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Research Article

Detecting cognitive decline in high-functioning older adults: The relationship between subjective cognitive concerns, frequency of high neuropsychological test scores, and the frontoparietal control network

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Abstract

Objective: Neuropsychologists have difficulty detecting cognitive decline in high-functioning older adults because greater neurological change must occur before cognitive performances are low enough to indicate decline or impairment. For high-functioning older adults, early neurological changes may correspond with subjective cognitive concerns and an absence of high scores. This study compared high-functioning older adults with and without subjective cognitive concerns, hypothesizing those with cognitive concerns would have fewer high scores on neuropsychological testing and lower frontoparietal network volume, thickness, and connectivity. **Method:** Participants had high estimated premorbid functioning (e.g., estimated intelligence ≥75th percentile or college-educated) and were divided based on subjective cognitive concerns. Participants with cognitive concerns ($n = 35$; 74.0 ± 9.6 years old, 62.9% female, 94.3% White) and without cognitive concerns ($n = 33$; 71.2 ± 7.1 years old, 75.8% female, 100% White) completed a neuropsychological battery of memory and executive function tests and underwent structural and resting-state magnetic resonance imaging, calculating frontoparietal network volume, thickness, and connectivity. **Results:** Participants with and without cognitive concerns had comparable numbers of low test scores (≤16th percentile), $p = .103$, $d = .40$. Participants with cognitive concerns had fewer high scores (≥75th percentile), $p = .004$, $d = .71$, and lower mean frontoparietal network volumes (left: $p = .004$, $d = .74$; right: $p = .011$, $d = .66$) and cortical thickness (left: $p = .010$, $d = .66$; right: $p = .033$, $d = .54$), but did not differ in network connectivity. **Conclusions:** Among high-functioning older adults, subjective cognitive decline may correspond with an absence of high scores on neuropsychological testing and underlying changes in the frontoparietal network that would not be detected by a traditional focus on low cognitive test scores.

Keywords: Cognitive aging; Aged; Cognitive dysfunction; Neuroimaging; Neuropsychological tests; Intelligence

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Introduction

Neuropsychologists often have difficulty detecting cognitive decline in older adults with high premorbid cognitive functioning because more neurological change must occur before cognitive test scores meet conventional criteria for defining mild or major cognitive impairment (Albert et al., 2011; American Psychiatric Association, 2013; Petersen et al., 1999). Current assessment methods and approaches to test interpretation are inherently limited in detecting potential cognitive decline in high-functioning examinees. Low scores have long been the standard for defining cognitive impairment in neuropsychological practice (Dubois et al., 2007; Heaton et al., 1991; Heaton et al., 2004; Petersen et al., 1999; Reitan & Wolfson, 1993), but in high-functioning older adults, decline from a high average or superior premorbid ability level may be present without any low scores on cognitive testing. In a longitudinal cohort of 204 high-functioning older adults, even average scores were predictive of dementia at a follow-up evaluation (Tuokko et al., 2003). In high-functioning individuals undergoing neuropsychological assessments, the *absence* of high scores, as opposed to the presence of low scores, may indicate cognitive decline and could correspond with an underlying disease process.

Prior research has extensively examined the normal frequency of an examinee obtaining one or more low test scores when administered a battery of neuropsychological tests, both across

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domains (Binder et al., 2009; Brooks et al., 2013; Brooks et al., 2009; Mistridis et al., 2015) and within specific domains, such as memory (Brooks et al., 2008; Brooks et al., 2007) and executive functions (Karr et al., 2017, 2018). Additional research has examined the *other side of the bell curve*, demonstrating that high scores are also commonly obtained by healthy examinees completing neuropsychological test batteries (Karr et al., 2020; Karr et al., 2022a; Karr & Iverson, 2020). For example, roughly half of adults (i.e., 48.9%) in the normative sample for the NIH Toolbox Cognition Battery (NIHTB-CB) obtained one or more scores ≥84th percentile (Karr & Iverson, 2020). Not surprisingly, individuals with higher estimated intelligence tend to obtain fewer low scores and more high scores (Iverson & Karr, 2021), meaning a very low base rate of high-functioning adults with no high scores on neuropsychological testing. For example, just 4.8% of healthy adults with high average intelligence obtained no test scores ≥75th percentile when interpreting seven scores from three tests on the Delis–Kaplan Executive Function System (D-KEFS) (Karr et al., 2020). As such, it would be clinically informative to assess whether fewer high scores on cognitive testing is associated with subjective cognitive concerns and underlying neurological differences.

Participants with subjective cognitive concerns present with subtly lower performances on cognitive testing (Burmester et al., 2016), and some of the largest cognitive effects of preclinical Alzheimer's disease occur within the domains of episodic memory and executive functions (Bäckman et al., 2005). The frontoparietal control network (FPCN) (Yeo et al., 2011) is involved in aspects of executive functions and memory (Badre & D'Esposito, 2007; Cabeza et al., 2008; Spreng et al., 2010; Vincent et al., 2008), and structural changes in frontal and parietal regions have been consistently observed in subjective cognitive decline (Rivas-Fernández et al., 2023). FPCN connectivity has predicted longitudinal changes in global cognition among healthy older adults (Buckley et al., 2017) and FPCN volume mediates the relationship between age and executive functions in healthy adults (Yao et al., 2020). Participants with and without subjective cognitive concerns may present with differences in FPCN volume and connectivity, potentially indicating underlying neurological changes that could lead to mild cognitive impairment or dementia.

For high-functioning older adults, subjective cognitive concerns may indicate decline that is not detected by the presence of low scores but may be related to the absence of high scores and the presence of latent neurological changes. The current study examined whether subjective cognitive concerns were associated with (a) the number of low and high scores on neuropsychological tests of memory and executive functions, and (b) the regional volume, cortical thickness, and connectivity of the FPCN. We hypothesized that high-functioning older adults with subjective cognitive concerns would have fewer high scores than those without subjective cognitive concerns, but a comparable number of low scores. These findings would indicate that objective decline has occurred but would not be detected by a traditional focus on low scores. We also hypothesized that subjective cognitive concerns would be associated with lower FPCN volume, thickness, and connectivity, indicating latent neurological change underlying subjective cognitive concerns.

Method

Participants

Participants were derived from an imaging sub-study of a longitudinal cohort study on self-regulation, brain, and cognitive health in older adults (D. R. Evans & Segerstrom, 2015; Geiger et al., 2019; Scott et al., 2019; Segerstrom et al., 2022). To be eligible, participants had to be 60 years or older and nonsmokers. They were excluded if they had autoimmune diseases; were taking opiates, corticosteroids, cytotoxic drugs, TNF blockers, or medications for dementia; received chemotherapy or radiation in the past 5 years or general anesthesia in the past 3 months; or were taking more than two of the following medication: α or β blockers or ACE inhibitors, hormone replacement, thyroid supplement, and antidepressant, anxiolytic, or hypnotic drugs. Overall, participants included in the study were healthy older adults. Apolipoprotein E genotype was not available for individual participants. This study was approved by the Institutional Review Board at the University of Kentucky and completed in accordance with the Helsinki Declaration.

Among 80 participants who underwent magnetic resonance imaging (MRI), participants were selected if they were estimated to have high premorbid functioning, operationally defined as either (a) scoring ≥75th percentile on the North American Adult Reading Test (NAART) (Blair & Spreen, 1989; Uttl, 2002) estimated full scale intelligence quotient (FSIQ) ($n = 60$) or (b) having completed a postsecondary degree ($n = 62$). There was a strong correspondence between these variables. Most participants scoring ≥75th percentile on the NAART had a college degree ($n = 54$, 90.0%) and most participants with a college degree scored ≥75th percentile on the NAART ($n = 54$, 87.1%). This resulted in a sample of 68 participants, who were further subdivided based on the presence or absence of subjective cognitive concerns, defined per self-report on the Medical Outcomes Study Cognitive Functioning Scale (MOS-Cog, with exact methodology described below). The demographic characteristics of the total sample and participants with subjective cognitive concerns ($n = 35$) and without subjective cognitive concerns ($n = 33$) are presented in Table 1. There were no significant differences between groups in terms of age, sex, race, education, household income, or NAART estimated FSIQ. The participants, by design, differed significantly on subjective cognitive concerns.

Measures

Subjective cognitive concerns

Participants completed the MOS-Cog (Stewart et al., 1992), a six-item questionnaire asking about past-month difficulty with general cognitive functions in everyday life (e.g., concentration, memory, problem solving). Participants responded to each item on a six-point scale, ranging from *all of the time* (1) to *none of the time* (6). The items were converted to 0–100 scale (i.e., 1 = 0, 2 = 20, 3 = 40, 4 = 60, 5 = 80, and 6 = 100) and averaged to arrive at a total score for the MOS-Cog (range: 0–100), with a higher score indicating fewer cognitive concerns. Participants were categorized as having or not having subjective cognitive concerns based on responses to MOS-Cog items. If participants endorsed one or more MOS-Cog items as *some of the time* (4), *a good bit of the time* (3), *most of the time* (2), or *all of the time* (1), they were categorized as having subjective cognitive concerns; and those who responded a *little of the time* (5) or *none of the time* (6) to all items were categorized as not having subjective cognitive concerns.

Neuropsychological tests

Participants completed the NAART (Blair & Spreen, 1989; Uttl, 2002), which is a word reading test used to estimate FSIQ; the Rey Auditory Verbal Learning Test (RAVLT) (Strauss et al., 2006), with

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Table 1. Participant demographics

	Total sample ($n = 68$)	Participants with subjective cognitive concerns ($n = 35$)	Participants without subjective cognitive concerns ($n = 33$)	Group comparison
Age (years), *M* (*SD*), range	72.6 (8.6), 60–95	74.0 (9.6), 60–95	71.2 (7.1), 62–85	$t = 1.42$, $p = .160$
Sex, %	–	–	–	$\chi^2 = 1.32$, $p = .250$
Female	69.1%	75.8%	62.9%	
Male	30.9%	24.2%	37.1%	
Race, %	–	–	–	Fisher's exact, $p = .493$
White	97.1%	94.3%	100%	
Black	2.9%	5.7%	0%	
Education, %	–	–	–	Fisher's exact, $p = .199$
Some College	8.8%	14.3%	3.0%	
College Degree	91.2%	85.7%	97.0%	
Household income, Mdn, range	$70k, $12k–$500k	$70k, $30k–$500k	$75k, $12k–$400k	$U = 499.5$, $p = .962$
NAART FSIQ, *M* (*SD*), range	116.9 (5.9), 94–125	117.0 (5.9), 101–125	116.7 (6.0), 94–123	$t = .25$, $p = .800$
MOS-Cog, *M* (*SD*), range	84.2 (12.1), 56.7–100	75.0 (9.4), 56.7–93.3	93.8 (4.7), 83.3–100	$t = 10.47$, $p < .001$, $d = 2.45$

Note. CI = Confidence Interval; MOS-Cog = Medical Outcomes Study Cognitive Functioning Scale; NAART FSIQ = North American Adult Reading Test estimated full scale intelligence quotient.

total learning for Trials 1–5 and delayed recall included as scores in the base rates analysis; the Trail Making Test (TMT) Parts A and B (Bowie & Harvey, 2006; Reitan, 1958), with time-to-completion for each part included as scores in the base rates analysis; the Controlled Oral Word Association Test (COWAT) (Benton et al., 1994), with the number of words produced across three trials included as scores in the base rates analysis; and the Digit Span (DS) and Letter-Number Sequencing (LNS) subtests from the Wechsler Adult Intelligence Scale, Fourth edition (WAIS-IV) (Wechsler, 2008), with the total scores for these subtests included in the base rates analysis. Age-adjusted scaled scores were derived using Mayo's Older Americans Normative Studies (MOANS) norms for the RAVLT (Steinberg et al., 2005), TMT Parts A and B (Steinberg et al., 2005), and COWAT (Steinberg et al., 2005) and using WAIS-IV norms for the DS and LNS (Wechsler, 2008). For all test scores, a score at or above the 75th percentile was considered a high score based on uniform labeling standards for performance test scores (Guilmette et al., 2020); and a score at or below the 16th percentile was considered a low score, based on recommended criteria for cognitive impairment (American Psychiatric Association, 2013).

Physical and mental health

Participants had heart rate, blood pressure, and Body Mass Index (BMI) measured. Participants completed the Geriatric Depression Scale (GDS), which is a 30-item questionnaire on past-week depression symptomatology (Yesavage et al., 1982). A higher scores indicates more severe depression and scores >10 indicate depression in older adults (Brink et al., 1982). Participants also completed a 10-item version of the Perceived Stress Scale (S. Cohen et al., 1983), which measures degrees of life stress in the past month. A higher score indicates a greater degree of life stress.

Imaging data acquisition

Participants were scanned using a 3-T Siemens TIM Trio scanner using an 8-channel array head coil between July 2015 and September 2017. A 3-T Siemens PRISMA scanner with a 20-channel array head coil was used between July 2018 and May 2019, with 38 of 64 participants scanned with the upgraded scanner. Structural and functional images were collected, on average, about two months after neuropsychological tests were completed ($M = 60.0$ days, $SD = 45.8$; Mdn = 46, range: 4–244). High-resolution T1-weighted images were collected using a magnetization-prepared rapid gradient-echo (MPRAGE) sequence (TR = 2530 ms; TE = 2.26 ms; FA = 7 degrees; resolution = 1 mm isotropic). Functional images were collected using a $T2^*$-weighted gradient-echo planar sequence (34 interleaved slices, TR = 2000 ms, TE = 27 ms, FA = 70°, FOV = 224 mm^2, matrix = 64×64, isotropic resolution = 3.5 mm).

Anatomical data preprocessing

The T1-weighted (T1w) image was corrected for intensity nonuniformity (INU) with N4BiasFieldCorrection (Tustison et al., 2010), distributed with Advanced Normalization Tools (ANTs) 2.2.0 (RRID:SCR_004757) (Avants et al., 2011; Tustison et al., 2021) and used as T1w reference. The T1w reference was skull-stripped with a Nipype implementation of the antsBrainExtraction.sh workflow from ANTs, using OASIS30ANTs as target template. Brain tissue segmentation of cerebrospinal fluid, white matter, and gray matter was performed on the brain-extracted T1w using fast (FSL 5.0.9, RRID:SCR_002823) (Zhang et al., 2001). Brain surfaces were

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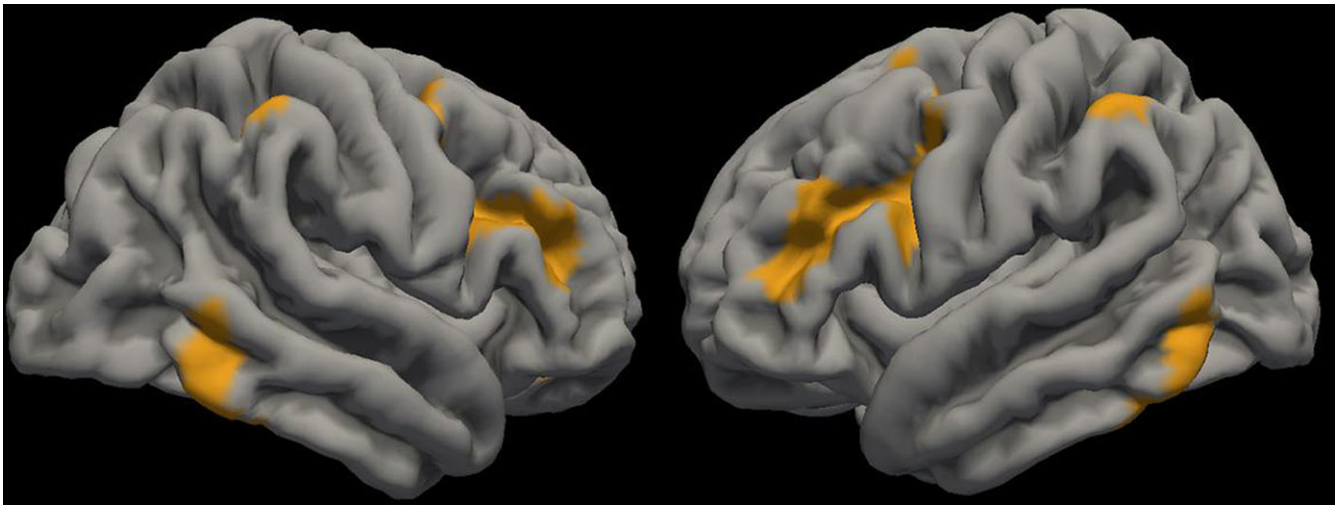

Figure 1. Frontoparietal control network parcellation used in the current study.

reconstructed using recon-all (FreeSurfer 6.0.1, RRID:SCR_001847) (Dale et al., 1999), and the brain mask estimated previously was refined with a custom variation of the method to reconcile ANTs-derived and FreeSurfer-derived segmentations of the cortical gray matter of Mindboggle (RRID:SCR_002438) (Klein et al., 2017). Volume-based spatial normalization to one standard space (MNI152NLin6Asym) was performed through nonlinear registration with antsRegistration (ANTs 2.2.0), using brain-extracted versions of both T1w reference and the T1w template. The following template was selected for spatial normalization: FSL\u2019s MNI ICBM 152 nonlinear 6th Generation Asymmetric Average Brain Stereotaxic Registration Model (RRID:SCR_002823; TemplateFlow ID: MNI152NLin6Asym) (A. C. Evans et al., 2012).

Resting-state preprocessing

Functional data were preprocessed using fMRIPrep 1.5.3 (Esteban, Markiewicz, et al., (2018); Esteban, Blair, et al., (2018); RRID: SCR_016216) (Esteban et al., 2019, 2020) based on Nipype 1.3.1 (RRID:SCR_002502) (Gorgolewski et al., 2011). A reference volume and its skull-stripped version were generated using a custom fMRIPrep methodology. Susceptibility distortion correction (SDC) was omitted. The BOLD reference was then co-registered to the T1w reference using bbregister (FreeSurfer) which implements boundary-based registration (Greve & Fischl, 2009). Co-registration was configured with six degrees of freedom. Head motion parameters with respect to the BOLD reference (transformation matrices, and six corresponding rotation and translation parameters) are estimated before any spatiotemporal filtering using mcflirt (FSL 5.0.9) (Jenkinson et al., 2002). The BOLD time series were resampled to surfaces in FreeSurfer (fsaverage5) space. The BOLD time series (including slice-timing correction when applied) were resampled onto their native space by applying the transforms to correct for head motion. These resampled BOLD time series are referred to as preprocessed BOLD.

The BOLD time series were resampled into standard space, generating a preprocessed BOLD run in MNI-152 space. A reference volume and its skull-stripped version were generated using a custom fMRIPrep methodology. Automatic removal of motion artifacts using ICA-AROMA (Pruim et al., 2015) was performed on the preprocessed BOLD on MNI space time series after removal of non-steady state volumes and spatial smoothing with an isotropic, Gaussian kernel of 6 mm FWHM. Corresponding non-aggressively denoised runs were produced after such smoothing. Additionally, the aggressive noise regressors were collected and placed in the corresponding confounds file. Several confounding time series were calculated based on the preprocessed BOLD: FD, DVARS, and three region-wise global signals. FD and DVARS are calculated for each functional run, both using their implementations in Nipype (Power et al., 2014). The three global signals are extracted within the cerebrospinal fluid, white matter, and whole-brain masks. Gridded resamplings were performed using ANTs, configured with Lanczos interpolation to minimize the smoothing effects of other kernels (Lanczos, 1964). Non-gridded resamplings were performed using mri_vol2-surf (FreeSurfer).

Resting-state time-series parcellation and analysis

The resulting images from ICA-AROMA run via fMRIPrep were further corrected by regressing out global signals cerebrospinal fluid and white matter, as well as a linear trend using fsl_regfilt. Subsequently, the data was also bandpass filtered between 0.01 and 0.1 Hz (Ciric et al., 2017). To construct resting-state connectivity matrices, the 7 Network 400 parcel variant was used (Schaefer et al., 2018), derived from a well-known atlas of resting networks (Yeo et al., 2011). The MNI registered atlas was used as a mask from which to extract time series from each of the 400 individual regions. All time series were correlated with one another to construct the final matrix. Time-series correlations for regions falling within the FPCN (presented in Figure 1) were averaged to generate a single value representing the connectivity between all regions in the network.

Anatomical parcellation & analysis

The anatomical scans for all participants were preprocessed using FreeSurfer. Using these transformations and the Schaefer atlas registrations in FreeSurfer space, the atlas was back projected onto the MPRAGE. Cortical thickness and volume were extracted using the FPCN as a single region of interest.

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Statistical analyses

There was a minimal missing cognitive test data (i.e., 1.5–4.4% missingness per variable), with a nonsignificant Little's test (Little, 1988), $\chi^2(31) = 22.07$, $p = .881$. Missing neuropsychological test data were imputed using an estimation–maximization method (Enders, 2010), because complete testing data was required in order to calculate the counts of low and high test scores for the full battery. Seven norm-referenced scaled scores ($M = 10$, $SD = 3$) were derived from the RAVLT, TMT Parts A and B, COWAT, and WAIS-IV DS and LNS subtests. The individual neuropsychological test scores, number of low scores (i.e., ≤16th percentile), the number of high scores (i.e., ≥75th percentile), and the three neuroimaging parameters (i.e., bilateral FPCN volume adjusted for intracranial volume, cortical thickness, and connectivity) were compared between participants with and without subjective cognitive concerns using t tests, with Cohen's d reported as a corresponding effect size (Cohen, 1988). The continuous MOS-Cog was also correlated with the count of low and high scores and the neuroimaging parameters in the full sample. Sensitivity analysis (Erdfelder et al., 2009) indicated that the sample had sufficient power ($1 - \beta \leq .80$) to detect a roughly large group difference ($d \geq .70$) and a medium correlation ($r \geq .33$).

Post hoc analyses included (a) an examination of differences in regional volume, thickness, and connectivity of the default mode network (DMN) to determine the specificity of group differences in the FPCN; (b) an evaluation of covariates (i.e., age, sex, physical and mental health variables) with low and high score counts and neuroimaging variables and analyses of covariance controlling for variables related to dependent variables of interest; (c) a comparison of FPCN volume, thickness, and connectivity by scanner upgrade (i.e., 8-channel versus 20-channel); and (d) a comparison of groups on alternative metrics for aggregating neuropsychological test performances, including an intraindividual standard deviation (ISD) as an estimate of intraindividual variability in test performances and the frequency of below average test performances (i.e., <50th percentile).

Results

Cognitive test performances

Participants with and without subjective cognitive concerns were compared on individual neuropsychological test performances (Table 2). Participants with subjective cognitive concerns performed significantly lower on only the COWAT and TMT Part A. A small portion of participants obtained one or more low neuropsychological test scores (i.e., 17.6%) and very few obtained two or more low scores (i.e., 4.4%). Participants without subjective cognitive concerns obtained a similar number of low scores as participants with subjective cognitive concerns (Table 3). Nearly all participants obtained one or more high neuropsychological test scores (i.e., 94.1%), with more than half obtaining four or more high scores (i.e., 58.8%). Participants without subjective cognitive concerns obtained a significantly greater number of high scores compared to participants with subjective cognitive concerns (Table 3). When using the MOS-Cog as a continuous variable, there were no significant associations between subjective cognitive concerns and the number of low scores, $r = -.04$, $p = .720$, or high scores, $r = .19$, $p = .123$.

Neuroimaging

Participants were compared on FPCN regional volume, cortical thickness, and connectivity (Table 4). Participants with subjective cognitive concerns had bilateral lower mean volume and cortical thickness of the FPCN, but did not differ from those without subjective cognitive concerns in network connectivity. None of the neuroimaging variables significantly correlated with the number of high or low scores. Larger FPCN volume significantly correlated with fewer cognitive concerns for the full sample (left: $r = .32$, $p = .009$; right: $r = .35$, $p = .005$). Higher thickness corresponded with fewer cognitive concerns, although the correlations were not statistically significant (left: $r = .24$, $p = .054$; right: $r = .21$, $p = .092$). Connectivity did not correlate with cognitive concerns ($r = -.07$, $p = .583$).

Post hoc analyses

DMN comparisons

To examine the specificity of FPCN differences, participants with and without subjective cognitive concerns were compared on cortical thickness, regional volume, and connectivity of the DMN (Table 4). There were no significant group differences on any neuroimaging variables, albeit right regional volume and bilateral cortical thickness were associated with approximately medium effect sizes (d range: .47–.49) that approached significance (p range: .055–.060).

Examination of covariates

Age was unrelated to the number of low scores, $r = -.08$, $p = .540$, and the number of high scores, $r = .01$, $p = .964$; and sex was unrelated to the number of low scores, $t = .21$, $p = .832$, $d = .06$ [95% Confidence Interval: −.46, .57], and the number of high scores, $t = .97$, $p = .334$, $d = .26$ [−.26, .77]. Age was related to bilateral FPCN cortical thickness (left: $r = -.30$, $p = .015$; right: $r = -.30$, $p = .016$) and volume (left: $r = -.38$, $p = .002$; right: $r = -.41$, $p < .001$), but not connectivity ($r = -.03$, $p = .835$). Sex was related to only left FPCN volume, $t = 2.24$, $p = .029$, $d = .61$ [.06, 1.16], with female participants having higher volume than male participants; but there were no group differences in cortical thickness (left: $t = 1.09$, $p = .281$, $d = .30$ [−.24, .84]; right: $t = .63$, $p = .532$, $d = .17$ [−.37, .71]), right volume ($t = 1.54$, $p = .128$, $d = .42$ [−.12, .96]), or connectivity ($t = 1.58$, $p = .119$, $d = .43$ [−.11, .97]).

Participants with and without subjective cognitive concerns were compared on physical and mental health variables (Table 5). Participants with and without subjective cognitive concerns did not differ in terms of BMI, heart rate, systolic or diastolic blood pressure, or depression. Based on GDS cutoff (i.e., >10), 25% of participants without subjective cognitive concerns and 37.5% of participant with subjective cognitive concerns reported at least mild depression. The groups differed on the PSS, associated with a medium-to-large effect size ($d = .71$). As a continuous variable, the MOS-Cog was significantly correlated with the PSS ($r = -.30$, $p = .015$), but not the GDS ($r = -.10$, $p = .435$). These variables were also examined as correlates of low and high score frequencies and FPCN neuroimaging variables. Higher depression scores correlated with fewer high neuropsychological test scores, $r = -.34$, $p = .007$, and more low scores, $r = .27$, $p = .029$, but no other physical or mental health variables significantly correlated with high or low score counts. Perceived stress and depression were not correlated with any FPCN neuroimaging variables. Greater BMI correlated with increased resting-state FPCN connectivity, $r = .29$, $p = .021$, and reduced FPCN volume in both hemispheres (i.e., left: $r = -.30$, $p = .016$; right: $r = -.29$, $p = .019$). The only other significant correlation indicated higher diastolic blood pressure

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Table 2. Mean performances on individual neuropsychological tests

	Total sample ($n = 68$)			Participants with subjective cognitive concerns ($n = 35$)			Participants without subjective cognitive concerns ($n = 33$)					
	M	*SD*	Range	*M*	*SD*	Range	*M*	*SD*	Range	*t*	*p*	*d* [95% CI]
RAVLT Trials 1-5	11.6	2.9	5–18	11.2	2.7	6–18	11.9	3.0	5–18	1.07	.289	.26 [−.22, .74]
RAVLT Delayed Recall	12.6	3.0	6–18	12.3	3.4	6–18	13.0	2.4	9–18	.98	.331	.24 [−.24, .71]
COWAT	12.3	2.3	6–18	11.7	2.5	6–18	12.9	2.1	8–16	2.15	.035	.52 [.04, 1.00]
WAIS-IV Digit Span	11.8	2.1	6–16	11.4	2.3	6–16	12.1	2.0	8–16	1.28	.204	.31 [−.17, .79]
WAIS-IV LNS	11.0	2.9	6–19	10.6	2.6	6–18	11.5	3.1	8–19	1.41	.163	.34 [−.14, .82]
TMT Part A	11.9	3.2	2–18	11.1	3.1	2–18	12.7	3.1	6–18	2.15	.036	.52 [.04, 1.00]
TMT Part B	12.3	2.7	5–18	11.8	3.0	5–17	12.9	2.3	7–18	1.80	.077	.44 [−.05, .91]

Note. All scores reflect scaled scores ($M = 10$, $SD = 3$). CI = Confidence Interval; COWAT = Controlled Oral Word Association Test; LNS = Letter-Number Sequencing; RAVLT = Rey Auditory Verbal Learning Test; WAIS-IV = Wechsler Adult Intelligence Scale, Fourth edition; TMT = Trail Making Test.

Table 3. Comparison of high-functioning participants with and without subjective cognitive concerns on number of low and high scores on neuropsychological testing

	Participants with subjective cognitive concerns ($n = 35$)		Participants without subjective cognitive concerns ($n = 33$)				
	M (*SD*)	Mdn (range)	*M* (*SD*)	Mdn (range)	*t*	*p*	*d* [95% CI]
Low score count (≤16th percentile)	0.4 (0.7)	0 (0–3)	0.2 (0.5)	0 (0–2)	1.66	.103	.40 [−.09, .88]
Low score count (<50th percentile)	1.8 (1.5)	2 (0–6)	0.8 (0.8)	1 (0–3)	3.48	<.001	.84 [.34, 1.32]
High score count (≥75th percentile)	3.1 (2.0)	3 (0–7)	4.4 (1.5)	5 (2–7)	2.95	.004	.71 [.22, 1.20]

Note. CI = Confidence Interval.

Table 4. Comparison of high-functioning participants with and without subjective cognitive concerns on volume, thickness, and connectivity of the frontoparietal control and default mode networks

			Participants with subjective cognitive concerns ($n = 32$)	Participants without subjective cognitive concerns ($n = 32$)			
Network	Variable	Hemisphere	*M* (*SD*)	*M* (*SD*)	*t*	*p*	*d* [95% CI]
Frontoparietal	Regional volume	Left	.0088 (.0009)	.0094 (.0008)	2.98	.004	.74 [.23, 1.25]
		Right	.0073 (.0007)	.0078 (.0006)	2.63	.011	.66 [.15, 1.16]
	Cortical thickness	Left	2.292 (.102)	2.364 (.115)	2.65	.010	.66 [.16, 1.16]
		Right	2.298 (.088)	2.343 (.078)	2.18	.033	.54 [.04, 1.04]
	Connectivity	–	.3768 (.1813)	.3356 (.1843)	−.90	.371	−.23 [−.72, .26]
Default mode	Regional volume	Left	.0128 (.00107)	.0132 (.00097)	1.46	.149	.36 [−.13, .85]
		Right	.0135 (.00105)	.0140 (.00108)	1.91	.060	.48 [−.02, .98]
	Cortical thickness	Left	2.427 (.122)	2.485 (.122)	1.90	.063	.47 [−.03, .97]
		Right	2.453 (.109)	2.504 (.100)	1.96	.055	.49 [−.01, .98]
	Connectivity	–	.4401 (.1780)	.3976 (.1733)	−.96	.337	−.24 [−.73, .25]

Note. CI = Confidence Interval; $n = 32$ per group due to three participants with subjective cognitive concerns missing. For regional volumes, units were mm^3, standardized by intracranial volume; for cortical thickness, units were mm; and for stationary connectivity, units were mean *r* value.

Table 5. Comparison of high-functioning participants with and without subjective cognitive concerns on physical and mental health variables

		Participants with subjective cognitive concerns ($n = 32$)	Participants without subjective cognitive concerns ($n = 32$)			
Domain	Variable	*M* (*SD*)	*M* (*SD*)	*t*	*p*	*d* [95% CI]
Physical health	Body mass index	26.6 (5.9)	25.7 (3.5)	.72	.476	.18 [.31, .67]
	Heart rate	65.1 (9.9)	66.5 (9.3)	.57	.574	.15 [−.36, .64]
	Systolic blood pressure	135.8 (19.6)	128.7 (21.1)	.49	.623	.35 [−.16, .85]
	Diastolic blood pressure	75.7 (7.1)	76.7 (9.2)	1.37	.177	.13 [−.37, .62]
Mental health	Perceived stress scale	19.4 (3.4)	17.3 (2.1)	2.84	.003	.71 [.20, 1.21]
	Geriatric depression scale	8.2 (4.1)	6.6 (4.8)	1.43	.157	.36 [−.14, .85]

Note. CI = Confidence Interval; $n = 32$ per group due to three participants with subjective cognitive concerns missing; For the Perceived Stress Scale and Geriatric Depression Scale, Levene's test of equality of variance was significant ($p < .05$) and equal variance was not assumed.

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was associated with greater FPCN cortical thickness in the right hemisphere, $r = .31$, $p = .014$.

Per these analyses, a series of analyses of covariance were conducted controlling for covariates that were related to either subjective cognitive concerns or the dependent variable of interest. Controlling for PSS and GDS, participants with and without subjective cognitive concerns significantly differed in their number of high scores, $F = 6.75$, $p = .012$, $\eta_p^2 = .10$, but not number of low scores, $F = 2.26$, $p = .138$, $\eta_p^2 = .04$. Controlling for age, sex, and BMI, the groups differed in FPCN volume in the left hemisphere, $F = 4.70$, $p = .034$, $\eta_p^2 = .07$, but not the right hemisphere, $F = 3.37$, $p = .072$, $\eta_p^2 = .05$. Controlling for age and systolic and diastolic blood pressure, participants differed in FPCN cortical thickness in the left hemisphere, $F = 4.41$, $p = .040$, $\eta_p^2 = .07$, but not the right hemisphere, $F = 3.57$, $p = .064$, $\eta_p^2 = .06$. Controlling for BMI, groups did not differ in FPCN connectivity, $F = .52$, $p = .474$, $\eta_p^2 = .01$.

Scanner upgrade

The scanner array head coil was upgraded from 8-channel to 20-channel during data collection. Post hoc analyses examined differences based on scanner. The groups were compared on FPCN variables, including volume (left: $t = .30$, $p = .769$; right: $t = 1.26$, $p = .211$), thickness (left: $t = .35$, $p = .732$; right: $t = .06$, $p = .952$), and connectivity ($t = 1.50$, $p = .140$), collectively indicating no group differences related to the scanner upgrade.

Alternative methods of neuropsychological test interpretation

To examine whether differences in high and low scores were attributable to differences in performance variability across neuropsychological tests, participants were compared on their ISD. The mean ISD for participants with subjective cognitive concerns were essentially identical ($M = 2.4$, $SD = 0.7$ for both groups) and did not significantly differ, $t = .11$, $p = .913$, $d = .03$ [−.45, .50]. Participants were also compared on number of scores<50th percentile, with results reported in Table 3. Participants with subjective cognitive concerns obtained more scores<50th percentile than participants without subjective cognitive concerns.

Discussion

This study compared high-functioning older adults (i.e., estimated FSIQ ≥75th percentile or college-educated) with and without subjective cognitive concerns on the number of low scores and high scores obtained on a seven-test neuropsychological battery and FPCN regional volume, cortical thickness, and connectivity. Whereas no difference was observed between groups in the number of low scores, participants with subjective cognitive concerns had fewer high scores ($M = 3.1$, $SD = 2.0$; Mdn = 3, range: 0–7) than those without subjective cognitive concerns ($M = 4.4$, $SD = 1.5$; Mdn = 5, range: 2–7), with a large effect size ($d = .71$ [95% CI: .22, 1.20]). Post hoc analyses indicated a large group difference in counts of scores<50th percentile as well ($d = .84$ [.34, 1.32]), with participants with subjective cognitive concerns ($M = 1.8$, $SD = 1.5$; Mdn = 2, range: 0–6) again having more scores below this cutoff than participants without subjective cognitive concerns ($M = 0.8$, $SD = 0.8$; Mdn = 1, range: 0–3). These differences in test performances were not attributable to intraindividual variability, which appears related to cognitive aging (Hultsch et al., 2008), but did not differ between groups in the current sample. Participants with subjective cognitive concerns also had lower bilateral FPCN volume and cortical thickness, with medium-to-large effect sizes (d range: .54–.74). Collectively, these findings indicate that high-functioning older adults who report subjective cognitive concerns (a) may be experiencing underlying neurological changes that do not correspond with obtaining low scores on neuropsychological testing, and (b) may be experiencing cognitive decline indicated by a reduction in high scores from a prior higher ability level.

Among high-functioning older adults, frontoparietal regions and network activity have been examined in the context of research on cognitive reserve, which is often estimated based on higher education, occupational attainment, and/or premorbid intelligence. The current sample would be considered to have high cognitive reserve per most research definitions (Stern et al., 2020). Higher premorbid IQ has been associated with less frontal activity in healthy older adults (Solé-Padullés et al., 2009; Steffener et al., 2011), whereas a higher cognitive reserve composite (e.g., based on premorbid IQ, education, and occupation) has been associated with greater gray matter volume in frontoparietal regions (Bartrés-Faz et al., 2009). Per these prior findings, increased functional activity and lower frontoparietal volume may correspond with an underlying decline in high-functioning older adults. There were no functional differences at resting-state observed in the current study, but lower bilateral volume and thickness in frontoparietal regions was observed. Participants with subjective cognitive concerns may be noticing changes that correspond with greater perceived cognitive difficulties in everyday life and a reduction in high scores on testing. These changes may be explained by underlying changes in frontoparietal or other regions.

Post hoc analyses were conducted that (a) controlled for relevant demographic and physical and health variables as covariates, and (b) examined the DMN to determine whether group differences were specific to the FPCN. The adjusted analyses indicated that group differences in frontoparietal volume and thickness were specific to the left hemisphere after controlling for demographic and physical health variables, which were associated with slightly larger effect sizes in unadjusted group comparisons. This finding indicates that volume differences between high-functioning older adults with and without subjective cognitive concerns are more pronounced in the left hemisphere, which aligns with research indicating that the left frontal cortex may underlie reserve capacity in both normal aging and Alzheimer's disease (Franzmeier et al., 2018). Group differences were not observed for the DMN, which has shown associations with cognitive aging (Hafkemeijer et al., 2012). Many effect sizes for the DMN were small-to-medium, and neared significance for some volume and thickness variables, meaning the sample was underpowered to detect more subtle effects than observed for the FPCN.

The neuroimaging findings add to a growing body of research on brain differences between older adults with and without subjective cognitive concerns (Parker et al., 2022). Researchers have compared older adults with subjective cognitive decline to healthy control participants, finding frontal differences (Archer et al., 2010; Hong et al., 2015; Kuhn et al., 2019; Toledo et al., 2015) and parietal differences (Archer et al., 2010; Hong et al., 2015) in regional volume and thickness. Researchers have also found differences on structural MRI in other brain regions not explored in the current study, including regions typically impacted in Alzheimer's disease, such as the entorhinal cortex (Fan et al., 2018; Meiberth et al., 2015; Ryu et al., 2017) and hippocampus (Archer et al., 2010; Hafkemeijer et al., 2013; Perrotin et al., 2015; Striepens et al., 2010). Although group differences in functional connectivity

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were not observed for the current sample, functional MRI studies have found decreased activation in frontal regions in subjective cognitive decline (Yasuno et al., 2015). In aggregate, neurological differences appear associated with subjective cognitive decline in older adults, with the current findings indicating volumetric and cortical thickness differences specific to the FPCN.

A key issue in detecting a degenerative process in high-functioning older adults is that much more cognitive and neurological change must occur before the individual would present with traditionally low cognitive test scores (e.g., ≤16th percentile) or the cognitive change would begin to interfere with activities of daily living. That said, the underlying change is still occurring, and early detection may allow for earlier intervention. In the absence of low test scores or functional impairment, subjective cognitive concerns have been associated with global amyloid burden in community-dwelling older adults (Buckley et al., 2019), increased risk for mild cognitive impairment and dementia (Jessen et al., 2020), and, in the current study, lower FPCN volume and thickness in high-functioning older adults. As opposed to awaiting low scores to present on testing, self-reported perceptions of cognitive change and an absence of high scores on neuropsychological assessment may align with underlying pathology that is not detected through a traditional focus on low scores.

A relatively sparse literature has examined neuropsychological methods for detecting potential cognitive decline in high-functioning older adults. Existing evidence suggests that the consideration of premorbid intelligence in normative comparisons captures cases of cognitive decline that may otherwise be overlooked. An early study examined the use of NAART FSIQ to adjust normative comparisons among 58 high-functioning older adults, finding that FSIQ-adjusted norms led to the detection of a possible Alzheimer's process that may have been missed when using age-adjusted norms alone (Rentz et al., 2000). In one sample of 42 highly intelligent older individuals, no participants had any cognitive impairments using age-based norms; but, when using IQ-adjusted norms, 47.6% were detected as having either executive or memory impairments, which predicted further decline at 3.5 years follow-up (Rentz et al., 2004). Traditional approaches to neuropsychological assessment may fail to detect cognitive decline in high-functioning older adults, leading researchers to develop IQ-based normative data for highly intelligent people, albeit with a limited sample size of 75 participants (Rentz et al., 2006). Researchers have even called for norms specific to high-level professions (e.g., physician-based normative data) (Gaudet & Del Bene, 2022).

As a way to control for baseline ability level, multiple approaches exist to estimate premorbid intelligence (Kirton et al., 2020), but there are rarely stratifications of normative data by IQ or score adjustments for IQ. More often, education is considered as a proxy for premorbid ability, either through demographic-adjusted scores or normative stratifications. In the current study, some participants with college degrees did not have a NAART FSIQ ≥75th percentile ($n = 8$; 11.7%), and some participants with NAART FSIQ ≥75th percentile did not obtain a college degree ($n = 6$; 8.8%). The use of education stratifications or adjustments may lead to a normative comparison sample that does not match the intelligence of a high-functioning examinee, rationalizing greater use of alternative approaches to detecting potential cognitive decline. These could include IQ-stratified norms or multivariate base rates of high scores to determine whether the number of high scores obtained on testing is fewer than expected.

Few studies have examined the normal frequency of high scores on neuropsychological test batteries, with multivariate base rates of high scores developed for only the D-KEFS (Karr et al., 2020) and the NIHTB-CB (Iverson & Karr, 2021; Karr & Iverson, 2020; Karr et al., 2022b). These studies have provided base rates of obtaining no high scores among healthy adults, with stratifications by estimated intelligence. When interpreting the seven D-KEFS test scores, just 4.8% of participants with a FSIQ ≥ 110 obtained no scores ≥75th percentile, making it uncommon to obtain no high scores among high-functioning adults. Per the current findings, subjective cognitive concerns are associated with both obtaining fewer high scores and underlying MRI-derived neurological changes among high-functioning older adults.

Multivariate base rates of high scores, with stratifications by intelligence, provide base rates of obtaining few or no high scores, and can allow for an indirect translation of the current findings into clinical practice. Take for example, a 68-year-old woman of high intelligence with a doctoral degree who works as a provost at an American university. Upon renewal of her appointment, multiple subordinate employees describe work performance changes, noting disorganization, forgetfulness, and inattentiveness. Her husband reports greater irritability. She reports more difficulty at work, noting greater difficulty with management responsibilities in the last year. She completes the Neuro-QoL Cognitive Function questionnaire (Cella et al., 2012; Gershon et al., 2012), reporting significant subjective cognitive concerns (T = 32). On neuropsychological assessment, she completes the WASI (FSIQ = 120); Wechsler Memory Scale (WMS-IV) subtests (Logical Memory – Immediate: Scaled Score [SS] = 12; Delayed: SS = 9) and Visual Reproduction (Immediate: SS = 12; Delayed: SS = 10); and D-KEFS tests, including Trail Making (Number-Letter Switching – Time-to-Completion: SS = 12), Verbal Fluency (Letter Fluency – Total Correct: SS = 11; Category Fluency – Total Correct: SS = 10; Category Switching – Total Correct: SS = 10; Category Switching – Total Switching Accuracy: SS = 9), and Color-Word Interference (Inhibition – Time-to-Completion: SS = 11; Inhibition/Switching – Time-to-Completion: SS = 11).

This examinee obtains two scores ≥75th percentile on WMS-IV Logical Memory and Visual Reproduction Immediate trials, but has average Delayed trial performances; and on the D-KEFS, all performances fall within the average range apart from Trail Making, which was 75th percentile. The base rates of high scores on the WMS-IV have not been published, but these findings indicate a reduction in performances at the delayed trial. For the D-KEFS, obtaining one score ≥75th percentile occurs among just 16.9% of healthy adults in the normative sample with WASI FSIQ ≥ 110 (Karr et al., 2020). This performance approximates ~ 1 *SD* below the mean in comparison to an IQ-matched normative comparison group. Considering self- and informant-reported subjective cognitive concerns and fewer high scores than expected, this examinee may be experiencing cognitive decline, despite obtaining no low test scores (i.e., ≤16th percentile).

A focus on methods for detecting potential cognitive decline in high-functioning older adults is warranted, as even average performances in cognition may correspond with reduced work capacity in high-level positions and cognitive decline in this population has been associated with broader health concerns, including increased risk of hospitalization (Chodosh et al., 2004) and reduced gait speed (Rosso et al., 2019), which may correspond with increased fall risk (Menant et al., 2014). Further, early interventions may be beneficial before underlying degeneration advances enough to produce low scores on cognitive testing.

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Dietary changes may be beneficial, with research demonstrating that antioxidants and beta-carotene may be protective against cognitive decline among high-functioning older adults (Hu et al., 2006). Many clinical trials have examined nonpharmacological interventions among older adults with subjective cognitive decline (e.g., exercise, cognitive training), finding evidence for a benefit on cognitive functioning (Smart et al., 2017).

This study provides insight into the correspondence between subjective cognitive concerns, the number of high scores obtained on neuropsychological testing, and underlying neurological differences, indicating that high-functioning older adults with subjective cognitive concerns tend to obtain fewer high scores and have lower FPCN volume and thickness. Although novel, this study has limitations that affect the generalizability of the findings. Subjective cognitive concerns were measured for the past month, as opposed to a longer onset; meaning such concerns may be transient rather than indicating long-term perceptions of decline. These concerns were correlated with perceived stress in the past month, but not mood in the past week. The sample size was relatively small and homogenous, consisting of primarily women (i.e., 69.1%), nearly all of whom were White (i.e., 97.1%), recruited from a single urban area in a midwestern state. Complete data was required to produce high and low score counts for individual participants, which led to imputation of some data. These findings may vary from results that would be obtained from a sample without missingness. By design, the sample was highly educated (i.e., 91.2% with a college degree), but involved limited representation of highly intelligent older adults without college degrees. Although there was substantial correspondence between NAART estimated FSIQ and college education, these variables are both proxies of premorbid functioning, and other variables, such as occupational complexity, were not considered when selecting this high-functioning sample. Per annual household income, there was a broad range of socioeconomic status of participants (i.e., range: $12,000–$500,000). The test battery was also brief, with just seven-test scores interpreted for analyses, which is much lower than the number of test scores typically obtained during a neuropsychological assessment. These findings offer preliminary evidence that subjective cognitive concerns and a lower number of high scores may indicate cognitive decline in high-functioning older adults, but future research is needed to examine more diverse samples using test batteries more consistent with neuropsychological practice. Such studies would both replicate the current findings and expand their generalizability and translation into practice.

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