Brain Research 1654 (2017) 95–101

Contents lists available at ScienceDirect

Brain Research

journal homepage: www.elsevier.com/locate/brainres

Review

Mental and physical skill training increases neurogenesis via cell survival in the adolescent hippocampus

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ARTICLE INFO

Article history:
Received 21 January 2016
Received in revised form
10 August 2016
Accepted 12 August 2016
Available online 13 August 2016

Keywords:
Learning and memory
Exercise
Sex differences
Hippocampus
Neurogenesis
Puberty

ABSTRACT

The adolescent hippocampus produces thousands more new neurons daily than the adult, yet many die within weeks of their generation (Cameron and McCay, 2001; Curlik, DiFeo & Shors, 2014; Shors et al., 2016). Learning new skills can increase their survival. The present study tested the effects of physical skill training on the survival of these newly generated cells in males and female rodents during puberty. Newly generated cells were labeled with BrdU, a marker of cell mitosis, and training began one week later, just as the new cells begin to die. Significantly more BrdU-labeled cells were present in the hippocampus of both sexes after engaging in the physical training experiences. The young animals were able to maintain their balance on a modified rotarod task throughout most trials of training and as a consequence expended considerable energy and endurance during each training trial. These data suggest that a combination of both exercise and skill training can increase brain plasticity through increases in neurogenesis in the adolescent hippocampus. This finding supports the premise behind a clinical intervention known as MAP Training, which combines mental and physical training to enhance brain health in humans (Shors et al., 2014; Alderman et al., 2016). Although theoretical at this stage, the positive consequences of MAP Training for brain function may be mediated through neurogenesis.

This article is part of a Special Issue entitled SI: Adolescent plasticity.

Contents

1. Introduction

Most young adults, especially adolescents enjoy learning new skills that require physical effort and training. It is assumed that engaging in these activities is beneficial for their normal growth and development but the benefits of these activities for brain health are less well described. It is well known that the adult brain as well as the adolescent brain continues to produce new neurons, many of which are produced in the dentate gyrus of the hippocampus. In previous studies, we determined that physical skill training in a rodent model of learning increased the survival of

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http://dx.doi.org/10.1016/j.brainres.2016.08.015
0006-8993/

newly-generated neurons in the adult hippocampus, a brain region necessary for many types of learning (Beylin et al., 2001; Curlik and Shors, 2011; Shors et al., 2012). Cell survival was determined through immunohistochemistry using a BrdU-labeling protocol. BrdU is a thymidine analog that is a marker of mitosis, and commonly used in studies to label cells that are dividing at the time of the injection. Laboratory rodents were trained to maintain their balance on a large rod that rotated 360°. The rod rotated either at a constant slow speed or increased its rotation speed on each trial. During each trial of the accelerating version of the task, the rod rotated from 4 to 40 RPMs, enhancing the effort (presumably both physical and mental aspects) necessary to remain on the rod. Animals that were trained on either a constant or accelerating speed version of this task expressed evidence of learning because the time that they remained on the rod increased over trials and days of training (Curlik et al., 2013). However, animals that were trained on the more difficult accelerating version of the task retained significantly more new neurons in their dentate gyrus than those trained with the slow constant speed task, which were not different from those tallied in animals that were not trained. These data support our previous studies, which indicate that nearly half of the new neurons in the hippocampus die within weeks of their birth unless new learning occurs and moreover, training with a physical skill task is an effective means for increasing neurogenesis via cell survival in the adult brain.

Most of the adult animals that were trained on the accelerating version of the rotarod task did not remain on the rod for the maximum length of the trial, suggesting that learning continued to occur, even after several days of training. However, many of the animals stepped off the rod, presumably because they had learned that there was no adverse consequence for doing so. Therefore, in a follow-up study, we increased the motivation to remain on the rod by placing cold water underneath. When the animals stepped off the rod, they would drop into the water. As expected, the animals were more likely to remain on the rod when the water was present than when it was not (DiFeo et al., 2015). In general, females performed better than the males on the more motivating task but both sexes demonstrated an increase in the number of surviving cells as a consequence of learning this novel physical skill. We have termed this task the “motirod” task, because it increases motivation to learn.

The onset of puberty in rodent models is accompanied and usually defined by the maturation of neuroendocrine systems that control reproductive function. Puberty onset occurs at approximately PND 35 ± 2 days in the female rodent and PND 42 ± 2 days in the male rodent. In both sexes, puberty continues for approximately 2 weeks, indicated by canalization of the vagina in females and balanopreputial separation of the foreskin from the glans of the penis in males. During this period of time, the female transitions from a two to a four-stage estrous cycle (Hodes and Shors, 2005). Also during this period of time, the hippocampus produces significantly more new neurons than an adult brain does (Curlik et al., 2014). But like the adult brain, many of these new cells are subject to programmed cell death. In one study, approximately 40% of newly generated cells in the granule cell layer and 80% of those in the hilus were no longer present three weeks after they were generated. However, pubescent animals that engaged in an effortful learning experience beginning one week after the new cells were generated retained the new cells that would have otherwise died. These findings are largely consistent with widely reported studies on the positive impact of learning on cell survival during adulthood (Curlik and Shors, 2011; Curlik et al., 2013; Shors et al., 2012). However, because nearly twice as many new neurons are generated during adolescence, learning can have an especially profound effect on cellular integrity in the hippocampus this stage of development.

As noted, adolescent children are motivated to and generally inclined toward learning new physical skills in school and elsewhere. Therefore, in the present experiments, we hypothesized that training with the accelerating version of the rotarod task with the motivating procedure would increase the number of surviving new cells in the hippocampus more than training with the accelerating task without the motivating procedure. Moreover, based on studies in adult rodents, we hypothesized that pubescent females would outperform the males and thereby retain more of the newly generated cells.

2. Methods

Male and female Sprague-Dawley rats were bred at Rutgers University in the Department of Psychology. At 28 days, animals were weaned and housed in groups in standard plastic shoebox style cages (44.5 cm long by 21.59 cm wide by 23.32 cm high). Animals were given access to food and water ad libitum and maintained on a 12:12 h light-dark cycle; the light cycle began at 7 a.m. and ended at 7 p.m. All handling and experiments were carried out in the light portion of the cycle. Experiments were conducted with full compliance with the rules and regulation specified by the PHC Policy on Human Care and Use of Laboratory Animals and the Guide for the Care and Use of Laboratory Animals. The Rutgers University Animal Care and Facilities Committee approved all procedures.

The rotarod (Four-station Rotarod for rat, Model #ENV575, MED Associates Inc., Georgia, VT, USA) is a cylindrical rod that is elevated 26.75 cm above a platform. The diameter of the rod is 7 cm. The rod can either accelerate or maintain a constant velocity over a five-minute period. To further enhance motivation to perform the task, we modified the standard version of the rotarod by placing cold water directly under the rod (approximately 55 mm deep). Animals were removed from the water as soon as they fell off the rod and immediately dried off with a towel. As noted, this version of the task is referred to as the “motirod”. Groups of animals were trained on either the standard accelerating rotarod (“rotarod”) or the modified motirod task. Rotarod and motirod training consisted of four trials per day over four consecutive days. Animals in both training conditions were placed on the rotarod while it was stationary, facing in the opposite direction in which it moved. Thus, animals had to move forward in order to remain on the rotating rod. Each trial began when the animal was placed on the rod in the correct orientation. The rod linearly accelerated from 1.47 cm/sec to 14.74 cm/sec over a five-minute period. After the first five minutes of a trial, the rod no longer accelerated and remained at a constant maximum velocity of 14.74 cm/sec. The latency to fall from the rod (in seconds) was the recorded behavioral dependent measure of the task. Animals were allowed to remain on the rod until they fell off or until 10 min had passed.

Four groups of pubescent animals were trained as followed: males trained on the rotarod ($n=6$), males trained on the motirod ($n=6$), females trained on the rotarod ($n=6$), and females trained on the motirod ($n=6$). All groups received one single intraperitoneal injection of 5-bromo-2-deoxyuridine (BrdU; 200 mg/kg; Sigma, Atlanta, GA, USA) at 28 days of age (PND 28). Additional groups of pubescent male ($n=6$) and female ($n=6$) rodents were injected with BrdU injection at the same time point but not trained (Fig. 1). Training began at PND 35 for all of the trained groups of animals.

Twenty-one days after the BrdU injection, animals were deeply anaesthetized with sodium pentobarbital (100 mg/kg) and transcardially perfused with 4% paraformaldehyde in 0.1 M phosphate buffer. The brains were extracted and post-fixed in 4% paraformaldehyde at 4 °C for 24–48 h to preserve the tissue structure

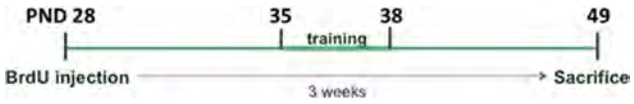

Fig. 1. Experimental timeline. Male and female rodents were injected once with BrdU (200 mg/kg) at approximately PND28. Animals were trained on one of two tasks beginning one week later. The cells were examined and counted three weeks after the one BrdU-injection, thus representing the cohort of newly-generated cells that had survived over the course of three weeks.

before being transferred to phosphate buffered saline (PBS). A vibratome was used to obtain 40 μm coronal sections through the entire rostral-caudal extent of the dentate gyrus in one hemisphere. This is the standard practice in our laboratory, as no differences in neurogenesis have been observed in the dentate gyrus of the right or left hemisphere (Anderson et al., 2011; Dalla et al., 2009). Every twelfth slice was mounted onto a superfrost glass slide (Fisher, Suwane, GA, USA) and allowed to air dry. Once dry, the tissue was then stained using standard peroxidase methods to visualize the cells that incorporated BrdU as described previously (Curlik and Shors, 2011). Tissue was pretreated with heated 0.1 M citric acid (pH 6.0), rinsed with 0.1 M PBS, incubated in trypsin for 10 min, and denatured in 2N HCl for 30 min with PBS rinses in between. The tissue was incubated overnight in primary mouse anti-BrdU (1: 200, Becton-Dickinson, Franklin Lakes, NJ, USA) and 0.5% Tween-20 (Vector Laboratories, Burlingame, CA, USA). The next day, tissue was rinsed and incubated in biotinylated anti-mouse antibody (1:200, Vector Laboratories) for 60 min and placed in avidin-biotin-horseradish peroxidase (1:100, Vectastain ABC Kit, Vector Laboratories) for 60 min. The tissue was placed in diaminobenzidine (DAB SigmaFrost tablets, Sigma, Atlanta, GA, USA) for four minutes, rinsed, counterstained with 0.1% cresyl violet, dehydrated, cleared, and coverslipped with Permount glue (Fisher Scientific, Fair Lawn, NJ, USA).

Quantitative analysis was performed blind to the experimental condition by coding each slide. Estimates of the total number of BrdU-positive cells were determined using a modified unbiased stereology protocol (Gould et al., 1999; West et al., 1991). The number of BrdU-positive cells in the dentate gyrus of each slice (granule cell layer and hilus) were counted by hand at 1000 × on a Nikon Eclipse 80i light microscope. We counted every 12th slice from either the right or left hemisphere of the hippocampus; therefore, the number of cells was multiplied by 24 to obtain an estimate of the total number of BrdU-positive cells in the entire dentate gyrus of both hemispheres.

3. Results

An independent samples *t*-test revealed no significant differences in weight between the pubescent males (mean = 92.55 g) and pubescent females (mean = 87.06 g) ($t_{1,25} = 2.08$, $p > 0.05$). The time spent on the rod during each trial was used as a dependent measure of performance. There were no interactions between the independent variables of sex (male versus female) or the type of physical skill training (rotarod versus motirod) ($p > 0.05$). However, as expected, there was a main effect of trials of training ($F_{(15,210)} = 8.53$, $p < 0.01$), suggesting the animals were learning to remain on the rod longer over trials as well as sessions of training. Separate repeated-measures analysis of variance revealed that the latency to fall from the rod increased as training progressed over the 16 trials in the four groups: male rotarod ($F_{(15,60)} = 2.47$, $p < 0.05$; Fig. 2A), male motirod ($F_{(15,30)} = 4.15$, $p < 0.01$; Fig. 2B), female rotarod ($F_{(15,75)} = 2.49$, $p < 0.05$; Fig. 2A) and female motirod ($F_{(15,45)} = 3.70$, $p < 0.001$; Fig. 2B). These results indicate that each of the four groups successfully learned either skill task. However, as shown in Fig. 2, most of the animals reached asymptotic performance after just one day of training (4 trials). The maximum time for each trial was 10-min. Therefore the increase in time across trials of training was blunted by a "ceiling" effect because most animals could not attain a higher score on each trial. Contrary to our hypothesis, males and females performed similarly on the two tasks and their performance was not significantly different ($p > 0.05$). Both sexes performed very well, especially during training with the motirod task.

To test the potential contribution of sex differences and training to the numbers of BrdU-labeled cells in the dentate gyrus, we conducted analysis of variance with sex (male versus female) and the type of training (rotarod versus motirod) as independent variables and number of BrdU-labeled cells as the dependent measure. There were no interactions between the type of training or sex on the number of BrdU-labeled cells ($p > 0.05$). Therefore the data between the sexes and tasks were collapsed for further analyses. There was a main effect of training, indicating that pubescent males and females retained significantly more BrdU+ cells in the total dentate gyrus than the untrained pubescent males and females ($n = 9$) ($F_{(1,26)} = 6.03$, $p < 0.05$; Fig. 3C). These effects were observed in both the GCL ($F_{(1,26)} = 4.53$, $p < 0.05$; Fig. 3D) and the hilus ($F_{(1,26)} = 4.71$, $p < 0.05$; Fig. 3E). These data suggest that training with the physical skill training tasks was associated with an increase in the number of BrdU-labeled cells in the hippocampus of the pubescent hippocampus three weeks after they were injected with BrdU and two weeks after the training began (Fig. 1).

4. Discussion

Adolescence is associated with increased brain plasticity and opportunities for new learning. In the present study, male and female rodents in early puberty were trained on one of two physical skill tasks, which require balance and sustained physical activity to master. Both sexes quickly and successfully learned the two motor skill tasks and their performances on either task were similar. We further examined the effects of these physical skill training tasks on the survival of newly generated cells in the hippocampus. Overall, training increased the number of cells previously labeled with BrdU, a marker of cell mitosis used to assess the survival of newly generated cells in laboratory studies. Therefore, training with these physical skill tasks was sufficient to increase the number of newly-generated cells in the hippocampal formation, as has been reported in adults that were trained on these same tasks (DiFeo et al., 2015). These findings are largely consistent with the previous study in adult rodents, with some important differences. For example, the adult animals did not learn these tasks as well as the adolescents, particularly adult males (DiFeo et al., 2015). In contrast, most of the pubescent animals in the present study reached the maximal level of performance within just a day or two of training, which indicates that most of the learning occurred very quickly in pubescent rats. Moreover, the numbers of cells that remained in the adolescents were considerably larger than in the adults. Because these are separate experiments, we cannot directly compare the data sets but it is nonetheless presumed that the young animals retain a large number of the new cells because they learn so well and so quickly, as well as the fact that they produce more new cells than do adults (Curlik et al., 2013).

4.1. Sex differences in performance

Sex differences in learning and performance are well accepted in animal models, although many of them can be explained by sex

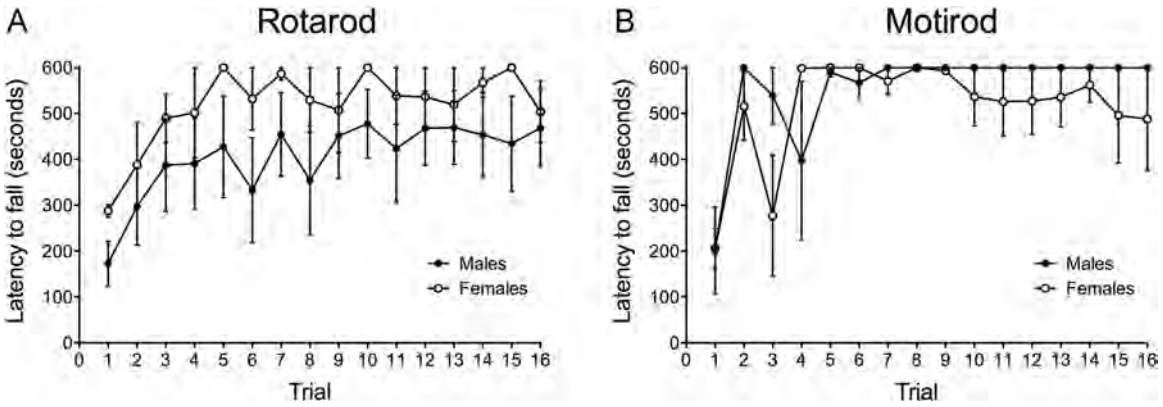

Fig. 2. Physical skill training. Groups of male and female rats in puberty were trained on the accelerating "rotarod" task, during which the rod increased its speed over each 10-min trial. During the motirod task, the rod similarly increased in speed over the 10-min trial, but if the animal quit performing, it dropped into a pool of water. Groups of males and females were trained with four trials of training for four consecutive days. Pubescent males and females readily learned to remain on the rotarod (A) or the motirod (B) during puberty. There was no sex difference in performance.

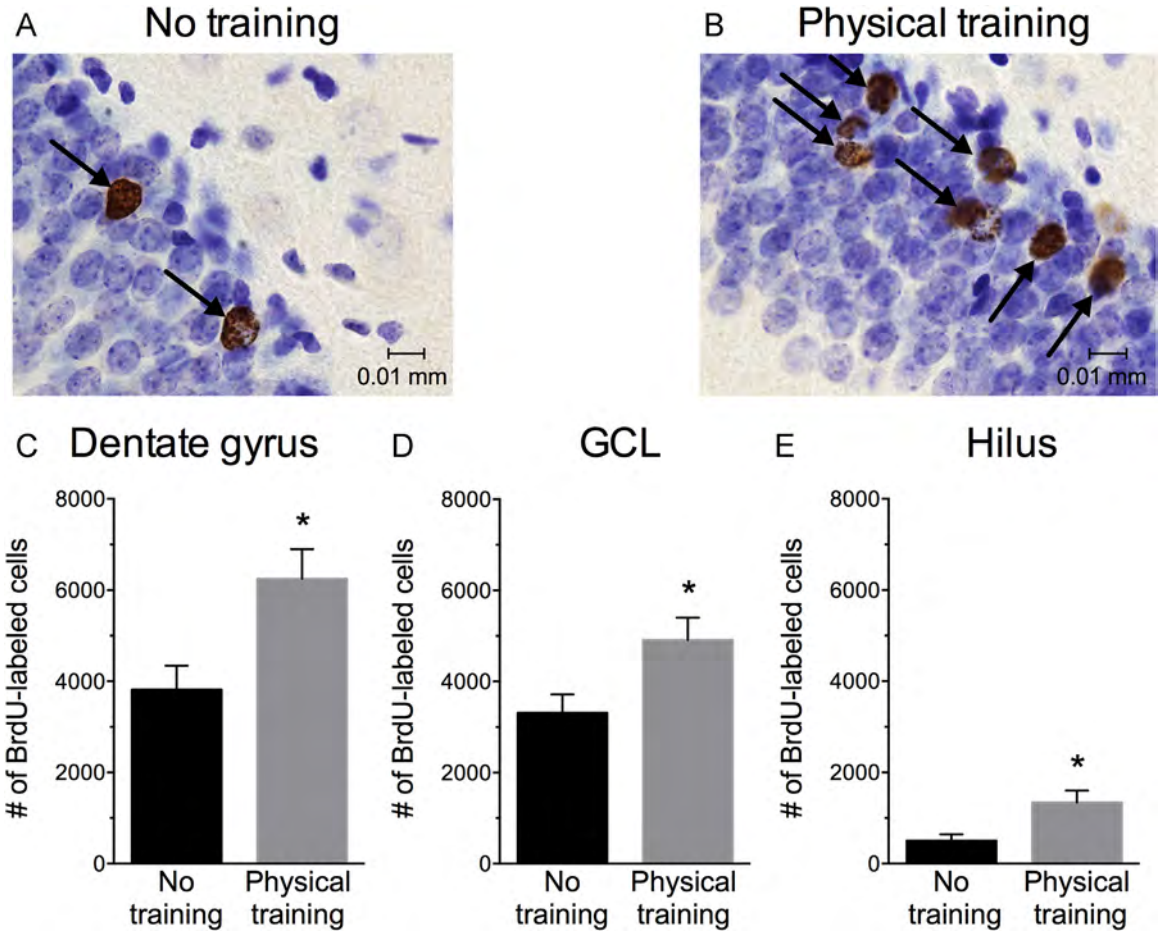

Fig. 3. Physical skill training and cell survival. Representative photomicrographs of immunohistochemistry for BrdU at 1000× from the dentate gyrus of an untrained pubescent animal (A) and a trained animal (B). Training with the physical tasks increased the number of BrdU-labeled cells in the hippocampus of pubescent male and female rats (C). These effects were observed in both the GCL (D) and the hilus (E).

differences in motor activity or weight (Shors, 2016). There were no significant differences in performance here but as noted, both sexes were performing near the maximum performance within just a few days of training, especially during training on the motirod task. It is not surprising that the animals learn the motirod task so well; by remaining on the rod, they avoid falling into the cold water. It is nonetheless surprising that the pubescent animals learn this task so much better than do adults. Pubescent rats tend to be more active than adults and weigh less, both factors of which may contribute to their sustained performance during training on these tasks (Dalla and Shors, 2009). As noted, we previously reported that adult females learned these two tasks faster than did males (DiFeo et al., 2015). We hypothesized that they were able to stay on the rod because they weigh less than the adult males. In other words, the sex difference in performance was probably not attributable to inherent differences in learning processes but rather one that is evoked by differences in physical characteristics (Shors, 2016). The adults also performed much worse than the

adolescents, as compared to the pubescent males and females. In the present study, adolescent males and females were similar in weight, which likely explains the absence of a sex difference in performance and their enhanced performance during training on either physical skill task.

4.2. Learning and cell survival

Adolescence is an important developmental stage during which the brain is undergoing extensive maturation and morphological changes (Romeo and McEwen, 2006), many of which occur within the hippocampus. For example, an overproduction of axons and synapses during early pubescence is followed by a rapid increase in dendritic pruning by the end of adolescence (Anderson et al., 2000; Giedd et al., 1999). Although some measures of plasticity decrease within the adolescent period (He and Crews, 2007), those related to neurogenesis tend to persist when compared to levels of production in adulthood (Curlik et al., 2013). As a consequence, learning has a disproportionate effect on the cells and other substrates within the brain of the pubescent animal. In a previous study, we reported that training to learn a Pavlovian conditioning task had a positive effect on cell survival. During training on this task, known as trace eyeblink conditioning, the animal must learn to associate stimuli across time. Learning this task (but not a similar one that is less difficult) increases the survival of newly generated neurons in the hippocampus of adult (Leuner et al., 2006) and pubescent rats (Curlik et al., 2013).

Not all types of learning increase the survival of new neurons in the hippocampus in adulthood. For example, delay eyeblink conditioning and a cued version of the Morris water maze, both hippocampal-independent tasks, do not rescue these cells from death (Beylin et al., 2001; Gould et al., 1999). But not all hippocampal dependent tasks are capable of rescuing cells either. Learning to associate two stimuli across a very short trace interval (250 ms) requires the hippocampus but does not enhance cell survival (Waddell et al., 2011). Moreover, non-hippocampal dependent tasks, such as contiguous trace eyeblink conditioning, during which the animal learns to associate the two stimuli better and faster because the first stimulus (the conditioned stimulus) is presented again with an unconditioned stimulus (US), did not rescue newly born adult DG cells from apoptosis (Dalla et al., 2007). Therefore, the types of tasks that increase cell survival are not necessarily dependent on the hippocampus (although most are) but rather are tasks that are effortful to learn, meaning more trials of training are necessary to achieve an optimal level of performance (Curlik and Shors, 2013; Dalla et al., 2007; Leuner et al., 2006, 2004; Waddell and Shors, 2008). Importantly, learning the accelerating rotarod does not require an intact hippocampus (Curlik et al., 2013), even though more cells remained in the hippocampus as a consequence of learning in adults and as reported here in adolescents. Therefore, it is proposed that effortful learning activates the hippocampus, regardless of its dependence on the structure for learning, to increase the survival of the newly generated cells.

4.3. Mechanisms to increase neurogenesis

The mechanisms through which learning increases neurogenesis are not known but are presumed to involve increased production of growth factors such as brain-derived neurotrophic factor (BDNF) or nerve growth factor (NGF) (Voss et al. 2013). A recent study investigated the effects of exercise on cognitive and brain function in teenagers (Lee et al., 2014). They reported that the concentrations of BDNF increased as a result of exercise and moreover interacted with exercise to predict cortical function. In another interesting report, Van Praag and colleagues reported that cathepsin-B secretion from the muscle after exercise was related to the production of new neurons in the hippocampus as well as potential increases in cognitive function in laboratory animals (Moon et al., 2016). They further demonstrated a positive effect of aerobic exercise on cathepsin-B in humans who exercised. Clearly, many systems are activated by aerobic exercise and potentially as many by mental training programs. Therefore, it will require considerable effort from the clinical and laboratory research communities to identify the necessary and sufficient mechanisms that enhance neurogenesis and cell survival as a result of physical training.

It is well accepted that aerobic exercise increases cell proliferation in the hippocampus but only a few report an increase in cell survival after the cells are produced (Hamilton and Rhodes, 2015; Kobilo et al., 2011; van Praag et al., 1999, Nokia et al., 2016). Previously, we examined the potential effects of aerobic exercise (versus rotarod training) on cell survival in the hippocampus of adult rodents. Animals were injected with BrdU once and then either given the opportunity to exercise in a running wheel in their home cage or were trained on the rotarod. Interestingly, numbers did not increase in animals that exercised with running wheels if the exercise began one week after the cells were labeled. We concluded from these data that the effect of rotarod training on neurogenesis was not attributable to exercise, per se, and that exercise itself did not increase cell survival, at least in adults (Curlik et al., 2014). Because young animals performed exceptionally well on the rotarod and motirod tasks in the present study, they would have exerted more physical effort than the adults did. The males and females trained on either task remained on the rotating rod for 5–7-min on the first day, 7–10-min on the second day, 8–10-min on the third day, and 8–10-min on the final day of training. Therefore, it is possible that some of the increase in cell number reported here is due to an increase in physical exertion and activity. That said, it is difficult to compare the effects of aerobic training for rodents in a running wheel to training on the rotarod task because the later involves more muscle strength and coordination and it may not be aerobic (Nokia et al., 2016). Moreover, in the present study, we did not assess the effects of rotarod or motirod training on cell proliferation itself. Nonetheless, we suggest that because training on these types of tasks involves both physical exercise and learning, they may be especially effective at increasing neurogenesis under these conditions.

The present data indicate that training on the rotarod and motirod tasks increased the number of BrdU-labeled cells in the pubescent dentate gyrus. We did not double label these cells; therefore we cannot confirm that they are in fact neurons. However, newly generated cells in the hippocampus of young animals mature into neurons with similar morphology and functional properties as adults (Ambrogini et al., 2004; Toni and Sultan, 2011) and in adults, the vast majority of BrdU-labeled cells differentiate into functional neurons and incorporate themselves into the existing hippocampal circuitry (Vivar and van Praag, 2013). In our previous studies, more than 80% of new cells in the GCL were double labeled with BrdU and neuron specific markers TuJ1 and NeuN after learning (Leuner et al., 2004). Similarly, double-labeled cells were present in the granule cell layer of the hippocampus more than two months after training, suggesting that they were relatively permanent and had been integrated into the circuitry of the hippocampus. That said, cells in the hilus of the dentate gyrus are less well characterized and some might not differentiate into neurons. In adult rodents, we observed very few new cells in the hilus and learning did not appear to increase their survival (Leuner et al., 2006). But in adolescents, the effects of physical skill training did extend to cells in the hilus. Interestingly, we reported similar increases in adolescent hilar cells after training with trace eyeblink conditioning (Curlik et al., 2014). It would be important to further

characterize these new cells and their incorporation into hippocampal circuitry, as well as their potential function in processes related to learning and memory during puberty.

4.4. Mental and physical (MAP) training

The positive benefits of physical activity itself on the cardiovascular, hormonal and muscular systems of the body are also well established in adolescents and young adults including decreased obesity and risk factors that predict cardiovascular disease later in life (Andersen et al., 2011; Tanha et al., 2011). Studies of adolescent children consistently report positive relationships between cardiovascular fitness and academic performance (Castelli et al., 2007; Chaddock et al., 2012; Van Dusen et al., 2011). More generally, aerobic exercise and physical activity improves and maintains cardiovascular fitness, which in turn positively impacts brain plasticity and function (Hillman et al., 2008). Some studies suggest a direct effect of physical activity on measures of cognition, such as memory and executive control (Berchtold et al., 2010; Hillman et al., 2009, 2008). However, aerobic exercise on its own, without a mental skill training component may not be as effective in improving health and function as combining mental and physical activities together (Alderman et al., 2016; Diamond and Ling, 2015; Sacco et al., 2015; Shors et al., 2014). And as one might expect, lifestyles that combine effortful training with physical activity are associated with overall well being in young and older adults (Hertzog et al., 2008; Sachdeva et al., 2015). However, few if any interventions directly combine these two types of activities. To meet this need, we recently developed a clinical intervention known as MAP Training, which stands for mental and physical training. The intervention includes 30-min of mental training with focused-attention mediation followed immediately by 30-min of aerobic exercise for physical training. This intervention, when practiced twice a week for 8 weeks resulted in a 40% decrease in depressive symptoms in young adults diagnosed with major depressive disorder, as well as in otherwise healthy controls. MAP Training was further associated with an increase in a neurophysiological correlate of cognitive control during training with the Flanker task, as assessed through electroencephalographic (EEG) activity and event-related potentials (ERPs) (Alderman et al., 2016). These measurements in humans were conducted within a week of the end of training. Therefore, some of these effects of MAP Training persist beyond the intervention environment. Therefore, we would suggest that some consequences of MAP training are mediated by structural changes in the brain and even perhaps through neurogenesis (Shors et al., 2014). Because neurogenesis cannot be measured in live humans, the connection between MAP Training and neurogenesis is theoretical at this point.

5. Conclusion

Over the past decade participation in youth sports in the United States increased more than 20%, with ~30–40 million young adults engaging in organized activities (Myer et al., 2011). The training procedures used in this laboratory study model these types of activities, at least to the extent that both require physical exertion, endurance and strength, along with gross motor skills for agility, balance and coordination. Unfortunately, many school systems have reduced or even eliminated their sports programs. Laboratory data and studies similar to the ones presented here suggest that physical skill training has positive effects on the structural integrity of the pubescent brain and underscore community efforts to increase and/or maintain physical activity and sports programs for our youth.

Acknowledgements

Supported by a Distinguished Investigator Award from the Behavioral Brain Health Foundation and National Alliance for Research on Schizophrenia and Depression (NARSAD) to TJS.

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