Cognitive, Affective, & Behavioral Neuroscience
https://doi.org/10.3758/s13415-021-00942-5

RESEARCH ARTICLE

# Diversity of daily activities is associated with greater hippocampal volume

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Accepted: 5 August 2021


## Abstract

Greater engagement in a range of daily activities is associated with better cognitive functioning (Lee et al., Lee et al., 2020). The hippocampus, a subcortical brain structure implicated in learning, memory, spatial navigation and other aspects of cognitive functioning, may be structurally sensitive to exposure to and engagement with novel experiences and environments. The present study tested whether greater activity diversity, defined as the range of common daily activities engaged in and the proportion of time spent in each, is associated with larger hippocampal volume. Greater diversity of activities, as measured using daily diaries across an 8-day period, was related to greater hippocampal volume averaged across the left and right hemispheres, even when adjusting for estimated intracranial volume, total activity time, sociodemographic factors, and self-reported physical health. These findings are broadly consistent with nonhuman animal studies, demonstrating a link between enriched environments and structural changes to the hippocampus. Future longitudinal and experimental work can elucidate causal and directional relationships between diversity of daily activities and hippocampal volume.

**Keywords** Activity diversity · Hippocampus · Daily experiences · Structural magnetic resonance imaging

## Introduction

A growing area of research emphasizes the ways in which increased diversity of experiences contributes to better health and well-being. Just as measures of biodiversity are thought to provide important information about environmental ecosystems beyond the sheer number of organisms in that ecosystem, measures of experiential diversity are thought to provide insight into psychological processes and outcomes beyond the aggregate or average of an individual person's experience. Borrowing from the concept of biodiversity, recent metrics of experiential diversity, such as emotion diversity (Quoidbach et al., 2014; Urban-Wojcik et al., 2020), stressor diversity (Koffer et al., 2016), and activity diversity (Lee et al., 2018; Lee et al., 2020), quantify the range (e.g., discrete types) and evenness (e.g., proportion of time spent) of one's emotion, stressors, and daily activities, respectively. Only recently have these diversity metrics been examined in relation to brain function (Heller et al., 2020). How brain structural differences may be associated with diversity of daily experiences, however, remains unknown.

### Activity Diversity

Activity diversity is a quantification of the range and evenness of participation in daily activities (Lee et al., Lee et al., 2018, 2020). Someone who has high activity diversity, for example, engages in a wide range of activities (such as working, doing chores, and leisure activities) and spends similar amounts of time in each of these activities, whereas someone with low activity diversity may spend most of their time doing one thing. Past research on activity diversity has shown that people, particularly older adults, who reported engaging in more diverse daily activities across an 8-day period had higher

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Published online: 01 October 2021

levels of psychological well-being as measured by a scale incorporating six different dimensions of eudaimonic well-being(Lee et al., 2018). Furthermore, individuals who increased the diversity of their daily activities between a baseline measurement and a follow-up approximately 10 years later also demonstrated trend level increases in their overall positive affect. Importantly, these associations held even while adjusting for total amount of time spent engaging in activities, demonstrating that the associated increases in psychological well-being and positive affect are not solely due to having a busier schedule (Lee et al., 2018).

In another study that used GPS tracking to log the locations each person visited, people reported higher levels of positive affect on days they logged more variable physical locations (Heller et al., 2020). This effect was stronger for people with greater functional coupling between the hippocampus, which is involved in learning, memory, and spatial navigation (Burgess et al., 2002; O'Keefe & Nadel, 1978; Rolls, 2010; Squire et al., 2004), and the ventral striatum, which responds to reward (Delgado et al., 2000; Haber & Knutson, 2010). The authors also tested whether the mere movement through different locations (i.e., "location diversity") or movement through areas that implicate diverse experiences (i.e., "experiential diversity") was most related to increases in positive affect. Using a measure of experiential diversity defined by movement through different sociodemographic regions (implicating more diverse experiences), they found that experiential diversity played a greater role than location diversity in changes in positive affect. These findings highlight a neural circuit that may be important for understanding the mechanistic relationship between experiential diversity and indicators of well-being and underscore the importance of experiential diversity (and not just location diversity). The authors did not report on the relationship between experiential diversity and brain structural differences.

Activity diversity also has recently been examined in relation to cognitive functioning (Lee et al., 2020). Participants in the Midlife in the United States II (MIDUS II) study with greater levels of activity diversity had better concurrent executive functioning, as measured using a brief telephone-administered cognitive battery (Lachman et al., 2014; Lachman & Tun, 2008). Individuals who increased their activity diversity from approximately 10 years earlier, or who had high activity diversity at both waves, also had higher executive functioning and episodic memory compared to their counterparts. These analyses adjusted for a number of covariates, including total activity time and self-reported physical health, demonstrating the unique relationship between the diversity of activities and cognition beyond overall activity frequency and perceived physical health. This study revealed that the construct of activity diversity is important not only to psychological well-being and emotional health, but also to cognitive functioning. Another study compared the frequency versus variety of activities and their relationship with cognitive function among healthy older adults (Bielak et al., 2019). Results showed that people who reported spending more time engaging in activities also tended to take part in a greater range of activities and that both greater frequency and greater range of activity was associated with better cognitive function.

## Activity Diversity and Hippocampal Volume

Engagement in diverse daily activities may be related to the structure and function of the hippocampus. The hippocampus is one of the few structures in the brain that demonstrates neurogenesis across the lifespan (Eriksson et al., 1998; Spalding et al., 2013). This neurogenesis supports the ability to incorporate newly experienced information with previously learned information (Garthe & Kempermann, 2013) and to navigate novel situations and environments (Kempermann, 2008). The impact of hippocampal neurogenesis on navigation is supported by nonhuman animal research such that mice living in enriched environments have more new hippocampal neurons than those in less enriched environments (Kempermann et al., 1997). Moreover, mice who explore a greater range of territory (termed "roaming entropy") exhibit more hippocampal neurogenesis than those who explore a more restricted range, even taking into account total amount of movement (Freund et al., 2013). Activity diversity, as a marker of exposure to and engagement with novel experiences and environments, may be related to hippocampal volume. Activity diversity is a unique construct that is similar to roaming entropy in terms of physical movement and spatial navigation but also captures a broad range of *experiences* across different social roles and settings (e.g., paid work, leisure, time with children, formal volunteering). For humans, the diversity of experiences when visiting diverse locations may matter more than just accounting for the fact that they are visiting more diverse locations in general (Heller et al., 2020).

Neuroimaging studies in humans complement rodent studies, providing correlational data linking hippocampal volume to the diversity of real-world experiences. For example, one study found a correlation between hippocampal volume and subjects' spatial navigation ability, both virtually and in real-space(Nedelska et al., 2012). A classic set of studies compared hippocampal volume between London taxi drivers, who undergo extensive navigational training, and people without such training (Maguire et al., 2000), and between London taxi drivers and London bus drivers, who rely on regular routes and thus do not have as much navigational knowledge of London (Maguire et al., 2006). In both studies, taxi drivers had greater posterior hippocampal volume than those in comparison groups. Moreover, hippocampal volume was positively correlated with the amount of time the individual had worked as a taxi driver. These findings suggest that

individuals with extensive experience navigating the physical world—and in particular, those who move about similar environments in a more diverse manner—have greater posterior hippocampal volume.

### Cognitive Functioning

Another potential link between activity diversity and hippocampal volume is their respective associations with cognitive functioning. Smaller hippocampal volume has been associated with poorer cognitive functioning in psychiatric samples, such as individuals with depression (Belleau et al., 2019; Campbell et al., 2004; Videbech & Ravnkilde, 2004), schizophrenia (Heckers, 2001), and posttraumatic stress disorder (Logue et al., 2018; Smith, 2005). In one study, patients with major depression had significantly smaller hippocampal volume than controls. Smaller hippocampal volume was related to worse performance on the Wisconsin Card Sorting Test, which is used to assess executive function (Frodl et al., 2006). Another study of normally aging older adults showed that greater hippocampal volume was related to better performance on a number of cognitive subscales from the NIH toolbox, including executive functioning, episodic memory, working memory, processing speed, and verbal learning (O'Shea et al., 2016). Using the subscales from the Montreal Cognitive Assessment, a screening tool for mild cognitive impairment, greater hippocampal volume also was significantly related to better delayed recall but was not related to attention or visual-spatial executive functioning (O'Shea et al., 2016). Note, however, that the aforementioned studies rely on specialized samples, and an association between hippocampal volume and cognitive functioning in healthy, younger samples is not always found (scene imagination, autobiographical memory, future thinking, and navigation in Clark et al., 2020; navigation ability in Weisberg et al., 2019; see also a meta-analysis on hippocampal volume and memory ability by Van Petten, 2004).

### The Present Research

Greater hippocampal volume has been associated with greater "roaming entropy" in mice (Freund et al., 2013) and more experience navigating diverse routes in familiar environments in humans (Maguire et al., 2000; Maguire et al., 2006). The present research, which used data from the MIDUS Refresher sample of U.S. adults, was designed to test the novel hypothesis that greater daily activity diversity (measured across the span of 8 days) would be associated with greater hippocampal volume even after accounting for total activity time. In recent research, greater activity diversity has been linked to better executive functioning and episodic memory (Lee et al., 2020)—cognitive processes that have previously been associated with greater hippocampal volume. A secondary goal of the present research was to test whether the association between activity diversity and cognitive functioning is mediated by hippocampal volume.

We hypothesized that (H1) greater activity diversity would be related to greater hippocampal volume. We also hypothesized that greater hippocampal volume would mediate the relationship between activity diversity and cognitive functioning as measured using (H2a) two indices from a phone-based cognitive battery (executive functioning and episodic memory; Lachman et al., 2014; Lachman & Tun, 2008) and (H2b) the cube-and-paper task (Gilbertson et al., 2007), a behavioral index of spatial reasoning. For each analysis, covariates of total activity time, estimated intracranial volume, and lag between measurement assessments were added where relevant along with demographic covariates of age, gender, education, and race. Furthermore, the covariate of self-reported health was included to test whether effects were independent of physical health status. Hypotheses 1 and 2a were preregistered[1] here: https://osf.io/afjyb.

## Method

The MIDUS study is a longitudinal national study of adults in the United States that began in 1994. Each wave of MIDUS consists of several subprojects; the second wave (MIDUS II; 2004-2009) was the first to include a neuroscience project. Due to the original sample aging, a refresher sample was recruited in 2011 (MIDUS Refresher) to again include representation across the adult age-span. Although many of the protocols were similar between MIDUS II and MIDUS Refresher, a scanner update between the two data collections resulted in much improved structural image quality for the MIDUS Refresher. The MIDUS Refresher structural imaging data were processed with the FreeSurfer image analysis suite, which is documented and freely available for download online (http://surfer.nmr.mgh.harvard.edu/). Unfortunately, the MIDUS II images were obtained with an older magnetic resonance imaging (MRI) scanner and suffered a severe intensity bias impacting automatic segmentation routines, especially in the anterior temporal lobes, such that the FreeSurfer-processed data did not pass quality control inspection at this time. Therefore, data from the MIDUS Refresher are the focus of this manuscript.

[1] Within hypothesis 2, only executive functioning and episodic memory variables were pre-registered(H2a); the measure of spatial reasoning was added after the first round of analyses (H2b). The composite of cognitive functioning (which simply averages scores from executive functioning and episodic memory tests) was also pre-registered but dropped from the present manuscript to avoid redundancy. In the pre-registration, the mediation analysis is broken down into two hypotheses, the first establishing the connection between hippocampal volume and cognitive function, the second performing a formal test of mediation.

## Participants

The primary sample included 52 individuals ($M_{age}$ = 46.58, *SD* = 9.85, *range*: 28-70) who participated in the daily diary subproject (during which daily activities were assessed), had structural MRI data collected during the neuroscience subproject, and had data for all pre-registered covariates. Participants were 52% female (48% male), primarily white (1 identified as black, 3 identified as "other"), and tended to be highly educated (83% had more than a high school education). Of this sample, 45 participants had data from the cognition subproject (during which executive function and episodic memory were assessed), 51 had data from the cube and paper test (assessing spatial reasoning), and 44 had data for all measures.

## Design and Measures

Each MIDUS subproject was conducted separately, and several months or years might elapse between data collection between subprojects. Time between subprojects was entered as a covariate in each analysis that includes variables from different subprojects to account for time lag between measures. Descriptive statistics and intercorrelations between continuous variables are provided in Table 1.

### Activity diversity

One subproject of the MIDUS study included an 8-day diary study, where participants were contacted each day to report on various features of their daily experience (Lee et al., 2018; Lee et al., 2020). As part of each daily interview, participants reported how much time in hours and minutes they had spent since the previous interview engaging in each of seven different activities: (1) in paid work, (2) with children, (3) doing chores, (4) on leisure, (5) in physical activities, (6) on formal volunteering, and (7) giving informal help to people not living with you (e.g., friends, neighbor, parent, other relatives, etc.). The total amount of time spent across the seven activities throughout the entire week was used as a covariate to ensure any relationship between activity diversity and hippocampal volume was not driven by greater overall activity.

Time in each activity was binarized into 0 (did not participate) and 1 (did participate). Each binary variable was then used to calculate activity diversity for each day using an adaption of Shannon's entropy (1948) in the formula below:

$$Activity\ Diversity = -\frac{1}{In\ (j)}\sum_{i=1}^{j}(P_i{*}InPi)$$

where j is the total number of activities and Pi is the proportion of a single activity over the sum of all activities engaged in. In our equation we multiplied the sum of the activity proportions by −1/ln(j), which converts the score into a positive scale ranging from 0 to 1, from the least to the most activity diversity. Scores were then averaged across the study period, allowing for a more representative window into an individual's average activity diversity.

### Hippocampal volume

Structural MRI data collection in the neuroscience project was conducted using a 3T MR750 GE Healthcare MRI Scanner (Waukesha, WI) with an 8-channel head coil. Data were derived from BRAVO T1-weighted structural images (TR = 8.2 ms, TE = 3.2 ms, flip angle = 12°, FOV = 256 mm, 256 x 256 matrix, 160 axial slices, inversion time = 450 ms) with 1-mm isotropic voxels. Processing was conducted using the FreeSurfer image analysis suite (v. 5.3.0; http://surfer.nmr.mgh.harvard.edu/). This process included motion correction and averaging of multiple volumetric T1-weighted images (when more than one was available; Reuter et al., 2010), removal of nonbrain tissue (Ségonne et al., 2004), automated Talairach transformation, segmentation of the subcortical white matter and deep gray matter volumetric structures (including the hippocampus; Fischl et al., 2002; Fischl et al., 2004), intensity normalization (Sled et al., 1998), tessellation of the gray matter white matter boundary, automated topology correction (Fischl et al., 2001; Ségonne et al., 2007), and surface deformation (Dale et al., 1999; Dale & Sereno, 1993; Fischl & Dale, 2000). Segmentation of hippocampal subfields was completed and subfields were grouped into head, body, and tail segments as in Iglesias et al. (2015). Also computed was an estimate of entire intracranial volume that can be used as a covariate to adjust for differences in overall brain size. Each participant's segmentation result was visually assessed for quality and edited manually as deemed necessary according to recommended procedures (http://freesurfer.net/fswiki/Edits). As was planned in the pre-registration, hippocampal volume was averaged across left and right hemispheres. Follow-up analyses probed for differences as a function of hemisphere as well as by anterior (head) vs. posterior (body + tail) segmentation.

### Cube and paper task

In the neuroscience subproject, participants also completed the cube and paper task (Gilbertson et al., 2007), a paper-based task where participants attempt to solve 20 spatial reasoning puzzles. This spatial processing requires participants to mentally discriminate between visual cues through mentalized orientation (cube rotation) and visualization (paper folding). Both processes fall within the concept of "allocentric" processing, in which deciphering visual cues depends on the ability to mentally compare objects based on their positioning relative to one another (compared with egocentric spatial

**Table 1** Descriptive statistics and intercorrelations between continuous variables

| Independent variable | *N* | *M* | *SD* | min. | max. | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1. Activity diversity | 52 | 0.74 | 0.12 | 0.36 | 0.92 | 1 | | | | | | | | | | | | |
| 2. Total activity time | 52 | 13.55 | 3.99 | 4.88 | 24.75 | 0.57** | 1 | | | | | | | | | | | |
| 3. Avg bilateral hippocampal volume | 52 | 425 | 43 | 342 | 537 | 0.21 | -0.05 | 1 | | | | | | | | | | |
| 4. Left hippocampal volume | 52 | 416 | 43 | 328 | 521 | 0.15 | -0.04 | 0.97** | 1 | | | | | | | | | |
| 5. Right hippocampal volume | 52 | 433 | 45 | 346 | 554 | 0.27† | -0.06 | 0.97** | 0.89** | 1 | | | | | | | | |
| 6. Estimated intracranial volume | 52 | 150,136 | 15,843 | 114,482 | 183,063 | 0.11 | 0.15 | 0.59** | 0.58** | 0.58** | 1 | | | | | | | |
| 7. Age | 52 | 46.58 | 9.85 | 28 | 70 | -0.23 | -0.4** | -0.30* | -0.31* | -0.28† | -0.27† | 1 | | | | | | |
| 8. Time lag (neuroscience - diary) | 52 | 0.22 | 1.04 | -0.92 | 2.58 | -0.15 | -0.11 | -0.15 | -0.10 | -0.19 | -0.03 | 0.10 | 1 | | | | | |
| 9. Time lag (cognition - diary) | 51 | -1.03 | 0.44 | -1.83 | -0.25 | -0.02 | 0.11 | -0.01 | 0.05 | -0.08 | 0.23 | -0.13 | 0.83** | 1 | | | | |
| 10. Self-rated physical health | 52 | 3.69 | 0.92 | 2 | 5 | 0.25† | 0.17 | 0.16 | 0.14 | 0.18 | -0.05 | -0.2 | 0.04 | -0.02 | 1 | | | |
| 11. Executive function (z-scored) | 45 | 0 | 1 | -2.17 | 2.56 | 0.12 | 0.28† | 0.17 | 0.25 | 0.09 | 0.41* | -0.29† | 0.29† | 0.35* | 0.18 | 1 | | |
| 12. Episodic memory (z-scored) | 45 | 0 | 1 | -2.70 | 1.84 | -0.09 | -0.12 | -0.21 | -0.13 | -0.27† | -0.07 | -0.14 | 0.27† | 0.23 | -0.12 | 0.34* | 1 | |
| 13. Cube and paper | 51 | 15.57 | 4.4 | 3 | 20 | 0.29* | 0.18 | 0.31* | 0.31* | 0.29* | 0.27† | -0.18 | 0.04 | 0.02 | 0.01 | 0.43** | 0.30† | 1 |

*Note.* Total activity time = number of hours of activity across the study period; hippocampal and intracranial volume is denoted in cm ^ 3; age = age at the time of the neuroscience project; time lag = the difference in years between the subprojects; executive function and episodic memory values are z-scored.

†$p < 0.10$; *$p < 0.05$; **$p < 0.01$.

processing, where the position of objects are assessed relative to the self). Previous research has demonstrated a link between smaller hippocampal volume and a deficit in allocentric spatial processing (Incisa Della Rocchetta et al., 2004). Performance on this task has implications for the ability to discriminate between situationally relevant contextual cues in the environment (Gilbertson et al., 2007), and thus may be related to the variety of activities (in conceivably variable environmental contexts) a person engages in during daily life.

In the task, each puzzle pictured a cube with either letters, numbers, or symbols on the sides, or pictured a square piece of paper with holes in it (see Figure 1 in Gilbertson et al., 2007 for an example). Each cube was explained to have 6 unique sides. Each piece of paper was depicted being folded (using a dotted line) and hole-punched (with the addition of a black circle on the paper). The participant was tasked with choosing one of the options that corresponded to the picture presented and required participants to mentally rotate (in the case of the cube) or fold/unfold (in the case of the paper) the image to match it with one of the options. The total number of correct responses was tallied for a score ranging from 0 to 20.

### Executive function and episodic memory

The MIDUS cognitive subproject involves assessment using the Brief Test of Adult Cognition by Telephone (BTACT;Lachman et al., 2014 ; Lachman & Tun, 2008). The BTACT includes seven subtests given to participants over the phone. Included was 1) an immediate and 2) delayed word list recall task to assess episodic verbal memory, 3) the digits backward span to assess working memory, 4) a category fluency test to assesses verbal ability, speed, and executive functioning, 5) the stop and go switch task to assess reaction time, attention, task-switching, and inhibitory control, 6) a number series task to assess fluid intelligence and reasoning, and 7) a backward counting test to assess speed of processing. See Lachman et al. (2014) and Lachman and Tun (2008) for a more detailed description of each of these tasks.

From these tests, two composite scores were computed as an indicator of different aspects of cognitive functioning based on confirmatory factor analysis. The immediate and delayed word lists task were combined into an indicator of episodic memory, and the remaining five were combined as a measure of executive functioning. To create the composites, the mean of the scores from each subtask was $z$-scored and averaged across each subsample for each domain (episodic memory and executive functioning), then $z$-scored again to equate each subsample's mean to 0 and the standard deviation to 1 as in previous research (Lachman et al., 2014; Lachman & Tun, 2008). For the stop and go switch task, as in previous research we used only cases that were considered "clean" based on no technical malfunctions, no distractions, sufficient participant understanding of the task, and at least 75% accuracy in each condition. Scores on the stop and go switch task were multiplied by −1 before combining with other tests so that higher scores indicated faster latency and mirrored the direction of the other tests, where higher scores indicate better cognitive functioning. See Table 2 for correlations between cognitive measure subtasks, hippocampal volume, and main covariates of interest.

## Statistical Power

Sample sizes for MIDUS subprojects were determined based on overarching project goals and not the specific analyses in this manuscript. A series of post-hoc power analyses were

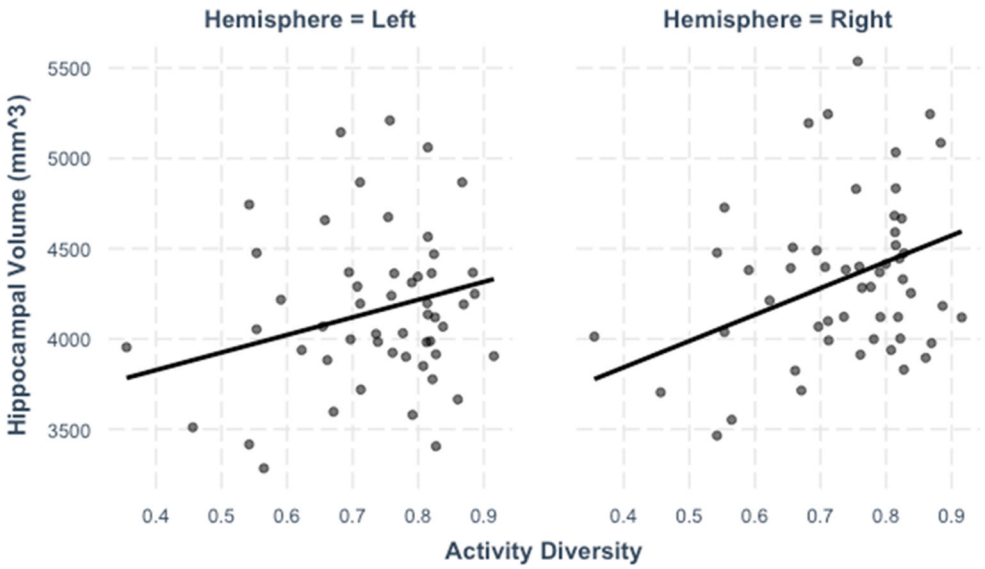


**Fig. 1** More activity diversity is related to greater hippocampal volume. *Note.* $N = 52$. Depiction of step 4 in the model. Points represent raw data; regression lines represent predicted values adjusting for covariates

**Table 2** Correlations between cognitive sub-tasks, hippocampal volume, and covariates

| Cognitive task | Avg bilateral HV | Left HV | Right HV | Est ICV | Age | Time lag | Phys health |
|---|---|---|---|---|---|---|---|
| **Executive function composite** | 0.17 | 0.25 | 0.09 | 0.41* | -0.29† | 0.20 | 0.18 |
| Digits backward | -0.09 | -0.03 | -0.14 | 0.36* | -0.13 | 0.27† | 0.09 |
| Category fluency | 0.21 | 0.25 † | 0.16 | 0.42** | -0.12 | 0.15 | 0.11 |
| Stop and go switch task | 0.04 | 0.07 | 0.01 | -0.08 | -0.30† | -0.17 | 0.12 |
| Number series | 0.27† | 0.32* | 0.21 | 0.44** | -0.24 | 0.27† | 0.12 |
| Backward counting | 0.15 | 0.24 | 0.05 | 0.26† | -0.21 | 0.15 | 0.19 |
| **Episodic memory composite** | -0.21 | -0.13 | -0.27† | -0.07 | -0.14 | 0.26† | -0.12 |
| Immediate word list recall | -0.04 | 0.02 | -0.09 | 0.13 | -0.16 | 0.16 | -0.12 |
| Delayed word list recall | -0.34* | -0.26† | -0.4* | -0.25 | -0.10 | 0.31* | -0.09 |
| **Cube and paper (spatial reasoning)** | 0.31* | 0.31* | 0.29† | 0.27* | -0.18 | 0.04 | 0.01 |

*Note.* $n = 45$ for all correlations, except for those involving cube and paper, where $n = 44$. Higher scores on the stop and go switch task indicate faster latency. HV = hippocampal volume; est ICV = estimated intracranial volume; age = age at neuroscience project; time lag = months between the neuroscience and cognition subprojects; phys health = self-reported physical health. †$p < 0.10$; *$p < 0.05$; **$p < 0.01$.

conducted using the pwr package in R (pwr 1.2-2; Champely, 2018) to assess whether the existing sample provided enough power to detect the expected effect size for each hypothesis. For 80% power in a two-sided test with a significance threshold of $p = 0.05$, we could detect an effect of $r = 0.37$ or higher for hypothesis 1 ($n = 52$), an effect of $r = 0.40$ for hypothesis 2a ($n = 45$), and an effect of $r = 0.38$ for hypothesis 2b ($n = 51$).

Because no studies thus far have examined the link between activity diversity and hippocampal volume, it is unclear whether hypothesis 1 is adequately powered. Regarding hypothesis 2a and 2b, previous work examining hippocampal volume, executive function, episodic memory, and visual-spatial executive function in older adults (age 71.9 ± 9.3 years) established effect sizes of $\eta_p^2 = 0.05$, $\eta_p^2 = 0.08$, and $r = 0.09$, respectively (O'Shea et al., 2016). To detect effects of this size with 80% power at a significance threshold of $p = 0.05$, power analyses estimate that we would need 160, 97, and 907 participants, respectively, revealing that analyses regarding hippocampal volume and cognitive outcomes in our sample are underpowered.

## Analytic Procedure

We used a hierarchical linear regression approach to test hypothesis 1. We first regressed bilateral hippocampal volume on activity diversity and total time spent in activities. In the second step, we added the estimate of intracranial volume to isolate relationships specific to the volume of the hippocampus (and not to size of the cranial cavity). In a third step, we added the remainder of the covariates that were pre-registered, including age, gender, education, race, and the time between the diary and neuroscience projects. A fourth step was added after the pre-registration to examine the influence of self-reported physical health as a covariate in the model.

For hypotheses 2a and 2b, we first performed hierarchical linear regressions to establish the relationship between hippocampal volume and cognitive function (based on previous literature; Belleau et al., 2019; Campbell et al., 2004; Frodl et al., 2006; Heckers, 2001; Logue et al., 2018; O'Shea et al., 2016; Smith, 2005; Videbech & Ravnkilde, 2004). The relevant cognitive function dependent variable was first regressed on hippocampal volume. Next, the estimate of intracranial volume was added to the model. Third, the remaining pre-registered covariates were added, including age, sex, education, race, and the time difference between the neuroscience and cognitive projects. Finally, a fourth step was added after the pre-registration examining the role of self-reported physical health. In the case that a significant relationship between hippocampal volume and any of the three cognitive function variables was detected in our sample we then would perform a formal test of mediation.

Each dependent variable was assessed for skew, and if significant skew was detected Q-Q plots were visually inspected to assess nonnormality. Cook's distance greater than 0.05 was used to identify outliers, however there were none in the present analyses. Each regression model was tested for heteroscedasticity using the Breusch-Pagan test for heteroscedasticity with the function bptest (lmtest package; Zeileis & Hothorn, 2002). When significant heteroscedasticity was detected we estimated corrected standard errors by specifying robust=TRUE in the summ.lm function from jtools (Long, 2019). This option employs the vcovHC function from the sandwich package (Zeileis, 2004; Zeileis, 2006) which uses heteroscedasticity-consistent covariance matrices to estimate corrected standard errors. The figure was produced using the function effectplot from jtools such that regression lines were plotted using partial residuals, which allows an illustration of the relationship between the independent and dependent variable while adjusting for effects of the other variables

in the model. Data points in the figure were based on raw data, uncorrected for covariates.

## Results

### Hippocampal Volume and Activity Diversity

To test hypothesis 1, we regressed averaged hippocampal volume on the index of activity diversity and total activity in step 1, added estimated intracranial volume in step 2, additional pre-registered covariates in step 3, and finally self-reported physical health (not pre-registered) in step 4. In all four models, and in support of hypothesis 1, engaging in more diverse daily activities was related to significantly larger bilateral hippocampi even after adjusting for covariates[2] (see Table 3 for full results). In the fully adjusted model, a one unit increase in activity diversity was associated with 1,217 $mm^3$ greater hippocampal volume. Given the entire range of activity diversity lies on a 0 to 1 scale and ranges between 0.36 to 0.92, a more applicable interpretation would show that a 1 SD increase in activity diversity (0.12) is related to 146 $mm^3$ greater hippocampal volume.

Follow-up analyses examining segment (anterior vs. posterior) and hemisphere (left vs. right) differences in the relationship between activity diversity and hippocampal volume were conducted using three series of linear mixed models: first with a fixed effect of segment, next with a fixed effect of hemisphere, and last with fixed effects of both segment and hemisphere. No significant interaction between segment and activity diversity emerged, $b = -82.73$, $t(52) = -0.46$, $p = 0.65$. A significant interaction between activity diversity and hemisphere, $b = 483.76$, $t(52) = 2.06$, $p = 0.045$, suggested that the positive relationship between activity diversity and hippocampal volume was larger for the right than left hippocampus. Computation of partial residuals revealed that, although greater activity diversity is indeed related to greater left and right hippocampal volume, this relationship is significant for the right hemisphere, $r_{partial} = 0.47$, $t(50) = 3.81$, $p < 0.001$, and only marginal for the left hippocampus, $r_{partial} = .23$, $t(50) = 1.67$, $p = 0.10$. Figure 1 displays these relationships. There was no significant three-way interaction between activity diversity, segment, and hemisphere.

### Hippocampal Volume and Cognitive Functioning

To test whether bilateral hippocampal volume mediates the relationship between activity diversity and cognitive function (hypotheses 2a and 2b), we first performed a series of hierarchical regressions to establish a relationship between hippocampal volume and cognitive function in our sample. The pairwise relationship between hippocampal volume and the cognitive function variable was examined in step 1. Step 2 added intracranial volume, step 3 added additional pre-registered covariates, and step 4 (which was not pre-registered) examined the role of self-reported physical health.

Hippocampal volume was not significantly related to executive function nor episodic memory in any of the four steps. Hippocampal volume was significantly related to cube and paper scores in the first step without covariates, $t(49) = 2.27$, $p = 0.03$, $r_{partial} = 0.31$, but not after the addition of covariates.[3] Our inability to detect a significant relationship between hippocampal volume and cognitive function in the present sample, a relationship that has been continually observed in previous research, may be due to a lack of power given the sample size. Because of this, we did not continue on to formal tests of mediation. In follow-up analyses, we explored the relationship between hippocampal volume and the delayed recall task given their significant correlation, $r(43) = -0.34$, $p = 0.02$ (Table 2). This relationship became only marginally significant when accounting for intracranial volume, $t(42) = -1.72$, $p = 0.09$, $r_{partial} = -0.26$, and became nonsignificant when adding in the remaining covariates, $t(36) = -1.24$, $p = 0.22$, $r_{partial} = -0.20$.

## Discussion

Previous research has demonstrated the relationship between engaging in a broader range of diverse experiences in daily life with better psychological well-being(Lee et al., 2018), cognitive functioning (Bielak et al., 2019; Lee et al., 2020), and emotional well-being(Heller et al., 2020). The present research tested the relationship between activity diversity and hippocampal volume, which often has been linked to learning (Rolls, 2010), memory (Squire et al., 2004), and spatial navigation (Burgess et al., 2002). We found that individuals who

[2] In supplementary analyses, we tested the interaction between age and activity diversity. The interaction was nonsignificant in each step (step 3: $t = 0.32$, $p = 0.75$; step 4: $t = 0.89$, $p = 0.381$). Thus, either the relationship between activity diversity and hippocampal volume is similar across age groups, or we do not have a sufficient sample size of older adults with a range of activity diversity (our sample includes only two individuals 65 years and older) to detect age differences in the relationship between activity diversity and hippocampal volume. Future work with an older age range may allow more insight into how major life events in later years might impact this relationship. See figure in supplementary analyses document at: https://osf.io/tcg83/?view_only=89799d5f0c93412d89d2c22489e922dc.

[3] Differences by segment (anterior vs. posterior) and hemisphere (left vs. right) also were explored using linear mixed models. No effect of segment was found. Although we found significant interactions between hemisphere and executive functioning, and hemisphere and episodic memory (but not between hemisphere and spatial reasoning), partial correlations revealed that the associations between hippocampal volume and each cognitive functioning variable was still non-significant (all $p$ values > 0.19). Thus, the significant interactions indicated a difference in direction/strength of the relationships by hemisphere, but did not change the nature of the results compared with when examined bilaterally. No significant three-way interactions between cognitive function, segment, and hemisphere emerged.

**Table 3** Linear regression of bilateral hippocampal volume on activity diversity and covariates

| Coefficient | Step 1 | | | | | Step 2 | | | | | Step 3 | | | | | Step 4 | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | *b* | 95%CI | *t* | *p* | $r_{partial}$ | *b* | 95%CI | *t* | *p* | $r_{partial}$ | *b* | 95%CI | *t* | *p* | $r_{partial}$ | *b* | 95%CI | *t* | *p* | $r_{partial}$ |
| Intercept | 3649.24 | 2903.33, 4395.15 | 9.83 | < 0.01 | | 1343.93 | 335.14, 2352.72 | 2.68 | 0.01 | | 2039.32 | 596.35, 3482.29 | 2.85 | 0.01 | | 1872.43 | 653.78, 3091.09 | 3.10 | < 0.01 | |
| Activity diversity | 1324.37 | 104.01, 2544.74 | 2.18 | 0.03 | 0.30 | 1256.94 | 299.84, 2214.04 | 2.64 | 0.01 | 0.36 | 1362.75 | 223.88, 2501.62 | 2.41 | 0.02 | 0.35 | 1217.48 | 263.89, 2171.07 | 2.58 | 0.01 | 0.37 |
| Total activity time | -28.00 | -63.92, 7.92 | -1.57 | 0.12 | -0.22 | -36.80 | -65.13, -8.46 | -2.61 | 0.01 | -0.35 | -50.10 | -88.36, -11.83 | -2.64 | 0.01 | -0.37 | -50.54 | -79.35, -21.74 | -3.54 | < 0.01 | -0.48 |
| Estimated intracranial volume | | | | | | 0.002 | 0.001, 0.002 | 5.64 | < 0.01 | 0.63 | 0.001 | 0.00, 0.002 | 3.13 | < 0.01 | 0.43 | 0.001 | 0.00, 0.002 | 3.05 | < 0.01 | 0.43 |
| Age (mean centered at 46.58) | | | | | | | | | | | -11.64 | -24.08, 0.80 | -1.89 | 0.07 | -0.28 | -10.15 | -20.47, 0.18 | -1.98 | 0.05 | -0.29 |
| Gender (female = ref) | | | | | | | | | | | 159.80 | -84.36, 403.95 | -1.32 | 0.19 | 0.20 | 205.90 | -27.65, 439.44 | 1.78 | 0.08 | 0.27 |
| Education (greater than HS = ref) | | | | | | | | | | | 37.01 | -254.79, 328.81 | 0.26 | 0.80 | 0.04 | 0.72 | -242.21, 243.65 | 0.01 | 1.00 | 0.00 |
| Race (white = ref) | | | | | | | | | | | 17.71 | -547.77, 583.19 | 0.06 | 0.95 | 0.01 | 10.33 | -326.13, 346.78 | 0.06 | 0.95 | 0.01 |
| Time lag | | | | | | | | | | | -48.59 | -150.67, 53.48 | -0.96 | 0.34 | -0.15 | -55.94 | -142.02, 30.15 | -1.31 | 0.20 | -0.20 |
| Self-rated physical heath | | | | | | | | | | | | | | | | 91.47 | -12.74, 195.68 | 1.77 | 0.08 | 0.26 |
| Model fit change statistics | $F(2, 49) = 2.45, p = 0.097, R^2 = 0.09$ | | | | | $F(3, 48) = 13.26, p < 0.001, R^2 = 0.45$<br>$F_{change} = 31.80, p < .001$ | | | | | $F(8, 43) = 6.28, p < 0.001, R^2 = 0.54$<br>$F_{change} = 1.59, p = .18$ | | | | | $F(9, 42) = 6.20, p < 0.001, R^2 = 0.57$<br>$F_{change} = 3.14, p = .08$ | | | | |

*Note*: N = 52: Hippocampal volume measured in mm^3. Confidence intervals and *p*-values for all regressors in step 3 obtained using heteroscedasticity consistent estimators: HS = high school; time lag = difference in months between the neuroscience and diary subprojects.

engaged in more diverse activities had significantly greater bilateral hippocampal volume, even after adjusting for total intracranial volume, total time engaged in activities during the study period, age, gender, education, race, perceived physical health, and time lapse between study measures. Results were consistent for both the anterior and posterior regions of the hippocampus. When examining laterality, the relationship between activity diversity and the hippocampus was statistically significant for the right, and marginally significant for the left, hippocampus. These findings establish the relationship between activity diversity and hippocampal structure and provide a framework for further inquiry.

## Activity Diversity and the Hippocampus

Hippocampal neurogenesis is sensitive to environmental stimulation (Freund et al., 2013; Kempermann, 2008). For example, mice living in enriched compared with nonenriched environments have more new hippocampal neurons (Kempermann et al., 1997). Similar to how enriched environments impact hippocampal structure, it is possible that engaging in more diverse daily activities does so as well. However, the results presented here are correlational in nature and thus the direction of the relationship between activity diversity and hippocampal structure remains unknown. It is equally possible that people with greater hippocampal volume have greater capacity to engage in a wider variety of activities. Indeed, past research has shown that smaller hippocampal volume could be a *predispositional* factor in cognitive dysfunction and psychiatric illness (Gilbertson et al., 2002; Gilbertson et al., 2007). Our preliminary finding thus calls for longitudinal research to establish the temporal directionality between activity diversity and hippocampal volume. Planned follow-ups of the MIDUS Refresher sample will aid in teasing apart this relationship, where we will be able to test whether activity diversity at time 1 is related to changes in hippocampal volume between time points.

Previous research has demonstrated that spatial navigation abilities may be linked specifically to larger posterior (rather than anterior) hippocampal volume (Maguire et al., 2000; Maguire et al., 2006). In studies of London taxi drivers, only the posterior hippocampus was larger among taxi drivers compared with their counterparts; in fact, the anterior hippocampus was larger among nontaxi drivers and bus drivers compared with the taxi drivers (Maguire et al., 2000; Maguire et al., 2006). In our sample, however, the relationship between activity diversity and hippocampal volume was similar for both the anterior and posterior regions of the hippocampus.

One important factor not considered in the present research is the role of life stress in the relationship between activity diversity and hippocampal volume. Previous research has shown that hippocampal volume is highly sensitive to stress (see review by Kim et al., 2015). The role of cumulative life stress, as well as daily stress, in the relationship between activity diversity, hippocampal volume, and cognitive functioning should be a topic of future research. Future research also should attempt to examine whether engaging in certain activities are more strongly related to hippocampal volume. It may be that certain activities (such as physical activity and exercise) may be driving the relationship between hippocampal volume and activity diversity, particularly given the observed relationship between aerobic fitness and hippocampal volume (Erickson et al., 2009, 2011).

## Hippocampal Volume and Cognitive Functioning

In previous research, the hippocampus has been associated with various aspects of cognitive functioning, such as learning (Rolls, 2010), memory (Squire et al., 2004), and spatial memory and navigation (Burgess et al., 2002). In our sample, hippocampal volume was only related to spatial reasoning when not adjusting for sociodemographic variables and was not significantly related to executive functioning or episodic memory in any model. This was the case for both anterior and posterior regions of the hippocampus.

When examining the cognitive subtest of delayed recall, a significant *negative* bivariate correlation was found, but adding in additional covariates nullified the relationship. Although at first glance this negative correlation is surprising, a meta-analysis of 33 studies found a negative correlation between hippocampal volume and memory ability in younger adults, and noted the variability in the direction of this relationship among studies of older adults (Van Petten, 2004). More research is needed to better understand the nature of the relationship between hippocampal volume and memory ability as people get older. One potential explanation for the lack of a relationship between hippocampal volume and cognitive function when including covariates is our lack of power to detect the effect. Larger sample sizes may allow us to detect the effects even when adjusting for sociodemographic covariates.

It is likely that the subregions of the hippocampus are involved in different cognitive functions and that more granular segmentation of the hippocampus beyond anterior vs. posterior would reveal differential relationships with various aspects of cognitive functioning. For example, one large study of hippocampal volume in over 5,000 adults examined 12 subregions of the hippocampus in relation to a battery of cognitive measures and risk for dementia, finding that different subregions held differing relationships with various aspects of cognitive functioning (Evans et al., 2018). Given the relatively small size of our sample compared to that of Evans and colleagues, and the risk of inflating the false discovery rate, we limited our subregion analyses only to anterior vs. posterior hippocampal volume and did not delve into more granular segmentation.

Another potential explanation for our disparate findings is that the link between hippocampal structure and cognitive functioning often has been made in samples of individuals experiencing psychological dysfunction or cognitive impairment (Belleau et al., 2019; Campbell et al., 2004; Frodl et al., 2006; Heckers, 2001; Nedelska et al., 2012; Smith, 2005). For example, Nedelska et al. (2012) only saw a significant relationship between spatial navigation and hippocampal volume in people with cognitive impairment and not in cognitively healthy individuals. In fact, two recent studies using large samples of healthy, younger adults demonstrated null relationships between hippocampal volume and navigation ability (Weisberg et al., 2019) and hippocampal volume and autobiographical memory, navigation, and other cognitive tasks (Clark et al., 2020). The MIDUS neuroscience sample is on average older than these studies and the participants that compose our sample are possibly healthier even than our average MIDUS participants, as participation in the neuroscience project requires travel to our laboratory and enduring 2 days of study-related activities. Perhaps hippocampal volume is an indicator of cognitive function only in cases of clinical dysfunction or specialized samples.

### Measuring Activity Diversity

The construct of activity diversity is meant to be sensitive to a wide variety of activities in daily life. However, our construct was limited to only seven activities. Although our activities may capture a broad range of experiences across different social roles and settings (e.g., paid work, leisure, time with children), our measure is not inclusive of discrete activity types that may be important for active lifestyles. In an ideal study of activity diversity, participants would provide an exhaustive list of activities they participated in throughout the day that could later be coded by trained researchers into a longer list of discrete categories. This method would allow for a richer view of the range of activities people engage in on a day-to-day basis and would allow for a closer follow-up of whether certain activities are more important for psychological and cognitive health than others, for example, teasing apart the contributions of activities increasing social connection and engagement as well as physical and mental activity to better understand how diversity may still be important. Despite this, even our limited measure of activity diversity reveals the significance of engaging in more diverse daily activities; those who have greater activity diversity in their daily lives have greater psychological well-being(Lee et al., 2018), have better executive functioning (Lee et al., 2020), and now we see even have greater hippocampal volume. The positive associations of activity diversity with these outcomes were independent of total time spent in the activities, highlighting the unique importance of experiential diversity in health and functioning. Future research employing a more liberal assessment of daily activities might provide additional insights into the construct of activity diversity. One strength of our activity diversity measure, however, is that we have eight days (compared to only one day, for example) of activity data. This allows a more representative window into an individual's *average* activity diversity. With more repeated assessments, the more confident we can be that our measure yields a reliable estimate of how diverse an individual's activities are on any given typical day, and that relationships found between this behavioral measurement and brain structure are not spurious results of study design.

## Conclusions

In the present research, we demonstrated that individuals who engage in a more diverse range of daily activities assessed across an 8-day study period had greater hippocampal volume. This research builds on past studies linking greater diversity in daily experiences with better psychological well-being(Lee et al., 2018), better emotional well-being(Heller et al., 2020), and better cognitive functioning (Lee et al., 2020). Additional research is needed to delineate whether engaging in more diverse activities leads to structural enhancement of the hippocampus, people with larger hippocampi are more prone to engaging in a more diversely active lifestyle, or if other biopsychosocial risk factors (such as stress or exercise) instead drive this relationship. This study suggests, however, that activity diversity may capture elements of an enriched environment, and may have important links to brain structure.

**Funding** MIDUS has been supported by The National Institute on Aging (P01-AG020166, U19 AG051426). DWG is supported by the National Institute of Mental Health (K01-MH117222).

**Data availability** Raw data of non-neuroscience data are available for download by searching for "MIDUS Refresher" at https://www.icpsr.umich.edu/web/pages/ICPSR/index.html and for structural MRI data by contacting Stacey Schaefer (stacey.schaefer@wisc.edu) or Barry Radler (bradler@wisc.edu).

## Declarations

**Conflicts of interest/Competing interests** Dr. Richard J. Davidson is the founder, president, and serves on the board of directors for the non-profit organization, Healthy Minds Innovations, Inc. In addition, Dr. Davidson served on the board of directors for the Mind & Life Institute from 1992-2017

**Ethics approval** The Midlife in the United States subprojects were all granted approval from relevant institutional review boards.

**Consent to participate** All participants were fully briefed about study procedures ahead of data collection. Data was only collected from participants who consented to study procedures.

**Consent for publication** Not applicable.

**Code availability** Scripts used to clean and analyze data for this manuscript can be found here: https://osf.io/tcg83/?view_only=89799d5f0c93412d89d2c22489e922dc

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