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Task-based functional connectivity of the Useful Field of View (UFOV) fMRI task

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Abstract Declines in processing speed performance occur in aging and are a critical marker of functional independence in older adults. Numerous studies suggest that Useful Field of View (UFOV) training may ameliorate cognitive decline in older adults. Despite its efficacy, little is known about the neural correlates of this task. The current study is the first to investigate the coherence of functional connectivity during UFOV task completion. A total of 336 participants completed the UFOV task while undergoing taskbased functional magnetic resonance imaging (fMRI).

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Ten spherical regions of interest (ROIs), selected a priori, were created based on regions with the greatest peak BOLD activation patterns in the UFOV fMRI task and regions that have been shown to significantly relate to UFOV fMRI task performance. We used a weighted ROI-to-ROI connectivity analysis to model task-specific functional connectivity strength between these a priori selected ROIs. We found that our UFOV fMRI network was functionally connected during task performance and was significantly associated to UFOV fMRI task performance. Withinnetwork connectivity of the UFOV fMRI network showed comparable or better predictive power in accounting for UFOV accuracy compared to 7 resting

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S. Wu Department of Biostatistics, College of Public Health and Health Professions, University of Florida, Gainesville, FL, USA state networks, delineated by Yeo and colleagues. Finally, we demonstrate that the within-network connectivity of UFOV fMRI task accounted for scores on a measure of "near transfer", the Double Decision task, better than the aforementioned resting state networks. Our data elucidate functional connectivity patterns of the UFOV fMRI task. This may assist in future targeted interventions that aim to improve synchronicity within the UFOV fMRI network.

Keywords Useful field of view · UFOV · Functional connectivity · Cognitive aging

Introduction

The exponential growth and prolonged lifespan of the older adult population have resulted in a vital need to address the detrimental effects of age-related cognitive decline. One cognitive domain that exhibits clear decline within the context of non-pathological aging is processing speed [1]. Processing speed is typically defined as the speed in which an individual can perceive a given stimulus (usually amongst distractors), interpret the information, and produce a response [2, 3]. A substantial body of literature has demonstrated that age-related declines in processing speed occur alongside declines across other cognitive domains and related functional abilities. Specifically, age-related declines in processing speed have been associated with poorer working memory, attention and problem solving, greater medical expenditures, poorer timed instrumental activities of daily living (IADL) scores, higher self-reported difficulties completing IADLs, increased driving accident rates, and greater motor vehicular crash risk [4–10].

Computerized training interventions have proven efficacious in slowing cognitive decline in older adults, particularly within the domain of processing speed. Interventions using the Useful Field of View (UFOV) task have long demonstrated robust, reliable, and durable cognitive training gains [11, 12]. Although several iterations of this task exist, the UFOV task requires participants to identify a central target presented for a brief period of time in addition to a peripheral target. Difficulty is moderated through the presentation time of targets and the addition of distractors in the periphery. Interventions employing UFOV-specific training have shown demonstrable improvement in driving outcomes [13, 14], self-reported cognition [15], and health-related quality of life [5, 16], as well as fewer difficulties in completing IADLs [17, 18].

Despite the fact that UFOV-based interventions have reliably shown deceleration of functional and cognitive declines in processing speed, little is known about the underlying neurocognitive mechanisms of task performance. Recent research suggests that differential patterns of blood-oxygen level dependent (BOLD) activation are associated with UFOV task completion and performance. Following a UFOV-based intervention, Ross and colleagues observed decreased BOLD activation patterns in several regions, including the supplementary motor area (SMA) and dorsolateral prefrontal cortex (DLPFC), suggesting greater neural efficiency in these regions [19]. A cross-sectional study performed by Kraft and colleagues found significant activation of the DLPFC, ventrolateral prefrontal cortex (VLPFC) and SMA, inferior temporal gyrus, precentral gyrus, and superior parietal lobules. Furthermore, these regions were significantly activated when accounting for task accuracy, signifying the importance of these regions in UFOV task performance [20].

Accumulating evidence also suggests that restingstate functional connectivity is associated with UFOV task performance. Functional connectivity refers to concurrent temporal correlations of BOLD signal activation across anatomically remote brain regions via distributed networks [21-24]. Decreased resting-state functional connectivity within-network and increased connectivity between-networks (known as decreased network segregation) have been associated with poorer cognitive performance in an older adult population [25–29]. Within the UFOV literature, resting-state functional connectivity in the cingulo-opercular network (CON) and frontoparietal control network (FPCN) was associated with better performance on an adapted version of the UFOV task, the Double Decision task [30]. Hardcastle and colleagues also found that strengthened resting-state FPCN connectivity was associated with better Double Decision performance following a multidomain cognitive training intervention, suggesting that regions within the FPCN may be important for UFOV task performance [31]. These findings correspond with the findings of Ross and colleagues, who also assessed resting-state functional connectivity following a UFOV intervention. Notably, they found significant increases

in resting-state functional connectivity between the anterior insula and anterior cingulate cortex (ACC) and between the dorsolateral prefrontal cortex (DLPFC) and supplementary motor area (SMA) [19].

Although previous research has identified individual regions activated during task performance, as well as resting-state networks associated with UFOV performance, no studies have looked at the engagement of functional networks or functional network segregation during UFOV task performance. Therefore, we aimed to evaluate task-based functional connectivity of the UFOV task, using a modified UFOV task designed for in-scanner presentation, the UFOV fMRI task [32]. This task requires participants to identify targets both in the center of the screen and in the periphery. To assess the viability of a UFOV task-based functional connectivity network in predicting UFOV performance, 10 a priori ROIs were derived from BOLD activation patterns previously implicated in UFOV task performance [20]. Thus, we aimed to assess if regions that were functionally activated in the UFOV fMRI task were temporally correlated via functional connectivity and related to task performance. Furthermore, we compared within-network connectivity of the UFOV functional network to within-network connectivity of 7 restingstate functional connectivity networks (Yeo et al., 2011) in predicting UFOV task performance and a "near-transfer" task, Double Decision performance. We hypothesize that the 10 a priori ROIs delineated in Kraft et al. (2021) will be temporally connected during UFOV task completion and will be associated with UFOV task performance. We further hypothesize that within-network connectivity of these 10 ROIs will predict both UFOV in-scanner performance and Double Decision performance better than the 7 resting-state functional connectivity networks. Additionally, given findings of decreased segregation in older adults, we explored the impact of network segregation between higher-order resting state networks and UFOV performance [25-27].

Materials and methods

Participants

Data from 359 healthy older adults were collected at the University of Florida and University of Arizona as part of an ongoing phase III clinical trial, the Augmenting Cognitive Training in Older Adults (ACT) study (R01AG054077). Participants in this study ranged in age from 65 to 89, had no history of head injury with loss of consciousness greater than 20 min, had no previous diagnosis of neurological or major psychiatric disorders, and were able to undergo an MRI (for further details of inclusion/exclusion criteria, see [32]). Participants were excluded if they met criteria for possible mild cognitive impairment (MCI), which were derived from the Uniform Data Set (UDS), a widely validated tool created by the National Alzheimer's Coordinating Center (NACC) to assess MCI and Alzheimer's disease [33]. Possible MCI was defined as 1.5 standard deviations below age-, sex-, and education-adjusted scores in performance of at least one of the five following cognitive domains: general cognition, visuospatial functioning, memory, executive functioning/working memory, and language.

Measures

Useful field of view (UFOV) fMRI task

The UFOV task used in the current study was an adaptation of the third subtask of the original UFOV task and is specific to fMRI presentation [34]. Successful completion of this task requires participants to attend to a target presented in the middle of the display, as well as a target in the periphery amongst distractors. All participants completed the UFOV fMRI task in the scanner, with a total run time of 10 min, 32 s (E-Prime version 2.0; Psychology Software Tools Inc., Pittsburgh, PA, USA).

Each trial began with a *fixation* cross, presented for an average duration of 5000 ms. During the *stimulus* portion of the task, participants must attend to a target in the center of the screen (either a car or a truck), as well as locate a target (a car) presented in one of eight radial locations in the periphery, amongst distractors. The stimulus screen was presented for 500 ms; a mask screen was then presented for an average of 3000 ms. During the *probe* portion of the task, the participant performed a forced choice response in which they had to decide if the object in the center of the screen and the location of the car in the periphery were the same as on the previous stimulus screen. All participants received 56 trials of the UFOV fMRI task in-scanner, with 0 to 47 distractors during the *stimulus* screen (Fig. 1).

This adapted UFOV task, known as the UFOV fMRI task, differed from the original UFOV task in a number of ways [20]. The *stimulus* screens and *probe* screens were presented for static durations of 500 ms and 2500 ms, respectively, to adequately capture hemodynamic responses. This is in contrast to the original UFOV test, in which scores are a function of the briefest display duration in which participants could respond correctly on at least 75% of trials. Additionally, during the probe portion of the task, participants were required to make a forced choice response, as opposed to assessing the radial location of the peripheral target.

POSIT Brain HQ Double Decision

The POSIT Brain HQ Double Decision task is a wellknown adaptive cognitive training paradigm, based on the original UFOV task [19, 35, 36]. Like the UFOV fMRI task, the Double Decision task requires participants to identify which central target was presented on the screen (either a car or a truck) and the location of the peripheral target (a Route 66 sign) (Fig. 2). As this is an adaptive training paradigm, the targets were presented for variable lengths of time depending on participant accuracy, with longer presentation times following incorrect trials and shorter presentation times following correct trials. There were 25 presentations total and possible presentation times ranged from 32 to 2600 ms. The task was set at a moderate difficulty to start, with a starting presentation time of 501 ms and 7 distractors. Participants' scores were

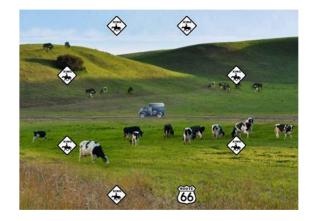


Fig. 2 Example of the POSIT Double Decision paradigm. Reproduced/adapted from POSIT Brain HQ, used with permission

calculated as the average presentation time of correct responses in log ms, as reaction time was skewed positively. Lower scores on the task equated to faster processing speed. All participants performed the Double Decision task at their first visit, within 60 days of their MRI visit.

MRI acquisition

Structural MRI data was collected using T1-weighted magnetization prepared rapid gradient echo (MPRAGE) via a Siemens 3 T Prisma scanner with a 64-channel head coil (University of Florida site, n=231) or via a Siemens 3 T Skyra scanner with a 32-channel head coil (University of Arizona site, n=105). T1-weighted structural scans were collected with the following parameters at both sites: repetition

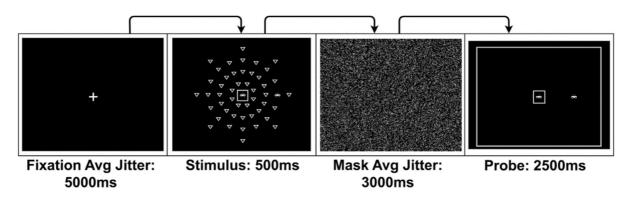


Fig. 1 Useful field of view task [32]

time (TR)=1800 ms; echo time (TE)=2.26 ms; flip angle=8°; field of view=256 mm×256 mm×176 m m; voxel size=1mm³. Task-based fMRI scans were collected using multi-slice interleaved echo planar imaging (EPI-BOLD) with the following parameters: repetition time (TR)=3000 ms; echo time (TE)=30.0 ms; flip angle=70°; field of view=240 mm×240 mm×132 mm; voxel=3 mm³, for a total of 209 volumes. The total run time of the task-based fMRI sequence was 10 min and 32 s. Scan cards were identical between the two study sites to ensure harmonization of MRI data acquisition.

Functional neuroimaging processing and analyses

Structural and functional MRI images were preprocessed using the CONN toolbox within the MATLAB suite (CONN version 18b, SPM12, MATLAB 2019b) [37]. We used the default preprocessing pipeline within CONN, composed of functional realignment and unwarping, functional centering of the image to (0, 0, 0) coordinates, slice-timing correction, structural centering to (0, 0, 0) coordinates, structural segmentation and normalization to MNI space, functional normalization to MNI space, and spatial smoothing (set at 8 mm full-width half maximum Gaussian smoothing kernel). The Artifact Rejection Toolbox (ART) was used to identify motion outliers (set at the 97th percentile, with motion threshold set at 0.9 mm and global BOLD signal deviation set at z = +/-5) and to flag outlier scan acquisitions. Following the pre-processing pipeline, the data were run through CONN's default denoising pipeline, to estimate and account for noise factors. During the denoising process, an anatomical component-based noise correction procedure (aCompCor) extracted five noise components from white matter and CSF, which primarily reflect signal related to cardiac and respiratory fluctuations [38]. Additionally, subject-specific motion parameters were identified, outlier scans were accounted for via scrubbing, and temporal band-pass filtering (0.008-0.09 Hz) was applied to exclude signals not related to BOLD signals, such as scanner frequency drift [39, 40]. In the current study, we chose not to discard the first several volumes unless the volume was identified to be an outlier via ART toolbox. In all instances, we incorporated scrubbing information as a first-level covariates. This method allows for accurate representation of onset time of various components of the UFOV task (particularly given that the fixation cross and mask are jittered for varying lengths of time, Fig. 1). Participants were subsequently excluded if less than 50% of functional volumes remained after motion scrubbing; this demonstrates substantial motion, in accordance with Yeo 2015 recommendations [41].

Of the 359 participants included in the current study, 3 participants were removed due substantial motion, defined above as having less than 50% of functional volumes remaining following scrubbing (104 functional volumes or less). Twelve participants were excluded for responding to less than 50% of trials on the UFOV in-scanner task, and an additional 8 participants who received a 20-channel head coil, as opposed to a 64-channel head coil, were excluded. In total, 336 participants were included in the final analyses (Table 1). All protocol procedures were approved through the University of Florida and University of Arizona Institutional Review Boards. All participants provided written informed consent prior to the start of any study procedures. See Table 1 for demographic information.

To assess connectivity of regions associated with the UFOV task, we created spherical ROIs using the WFU PickAtlas in SPM12 [42]. These spherical regions were centered on regions with

Table 1Sampledemographics		University of Florida (<i>n</i> =231)	University of Ari- zona ($n = 105$)	Combined $(n=336)$	
	Age mean (SD)	71.62 (5.38)	71.42 (4.42)	71.56 (5.09)	
	Years of education mean (SD)	16.30 (2.48)	16.37 (2.01)	16.32 (2.34)	
	Sex M:F	90:141	29:76	119:217	
SD standard deviation	UFOV % accuracy mean (SD)	60.10 (13.00)	62.02 (12.82)	60.70 (12.96)	

the greatest peak BOLD activation patterns in the UFOV fMRI task, specifically associated with UFOV fMRI task performance [20]. Spherical ROIs were titrated to either 9 mm or 10 mm to capture significant regions of activation without overlapping. The details of the spherical ROIs can be found in Table 2 and visualization in Fig. 3.

We used a weighted ROI-to-ROI connectivity analysis to model task-specific functional connectivity strength between a priori ROIs [20]. All task conditions (stimulus, probe, mask, and rest) were modeled. Weighted ROI-to-ROI connectivity was computed via a weighted least squares linear model, with weights defined as a condition-specific timeseries convolved with a canonical hemodynamic response function [43]. Thus, connectivity values in the following analyses are Fisher z-transformed bivariate correlations between ROI's BOLD time series that quantify associations in activation during task conditions. The following analyses were all corrected at a false discovery rate (FDR) seedlevel correction of p = 0.05 [44].

UFOV functional network and UFOV accuracy

We assessed whether within-network task-based functional connectivity of the above ROIs, henceforth called the UFOV functional network, was associated with UFOV fMRI accuracy. Task accuracy was calculated as the number of correct responses divided by 56 total trials. This serves as a confirmatory analysis that connectivity within the UFOV network as a whole did in fact capture activation related to task performance. Average within-network connectivity was calculated as the mean of the pairwise correlations between each of the ROIs of the UFOV functional network throughout completion of the total trial. The total trial was modeled as the onset times of the fixation cross, stimulus, mask, and probe screens for each participant (Fig. 1). General linear regressions were conducted in SPSSv27 to assess the

Table 2 Spherical ROIs	ROI	x	У	Z	Volume (mm ³)	Radius (mm)	T statistic
	L Pars Opercularis	- 38	4	26	729	9	5.21
	L Pars Triangularis	-46	20	30	729	9	5.19
	L Supplementary Motor Area	2	8	60	729	9	4.35
	L Inferior Temporal Gyrus	-44	-60	-6	1000	10	4.87
	L Middle Occipital Gyrus	-26	-68	34	1000	10	5.68
	R Inferior Temporal Gyrus	48	-60	-6	1000	10	4.29
Coordinates refer to x,y,z, location in MNI152 space. T statistic refers to strength of peak BOLD activation, found in Kraft et al. (2021)	R Pars Triangularis	42	34	24	1000	10	4.74
	R Precentral Gyrus	44	2	24	1000	10	4.77
	R Supplementary Motor Area	6	18	46	1000	10	5.51
	R Superior Parietal Lobule	28	-60	52	1000	10	6.12

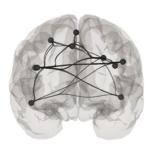






Fig. 3 UFOV network displayed on anterior, superior, and lateral right hemisphere views, displayed on grey matter mask

relationship of average connectivity of the UFOV network on UFOV fMRI task performance, controlling for age, sex, years of education, and scanner type.

Resting state networks and UFOV accuracy

We then compared the efficacy of the UFOV functional network in predicting UFOV fMRI task performance to reliable, well-established resting state networks. To accomplish this, we used a widely validated, publicly available parcellation, composed of 7 resting state networks [45]. Fig. 4 shows the parcellation of the 7 resting-state networks, modeled onto the MNI152 template. Average within-network connectivity values were calculated as the mean of the pairwise correlations between the ROIs within each resting state network. We assessed the relationship of average within-network connectivity of these 7 networks on UFOV fMRI task performance, controlling for age, sex, education, and scanner, via linear regression using an FDR threshold of p = 0.05 for multiple comparisons correction [44].

UFOV functional network + resting state networks and double decision performance

Additionally, we wanted to evaluate the generalizability of the UFOV functional network as well as the 7

resting state networks to a widely used UFOV train-
ing paradigm, the Double Decision task. At present,
the Double Decision training paradigm serves as the
prevalent implementation for UFOV training inter-
ventions in recent and ongoing clinical trials [11, 12,
19, 32]. We assessed the relationship of average net-
work connectivity of the UFOV functional network
and the 7 resting state networks to Double Decision
performance outside the scanner, controlling for
age, sex, education, and scanner type, using an FDR
threshold of
$$p=0.05$$
 for multiple comparisons cor-
rection between the 7 network regressions [44].

Higher-order network segregation and UFOV performance

Finally, we aimed to explore the relationship between segregation of higher-order resting state networks and UFOV performance. We calculated network segregation of the dorsal attention network (DAN), default mode network (DMN), FPCN, and CON using the formula delineated by Chan and colleagues:

where \overline{Z}_{w} is the mean Fisher z-transformed correla-

tion between all nodes within a network and Z_b is the

System segregation :
$$\frac{\overline{Z}_w - \overline{Z}_b}{\overline{Z}_w}$$

Default ModeFrontoparietal
ControlCingulo-OpercularDorsal AttentionLimbicSomatomotorVisualAImage: SomatomotorImage: SomatomotorImage: SomatomotorImage: SomatomotorImage: SomatomotorImage: SomatomotorImage: SomatomotorBImage: SomatomotorImage: SomatomotorImage: SomatomotorImage: SomatomotorImage: SomatomotorImage: SomatomotorImage: SomatomotorCImage: SomatomotorImage: SomatomotorIma

Fig. 4 Resting-state networks displayed on grey matter mask with A. anterior B. superior and C. right lateral hemisphere views. Each network is color-coded; however, the colors do not depict correlation strength [28]

mean Fisher z-transformed correlation between the nodes of one network to the nodes of another network. We then ran a general linear regression to assess the relationship of system segregation between the four higher-order resting state network on UFOV fMRI task performance, controlling for age, sex, years of education, and scanner type. We used an FDR threshold of p=0.05 for multiple comparisons correction between the 12 system segregation comparisons.

Results

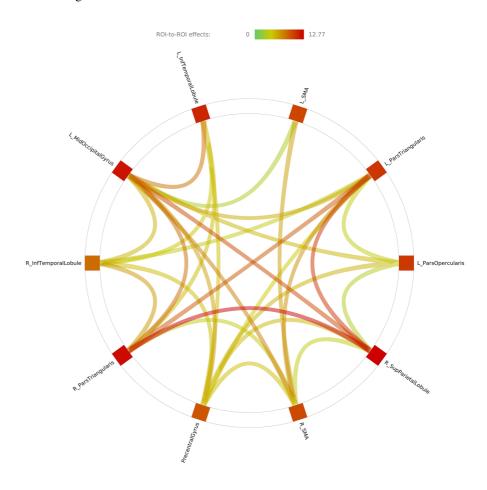
UFOV functional network and UFOV accuracy

We first aimed to assess whether regions functionally activated during the UFOV fMRI task were (1) functionally connected and (2) subsequently related to UFOV fMRI performance. ROI-to-ROI analysis showed significantly greater functional connectivity between the 10 a priori ROIs during whole trial

Fig. 5 Connectome ring of ROI-to-ROI task-based functional connectivity using the 10 a priori spherical ROIs. The color of the connections and color bar refer to connectivity t-values. Specific *p* values of ROI-to-ROI connections can be found in Supplemental Table 1 task completion (all FDR corrected p values < 0.05). No ROIs showed decreased functional connectivity with any other ROI. Fig. 5 shows the strength of connectivity between each of the ROIs within the UFOV functional network. Supplemental Table 1 contains statistical information regarding significant connections between nodes within the UFOV functional network. After confirming that these regions were indeed functionally connected, we evaluated the relationship of within-network functional connectivity of the UFOV network to UFOV fMRI task performance. After controlling for age, sex, years of education, and scanner type, greater within-network connectivity of the UFOV functional network was associated with higher accuracy of the UFOV fMRI task ($R^2 = 0.114$, $sr^2 = 0.141, \beta = 0.147, p = 0.008)$ (Fig. 6).

Resting state networks and UFOV accuracy

Given our findings of a significant relationship between UFOV fMRI performance and UFOV



network functional connectivity, we then sought to compare these results to the 7 resting-state networks. After controlling for covariates and performing FDR corrections, greater within-network connectivity only within the CON (R^2 =0.134, sr^2 =0.202, β =0.217, pFDR <0.001) and FPCN (R^2 =0.116, sr^2 =0.150, β =0.158, pFDR=0.014) were associated with higher accuracy on the UFOV fMRI task (Figs. 7 and 8). No other resting state networks were significantly related to UFOV fMRI task performance (all pFDR >0.05).

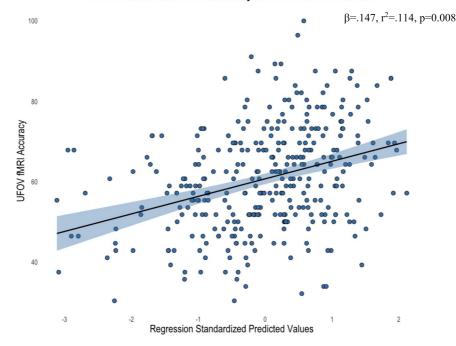
UFOV functional network + resting state networks and double decision performance

Following the above significant relationships between within-network connectivity of the UFOV functional network, CON, and FPCN to UFOV accuracy, we then evaluated the generalizability of these networks to the Double Decision task, a commonly used cognitive training intervention paradigm based on the original UFOV task. We ran the regressions from both the UFOV functional network and resting-state network analyses, substituting UFOV fMRI performance for Double Decision performance. After controlling for age, sex, years of education, and scanner type, greater within-network connectivity of the UFOV functional network was associated with faster presentation times, and thereby better performance, on the Double Decision task (R^2 =0.159, sr^2 =-0.116, β =-0.114, p=0.034) (Fig. 9).

Notably, none of the 7 resting state networks were associated with POSIT Double Decision performance (all pFDR > 0.05).

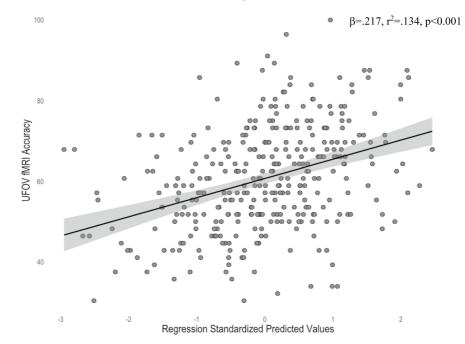
Higher-order network segregation and UFOV performance

Finally, we assessed the relationship between higherorder network segregation and UFOV accuracy. After controlling for age, sex, years of education, and



UFOV Network Functional Connectivity and UFOV fMRI Performance

Fig. 6 Scatterplot depicting the significant relationship between average within-network connectivity of the UFOV network and accuracy on the UFOV fMRI task, controlling for age, sex, years of education, and scanner type (standardized predicted values). Standardized predicted values are calculated by subtracting the mean predicted value of within-network connectivity of the UFOV network (given the mean age, sex, education, and scanner type) from the individual's predicted value of within-network connectivity of the UFOV network (given an individual's age, sex, education, and scanner type). This difference is divided by the standard deviation of the predicted values to allow for comparisons between individuals controlling for demographics. Standardized predicted values have a mean of 0 and a standard deviation of 1. Shaded region represents the 95% confidence interval of the regression line



CON Functional Connectivity and UFOV fMRI Performance

Fig. 7 Scatterplot depicting the significant relationship between average within-network connectivity of the CON and accuracy on the UFOV fMRI task, controlling for age, sex, years of education, and scanner type (standardized predicted values). Standardized predicted values are calculated by subtracting the mean predicted value of within-network connectivity of the CON (given the mean age, sex, education, and scanner type) from the individual's predicted value of within-

scanner type, no significant relationships between network segregation and UFOV performance remained (all pFDR and *p*-uncorrected values > 0.05).

Discussion

Prior evidence suggests that UFOV-based interventions provide lasting transfer effects in processing speed, a domain sensitive to age-related cognitive decline. Despite this, little is known about the neurocognitive correlates of the UFOV task. The current study was the first to assess task-based functional connectivity during UFOV performance. We assessed functional connectivity between a priori ROIs derived from BOLD activation patterns previously implicated in UFOV task performance [20]. We further assessed the viability a UFOV functional network by comparing its network connectivity network connectivity of the CON (given an individual's age, sex, education, and scanner type). This difference is divided by the standard deviation of the predicted values to allow for comparisons between individuals controlling for demographics. Standardized predicted values have a mean of 0 and a standard deviation of 1. Shaded region represents the 95% confidence interval of the regression line

to canonical resting state networks on both UFOV task performance and on a closely related task, the Double Decision task. Such findings may provide insight into potential neural targets to optimize UFOV training gains.

Analyzing the relationship between the UFOV functional network and UFOV accuracy, we observed greater within-network functional connectivity of the UFOV functional network associated with higher accuracy on the UFOV fMRI task. Nodes within the UFOV functional network included the bilateral pars triangularis, inferior temporal gyrus, and supplementary motor areas (SMA), as well as the left pars opercularis, left middle occipital gyrus, right precentral gyrus, and right superior parietal lobule. Several of these regions have previously been associated with out-of-scanner UFOV performance, including the ACC and DLPFC [19]. However, in comparison to established resting-state networks, we were surprised

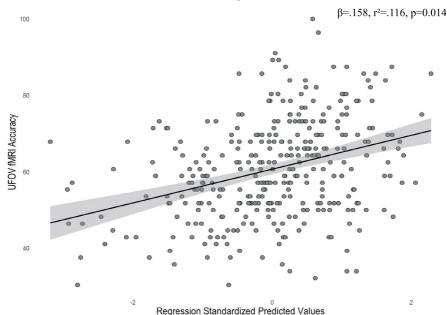


Fig. 8 Scatterplot depicting the significant relationship between average within-network connectivity of the FPCN and accuracy on the UFOV fMRI task, controlling for age, sex, years of education, and scanner type (standardized predicted values). Standardized predicted values are calculated by subtracting the mean predicted value of within-network connectivity of the FPCN (given the mean age, sex, education and scanner type) from the individual's predicted value of within-

to find that within-network connectivity of the FPCN and CON predicted UFOV task performance equally well or better than our UFOV functional network. This may be due, in part, to the overlap of our ROIs to regions implicated in the FPCN and CON networks.

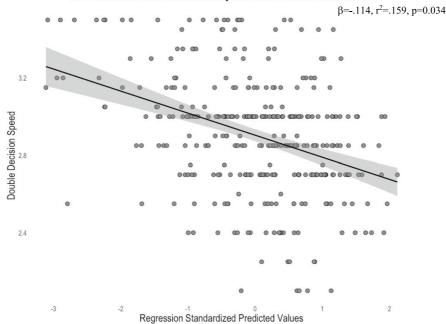
The FPCN, a functional connectivity resting state network critical in higher-order cognition, is associated with directing attention to relevant stimuli, manipulation of stimuli, and set-shifting abilities [29, 46, 47]. Maintenance of functional connectivity within this network is essential for cognitive control, especially in older adults. Our findings align with the findings of Hardcastle and colleagues, who found evidence of strengthened resting-state frontoparietal control network (FPCN) connectivity following an intervention using the UFOV task [31].

The superior portion of our 9 mm ROIs centered on the pars triangularis and pars opercularis makes up parts of the DLPFC, while the inferior portions comprise much of the VLPFC. This is noteworthy, since

network connectivity of the FPCN (given an individual's age, sex, education, and scanner type). This difference is divided by the standard deviation of the predicted values to allow for comparisons between individuals controlling for demographics. Standardized predicted values have a mean of 0 and a standard deviation of 1. Shaded region represents the 95% confidence interval of the regression line

the lateral prefrontal cortex, comprising the DLPFC/ VLPFC, is a hub region of the FPCN (for graphical depiction of the FCPN, see [41, 46]). The DLPFC's corresponding ROI in the UFOV functional connectivity network, the pars triangularis, exhibited some of the strongest ROI-to-ROI task-based functional connectivity. The role of the DLPFC in UFOV performance has also been highlighted by Ross and colleagues, who found significant strengthened restingstate functional connectivity between the DLPFC and ACC following a UFOV intervention [19].

The temporal region of the FPCN, centered within our a priori inferior temporal gyrus ROI, demonstrated significant task-based functional connectivity during the UFOV task. In the current study, we saw significant cross-hemispheric connections between the left and right inferior temporal gyrus, as well as widespread cross-hemispheric connections to nearly all other nodes within the UFOV functional network. Our findings suggest that strong cross-hemispheric



UFOV Network Functional Connectivity and Double Decision Performance

Fig. 9 Scatterplot depicting the significant relationship between average within-network connectivity of the UFOV network and faster Double Decision presentation, controlling for age, sex, years of education, and scanner type. Standardized predicted values are calculated by subtracting the mean predicted value of within-network connectivity of the UFOV network (given the mean age, sex, education, and scanner type) from the individual's predicted value of within-network con-

communications between key regions of the FPCN, particularly the DLPFC and inferior temporal gyrus, are essential in UFOV task performance, and this may be particularly true in aging. Foundational work by Cabeza and colleagues demonstrated that under task-based demands, older adults experience less lateralization of BOLD activation, suggesting a compensatory mechanism in maintaining cognitive performance [48, 49]. It is possible that cross-hemispheric functional connectivity during UFOV completion, particularly within our older adult sample, may support compensation, as described by Cabeza and colleagues.

In addition to the FPCN, we observed overlap of our UFOV functional network ROIs with other established functional connectivity networks [45]. The inferior portion of the 10 mm ROI centered on the right supplementary motor area (SMA) is composed of regions of the anterior cingulate cortex nectivity of the UFOV network (given an individual's age, sex, education, and scanner type). This difference is divided by the standard deviation of the predicted values to allow for comparisons between individuals controlling for demographics. Standardized predicted values have a mean of 0 and a standard deviation of 1. Shaded region represents the 95% confidence interval of the regression line

(ACC). Our ROI overlaps with the medial portion of the CON network, centered at the ACC, and this region is a key hub in the CON network. Similar to the FPCN, the CON network is a higher-order resting state network involved in monitoring task performance, maintenance of task rules, and set-shifting abilities [50]. These results again corroborate the findings of strengthened functional connectivity between the ACC and DLPFC following a UFOV intervention, underscoring these regions' crucial role in UFOV task performance [19]. Moreover, the posterior node of the DAN is encompassed by our 10 mm ROI centered on the right superior parietal lobule. This higher-order resting state network is implicated primarily in orientation to task-relevant stimuli, specifically location of visual stimuli [51, 52]. Previous research has shown that following a visual search intervention, within-network connectivity of the DAN was significantly strengthened [53]. Recent research has further suggested that connections among the superior parietal lobule, ACC, and DLPFC relate to individual performance on a visual search task, all of which are implicated in the current study [54].

We also identified unique regions associated with UFOV task performance not encompassed by the FPCN, CON, or DAN, including ROIs centered on the left SMA, the left middle occipital gyrus, and the right precentral gyrus. Both the SMA and the visual cortex have been implicated in UFOV task performance, and both regions had significant increases in resting-state functional connectivity following a UFOV intervention [19]. The significance of coherent functional connectivity in the middle occipital gyrus is unsurprising, given the visual nature of the UFOV task. The SMA is activated during anticipation and completion of motor tasks and also involved in reaction time maintenance [55–57]. A rapidly growing body of evidence has further suggested the role of the precentral gyrus in UFOV task performance [19]. Consistent with this, the precentral gyrus demonstrated some of the most robust activation patterns when completing the UFOV task in the present study, and structural degradation of this region was associated with poorer performance on an analogous Double Decision task [20, 58]. The motor cortex is contained within the precentral gyrus, a region that plays a critical role in motor planning and completion of motor tasks [59]. These findings suggest that motor planning is an integral part in UFOV task completion and may further explain the role of the precentral gyrus in UFOV task performance.

We then aimed to evaluate the generalizability of within-network connectivity of the UFOV network to scores on a "near-transfer" task, the Double Decision task. We found that the within-network connectivity of UFOV fMRI task predicted scores on the Double Decision task, better than the 7 resting state networks. This finding is significant, given that the Double Decision task is the most prevalent implementation of adaptive UFOV training in clinical trials. The Advanced Cognitive Training for Independent and Vital Elderly (ACTIVE) study was the largest clinical trial of its time to investigate the longitudinal effects of cognitive training using the Double Decision task (n=2832) [11]. They found that cognitive improvements stemming from a Double Decision based intervention lasted 2 years following cessation of intervention, and resultant work found that these gains can last up to 10 years following intervention [11, 12]. Further studies found that each UFOV training session was associated with up to a 29% reduction in dementia prevalence 10 years following the end of intervention in the ACTIVE study [60]. Such improvements extend beyond cognition—UFOV and Double Decision-based interventions have been associated with better driving outcomes [13, 14], better self-reported cognition [15], fewer difficulties in completing IADLs [17, 18], and improved healthrelated quality of life [5, 16]. The overwhelming evidence of efficacy regarding the Double Decision task makes the UFOV functional network an important target for future interventions.

It is interesting to note that the relationship between functional segregation of the four higherorder resting state networks and UFOV task performance was not significant. Functional segregation of networks is essential in cognitive aging, as research has found that increased system segregation is associated with cognition and these relationships exists independent of the aging process [27]. It should be emphasized that we cannot state that system segregation is irrelevant in task performance; rather, withinnetwork connectivity, as opposed to between-network connectivity, may be driving UFOV performance. Future research should investigate how metrics of system segregation, including participation coefficients, influence UFOV task performance.

Limitations and future directions

While this study provides novel insights into taskbased functional connectivity of the UFOV cognitive paradigm, results from this work must be interpreted within the context of limitations. Our sample was highly educated, with 69% of our sample achieving a bachelor's degree or higher; 83.14% of our sample identified as "White/non-Hispanic," which limits generalizability of our findings to Black, Asian American and Pacific Islander, Indigenous, and Hispanic or Latinx populations. As the aging population becomes more ethnically and racially diverse, we must overcome barriers to research participation that disproportionately impact individuals from marginalized populations to promote more inclusive aging research.

This study was cross-sectional and thus can make no inferences regarding dynamic changes in

task-based functional connectivity during the aging process. Future work should analyze longitudinal changes in UFOV task-based functional connectivity, given that both UFOV performance and functional connectivity network segregation are impacted during the cognitive aging process [12, 26, 61]. In the present study, we conducted an ROI-to-ROI taskbased analyses using a priori ROIs built from a subset of participants used in the current sample [20]. This method allowed us to focus on functional connectivity metrics among regions that had previously shown activation during the UFOV fMRI task and were related to UFOV task performance. Future studies should replicate these findings using a variety of functional connectivity techniques (e.g., independent components analysis, voxel-wise approaches, graph theory approaches).

Improving replicability and reproducibility of fMRI studies remains essential in the field of cognitive neuroscience. In the current study, we adopted several of the recommendations delineated by Poldrack and colleagues, including the collection of larger samples to improve power, using statistical thresholding procedures such as FDR corrections, and restricting analyses to a priori ROIs [62]. However, limitations using fMRI persist, including temporal resolution limitations, susceptibility to motion and tightly constrained environments. Moreover, MRI contraindications and cost of imaging may further reduce generalizability to a broader population. Functional near-infrared spectroscopy (fNIRS) is an inexpensive, non-invasive neuroimaging technique in which near-infrared light is shined into the head and measures changes in concentrations of oxygenated and deoxygenated hemoglobin (for reviews, see [63] and [64]). Measurements of hemodynamic response in fNIRS and BOLD responses in fMRI have been shown to produce similar results, even within taskbased designs [65, 66]. fNIRS has also been shown to be less susceptible to motion, and no contraindications exist for fNIRS [65] Despite the limitations of fNIRS, including spatial resolution and penetration depth, future research should investigate alternative neuroimaging techniques.

Finally, recent studies have investigated the role of non-invasive brain stimulation techniques, such as transcranial direct current stimulation and transcranial alternating current stimulation, in increasing within-network modularity in higher-order resting-state networks [67, 68]. Given the crucial role of within-network synchrony, particularly in the context of aging, future work should explore modulating these networks to offset the deleterious effects of cognitive decline.

Conclusion

To date, this is the first study that has assessed taskbased functional connectivity during completion of a widely efficacious paradigm in improving cognition, the UFOV task. Notably, we provide evidence that coherence within 10 a priori ROIs significantly predicts UFOV task performance. Synchronicity in this network, which we termed the UFOV functional network, predicted UFOV performance. Additionally, enhanced within-network connectivity of the UFOV functional network predicted better performance on a measure of "near-transfer," the Double Decision task. Collectivity, these findings provide insight into potential targets to optimize the efficacy of the UFOV paradigm in slowing cognitive aging.

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Author contribution JK and AW contributed to the conception and design of this specific study. JK extracted data, performed statistical analyses, and wrote the first draft of the manuscript. HH and CH contributed to data analyzing and processing. EP, GH, SW, SD, GA, MM, RC, and AW were involved in project administration. All authors contributed to manuscript revisions, read, and approved the submitted version.

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Data availability Data are managed under the data sharing agreement established with NIA and the parent R01 clinical trial Data Safety and Monitoring Board in the context of an ongoing Phase III clinical trial (ACT study, R01AG054077). All trial data will be made publicly available 2 years after completion of the parent clinical trial, per NIA and DSMB agreement. Requests for baseline data can be submitted to the ACT Publication and Presentation (P&P) Committee and will

require submission of a data use, authorship, and analytic plan for review by the P&P committee (ajwoods@php.ufl.edu).

Declarations

Conflict of interest The authors declare no competing interests.

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