

Review

Mental and Physical (MAP) Training: A neurogenesis-inspired intervention that enhances health in humans [☆]Tracey J. Shors ^{a,b,d,*}, Ryan L. Olson ^c, Marsha E. Bates ^e, Edward A. Selby ^b, Brandon L. Alderman ^c^a Behavioral and Systems Neuroscience, Rutgers University, United States^b Department of Psychology, Rutgers University, United States^c Department of Exercise Science, Rutgers University, United States^d Center for Collaborative Neuroscience, Rutgers University, United States^e Center of Alcohol Studies, Rutgers University, United States

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ABSTRACT

New neurons are generated in the hippocampus each day and their survival is greatly enhanced through effortful learning (Shors, 2014). The numbers of cells produced can be increased by physical exercise (van Praag, Kempermann, & Gage, 1999). These findings inspired us to develop a clinical intervention for humans known as Mental and Physical Training, or MAP Training. Each session consists of 30 min of mental training with focused attention meditation (20 min sitting and 10 min walking). Meditation is an effortful training practice that involves learning about the transient nature of thoughts and thought patterns, and acquiring skills to recognize them without necessarily attaching meaning and/or emotions to them. The mental training component is followed by physical training with 30 min of aerobic exercise performed at moderate intensity. During this component, participants learn choreographed dance routines while engaging in aerobic exercise. In a pilot “proof-of-concept” study, we provided supervised MAP Training (2 sessions per week for 8 weeks) to a group of young mothers in the local community who were recently homeless, most of them having previously suffered from physical and sexual abuse, addiction, and depression. Preliminary data suggest that MAP Training improves dependent measures of aerobic fitness (as assessed by maximal rate of oxygen consumed) while decreasing symptoms of depression and anxiety. Similar changes were not observed in a group of recently homeless women who did not participate in MAP Training. It is not currently possible to determine whether new neurons in the human brain increase in number as a result of MAP Training. Rather these preliminary results of MAP Training illustrate how neuroscientific research can be translated into novel clinical interventions that benefit human health and wellness.

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1. Introduction

Tens of thousands of new neurons are produced each day in a “normal” adult brain. Many of these cells are produced in the hippocampus, a brain region necessary for various types of learning (Fig. 1A). The cells are produced in a part of the hippocampus known as the dentate gyrus, whose primary neuronal phenotype is the granule neuron (Fig. 1B). Once the new cells differentiate into granule neurons (Fig. 1C), they produce axons and dendrites and eventually express action potentials, as they become incorporated into the rest of the brain (van Praag et al., 2002). In animal studies, it has been determined that newly-generated cells in the dentate

gyrus are especially responsive to environmental conditions that humans often experience (Fig. 2; Shors, Anderson, Curlik, & Nokia, 2011). For example, stressful life experiences significantly decrease cell production as does daily drinking of moderate amounts of alcohol, an amount comparable to the legal driving limit (Anderson, Nokia, & Shors, 2012). However, not all life experiences decrease cell production in animal models. Most notably, aerobic exercise greatly increases the number of cells that are made. Animals that are given the opportunity to run on a daily basis can produce nearly twice as many new cells as sedentary controls (van Praag, Kempermann, & Gage, 1999).

2. Neurogenesis and effortful learning

The newly-generated cells in the hippocampus do not necessarily survive. Indeed, more than half of them die and do so within

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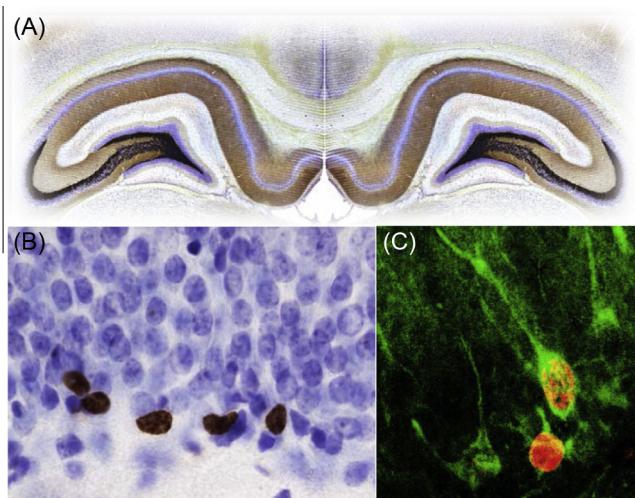


Fig. 1. The hippocampus (A; Timm stain; Shors, 2014) produces thousands of new neurons each day (B). The new cells (shown labeled with BrdU in brown) reside in the granular layer of the dentate gyrus (B; Shors, 2014). If they survive and many do in response to learning, most differentiate and mature as granule neurons (double labeled with BrdU in red and TuJ1 in green; Leuner et al., 2004). (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

several weeks of being born, often before they have fully differentiated into neurons (Anderson, Sisti, Curlik, & Shors, 2011). Nevertheless, a great number of these newly-generated cells can be “rescued” from death if animals engage in an effortful learning experience. In 1999, Drs. Shors and Gould reported that new neurons in the rat hippocampus are rescued from death by new learning and may even be involved in learning (Gould, Beylin, Tanapat, Reeves, & Shors, 1999; Shors, 2001). Since then, it has been determined that not all types of training keep new neurons alive. Rather training tasks that are difficult to learn are the most effective (Curlik & Shors, 2011; Waddell, Anderson, & Shors, 2010; Waddell & Shors, 2008). Moreover, learning itself is critical. Animals that learn well retain more cells than animals that are trained but do not learn as well (Dalla, Bangasser, Edgecomb, & Shors,

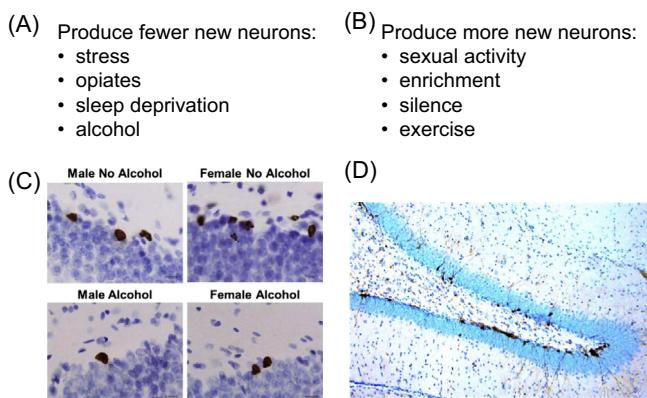


Fig. 2. Numbers of new neurons in the rodent hippocampus decrease after stressful life experience (Kozorovitskiy & Gould, 2004), opiate use (Eisch, Barrot, Schad, Self, & Nestler, 2000), sleep deprivation (Hairston et al., 2005) and alcohol consumption (Nixon & Crews, 2002) (A), while numbers increase with sexual activity (Leuner, Glasper, & Gould, 2010), environmental enrichment (Kempermann, Kuhn, & Gage, 1997), silence (Kirste et al., 2013) and physical exercise (Fabel et al., 2009; van Praag et al., 1999) (B). Fewer new cells were produced in response to moderate amounts of alcohol. New cells are shown labeled with BrdU (brown) in both males and females (Anderson et al., 2012) (C) while intense exercise training produced more new neurons. New neurons (brown) are shown labeled with doublecortin (Nokia et al., 2014) (D). (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

2007). Within animals, those that learn but require more trials of training to learn, retain more of the new cells (Curlik & Shors, 2011; Waddell & Shors, 2008). Overall, these data indicate that learning keeps new neurons alive, provided that the training experience is both effortful and successful.

Learning a new physical skill can also increase the survival of new neurons in the hippocampus (Curlik, Maeng, Agarwal, & Shors, 2013; Fig. 3). During one such task, a laboratory rodent learns to balance on a rod as it rotates faster and faster during one trial of training. Over trials, the animals learn to remain on the rod, despite the increase in speed. Learning this type of motor skill might be comparable to mastering a new sport or learning a new dance routine in humans (Sherwood & Jeffery, 2000). Training with the physical motor skill increased the number of surviving neurons in the adult hippocampus. Consistent with previous studies, only animals that learned the new skill retained the new cells. Animals that did not learn retained only as many new cells as those that were not trained. Also consistent with previous findings, we determined that the task conditions must be sufficiently difficult to learn in order to rescue the new cells from death. For example, training on a relatively easy version of the task, during which the rod rotates slowly and consistently throughout a trial does not increase the number of surviving cells. Finally, *individual differences in performance were once again important*. Animals that learned well retained the most new neurons. Together these various studies indicate that learning can rescue new neurons from death but the experience must be new and effortful – and learning itself must occur. These effects on cell survival were not attributable to exercise, *per se*. Animals that exercised during the same time period did not retain more cells than animals that did not exercise.

To summarize, behaviors such as aerobic exercise increase the production of new neurons in the adult hippocampus while effortful and successful learning keeps a significant number of those cells alive (Curlik and Shors, 2011). As noted, once the new cells are rescued from death, they remain in the hippocampus for months at least, by which time they have acquired the characteristics of mature neurons, including the ability to produce action potentials (Leuner et al., 2004; van Praag et al., 2002). Because humans also generate new neurons throughout life (Eriksson et al., 1998; Mangunas et al., 2007; Spalding et al., 2013), it is assumed that aerobic exercise increases their numbers as it does in rodents and indirect evidence supports this premise. For example, exercise training on a treadmill increased blood flow to the human dentate gyrus (Pereira et al., 2007) and similar exercise regimens have increased hippocampal volume (Erickson et al., 2011). With respect to learning, it is assumed that effortful training procedures which engage skill learning would, in turn, keep a great number of newly-generated cells alive in the hippocampus, although this particular assumption cannot be tested in humans at this point in time. Based on these laboratory studies and assumptions, we developed a clinical intervention that combines mental and physical training, referred to as MAP Training.

3. The MAP Training intervention

MAP Training is a clinical and practical intervention, which was inspired by research connecting neurogenesis with learning and exercise. This intervention is based on animal laboratory studies demonstrating that physical exercise increases the number of cells produced while mental training keeps the cells alive (Fig. 4; Curlik and Shors, 2013; van Praag et al., 1999). We propose that the combination of the two activities is better than either one alone, again based on evidence that new neurons are kept alive by learning once they are produced. For the intervention, we chose activities that humans can readily engage in and yet are known to enhance mental and physical health (Chiesa & Serretti, 2010; Davidson & McEwen,

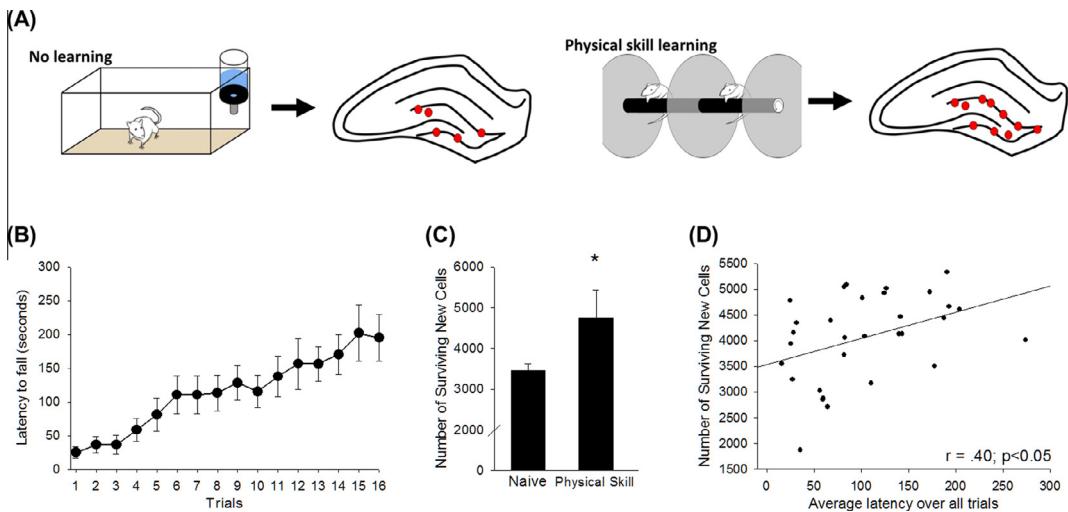


Fig. 3. Animals were not trained (No learning) or provided the opportunity to learn a new physical skill (Physical skill learning). During training, rodents learned to remain on a rod that rotated faster and faster during each trial (A). They learned to remain on the rod longer over trials of training (B). Those that were trained and learned (Physical Skill) retained more newly-generated cells than those that were not trained (Naive) (C). Those that learned well retained more new cells than those that did not learn well (D) (Adapted from [Curlik and Shors, 2013](#) and [Curlik et al., 2013](#)).

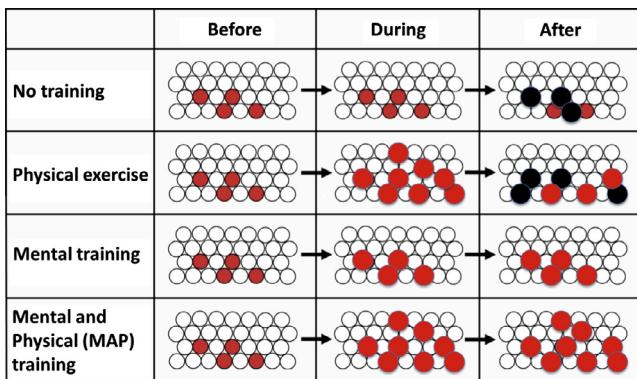


Fig. 4. MAP Training in humans was translated from laboratory studies about neurogenesis in the hippocampus. With no training, many new cells (red filled circles) die (black filled circles) in the dentate gyrus of the hippocampus. With physical exercise, more are produced, but some still die. With mental training, most cells survive as long as the process is effortful and learning occurs. Theoretically, a combination of physical exercise and mental training which is sustained over time should increase the number of new neurons that ultimately reside in the adult brain (adapted from [Curlik and Shors, 2013](#)). (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

2012; Herring, Puetz, O'Connor, & Dishman, 2012; Heyward, 1998; Hofmann & et al., 2010; Kabat-Zinn, 1990; van Vugt, Hitchcock, Shahar, & Britton, 2012). Our goal was to translate the neurogenesis/learning data into a clinical intervention that can be easily disseminated and practiced by everyone in our community. Therefore, we did not choose eyeblink conditioning or spatial maze learning because those training tasks would not be especially easy to administer in humans and they would not necessarily provide "new" learning experiences across repeated training sessions (Nokia, Sisti, Choski, & Shors, 2012). But more importantly, we wanted to provide the participants with an opportunity to learn new skills that once acquired, they could continue to use in their everyday lives to maintain increases in mental and physical health outcomes.

4. MAP Training methods

For the mental training component, participants engaged in the practice of focused attention meditation. We chose this particular

meditation procedure, because it is challenging to learn and practice. (Recall that new neurons in animal models are rescued from death by tasks that are challenging to learn; [Waddell et al., 2010](#); [Curlik and Shors, 2011](#); [Shors, 2009, 2014](#)). During the initial session, participants were instructed to sit on a Zafu cushion in an upright position with legs crossed and hands folded together in the middle of the lap. They were instructed to breathe slowly and "watch" their breath, counting each one as the final air is expelled during exhalation. As thoughts arise, participants new to meditation typically lose count of the breath. At this point, they were told to let go of the thought(s) without judgment and return to counting each breath, beginning again with the number one. With practice, a person learns how difficult it is to pay attention to the breath. As a consequence, he or she learns that thoughts are transient yet powerful because they interfere with concentration. With practice, the person learns to let go of these recurring thoughts about the past as well as worrisome thoughts projecting into the future. Focused attention meditation is an effortful learning experience, during which one learns to be present in this moment while being less reactive to ongoing thoughts and emotions.

After 20 min of sitting meditation, participants were instructed to stand to begin 10 min of walking meditation. Walking meditation is similar in principle to sitting meditation. However, instead of focusing on the breath, individuals focus on the movement of the feet. In our program, we adopted a very slow walking practice. Individuals gathered in a circle, walking slowly with hands folded behind their back. They were instructed to keep their attention focused in each foot as the weight transferred from one foot to the next, from the heel to the ball of the foot to the toe. As a person walks, once again, thoughts tend to arise and interfere with concentration. And once again, participants were instructed to bring their focus of attention back to the feeling of their feet. With practice, one learns to redirect the focus of attention back to the body. Walking meditation is an effortful training experience during which individuals learn to be present in this moment even while moving forward.

The mental training component was immediately followed by the physical component of MAP Training, during which individuals engaged in 30 min of directed aerobic exercise. It is well established that aerobic exercise promotes mental and physical health ([Arena, Myers, & Guazzi, 2010](#); [Charansonney, 2011](#); [Dishman et al., 2006](#); [Herring, Puetz, O'Connor, & Dishman, 2012](#)), and as noted, it

increases the number of new neurons produced in the hippocampus of laboratory animals (Nokia et al., 2014; van Praag et al., 1999). For the study presented here, participants exercised in a group while learning choreographed dance routines similar in style to the widely popular dance program Zumba. Before beginning, all participants were provided a pedometer to tally the number of steps accrued during the session as well as a heart rate monitor (Polar Electro, Finland) to assess heart rate throughout the session and monitor exercise intensity. Each session began with a short warm-up (3 min) followed by 25 min of aerobic-based dance exercise training at a moderate intensity, followed by a 2–3 min cool down period. During each session, participants were taught new sequences of physical motor skills set to music of popular songs. This component of MAP Training has been especially well received by the women, presumably because it elevates mood and social interaction while decreasing rumination (Nolen-Hoeksema, 1991; Nolen-Hoeksema, 2012; Sherwood & Jeffery, 2000).

5. Preliminary data from underserved individuals in the community

The MAP Training intervention has produced positive results in three study populations so far. In the present review, we present preliminary data from one population. The participants in this study were all young women (18–36 years; mean 25 ± 5) who were recently homeless, having suffered months and in some cases years of poverty and trauma, as well as addictive behaviors. Nearly all of the women reported being sexually and/or physically abused either as children or young adults. They were rescued from the streets and given housing and food in a residential center, where they live with their children. We provided MAP Training in a large conference room at their residence. The sessions occurred twice a week for 8 weeks. The participants had not engaged in organized meditation or aerobic exercise prior to MAP Training. Therefore, we propose that the 16 sessions of MAP Training resulted in consistent and effortful learning experiences over time, at least as can be assessed through verbal communication and observation. In this review, we present preliminary data from a group of women ($n = 8$) who completed all 8 weeks of supervised MAP Training, as well as a group ($n = 6$) of previously homeless women who resided at the center but did not participate in or complete MAP Training. Instead of MAP Training, the treatment-as-usual (TAU) group participated in group activities which did not include aerobic exercise or focused attention meditation.

6. Physical health outcomes

Before MAP Training, participants were informed about the study and provided written informed consent that was approved by the Institutional Review Board at Rutgers University. On a separate day, participants were transported from the residence to the Exercise Psychophysiology Laboratory at Rutgers University for baseline testing. After MAP Training or an equivalent amount of time at the center without MAP Training (i.e., treatment-as-usual controls), participants again returned to the laboratory for post-testing. During the baseline and post-intervention assessments, the Mini International Neuropsychiatric Interview (M.I.N.I.) and a series of mental and physical health outcomes were administered, including tasks of attention, hippocampal-dependent learning, event-related brain potentials (ERPs) through EEG, heart rate variability, maximal oxygen consumption, and psychological outcomes. In this review, we present preliminary data for several of these health outcomes (Fig. 5).

The first physical outcome measure reported here is VO_2 peak, which is the maximum rate of oxygen consumption during incremental exercise and is widely considered the gold standard measurement of aerobic physical fitness. Specifically, cardiorespiratory fitness (VO_2 peak) was assessed through a submaximal exercise test using a motor-driven treadmill and a modified Bruce protocol (Bruce et al., 1975). The speed of the treadmill was initially set at 1.7 mph and was increased to 2.5, 3.4, 4.2, 5.0, and 5.5 mph at 3-min intervals throughout the test. The treadmill incline was initially at a 10% grade and was subsequently increased by 2% every 3 min until participants reached 85% of age-predicted maximal HR (220 bpm – age in years), at which time the test was terminated. A Polar heart rate (HR) monitor (Polar Electro, Finland) was used to measure HR throughout the test. Oxygen consumption was measured through indirect calorimetry using a Parvo MedicsTrueOne 2400 Metabolic Measurement Cart (Parvo Medics, Inc., Sandy, UT) averaged over 15-s intervals. VO_2 peak ($\text{mL kg}^{-1} \text{min}^{-1}$) was established from direct expired gas exchange data from the metabolic system and was predicted by extrapolating the linear regression between HR and measured oxygen consumption measured up to the age-predicted maximal HR (ACSM, 2013). A 3–5 min cool-down period was then performed at preferred walking speed and 0% grade to ensure participants returned to near baseline cardiovascular values.

After MAP Training, maximal oxygen consumption (VO_2 peak) increased from numbers in ranges considered fair to good ($30\text{--}35 \text{ mL kg}^{-1} \text{ min}^{-1}$) into those considered excellent and even superior ($>40 \text{ mL kg}^{-1} \text{ min}^{-1}$) for women of this age group (Fig. 5A). These data are consistent with their performance during MAP Training. During each session of MAP Training, participants wore heart rate monitors in order to evaluate maximum, minimum and average heart rates during each component of MAP Training. During meditation, the average heart rate was 77 beats/min, and this increased to an average of 137 beats/min with an average maximum of 167 beats/min during exercise. Participants also wore pedometers to monitor the number of steps that were taken during each session. The average number of steps per training session exceeded 2330, with a range between 1006 and 3791 steps.

For a comparison group, we also tested a group of women ($n = 6$) who were recently homelessness and received treatment as usual (TAU) at the center but did not participate in or complete MAP Training. The mean VO_2 peak for the TAU group was $34.68 \pm 3.47 \text{ mL kg}^{-1} \text{ min}^{-1}$ during the pretesting baseline period and $36.43 \pm 2.93 \text{ mL kg}^{-1} \text{ min}^{-1}$ after 8 weeks of living at the center with no significant change across time ($p > 0.05$). Analysis of variance revealed a significant interaction between MAP Training and time between VO_2 peak assessments, $F(1,10) = 11.66$, $p < 0.01$. Only the group that completed MAP Training expressed an increase in oxygen consumption ($p < 0.05$). Therefore, participation in the MAP Training program, and not their new living conditions, significantly increased aerobic fitness. This was expected because the participants did not regularly participate in aerobic exercise and VO_2 would not be expected to increase in response to changes in improvements in food, shelter, medicine, etc. These data suggest the physical training component of MAP Training enhanced the cardiovascular fitness and endurance capacity of the participants. Of relevance, increases in VO_2 peak have been associated with an increased volume of the hippocampus in humans (Erickson et al., 2009). Most importantly, VO_2 peak is one of the best predictors of all-cause mortality and cardiovascular disease (Kodama et al., 2009).

7. Mental health outcomes

After 16 sessions of MAP Training (twice a week for eight weeks), participants expressed significant changes in mental health

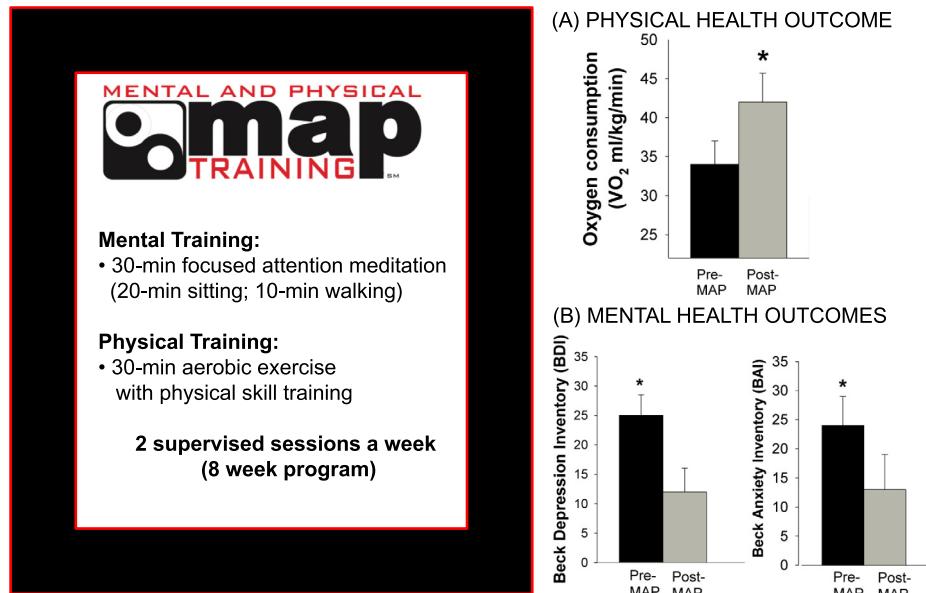


Fig. 5. In a preliminary “proof-of-concept” study, MAP Training was provided twice a week for 8 weeks to underserved women in our community who were recently homeless ($n = 8$). Maximal rate of oxygen consumed (VO_2 peak) was assessed during a stress test before and after MAP Training. After 16 sessions of training, participants increased their aerobic fitness, as indicated by an increase in oxygen consumption (A). Before training, participants expressed elevated symptoms of depression and anxiety as assessed with Beck Inventories. After MAP Training, symptoms of depression and anxiety were significantly reduced (B). A group of recently homeless women receiving treatment as usual (TAU) but who did not participate or complete MAP Training ($n = 6$) did not express significant changes in VO_2 , BDI or BAI.

outcomes. Before training, participants reported elevated symptoms of depression consistent with a diagnosis for major depressive disorder (MDD), as assessed with the Beck Depression Inventory (BDI-II; Beck, Steer, & Carbin, 1988a). After 8 weeks of MAP Training, mean BDI scores decreased significantly. As shown in Fig. 5B, BDI scores after MAP Training were less than half what they were before MAP Training. Before training, the participants also expressed elevated symptoms of anxiety as detected with the Beck Anxiety Inventory (Beck, Epstein, Brown, & Steer, 1988b). Following MAP Training, BAI scores were significantly reduced, suggesting that participants were experiencing fewer symptoms of anxiety. The same mental health outcomes were assessed in a comparison group of previously homeless women who live at the center but who did not participate in or complete the MAP Training program ($n = 6$). No change in BDI [$F(1,5) = 0.14$; $p = 0.72$] or BAI [$F(1,5) = 1.21$; $p = 0.32$] scores were found over the course of 8 weeks in women living under similar conditions without participation in MAP Training. With respect to depression, there was a significant interaction between MAP Training and time of assessment, $F(1,12) = 7.61$; $p < 0.05$. As noted, only those who participated in the MAP Training intervention reported decreases in depression symptoms. With respect to anxiety, there was no interaction between the intervention and time between testing periods (pre to post assessment) because both groups (MAP Trained and TAU) reported a decrease in anxiety symptoms over time. This is not surprising because the participants in the center program also experience other changes in their lives that are known to enhance mental health, including other psychological programs and group therapies, as well as medical assistance and nutritious food and the comforts of heat and shelter. Therefore, we are not claiming that 8 week of MAP Training is responsible for all of the positive mental and physical health outcomes, but rather that it synergistically enhances the health outcomes that were observed, especially those related to depression. It is further noted that we have observed similar outcomes in a group of clinically depressed adults and

otherwise healthy controls. In these studies, we also observed a significant decrease on BDI scores after MAP Training, even in the healthy control group (Alderman, Olson, Bates, Selby, & Shors, 2014b; Alderman et al., 2014a).

8. Relevance to neurogenesis and learning

A recent study reported that female rodents that experience early life stressors produce fewer hippocampal neurons (Loi, Koricka, Lucassen, & Joëls, 2014), while another study reported less complex arborization in cells that are produced under stressful conditions (Leslie et al., 2011). These findings in laboratory studies may have some potential relevance to the population of homeless women that we have been studying, because they have experienced a number of early life stressors. That said, it is important to note that we do not know whether the women began training with fewer new neurons nor do we know whether the positive outcomes of MAP Training are due to an increase in neurogenesis and/or the survival of new neurons in the hippocampus. The MAP Training intervention was “inspired” by neuroscientific data from laboratory experiments but further studies and analyses will be necessary in order to identify the mechanisms of action. This study represents the translational interface between basic scientific discoveries and clinical medicine application with the goal of improving public health.

9. Conclusion

Overall, preliminary findings presented here suggest that MAP Training enhances mental and physical health outcomes for young women who have experienced a number of traumatic events and stressors in their lives, including poverty, homelessness, abuse and addiction. We have also been providing the intervention to a large group of depressed adults as well as a group of healthy

control participants, and have observed similarly positive results in mental and physical health outcomes (Alderman et al., 2014a; Alderman et al., 2014b). The MAP Training intervention is well accepted among participants, inexpensive to administer, and can be reasonably used in many clinical and community populations. Indeed, we anticipate that MAP Training can be used to enhance mental and physical health in men and women from all walks of life – from the college student struggling with depression to the housewife addicted to pain medications to the soldier coming home from war. In our opinion, the number of people that could benefit from MAP Training is limitless.

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