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Gender differences in the mesocorticolimbic system during computer game-play

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Abstract

Little is known about the underlying neural processes of playing computer/video games, despite the high prevalence of its gaming behavior, especially in males. In a functional magnetic resonance imaging study contrasting a space-infringement game with a control task, males showed greater activation and functional connectivity compared to females in the mesocorticolimbic system. These findings may be attributable to higher motivational states in males, as well as gender differences in reward prediction, learning reward values and cognitive state during computer video games. These gender differences may help explain why males are more attracted to, and more likely to become "hooked" on video games than females.

Keywords: fMRI; Game; Gender differences; Amygdala; Orbitofrontal cortex; Nucleus accumbens

1. Introduction

It has been shown that there tends to be a larger dependence to video games in males than females (Griffiths and Hunt, 1998). Several neuroimaging studies have examined the neural processes underlying playing computer games. In one neuroimaging study using positron emission tomography (PET), increased release and binding of dopamine in the ventral striatum and positive correlation with subject performance were observed (Koepp et al., 1998). Another study showed decreased dorsal prefrontal activation while playing video games using near infrared spectroscopy (NIRS) (Matsuda and Hiraki, 2006). These findings are of interest in the context of putative associations between computer games, addiction and the reward system (Griffiths and Hunt, 1998). No studies, however, have examined gender differences in neural activation during video gaming.

In the present study, we acquired functional magnetic resonance images (fMRI) as subjects performed a simple computer game. The goal of the computer game (to gain "space") was made implicit in order to dissociate the effect of low-level motor performance from the effect of goal achievement, and to provide identical instructions during the Game and Control conditions. We hypothesized that the mesocorticolimbic reward system would show greater activation and functional connectivity in males compared to females.

2. Materials and methods

2.1. Subjects

Twenty-two healthy Stanford students (19–23 years) participated in the study (11 females). All gave informed consent according to procedures approved by Stanford University School of Medicine and with the latest version of the Declaration of Helsinki. All subjects were right-handed and had no clinical psychiatric symptoms or problems as indicated by history or testing. There were no gender differences in age, psychological symptoms (Symptom Checklist-90-R) or personality traits (NEO

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Personality Inventory – revised) (P's > 0.05). Results from a survey showed that there were no gender differences in the degree to which subjects played computer/video games or utilized a computer in everyday activities ($P > 0.05$).

2.2. Task and stimuli

There were a total of 40 blocks of either a 24-s Game or Control conditions and rest conditions between each condition. At the beginning of each condition Game or Control, a vertical line (wall) was centered in the middle of a 1024 × 780 pixel screen. Balls with 20-pixel diameter appeared on one-half of the screen from the side at 40 pixel/s, and 10 balls were constantly on the screen at any given time Fig. 1a). *One's own space* was defined as the space behind the wall and opposite side to where the balls appeared. The ball disappeared whenever clicked by the subject. Anytime a ball hit the wall before it could be clicked, the ball was removed and the wall moved at 20 pixel/s, making the *space* narrower. Anytime all the balls were at least 100 pixels apart from the wall, which was measured every second, the wall moved such that the *space* became wider. Task instructions intentionally omitted any reference to goals or strategies, or the fact that the "wall" did not move in the control condition. The only instruction provided throughout the task was to "click on as many balls as possible". Low-level motor performance was defined as the total number of balls clicked throughout the Game or Control conditions throughout the scan. "Goal achievement" (i.e., amount of space gained/maintained) was measured as the mean position of the wall throughout the task "[(final position) – (initial position)]/(screen width)". Finally, learning of the goal was defined as the change in the amount of space during each block from the beginning until the end of the scan. The only difference between the Game and Control conditions was that the wall position was fixed (non-contingent) in the Control condition.

2.3. MRI acquisition

Data were collected using a 3.0-T Signa scanner (General Electric, Milwaukee, WI, USA). A T2*-weighted gradient echo spiral pulse sequence was used: TR = 2 s, TE = 30 ms, flip angle = 80°, FOV = 20 cm, matrix = 64 × 64, 28 oblique slices, and resolution = 3.125 × 3.125 × 4.0 mm with a 0.5 mm gap.

2.4. Data analysis

Statistical analysis was performed using Statistical Parametric Mapping software (SPM2; Wellcome Department of Cognitive Neurology, London, UK). Each subject's data were realigned, normalized, and smoothed with a Gaussian

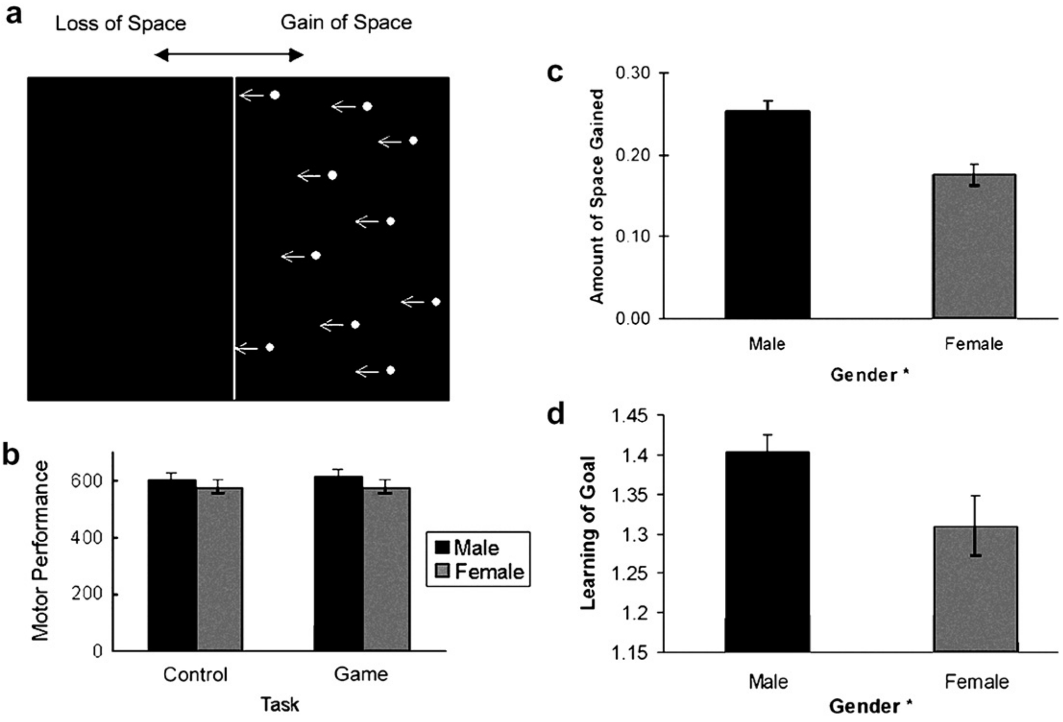

Fig. 1. Task design and performance. (a) Schematic diagram of task. (b) Low-level motor performance, defined as the total number of balls clicked during the Game or Control conditions throughout the scan. A two-way repeated measures analysis of variance (ANOVA) revealed that there was no significant effect ($P > 0.60$). (c) Amount of space gained defined as the mean position of the wall throughout the task. A larger number indicates gaining more space. Significantly more space was gained during the Game condition in males compared to females ($P < 0.05$). (d) Learning of goal defined as the change in the amount of space from the beginning until the end of the scan. The effect was significantly greater in males compared to females ($P < 0.05$). Error bars represent standard error of the mean.

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filter (4 mm full-width-half-maximum). Individual subject data were high pass filtered at 120 s, and analyzed using a fixed effects model modeling the Game and Control condition (rest was modeled implicitly).

Group analyses were performed with a random effects model. One-sample *t*-tests were first conducted across all subjects for the contrast [Game + Control] > Rest. The contrast Game > Control was then examined across the entire sample to examine regions that show activation when there was a goal.

The nucleus accumbens (NAc), amygdala (AMYG) and orbitofrontal cortex (OFC) were chosen as regions of interest (ROIs) based on information from previous studies of video game playing, reward and addiction (see Section 1 and Section 4 for details). Anatomical ROIs of the bilateral (Bil) NAc, OFC, and AMYG were created using the WFU PickAtlas and the location was confirmed in each subject's native space. All subsequent analyses were performed utilizing these regions. Two-sample *t*-tests were conducted between males and females for the contrast Game > Control.

Further, we were interested in assessing the *interactions* among the network constituents during the space-infringement task relative to the non-space infringement control task, hence performed PPI analysis as described in (Gitelman et al., 2003). We chose the NAc as the seed region based on prior literature that the NAc would play a key role in modulating activity of other ROIs (see Section 1 and Section 4 for details). We chose NAc in the left hemisphere because, as outlined in Section 3 the contrast Game > Control revealed left (Lt) NAc to display significant activation, with no significant gender difference (peak Talairach coordinates x −10, y 10, z −2).

Statistical threshold of $P = 0.05$ false discovery rate corrected was used for whole brain analysis. When no regions survived and where specified, a threshold of $P = 0.001$ uncorrected, extent threshold = 10 was employed as exploratory analyses. $P = 0.05$ small volume corrected was used for ROI analyses.

3. Results

3.1. Behavior results

A two-way repeated measures analysis of variance (ANOVA) of low-level motor performance revealed that there was no significant Gender (Male, Female) × Task (Game, Control) interaction ($F_{(1,20)} = 0.432$, $P = 0.52$), nor main effect for Gender ($F_{(1,20)} = 0.085$, $P = 0.77$) or Task ($F_{(1,20)} = 0.29$, $P = 0.60$) (Fig. 1b). This indicates that brain activation results below are unlikely to be due to low-level motor performance. Amount of space gained however, was significantly greater in males compared to females ($t_{(20)} = 2.57$, $P = 0.018$; Fig. 1c). Further, there was a learning effect in that males showed a greater propensity for successfully gaining space than females ($t_{(20)} = 2.21$, $P = 0.039$; Fig. 1d).

3.2. Brain activation profiles associated with playing computer games across genders

Brain regions that showed significant activation during computer games ([Game + Control] > Rest) included areas known to be involved in visual processing, visuo-spatial attention, motor function, and sensori-motor transformation (Fig. 2a and Table 1a). For the contrast Game > Control, there was no significant effect at the stringent threshold. At a more liberal threshold, however, there was significant activation in the right (Rt) insula, Rt dorsolateral prefrontal cortex (DLPFC), bilateral premotor cortices and precuneus. ROI analyses revealed significant activation in Lt NAc and Rt OFC.

3.3. Gender difference in brain activation profiles

Because of our particular interest in gender differences, we performed a direct comparison between males and females for the contrast Game > Control. We found significantly greater activation in males compared to females in the Rt NAc, bilateral OFC and Rt AMYG (Fig. 2b, Table 1b) but no regions showed greater activation for females compared to males. Further, we compared the contrast Control > Rest to investigate the possibility that these differences could arise from differences in activation levels during the control condition, and found no significant gender differences.

Males compared to females also showed significantly greater functional connectivity between Lt NAc and bilateral OFC and between Lt NAc and Rt AMYG (Fig. 2c and Table 1c, 223 voxels). In contrast, females compared to males showed one small cluster (10 voxels) in the Rt OFC (Fig. 2c and Table 1c).

3.4. Gender specific covariance of behavior and brain activation profiles

Males showed positive correlation between goal achievement and Game > Control brain activation (contrast estimates, i.e., effect size calculated as the linear combination of beta parameters) in Lt NAc (rho = 0.61, $P = 0.047$) and Rt AMYG (rho = 0.88, $P < 0.001$) and with functional connectivity between Lt NAc and Lt OFC ($\rho = 0.66$, $P = 0.026$). Females, on the other hand, showed negative correlation with functional connectivity between Lt NAc and Lt OFC ($\rho = -0.69$, $P = 0.019$). Finally, in males only, learning of goal (change in space gained) was positively correlated with Rt AMYG activation ($\rho = 0.68$, $P = 0.021$). None of these activation profiles showed significant correlation with low-level motor performance (P's > 0.05).

4. Discussion

Our study provides novel evidence suggesting (1) an overlap between the neural basis of space-infringement computer games and the neural circuitries involved in reward and addiction and (2) gender differences in brain activation and functional connectivity patterns. We excluded possible confounds due to neuropsychological profiles, lower-level motor performance, and computer and video-game experience.

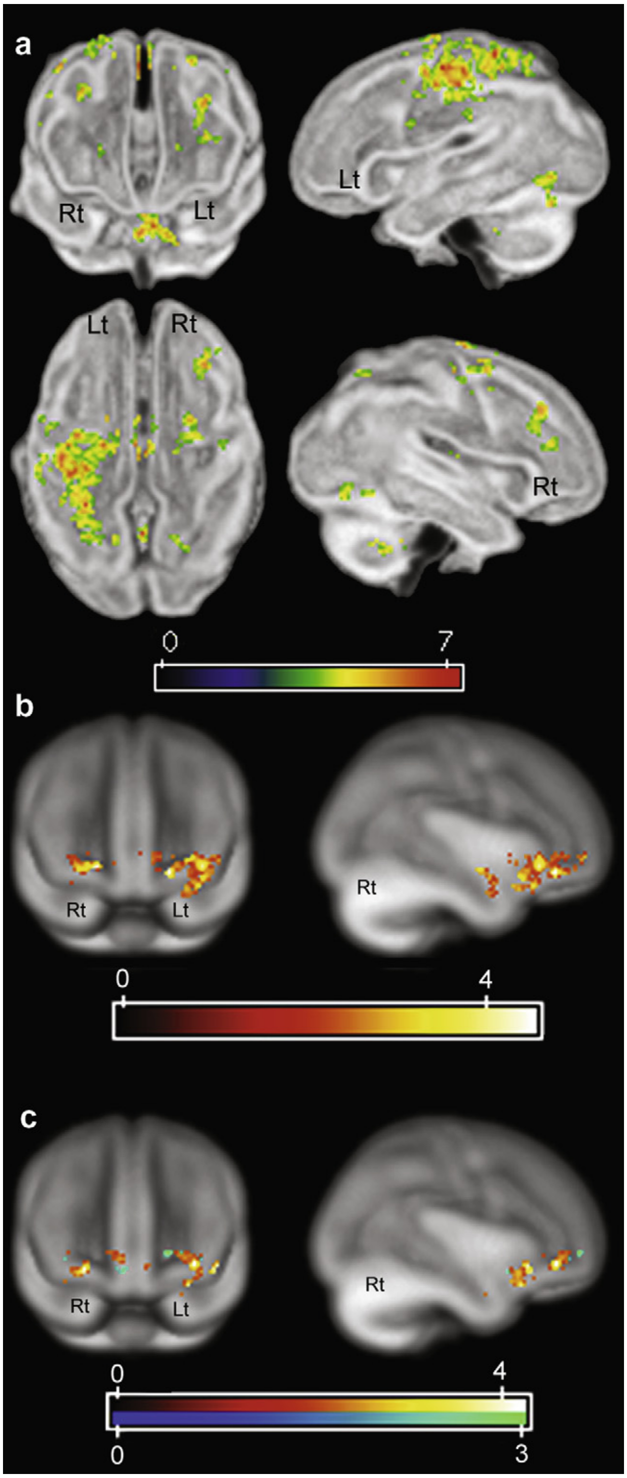

Fig. 2. Brain activation profiles. (a) Brain activation for the Contrast (Game + Control) > Rest. $P_{\text{corrected}} = 0.05$. (b) Gender differences in brain activation for the Contrast Game > Control. Regions that showed greater activation for males compared to females. No regions showed greater activation for females compared to males. $P_{\text{corrected}} = 0.05$. (c) Gender differences in task-specific functional connectivity. Warm color indicates regions that showed greater activation for males compared to females. Cold color indicates regions that showed greater activation for females compared to males. $P_{\text{corrected}} = 0.05$.

Across the entire subject group, we found significant brain activation in regions typically associated with reward (for a review, see (Knutson and Cooper, 2005)) and addiction, including the NAc and OFC. The OFC is involved in coding stimulus reward value (Anderson et al., 2003), and in concert with the ventral striatum (NAc) (O'Doherty et al., 2002), is implicated in representing predicted future reward. Such representations can be used to guide action selection for reward, a process that depends, at least in part, on OFC (Lauwereyns et al., 2002).

In addition, our whole brain analyses showed additional activation in the insula, DLPFC, precuneus and premotor cortex during the Game compared to the Control condition. Insular activity could signal autonomic arousal (Critchley et al., 2003), the premotor cortex may be involved together with the LPFC during action preparation for reward (O'Doherty, 2004) and the DLPFC in maximizing reward or to modify behavioral strategies (Knutson and Cooper, 2005). While precuneus activation has not been reported in the reward literature, this region has been shown to be involved in a neural network functionally specialized for the processing of spatially guided behavior (Cavanna and Trimble, 2006).

Neural substrates of drug use and addiction such as the AMYG, NAc and OFC, DPFC and insular cortex also overlap with our current findings (Kalivas and Volkow, 2005). Associations between playing video games, the reward system and addiction have been previously suggested (Griffiths and Hunt, 1998); however, activation profiles in these regions during video game-playing have not been shown.

Supporting our *a priori* hypotheses, significant gender differences in brain activation and task-specific functional connectivity were observed within the mesocorticolimbic reward circuitry, with males generally exhibiting greater activation and connectivity. The only observed gender difference in performance was that males were more effective in gaining space and learned the implicit goal faster than females. Thus, it is of interest that prominent gender differences would be observed in regions implicated in reward and addiction during a simple computer game. One explanation for this finding is that the goal to "gain more space" acted as a reward for males relative to females, whether or not it was consciously perceived as rewarding by the subjects (Kaya and Weber, 2003). Several anecdotal observations after the imaging session indicated that the subjects did not focus on the space-infringement nature of the task, supporting the premise that an implicit reinforcer (i.e., acquired space) can activate the reward circuitry.

Of additional interest are the significant associations between goal achievement and learning and brain activation profiles occurring predominantly in males. Results showing significant associations of goal achievement with

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Table 1
Brain activation profiles

Lobe	Region		Brodmann area	Talairach coordinates			T	$P_{\text{corrected}}$	Volume (voxels)
	Hemisphere	Gyrus		x	y	z			
(a) *[Game + Control] > Rest contrast: males and females combined*									
Frontal	Right	Medial–superior frontal gyrus	6	0	−11	52	7.25	0.01	457
		Superior, middle frontal gyrus	9	36	37	31	5.57	0.01	78
		Middle frontal gyrus	6	26	7	53	5.26	0.02	92
		Middle frontal gyrus	10	36	42	15	4.83	0.02	28
	Left	Inferior frontal gyrus	9	−55	5	22	4.10	0.03	10
		Precentral gyrus	6	−51	2	37	4.29	0.03	10
	Right	Precentral gyrus	6	44	−7	50	3.88	0.04	10
Frontal, parietal	Left	Post-, pre-central gyrus	5, 3, 4	−32	−40	61	6.81	0.01	1378
Parietal	Left	Post-, pre-central gyrus	3, 2	−55	−19	40	4.67	0.02	61
	Right	Superior parietal lobule	7	20	−59	55	4.28	0.03	18
	Left	Inferior parietal lobule	40	−50	−28	27	4.46	0.02	12
		Precuneus	7	−16	−59	55	4.41	0.03	14
Occipital	Left	Inferior temporal, middle occipital gyrus	19	−46	−74	−1	5.14	0.02	70
		Fusiform gyrus	19	−40	−75	−15	5.33	0.02	16
	Right	Middle occipital gyrus	19	44	−74	−6	4.70	0.02	40
		Middle occipital gyrus	19	46	−59	−7	4.43	0.03	12
Sub-lobar	Left	Lentiform nucleus, putamen		−22	2	−3	6.89	0.01	126
		Thalamus, ventral anterior nucleus		−12	−3	11	5.44	0.02	50
		Thalamus, mammillary body		−12	−18	−1	4.22	0.03	13
	Right	Thalamus, ventral lateral nucleus		18	−13	12	4.18	0.03	18
(b) *Game > Control Contrast*									
Males > Females									
Frontal	Left	Orbitofrontal cortex, gyrus rectus	11	−34	34	−10	3.69	0.001	115
			11	−18	38	−10	2.82		
	Right	Orbitofrontal cortex	10	18	44	−7	3.72	0.001	375
Sub-lobar	Right	Nucleus accumbens		8	9	−10	2.70	0.007	17
		Amygdala	38	30	−3	−22	2.76	0.006	29
Females > Males									
n/a									
(c) *Functional connectivity With Nac*									
Males > Females									
Frontal	Left	Orbitofrontal cortex	47	−30	30	−12	4.22	<0.001	75
	Right	Orbitofrontal cortex	11	12	50	−9	4.18	<0.001	128
Limbic	Right	Amygdala		30	−1	−23	2.60	0.009	20
Females > Males									
Frontal	Right	Orbitofrontal cortex	10	−27	45	−20	3.02	0.003	10

NAc activation, AMYG activation and connectivity between NAc and OFC, are consistent with the role of the OFC in the representation of stimulus reward value (Anderson et al., 2003) and the AMYG (Canli et al., 2002) and the ventral striatum (NAc) (O'Doherty et al., 2002) in representing predicted future reward. The findings of the AMYG are also in line with previous findings showing modulatory effects of dopamine to affective stimuli in the AMYG (Takahashi et al., 2004; Tessitore et al., 2002). Further, the significant association between learning and AMYG activation is consistent with a recent study in monkeys highlighting the role of the this region in learning the value of stimuli (Paton et al., 2006). While there were no significant differences in low-level motor task performance, it is also possible that other components such as aggressive behavior may have contributed to the gender differences in activation we saw in regions such as the AMYG (Takahashi et al., 2006). Overall, our findings suggest that males code the space-infringement task as more rewarding relative to females. If true, this gender difference may have contributed to differences in the amount of space gained and learning between males and females.

Our results are consistent with the growing literature describing gender differences in brain function (e.g., viewing (rewarding) sexual stimuli (Hamann et al., 2004), emotional films (Cahill et al., 2001), humor processing (Azim et al., 2005), and during rest (Kilpatrick et al., 2005)). Gender differences in brain function shown here are also consistent with the behavioral literature on drug intake and addiction (D'Souza et al., 2002) which has been related to disparities in the sensitivity of the male and female brain to drug stimuli (Cicero et al., 1997; Munro et al., 2006) (but note opposite gender effects observed in (Riccardi et al., 2006) in other regions of the brain).

There are many studies that will eventually need to be performed: (1) identification of the specific cognitive aspects of the game (e.g., motivational states, reward prediction and learning reward values) that contribute to these

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gender differences, (2) examination of gender differences during other types of games, (3) individual subject analysis in native space especially in examining small subcortical brain regions, and (4) investigation of subject populations in other age groups and from different cultural backgrounds. While the lack of significant difference in computer/video game-play between genders suggest that motivational level were similar between females and males, studies that tease apart gender differences from possible confounds such as difference in motivational states are warranted.

To our knowledge, this is the first fMRI study of computer video game playing examining neural systems related to reward and addiction. We show novel evidence that gender differences exist in the mesocorticolimbic reward system during an implicit space-infringement task with greater activation and functional connectivity observed in males than in females. The overlap with neural processes underlying addiction may help us understand the greater propensity of males for playing video games in a repetitive manner.

5. Contributtions

A.L.R. conceived the experiment, K.E.B. wrote the ‘territory simulator’, F.H., C.W., and S.R.K. carried out the experiment and data analysis. F.H. and A.L.R. co-wrote the manuscript.

6. Conflict of interest

None.

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