

## Supplementary Information

### *Effects of estrogen on spatial navigation and memory*

by G Joue, T Navarro-Schröder, J Achtzehn, S Moffat, N Hennies, J Fuß, C Döller, T Wolbers & T Sommer.

### **Additional Results**

Details of regression models and results are shown in Table [S1](#).

women become more relaxed in test situations over time and hence perform better.

### **Relation to the classic non-navigation-based spatial task: mental rotation**

Other tasks testing general spatial ability are often conflated with spatial navigation. A common such task is the mental rotation task (e.g. of 3-D blocks: [Shepard and Metzler 1971](#); or perspective line drawings of objects: [Vandenberg and Kuse 1978](#)). Mental rotation performance has been found to be correlated with faster wayfinding through a maze, virtual ([Moffat et al, 1998](#)) or real ([Malinowski, 2001](#)), and with fewer errors but only after the maze environment has been learned – but also correlated with tasks involving an egocentric strategy ([Moffat et al, 1998](#)). Indeed, mental rotation tasks can be solved with either egocentric or allocentric views ([Zacks et al, 2002](#)) and is arguably not a naturalistic task with weak and variable correlation with other spatial navigation tasks.

Mental rotation performance have been reported to fluctuate with E2, though reports are not consistent in women ([Noreika et al, 2014](#); [Shirazi et al, 2021](#); [Vashro and Cashdan, 2015](#)) or in men ([Peragine et al, 2020](#)). Otherwise, males tend to perform better, though this advantage decreases when more items are tested ([Voyer et al, 1995](#)), suggesting that performance differences stem from stress more than ability and that

**Table S1** Regression model predictions of (back-transformed) spatial navigation metrics reflecting strength of cognitive maps and spatial orientation.

<i>predictor</i>	<i>metric estimates</i>					
	dist/path <sup>(O)</sup> $e^{\log-norm}$	idle time <sup>(O)</sup> $e^{\log-norm}$	y-flips <sup>(O)</sup> <i>CMP</i>	LISAS <sup>(O),1</sup> <i>log-log</i>	sinuosity <sup>(O),2</sup> $e^{\log-norm}$	pt RT <sup>(T)</sup> <i>inv.G</i> ( $10^{-3}$ )
(Intercept)	2996.0*	9.6*	1.2*	3.6*	0.01*	5.2*
	[2367.1, 3792.0]	[7.7, 12.1]	[1.2, 1.3]	[3.5, 3.7]	[0.01, 0.02]	[3.6, 7.1]
Sex <sub>M</sub>	<b>1.2</b>	<b>0.7*</b>	<b>1.3*</b>	<b>-0.2*</b>	<b>1.3*</b>	-0.6
	[1.0, 1.3]	[0.5, 0.9]	[1.3, 1.4]	[-0.3, -0.1]	[1.1, 1.4]	[-3.0, 1.7]
Grp <sub>E2</sub>	1.1	1.2	<b>1.2*</b>	-0.02	0.90 <sup>+</sup>	<b>-1.9<sup>+</sup></b>
	[1.0, 1.2]	[0.9, 1.6]	[1.1, 1.2]	[-0.1, 0.1]	[0.8, 1.0]	[-4.1, 0.2]
Sex <sub>M</sub> :Grp <sub>E2</sub>	0.9	0.9	<b>0.8*</b>	0.08		1.3
	[0.8, 1.1]	[0.6, 1.2]	[0.8, 0.9]	[-0.1, 0.2]		[-1.6, 4.3]
<sup>1</sup> log( <i>t</i> <sub>loc<sub>l</sub></sub> ) or <sup>2</sup> <i>t</i> <sub>path<sub>p</sub></sub>				<b>-0.2*</b>	<b>1.0*</b>	
				[-0.2, -0.2]	[1.0, 1.0]	
<sup>1</sup> Sex <sub>M</sub> :log( <i>t</i> <sub>loc<sub>l</sub></sub> ) or <sup>2</sup> Sex <sub>M</sub> : <i>t</i> <sub>path<sub>p</sub></sub>				<b>-0.02*</b>	<b>1.0*</b>	
				[-0.04, -0.00]	[1.0, 1.0]	
Grp <sub>E2</sub> :Sex <sub>M</sub> :log( <i>t</i> <sub>loc<sub>l</sub></sub> )				<b>-0.03*</b>		
				[-0.1, -0.01]		
<i>R</i> <sup>2</sup>	0.0 <sup>M</sup> /0.5 <sup>C</sup>	0.1 <sup>M</sup> /0.6 <sup>C</sup>		0.2 <sup>M</sup> /0.5 <sup>C</sup>	0.01 <sup>M</sup> /0.13 <sup>C</sup>	
Deviance					2.1	
N <sub>obs</sub>	3732	3732	3732	24031	24148	129
N <sub>group<sub>Ss</sub></sub>	129	129		129	129	
N <sub>group<sub>path</sub></sub>	36	36				
σ <sup>2</sup>	0.5	0.3		0.1	1.02	
τ <sub>Ss</sub>	0.1	0.3		0.1	0.1	
τ <sub>path</sub>	0.4	0.1				
<sup>1</sup> τ <sub>loc<sub>l</sub> Ss</sub> or <sup>2</sup> τ <sub>path<sub>p</sub> Ss</sub>					0.06 – 0.1	0.00

Task for each metric is shown as a superscript: <sup>(O)</sup> arena, <sup>(T)</sup> town

Metrics: distances to target locations (dist/path), idle time while navigating (idle time), navigation direction changes along the y-axis (y-flips), trade-off between spatial accuracy and time spent navigating (LISAS), sinuosity of navigation paths, and time to complete pointing/dead-reckoning task (pt RT)

The residual variance (σ<sup>2</sup>) is reported with between-group variance for random intercept (τ; *loc* location, *Ss* subjects) and random slope (τ<sub>*x*|*y*</sub> for slope *x* given *y*) where applicable.

*CMP*: Conway-Maxwell Poisson

*inv.G*: inverse Gaussian with link  $1/\mu^2$  for response time for pointing (pt RT)

*R*<sup>2</sup> variants: <sup>M</sup>Marginal/Fixed effects, <sup>C</sup>Conditional/Total

Null hypothesis values: \* outside the 95% confidence interval or <sup>+</sup> at the bounds of the interval.

Colon indicates interaction

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