and Medical Characteristics (*n*=29)

	Intervention Group (<i>n</i> =16)		Control Group (<i>n</i> =13)		<i>p</i> -value
	Mean	Standard Deviation	Mean	Standard Deviation	
Age (years)	52.3	8.0	53.2	8.6	0.75
Years Living with HIV	15.5	9.3	15.0	7.6	0.81
Years Taking HIV Antiretroviral Medications	11.4	7.8	13.5	8.5	0.37
Current CD4+ T-Cell Count (cells/mm ³)	657	347	665	331	0.95
CD4+ T-Cell Nadir cells/mm ³	294	212	209	117	0.24
Body Mass Index (kg/m ²)	32.6	10.1	27.1	6.3	0.10*
Hip-to-Waist Ratio	0.95	0.05	0.93	0.11	0.57
Mean Blood Pressure (mmHG)	127/82	16.3	126/83	17.8	0.74

Table 2:**Baseline Neurocognitive, Neurocognitive Processing, and Self-Management Variables**

	Theoretical Range	Recommend Range	Median	Interquartile Range (25%, 75%)
Neurocognitive Processing Variables				
Chronic Disease Self-Efficacy	10–60	Higher scores indicate more self-efficacy	44	38, 52
Patient Activation Scale	0–100	Higher scores indicate more patient activation	75.5	56, 83.7
Decision Making Capacity (Iowa Gambling Test)				
T-score Demographically Matched	0–100	39: Impaired Decision Making Capacity 40–44: Less Than Average Decision Making Capacity 45: Nonimpaired Decision Making Capacity	46	42, 47
Attention (Flanker Test) (<i>n</i> =8)				
Percent of congruent trials correct	0–100	Higher scores indicate more attention	96	70, 98
Congruent trial reaction time (ms)		Lower scores indicate more attention	523	506, 724
Percent of incongruent trials correct	0–100	Higher scores indicate more attention	95	72, 98
Incongruent trial reaction time (ms)		Lower scores indicate more attention	534	499, 819
fMRI-Derived Neurocognitive Processing				
Empathetic Network (DMN) Task Differentiation	unlimited	Higher scores indicate greater task differentiation	0.161	0.064, 0.259
Analytic Network (TPN) Task Differentiation	unlimited		0.174	0.046, 0.240
Self-Management Variables				
Physical Activity				
Minutes in Moderate-to-Vigorous Physical Activity per week	unlimited	75–150 minutes per week	31.9 ()	0, 64.2
Steps per day	unlimited	10,000 per day	5753	4334, 9701
Dietary Intake				
Healthy Eating Index	0–100	Higher indicates better diet	45	39, 58
% of Daily Diet from Carbohydrates	0–100	Lower typically indicates better diet	50.4	40.4, 59.0

Table 3:The effect of the System Change intervention on Self-Management Outcomes ($n=29$)

	Predictors	Estimate	Std. Error	p-value
Moderate to Vigorous Physical Activity (minutes per day)	Time	-2.81	5.58	0.62
	Intervention Group	5.83	4.98	0.25
	time-by-group	-3.37	7.29	0.65
Total Healthy Eating Index 2010	Time	-8.84	4.05	0.04
	Intervention Group	-1.87	4.65	0.69
	time-by-group	10.02	5.55	0.08

Table 4:

Effect of the SystemCHANGE Intervention on fMRI-derived neurocognitive processing using linear mixed effects model

Variable	Task Positive Network			Default Mode Network		
	β Coefficient	95% Confidence Interval	p-value	β Coefficient	95% Confidence Interval	p-value
Intercept	0.16	0.08,0.23	<0.01*	0.15	0.07, 0.23	<0.01*
Intervention	-0.01	-0.10, 0.10	0.01*	0.04	-0.06, 0.15	0.47
Time	-0.13	-0.24, -0.04	0.98	0.05	-0.08, 0.18	0.45
Time-by-group interaction	0.14	0.01, 0.27	0.05*	-0.15	-0.33, 0.01	0.11