Effects of training strategies implemented in a complex videogame on functional connectivity of attentional networks

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ABSTRACT

We used the Space Fortress videogame, originally developed by cognitive psychologists to study skill acquisition, as a platform to examine learning-induced plasticity of interacting brain networks. Novice videogame players learned Space Fortress using one of two training strategies: (a) focus on all aspects of the game during learning (fixed priority), or (b) focus on improving separate game components in the context of the whole game (variable priority). Participants were scanned during game play using functional magnetic resonance imaging (fMRI), both before and after 20 h of training. As expected, variable priority training enhanced learning, particularly for individuals who initially performed poorly. Functional connectivity analysis revealed changes in brain network interaction reflective of more flexible skill learning and retrieval with variable priority training, compared to procedural learning and skill implementation with fixed priority training. These results provide the first evidence for differences in the interaction of large-scale brain networks when learning with different training strategies. Our approach and findings also provide a foundation for exploring the brain plasticity involved in transfer of trained abilities to novel real-world tasks such as driving, sport, or neurorehabilitation.

Introduction

Some training strategies are more effective than others for learning new skills (Kramer et al., 1999; Schmidt and Bjork, 1992), presumably because those strategies differ in how they draw upon brain processes associated with learning. A growing number of neuroimaging studies find learning-induced changes in brain structure and function as a result of practice (Draganski et al., 2004; Dux et al., 2009; Erickson et al., 2007; Scholz et al., 2009), but no prior studies have examined the effect of training strategy and related

learning on the plasticity of brain function after extensive practice in a complex cognitive task. To the extent that different learning strategies differentially affect functional brain organization, we should be able to measure those changes by comparing functional brain organization before and after training. We used functional connectivity analyses of fMRI data to examine changes in the interactions among brain regions as a result of complex skill learning.

For skill learning, the nature of practice can be just as important as its amount. Variability in the emphasis, the medium, and/or the schedule of practicing sub-components of a skill can enhance both the learning and retention of skills as well as their transfer to other tasks; such benefits of variable emphasis training have been shown across a range of domains, including motor skill and verbal learning (Schmidt and Bjork, 1992), complex videogames (Boot et al., 2010; Fabiani et al., 1989; Gopher et al., 1989), and multitasking (Kramer et al., 1999, 1995). Take as an example the skill of hitting a forehand in tennis. One approach would be to practice the skill of hitting a forehand by spending an hour each day practicing the entire stroke and trying to hit the ball in the court. This would be consistent, or fixed priority (FP) training. Another approach would be to divide the

hour into 15-minute segments with an emphasis on a different aspect of the swing for each segment (e.g., the backswing, point of contact, footwork, and follow-through), all while still completing the entire stroke. This training strategy utilizes variability in emphasis on subcomponents of the task, and is an example of variable priority (VP) training. In the context of learning a complex cognitive task, it is thought that VP training facilitates the formation of efficient, automatic higher-level schemas from what were initially effortful strategies of controlled, voluntary attention and action (Gopher et al., 1989).

Despite the proven advantages of VP training, little research has examined why, neurobiologically, it is more effective. Some research suggests that FP and VP training may depend on different brain networks for the consolidation of learning (Kantak et al., 2010): in motor learning, consolidation following FP practice depended on the primary motor cortex, whereas consolidation after VP practice depended on the dorsolateral prefrontal cortex. Also, consolidation following motor training that required continuous updating of the parameters for manually tracking a moving object, a form of VP training, was associated with increased synchrony among brain regions in a fronto-parietal brain network (Albert et al., 2009). Together these studies suggest that FP and VP learning strategies encourage the use of different brain networks during skill acquisition, consolidation and retention: consistent, FP practice affects neural networks that acquire and implement stimulus-response representations, whereas VP practice affects neural networks representing higher-order relationships between goals and actions (Kantak et al., 2010).

Intriguingly, these distinct neural networks roughly map onto the procedural and declarative learning and memory systems (Robertson, 2009; Squire, 1992). The procedural learning system relies on the primary motor cortex and the striatum, including the caudate nucleus and putamen, whereas the declarative learning system relies on brain structures in the medial temporal lobe (MTL) such as the hippocampus (Poldrack et al., 2001; Squire, 1992). Consistent with the idea that the differences between FP and VP training might result from separate underlying learning and memory systems, medial temporal brain regions involved with declarative memory are associated with more flexibility and greater transfer of learning to novel contexts compared to learning mediated by the procedural memory system (Myers et al., 2003; Reber et al., 1996). In addition, successful encoding by the declarative memory system is linked to greater attention and working memory capacity (Craik et al., 1996; Foerde et al., 2006), which has been associated with a fronto-parietal brain system (Olesen et al., 2004). Thus the procedural and declarative systems do not act in isolation to facilitate skill acquisition and are likely biased differentially through their interaction with higher-order networks, such as the fronto-parietal network.

Here, we sought to characterize training-induced changes in functional connectivity in three well-established brain systems involved in higher-order cognition, including the fronto-executive (also referred to as the cingulo-opercular network) and fronto-parietal systems (Dosenbach et al., 2007), and the default mode network (DMN) (Buckner et al., 2008). These brain systems were targeted among other identified systems in the literature based on their known involvement in attention and executive function compared to systems involved in lower-level sensory and representational processes (e.g., Smith et al., 2009). The fronto-parietal system is involved in skill learning (Albert et al., 2009), and functionally, there is reason to believe the other two networks would also be important. Anatomically, the fronto-executive network includes the anterior prefrontal cortex, insular and frontal operculum cortices, the temporo-parietal junction, and the dorsal posterior and anterior cingulate gyri. This network also overlaps somewhat with the ventral attention network described in Corbetta et al.'s (2008) theory of attention. Functionally, within the context of cognitive control, the fronto-executive network is involved in sustained task-set mainte-

nance, error feedback for tuning top-down control, and maintaining associations between actions and their outcomes (Dosenbach et al., 2006, 2007; Rushworth et al., 2004). Thus, we expect this network to be involved in maintaining game rules and stimulus-response mappings over prolonged time periods. Because of the emphasis on sustained maintenance of rules and of stimulus-response mappings, this network may be preferentially important for learning with FP training.

The fronto-parietal network includes the inferior parietal cortices, the supplementary motor cortex, the frontal eye-fields, primary and extrastriate visual cortices, the inferior frontal cortex, and some overlapping portions of the temporo-parietal junction with the fronto-executive network, and has been implicated in top-down distribution of attention, instantiation of task-set and response-set mappings (e.g., to a cue that signals "task switch"), and working memory (Corbetta and Shulman, 2002; Dosenbach et al., 2006, 2007; Olesen et al., 2004). Note this network overlaps significantly with the dorsal attention network described in Corbetta et al.'s (2008) theory of attention. We expect this network to be involved in the spatial distribution of attention, in keeping relevant game events in working memory, and in facilitating the encoding of game information into the declarative system. Therefore, we expect the fronto-parietal system to be important for learning with VP training. Additionally, its involvement in instantiation of stimulus-response mappings may also make it important for learning during FP training.

The DMN includes the posterior cingulate, ventral and superior frontal medial cortices, and bilateral lateral occipital, middle frontal, hippocampal and parahippocampal, and middle temporal cortices (Buckner et al., 2008; Fox et al., 2005). Hypothesized functional roles of the DMN include memory consolidation, self-referential thought, mind-wandering, and autobiographical memory (Buckner et al., 2008; Schilbach et al., 2008), but the functional integrity of the DMN has also been implicated in executive control processes (Andrews-Hanna et al., 2007; Hampson et al., 2006; Voss et al., 2010). Therefore, the DMN may be involved in the general capacity to regulate competition between endogenous and exogenously directed attention, and in the successful completion of higher-level executive function tasks. We don't expect the DMN to be preferentially important for learning with either training strategy.

In sum, we used functional connectivity analyses of fMRI data to examine the following three research questions: 1) How does functional brain organization change after extended training on a complex cognitive task? 2) Do FP and VP training result in quantitative and/or qualitative differences in functional brain re-organization? 3) Is functional brain re-organization related to performance gains? When mastering a complex skill, learning should be associated with increased within-network connectivity of the fronto-executive, fronto-parietal, and DMN systems, regardless of training strategy. If training effectively alters how the brain functions under all states of cognition, training-induced plasticity should extend to cognitive tasks outside of the trained skill (i.e., domain-general enhanced connectivity). The pattern of change in these networks may also interact with the procedural and declarative memory systems. Given that consolidation following FP training depends on neural networks that acquire and implement stimulus-response representations, we hypothesized that FP training would be associated with increased interactions between the fronto-parietal and procedural learning systems. Since FP training is likely to lead to a more rigid, sustained rule set, we also hypothesize that FP training would encourage interaction between the fronto-executive and declarative systems. In contrast, given the role of the fronto-parietal network in consolidation following VP training, and the involvement of the declarative system in supporting the type of flexible skill knowledge that VP training produces, we hypothesize that VP training may be associated with increased interactions between the fronto-parietal and declarative learning systems. Finally, we expected that changes in

functional connectivity would be associated with improvement in the trained task.

Materials and methods

Participants

Participants were recruited from the Urbana–Champaign community through campus fliers, email advertisements, and postings on a lab website. Given that the trained task, Space Fortress (SF), is a complex videogame, interested participants completed a survey of their videogame habits, and if they reported playing videogames less than 3 h/week over the past 2 years, they visited the lab for further screening. All participants had normal or corrected-to-normal visual acuity, normal color vision, normal hearing, were right-handed, and reported being on no medications that could affect their cognitive function. Participants also passed an aiming task to ensure that they could use a joystick. Finally, participants met criteria for participating in an MRI study, including no previous head trauma, no previous head or neck surgery, no diagnosis of diabetes, no neuropsychiatric or neurological conditions including brain tumors, and no metallic implants (including braces) that could interfere with or cause injury due to the magnetic field. Eligible participants signed an informed consent approved by the University of Illinois Institutional Review Board before participating. Forty-two participants initially qualified for the study, and 39 completed the training; 29 of those participants were included in the imaging analysis (see Table 1). Exclusion from the imaging analysis occurred due to excessive motion or incomplete data at either pre- or post-training. Participants were paid $15/h for testing and training.

Videogame training with Space Fortress

Our training task was Space Fortress, a videogame originally developed by cognitive psychologists as a tool to study how different training strategies affect learning (Donchin et al., 1989). It requires complex motor control, working memory, and monitoring. For example, players must control the movement of their ship in a frictionless environment, continually monitor the number of times they have successfully shot the enemy fortress, keep track of whether mines firing at their ship are "friends" or "foes," and monitor a stream of symbols that determine their ability to gain bonus points or resources. Maximizing the overall score requires mastery of each sub-component. While motor control is thought to be the most important skill to learn first, it must be acquired while also performing the working memory and monitoring tasks. A detailed description of Space Fortress is provided in the Supplementary materials.

Training procedures

Participants learned the basic rules of Space Fortress via a short instructional video and they then completed a pre-training 2-hour MRI session (described in imaging procedures) in a 3-Tesla Siemens Allegra scanner at the Biomedical Imaging Center at the University of Illinois at Urbana–Champaign. Training consisted of ten 2-hour training sessions (20 h total), with approximately 3–5 sessions per week (see Boot et al., 2010 for a detailed description of the training procedures). Each session consisted of 36 three-minute games using one of two learning strategies: fixed priority (FP) or variable priority (VP). For FP training (n = 14), participants focused on all aspects of the game during learning. For VP training (n = 15), participants shifted their emphasis to distinct game components while playing the game (see Table 1 for group demographics). During each training session, all participants played a total of 3 pre-training and 3 post-training games without an instructed strategy. Scores for these sets of games provided an assessment of learning progress (see Fig. 1). Thus during each training session, participants played 30 "training" games. The FP group tried to maximize their total score on each game. The VP group focused on improving and monitoring different sub-components. Their 30 games were divided into 5 blocks of 6 games each, with a different sub-component of the game emphasized in each block. Importantly, the VP subjects were instructed to emphasize that sub-component, but not to ignore other aspects of the game. On even-numbered sessions, participants emphasized sub-components in the following order: Control (emphasize ship control by keeping the ship within a pre-defined hexagonal area surrounding the fortress), Velocity (emphasize ship control by moving the ship with slow, controlled moves), Speed (emphasize speed and accuracy when dealing with Mines), Points (emphasize shooting and destroying the fortress while protecting the ship from the fortress's shots), and Total (emphasize maximizing total score). On odd-numbered sessions, the order was reversed.

Learning rate was quantified using growth curve analyses of individual performance across training sessions. The best fitting curve for total game scores (y) as a function of time (t, where 1 unit of time is the average score from a 3-game pre-training or post-training set) was expressed by the following function: $y = a + r \times \ln(t)$, where a refers to a participant's intercept or fitted pre-training game score and r refers to the rate or fitted slope of their learning curve. After 20 h of training, participants completed an MRI session identical to their pre-training MRI session. During game play in pre and post MRI sessions all participants were asked to focus on all aspects of the game and maximize their total score.

Imaging procedures

High resolution T1-weighted brain images were acquired using a 3D MPRAGE (Magnetization Prepared Rapid Gradient Echo Imaging) protocol with 144 contiguous axial slices, collected in ascending fashion parallel to the anterior and posterior commissures, echo time (TE) = 3.87 ms, repetition time (TR) = 1800 ms, field of view (FOV) = 256 mm, acquisition matrix 160 mm × 192 mm, slice thickness = 1.3 mm, and flip angle = 8°.

For the fMRI tasks, T2* weighted images were acquired using a fast echo-planar imaging (EPI) sequence with Blood Oxygenation Level Dependent (BOLD) contrast (64 × 64 matrix, 3.4375 × 3.4375 × 4 mm

Table 1
Participant demographics for overall sample and by sub-groups.

Group	FP	FP-low	FP-high	VP	VP-low	VP-high	Overall
N	14	6	8	15	8	6	29
Age (SD)	21.64 (2.31)	22.17 (1.17)	21.25 (2.92)	22.80 (3.34)	22.50 (3.96)	23.67 (2.58)	22.24 (2.90)
Years of education (SD)	16.00 (2.14)	16.17 (1.33)	15.88 (2.68)	16.40 (2.71)	15.88 (2.37)	17.50 (3.08)	16.21 (2.41)
% Male	29%	0%	50%	33%	25%	50%	31%
Baseline Space Fortress score (SD)	404.64 (1938.16)	−1452.55$_a$ (840.84)	1797.54$_a$ (1139.10)	−63.15 (1743.38)	−1042.75$_b$ (692.99)	1687.88$_b$ (1094.52)	162.67 (1822.19)

Data rows and columns with like subscripts denote groups that differed significantly in terms of age, education, or baseline SF score (determined by t-test) or gender (determined by Fisher's exact test). FP = fixed priority; FP-low = fixed priority participants with low initial game scores; FP-high = fixed priority participants with high initial game scores; VP = variable priority; VP-low = variable priority participants with low initial game scores; VP-high = variable priority participants with high initial game scores.
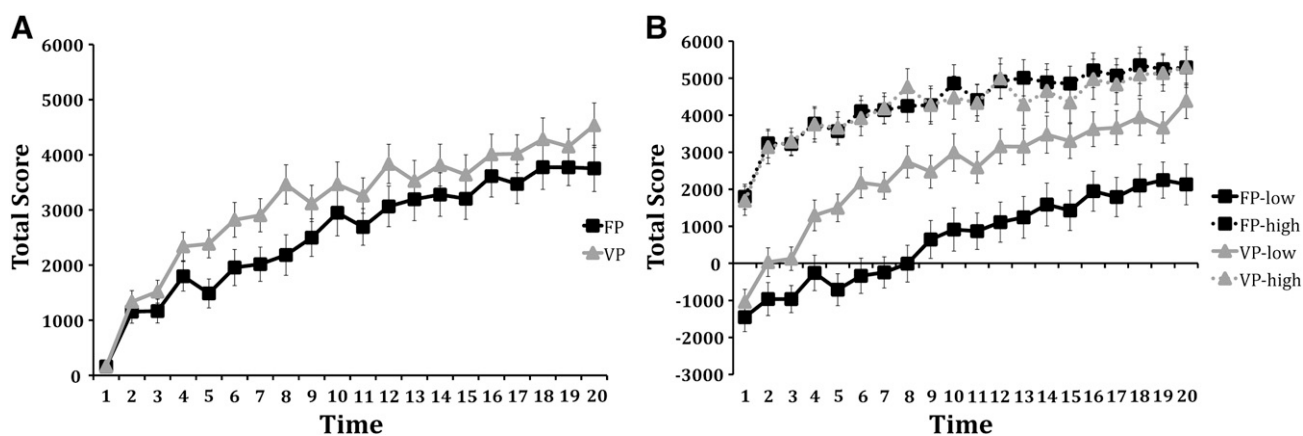
Fig. 1. Behavioral training effects by (A) training strategy group and by (B) training strategy group × starting performance, for participants in the current study. One unit of time (along x-axis) refers to one three-game set at either pre or post a given training session (there were 10 training sessions); FP = fixed priority; FP-low = fixed priority participants with low initial game scores; FP-high = fixed priority participants with high initial game scores; VP = variable priority; VP-low = variable priority participants with low initial game scores; VP-high = variable priority participants with high initial game scores.

voxel size, TR = 2000 ms, TE = 25 ms, and flip angle = 80). A total of 13 functional runs were acquired, consisting of seven 46-second blocks of passively watching (PW) a sample Space Fortress game played by an expert, interleaved with six blocks of active task. The six active task blocks included two runs of an oddball task (OB), which required counting the number of high-pitch tones among low-pitch distracter tones, two runs of playing Space Fortress (SF), and two runs of playing Space Fortress while also performing the oddball task (SF + OB). In the context of the current study, the OB task enabled us to assess the specificity of functional changes, whereas the SF + OB task was designed to increase the difficulty of the SF task by adding a parallel task that would utilize additional resources. However, this manipulation was irrelevant to the specific questions examined here, and comparison of the functional connectivity maps for the SF and SF + OB conditions showed minimal differences; therefore, we collapsed across all blocks containing SF game play to increase statistical power (described in further detail below). Each active run was comprised of 120 BOLD volume acquisitions, and lasted for 4 min. The order of runs for different task conditions was counterbalanced within session, but each subject received the runs in the same order (PW,OB,PW,SF,PW,SF + OB,PW,SF + OB,PW,SF,PW,OB,PW). Due to the shorter length of the PW runs, which may compromise the comparability of functional connectivity estimates for these runs compared to active state runs, PW runs were not included in the current analyses.

fMRI preprocessing

fMRI analyses were carried out using the FSL software package and MATLAB. To examine functional connectivity in select brain systems, or the extent to which distributed networks activated cohesively in space and time, we followed a standard pipeline that is used for functional connectivity analysis (Fox et al., 2005; Voss et al., 2010). This includes typical functional image processing steps such a brain extraction (Smith, 2002), motion correction (Jenkinson et al., 2002), spatial smoothing (6 mm FWHM), as well as an additional temporal filtering step to ensure the fMRI signal is within a frequency band of .008 < f < .08 Hz, which is optimal for functional connectivity analyses (Cordes et al., 2001). Following preprocessing, the fMRI signal was further corrected for potential sources of noise, including signal variance from white matter, cerebral spinal fluid, and motion-induced signal fluctuations, and signal from a global brain mask to remove the mean brain signal. Signal correction was done by regressing the mean time series from each of the nuisance brain regions and motion correction parameters (six directions) as independent variables

predicting the observed fMRI signal as the dependent variable. The residual volume from this analysis was saved and used for all functional connectivity analyses.

Functional connectivity seeding analysis

First we conducted a whole-brain analysis of three cognitively relevant brain systems (fronto-executive, fronto-parietal, and DMN). These brain networks were derived based on three seeds from the literature that are known to be primary hubs for each of the respective networks (fronto-executive: right anterior lateral prefrontal (RALPFC) seed MNI 32, 40, 28 (Krienen and Buckner, 2009); fronto-parietal: right inferior parietal (RIP) seed MNI 26, −62, 52 (Fox et al., 2005); DMN: posterior cingulate cortex (PCC) seed MNI 8, −56, 30 (Voss et al., 2010)). These particular seed coordinates were chosen relative to others because they were found to yield the most replicable statistical maps of the intended network across participants, and were found to overlap most consistently with statistical peaks in comparable network maps derived from a multivariate analysis with tensor PICA in FSL (Beckmann et al., 2005) in an independent data set of young adults (Voss et al., 2010). Functional connectivity analysis consisted of extracting the corrected time-series (i.e., from the residual volume described above) from seeds with spherical regions of interest (ROIs) around their coordinate locations; ROIs were comprised of approximately 9 functional voxels. Next, to derive a statistical map of a given functional network, we computed the cross-correlation of the seed time series with every other voxel in the brain (see Fig. 2). Specifically, voxel-wise Pearson correlation coefficients between the corrected time series of the seed region and the time series of each voxel in the residual image were computed in MATLAB. These statistical maps were converted to Fisher's z maps using Fisher's r-to-z transformation (Zar, 1996) to improve normality. This procedure was done separately for each fMRI run. Individual-level analyses of voxel-wise functional connectivity were then aggregated within subjects for greater statistical power, using ordinary least squares (OLS) in FSL's FEAT tool. Runs were aggregated at this fixed-effects level into two conditions of interest: OB, and SF (where SF and SF + OB runs were aggregated together). Finally, individual-level fixed-effects statistical maps were forwarded to a mixed-effects OLS group analysis that considered between-subjects variations (Beckmann et al., 2003).

In the mixed-effects between-subjects analysis, we examined participants' change in functional connectivity in each network as a function of time and group. For all analyses, the statistical threshold for group statistical maps was set to voxel and cluster correction of
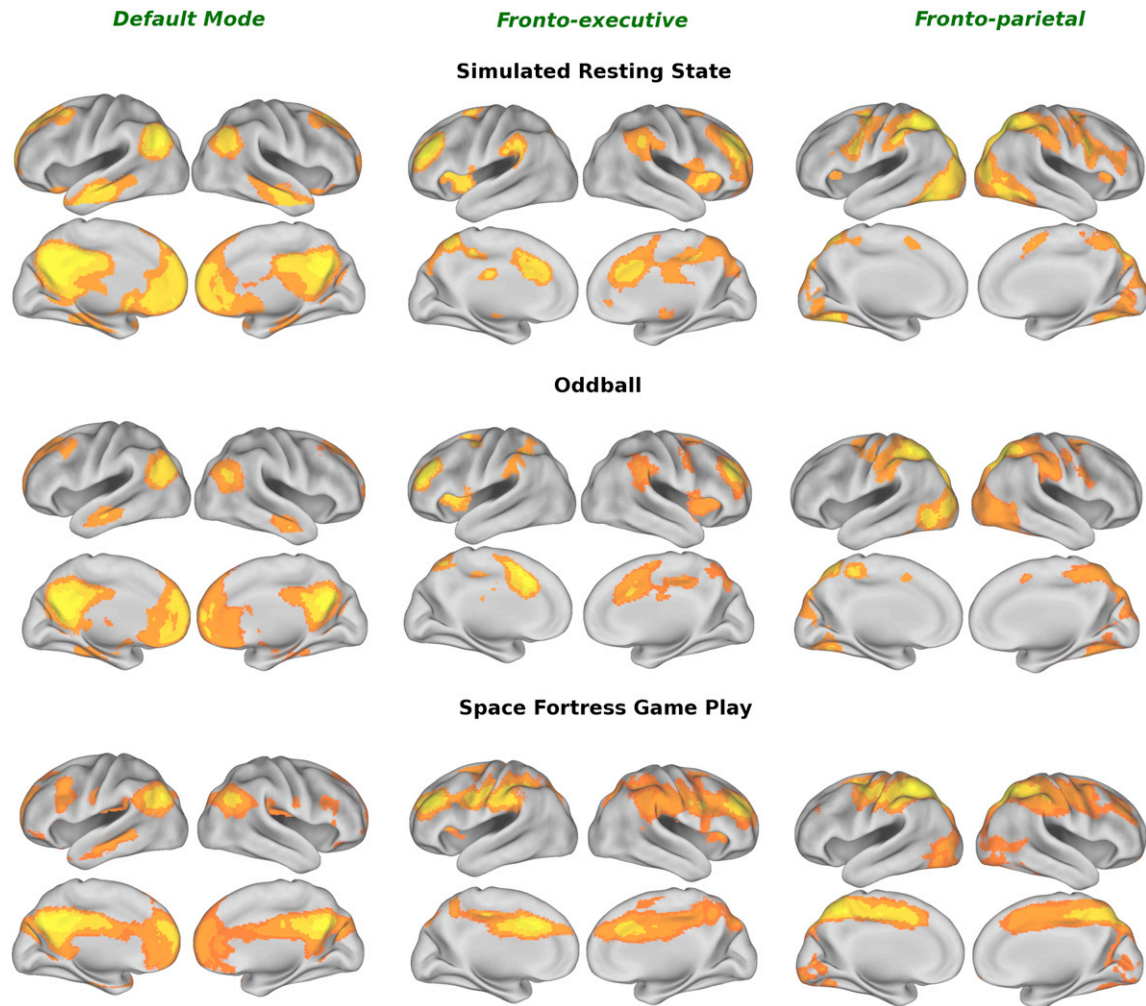
Fig. 2. Large-scale functional networks were recovered during 4-minute fMRI runs of real-time game play. In the above figure 'Simulated Resting State' visualizes the three networks in 32 young adults in a separate study during task-independent rest (Voss et al., 2010). Overlap between the FE and the FP systems during game-play is expected, as they are theorized to act in parallel during cognition. However, this does not mean we could not distinguish group differences in the two systems as a function of learning, as will be evident in the results that follow. Statistical maps are shown such that R = R and L = L, surface visualization is on the PALS-B12 atlas using CARET (http://brainvis.wustl.edu); each represent voxel-wise z-statistics transformed from fisher's z correlation estimates, statistical maps shown with voxel and cluster correction threshold of $p<.05$.

$p<.05$. First, we determined which voxels exhibited greater functional connectivity post-training relative to pre-training (Post>Pre) for each network across all subjects. Second, we examined whether the differences for the Post>Pre contrast differed by training group (group×time interaction). Third, we extracted the functional connectivity estimates for each person in functional-anatomic ROIs and correlated them with individual learning rates (brain−behavior relationship).

Results

Behavioral learning during videogame training

The subjects in this longitudinal imaging study are a subset of those from a larger behavioral study (Boot et al., 2010). Consequently, we will first describe the behavioral results for this subset. Unlike the behavioral results for the full study (Boot et al., 2010), we found no significant difference in training effectiveness for VP and FP training.

For all repeated measures ANOVAs, average Total Score from each 3-game set at the start and end of each session was the within-participant factor, training strategy was the between-groups factor, and baseline game performance was entered as a covariate. Note that in cases where the sphericity assumption violated based on Mauchly's test ($p<.05$), adjusted degrees of freedom are reported based on the

Huynh–Feldt adjustment. As illustrated in Fig. 1A, both groups significantly improved in their performance ($F(4.64, 120.77)=82.59$, $p<.001$, $pr\ \eta^2=.76$), but their improvement was comparable across conditions throughout training ($F(4.65,120.77)=1.45$, $p=.22$, $pr\ \eta^2=.05$) and overall (no main effect of strategy, $F(1,26)=1.94$, $p=.18$, $pr\ \eta^2=.07$). The lack of a significant interaction for our subset of the subjects may have resulted from limited statistical power. Although not significant, the trends were in the same direction as in the larger behavioral analysis.

VP training typically produces the greatest benefits for those with poor initial performance (Gopher et al., 1989), a pattern we replicated: VP training was particularly effective for those with low initial Space Fortress scores. For this analysis, we divided participants in each training group into two groups based on a median split of their total score at baseline. We then performed a repeated measures ANOVA, with average Total Score from each 3-game set at the beginning and end of each training session as the within-participant factor and training strategy and initial performance as between-groups factors. As illustrated in Fig. 1B, training improved videogame performance for all participants, $F(5.3,134.1)=84.70$, $p<.001$, $pr\ \eta^2=.79$. Furthermore, while the VP group improved more than FP overall, reflected here by a main effect of strategy in favor of VP, ($F(1,23)=4.36$, $p<.05$, $pr\ \eta^2=.16$), improvement was significantly greater for initially low performing VP participants, whereas training

Table 2
Statistical map peak summary for each training effect in each group and the group×time interactions during game play.

2a) FP Post>Pre

Cluster anatomical description	ROI abbreviation	MNI coordinates (x, y, z)	Z score	Voxels
Default mode				
None				
Fronto-executive				
R. inferior temporal gyrus	RITG	62, −52, −20	3.99	626
R. hippocampus/parahippocampus	RHPC	22, −8, −26	3.40	302
L. hippocampus/parahippocampus	LHPC	−22,4, −26	3.26	167
L. thalamus	LTHAL	−22, −24,2	2.74	128
L. insular cortex	LIC	−38,0, −6	2.68	27
R. lingual gyrus	LLG	22, −62, 2	2.33	29
Fronto-parietal				
R. inferior frontal gyrus extending into R. caudate, putamen, frontal and central operculum, and precentral gyrus	RMOT	30, 28, 12	3.88	2470
L. caudate extending into L. putamen, inferior frontal gyrus, frontal and central operculum, and precentral gyrus	LMOT	−20, 18, 8	3.22	1572
L. thalamus	LTHAL	−20, −20, 16	3.09	696
L. anterior cingulate gyrus	LACG	−6, 6, 30	2.48	243

2b) FP (Post>Pre)>VP (Post>Pre), group×time interaction

Cluster anatomical description	ROI abbreviation	MNI coordinates (x, y, z)	Z score	Voxels
Default mode				
None				
Fronto-executive				
R. hippocampus extending into:	RHC	22, −6, −26	3.98	8116
R. parahippocampus	RPHC	14, −8, −24	3.94	
R. middle temporal gyrus	RMTG	74, −40, −8	3.71	
L. hippocampus/parahippocampus	LHPC	−18, −24, −18	3.52	
L. inferior temporal gyrus	LITG	−44, −16, −22	3.50	
L. hippocampus	LHC	−30, −10, −22	3.26	
L. middle temporal gyrus	LMTG	−58, −20, −20	2.87	
Fronto-parietal				
L. thalamus extending into:	LTHAL	−20, −20,18	4.29	12216
R. caudate	RCAUD	16, −12,20	4.26	
L. central opercular cortex	RCOP	−56, −16,10	3.91	
L. inferior frontal gyrus and frontal pole	LIFG	−54,40,6	3.89	
R. anterior cingulate cortex	RACG	6,8,32	3.68	
R. precentral gyrus	RPCG	50,6,26	2.72	
L. precentral gyrus	LPCG	−48, −2,30	2.68	

2c) VP Post>Pre

Cluster anatomical description	ROI abbreviation	MNI coordinates (x, y, z)	Z score	Voxels
Default mode				
None				
Fronto-executive				
None				
Fronto-parietal				
R. superior temporal gyrus	RSTG	56, −10, −8	4.31	47
R. putamen extending into R. insular cortex and R. pallidum	RPUT	32, −4, −6	3.50	545
L. posterior cingulate gyrus extending into R. cingulate gyrus	LPCG	−14, −48, 4	3.46	219
L. lateral precuneus cortex extending into L. intracalcarine cortex and L. lingual gyrus	LPREC	−24, −60, 12	3.17	450
R. temporal fusiform cortex extending into R. inferior temporal cortex	RTFG	42, −14, −24	2.78	58
R. middle temporal gyrus	LMTG	44, −24, −8	2.74	71
R. middle temporal gyrus/temporal pole	RMTG	58,6, −26	2.71	33

2d) VP (Post>Pre)>FP (Post>Pre), group×time interaction

Cluster anatomical description	ROI abbreviation	MNI coordinates (x, y, z)	Z score	Voxels
Default mode				
None				
Fronto-executive				
None				
Fronto-parietal				
R. superior temporal gyrus extending into:	RSTG	56, −10, −8	4.53	9736
L. middle temporal gyrus	LMTG	−40, −38, −2	4.50	
R. insular cortex	RIC	38, 6, −10	3.86	
L. frontal medial cortex	LFMC	−4, 16, −16	3.50	
R. hippocampus	RHC	30, −26, −14	3.39	
L. hippocampus	LHC	−22, −12, −16	3.34	
L. hippocampus	LHC	−30, −22, −18	2.85	

strategy did not matter for those individuals with initially high game proficiency ($F(1,23) = 4.96$, $p < .05$, pr $\eta^2 = .18$). Despite the VP advantage for initially low performers, the difference in learning rate (slope) was not significant across the entire training period ($F(5.8,134.10) = 1.72$, $p = .15$, pr $\eta^2 = .07$). Rather, the difference in slopes was most pronounced, and statistically different, only in the first half of training ($F(4.8, 109.8) = 2.86$, $p < .05$, pr $\eta^2 = .11$).

Functional brain organization following videogame training

As shown in Fig. 2, we extracted known functional brain networks from continuous runs of real-time videogame play. This novel methodology provides a new tool for imaging complex cognitive task performance, while also allowing for the exploration of individual differences in the connectivity of such networks.

Among all possible tests, only one network – the DMN – showed a trend for change from pre-training to post-training functional connectivity that did not depend on training strategy (i.e., across all participants). Specifically, there was greater connectivity between the PCC seed and a region in the left hippocampus (peak $Z = 2.96$, MNI: -18, -32, -12). The cluster extended approximately 30 anatomical voxels, but did not pass cluster correction at $p < .05$. Therefore this result should be interpreted conservatively. These functional connectivity changes were specific to game play; there were no significant post-pre differences across subjects in the oddball task.

Effects of training strategy on functional brain organization

We first present results for whole-brain analyses of training-induced changes in functional connectivity for each group separately, followed by results for whole-brain analyses of group × time interactions. For all main effects and interaction results, refer to Table 2 (a–d) for MNI coordinates, local maxima, and cluster extent.

Table 2a and c list brain regions that showed training-related increases in functional connectivity for the FP and VP groups, respectively. Neither group showed main effects in the DMN, whereas

a distinct spatial pattern emerged for the fronto-executive and fronto-parietal systems. Specifically, the FP group showed increased functional connectivity between the fronto-executive system and regions including several temporal lobe regions (right inferior temporal gyrus, and left and right hippocampus/parahippocampal cortex), the left thalamus and insular cortex, and right lingual gyrus. In contrast, the VP group did not show training-induced changes in functional connectivity in the fronto-executive network. In the fronto-parietal system, the FP group showed increased functional connectivity with regions associated with motor control (left and right caudate nucleus, putamen, inferior frontal gyri, frontal and central operculum, and precentral gyri) and conflict regulation (anterior cingulate cortex). In contrast, the VP group showed increased connectivity of the fronto-parietal system with several regions in the temporal cortex (right superior temporal gyrus, temporal fusiform cortex, and left and right middle temporal gyri), as well as with the right putamen and posterior cingulate cortex. Finally, neither the FP or VP group showed changes in functional connectivity in the DMN, fronto-executive, or fronto-parietal systems during the oddball task.

In order to further highlight changes in functional connectivity associated with training strategy, we next examined group differences in a Post > Pre contrast (group × time interaction) for a) all game blocks collapsed (2 blocks of SF and 2 blocks of SF + OB) and b) the oddball blocks. Figs. 3 and 4 illustrate the results during game play for the fronto-executive and the fronto-parietal networks, respectively, and show how training strategy affected functional networks during game play. The FP group showed increased connectivity between the executive system and the bilateral medial and lateral temporal lobe, whereas the VP group showed no differential changes in connectivity with the executive system (see Table 2b and d, Fig. 3). In the fronto-parietal system, however, the FP group showed increased connectivity with areas of motor control such as the primary left and right motor cortices and the basal ganglia, as well as the left opercular cortex and inferior frontal gyrus, and right anterior cingulate, whereas the VP group showed increased connectivity with bilateral medial and lateral temporal lobe, as well as the medial prefrontal cortex (see Table 2b and d, Fig. 4). Given that the hippocampus is a critical locus for the
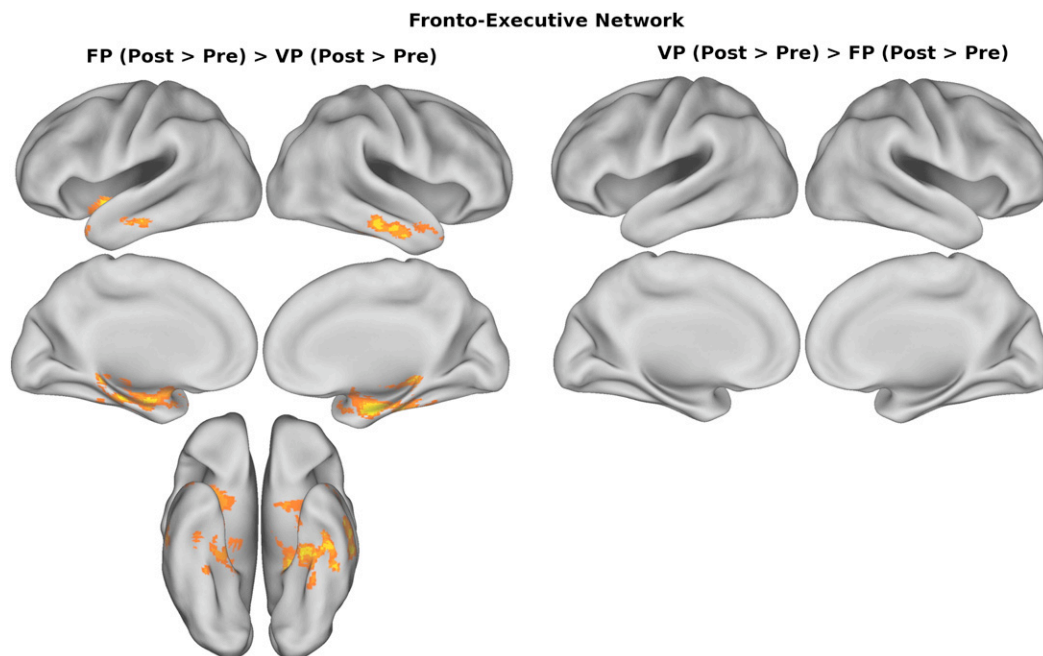
Fig. 3. Training-related changes in functional connectivity in the fronto-executive system. Statistical maps are shown such that R = R and L = L, surface visualization is on the PALS-B12 atlas using CARET (http://brainvis.wustl.edu); each represent voxel-wise z-statistics transformed from fisher's z correlation estimates, statistical maps shown with voxel and cluster correction threshold of $p < .05$; z-maximum in each statistical map matches the corresponding statistical peak shown in Tables 2b and d.

Fronto-parietal Network

FP (Post > Pre) > VP (Post > Pre)   VP (Post > Pre) > FP (Post > Pre)
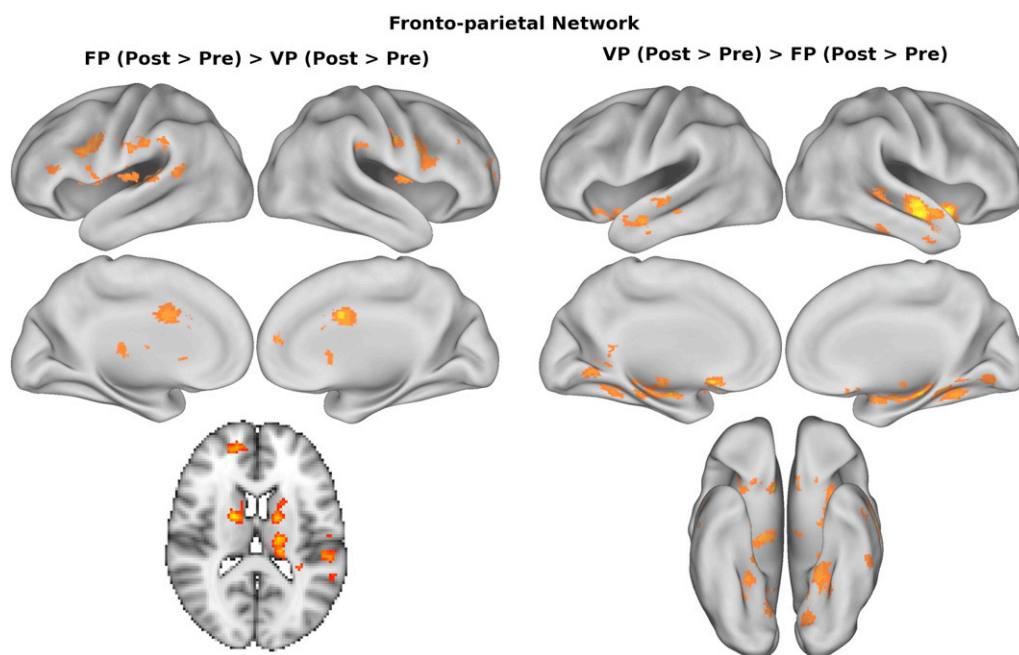
Fig. 4. Training-related changes in functional connectivity in the fronto-parietal system. Statistical maps are shown such that R = R and L = L, surface visualization is on the PALS-B12 atlas using CARET (http://brainvis.wustl.edu); each represent voxel-wise *z*-statistics transformed from fisher's *z* correlation estimates, statistical maps shown with voxel and cluster correction threshold of *p* < .05; *z*-maximum in each statistical map matches the corresponding statistical peak shown in Table 2b and d. Statistical map rendered on axial plane is overlayed onto the MNI152 FSL template at plane Z = 14.

declarative memory system, while the primary motor system and the basal ganglia are integral to procedural memory (Squire, 1992), FP and VP training strategies apparently facilitate the use of distinct systems for learning and memory during skill acquisition.

Finally, similar to the main effects for training groups described above, there were no statistically significant group × time interactions in the DMN, fronto-executive or fronto-parietal systems during the oddball task. This suggests game-specific functional plasticity, reflecting the functional systems being used during skill learning and implementation.

Functional plasticity and learning

VP and FP training of Space Fortress appear to strengthen the role of the declarative and procedural brain systems, respectively. To highlight this phenomenon we focused on the changes in functional connectivity during training between the key structures linked to these two systems (the MTL and basal ganglia, respectively, based on an ROI approach) and the fronto-parietal and fronto-executive networks. Further, to determine whether these connectivity changes are relevant to behavior, we examined their relationship with learning rate by (a) comparing the average connectivity changes in high and low learners (based on initial performance), and (b) correlating individual connectivity changes with learning rate, while controlling for individual differences in baseline performance. Results of both analyses are shown in Fig. 5.

Panels 5A and 5B present difference scores in MTL and basal ganglia connectivity, with the fronto-parietal and fronto-executive systems, respectively. Panel 5A illustrates the group × time interaction from the whole-brain analyses presented above. However an important result illustrated in the bar graph is the coupling of increases in connectivity for one training strategy with decreases in connectivity (increasingly negative correlation) for the other training strategy, supporting the hypothesis that they are based on competing memory systems. This pattern was reflected in significant interactions obtained in mixed-design ANOVAs, with brain network as the within-subjects factor and training strategy as the between-subjects factor:

for the MTL $F(1,27) = 26.52$, $p < .001$, $pr\ \eta^2 = .50$ and for the caudate nucleus, $F(1,27) = 4.32$, $p < .05$, $pr\ \eta^2 = .14$. Panel 5B further shows that this pattern was particularly evident in subjects with the lowest initial scores (i.e., those with the most to learn). Therefore we can hypothesize that the greatest functional plasticity would be present in those individuals experiencing the most behavioral learning. A trend towards this group pattern was shown by a marginally significant interaction based on a mixed-design ANOVA, with brain network as the within-subjects factor and training strategy and initial performance as between-groups factors, for connectivity with the MTL $F(1,24) = 3.20$, $p = .08$, $pr\ \eta^2 = .12$ but this time not with the caudate nucleus, $F(1,24) = .83$, *ns*, $pr\ \eta^2 = .03$.

To further test whether these connectivity changes are relevant to behavior, we examined whether individual connectivity changes associated with learning rate, while controlling for individual differences in baseline performance. A multiple linear regression predicting learning rate (after controlling for baseline performance) from group and the interaction between group and change in network connectivity showed that the fronto-parietal-MTL connection was most adaptive for skill learning, but only for the VP group. This was reflected by a statistically significant interaction between group and change in fronto-parietal–MTL connectivity ($\beta = .43$, $p < .05$), and a non-significant interaction between group and change in fronto-executive–MTL connectivity ($\beta = -.20$, *ns*). As illustrated in Fig. 5C, the fronto-parietal–MTL interaction resulted from a positive association between changes in connectivity and learning rate for the VP, but not FP, group. In a separate model, there were no statistically significant interactions between group and change in network-caudate nucleus connectivity (fronto-parietal: $\beta = -.20$, *ns*; fronto-executive: $\beta = -.13$, *ns*).

To ensure that these patterns represented communication between networks of regions and not particular network seed ROIs, we repeated these analyses using a mask of the entire network for the fronto-parietal and fronto-executive systems as seeds (masks illustrated in Supplementary materials). With this analysis, there was still a significant group × time (network change) interaction for the MTL, $F(1,27) = 9.70$, $p < .05$, $pr\ \eta^2 = .26$, however the interaction for
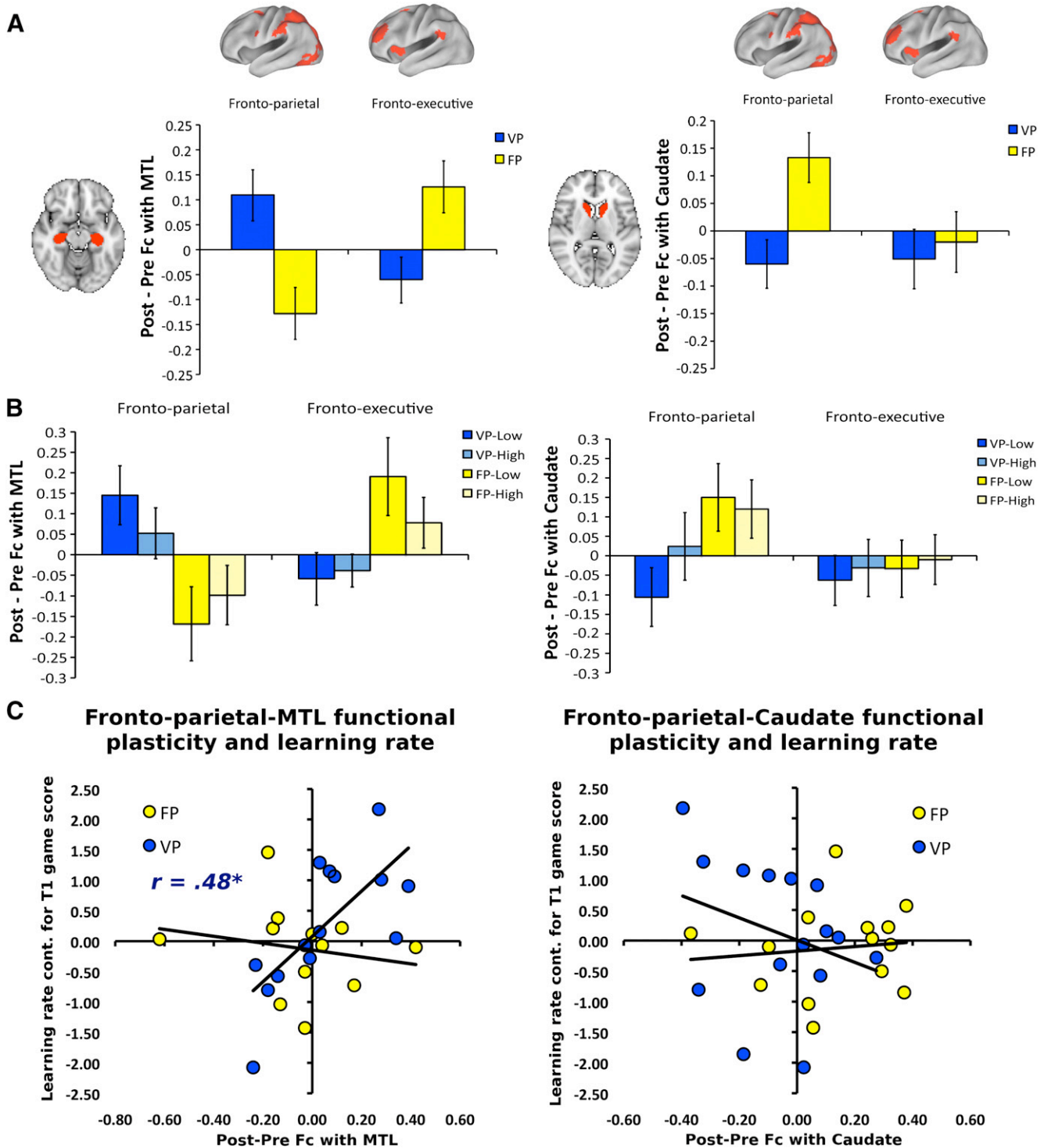
Fig. 5. Changes in functional connectivity are behaviorally relevant. A) Pattern of group×time interactions for functional connectivity between the fronto-parietal and fronto-executive networks and the MTL and Caudate ROIs; B) Pattern of group×time interactions for sub-groups of low and high initial scorers; C) Only the pattern of change for the VP group between the FP and MTL systems is correlated with learning rate; displayed correlation is the partial correlation between learning rate (controlled for baseline) and change in functional connectivity with the MTL for the VP training group.

the caudate nucleus became marginally significant, $F(1,27)=3.46$, $p=.07$, $pr\,\eta^2=.11$. When groups were sub-divided into low and high initial performers, the group×time×initial performance interaction based on connectivity with the MTL again remained marginal, $F(1,24)=3.16$, $p=.08$, $pr\,\eta^2=.12$, and the interaction based on connectivity with the caudate nucleus remained non-significant, $F(1,24)=.43$, ns, $pr\,\eta^2=.02$. In addition, the interaction between change in fronto-parietal–MTL connectivity and learning rate, in favor

of the VP group, became even stronger when the fronto-parietal mask was used as the seed ($\beta=.54$, $p<.01$), whereas the interaction between fronto-parietal–caudate nucleus connectivity and learning rate remained non-significant ($\beta=-.29$, ns). Lastly, the interaction between change in connectivity between the fronto-parietal system and caudate nucleus became statistically significant ($\beta=-.49$, $p<.05$), whereas the interaction for the fronto-executive system remained non-significant ($\beta=.03$, ns).

Two tables in the supplementary information list the means and standard deviations of functional connectivity between the fronto-parietal and fronto-executive systems and the MTL and the caudate nucleus. Table S1 lists pre-training, post-training, and percentage change from pre to post for both training groups, and Table S2 lists the same information for training groups subdivided by initial performance. Note from these tables that the correlations between the networks and the MTL and caudate nucleus are negative at both pre and post-test. This is likely a side-effect of global signal regression during preprocessing, which has been shown to improve the functional–anatomic mapping of functional connectivity estimates (Fox et al., 2009), but also forces the distribution of individual-level correlations to be centered around zero (Murphy et al., 2009). Therefore, at this time the pattern of correlations is most consistent with the idea that these networks and sub-systems are not strongly, or consistently functionally connected over extended periods of time. Thus a decreasing negative correlation as a function of training can still reflect a meaningful increase in functional connectivity (e.g., greater number of transient interactions), or communication patterns between networks and sub-systems, as also suggested by the pattern of brain–behavior associations.

Discussion

Consistent with earlier work (Gopher et al., 1989), learning Space Fortress with VP training enhanced skill acquisition, particularly for people with initially poor performance. For the first time, we showed that the VP training advantage is linked to the interaction of the declarative learning system with a fronto-parietal network implicated in attentional control and working memory. In contrast, FP training is linked to the interaction of the procedural learning system with the fronto-parietal network and enhanced interaction between the fronto-executive and declarative systems. Additionally, for the VP group, increased connectivity between the fronto-parietal and declarative systems was associated with enhanced learning—those who had the most to learn also showed the most functional plasticity.

The pattern of opposing systems involved in learning is consistent with the idea that attributes of a training strategy can bias the relative engagement of learning and memory systems during skill acquisition (Foerde et al., 2006; Poldrack et al., 2001). For instance, the declarative memory system is facilitated when focused attention allows the fronto-parietal system to encode new information into memory (Craik et al., 1996; Foerde et al., 2006). In VP training, participants emphasize learning each skill separately across different blocks, but do so in the context of the whole task. This combination of emphasis and integration facilitates the formation of higher-order relationships between task components in relation to the overall task. For example, during VP training participants learn more about the emphasized components of the task and about the relative benefits and costs to performance when emphasis on particular subcomponents is increased or decreased. This more flexible form of learning is also consistent with transfer of training benefits of VP-based training to other laboratory (Kramer et al., 1995, 1999) and real-world (Gopher et al., 1994) tasks. In contrast, FP training requires rapid acquisition of motor sequences involving all game components at once, thereby putting unrealistic demands on working memory capacity and in turn increasing distraction and encouraging procedural learning. Indeed, the procedural system is facilitated when participants are distracted with continuous monitoring of a secondary task (Foerde et al., 2006).

Also consistent with our predictions, the fronto-executive system was preferentially involved in FP training. Specifically, the FP group showed increased connectivity between the fronto-executive system and the declarative system, whereas the VP group did not show any areas of increased functional connectivity with the fronto-executive system. We believe this corresponds to the cognitive functions supported by each brain network. The increased association between the executive and declarative system for the FP group may reflect learning of specific stimulus-response mappings and motor sequences during training, and maintenance of these motor programs in a sustained "task set" for Space Fortress game play. This result is complemented by the FP group's increased interaction between the fronto-parietal and procedural systems, which may reflect their learned ability to continually respond to the stimuli they are attending to with specific, pre-programmed action sequences. In this context, the plasticity associated with VP training may represent a more efficient system such that whereas the FP group is coordinating two interacting cognitive control systems, the VP group seems to have consolidated the task set into higher-order schemas (Gopher et al., 1989; Yechiam et al., 2001) that only need to interact flexibly with the fronto-parietal attention system.

Some questions may be raised, however, when considering our results in regard to a previous study that found baseline dorsal striatal volume, but not hippocampal volume, was associated with increased skill acquisition in the VP group but not the FP group (Erickson et al., 2010). The two studies examine different aspects of how individual differences account for learning in the context of VP training: one implies that the initial functional capacity of the dorsal striatum is important for predicting learning (Erickson et al., 2010), whereas we find that the dorsal striatum is not involved in the plasticity of functional interactions that occur from learning. One way to investigate this discrepancy is to test whether the procedural system is associated with learning only during a particular phase of learning for the VP group. To explore this possibility, we examined the association between functional plasticity and skill learning in four phases of training; detailed results from these analyses are presented in the Supplementary materials. Consistent with the literature, results for the VP group suggest that the declarative system facilitates learning most in the early phases of skill acquisition (Poldrack and Packard, 2003), yet the procedural system was not associated with learning in any phase. Perhaps greater striatal volume reflects an increased capacity to efficiently manage multiple response mappings within the domain of the procedural memory system (Cools et al., 2006), thereby increasing the capacity for the fronto-parietal and declarative systems to interact free of interference from a parallel, frontally-mediated relationship with the procedural system. Future research is needed to further understand the interplay between individual differences in brain structure and functional plasticity.

Not all of our hypotheses were supported. We predicted that increased connectivity within each of the three cognitively relevant brain systems would occur during both game-play and a cognitive task unrelated to the game. This predicted pattern of results would have reflected a fundamental (domain-general) increase in network integrity as a result of Space Fortress training. That we did not see increased connectivity within-networks during either game play or an unrelated cognitive task suggests that training primarily induced functional plasticity in context-specific interactions between cognitive control networks and learning and memory systems. However, future investigations of this kind should aim to also characterize the multidimensional nature of training-related changes in patterns of brain activation (Bullmore and Sporns, 2009). Such multivariate analyses are advantageous because they can characterize the nature of functional interactions among all voxels in the brain simultaneously (Hayasaka and Laurienti, 2009; Sepulcre et al., 2010) and may produce increased sensitivity to training-induced network plasticity.

Overall, our results demonstrate the usefulness of functional neuroimaging in better understanding how people learn new skills and improve their performance. By combining real-time fMRI monitoring and neurofeedback during training, future research may be able to monitor the effects of training parameters on changes in the interaction of brain systems, perhaps improving the ability to adopt the most effective learning strategies. Ultimately these techniques

may also help characterize how training-induced changes in functional connectivity are related to retention and transfer of learned skills to real-world environments such as driving, sport, or neurorehabilitation. For example, successful transfer of training may require both context-specific functional plasticity as well as functional plasticity of resting networks. In sum, the current study gives us novel insight into the mechanisms underlying the effectiveness of VP training while also demonstrating new possibilities for using functional neuroimaging to examine the brain at work.

Acknowledgments

Appendix A. Supplementary data

Supplementary data to this article can be found online at doi:10.1016/j.neuroimage.2011.03.052.

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