

Virtual Environmental Enrichment through Video Games Improves Hippocampal-Associated Memory

Gregory D. Clemenson and Craig E.L. Stark

Center for Neurobiology, Learning, and Memory, and Department of Neurobiology and Behavior, University of California, Irvine, Irvine, California 92697

The positive effects of environmental enrichment and their neural bases have been studied extensively in the rodent (van Praag et al., 2000). For example, simply modifying an animal's living environment to promote sensory stimulation can lead to (but is not limited to) enhancements in hippocampal cognition and neuroplasticity and can alleviate hippocampal cognitive deficits associated with neurodegenerative diseases and aging. We are interested in whether these manipulations that successfully enhance cognition (or mitigate cognitive decline) have similar influences on humans. Although there are many "enriching" aspects to daily life, we are constantly adapting to new experiences and situations within our own environment on a daily basis. Here, we hypothesize that the exploration of the vast and visually stimulating virtual environments within video games is a human correlate of environmental enrichment. We show that video gamers who specifically favor complex 3D video games performed better on a demanding recognition memory task that assesses participants' ability to discriminate highly similar lure items from repeated items. In addition, after 2 weeks of training on the 3D video game Super Mario 3D World, naive video gamers showed improved mnemonic discrimination ability and improvements on a virtual water maze task. Two control conditions (passive and training in a 2D game, Angry Birds), showed no such improvements. Furthermore, individual performance in both hippocampal-associated behaviors correlated with performance in Super Mario but not Angry Birds, suggesting that how individuals explored the virtual environment may influence hippocampal behavior.

Key words: environmental enrichment; hippocampus; neurogenesis; pattern separation; video games

Significance Statement

The hippocampus has long been associated with episodic memory and is commonly thought to rely on neuroplasticity to adapt to the ever-changing environment. In animals, it is well understood that exposing animals to a more stimulating environment, known as environmental enrichment, can stimulate neuroplasticity and improve hippocampal function and performance on hippocampally mediated memory tasks. Here, we suggest that the exploration of vast and visually stimulating environments within modern-day video games can act as a human correlate of environmental enrichment. Training naive video gamers in a rich 3D, but not 2D, video game, resulted in a significant improvement in hippocampus-associated cognition using several behavioral measures. Our results suggest that modern day video games may provide meaningful stimulation to the human hippocampus.

Introduction

In rodents, there is a long history of the influence of environmental enrichment on hippocampal function. Environmental enrichment leads to increases in hippocampal neurogenesis, synaptogenesis, neurotrophic factors, and a dramatic improvement

on hippocampus-dependent learning and memory tasks (Kempermann et al., 1997; van Praag et al., 1999; Olson et al., 2006; Fabel et al., 2009; Birch et al., 2013; Freund et al., 2013; Zhao et al., 2014; Clemenson et al., 2015). One critical component is the exploration that occurs when presented with a large, novel environment (Freund et al., 2013).

We are interested in whether the environmental enrichment manipulation used in animals has relevance to humans. There are a number of similarities that exist between humans and rodents in terms of hippocampal function and the mechanisms involved. For example, in the rodent, the hippocampus has long been thought to play a critical role in spatial learning and navigation (Tolman, 1948; O'Keefe and Nadel, 1978), and it is clear that there are underlying neural networks in the rodent hippocampus that respond to space (O'Keefe and Dostrovsky, 1971; Morris, 1981, 1984; Hafting et al., 2005). With the use of virtual environ-

Received July 2, 2015; revised Oct. 8, 2015; accepted Oct. 30, 2015.

Author contributions: G.D.C. and C.E.L.S. designed research; G.D.C. performed research; G.D.C. analyzed data; G.D.C. and C.E.L.S. wrote the paper.

This research was supported in part by James S. McDonnell Foundation Grant 624748 (G.D.C.) and National Institute of Aging Grant R01-AG034613. We thank Fred Gage for his input and guidance on the project and Ryan Abrigo and Neil Patel for their assistance in data collection.

The authors declare no competing financial interests.

Correspondence should be addressed to Craig E. Stark, University of California, Irvine, 320 Queshey Research Laboratory, Irvine, CA 92697. E-mail: cestark@uci.edu.

DOI:10.1523/JNEUROSCI.2580-15.2015

Copyright © 2015 the authors 0270-6474/15/3516116-10\$15.00/0

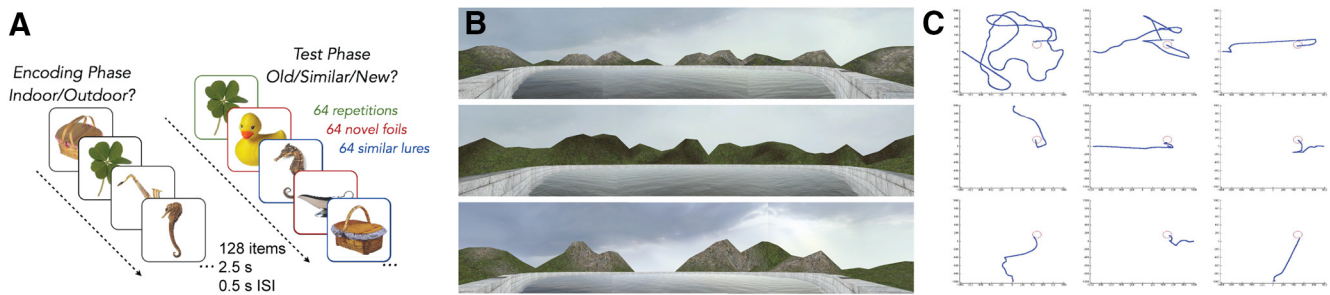


Figure 1. Behavioral task paradigms and example images of the vWM. **A**, Schematic of the MST. **B**, Three virtual environments used for the vWM task. **C**, Example path traces for a single participant during the vWM.

ments, studies in humans and rodents have shown that the hippocampus is active during the navigation of these virtual environments (Maguire et al., 1998; Harvey et al., 2009; Woollett et al., 2009; Schmidt-Hieber and Häusser, 2013). Grid- and place-like cells in the human entorhinal cortex and hippocampus have even been identified during navigation tasks performed within virtual environments (Ekstrom et al., 2003; Jacobs et al., 2013). Thus, in both species, there is evidence that the hippocampus is involved in (albeit not limited to) spatial memory. There is even evidence in humans demonstrating structural changes in the hippocampus with large amounts of spatial training and expertise (Maguire et al., 2000; Woollett et al., 2009; Kühn et al., 2014).

Within the hippocampus, a number of computational models propose that the dentate gyrus (DG) facilitates rapid memory encoding via a computation known as pattern separation (Yassa and Stark, 2011). Pattern separation can be defined as the process of making the representation of two similar experiences distinct from one another to facilitate rapid storage without interference. This process has been shown in rodents to be modified by neurogenesis (Clelland et al., 2009; Sahay et al., 2011; Clemenson et al., 2015). Although neurogenesis exists in the human hippocampus (Eriksson et al., 1998; Manganas et al., 2007; Spalding et al., 2013), imaging techniques are not to the point that we can observe the generation of newborn neurons in the human hippocampus. However, we do have a behavioral task in humans, the Mnemonic Similarity Task (MST; Kirwan and Stark, 2007; Stark et al., 2013), that was designed to index pattern separation by assessing behavioral and/or neural responses to highly similar lure items after a study exposure. This task has been shown to specifically activate the DG/CA3 region of the hippocampus (Bakker et al., 2008; Lacy et al., 2011) and be selectively impaired after hippocampal damage (Kirwan et al., 2012). It is also highly sensitive to aging and age-related alterations of hippocampal function (Yassa and Stark, 2011) that have been shown to correlate with both neurogenesis and pattern separation (Creer et al., 2010).

Here we test the hypothesis that the exploration of a virtual environment within a 3D video game stimulates the hippocampus and leads to an enhancement in both spatial memory and mnemonic discrimination. We show that video gamers who focus on video games that center around complex 3D virtual worlds are better at mnemonic discrimination when compared with video gamers who focus on simpler 2D video games and non-video gamers, despite showing no differences in visual perception. In addition, training naive video gamers for 2 weeks on the complex 3D video game *Super Mario 3D World* improves both mnemonic discrimination and spatial memory on a virtual version of the Morris water maze task.

Materials and Methods

Experiment 1A

Participants. Participants were recruited online through the University of California, Irvine (UCI) Sona Systems experiment management system, which organizes the participation of UCI students in psychology experiments for course credit. Thirty-nine self-described video gamers (VG group; 15 male) and 29 self-described non-video gamers (NVG group; 8 male) were recruited for participation in the pilot study.

Video game questionnaire. All participants were required to take an online questionnaire to determine individual game experience. Participants answered a variety of questions designed to assess not only how much time was spent gaming but also the types of games played, experience, competitiveness, and performance in all game genres.

Enumeration task. The enumeration task was derived from previous video game studies (Green and Bavelier, 2006; Wilms et al., 2013) and consists of asking participants to determine how many dots were shown on a screen after a very rapid presentation. Each trial consisted of a fixation cross presented for 500 ms, followed by a random number of dots (1–9) for 100 ms, and lastly followed by a visual mask of 50 random lines presented for 500 ms. After each trial, participants were asked to identify the number of dots presented on the screen as accurately as possible using the keyboard (1–9) to input their answer. After the visual mask, the computer screen stayed blank (white) until a choice was made. There were 90 trials total, 10 trials for each of the possible 1 through 9 dots.

MST. The MST is a recognition memory task originally designed to tax the process of pattern separation (Kirwan and Stark, 2007). The MST consists of an incidental encoding phase and a test phase (Fig. 1A) in which participants are shown color photos of objects. During the encoding phase, participants were shown 128 pictures of everyday objects [2000 ms duration, 500 ms interstimulus interval (ISI)] and were asked to make indoor/outdoor judgments about each object, using a keyboard to make each choice. During the testing phase (64 objects per condition, 192 total trials), participants were again shown pictures of everyday objects, including the following: (1) those that were exactly the same as an encoded item (repetition); (2) those that were similar to an encoded item (lure); or (3) those that were novel and unrelated to any encoded items (foil). For each presented object, the participant had to determine whether the object was “old,” “similar,” or “new” when compared with objects seen during the training phase (2500 ms duration and response window, 500 ms ISI).

The MST provides two measures: a lure discrimination index (LDI) and a recognition memory score. The LDI attempts to index hippocampal function by assessing how well participants can reject highly similar lure items and not succumb to viewing these items as old (thus demonstrating the preservation of unique, detailed memories and a lack of interference). The LDI is calculated as the probability of correctly calling a lure object similar minus the probability of incorrectly calling a foil object as similar (to correct for biases in use of the similar response). The second measure of the MST is a traditional recognition memory measure, calculated as the probability of correctly calling repeated objects old minus incorrectly calling foil objects old (i.e., hits minus false alarms). As

noted, the LDI measure is highly reliant on the hippocampus and its connectivity, whereas the recognition memory measure is not highly sensitive to hippocampal function.

Experiment 1B

Participants. Participants were recruited on site, over a single day, while participating at the 2015 Winter GameFest at University of California, San Diego. As is typical at such tournaments, gamers were highly specialized in their gaming and focused almost exclusively on a single game. Here, we chose competitive Super Smash Bros Brawl (SB: an extremely fast-paced 2D fighting game) players and competitive League of Legends (LOL: a 3D real-time strategy game) players. A total of 13 SB players and 19 LOL players were tested.

MST. The same MST from Experiment 1A was used here.

Experiment 2

Participants. Participants were recruited locally through campus fliers posted around the UCI campus. A total of 69 self-described naive video gamers were recruited for this study and were aged 18 to 22 years. These participants were divided randomly into three experimental groups: NG control group ($n = 24$; 8 male), 2D active control ($n = 22$, 8 male), and 3D experimental group ($n = 23$; 6 male). We did not observe gender differences in any behavioral measure.

Experimental design. The active controls played the 2D game Angry Birds (AB), and the experimental group played the 3D game Super Mario 3D World (SM). The design consisted of three testing sessions (Pretest, Posttest 1, and Posttest 2) separated by 2 weeks of either video game training or no contact. For the AB and SM groups, the first 2 week interval contained daily playing (30 min) of their respective game, whereas the NG group had no contact. For all three groups, the second 2 week interval involved no contact. All participants were given the enumeration task, the MST (counterbalanced image sets), and the virtual water maze task (vWM; counterbalanced environments) for the Pretest, Posttest 1, and Posttest 2. Unfortunately, several participants could not complete the experiment (e.g., some individuals were particularly sensitive to the vWM and were unable to finish because of nausea). We excluded these from the analyses, and specific counts are reported in the figure legends with each respective experiment.

Video game questionnaire. A modified version of the questionnaire from Experiment 1 was used. Although we stressed the desire for naive gamers, it is likely that, at one point, they have had watched or even played games. The cognitive training study questionnaire was designed to assess both direct and indirect video game experience.

Enumeration Task. For the enumeration task, there was no change from Experiment 1A.

MST. The same MST from Experiment 1A was used here. Separate sets of objects were used for the three different test phases (counterbalanced).

vWM. The vWM was created using the Source Engine (Valve Corporation), designed to mimic the rodent Morris water maze task (Fig. 1B). Using the mouse and keyboard (mouse to look and spacebar to move forward), participants could move virtually in a pool-like 3D environment and navigate using extramaze cues. Participants completed a total of 12 self-directed trials, starting from a random location, and were given 30 min to complete all 12 trials. There was no time limit for individual trials to allow them to gain a better understanding of the platform location (Chrastil and Warren, 2012). Time was recorded continuously, and the coordinate location of the user was recorded every 250 ms (Fig. 1C).

Virtual water maze environments. Three different vWM environments were used for each testing session (counterbalanced). All consisted of mountainous cues in an outdoor environment (Fig. 1B).

Virtual water maze probe trials. All participants received two probe trials, 2 weeks after learning the platform location. Probe 1 tested memory for the platform location learned during Pretest. Probe 2 tested memory for the platform location learned during Posttest 1. During the probe trial, the platform was removed, and participants were given 60 s to search for the missing platform from a novel starting location. All participants were told that the hidden platform was in the same location as before.

Video games. All games were played on the Wii U on a 32-inch high-definition LED television. Participants came into our testing facility on 10 consecutive days (except weekends) and played for a total of 30 min every day. An experimenter was present during training periods to ensure that participants played the entire time. Video game performance measures (score, number of levels, and number of achievements) were recorded by the Wii U. For each performance measure, an individual index score was calculated as a fraction of the total group score (individual score/total group score).

Results

Experiment 1A

If video game exposure provides environmental enrichment and if this enrichment leads to an alteration of hippocampal function (and perhaps DG function in particular), we should be able to observe an effect of previous gaming experience on behavioral performance on hippocampal-associated tasks. Experiment 1 tests this hypothesis by assessing the relationship between gaming experience (via a questionnaire) and memory performance using the MST and speed of visual processing using an enumeration task.

No effect of previous gaming experience on enumeration

Although previous studies have observed a relationship between action video gamers and visual perception using an enumeration task (Green and Bavelier, 2006), we found no difference in either speed (two-way ANOVA with repeated measures: $F_{(1,46)} = 1.34$, $p = 0.25$) or accuracy (two-way ANOVA with repeated measures: $F_{(1,46)} = 0.91$, $p = 0.34$). However, it should be noted that our video game group did not specialize in one particular genre of video game (whereas the Green and Bavelier group tested action-video gamers specifically) but rather commonly played games from a number of video game genres.

Video game experience related to mnemonic discrimination

As noted, the MST provides both a simple recognition memory measure and a hippocampally mediated LDI measure. If video games are providing a form of environmental enrichment that alters hippocampal function, we would expect an effect of gaming on the LDI measure without any requisite effect on the recognition memory measure. On the simple recognition memory measure, no difference was observed between the VG and the control (CON) groups ($t_{(66)} = 1.15$, $p = 0.25$). However, on the LDI measure (Fig. 2A), the VG group showed better mnemonic discrimination than the CON group ($t_{(66)} = 3.17$, $p < 0.005$).

Although we observed a highly reliable difference in LDI between the VG and CON groups, we were ultimately interested in the underlying factors that might account for this effect. Thus, we analyzed the questionnaire to determine possible video gaming habits and experiences that might account for the observed effect. Surprisingly, we did not find a correlation between the LDI and any measure of video game experience and performance. The amount of time spent playing, in both years spent playing ($r^2 = 0.02$, $p = 0.38$) and hours spent playing daily ($r^2 = 0.002$, $p = 0.76$), did not correlate with performance on the LDI. In addition, game genre such as action video games did not correlate with LDI scores (fighting, $r^2 = 0.03$, $p = 0.26$; first-person shooter, $r^2 = 0.017$, $p = 0.41$; real-time strategy, $r^2 = 0.01$, $p = 0.45$; action/adventure, $r^2 = 0.02$, $p = 0.33$; massively multiplayer online role-playing game, $r^2 = 0.05$, $p = 0.15$; racing, $r^2 < 0.00001$, $p = 0.99$; sports, $r^2 = 0.009$, $p = 0.56$; simulation, $r^2 = 0.006$, $p = 0.61$; platform, $r^2 = 0.005$, $p = 0.66$). One problem we encountered while trying to classify video games into game genres was that, oftentimes, video games fell into a range of genres and can be difficult to fit in one particular genre.

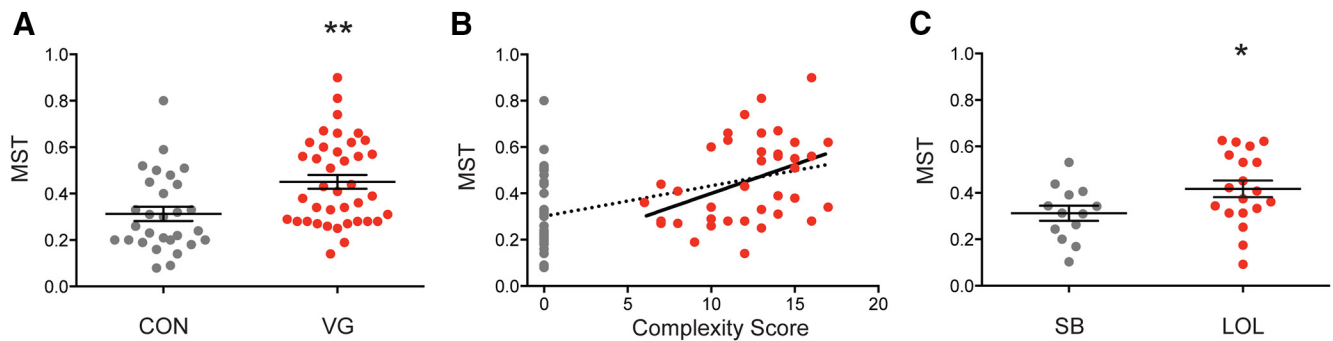


Figure 2. Lure discrimination performance of self-described video gamers and competitive video gamers on the MST. **A**, The CON group ($n = 29$) compared with VG group ($n = 39$) on the MST task. **B**, Scatter plot of video game complexity scores of video gamers (in red, $n = 39$) and non-video gamers (in gray, $n = 29$) paired with MST scores. The solid black line is a linear regression of only video gamers, and the dotted black line is a linear regression of both video gamers and non-video gamers. **C**, MST scores of competitive 2D video gamers (SB, $n = 13$) and competitive 3D video gamers (LOL, $n = 19$). All data are presented as mean \pm SEM; * $p < 0.05$, ** $p < 0.01$.

Game perspective relates to mnemonic discrimination

The hippocampus is often thought to carry an allocentric or “map” representation of the environment as opposed to an egocentric or “route” representation (Burgess, 2008). With this in mind, we investigated specific video games on which the VG group focused and the perspectives used in these games. We asked participants to list the three video games that they played the most and then classified these games into different viewpoint perspectives. Although most video games can easily be separated into a 2D or 3D viewpoint, they can be further subdivided. 2D video game subdivisions include the following viewpoints: (1) static (Tetris); (2) side-scrolling (Super Mario Bros or Sonic the Hedgehog); (3) top-down (The Legend of Zelda); and (4) pseudo-3D (Diablo). In addition, 3D video games can include first-person (Halo or Destiny), third-person (Grand Theft Auto V or Super Mario 64), and third-person omniscient (LOL, Defense of the Ancients 2) viewpoints. Although many video games contain an environment (2D or 3D), the amount of complexity and spatial information that can be learned from this environment increases as one moves from a 2D to a 3D perspective. Pseudo-3D is a fixed viewpoint, but the viewing angle allows for multiple dimensions of the environment to be seen. Third-person omniscient is a 3D perspective in which the camera can be moved independent of the player to allow the user to view more of the map.

The top three games of all participants were divided into these categories and given a complexity score based on the viewpoint (2D static being the lowest and third-person omniscient being the highest). We refer to this as a “complexity” score because we cannot determine from the data at hand whether the relevant aspect is the viewpoint itself, the amount of information being presented, the amount of spatial information or number of spatial relationships being presented, or some combination thereof. Each individual received a total complexity score, based on their top three video games, which was paired with their MST LDI score. We observed a positive correlation between the complexity score and LDI ($r^2 = 0.17$, $p < 0.01$; Fig. 2B), demonstrating that video gamers who focused on more complex 3D video games performed better on the LDI. Adding non-gamers (with a score of 0) had little effect on the analysis ($r^2 = 0.2$, $p < 0.0001$), suggesting that video gamers who focused more on 2D video games performed similarly on the hippocampal-associated task to non-video gamers.

Experiment 1B

Experiment 1A showed that people who play spatially complex 3D video games have higher LDI scores in the MST than those

who play 2D games or non-gamers. Although we collected simple metrics of how much time individuals spent playing video games, it is difficult to objectively measure how “good” each individual is at video games, and differences here in our two groups could potentially confound our results. In Experiment 1B, we further tested our hypothesis by examining individuals who perform at an extremely high level of game play in either 2D or 3D video games. By testing competitive gamers on the MST, we sought to replicate the results of Experiment 1A (2D vs 3D video games) while controlling for and addressing any concerns that differences in motivation or skills/experience required to play at a competitive level of video games might affect the results.

Consistent with the results of Experiment 1A, the competitive players of a complex 3D game (LOL) performed better on the LDI measure than the 2D game group (SB; Fig. 2C; $t_{(30)} = 2.07$, $p < 0.05$), despite no difference in simple recognition memory ($t_{(30)} = 0.06$, $p = 0.9$). These data are consistent with results from Experiment 1A, supporting our previous hypothesis and suggesting that the 3D video games themselves are influencing hippocampal function regardless of how good the individual is.

Experiment 2

Whereas Experiments 1A and 1B suggested that people who play 3D video games have higher LDI scores than 2D and non-video gamers, it was unclear whether playing 3D video games actually improved their ability to perform on the MST or whether people with higher LDI scores tended to gravitate toward 3D video games. To determine whether playing 3D video games can increase performance on the MST, we used an intervention on naive video gamers in Experiment 2 (Fig. 3A,B).

No effect of training on the enumeration task

As in Experiment 1A, we measured basic visual processing ability using the enumeration task, measuring error rate as a measure of visual accuracy and reaction time as a measure of visual processing speed. Although performance in all groups decreased as the number of visual stimuli increased, we did not find any significant differences between the three groups in either error rate (two-way repeated-measures ANOVA: Pretest, $F_{(2,63)} = 0.6471$, $p = 0.52$; Posttest 1, $F_{(2,60)} = 0.3076$, $p = 0.73$; Posttest 2, $F_{(2,60)} = 0.2143$, $p = 0.8$) or reaction time (two-way repeated-measures ANOVA: Pretest, $F_{(2,56)} = 0.7275$, $p = 0.48$; Posttest 1, $F_{(2,55)} = 0.1699$, $p = 0.84$; Posttest 2, $F_{(2,56)} = 0.2923$, $p = 0.74$). Thus, the NG, AB, and SM groups were equivalent in all measures.

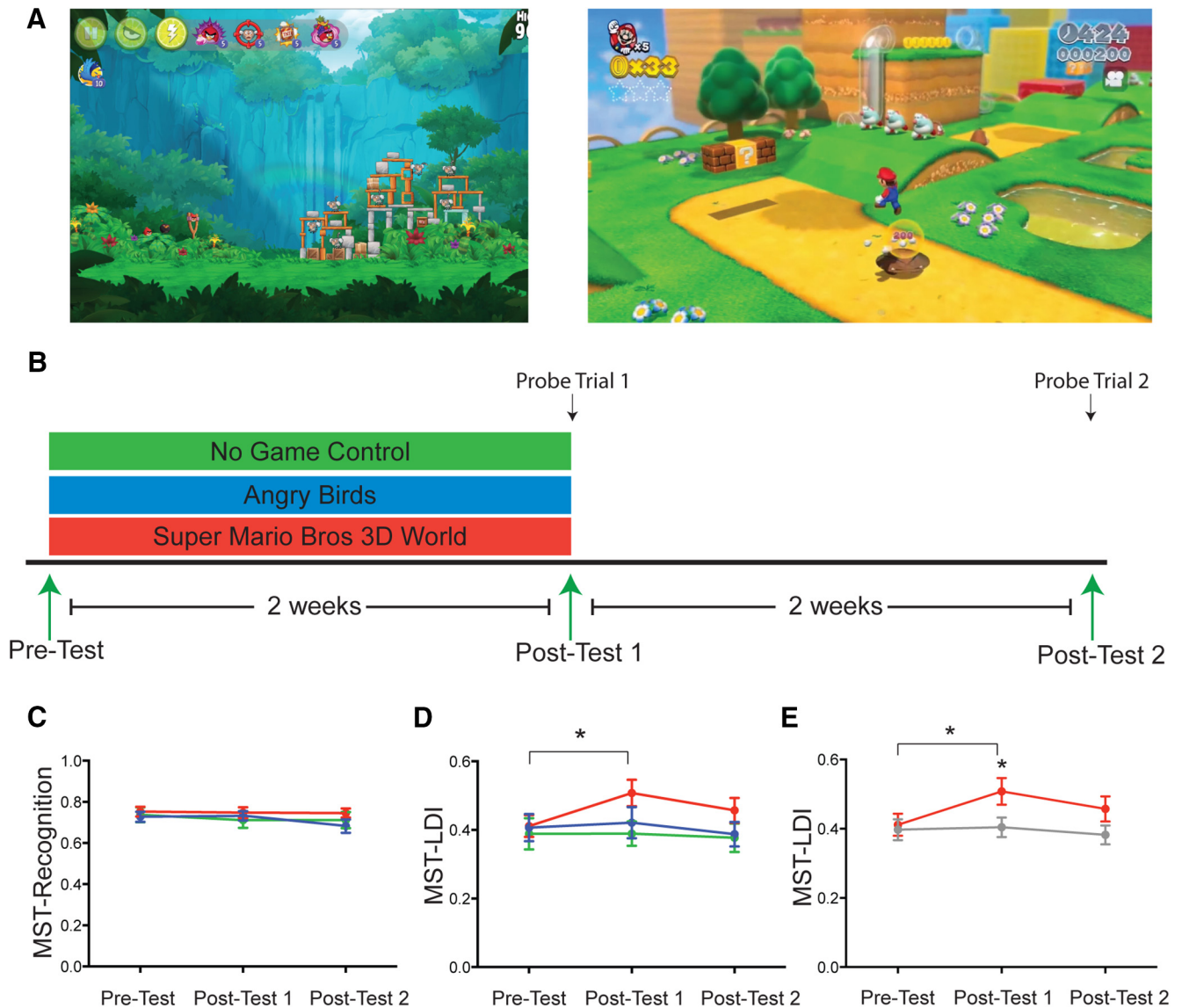


Figure 3. Results of the video game intervention. **A**, Screenshot of Angry Birds (left) and Super Mario 3D World (right). **B**, Timeline of the intervention study and testing sessions. **C**, MST recognition performance of the NG ($n = 24$), AB ($n = 21$), and SB ($n = 23$) groups during the Pretest, Posttest 1, and Posttest 2. **D**, MST lure discrimination performance of the NG ($n = 24$), AB ($n = 21$), and SM ($n = 23$) groups during the Pretest, Posttest 1, and Posttest 2. **E**, MST lure discrimination performance of the combined controls ($n = 45$) and SB group ($n = 23$) during the Pretest, Posttest 1, and Posttest 2. All data are presented as mean \pm SEM. * $p < 0.05$.

Table 1. Average values of individual components of the MST for the SM and CON groups for Pretest and Posttest 1

	Pretest			Posttest 1		
	Old	Similar	New	Old	Similar	New
SM						
Target	0.793 \pm 0.024	0.145 \pm 0.015	0.062 \pm 0.014	0.778 \pm 0.026	0.163 \pm 0.023	0.059 \pm 0.014
Lure	0.293 \pm 0.024	0.548 \pm 0.027	0.158 \pm 0.022	0.209 \pm 0.026	0.64 \pm 0.037	0.15 \pm 0.029
Foil	0.04 \pm 0.006	0.136 \pm 0.019	0.823 \pm 0.022	0.03 \pm 0.008	0.132 \pm 0.018	0.84 \pm 0.02
CON						
Target	0.778 \pm 0.018	0.167 \pm 0.014	0.055 \pm 0.007	0.761 \pm 0.017	0.172 \pm 0.013	0.066 \pm 0.007
Lure	0.28 \pm 0.02	0.548 \pm 0.02	0.172 \pm 0.015	0.261 \pm 0.018	0.579 \pm 0.018	0.159 \pm 0.014
Foil	0.045 \pm 0.006	0.154 \pm 0.014	0.8 \pm 0.016	0.039 \pm 0.006	0.175 \pm 0.012	0.785 \pm 0.014

The MST LDI score was calculated using the formula described in the Materials and Methods. Data are presented as mean \pm SEM.

3D game training improved mnemonic discrimination

Before any training, the NG, AB, and SM groups performed similarly (Table 1, Fig. 3C,D). On both the MST recognition (one-way ANOVA: $F_{(2,66)} = 0.1811, p = 0.83$) and LDI (one-way ANOVA: $F_{(2,66)} = 0.0835, p = 0.92$) measures, no differences between groups existed here at baseline.

The first critical question was whether there was any effect of training on the MST measures. If Super Mario is serving as a suitable form of environmental enrichment and if this is driving a change in the hippocampus, we should observe an effect on the LDI without necessarily any effect on the recognition memory measure. To assess this, we calculated a simple difference score

for each participant (Posttest 1 – Pretest). Although no effects were observed for any group on the recognition memory measure (all p values >0.39), a reliable effect of training on the LDI measure was observed in the SM group ($t_{(22)} = 2.5$, $p < 0.02$) alone (AB, $p = 0.68$; NC, $p = 0.99$). Because there was no evidence for any differences between our two control groups, they were collapsed to increase power in the remainder of these analyses (Fig. 3E).

The second critical question is whether 2 weeks of training in Super Mario had a reliably larger effect than in the controls. Using this same difference score, we observed that, although there was no differential effect on recognition memory ($t_{(66)} = 0.24$, $p = 0.81$), there was a reliably larger effect the LDI measure after SM than the control conditions ($t_{(66)} = 2.03$, $p < 0.05$). In addition, we observed that the LDI measure at Posttest 1 was higher in the SM group than in the CON groups ($t_{(66)} = 2.16$, $p < 0.05$).

The third question is whether the effect of training persisted over a no-contact delay of 2 weeks. Here, results were equivocal. Although there was no reliable decrease in performance on the LDI measure between the two posttests in the SM group ($t_{(22)} = 1.6$, $p = 0.12$), the difference in performance between the SM group and the CON groups showed a similar, nonreliable trend ($t_{(66)} = 1.6$, $p = 0.11$). Thus, although an analysis of the full set of posttraining LDI data shows a main effect of group (two-way ANOVA with repeated measures: $F_{(1,66)} = 4.24$, $p < 0.05$) and no group \times time interaction ($F_{(1,66)} = 0.6$, $p = 0.44$), this level of performance at Posttest 2 in the SM group suggests the effects on the LDI observed after Super Mario 3D World training have begun to dissipate after 2 weeks without contact.

Importantly, although the MST contains multiple performance components, the LDI measure is based only on the ability to correctly identify lures item as similar minus incorrectly identifying foil object as similar. The changes we observe here are specifically attributable to an increase in the percentage of correctly calling a lure similar (Table 1).

3D game training improved vWM probe trial performance

In the vWM, all participants were able to learn the location of the hidden platform in the vWM, and there were no differences observed in performance of the task itself at Pretest (two-way ANOVA with repeated measures: significant main effect of time, $F_{(10,500)} = 4.98$, $p < 0.0001$; main effect of group, $F_{(2,50)} = 1.01$, $p = 0.37$), Posttest 1 (two-way ANOVA with repeated measures: significant main effect of time, $F_{(10,560)} = 2.73$, $p < 0.01$; main effect of group, $F_{(2,56)} = 0.34$, $p = 0.72$), or Posttest 2 (two-way ANOVA with repeated measures: significant main effect of time, $F_{(10,550)} = 2.35$, $p < 0.01$; main effect of group, $F_{(2,55)} = 2.32$, $p = 0.11$) as measured by total latency to the platform (Fig. 4A). Distance to the platform resulted in a similar outcome. In addition, using the optimal distance measure (see Materials and Methods) to collapse all vWM trials, there was no measureable improvement in vWM from Pretest to Posttest 1 (two-way ANOVA with repeated measures: significant main effect of time, $F_{(1,60)} = 4.99$, $p < 0.05$; main effect of group, $F_{(2,60)} = 0.6$, $p = 0.55$) and Posttest 1 to Posttest 2 (two-way ANOVA with repeated measures: main effect of time, $F_{(1,59)} = 0.44$, $p = 0.51$; main effect of group, $F_{(2,59)} = 0.09$, $p = 0.91$).

Such null effects are common because many strategies can be used to solve the vWM when the platform is present. In the rodent, spatial memory is typically assessed using a probe trial in which the platform is removed and searching behavior in the platform area is measured (see Materials and Methods; Morris 1981). We did not find differences in the initial first platform

crossing in either time (two-way ANOVA with repeated measures: main effect of time, $F_{(1,58)} = 0.0002$, $p = 0.99$; main effect of group, $F_{(2,58)} = 0.57$, $p = 0.56$) or distance (two-way ANOVA with repeated measures: main effect of time, $F_{(1,58)} = 0.21$, $p = 0.64$; main effect of group, $F_{(2,58)} = 0.62$, $p = 0.54$). However, using the amount of time spent searching for the platform, we observed an overall improvement of spatial memory in the SM group compared with the CON group (two-way ANOVA with repeated measures: significant main effect of group, $F_{(1,58)} = 5.51$, $p < 0.05$; Fig. 4B).

3D game performance related to mnemonic discrimination and vWM probe trial performance

Although all participants trained on the same respective video game, individual experience varied. Apart from simple instructions of how to use the controls and the general nature of the game, there were no restrictions on how to progress. Thus, participants were given the necessary tools to play the game but were allowed to explore the game however they pleased. This resulted in a variety of unique individual experiences. For example, some participants ran through each level quickly in attempts to complete the last level of the game, whereas some participants focused on collecting and finding all the unique secrets of the game and would often repeat levels to do so. To address the variability in game play, we recorded and analyzed multiple measures of video game performance. Within Super Mario, we recorded total score, levels completed, total stars found, and total stamps found. Stars and stamps are secret items that are hidden in each level of the game. In Angry Birds, we recorded total score, levels completed, and total stars received. Stars in Angry Birds were received based on the score after completing a level (higher score = more stars). We used an index score (see Materials and Methods) to normalize performance across multiple video game performance measures.

For the SM group, we found some evidence for a correlation between overall video game performance and the LDI measure of the MST immediately after training ($r^2 = 0.16$, $p = 0.06$). Breaking down performance measures further, we found that the LDI correlated significantly with the combined stars and stamps collected ($r^2 = 0.18$, $p < 0.05$; Fig. 4D) but not total score ($r^2 = 0.12$, $p = 0.11$) or levels completed ($r^2 = 0.08$, $p = 0.18$). Video game performance also correlated significantly with performance on Probe 2 ($r^2 = 0.29$, $p < 0.01$) but not Probe 1 ($r^2 = 0.06$, $p = 0.24$). Interestingly, there was absolutely no correlation in the AB group between video game performance and the LDI measure of the MST ($r^2 = 0.004$, $p = 0.77$; Fig. 4E), Probe 1 ($r^2 = 0.04$, $p = 0.42$) or Probe 2 ($r^2 = 0.04$, $p = 0.38$).

Discussion

In Experiment 1A, we tested self-described video gamers on a hippocampally mediated memory task that uses highly similar lures (the LDI metric of the MST) and discovered that people who play complex 3D video games perform better than people who focus on simpler 2D games. Furthermore, in Experiment 1B, we found that even in a highly competitive population of video gamers, those who specialize in a spatially complex 3D video game outperformed those who specialize in a 2D video game on this same metric. In Experiment 2, we tested whether we could induce the effect by training naive video gamers on a simple 2D game or a complex 3D game and discovered that we could induce the effect within a short, 2 week training protocol (and a parallel effect on probe-trial performance in a vWM) but only in the complex 3D game group. Interestingly, performance on both hippocampal-associated memory metrics correlated with the

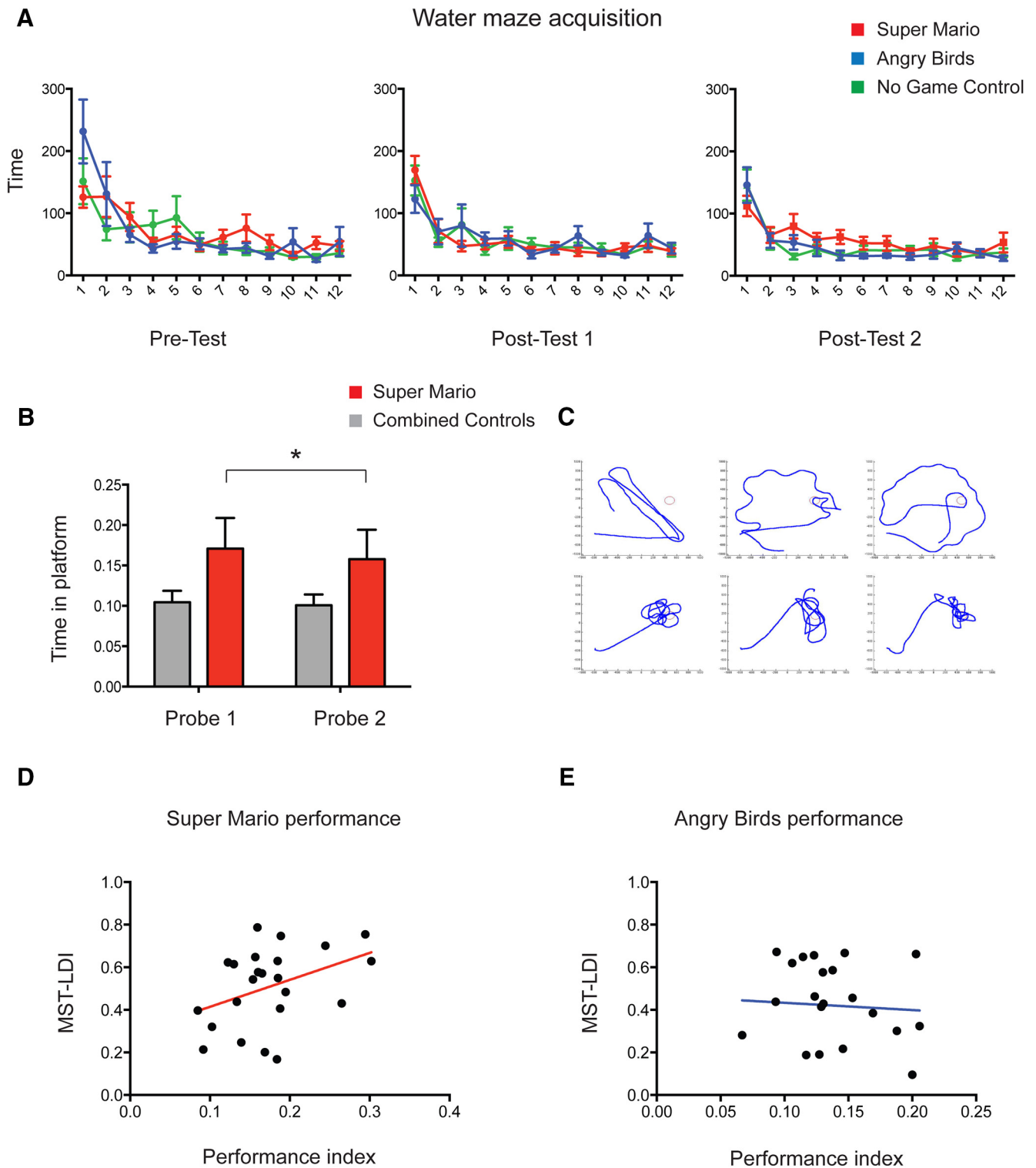


Figure 4. Virtual water maze and video game performance of CON, AB, and SM groups. **A**, Virtual water maze acquisition during Pretest (NG, $n = 18$; AB, $n = 15$; SM, $n = 20$), Posttest 1 (NG, $n = 21$; AB, $n = 17$; SM, $n = 21$), and Posttest 2 (NG, $n = 20$; AB, $n = 17$; SM, $n = 21$). **B**, Time in platform of Probe 1 (combined controls, $n = 38$; SM, $n = 22$) and Probe 2 (combined controls, $n = 38$; SM, $n = 22$). **C**, Example water maze probe traces demonstrating the use of both nonspatial (top 3) and spatial (bottom 3) strategies. **D**, Video game performance of the SM group ($n = 23$) compared with their MST lure discrimination performance. **E**, Video game performance of the AB group ($n = 22$). All data are presented as mean \pm SEM; * $p < 0.05$.

amount of exploration of the complex 3D world. Across all experiments, the benefits were specific to the hippocampus-associated behaviors.

Video games are part of a multibillion-dollar industry that is constantly evolving (Entertainment Software Association, 2015).

Advances in technology and online interactions have led to video games that are more engaging and immersive than ever before. Adding to the excitement are the vast complex environments in which these video games take place. Often, success in video games requires keen map knowledge to navigate these virtual environ-

ments to complete missions and objectives. Although human studies have shown that the hippocampus plays an active role in the navigation and spatial memory of virtual environments (Burgess et al., 2002), the environments in video games are far richer and more engaging than those used in typical laboratory tests (e.g., the vWM). Here we provide evidence consistent with our hypothesis that playing a complex 3D video game can stimulate the hippocampus, leading to an enhancement in hippocampus-associated behavior.

In Experiment 1A, we did not observe any correlation between the LDI measure of the MST and time spent playing. At first, this may seem counterintuitive and in contrast to our results from Experiment 2. The difference in LDI scores between complex 3D gamers and non-gamers in Experiment 1A is equivalent to ~30 years worth of age-related decline, and the gaming-induced boost in performance in Experiment 2 is equivalent to ~20 years of decline (Stark et al., 2013 showed a linear decline of 0.048 per decade). Thus, these are substantial effects and there is little reason to expect that they must scale linearly without bound. For example, although physical exercise can increase muscle mass, a decade of exercise will not lead to an order of magnitude more muscle gain than 1 year of exercise. In addition, results of Experiment 2 demonstrate that, despite all participants playing the same amount of time, video game performance was a better indicator of MST score.

Although Experiment 2 showed a difference in memory performance between Super Mario 3D World and Angry Birds training, there are a number of differences that make it difficult to isolate the relevant factor(s) from the data at hand. One clear difference is the complexity of the view (2D vs 3D), and a second is the amount of spatial and nonspatial information to be learned. In Super Mario 3D World, there is a rich array of information on each level that must be explored and learned that is simply not present in Angry Birds. Whether our results stem from the perspective, the richness or amount of information, or the spatial aspects of the information per se cannot be determined from the present data but is a clear avenue for future experiments.

It is unlikely that “engagement” is responsible for the differences we observe. In Experiment 1B, participants were highly competitive gamers who chose to spend significant amounts of time on specific games. In Experiment 2, participants in both groups reported enjoying the training, and nobody dropped out of either condition. Moreover, video games are created primarily for entertainment and therefore are designed to engage and captivate the user. Angry Birds (Rovio Entertainment) has built a successful franchise with two billion downloads on mobile apps alone. Angry Birds has proven to be an engaging and even addictive game, despite having no explorative component of the environment. Both Super Mario 3D World and Angry Birds created a fun and exciting experience that was pleasant for the naive gamers.

The limits of virtual reality may limit how well the vWM task measures hippocampal-associated spatial memory in humans. However, studies have shown that the hippocampus is active during navigation of the vWM (Rodriguez, 2010), and patients with hippocampal damage or lesions are impaired in the vWM (Bartsch et al., 2010; Goodrich-Hunsaker et al., 2010). We did observe an effect on probe trial performance, but results on other measures were inconclusive and may be indicative of a lack of sensitivity or specificity in young healthy individuals. At the very least, it is encouraging to see that our results are consistent with rodent literature that have observed specific effects in probe trial performance (van Praag et al.,

2005; Jessberger et al., 2009; Martinez-Canabal et al. 2013) and other human studies. Additionally, it is worth noting that video games may be influencing navigational strategies (West et al., 2015) that can be used to solve the vWM, because video games are likely stimulating other regions of the brain involved in navigation. We attempted to assess spatial search strategies, but we discovered that participants would often use a combination of search strategies, making it difficult to objectively measure performance.

Our observed effects on the vWM might be viewed as transfer from training on one 3D spatial navigation and memory task (Super Mario 3D World) to another (vWM), but there is nothing inherently spatial about the MST. We cannot rule out the possibility that the complexity of the 3D environment is allowing for multiple viewings of the same objects from different perspectives, which translates to better discrimination in the MST. However, if this skill were translating to the LDI measure of the MST, we would imagine a similar enhancement in the general recognition task as a better recognition of “similar” objects should also improve the recognition of “not similar” objects.

The LDI measure, like the water maze, has been linked strongly to hippocampal function, and it has been linked to activity in and connectivity with the DG and CA3 regions of the hippocampus (Bakker et al., 2008; Bennett and Stark, 2015). One interpretation of our results is that the long-term exploration of complex 3D worlds in video games may be influencing specific hippocampal processes, such as hippocampal neurogenesis. Adult hippocampal neurogenesis is found in the DG and has been shown to correlate with pattern separation (Clelland et al., 2009; Creer et al., 2010; Sahay et al., 2011; Clemenson et al., 2015). Similar to the behavioral and neurogenic benefits of environmental enrichment in rodents (Kempermann et al., 1997; Fabel et al., 2009; Freund et al., 2013; Clemenson et al., 2015), the exploration of these novel and highly engaging virtual environments may be working through a similar mechanism in humans. Although it is unclear which features of the enriched environment are most salient, exploration of these environments have been singled out as a prominent regulator of hippocampal neurogenesis (Freund et al., 2013). Although neurogenic effects of enrichment (which cannot be tested directly here) provide a tantalizing account for the effects observed here and their dynamics, we would like to stress that such accounts are speculative.

Our study is not the first to observe the effects of video games on the brain (Latham et al., 2013; Kühn et al., 2014), but by using both a 3D and an active 2D control condition, our data suggest that the spatial aspect of the environment may have a specific influence on hippocampus-dependent behavior. Because of their engaging experiences and enriching 3D virtual environments, the same video games that have been played for decades by children and adults alike may actually provide our brain with meaningful stimulation.

Results from this study add to the existing literature that playing video games may provide meaningful stimulation to the brain. However, it is important to be cautious when generalizing these results to other instances. Recently, >70 neuroscientists from universities and institutions around the world published a letter discussing the myths of “brain training” (Max Planck Institute for Human Development/Stanford Center on Longevity, 2014). In contrast to typical brain training, typical video games are not created with specific cognitive processes in mind but

rather designed to captivate and immerse the user into characters and adventure. Rather than isolate single brain processes, modern video games can naturally draw on or require many cognitive processes, including visual, spatial, emotional, motivational, attentional, critical thinking, problem solving, and working memory. It is quite possible that, by explicitly avoiding a narrow focus on a single or small set of cognitive domains and by more closely paralleling natural experience, immersive video games may be better suited to provide enriching experiences that translate into functional gains.

References

- Bakker A, Kirwan CB, Miller M, Stark CE (2008) Pattern separation in the human hippocampal CA3 and dentate gyrus. *Science* 319:1640–1642. [CrossRef Medline](#)
- Bartsch T, Schönfeld R, Müller FJ, Alfke K, Lepow B, Aldenhoff J, Deuschl G, Koch JM (2010) Focal lesions of human hippocampal CA1 neurons in transient global amnesia impair place memory. *Science* 328:1412–1415. [CrossRef Medline](#)
- Bennett IJ, Stark CEL (2015) Mnemonic discrimination relates to perforant path integrity: an ultra-high resolution diffusion tensor imaging study. *Neurobiol Learn Mem*. Advance online publication. Retrieved November 8, 2015. doi:10.1016/j.nlm.2015.06.014. [CrossRef Medline](#)
- Birch AM, McGarry NB, Kelly AM (2013) Short-term environmental enrichment, in the absence of exercise, improves memory, and increases NGF concentration, early neuronal survival, and synaptogenesis in the dentate gyrus in a time-dependent manner. *Hippocampus* 23:437–450. [CrossRef Medline](#)
- Burgess N (2008) Spatial cognition and the brain. *Ann N Y Acad Sci*, 1124: 77–97. [CrossRef Medline](#)
- Burgess N, Maguire EA, O'Keefe J (2002) The human hippocampus and spatial and episodic memory. *Neuron* 35:625–641. [CrossRef Medline](#)
- Chrastil ER, Warren WH (2012) Active and passive contributions to spatial learning. *Psychon Bull Rev* 19:1–23. [CrossRef Medline](#)
- Clelland CD, Choi M, Romberg C, Clemenson GD Jr, Fragniere A, Tyers P, Jessberger S, Saksida LM, Barker RA, Gage FH, Bussey TJ (2009) A functional role for adult hippocampal neurogenesis in spatial pattern separation. *Science* 325:210–213. [CrossRef Medline](#)
- Clemenson GD, Lee SW, Deng W, Barrera VR, Iwamoto KS, Fanselow MS, Gage FH (2015) Enrichment rescues contextual discrimination deficit associated with immediate shock. *Hippocampus* 25:385–392. [CrossRef Medline](#)
- Creer DJ, Romberg C, Saksida LM, van Praag H, Bussey TJ (2010) Running enhances spatial pattern separation in mice. *Proc Natl Acad Sci U S A* 107:2367–2372. [CrossRef Medline](#)
- Ekstrom AD, Kahana MJ, Caplan JB, Fields TA, Isham EA, Newman EL, Fried I (2003) Cellular networks underlying human spatial navigation. *Nature* 425:184–188. [CrossRef Medline](#)
- Eriksson PS, Perfilieva E, Björk-Eriksson T, Alborn AM, Nordborg C, Peterson DA, Gage FH (1998) Neurogenesis in the adult human hippocampus. *Nat Med* 4:1313–1317. [CrossRef Medline](#)
- Entertainment Software Association (2015) Essential facts about the computer and video game industry: 2015 sales, demographic and usage data. Washington, DC: Entertainment Software Association.
- Fabel K, Wolf SA, Ehniger D, Babu H, Leal-Galicia P, Kempermann G (2009) Additive effects of physical exercise and environmental enrichment on adult hippocampal neurogenesis in mice. *Front Neurosci* 3:50. [CrossRef Medline](#)
- Freund J, Brandmaier AM, Lewejohann L, Kirste I, Kritzler M, Krüger A, Sachser N, Lindenberger U, Kempermann G (2013) Emergence of individuality in genetically identical mice. *Science* 340:756–759. [CrossRef Medline](#)
- Goodrich-Hunsaker NJ, Livingstone SA, Skelton RW, Hopkins RO (2010) Spatial deficits in a virtual water maze in amnesic participants with hippocampal damage. *Hippocampus* 20:481–491. [CrossRef Medline](#)
- Green CS, Bavelier D (2006) Enumeration versus multiple object tracking: the case of action video game players. *Cognition* 101:217–245. [CrossRef Medline](#)
- Hafting T, Fyhn M, Molden S, Moser MB, Moser EI (2005) Microstructure of a spatial map in the entorhinal cortex. *Nature* 436:801–806. [CrossRef Medline](#)
- Harvey CD, Collman F, Dombeck DA, Tank DW (2009) Intracellular dynamics of hippocampal place cells during virtual navigation. *Nature* 461: 941–946. [CrossRef Medline](#)
- Jacobs NS, Allen TA, Nguyen N, Fortin NJ (2013) Critical role of the hippocampus in memory for elapsed time. *J Neurosci* 33:13888–13893. [CrossRef Medline](#)
- Jessberger S, Clark RE, Broadbent NJ, Clemenson GD Jr, Consiglio A, Lie DC, Squire LR, Gage FH (2009) Dentate gyrus-specific knockdown of adult neurogenesis impairs spatial and object recognition memory in adult rats. *Learn Mem* 16:147–154. [CrossRef Medline](#)
- Kempermann G, Kuhn HG, Gage FH (1997) More hippocampal neurons in adult mice living in an enriched environment. *Nature* 386:493–495. [CrossRef Medline](#)
- Kirwan CB, Stark CE (2007) Overcoming interference: an fMRI investigation of pattern separation in the medial temporal lobe. *Learn Mem* 14: 625–633. [CrossRef Medline](#)
- Kirwan C, Hartshorn A, Stark SM, Goodrich-Hunsaker NJ, Hopkins RO, Stark CE (2012) Pattern separation deficits following damage to the hippocampus. *Neuropsychologia* 50:2408–2414. [CrossRef Medline](#)
- Kühn S, Gleich T, Lorenz RC, Lindenberger U, Gallinat J (2014) Playing Super Mario induces structural brain plasticity: gray matter changes resulting from training with a commercial video game. *Mol Psychiatry* 19: 265–271. [CrossRef Medline](#)
- Lacy JW, Yassa MA, Stark SM, Muftuler LT, Stark CE (2011) Distinct pattern separation related transfer functions in human CA3/dentate and CA1 revealed using high-resolution fMRI and variable mnemonic similarity. *Learn Mem* 18:15–18. [CrossRef Medline](#)
- Latham AJ, Patston LL, Tippett LJ (2013) The virtual brain: 30 years of video-game play and cognitive abilities. *Front Psychol* 4:629. [CrossRef Medline](#)
- Max Planck Institute for Human Development/Stanford Center on Longevity (2014) A consensus on the brain training industry from the scientific community. Stanford, CA: Stanford Center on Longevity.
- Maguire EA, Burgess N, Donnett JG, Frackowiak RS, Frith CD, O'Keefe J (1998) Knowing where and getting there: a human navigation network. *Science* 280:921–924. [CrossRef Medline](#)
- Maguire EA, Gadian DG, Johnsrude IS, Good CD, Ashburner J, Frackowiak RS, Frith CD (2000) Navigation-related structural change in the hippocampi of taxi drivers. *Proc Natl Acad Sci U S A* 97:4398–4403. [CrossRef Medline](#)
- Manganas LN, Zhang X, Li Y, Hazel RD, Smith SD, Wagshul ME, Henn F, Benveniste H, Djuric PM, Enikolopov G, Maletic-Savatic M (2007) Magnetic resonance spectroscopy identifies neural progenitor cells in the live human brain. *Science* 318:980–985. [CrossRef Medline](#)
- Martinez-Canabal A, Akers KG, Josselyn SA, Frankland PW (2013) Age-dependent effects of hippocampal neurogenesis suppression on spatial learning. *Hippocampus* 23:66–74. [CrossRef Medline](#)
- Morris R (1984) Developments of a water-maze procedure for studying spatial learning in the rat. *J Neurosci Methods* 11:47–60. [CrossRef Medline](#)
- Morris RG (1981) Spatial localization does not require the presence of local cues. *Learn Motiv* 12:239–260. [CrossRef](#)
- O'Keefe J, Dostrovsky J (1971) The hippocampus as a spatial map: Preliminary evidence from unit activity in the freely-moving rat. *Brain Res* 34: 171–175. [CrossRef Medline](#)
- O'Keefe J, Nadel L (1978) *The hippocampus as a cognitive map*. Oxford, UK: Clarendon.
- Olson AK, Eadie BD, Ernst C, Christie BR (2006) Environmental enrichment and voluntary exercise massively increase neurogenesis in the adult hippocampus via dissociable pathways. *Hippocampus* 16:250–260. [CrossRef Medline](#)
- Rodriguez PF (2010) Human navigation that requires calculating heading vectors recruits parietal cortex in a virtual and visually sparse water maze task in fMRI. *Behav Neurosci* 124:532–540. [CrossRef Medline](#)
- Sahay A, Scobie KN, Hill AS, O'Carroll CM, Kheirbek MA, Burghardt NS, Fenton AA, Dranovsky A, Hen R (2011) Increasing adult hippocampal neurogenesis is sufficient to improve pattern separation. *Nature* 472: 466–470. [CrossRef Medline](#)
- Schmidt-Hieber C, Häusser M (2013) Cellular mechanisms of spatial navigation in the medial entorhinal cortex. *Nat Neurosci* 16:325–331. [CrossRef Medline](#)
- Spalding KL, Bergmann O, Alkass K, Bernard S, Salehpour M, Huttner HB, Boström E, Westerlund I, Vial C, Buchholz BA, Possnert G, Mash DC,

- Druid H, Frisén J (2013) Dynamics of hippocampal neurogenesis in adult humans. *Cell* 153:1219–1227. [CrossRef Medline](#)
- Stark SM, Yassa MA, Lacy JW, Stark CE (2013) A task to assess behavioral pattern separation (BPS) in humans: data from healthy aging and mild cognitive impairment. *Neuropsychologia* 51:2442–2449. [CrossRef Medline](#)
- Tolman EC (1948) Cognitive maps in rats and men. *Psychol Rev* 55:189–208. [CrossRef Medline](#)
- van Praag H, Kempermann G, Gage FH (1999) Running increases cell proliferation and neurogenesis in the adult mouse dentate gyrus. *Nat Neurosci* 2:266–270. [CrossRef Medline](#)
- van Praag H, Kempermann G, Gage FH (2000) Neural consequences of environmental enrichment. *Nat Rev Neurosci* 1:191–198. [CrossRef Medline](#)
- van Praag H, Shubert T, Zhao C, Gage FH (2005) Exercise enhances learning and hippocampal neurogenesis in aged mice. *J Neurosci* 25:8680–8685. [CrossRef Medline](#)
- West GL, Drisdelle BL, Konishi K, Jackson J, Jolicoeur P, Bohbot VD (2015) Habitual action video game playing is associated with caudate nucleus-dependent navigational strategies. *Proc Biol Sci* 282:2014–2952. [CrossRef Medline](#)
- Wilms IL, Petersen A, Vangkilde S (2013) Intensive video gaming improves encoding speed to visual short-term memory in young male adults. *Acta Psychol (Amst)* 142:108–118. [CrossRef Medline](#)
- Woollett K, Spiers HJ, Maguire EA (2009) Talent in the taxi: a model system for exploring expertise. *Philos Trans R Soc Lond B Biol Sci* 364:1407–1416. [CrossRef Medline](#)
- Yassa MA, Stark CE (2011) Pattern separation in the hippocampus. *Trends Neurosci* 34:515–525. [CrossRef Medline](#)
- Zhao C, Jou J, Wolff LJ, Sun H, Gage FH (2014) Spine morphogenesis in newborn granule cells is differentially regulated in the outer and middle molecular layers. *J Comp Neurol* 522:2756–2766. [CrossRef Medline](#)