Sex differences in spatial navigation and perception in human adolescents and emerging adults ☆

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ABSTRACT

Males typically outperform females on spatial tasks, beginning early in life and continuing into adulthood. This study aimed to characterize age and sex differences in human spatial ability using a virtual Water Maze Task (vWMT), which is based on the classic Morris water maze spatial navigation task used in rodents. Performance on the vWMT and on a task assessing visuospatial perception, Mental Rotations Test (MRT), was examined in 33 adolescents and 39 emerging adults. For the vWMT, significant effects of age and sex were observed for path length in the target region (narrower spatial sampling), and heading error, with emerging adults performing better than adolescents, and an overall male advantage. For the MRT, males scored higher than females, but only in emerging adulthood. Overall, sex differences in visuospatial perception (MRT) emerge differently from those observed on a classic navigation task, with age and sex-specific superior vWMT performance likely related to the use of more efficient strategies. Importantly, these results extend the developmental timeline of spatial ability characterization to include adolescent males and females performing a virtual version of the classic vWMT.

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1. Introduction

As early as infancy, children have the ability to localize spatial information based on the relationship between an event and environmental features (Keating et al., 1986). There are ample data available from cohorts studied in early childhood (5 years of age and younger) demonstrating the development of place learning (Hupbach et al., 2011; Ribordy et al., 2013; Sluzenski et al., 2004) and scene recognition (Chai et al., 2010) abilities. In general, the ability to process spatial and contextual information appears to mature around age eight on a variety of large-environment spatial tasks (Overman et al., 1996) and around age 9 on a computerized spatial navigation task (Laurance et al., 2003). Not surprisingly, dynamic and rapid structural and functional brain changes beyond childhood and into adolescence (Blakemore, 2012; Paus, 2005; Spear, 2000) underlie significant improvements across a variety of cognitive domains (Casey et al., 2005; Paus, 2005), including spatial ability (Klingberg, 2006; Piper et al., 2011; Sowell et al., 2001). Results from a functional magnetic resonance imaging (fMRI) study of scene complexity demonstrated greater activation of a brain region implicated in spatial processing, the parahippocampal gyrus (PHG), for high-complexity versus low-complexity scenes in healthy participants ages 8–24 years (Chai et al., 2010). Differences in brain activation not only increased with age, but also were associated with superior memory formation.

The Morris Water Maze Task (WMT) was developed in 1981 as an alternative to the radial arm maze to study spatial learning in rodents (Wenk, 2004). The Morris WMT has since been used extensively in animal research to probe spatial memory ability (Morris, 1984), with many variants of this task being used over the past 30 years to study the neurobiology (Clark et al., 2013) and neuropharmacology (Cha et al., 2007; Markwiese et al., 1998; Swartzwelder et al., 2014) of spatial learning, as well as for developing neurobiological models of neurocognitive disorders (D'Hooge and De Deyn, 2001). Successful spatial learning in the WMT is characterized by execution of (more or less) direct trajectories to a hidden, submerged escape platform from multiple starting locations

and persistence in searching at the platform location when it is removed for a probe trial. It is generally accepted that optimal performance in the WMT is based on the use of spatial information provided from visual environmental cues, for example, based on the fixed spatial relationship between the platform and the available visual cues (O'Keefe and Nadel, 1978) or the contributions of visual cues to the selection of trajectories to the platform location (Knierim and Hamilton, 2011). The hippocampus plays an integral role in memory function; it is critical for processing spatial and contextual information and for generating and maintaining representations utilized for navigating in space (Jarrard, 1993; O'Keefe and Nadel, 1978; Wegman et al., 2014). To this end, rodents with hippocampal lesions have been shown to exhibit deficits in spatial learning on this task, as evidenced by an inability to efficiently navigate to the hidden platform (Morris et al., 1982; Sutherland et al., 1982). Prominent sex differences also have been reported in rodents on the WMT, with adult male rats demonstrating better navigation to the hidden platform than female counterparts (Keeley et al., 2013; Perrot-Sinal et al., 1996; Roof and Stein, 1999; Saucier et al., 2008), although some studies report no differences (Bucci et al., 1995). While most examination of developmental differences in performance of the WMT in rodents has been within the context of alcohol or drug challenges (Cha et al., 2007; Markwiese et al., 1998; Sircar and Sircar, 2005), or hormone manipulations (Roof, 1993), there is some limited evidence of age-related improvements in acquisition (reduced escape latency and shorter swim distances) and retention (more time spent in goal quadrant) from adolescence to adulthood (Markwiese et al., 1998).

It has recently become possible to translate WMT findings from preclinical to clinical populations (Hamilton et al., 2009), given the development of virtual versions of the WMT (vWMT) to assess spatial ability in humans (Hamilton et al., 2009; Astur et al., 2002; Driscoll et al., 2005; Herting and Nagel, 2012; Moffat and Resnick, 2002; Newhouse et al., 2007; Sneider et al., 2011, 2013a,b; Woolley et al., 2010). Although to date no human developmental data are available to assess age-related improvements in performance on the vWMT, a cross sectional comparison of healthy volunteers across a large age span (6–67 years of age) demonstrates superior performance in adolescents and younger–adults relative to children and relative to older individuals on a variant of a spatial memory task, the Memory Island task (Piper et al., 2011). Furthermore, effects of age and sex examined in a modified version of the WMT in young adults and older adults (mid-50s) indicated that young adults performed better than older adults, again with a male advantage being evident in both age groups (Schoenfeld et al., 2010). In a virtual version of the WMT, a study of 8–10 year old prepubertal children likewise showed a male advantage in spatial ability, with boys performing better on the retention trial (probe) than girls (Newhouse et al., 2007). On the other end of the age spectrum, WMT performance declines with aging (Driscoll et al., 2005). In addition, WMT performance examined in combination with functional magnetic resonance imaging (fMRI) has been useful for elucidating underlying neurobiology associated with performance differences in healthy adults and in substance abusers, confirming that the hippocampus shows significant activation during task performance (Sneider et al., 2013b). From a translational perspective, impaired spatial navigation on the virtual WMT has been observed in patients with unilateral hippocampal resections (Astur et al., 2002) and in amnesic participants with hippocampal damage (Goodrich-Hunsaker et al., 2010), which is similar to observations found in animal hippocampal lesion studies. Thus, applications of the virtual WMT have been invaluable for investigating spatial learning and memory and for validating rodent models of neurocognitive disorders and treatments for memory disorders in humans (D'Hooge and De Deyn, 2001). While new tasks and quantitative statistical approaches for assessing place learning have

Table 1
Participant demographics.

	Adolescents (n = 33)	Young adults (n = 39)	p
Age (years)	13.6 ± 0.9 (range 12.3–15.0)	21.6 ± 1.7 (range 18.5–25.5)	<.001
Education (years)	7.5 ± 1.48	14.7 ± 1.5	<.001
SES[a]	50.1 ± 11.1	50.6 ± 11.0	.87
Handedness	28R, 4L, 1A	37R, 2L	–
Female	52%	44%	–
Ethnicity[b]	97% Non-Hispanic	97% non-Hispanic	–
Race[c]	85% Caucasian	64% Caucasian	–

Data represent mean values ± SD. *Abbreviations*: SES, socioeconomic status.
[a] SES unavailable for n = 1 adolescent and n = 1 emerging adult.
[b] Ethnicity: Hispanic vs. non-Hispanic.
[c] Race: Caucasian vs. non-Caucasian (classification consisted of Asian, African American, and other).

become available and have been applied to study participants age 18 and older (Furman et al., 2014; Nardi et al., 2011), to date, the virtual WMT has been underemployed for elucidating the neurobiological role of the hippocampus during adolescence, a time when the brain is rapidly developing and when the hippocampus is particularly vulnerable to insults such as alcohol and drug use (Chin et al., 2010), and is structurally and functionally altered in adolescents with depression and other psychiatric conditions (Whittle et al., 2014).

Accordingly, the purpose of the present study is to fill a critical gap in the literature regarding healthy developmental changes in spatial ability, along with an examination of sex differences, using a virtual version of the classic WMT. Given reports that visual perception may influence spatial learning on tests such as the vWMT (Astur et al., 2004), the Mental Rotations Test (MRT) also was administered to assess visuospatial ability. Performance on mental rotation tests likewise demonstrate robust sex differences, with men demonstrating better performance than women (Astur et al., 2004; Linn and Petersen, 1985; Parsons et al., 2004), and sex differences in children as early as kindergarten, with kindergarten boys outperforming age-matched girls on rotational and translational elements of a spatial transformation task (transforming two separate halves of a shape into a whole shape) (Levine et al., 1999) and in preadolescents on house plans, mirror images and 3D object rotation tasks (Kerns and Berenbaum, 1991). Inclusion of the MRT permits an ability to dissociate whether hypothesized developmental improvements and male-related advantages in spatial ability reflect better memory-related function or better visuospatial perception, or both.

2. Method

2.1. Participants

The study sample consisted of 33 healthy adolescents (ranging in age from 12.3 to 15.0 years, mean age 13.6 ± 0.9 years) and 39 healthy emerging adults (ranging in age from 18.5 to 25.5 years, mean age 21.6 ± 1.7 years). Demographic details are provided in Table 1, including socioeconomic status (SES) (Barratt, 2006) and handedness. Participants were recruited through local advertisement and screened by telephone interview to ensure they met criteria for inclusion in the study. All aspects of the clinical research protocol were reviewed and approved by the Institutional Review Board of McLean Hospital (Belmont, MA, USA). After a complete description of the study, all participants and their parent(s) or guardian(s) (adolescent group only) provided written informed

assent or consent. All participants received monetary compensation for study completion.

2.2. Clinical assessment

A trained psychologist conducted diagnostic clinical interviews in adolescents using the Kiddie-Schedule for Affective Disorders and Schizophrenia (K-SADS-E) (Puig-Antich et al., 1980) and in emerging adults using the Structured Clinical Interview for the Diagnostic and Statistical Manual (DSM-IV) Non-Patient Edition (SCID-I/NP) (First et al., 1997). All participants were free of Axis-I psychiatric diagnoses, neurological illness, and severe medical problems. Participants also completed urine screening to rule out current psychoactive substance use (Triage® Drugs of Abuse Panel: Immediate Response Diagnostics, Biosite, San Diego, CA), as negative urine toxicology results were required for study inclusion in the concurrent neuroimaging study (Silveri et al., 2013). Adolescent participants reported no current or <3 lifetime alcohol drinking bouts. Emerging adults reported consumption of 1.8 ± 1.2 alcoholic beverages per drinking bout (averaged over the three months prior to study participation). Given that menstrual cycle phase has been reported to influence memory performance in females (McCormick and Teillon, 2001), menstrual cycle phase was recorded for all females participants using self-report: 50.0% of adolescent and emerging adult females were in their follicular phase (cycle days 3–13), 14.7% were in their non-follicular phase (days 14–28), 17.6% of adolescent females had not yet begun cycling or reported less than one month since first menses, and menstrual cycle phase information was unavailable for the remaining female participants.

2.3. Spatial ability: virtual Water Maze Task

A PC-compatible laptop (screen resolution: 800×600) was used to control the presentation of the virtual environment and vWMT data collection. The vWMT program (Hamilton et al., 2009) was written in C (DH), with a field of view = 50° (first-person perspective). Distances in virtual space were measured in arbitrary units: virtual room 16 (width) × 3 (height) units. Distal room walls only differed by placement of four unique abstract pictures (3×3 units) on each wall, which served as landmarks. The circular pool was located in the center of the square room and had a diameter of 3.2 units, with a perimeter wall that extended approximately 0.66 units above the surface of the water. The platform was either hidden or visible as specified in the experiment and was located in the northeast (NE) quadrant for all trials. Navigation was controlled using a joystick, which allowed right, left and forward movement but not backward movement. The fixed full rotation duration and time to traverse the pool at its widest point in a straight line is approximately 2.5 s and 4 s, respectively. A visual message was displayed on the screen when the platform was located: "Platform found". If the platform was not located within 60 s, the platform became visible and the following message was displayed on the screen: "The platform is visible, swim to it". The inter-trial interval (ITI) was one second (1 s).

Participants completed a training phase that consisted of four visible platform trials in a virtual environment featuring distinct spatial cues from the experimental virtual environment. Subsequently, participants completed three experimental conditions: Learning (Hidden trials), Retention (Probe trial), and Motor Control (Visible trials). The Learning condition included 16 hidden platform trials (1 trial starting in each quadrant (NW, NE, SW, SE), 4 trials per 4 blocks). The Probe trial lasted for 30 s, during which time the platform was removed from the pool, unbeknownst to participants. The Motor Control condition included 8 visible platform trials (1 trial
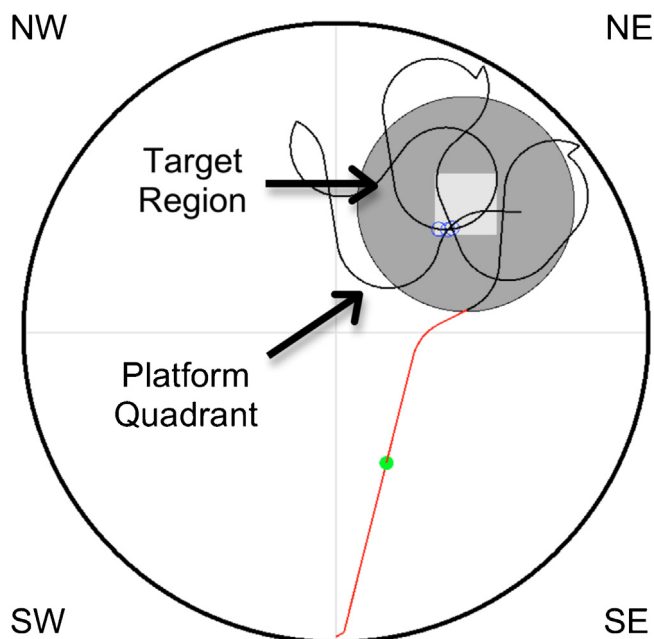
Fig. 1. Schematic representation of the virtual pool, denoting four quadrants (light gray lines: NW, NE, SW, SE). The large gray circle represents the target region, which is 25% of the pool diameter centered on the platform (white square), located in the NE quadrant.

starting in each quadrant (NW, NE, SW, SE), 4 trials per 2 blocks). For additional task details, see Sneider et al. (2013a,b).

2.3.1. Dependent measures: platform trials

For both Learning (hidden) and Motor (visible) platform trials, time to enter the platform area and path length were recorded for each trial, 4 trials per 4 blocks (escape latency, s). Path length of the pool diameter was recorded for each trial block.

2.3.2. Dependent measures: no-platform probe trial

For analysis purposes, a notional circular region (the critical region) with a diameter equal to 25% of the pool diameter was centered on the platform location used during training (Fig. 1). The path length to first enter this region and the total percentage of the overall path length within this region were calculated. Heading error (angular deviation from a direct path from the release point to the platform) was determined at the point where the cumulative path length first exceeded an amount equal to 25% of the pool diameter. The path length to enter and percentage of total path length spent within the quadrant containing the escape platform were also calculated. Collectively, these dependent measures provide information about initial trajectory to the platform location and search persistence at this location on different spatial scales. Chance values for percent of total path length in the quadrant and percent of total path length in the region were approximately 25% and 5%, respectively.

Independent raters blind to participant age and sex determined navigation strategies during performance on the Probe trial to be either: (1) a direct strategy, where participants navigated directly to the platform location from the starting location, or (2) a non-direct strategy, where participants navigated in a circuitous or random route that was not in the direction of the platform quadrant (NE) (Astur et al., 2004). While there are several types of non-direct strategies: zigzag, circuitous, random, landmark, these strategies were coded as "non-direct". Two coders viewed individual output files of navigation maps produced during task performance to
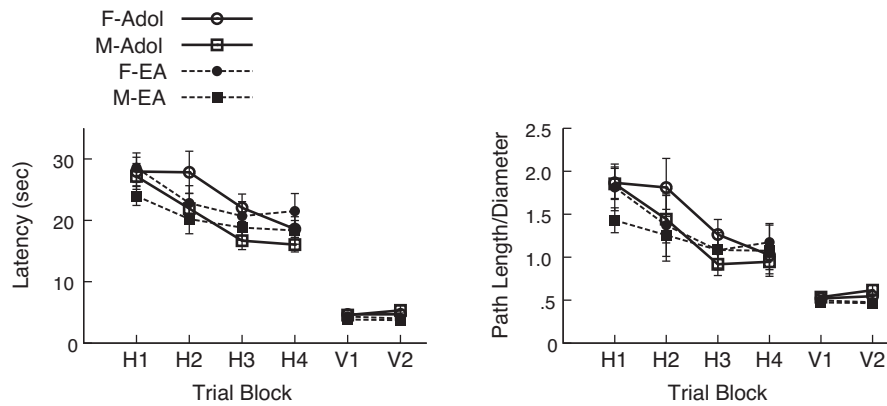
Fig. 2. Mean (+SEM) vWMT measures during the training (left) and visible (right) trials for males and females at each age (adolescent vs. emerging adult (EA)): (A) Latency (s) across hidden trial blocks (left) and visible trial blocks (right) and (B) Path length to enter the platform region across 4 hidden trial blocks (left) and visible trial blocks (right). Adolescent females and males represented with solid lines and open circles/squares, respectively, and emerging adult females and males represented with dashed lines and closed circles/squares, respectively.

classify strategy. The intraclass correlation coefficient between raters for strategy coding was ICC = 0.95, $p < .001$.

2.4. Visuospatial perception: Mental Rotations Test

A paper pencil version of the MRT was administered to assess visuospatial perception (Vandenberg and Kuse, 1978). In this 12-item task, participants had a time limit of 4-min to match target 3-D cube figures to two of four rotated versions of the reference item. For each item, participants were asked to select the two correct figures from four options. One point is given for each correctly identified rotated figure, with a maximum total score of 24 points. This timed task required participants to visualize how an object would look if it were rotated.

3. Statistical analyses

For the vWMT, Learning trial data were analyzed using three-way (Age × Sex × Block (4 trials)) mixed-model repeated measures analyses of variance (ANOVAs), with Age and Sex as between-subject variables and Block as a within-subject variable. The primary outcome variables of interest for Learning trial and Motor Control trial analyses were escape latency and path length (expressed as the ratio to the pool diameter). To evaluate Probe trial performance, two-way (Age × Sex) ANOVAs were conducted for path length to enter the target quadrant, path length to enter the target region, the percent path length traveled in the target quadrant and target region, and the initial heading error. Planned analyses were conducted for each "persistence" measure (% path length in region and quadrant) to evaluate whether each group (combination of sex and age) performed significantly above these approximate chance thresholds (25% and 5%) using one sample t-tests for each age/sex, with test values set to 25% and 5%, respectively. Chi-square non-parametric analyses were conducted to compare navigation strategies employed (i.e., direct strategy versus the non-direct strategy) between groups. For the MRT, Total score was analyzed using a two-way (Age × Sex) ANOVA. Follow-up analyses were conducted using paired t tests for repeated measures and ANOVAs for univariate analyses to determine sources of differences when interactions were statistically significant. Effect size (ES) F was calculated for significant main effects and interactions using G*power (Version 3.0.6). Based on previous work (Astur et al., 2004), correlations between age and vWMT and MRT performance were conducted separately for each sex using Pearson's correlation

coefficients. SPSS 18.0 (SPSS, Chicago, IL) was used for all statistical analyses ($\alpha = .05$).

4. Results

4.1. Demographic and clinical variables

No age or sex differences (within each age epoch) were observed for demographic variables (Table 1).

#### 4.2. Spatial ability: virtual Water Maze Task

4.2.1. Learning – hidden platform trials

Mean performance over trial blocks for latency (s) and path length/diameter measures for hidden platform trial blocks are presented in Fig. 2. A significant main effect of Block was observed for latency ($F(3,204) = 25.7$, $p < .001$; ES = .61), with shorter swim latencies observed by Block 4 (H4) on Learning trials (Fig. 2, left), as well as an Age × Block interaction for latency ($F(3,204) = 2.9$, $p = .04$; ES = .21). Follow-up paired t tests for the interaction demonstrated that while all groups exhibited significant learning, adolescents exhibited shorter latencies between Block 2 and Block 3 ($t(32) = 3.74$, $p = .001$), whereas emerging adults exhibited shorter latencies between Block 1 and Block 2 ($t(38) = 3.06$, $p = .004$). A significant main effect of Block also was observed for path length/diameter ($F(3,204) = 17.1$, $p < .001$; ES = .50), with shorter path length/diameter being observed by Block 3 ($t(71) = 3.4$, $p = .001$) (Fig. 2, right). No significant main effects of Age or any interactions were observed for path length/diameter, nor were there significant main effects of Sex for either measure.

4.2.2. Motor – visible platform trials

Mean performance over trial blocks for latency (s) and path length/diameter measures for visible platform trial blocks are presented in Fig. 2. Significant main effects of Age were observed for latency to reach the platform [Adolescent > Emerging Adult; $F(1, 67) = 11.66$, $p = 0.001$; ES = 0.42] and path length [Adolescent > Emerging Adult; $F(1, 67) = 18.42$, $p < 0.001$; ES = 0.53] (Fig. 2, left). A significant Age × Block interaction also was observed for path length/diameter [$F(1, 67) = 6.03$, $p = 0.017$; ES = 0.29]. Post hoc analyses indicated that adolescents showed a trend toward shorter path length/diameter Block 2 (V2) compared to Block 1 (V1) [$F(1, 32) = 3.50$, $p = 0.07$; ES = 0.33], whereas the main effect of Block reached significance in emerging adults, with significantly shorter path length/diameter observed on Block 2 (V2) versus Block 1 (V1)
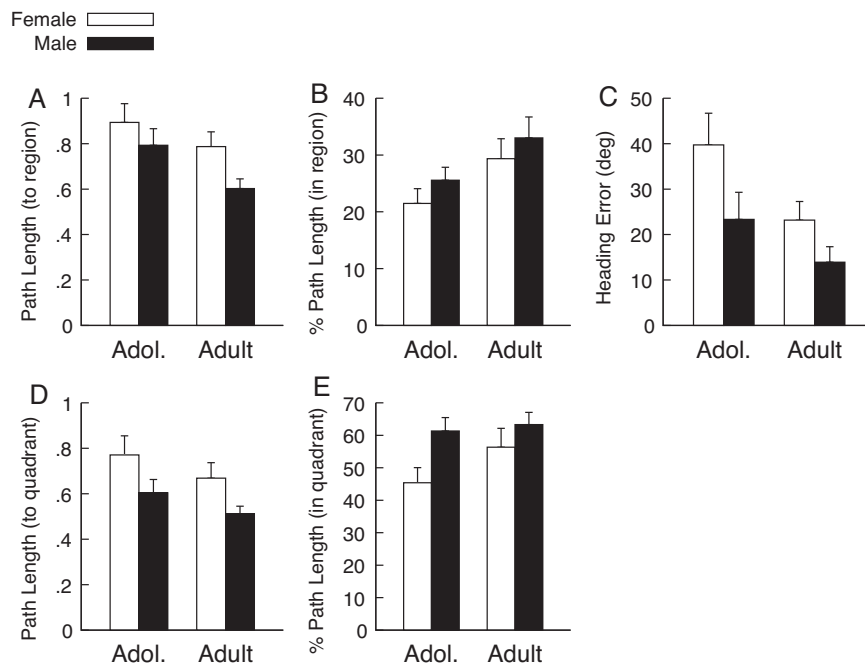
Fig. 3. Mean (+SEM) vWMT measures during the no-platform probe trial for males and females at each age (adolescent vs. emerging adult (EA)): (A) path length to enter the platform region, (B) percentage of overall path length in the platform region, (C) heading error, (D) path length to enter the platform quadrant, and (E) percentage of overall path length spent in the platform quadrant.

$[F(1, 37) = 5.14, p = 0.029;$ ES = 0.36] (Fig. 2, right). No significant main effects of or interactions with Sex were observed.

4.2.3. No-platform probe trial

Mean performance for Probe trial dependent measures are presented in Fig. 3. There were significant effects of Age for path length to enter the target region [Emerging Adult < Adolescent; $F(1, 68) = 5.19, p = 0.026;$ ES = 0.27], percentage of total path length in the target region [Emerging Adult > Adolescent; $F(1, 68) = 5.56, p = 0.021;$ ES = 0.28], and heading error [Emerging Adult < Adolescent; $F(1, 68) = 6.45, p = 0.013;$ ES = 0.30]. Although similar trends were observed for the path length to enter the platform quadrant (Emerging Adult < Adolescent) and percentage of overall path length in the platform quadrant (Emerging Adult > Adolescent), neither reached statistical significance. There were significant Sex effects for path length to enter the target region [Males < Females; $F(1, 68) = 4.78, p = 0.032;$ ES = 0.27], heading error [Males < Females; $F(1, 68) = 6.26, p = 0.015;$ ES = 0.30], path length to enter the platform quadrant [Males < Females; $F(1, 68) = 6.95, p = 0.01;$ ES = 0.32], and percentage of overall path length in the platform quadrant [Males > Females; $F(1, 68) = 6.18, p = 0.015;$ ES = 0.30]. Males demonstrated a higher percentage of overall path length in the target region, however, this effect did not reach statistical significance. There also were no significant Age × Sex interactions observed for any measure (all $ps > 0.333$). Percentage of overall path length was significantly different than chance for all participants for both the region (5%) and the quadrant (25%) analyses ($p = .000$, for all one sample t-tests).

4.2.4. Navigation strategies

No significant Strategy preference was observed on the Probe Trial for adolescents: 52% ($n = 17$) of adolescents utilized a direct strategy and 48% ($n = 16$) of adolescents utilized a non-direct strategy to reach the platform ($\chi^2(1,33) = .03$, ns). In contrast, emerging adults demonstrated a significant Strategy preference, with a greater percentage of emerging adults using a direct strategy

(74%, $n = 29$) than a non-direct strategy (26%, $n = 10$) ($\chi^2(1,39) = 9.3$, $p = .002$). In addition, significantly more emerging adult males (69%, $n = 20$) used a direct strategy relative to emerging adult females (31%, $n = 9$) ($\chi^2(1,29) = 4.2, p = .04; p = .38$). This pattern of sex differences was not observed between male and female adolescents (Fig. 4).

4.3. Spatial perception: Mental Rotations Test

There was a significant main effect of Sex ($F(1, 63) = 12.0$, $p = .001$; ES = 0.44), and a significant Age × Sex interaction ($F(1, 63) = 7.01, p = .01$; ES = .33) for total score on the MRT. However, the Age main effect did not reach significance ($F(1,63) = 3.3, p = .07$). Follow-up analyses revealed that emerging adult males exhibited higher scores than emerging adult females ($F(1, 34) = 17.1, p < .001$; ES = .72), whereas no differences were observed between adolescent males and females (Fig. 5).
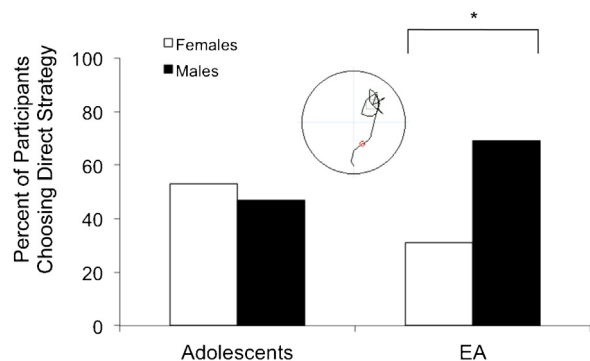
Fig. 4. Percent of participants using a direct strategy on the Probe trials, displayed by age group and broken down by sex, adolescent group (left panel) and emerging adults (right panel), *$p < .05$.
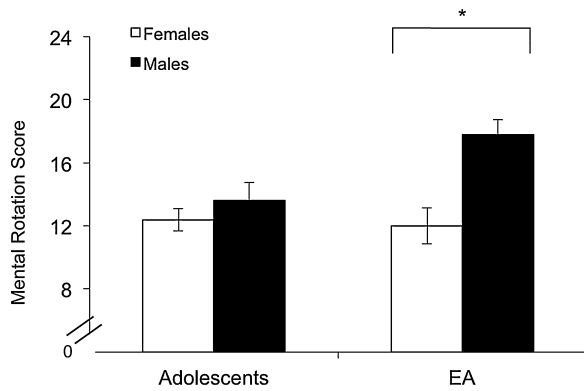
Fig. 5. Mean (+SEM) MRT total score in adolescent females and males (left panel, open and closed bars, respectively) and emerging adult females and males (right panel, open and closed bars, respectively), *p < .05.

4.4. Correlations: age and performance

Age was significantly correlated with heading error on the vWMT in females ($r(34) = -.329$, $p = .029$), but not with any other vWMT measure or with MRT total score. In contrast, in males, Age was significantly correlated with path length to enter the target region ($r(38) = -.369$, $p = .011$) and percent path length in the target region ($r(38) = .279$, $p = .045$) on the vWMT, and total score on the MRT ($r(35) = .521$, $p = .001$). Further, MRT total score was significantly correlated with path length to enter the target region ($r(35) = -.333$, $p = .025$), percent path length in the target region ($r(35) = .411$, $p = .007$) and heading error ($r(35) = -.333$, $p = .025$), and percentage of overall path length in the platform quadrant ($r(35) = .292$, $p = .044$) again only in males. However, based on these correlations, when MRT total score was included in mediation analyses as a covariate, it was found not to be significant for any vWMT measure.

5. Discussion

To date, there have been a number of reports examining vWMT performance in adults, as well as a growing number of studies conducted in children. The results of the present study, however, are the first to demonstrate human evidence for age-related improvements and sex-specific differences in spatial performance on the WMT specific to adolescence compared with emerging adults.

All participants demonstrated significant evidence of learning on the vWMT, with a steeper learning curve being observed in emerging adults than in adolescents, (i.e., emerging adults reached asymptote at an earlier Block than adolescents during learning/hidden platform trials). Emerging adults also demonstrated better retention of the platform location than adolescents, as indicated on the Probe trial. Collectively, vWMT Probe outcome measures indicate that emerging adults outperformed adolescents in searching near the platform location, on both initial trajectory (path length to enter the target region) and persistence (percent path length within the target region). The pattern of significant results also suggests that measures derived from more narrow spatial scale at the target location are more sensitive to age effects within the sampled range of ages (i.e., measures taken at the level of the entire platform quadrant may not be sufficiently sensitive to detect age effects).

With regard to sex differences, there were no significant differences on learning trials, nor were there significant interactions with sex. However, most measures of navigation during the Probe trial revealed better performance in male participants, albeit the effect for persistence in searching at the target region (a more narrow

spatial sampling) failed to reach significance. This observation suggests that measures derived from a broader spatial sampling may be more sensitive to sex differences, although it is noted that the difference between males and females in spatial search was similar in magnitude for both narrow (target region) and broader (target quadrant) spatial scales. Correlational analyses corroborated age and sex differences in performance of the vWMT, suggesting that spatial ability improves with age, to a larger extent in males (older age associated with shorter path length to enter and higher percent path length in the target region) than females (older age associated only with smaller heading error).

Performance on a test isolating visuospatial perception, the MRT, also was assessed, again revealing age-related improvements that were consistent with previous studies (Andreano and Cahill, 2009; Astur et al., 2004; Voyer, 2011). Importantly, for males in the present study, better vWMT performance (shorter path length to enter and higher percent path length in the target region, and smaller heading error) was correlated with higher MRT total score. A similar correlation has also been reported between performance on these tasks in young adults (Astur et al., 2004). Despite the observed male vWMT/MRT relationship in this study, MRT total score included as a covariate was not significant in a mediation analysis of vWMT performance, suggesting that mental rotation ability does not simply account for sex differences in spatial navigation.

The present findings are also consistent with the rodent literature demonstrating age-related improvements in acquisition (reduced escape latency and shorter swim distances) and retention (more time spent in goal quadrant), observed from adolescence to adulthood (Akers and Hamilton, 2007; Carman and Mactutus, 2001). Specifically, spatial navigation abilities emerge very early in rat development (i.e., generally around postnatal days 19–22) (Carman and Mactutus, 2001; Carman et al., 2002; Castro et al., 1987; Akers and Hamilton, 2007; Brown and Whishaw, 2000). Overall, preweanling rats have been shown to successfully learn to navigate to the platform in place and cued versions of the WMT. An age-related improvement in human spatial ability also was observed in participants between ages 6 and 67 on the Memory Island task. In that task, adolescents and younger–adults outperformed children and older ages (Piper et al., 2011). The overall male advantage on spatial ability on the vWMT, observed in the present study regardless of age, also is consistent with previous work in adults (Astur et al., 2004) and in prepubertal children (Newhouse et al., 2007), extending the literature to now include adolescents. Similarly, a comparison of twenty- and fifty-year-olds on a vWMT and on the MRT demonstrated that emerging adults outperformed older adults, and males outperformed females, although no age or sex differences were observed for mental rotation ability (Schoenfeld et al., 2010). Taken together, age-related changes in spatial abilities across the lifespan appear to follow an inverted U-shape pattern, in which adolescents improve significantly in ability by emerging adulthood, and overall, emerging adults exhibit superior WMT performance relative to younger and older counterparts.

Differences in spatial processing on the vWMT may be related to differences in the strategy employed to solve the task (Liu et al., 2011; Rodgers et al., 2012) and possibly greater confidence in navigating toward and identifying the platform location when the platform is not visible. That is, significantly more emerging adult males employed a direct navigation route, which relies on a more efficient spatial strategy that is a more efficient means to solve the task. For adolescents and emerging adult females, however, approximately half used a direct approach and the other half used a non-direct approach to complete the task. This finding is consistent with prior work (Astur et al., 2004). Notably, unlike emerging adults, this study documents that the superior performance observed in adolescent

males versus females was not due to differences in the strategy employed to solve the task. In a study combining the vWMT with eye tracking during task performance, young adults who employed direct navigation routes during training were found to primarily look at the distal room environment early in the trial, and at the pool later in the trial (Hamilton et al., 2009). In contrast, participants employing less efficient, non-direct routes were found to transiently look at distal cues, focusing more on the pool throughout the task. Thus, age and sex differences in establishing directionality of the initial trajectory, relative to distal room cues, and the ability to interpret relative distance to the platform within the pool (Hamilton et al., 2007) may also contribute to the observed differences in adolescent versus emerging adult males and females.

It is plausible that females, regardless of age, navigate away from the correct platform quadrant during the Probe trial in the absence of confirmation that they have successfully reached the platform, as the platform is removed in this condition unbeknownst to participants, thereby reducing reinforcement of choosing a direct strategy. To this end, in adults, sex differences in wayfinding strategies have been reported, with men reporting greater preference for an orientation strategy (e.g., maintain sense of own position relative to geographical reference points) relative to women who reported greater preference for a route strategy (e.g., use of signs or directions from another person) (Lawton, 1996; Lawton and Kallai, 2002). Further, women reported greater wayfinding anxiety (i.e., spatial anxiety) than men, which was attributed to personal safety in environments related to choosing a more familiar route which may not be the most direct per se (Lawton, 1996; Lawton and Kallai, 2002). Orientation strategy was significantly correlated with spatial ability, whereas the route strategy was anticorrelated with spatial anxiety. Thus, age-related changes in spatial ability could potentially be attributed to differences in anxiety related to wayfinding. In contrast, generational changes in gender roles could provide more opportunities for exposure to wayfinding across sexes, which could perhaps offset negative influences of anxiety on spatial ability in today's younger generations (Lawton, 1994).

From a neurobiological perspective, fMRI studies in adults provide evidence that women show a pattern of hippocampal activation that is unique from men during vWMT performance: women activate right hippocampus, bilateral parahippocampal area, and right mid-cingulate, whereas men activate left hippocampus, left parahippocampal area, left mid-cingulate, and right anterior cingulate during task performance (Sneider et al., 2011). An fMRI vWMT investigation to probe neural correlates of spatial ability in adolescents is therefore warranted to better understand neurobiological underpinnings of age and sex differences in task performance, particularly since evidence from structural MRI studies point to differences in hippocampal tissue volumes between girls and boys (ages 8–15 years) that likely influence spatial ability (Neufang et al., 2009). Moreover, a recent review of neurobiological differences between virtual reality navigation and real-world navigation tasks, suggests additional involvement of vestibular, motor and proprioceptive systems during virtual navigation (Taube et al., 2013). Thus, potential age and sex differences in activation of regional (hippocampal) and multi-regional networks need to be taken into account when investigating neural contributions to spatial cognition.

One limitation that should be considered when interpreting the current study results is that joystick use/video game experience was not directly assessed in the study participants, which could contribute to performance differences between groups. This is unlikely, however, given that adolescents typically have more video game exposure than young adults (Rideout et al., 2010), which would result in better, not worse performance. Further, Schoenfeld et al. (2010) reported that vWMT performance was not significantly correlated with computer game experience. Nonetheless, future studies of spatial ability in adolescent cohorts must account for joystick experience. A limitation to consider for the MRT is that the time limit imposed in the test (4 min limit for task completion) could be a potential factor contributing to sex-related performance differences, or lack thereof (Voyer, 2011), and accordingly, could be empirically examined in future studies. Finally, the influence of hormone fluctuations associated with menstrual cycle phase was not directly assessed in the present study. Cycle phase is a relevant factor, as better spatial ability has been reported during the follicular phase of the menstrual cycle in adult women (McCormick and Teillon, 2001). However, exploratory analyses based on self-report in a subset of female participants in the present study yielded evidence of similar task performance across follicular and non-follicular phases. It will be necessary in future studies to empirically investigate age-related differences in memory performance relative to sex hormone levels in adolescence.

The current findings have important practical applications. Previous studies conducted in first grade boys and girls demonstrate that interventions (e.g., skill-building) that encourage the use of spatial strategies for processing visuospatial information can improve spatial ability, thereby mitigating performance differences between sexes (Tzuriel and Egozi, 2010). Thus, intervention and education efforts that encourage the use of direct navigation strategies could help improve performance via identification of important visuospatial cues, and accordingly, improve spatial ability at any age, but particularly in those that have suboptimal task performance. To this end, Uttal et al. (2013) recently conducted a meta-analysis demonstrating that training can enhance spatial reasoning in male and female children and adults. Other training methods that can enhance spatial ability include exposure to video games geared toward spatial attention and mental rotation, which also have been shown to reduce sex differences in spatial skills (Feng et al., 2007).

In conclusion, this is the first study to establish sex-specific performance differences in adolescents relative to emerging adults on a vWMT. Significant sex differences were evident in both age groups, with males performing better than females on the vWMT regardless of age, but no sex differences were apparent in the adolescent group on mental rotation ability. Furthermore, measures derived from a more narrow spatial scale at the target location were shown to be more sensitive for identifying age effects. Utilization of a more efficient strategy for locating the platform, the direct strategy, yielded better vWMT performance in emerging adult males, although strategy choice did not account for sex differences in the adolescent cohort, nor did visuospatial perception ability. Overall, the present study provides important information regarding the developmental profile of spatial ability in adolescents as compared to a slightly older cohort, emerging adults. The WMT is one the most frequently used tools to assess spatial memory in animal models, and virtual analogs of this classic task have provided invaluable applications for translational research on the study of learning and memory. Future studies should address four major areas to advance the literature on developmental improvements in spatial ability: (1) how other types of memory ability relate to spatial ability; (2) the influence of motoric ability, such as joystick use or keyboard manipulation, on performance; (3) the role of developmental maturation of the neural circuitry underlying learning and memory on vWMT performance; and (4) the impact of biological influences, such as sex-related hormones, on spatial navigation. Future work should also address whether spatial abilities are vulnerable to environmental influences during adolescence, such as exposure to alcohol or drugs (Sneider et al., 2013a,b), and whether spatial abilities can be enhanced across the lifespan.

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