



# Meditation and Aerobic Exercise Enhance Mental Health Outcomes and Pattern Separation Learning Without Changing Heart Rate Variability in Women with HIV

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## Abstract

Mental and physical (MAP) training targets the brain and the body through a combination of focused-attention meditation and aerobic exercise. The following feasibility pilot study tested whether 6 weeks of MAP training improves mental health outcomes, while enhancing discrimination learning and heart rate variability (HRV) in a group of women living with human immunodeficiency virus (HIV) and other stress-related conditions. Participants were assigned to training ( $n = 18$ ) or no-training control ( $n = 8$ ) groups depending on their ability and willingness to participate, and if their schedule allowed. Training sessions were held once a week for 6 weeks with 30 min of meditation followed by 30 min of aerobic exercise. Before and after 6 weeks of training, participants completed the Behavioral Pattern Separation Task as a measure of discrimination learning, self-report questionnaires of ruminative and trauma-related thoughts, depression, anxiety, and perceived stress, and an assessment of HRV at rest. After training, participants reported fewer ruminative and trauma-related thoughts, fewer depressive and anxiety symptoms, and less perceived stress ( $p$ 's  $< 0.05$ ). The positive impact on ruminative thoughts and depressive symptoms persisted 6 months after training. They also demonstrated enhanced discrimination of similar patterns of information ( $p < 0.05$ ). HRV did not change after training ( $p > 0.05$ ). Combining mental and physical training is an effective program for enhancing mental health and aspects of cognition in women living with HIV, although not necessarily through variance in heart rate.

**Keywords** HIV · Trauma · Rumination · Memory · Meditation · Exercise · Heart rate variability · Pattern separation

## Introduction

Living with a chronic condition takes a toll on overall health and well-being. For example, the effects of human immunodeficiency virus (HIV) are widespread throughout the body including the brain, even with consistent regimes of antiviral medication (Asahchop et al., 2017; Kaul et al., 2001; Kovalevich & Langford, 2012). As a result, people

with HIV experience chronic problems with central and peripheral nervous system function. Living with HIV also impacts mental health, particularly among women. Women with HIV are twice as likely to experience trauma compared to women without HIV (Machtinger et al., 2012). The diagnosis itself can elicit stress-related symptoms (Katz & Nevid, 2005) as well as posttraumatic stress disorder, which accelerates viral progression (Hou et al., 2020). Up to 20% of women with HIV also meet criteria for major depressive disorder, which is four times higher than rates among non-HIV women (Morrison et al., 2002); they also are more likely to exhibit generalized anxiety disorder (Beer et al., 2019). Anxiety symptoms can exacerbate the likelihood of engaging in risk-taking behaviors (e.g., unprotected sex), living with unmet medical needs, and hospitalization (Beer et al., 2019). Health-related anxiety among women with HIV also contributes to difficulty sleeping and concentrating at school or work, as well as decreases in appetite (Schulte et al., 2018). Among women living with HIV, mental health

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issues can reduce access to HIV care and reproductive services (Orza et al., 2015).

In a previous study, we reported that women living with HIV were experiencing a relatively high degree of perceived stress in their everyday lives, as well as heightened symptoms of depression and anxiety (Millon & Shors, 2021; Nightingale et al., 2010; Yanes et al., 2012). They also indicated that they were less likely to sense and trust bodily sensations (i.e., interoceptive awareness) and had difficulty regulating thoughts and feelings related to these sensations (Millon & Shors, 2021). Black women with HIV in particular are at increased risk for major depression and suicidal behaviors, in part because they frequently experience gendered and racial discrimination (Thompson & Dale, 2021). Health disparities contribute to HIV transmission and compromise access to care, particularly within racially minoritized Black and brown communities, where HIV is most prevalent (CDC, 2011). Racially minoritized individuals living with HIV also experience racial and economic discrimination and stigma from healthcare providers (Bird & Bogart, 2001), which can limit their access and adherence to care (Pellowski et al., 2013). Furthermore, racially minoritized women are more likely to live below the poverty line and experience inequity, which can increase risk of HIV transmission and reduce adherence to HIV treatment (Pellowski et al., 2013). Overall, these racial, social, and economic factors exacerbate the physical and mental health challenges of living with HIV.

Despite the alarming statistics on the mental and physical health challenges for HIV populations, there are few available interventions or lifestyle programs that are specifically designed for people with HIV (Hutton et al., 2020). The majority of behavioral health interventions are aimed at reducing transmission and improving antiretroviral therapy adherence. Some programs focus on targeting social contextual factors linked to HIV/AIDS that provide access to clean syringes, health care and stable housing, as poverty increases the risk of acquiring HIV (Adimora & Schoenbach, 2005), but few interventions target mental health (Waldron et al., 2021). Among the intervention studies that do exist, participants are rarely followed over time, and therefore it is difficult to determine the long-term benefits. For example, cognitive-behavioral interventions reduce depression and anxiety in people with HIV but the follow-up period was brief (Spies et al., 2013).

In the present pilot study, we had the opportunity to provide an intervention to a small population of women living with HIV in the inner city of Newark, most of whom were middle-aged, lower socioeconomic status, and self-identified as Black. The program we offered is referred to as MAP Training because it combines mental and physical training. The mental training consists of 30 min of focused-attention meditation and the physical training consists of 30 min of

aerobic exercise (Shors et al., 2014). Clinical and community studies indicate that the program, when practiced over weeks, can increase aspects of mental health, especially reducing symptoms of depression and the occurrence of ruminative thoughts. For example, women with sexual violence history who engaged in 6 weeks of MAP Training reported fewer numbers of ruminative and trauma-related cognitions, as well as greater self-worth (Millon et al., 2018; Shors & Millon, 2016; Shors et al., 2018). In another study, women with substance dependence were less anxious and acquired greater cardiovascular fitness (measured as  $VO_2$ ) (Shors et al., 2014). In yet another study, the training decreased ruminative thoughts and depressive symptoms by 40% in adults with major depressive disorder, while increasing synchronized brain activity during tests for cognitive control (Alderman et al., 2016). The program also decreased perceived stress while increasing quality of life, this time in medical students (Lavadera et al., 2020). Recently, we reported that MAP Training reduced stress and improved well-being among school teachers during the COVID-19 pandemic (Demmin et al., 2021). Most importantly, the combination of meditation and aerobic exercise has been more effective for trauma and rumination than either activity alone (Shors et al., 2018). Importantly, MAP Training is not meant to be a substitute for psychotherapy or medication, but rather a behavioral health intervention that improves the fitness of the brain and body.

The MAP training program was adapted from laboratory studies indicating that mental and physical training activities in laboratory animals increase neurogenesis in the adult brain. In particular, Shors, Gould, and colleagues reported that mental training with standard learning procedures in rodents increased the survival of new neurons in the hippocampus (Gould et al., 1999), while other groups reported that physical training with aerobic exercise increased the number of new neurons that are generated in the hippocampus (van Praag et al., 1999). These findings were translated into the MAP Training program, with meditation as mental training and aerobic exercise for physical training (Millon & Shors, 2019). Neurogenesis is not measurable in the human brain while someone is alive; however, MAP Training does not necessarily depend on changes in neurogenesis for its efficacy. In previous studies, we have determined that weekly training tends to decrease depression and anxiety as well as measures of rumination and stress (Alderman et al., 2016; Lavadera et al., 2020; Shors et al., 2014, 2018). So far, however, we have not identified the mechanisms through which the combination of mental and physical training enhances mental health. In laboratory studies, animals with fewer new hippocampal neurons are reportedly less able to discriminate very similar patterns of information, whereas animals with more neurogenesis were better able to discriminate between the patterns (e.g., Clelland et al., 2009; Drew et al., 2010;

Snyder et al., 2005). These findings in animal models are supported by similar albeit indirect findings in humans (Bakker et al., 2008; Clelland et al., 2009; Kirwan et al., 2012; Lacy et al., 2011; Stark et al., 2013). Thus, we hypothesized that MAP Training would enhance discrimination learning, a process that could influence well-being in humans living with a chronic health condition.

It is reasonable to hypothesize that changes in autonomic nervous system (ANS) function may contribute. The MAP Training program activates both branches of the ANS, with most people experiencing a slow heartbeat during meditation, followed by a dramatic increase during aerobic exercise. Slow breathing during meditation increases baroreflex sensitivity and reduces sympathetic activity (Joseph et al., 2005). Conversely, high intensity aerobic exercise engages the sympathetic branch, with parallel increases in heart rate and arterial pressure via the baroreflex, thus allowing for increased blood pressure during exercise (Fu & Levine, 2013). Dramatic changes in heart rate such as these reflect a healthy ANS that can respond quickly to danger as well as physical activity and rest (e.g., Shaffer & Ginsberg, 2017). The general health of the ANS can be estimated by time variations between successive heartbeats or heart rate variability (HRV), which reflects cardiac flexibility and adaptability (Lehrer & Eddie, 2013). Pathologies like HIV can impact HRV, such that heart oscillations become more regular and noncomplex, thereby increasing risk of illness or death (Lehrer & Eddie, 2013). For example, people living with HIV experience hypersensitivity of the ANS as measured with cardiovascular reflex tests (e.g., Rogstad et al., 1999). There is also evidence that physical fitness is associated with greater HRV, as people with HIV who are more physically active exhibit lower resting heart rates, increased levels of maximal oxygen uptake, higher baroreflex sensitivity, and greater high-frequency HRV than those who are less physically active (Spierer et al., 2007). Thus, greater aerobic fitness (e.g., higher maximal oxygen uptake) might be related to higher HRV in people with HIV. However, very few studies have attempted to enhance physical health in people with HIV by targeting HRV with aerobic exercise. Black women with HIV particularly may benefit from aerobic exercise interventions that target HRV, as they exhibit significantly higher rates of abnormalities in cardiac structure and function (Mondy et al., 2011) relative to non-HIV Black women. These abnormalities are concerning because they are predictive of heart failure and all-cause mortality (e.g., Fisher et al., 2005).

HRV is measured from the electrocardiogram (ECG) or pulse, and then assessed according to time and/or frequency domains (Sayers, 1973; Shaffer & Ginsberg, 2017; Task Force, 1996). Common time measurements include the standard deviation of normal beat-to-beat intervals or SDNN (in milliseconds), which tends to reflect general autonomic

flexibility, and the root-mean-squared of standard deviation normal-to-normal or RMSSD, which reflects respiratory sinus arrhythmia, generally a measure of vagus nerve activity. Measurements related to frequency are assessed via power spectral analyses, which estimate variance in heart rhythms in specific frequency ranges (Stein & Kleiger, 1999). In a healthy heart, the parasympathetic system predominates at rest and mediates both low (0.04–0.15 Hz) and high-frequency (0.15–0.4 Hz) oscillations, to the extent that cholinergic antagonists can reduce these responses (Akselrod et al., 1981; Billman, 2013; Reyes del Paso et al., 2013; Shaffer & Ginsberg, 2017). The sympathetic system has minimal effects on high-frequency HRV, but drives the low end of the low-frequency range (Billman, 2013). Although the ratio between low and high-frequency activity has been cited as a measure of autonomic balance between sympathetic and parasympathetic branches (Pagani et al., 1984, 1986), there is evidence that it reflects parasympathetic function (Billman, 2013; Reyes del Paso et al., 2013). Low-frequency HRV in a range surrounding 0.1 Hz also can reflect activity of the baroreflex, which regulates blood pressure (Goldstein et al., 2011; Shaffer & Ginsberg, 2017) via the brainstem (Gerlach et al., 2019), while projections from frontotemporal to limbic brain regions regulate changes in mood state (e.g., Schumann et al., 2021). In the present study, we assessed both low- and high-frequency activity during ECG recording before and after the 6-week MAP Training program. Our goal was to detect potential changes in ANS function that might account for potential increases in mental health outcomes. We assessed several canonical time (e.g., SDNN, RMSSD) and frequency (e.g., low-frequency, high-frequency, low/high frequency ratio) measures.

In the present study, we recruited women living with HIV, who ranged in age from young adulthood to elderly (e.g., 60 or above). Meta-analyses on physical exercise interventions for people with HIV report high adherence rates (e.g., 75% or above) and document that exercise is safe and feasible (Dolan et al., 2006a; O'Brien et al., 2016). However, the majority of intervention studies tend to target men rather than women (Brown & Vanable, 2008; Crepaz et al., 2014; Spaan et al., 2020). Although meditation studies for people with HIV have been effective at improving mental health, adherence rates can be low (e.g., Ramirez-Garcia et al., 2019a, 2019b). Given these data, we sought to determine whether a more comprehensive mental and physical training program targeting the brain and body was beneficial and feasible for women with HIV.

## Method

### Participants and Procedure

Thirty-nine adult women with HIV ( $M_{\text{age}} = 45$  years, range 22–68 years, 95% Black/African-American, 2.5% Latina, 2.5% White) were recruited from the François-Xavier Bagnoud Center and St. Clare's Housing Program in Newark, NJ. Inclusion criteria were: (1) women over age 18; (2) HIV-positive; (3) not engaged in a regular exercise program (<3 days/wk for 20 min or less per session over the past month); (4) not engaged in any formal meditation practice (not meditating more than 30 min total per week and less than 200 h in lifetime); (5) free from physical limitations or contraindications to exercise; and (6) able and willing to provide informed consent. Exclusion criteria were those who were (1) pregnant; (2) had severe psychopathology; or (3) at high risk for suicide as determined by self-report questionnaires and the counseling supervisors at the site locations. If an individual met any of the exclusion criteria, she was compensated for her screening time and provided further resources as appropriate but did not continue further in the study.

At the start of the study, participants were attending group counseling, which continued throughout the MAP sessions; MAP was provided as an adjunct to participants' ongoing counseling and medication regimens. Following initial assessments, participants were scheduled for weekly MAP sessions for 6 weeks in a group setting. After training, participants returned for post-training assessments, and completed questionnaires 3 and 6 months post-training. Participants were assigned to training groups depending on their ability and willingness to participate, and if their schedule allowed. Training participants were compensated \$100 total for assessments and 6 weeks of training, and \$20 each for 3-month and 6-month follow-up testing. No-training controls who did not participate in the full course of training and only completed initial and follow-up assessments were paid up to \$60. Eleven women did not complete all test assessments and were omitted from data analyses; two of those were unable to return because of the COVID-19 pandemic and were compensated \$60. Eight out of 32 women who initially started in the MAP training group dropped out of training (adherence rate ~75%). Final groups numbers were  $n = 18$  for the training group and  $n = 8$  for no-training controls. All participants provided written informed consent in accordance with the Declaration of Helsinki. Procedures were approved by the Institutional Review Board at Rutgers University. All research staff were certified by the Collaboration Institutional Training Initiative (CITI) for Human Subjects Research.

### Measures

After consent, participants were assessed on outcomes as follows:

- *Trauma history*: the history of traumatic events was assessed with the Life Events Checklist for DSM-5 (LEC-5; Weathers et al., 2013). The LEC assesses exposure to 16 events related to stress and trauma, including physical and sexual assault.
- *Ruminative thoughts*: the frequency and type of ruminative thoughts were assessed with the Ruminative Responses Scale (RRS; Treynor et al., 2003). The RRS measures how often a person engages in repetitive thoughts related to the past, blame, brooding, depression, and sadness. Scores range from 22 to 88. Healthy young adults self-report rumination scores averaging around 42–44, women with sexual violence history report average scores in the 50's, and depressed individuals report scores closer to or above 60 (Millon et al., 2018; Nolen-Hoeksema et al., 1999; Shors et al., 2017).
- *Depressive symptoms*: the Beck Depression Inventory-II (BDI-II; Beck et al., 1996) assessed the severity of depressive symptoms related to sadness, guilt, and changes in appetite/weight/interest in sex. BDI scores from 0–13 indicate minimal depression, 14–19 indicate mild depression, 20 and above indicate moderate to severe depression (Beck et al., 1996).
- *Perceived stress*: the Perceived Stress Scale (PSS; Cohen et al., 1983) assessed a person's self-reported ability on how well she could handle events in the past month. PSS scores ranging from 0–13 are considered low perceived stress, 14–26 indicate moderate perceived stress, and 27–40 indicate high perceived stress.
- *Posttraumatic cognitions*: thoughts and emotions related to a very stressful past event were assessed with the posttraumatic cognitions inventory (PTCI; Foa et al., 1999). Higher PTCI scores (i.e., greater than 130) are indicative of more posttraumatic cognitions and are associated with greater numbers of PTSD symptoms (Foa & Rauch, 2004). The prompt was altered to reflect responses to a very stressful event rather than a traumatic event, because not all participants had experienced a traumatic life event.
- *Anxiety symptoms*: the Beck Anxiety Inventory (Beck et al., 1988) has been used in clinical populations to assess somatic and cognitive symptoms of anxiety. BAI scores less than 10 indicate minimal anxiety, 10–19 indicate mild to moderate anxiety, and greater than 20 indicate severe anxiety.
- *Discrimination learning*: participants completed the Behavioral Pattern Separation (BPS) task, also referred to as the Mnemonic Similarity Task (Bakker et al.,



2008; Stark et al., 2013). During the initial encoding phase, participants categorized 128 common objects as “indoor” or “outdoor” with a button press. Immediately following, participants were given a surprise recognition test in which they were shown repetitions of previously-viewed objects (64 targets), objects similar but not identical to those in the prior set (64 lures), and novel objects (64 foils). Participants were asked to categorize the items as “old”, “similar”, or “new” with a button press. There were two versions of the BPS task. Participants completed version A prior to training and version B after training. Both versions contained everyday household objects but versions A and B included different objects so as to avoid practice effects.

- *Heart rate variability (HRV)*. HRV was assessed while recording ECG during a 5-min rest period.
- *Rest period procedure*. During the rest period, participants were instructed to breath normally and count their breaths to themselves. If they lost count, they were instructed to begin counting again at one. The researcher alerted participants that they would be asked for the highest number of breaths counted at the end of the session. When the researcher verbally cued the participant, she began counting in silence until the researcher instructed the person to stop five minutes later. The researcher recorded the number of breaths the participant counted. Upon completion of the breathing task, electrodes were removed. This breathing exercise served to focus the participants’ attention on their breath, and mimicked the practice engaged during MAP Training.

### MAP Training Intervention

Each MAP training session began with 20 min of silent seated meditation, followed by 10 min of very-slow walking meditation, ending with 30 min of aerobic exercise. During the seated meditation component, participants were instructed to sit on the floor on a zafu pillow or on the edge of a straight-backed chair, with their upper torso upright. They were then instructed to place their hands together in their lap, with their right hand on the bottom and thumbs slightly touching. They were asked to either close their eyes or gaze at the floor a few feet in front of them. The participants were instructed to take a deep breath and then to focus their attention on their breath, noticing as the air travelled into and out of their body. They were instructed to breath normally while counting the pauses between the exhale and the inhale. They were to begin counting at one and when they lost count, instructed to return counting again at one. A timer was set for 20 min.

When the timer sounded, participants were instructed to move their legs around to get oxygen flowing again and then

to stand up and gather in a circle, facing in one direction. Participant were asked to focus their attention in their feet as they walked slowly in a circle, with their arms clasped loosely behind their back. Again, as their attention drifted from the point of focus, participants were instructed to notice the interruption in concentration, and return their attention to their feet. A timer was set for 10 min.

When the timer sounded, participants were instructed to place their fingers alongside their neck and to count the number of pulses in 10 s. This number was multiplied by 6 to estimate resting heart rate. Immediately following, participants engaged in a group aerobic exercise class to popular music. The choreographed exercise routines included kicking, jumping, and running in place. Participants who could not engage in high-impact activity were asked to move their arms rapidly up and down above their heads, as done during a jumping jack but without using the legs. After about 20 min of exercise, participants again took their own heart rate using their finger pressed at the neck and were encouraged to achieve at least 60% of their maximum. This number is calculated by subtracting age from 220 and multiplying by 0.6. The session ended with a 5 min cool-down, with stretching and slow walking in a circle to music.

### Data Analyses

Mental health outcomes were analyzed using the SPSS statistical package (IBM, 2019). Repeated measures analyses of variance (ANOVAs) were conducted to determine whether RRS, BDI, PTCI, PSS, and BAI scores measured at the second assessment significantly differed from scores at initial assessment ( $\alpha=0.05$ ) in those who trained ( $n=18$ ) as compared to no-training controls ( $n=8$ ).

Discrimination learning during the pattern separation task was analyzed with percent accuracy scores in response to the novel, old, and similar items. Novelty detection was calculated as the percent of novel items correctly rated as “new.” The recognition memory score was calculated as the percent of familiar objects correctly rated as “old” minus the percent of new objects incorrectly rated as “old” (i.e., hits minus false alarms). Higher recognition memory scores indicated better recognition memory ability. Repeated measures ANOVAs were performed to determine whether post-training scores changed significantly after the 6-week MAP Training program. Data from participants who performed better than 80% on the recognition memory part of the task ( $n=8$ ) were further analyzed for pattern separation, which was calculated as the difference between the percent of similar objects correctly rated as “similar” minus the percent of novel objects incorrectly rated as “similar.” Pattern separation ability is considered a higher-order cognitive process than recognition memory as individuals who are able to perform well on recognition memory are

not always able to complete pattern separation tasks (e.g., Stark et al., 2013). In general, a higher pattern separation score indicated greater discrimination learning. A negative score would emerge if a participant incorrectly categorized more novel objects as “similar” than correctly categorized similar objects as “similar.”

To analyze HRV, ECG data were collected from the wrists using a J&J Engineering C2 + physiograph. Raw ECG data were digitized at 1024 samples per second and imported to WinCPRS® (Absolute Aliens Oy, Turku, Finland) or ARTii-FACT (Kaufmann et al., 2011) to extract time intervals between R-R waves (one heartbeat to the next) or interbeat (IBI) intervals. Kubios HRV software was used to analyze events during beat-to-beat intervals as follows (Tarvainen et al., 2014): standard deviation of normal-to-normal interbeat intervals (SDNN; msec), root-mean-square of differences between successive normal-to-normal interbeat intervals (RMSSD; msec), low-frequency power (msec<sup>2</sup>), high-frequency power (msec<sup>2</sup>) and the ratio of low-/high-frequency HRV. R-waves were visually inspected for movement artifacts or electrical noise for each participant in Kubios. Three participants' data were removed from analyses due to movement or noise, leaving a sample of 15 for analysis. HRV measures were normalized using log transformations. Paired t-tests were performed to determine whether HRV outcomes significantly changed after training when compared to before training ( $n = 15$ ).

## Results

### Trauma History and Mental Health Outcomes

Eighteen women (67%) reported a history of physical and/or sexual assault whereas nine women (33%) reported no history, as assessed with the LEC. Prior to the MAP Training program, mental health outcome measures extracted from the BDI, BAI, PSS, PTCI were not different between groups,  $p$ 's > 0.05. However, RRS scores at baseline were significantly higher among no-training controls ( $M = 49$ ,  $SE = 4$ ) when compared to those in the training group prior to the intervention ( $M = 35$ ,  $SE = 5$ ),  $p = 0.03$ .

There was a significant interaction between training group and time for both RRS (ruminative thoughts) and BDI (depressive symptoms) scores. RRS scores decreased by 19% post-training ( $M = 40$ ,  $SE = 3$ ) versus pre-training ( $M = 49$ ,  $SE = 4$ ), [ $F_{(1, 24)} = 17.37$ ,  $p = 0.00$ , partial  $\eta^2 = 0.42$ ]. (Fig. 1A). BDI scores decreased by 41% post-training ( $M = 11$ ,  $SE = 2$ ) versus pre-training ( $M = 19$ ,  $SE = 2$ ), [ $F_{(1, 24)} = 4.83$ ,  $p = 0.04$ , partial  $\eta^2 = 0.17$ ] (Fig. 1B).

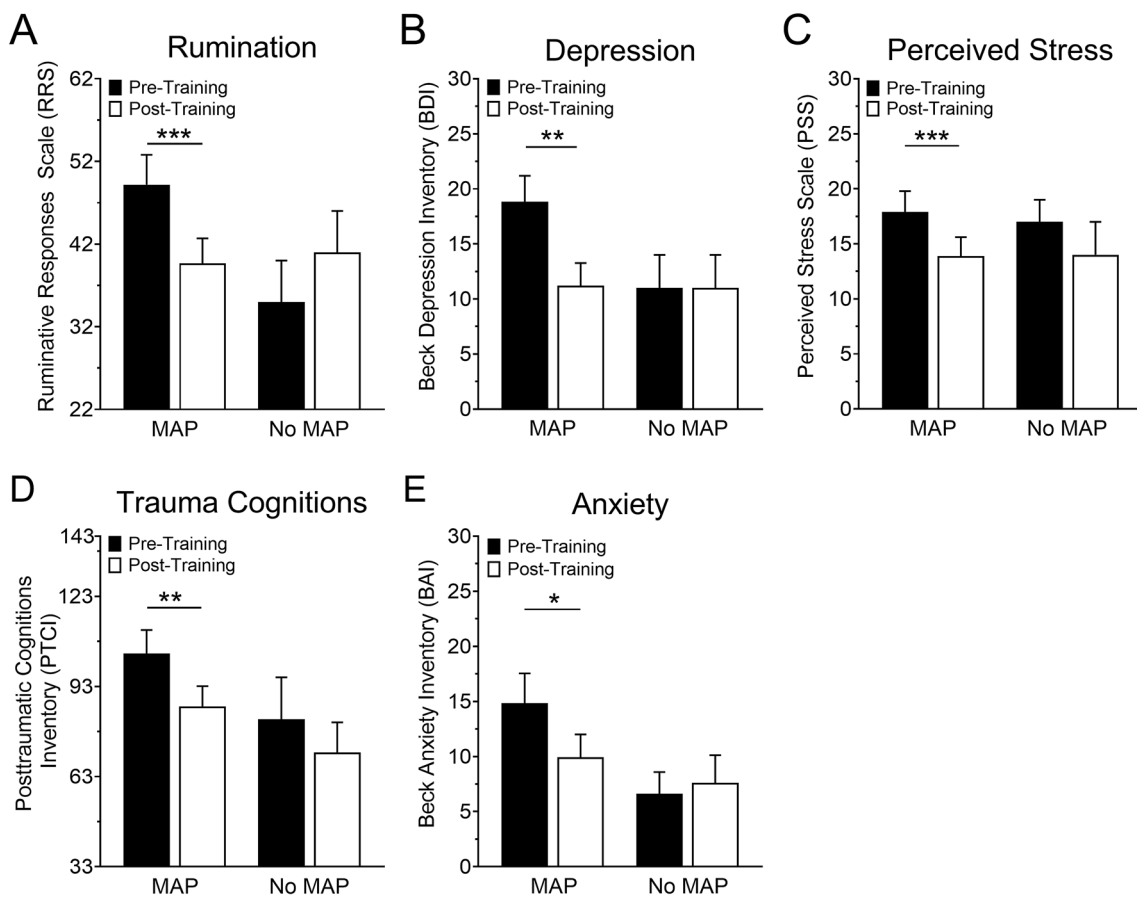
Pairwise comparisons indicated PSS (perceived stress) scores were reduced post-training ( $M = 14$ ,  $SE = 2$ ) versus

pre-training ( $M = 18$ ,  $SE = 2$ ), [ $F_{(1, 24)} = 8.87$ ,  $p = 0.01$ , partial  $\eta^2 = 0.27$ ] (Fig. 1C) but not for those who did not train ( $p = 0.21$ ). There was not a significant group by time interaction for PSS scores,  $p = 0.41$ . Pairwise comparisons indicated PTCI (post-traumatic thoughts) scores were reduced 17% post-training ( $M = 86$ ,  $SE = 7$ ) versus pre-training ( $M = 104$ ,  $SE = 8$ ), [ $F_{(1, 24)} = 6.67$ ,  $p = 0.02$ , partial  $\eta^2 = 0.22$ ] (Fig. 1D) but not for those who did not train ( $p = 0.25$ ). There was not a significant group by time interaction for PTCI scores,  $p = 0.54$ . Similarly, MAP Training reduced the BAI (anxiety) scores by approximately 33%, when comparing post-training ( $M = 10$ ,  $SE = 2$ ) to pre-training ( $M = 15$ ,  $SE = 3$ ), [ $F_{(1, 24)} = 4.99$ ,  $p = 0.04$ , partial  $\eta^2 = 0.17$ ] (Fig. 1E). There was not a significant group by time interaction for BAI scores,  $p = 0.15$ .

RRS, BDI and PSS scores were re-assessed 3 months ( $n = 17$ ) and 6 months ( $n = 6$ ) following the end of training. (PTCI and BAI scores were not assessed at 3-month and 6-month follow-up to reduce participant burden). The decrease in RRS scores remained significant at 6-month follow-up ( $M = 36$ ,  $SE = 5$ ),  $t(5) = 2.89$ ,  $p = 0.03$ , Cohen's  $d = 1.18$  but not at 3-month follow-up ( $M = 42$ ,  $SE = 3$ ),  $p = 0.24$ . However, scores were reduced by 16% at 3-month follow-up and by 27% at 6-month follow-up (Fig. 2A). The decrease in BDI scores remained at 3-month ( $M = 10$ ,  $SE = 2$ ),  $t(16) = 3.79$ ,  $p = 0.002$ , Cohen's  $d = 0.76$ , and 6-month ( $M = 8$ ,  $SE = 3$ ),  $t(5) = 3.57$ ,  $p = 0.016$ , Cohen's  $d = 1.21$ , follow-up, with a nearly 50% decrease at 3-month follow-up. The reduction in perceived stress after training was not sustained at 3-month or 6-month follow-up (Fig. 2C).

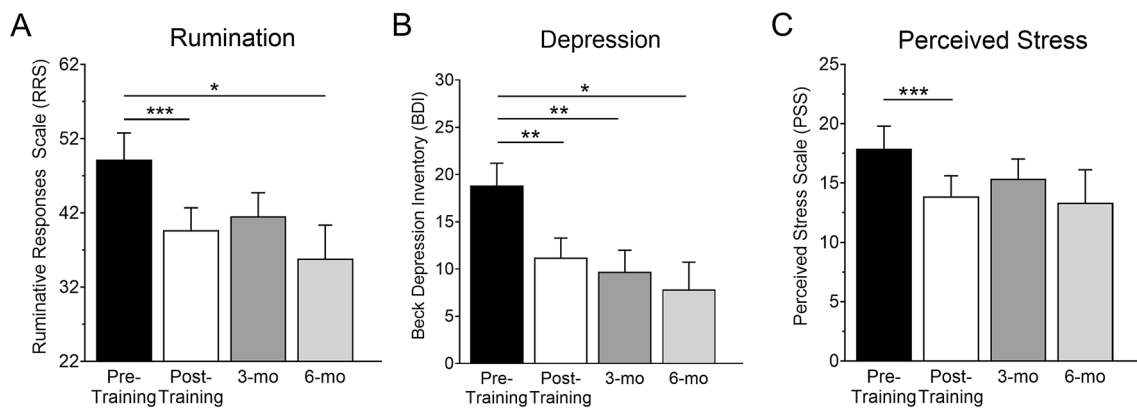
### Discrimination Learning with a Pattern Separation Task

Novelty detection accuracy (the percentage of correct responses to novel objects) and pattern separation accuracy (the percentage of correct responses to similar objects) scores did not significantly differ between groups before training,  $p$ 's > 0.05 (Table 1). Novelty detection accuracy did not significantly change after training ( $M = 0.62$ ,  $SE = 0.06$ ) compared to before training ( $M = 0.70$ ,  $SE = 0.05$ ), [ $F_{(1, 22)} = 0.55$ ,  $p = 0.47$ , partial  $\eta^2 = 0.02$ ] (Fig. 3B). Participants who were at least 80% accurate during recognition memory were selected for further analyses ( $n = 8$ ) and their pattern separation scores increased after training,  $t(7) = -2.53$ ,  $p = 0.04$ , Cohen's  $d = 0.89$  (Fig. 3C). Correlations between the pattern separation scores and mental health outcomes were not significant ( $p$ 's > 0.05).



**Fig. 1** Women with HIV reported significantly fewer **A** numbers of ruminative thoughts and **B** symptoms of depression compared to women who did not train with 6 weeks of combined meditation and aerobic exercise. Women who trained also reported significant reduc-

tions in **C** perceived stress, **D** trauma-related cognitions, and **E** anxiety symptoms, while responses in women who did not train did not change. \* $p < 0.05$ , \*\* $p < 0.01$ , \*\*\* $p < 0.001$



**Fig. 2** **A** Decreases in rumination as assessed with the Ruminative Responses Scale persisted for 6 months but not 3 months. **B** Decreases in depressive symptoms as assessed with the Beck Depression Inventory persisted 3 months and 6 months after training. **C**

Decreases in perceived stress as assessed with the Perceived Stress Scale decreased after training but not 3 months and 6 months after training. \* $p < 0.05$ , \*\* $p < 0.01$ , \*\*\* $p < 0.001$

**Table 1** Group means and standard deviations (in parentheses) for percent endorsed for each stimulus and response type, and recognition memory and pattern separation scores

	Targets (old)				Lures (similar)				Folios (new)				Recognition memory		Pattern separation
	Old		New		Old		New		Old		New		Similar	New	
	Similar	New	Similar	New	Similar	New	Similar	New	Old	New	Similar	New			
<b>Training</b>															
Baseline	0.81(0.12)	0.13 (0.09)	0.06 (0.05)	0.54 (0.21)	0.32 (0.22)	0.14 (0.09)	0.10 (0.15)	0.20 (0.14)	0.69 (0.18)	0.71 (0.21)	0.12 (0.24)				
Follow-up	0.73 (0.19)	0.19 (0.13)	0.08 (0.08)	0.52 (0.17)	0.38 (0.19)	0.10 (0.06)	0.14 (0.20)	0.23 (0.13)	0.63 (0.24)	0.59 (0.31)	0.15 (0.23)				
<b>No training</b>															
Baseline	0.57 (0.28)	0.25 (0.24)	0.18 (0.14)	0.45 (0.18)	0.34 (0.28)	0.22 (0.15)	0.20 (0.17)	0.25 (0.22)	0.55 (0.23)	0.36 (0.35)	0.09 (0.11)				
Follow-up	0.40 (0.35)	0.28 (0.25)	0.32 (0.31)	0.30 (0.27)	0.33 (0.24)	0.36 (0.25)	0.15 (0.13)	0.30 (0.19)	0.56 (0.22)	0.25 (0.42)	0.03 (0.16)				

Data from training ( $n = 18$ ) and no-training ( $n = 8$ ) groups at baseline and follow-up testing 6 weeks apart

## Physiological Outcomes

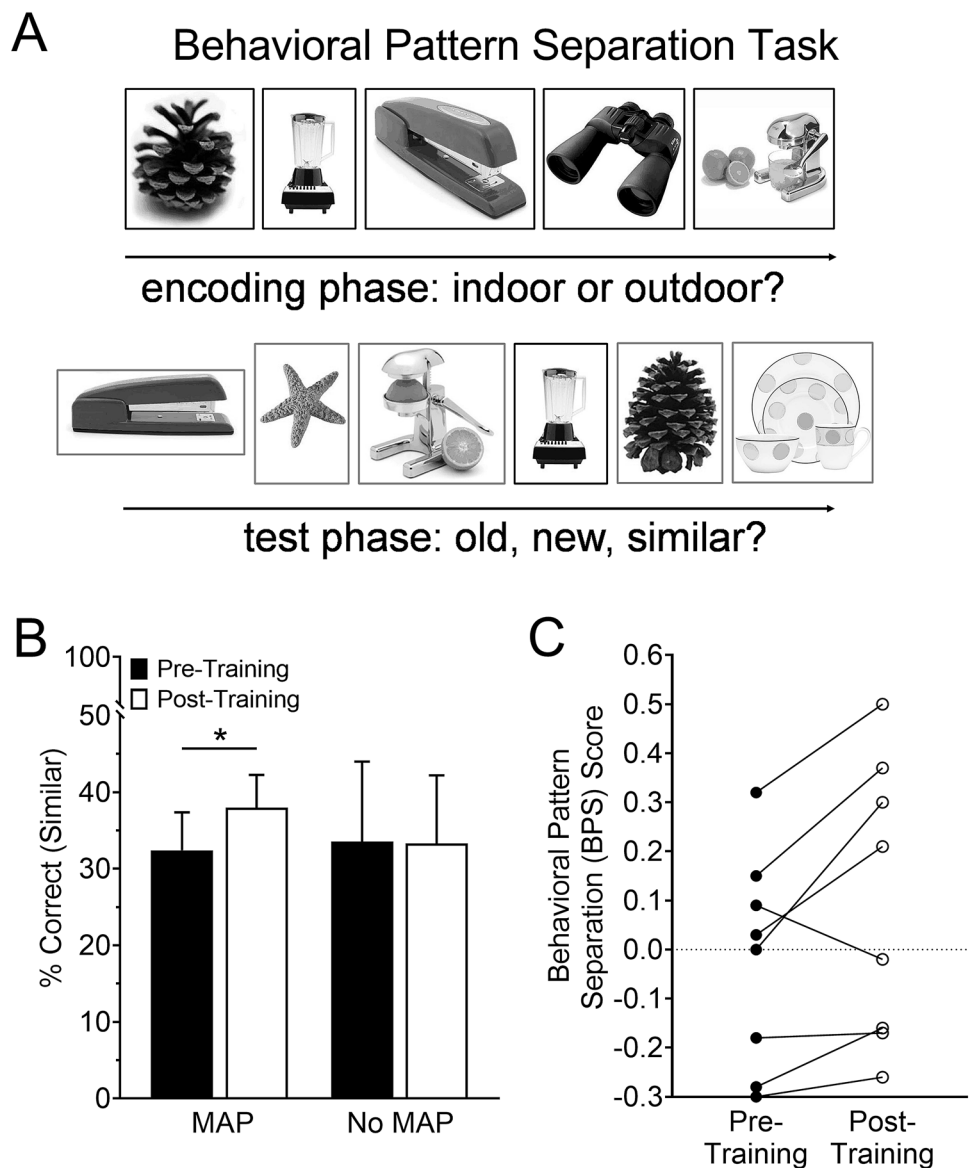
HRV measures were analyzed in women who engaged in 6 weeks of combined silent meditation and aerobic exercise training. None of the HRV measures changed significantly after training ( $p$ 's > 0.05). Group means, standard deviations, standard errors of means, and effect sizes of HRV outcomes are reported in Table 2. Total number of breaths counted during the 5-min rest period did not change as a result of training,  $t(10) = -0.27$ ,  $p > 0.05$ .

## Discussion

Living with a chronic condition such as HIV impacts the brain and the body, contributing to disruptions in mental and physical health (Gore-Felton & Koopman, 2008; Ivanova et al., 2012; Looby et al., 2018). Here we were interested in determining whether an intervention that targets both mental and physical health would benefit women living with HIV. The program, known as MAP Training and trademarked as *MAP Train My Brain*<sup>TM</sup> combines 30 min of mental training with meditation followed by 30 min of aerobic exercise. Similar interventions have proved appealing for people living with HIV. For example, a meta-analysis of physical exercise interventions for people with HIV report high adherence rates (e.g., 75% or above; Dolan et al., 2006a, 2006b; O'Brien et al., 2016), although adherence for meditative practices were less robust (Ramirez-Garcia et al., 2019b). To date, most interventions for people with HIV have targeted men (Brown & Vanable, 2008; Crepez et al., 2014; Spaan et al., 2020). Given these limitations, we tested whether a relatively simple and cost-effective intervention that combines both mental and physical training would benefit women with HIV who were living in Newark, New Jersey and who frequented clinics in the area for their antiviral medication and clinical support. In this study, women who engaged in the program once a week for 6 weeks reported significantly fewer depressive and anxiety symptoms as well as significantly less perceived stress. They also reported fewer ruminative and traumatic thoughts after training. The effects on rumination and depression were long-lasting, persisting up to 6 months after the training. The only measure that did not persist over time was that of perceived stress, which reflects feelings of stress during recent and present day life. The majority of participants reported that they continued the program after the 6 weeks of training, supporting study feasibility. Thus, the intervention seems to induce relatively long-lasting effects in overall mental health with and without continued practice and with the exception of perceived stress, potentially as it is a measure of more recent and present day experience.



**Fig. 3** **A** Behavioral Pattern Separation Task adapted from Stark and colleagues (2013). Participants initially encoded a series of everyday objects. The encoding phase was immediately followed by a surprise recognition test that had 64 identical images to those from the encoding phase (old), 64 novel objects not previously seen, and 64 objects similar to what participants had seen before in the encoding phase but not exactly the same. **B** Women with HIV who engaged in 6 weeks of training significantly improved on pattern separation accuracy (assessed by the percentage of correct responses to similar items), while performance in women who did not train did not change  $*p < 0.05$ . **C** Women with HIV with recognition memory scores of 80% or above prior to training ( $n = 8$ ) were assessed on pattern separation scores (calculated as the percentage of correct responses to similar objects minus the percentage of incorrect similar responses to novel objects). Their performance improved after 6 weeks of combined meditation and aerobic exercise training ( $p < 0.05$ )



In a previous study with this population, women who reported a greater tendency to ruminate also reported higher levels of perceived stress, as well as greater numbers of anxiety and depressive symptoms, suggesting there is a relationship between these outcomes within individuals (Millon & Shors, 2021). A factor analysis of these data identified a primary factor, which we termed “mental health” because it accounted for about 66% of the variance for all the mental health outcomes. This factor accounted for 94% of the variance in ruminative thoughts, as well as most of the variance in the measures of anxiety and depression reported by the individuals (Millon & Shors, 2021). Thus, rumination emerged as an especially strong predictor of overall mental health and may be a target for improving other mental health symptoms related to stress and trauma, including those that emerge while living with HIV. In the present study, women

with HIV did report a relatively high degree of ruminative thoughts that decreased by nearly 20% in those who completed the 6-week training program. This effect was significant and similar to other reports with differing populations engaging in the same training program (Alderman et al., 2016; Lavadera et al., 2020; Shors et al., 2018). Thus, targeting rumination may be a useful strategy for decreasing other measures of stress, including those related to depression and anxiety.

**MAP Training Enhanced Discrimination Learning/ Pattern Separation**

Pattern separation is a type of discrimination learning that is used to describe a computational process that transforms similar inputs into distinct, non-overlapping outputs (Marr,

**Table 2** Heart rate variability measures (log-transformed) prior to and after combined meditation and aerobic exercise training ( $n = 15$ )

	Pre-training			Post-training			<i>p</i>	Cohen's <i>d</i>
	Mean	SD	SEM	Mean	SD	SEM		
SDNN	3.14	0.67	0.17	3.18	0.65	0.17	>0.05	0.09
RMSSD	3.16	0.79	0.20	3.19	0.78	0.20	>0.05	0.06
VLF Power (ms <sup>2</sup> )	3.33	1.23	0.32	3.07	0.90	0.23	>0.05	0.21
LF Power (ms <sup>2</sup> )	5.21	1.19	0.31	5.31	1.17	0.30	>0.05	0.09
HF power (ms <sup>2</sup> )	5.40	1.55	0.40	5.27	1.53	0.40	>0.05	0.13
LF/HF ratio	-0.20	0.77	0.20	0.05	0.91	0.24	>0.05	0.23

1971; McClelland et al., 1995). This type of learning is often associated with the anatomy of the hippocampal formation and the presence of newly generated neurons in the dentate gyrus (e.g., Clelland et al., 2009; Drew et al., 2010; Snyder et al., 2005). To explore this relationship in humans, Stark and colleagues developed the Behavioral Pattern Separation Task, also known as the Mnemonic Similarity Task (Bakker et al., 2008; Clelland et al., 2009; Kirwan et al., 2012; Lacy et al., 2011; Stark et al., 2013). We used this task in the present study. Before and after the 6-week training program, participants were asked to detect differences in objects that were either the same or slightly different from objects they had viewed beforehand. The participants who completed the training and performed well on the recognition aspect of the task were better able to discriminate between very similar patterns of information (Fig. 3). It is not clear how such a change in learning would translate into the everyday lives of participants living with HIV. Most of the participants experienced past traumas and were currently experiencing trauma-related cognitions while living in an inner city environment. Thus, it is hypothesized that even a minor enhancement in this kind of skill learning may have some benefit, as people navigate in an environment within which they must distinguish between potentially dangerous contexts and those that are similar but safe (e.g., Jovanovic et al., 2012; Sangha et al., 2020; Thome et al., 2018).

As noted, learning to discriminate similar patterns of information is most often associated with the hippocampus, a part of the brain used for generating new memories (Bakker et al., 2008; Clelland et al., 2009; Kirwan et al., 2012; Lacy et al., 2011; Stark et al., 2013). But the mental and physical activities that were used in the MAP Training intervention likely activate multiple brain regions. For example, the practice of meditation alone engages a broad range of executive and/or cognitive control networks (e.g., dorsolateral prefrontal cortex, inferior frontal gyrus), as does aerobic exercise alone (Ji et al., 2017; Voss et al., 2010; Weng et al., 2017). In contrast, engaging in ruminative thinking reportedly decreases activity in similar regions, while increasing activity in regions involved in self-referential thinking, especially within the temporal lobe (Kaiser et al., 2019; Nejad et al., 2013, 2019; Zhou et al., 2020).

Perhaps the intervention preferentially engages networks engaged in cognitive control processes to reduce ruminative thinking and enhance aspects of cognition, including the improvement in pattern separation that we report here. For example, the medial temporal lobe was reportedly more active while people were engaging in the pattern separation task used in the present study (Nash et al., 2021). Although speculative at this point, interventions that enhance activity in medial temporal brain regions might be beneficial not only for discrimination learning but also for breaking away from cognitive processes involved in rumination.

To date, most intervention studies aimed at enhancing cognition in people with HIV have been conducted in men. For example, men with HIV who regularly exercised performed better on a motor speed task compared to men who did not exercise (Honn et al., 1999); similar effects were observed for working memory (Dufour et al., 2013). Men with HIV reported fewer cognitive problems after a randomized control trial of weekly aerobic and resistance training over 6 months (Fillipas et al., 2006). However, these effects may depend on the type of activity. One study reported no change in cognition after a yoga intervention, which was not aerobic (Quigley et al., 2020). Therefore, the increase in pattern separation in women with HIV reported here is novel. However, we had access to a relatively small group and after eliminating those who did not perform well on the basic memory skills, it was a smaller sample. Nonetheless, the changes were significant and perhaps meaningful for their ability to distinguish between similar patterns of information in their everyday lives.

### Heart Rate Variability Related to Aerobic Exercise and Meditation

In contrast to the broad effect on mental health outcomes, there was no appreciable change in any measure related to HRV. Several outcomes were assessed including canonical time (e.g., SDNN, RMSSD) and frequency (e.g., low-frequency, high-frequency, low/high frequency ratio) measures. In general, these measures provide an estimate of the health of the ANS and its ability to respond adaptively to stressors in the environment. Changes in HRV following short-term

physical training depend on a variety of factors, including the duration and type of training, as well as a person's baseline vagal and sympathetic activity prior to training (e.g., Grässler et al., 2021). A positive response to MAP Training, and in particular an increase in high-frequency HRV, might have indicated greater parasympathetic activation of the ANS, and potentially decreased risk for related physical health issues such as cardiovascular disease.

The absence of a meaningful change was somewhat surprising but not entirely unexpected. HRV is often used as an indicator of overall physical health because people who are more aerobically fit tend to have higher HRV (e.g., De Meersman, 1993), while those with heart disease and other risk factors have less (Kleiger et al., 1987; Tsuji et al., 1994; Vaishnav et al., 1994). Some studies suggest that mental health is also related to HRV, and those with depression exhibit reduced HRV (Sgoifo et al., 2015). Certainly, aerobic training can increase HRV (e.g., Reardon & Malik, 1996). For example, post-menopausal women who regularly endurance trained (quantified as running an average of 32 miles per week) had greater HRV compared to women who did not regularly exercise (Davy et al., 1996). However, it is difficult to change HRV with one session a week for 6 weeks (Davy et al., 1996; Masroor et al., 2018). Most studies indicate that more sustained exercise is necessary to change HRV. For example, HRV increased with training five times a week for four weeks in sedentary middle-aged women (Masroor et al., 2018). Another study reported greater SDNN in people living with HIV following eight weeks of aerobic exercise, practiced three times a week (Quiles et al., 2020), but no difference in frequency-domain measures of HRV (Quiles et al., 2020). Another study assessed HRV prior to, during, and after 20 min of treadmill exercise (performed at 60% of maximum oxygen intake) (Borges et al., 2012). People with HIV had less SDNN and low- and high-frequency HRV at rest, as well as significantly less low- and high-frequency HRV compared to controls (Borges et al., 2012).

It is hard to compare our data to others who have assessed HRV in HIV populations because there are so few studies and most were conducted in men. The SDNN and low-frequency HRV measures reported in our study were lower than those reported by Borges and colleagues (2012); however, only three females participated. For the most part, men have higher HRV than women (e.g., Koenig & Thayer, 2016) though age is also a factor (Stein et al., 1997). The SDNN values in our study were also lower than those reported by Quiles and colleagues (2020), both before and after their aerobic exercise intervention. Also, we did not measure HRV in people without HIV so we are not able to report on the impact of HIV itself on HRV; however, others have reported decreased low- and high-frequency HRV in people with AIDS (Neild et al., 2000). With respect to meditation, effects on HRV are even less consistent (Amihai &

Kozhevnikov, 2014; Cysarz & Büssing, 2005; Lehrer et al., 1999; Léonard et al., 2019). In summary, 6 weeks of MAP Training were not sufficient to alter persistently common measures of HRV and thus are unlikely to account for the improvement in mental health outcomes that were observed here and in our other studies (Alderman et al., 2016; Lavadera et al., 2020; Shors et al., 2014, 2018).

## Feasibility and Limitations

This pilot study demonstrated that 6 weeks of combined meditation and aerobic exercise is beneficial for women living with a chronic virus in an urban city, many of whom were suffering from a variety of mental and physical health challenges. Yet, there were several limitations to the study. First, we did not test participants without HIV and therefore, cannot compare our results to those in people without HIV. In addition, the study was not a randomized control trial and sample sizes were unequal. We did retain ~75% of the sample throughout the study, which is a higher rate than reported in prior studies with this intervention (Alderman et al., 2016; Shors et al., 2018). Although most outcome measures did not differ between groups prior to training, the women who volunteered for the training did report more ruminative thoughts, which might have accounted for their willingness to participate in training. In addition, we did not assess other measures of cognition, in part because of time limitations. There was no change in novelty detection or recognition memory as a result of training. Finally, we did not collect data on viral load or CD4 cell counts, and therefore are not able to determine whether training improved physical health indicators of HIV status.

## Conclusion

Overall, a combination of mental and physical exercise, known as MAP Training, appears to be an effective therapy for women who live each day with a chronic disease that impacts the health of their brain and body. In particular, this pilot study demonstrated that an intervention that targets mental and physical health is feasible for a female HIV population suffering from multiple stressors to their physical and mental health and living with few socioeconomic resources. Mental health outcomes, including ruminative and trauma-related thoughts, as well as symptoms of depression, anxiety, and perceived stress, were significantly reduced after 6 weeks of training with meditation and aerobic exercise. HRV did not change after training, but learning to discriminate very similar patterns of information was enhanced. The MAP Training program is relatively easy to implement and it does not depend on extraordinary finances or specialized

equipment. Based on the pilot data presented here, it may be a manageable fitness program for people who are living with a chronic illness and have limited resources for maintaining everyday health and wellness.

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## Declarations

**Conflict of interest** The authors declare that they have no conflict of interest.

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