

# **Body mass index moderates brain dynamics and executive function: A structural equation modeling approach**

Running title: Body mass index impacts on brain dynamics and executive function

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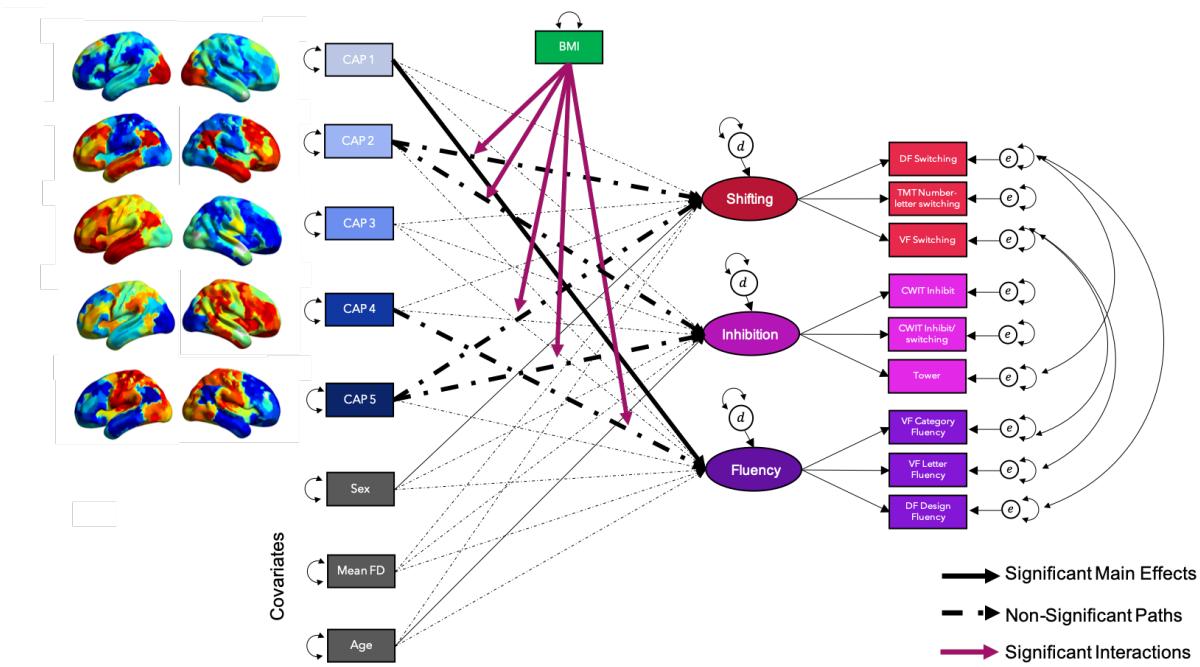
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## Graphical Abstract



## Abstract

Obesity is associated with negative physical and mental health outcomes. Being overweight/obese is also associated with executive functioning impairments and structural changes in the brain. However, the impact of body mass index (BMI) on the relationship between brain dynamics and executive function (EF) is unknown. The goal of the study was to assess the modulatory effects of BMI on brain dynamics and EF. A large sample of neuroimaging and neuropsychological assessment data collected from 253 adults (18-45 years; mean BMI  $26.95 \text{ kg/m}^2 \pm 5.90 \text{ SD}$ ) from the Nathan-Kline Institute (NKI) were included ([http://fcon\\_1000.projects.nitrc.org/indi/enhanced/](http://fcon_1000.projects.nitrc.org/indi/enhanced/)). Participants underwent resting-state functional MRI and the Delis Kaplan Executive Function System (D-KEFS) test battery (1). Time series were extracted from 400 brain nodes and used in a co-activation pattern analysis (CAP). *K*-means clustering was used to determine the dynamic co-activation patterns. Dynamic CAP metrics including dwell time (DT), frequency of occurrence, and transitions were computed. Multiple measurement models were compared based on model fit with indicators

from the D-KEFS assigned *a priori* (shifting, inhibition, and fluency). Multiple structural equation models were computed with interactions between BMI and the dynamic CAP metrics predicting the three latent factors of shifting, inhibition, and fluency. Models with non-significant interactions were assessed for main effects of BMI and CAP metrics predicting the latent factors. A three-factor model (shifting, inhibition, and fluency) resulted in the best model fit. BMI was significantly associated with shifting and inhibition scores. CAP 1 DT (visual network) was significantly associated with inhibition. Significant interactions were present between BMI and CAP 2 (lateral frontoparietal (L-FPN), medial frontoparietal (M-FPN) and limbic nodes) and CAP 5 (dorsal frontoparietal (D-FPN), midcingulo-insular (M-CIN), somatosensory motor, and visual network nodes) DTs associated with both shifting and inhibition. Additionally, there was a significant interaction between BMI and CAP 4 (L-FPN, DAN, limbic, and M-CIN) DT associated with fluency. In all significant models except for inhibition, a higher BMI was associated with a positive relationship between CAP DTs and EF. Conversely, in average and low BMI participants, a negative relationship was seen between CAP DTs and EF. Our findings indicate that BMI moderates the relationship between brain dynamics of networks important for cognitive control and EF components including shifting, inhibition, and fluency. Furthermore, higher BMI is linked with altered brain dynamic patterns associated with EF.

### **Lay Summary**

Being overweight or obese is a major public health concern and impacts not just physical health symptoms, but also cognitive functioning and brain structure and function. However, little is known about how weight or body mass index (BMI) impacts the relationship between brain dynamics, or time-varying brain network connections, and executive function in the domains of

inhibition, shifting, and fluency. Using co-activation pattern analysis, a method to examine dynamic relationships among brain networks, and structural equation modeling, we identified various co-activation patterns that were moderated by BMI when predicting inhibition, shifting, and fluency. Our findings provide novel information showing that the relationship between various co-activation patterns and executive function depends on BMI. Our results suggest this relationship is specifically altered in overweight/obese individuals and BMI should be considered when studying brain network dynamics and executive function.

## **Introduction**

Overweight and obesity are prevalent in one-third of the world population (2) and 42.4% of adults in the United States (3). Obesity accounts for over 2.8 million deaths per year (4), and a body mass index (BMI)  $\geq 30$  is additionally a risk factor for greater complications as a result of the novel coronavirus (COVID-19) (5). Overweight (BMI 25 to  $< 30$ ) and obesity are typically considered physical health conditions associated with comorbid conditions such as type II diabetes and cardiovascular disease (6). In addition to these health concerns, obesity is increasingly being linked with cognitive impairments and brain alterations (7–9). Cognitive impairments are found to worsen with increasing BMI (10,11) throughout the lifespan (11). Additionally, obesity during midlife is associated with greater risks of dementia in later-life (12) and brain atrophy (13).

Accumulating evidence supports cognitive impairment in the form of executive function (EF) deficits in overweight/obese individuals (14,15). EFs are higher order cognitive processes that enable goal-oriented behaviors (16,17) and are important for various aspects of daily functioning including maintaining a job (18), social functioning (19,20), and well-being (21). EFs can be divided into distinct but related components (22) including inhibition, cognitive flexibility, and updating (23,24). A recent meta-analysis revealed that individuals with obesity primarily show impairments on EF tasks that require inhibition, cognitive flexibility, working-memory, decision-making, verbal fluency, and planning (15). Additionally, impairments in EF and overweight/obesity are associated with negative impacts on mental health such as anxiety and depression (25–28).

A common neuropsychological test used to assess EF is the Delis-Kaplan Executive Function System (D-KEFS; (1). The D-KEFS consists of nine tests of varying EF components;

however, composite scores within the tests have been tested as construct-specific factors rather than stand-alone tests (29,30). The use of latent variables as dependent variables reduces the task impurity problem by tapping into the underlying construct rather than relying on one impure measure of a task. The latent variable is characterized by statistical extraction of the variance shared by multiple tasks that are thought to require the same executive control ability, resulting in a purer measure of the ability (31,32). The D-KEFS does not include direct tests within the latent factor of updating (i.e., continuously monitoring working memory and updating content), which is thought to be one of three EF constructs in well known latent models of executive functioning (23). Subsequently, the three constructs instead include shifting, inhibition, and fluency (33). The three latent factors of D-KEFS are defined as: 1) shifting or the mental ability to switch or shift in response to changing stimuli (an index of cognitive flexibility) (34), 2) inhibition or the ability to control one's behavior and thoughts to inhibit responses (16), and 3) fluency, thought to underlie executive control and updating (35), fluency in generating new designs (i.e., creativity) (36), and an index of verbal abilities.

Recent studies examining brain functional connectivity (FC) in overweight/obesity have identified alterations in brain networks rather than specific brain regions that may impact EF. Studies have reported network alterations among the midcingulo-insular/salience network (M-CIN), medial frontoparietal/default network (M-FPN), and lateral frontoparietal/central executive network (L-FPN) in overweight/obese individuals (37–39). The M-CIN plays a role in detecting salient information and coordinating transitions between the L-FPN and M-FPN; The L-FPN is involved in executive or control processes; The M-FPN is involved in self referential thoughts and monitoring of the environment (40). The dynamic relationships among these three core neurocognitive networks are additionally thought to enable flexible cognition (40,41), important

for EFs. Alterations among the M-CIN, L-FPN, and M-FPN in overweight/obesity provides further support for altered reward processing and EF, and cognitive and emotional processing of salient food cues (42). Alterations among these networks have also been previously associated with various neuropsychiatric disorders (43), suggesting these networks are important treatment targets for populations such as obese individuals.

Evidence of brain alterations among the three large-scale neurocognitive networks provide important insights into potential neural mechanisms underlying behavior; however, whole brain FC studies have revealed alterations among other regions in overweight/obese individuals. FC alterations have been observed between the aforementioned three large-scale networks and visual (39,44,45), limbic (46), sensorimotor (39,47), and dorsal frontoparietal networks (D-FPN; dorsal attention) (39). These findings suggest it is important to examine whole-brain network relationships in overweight/obesity. Further, brain regions important for monitoring external and internal processes are altered in overweight/obesity and may reduce network flexibility supporting EF and adaptive behavior.

There are very few studies to date that have examined the relationship among EF, BMI, and the brain (48,49), and no study to date examining BMI as a moderator of the relationship between brain network dynamics and EF. Brain network dynamics have previously been shown to predict EF performance irrespective to BMI (50). Recent work has also shown that brain network dynamics of the L-FPN, thought to underlie EFs, was correlated with BMI (51). Therefore, it is plausible to consider whether the relationship between brain dynamics and EF may depend on the individual's BMI. Although the studies reviewed support a link between BMI, EF, and the brain, the directionality remains unclear. Previous work has suggested bi-directional relationships among all factors (11,37), and have shown the brain may be a predictor,

mediator, or dependent variable related to BMI and cognition (52). However, there is evidence that the relationship between the brain and EF may change as a result of BMI. For example, a low-grade inflammatory response characterized in obesity has been shown to alter the brain and cause EF impairments (15,53). Although this supports a causal link from BMI to the brain and EF, this also highlights the importance to examine the change in the relationship between the brain and EF across dimensional levels of BMI.

Although FC and structural methods have provided insight into brain organization differences in overweight/obese individuals, recent developments in neuroimaging posit dynamic methods, such as sliding window correlations (54,55) and co-activation patterns (CAPs) (54,56), may be applied to capture time-varying changes in the brain architecture (see (57)). Further, dynamic or time-varying methods may, in some cases, better capture relationships between brain function and cognition and behavior than static FC methods (58,59). Dynamic methods have also been shown to reveal relationships with BMI and behavior where static methods were unable to (51). CAPs, in particular, identify critical co-activating patterns that recur across time by averaging time points with similar spatial distributions of brain activity at either the whole-brain or region-of-interest level (60). Further, CAPs require the specification of fewer assumptions than sliding window methods as they do not rely on arbitrary definitions of window size. CAPs have also been utilized to study neuropsychiatric disorders such as autism (61,62) and dynamic network changes across the lifespan (Kupis et al., submitted). Despite the advantages to using dynamic MRI methods over static MRI methods, no study to date has examined dynamic brain network alterations during rest across BMI or its association with EF. Further, exploring relationships among brain networks using brain dynamics has shown to be beneficial for the study of EF due to the various networks underlying EF (50).

The current study aims to explore BMI as a moderator of the relationship between whole brain CAP dynamics and EF, indexed by latent factors of shifting, fluency, and inhibition, using structural equation modeling. Examination of the dynamic interactions among the M-CIN, L-FPN, and M-FPN have provided important information about the network interactions subserving cognition, however, large-scale network interactions with other brain regions, such as the visual network, also lends insight into flexible cognition (63). Therefore, whole-brain network co-activations were assessed in this study. We hypothesized that a higher BMI would be associated with an altered relationship between brain network dynamics among the M-CIN, M-FPN, and L-FPN and shifting, an index of cognitive flexibility (34).

## Methods

### *Participants*

The current study included a sample of 253 adults (18-45 years) from the publicly available Nathan-Kline Institute-Rockland Sample ([http://fcon\\_1000.projects.nitrc.org/indi/enhanced/](http://fcon_1000.projects.nitrc.org/indi/enhanced/)). Inclusionary criteria were 1) available neuroimaging and behavioral data 2) no current DSM diagnosis 3) mean framewise displacement (FD) < 0.5 mm (**Table 1**). Institutional Review Board Approval was obtained for this project and written informed consent was obtained for all study participants.

### **Table 1**

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	<b>N = 253</b>
	<b>mean ± SD (minimum - maximum)</b>
BMI (kg/m <sup>2</sup> )	26.95 ± 5.90 (16.26 - 49.96)
Age (years)	28.44 ± 7.55 (18.15 - 44.82)
Mean FD (mm)	0.23 ± 0.09 (0.08 - 0.49)
Sex	105 M/ 148 F
DF Switching	8.59 ± 2.94 (1.00 - 16.00)
TMT	9.97 ± 2.83 (1.00 - 15.00)
VF Switching	10.47 ± 3.56 (1.00 - 19.00)
CWIT Inhibition	10.26 ± 2.89 (1.00 - 16.00)
CWIT Inhibition/Switching	9.89 ± 3.04 (1.00 - 14.00)
Tower Total Achievement	9.99 ± 2.36 (2.00 - 19.00)
VF Letter Fluency	10.61 ± 3.44 (1.00 - 19.00)
VF Category Fluency	11.28 ± 3.64 (2.00 - 19.00)
DF Composite Score	10.42 ± 2.69 (4.00 - 18.00)

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Note: BMI, body mass index; FD, framewise displacement; DF, Design Fluency; TMT, Trail Making Test; VF, Verbal Fluency; CWIT, Color-Word Interference.

## Measures

### *Body Mass Index*

BMI was calculated from weight in kilograms divided by height in meters squared ( $\text{kg}/\text{m}^2$ ) for all participants. Weight and height were measured during the study visit by study staff. Participants ranged in their BMI from underweight (< 18.5 BMI), healthy weight (18.5 to < 20 BMI), overweight (25 to < 30 BMI) and obese (30 or higher BMI). For the purpose of this

study overweight/obesity are discussed interchangeably. See **Figure S1** for a graphical distribution of BMI in this sample.

### *Shifting*

The Delis-Kaplan Executive Function System (D-KEFS) was administered to all participants (1). The tasks with shifting (an index of cognitive flexibility) conditions within the D-KEFS include the Trail Making Test (TMT), the Design Fluency (DF) Test, and the Verbal Fluency (VF) Task. The TMT consists of five conditions, including the Number-Letter Switching condition (64). During the Number-Letter Switching condition, subjects switch back and forth between connecting numbers and letters (i.e., 1, A, 2, B etc.) (65). The DF test consists of three conditions including a Switching Condition. In the Switching Condition, participants are asked to alternate between connecting empty and filled dots. Lastly, the VF test consists of three conditions, including the Category Switching condition. During the Category Switching condition, participants alternate between saying words from two different semantic categories.

### *Inhibition*

The D-KEFS tasks with inhibition conditions included the color-word interference task (CWIT) and the Tower Test. The CWIT is a modified Stroop task and consists of four conditions including an inhibition and inhibition/switching condition. In the CWIT Inhibition Condition, the participant is presented with color names that are written in incongruent ink color. The participant is required to name the ink color and ignore the written word. Therefore, participants have to inhibit saying the more automatic written word response. In the Inhibition/Switching Condition, participants are presented with a page containing the words “red”, “green”, and “blue”, written in red, green, or blue ink. Some of the words are contained in a box and the subject must switch between saying the color of the ink (word is not inside a box) or the color of

the word (word inside a box). The Tower Test examines the participant's ability to plan and carry out steps to attain a desired goal.

### *Fluency*

The D-KEFS tasks with fluency conditions included the VF Test and the DF Test. The fluency measures in the VF Test include the Letter Fluency and Category Fluency conditions. In both conditions, participants must generate as many words as possible within 60 seconds, beginning with either a specific letter or within a specific category. The DF Test included trials where participants had to connect either empty or filled dots.

### *MRI Protocol*

Three-dimensional magnetization-prepared rapid gradient-echo imaging (3D-MP-RAGE) structural scans and multiband (factor of 4) EPI sequenced resting-state fMRI (rsfMRI) were acquired using a Siemens TrioTM 3.0 T MRI scanner. Scanning parameters were: TR = 1400 ms, 2 x 2 x 2 mm, 64 interleaved slices, TE = 30 ms, flip angle = 65 degrees, field of view (FOV) = 224 mm, 404 volumes. Participants were instructed to keep their eyes open and fixate on a cross in the center of the screen during the 9.4-minute rsfMRI scan. For detailed MRI protocol information see: [http://fcon\\_1000.projects.nitrc.org/indi/pro/nki.html](http://fcon_1000.projects.nitrc.org/indi/pro/nki.html).

### *Preprocessing and Postprocessing*

Preprocessing steps were conducted using the Data Preprocessing Assistant for Resting-State fMRI Advanced edition (DPARSF-A, (66), which uses FSL and SPM-12 (<https://www.fil.ion.ucl.ac.uk/spm/software/spm12/>), and were as follows: removal of the first 5 volumes to allow scanner signal to reach equilibrium, despiking, realignment, normalization directly to the 3 mm MNI template, and smoothing (6 mm FWHM).

Independent component analysis (ICA) was conducted using FSL's MELODIC by means of automatic dimensionality estimation. The ICA-FIX classification algorithm was applied to the data (FMIRB's ICA-FIX; (67) using a subset of the participants to train FIX. ICA-FIX then classified ICA into noise and non-noise components for the resting-state fMRI data for individual subjects. The fMRI data also underwent nuisance covariance regression (linear detrend, Friston 24 motion parameters, global mean signal), despiking using AFNI's 3dDespike algorithm, and bandpass filtering (0.01-0.10 Hz). Information about the data without global mean signal regression is included in the **Supplementary Materials**.

#### *Parcellation*

A 400 node parcellation was used containing nodes within 17 networks (68) :[https://github.com/ThomasYeoLab/CBIG/tree/master/stable\\_projects/brain\\_parcellation/Schaefer2018\\_LocalGlobal](https://github.com/ThomasYeoLab/CBIG/tree/master/stable_projects/brain_parcellation/Schaefer2018_LocalGlobal)). The parcellation incorporates local gradient and global similarity approaches from task-based and resting-state functional connectivity.

#### *Co-activation Pattern (CAP) Analysis*

The time series were extracted from the 400 nodes for each subject and were converted to z-statistics and concatenated into one (nodes x timepoints) matrix (where the number of timepoints is 399 TR x 253 subjects). The matrix was then subjected to  $k$ -means clustering to determine the optimal number of clusters. The elbow criterion was applied to the cluster validity index (the ratio between within-cluster to between-cluster distance) for values of  $k = 2-20$  and an optimal value of  $k = 5$  was determined (**Figure S2**).

$K$ -means clustering (squared Euclidean distance) was then applied to the matrix using the optimal  $k = 5$  to produce 5 CAPs (“brain states”). CAP metrics were calculated and included: a) dwell time (DT), calculated as the average number of continuous TRs that a participant stayed in

a given brain state, b) frequency of occurrence of brain states, calculated as an overall percentage that the brain state occurred throughout the duration of the resting-state fMRI scan compared to other brain states, and c) the number of transitions, calculated as the number of switches between any two brain states.

### *Statistical Analysis*

The normative data were age-corrected for all D-KEFS variables. All data were screened for outliers, missingness in data, and tests of assumptions. Additionally, each CAP was assessed prior to statistical modeling to determine if the brain regions co-activated in each CAP had theoretical support behind including the CAP in the models. Using a two step procedure, a measurement model was evaluated first to ensure an acceptable fit for the data, then a structural moderated model was examined. Confirmatory factor analysis (measurement model) and structural equation modeling (SEM) were conducted in MPlus (69) using maximum likelihood to estimate model parameters and full information maximum likelihood approach to allow data to be included regardless of the pattern of missingness in the data. Code for all MPlus analyses are publicly available ([https://github.com/lkupis/NKI\\_BMI](https://github.com/lkupis/NKI_BMI)). Covariates included mean FD, age, and sex. All models were assessed for goodness of fit by examining:  $\chi^2$ , comparative fit index (CFI), standardized root-mean square residual (SRMR), and root mean square error of approximation (RMSEA).  $\chi^2 > .05$ ,  $CFI \geq .95$ , SRMR values  $\leq .08$ , and RMSEA values  $\leq .06$  indicated good model fit.

### *Confirmatory Factor Analysis*

A three-factor model was tested based on prior findings of a three-factor model using the D-KEFS (33). The three factors were shifting, inhibition, and fluency. Additionally, all indicators used were scaled or age adjusted scores ( $M = 10$ ,  $SD = 3$ ).

The indicators for shifting included the TMT Number-Letter Switching Condition, the DF Switching Condition, and the VF Switching Condition scores. The shifting indicator in the TMT condition was the Number-Letter Switching-Total score or time-to-completion. The shifting indicator in the DF Switching Condition was the Switching Total Correct score or the number of unique designs drawn. The shifting indicator in the VF test was the total correct number of category switches made.

The indicators for inhibition included the CWIT Inhibition and Inhibition/Switching Conditions and Tower total achievement score. The inhibition indicator for the CWIT Inhibition Condition was the total number of correct responses. The inhibition indicator in the Tower Test was the Total Achievement score or the sum of points given in each trial. The CWIT shifting indicator included the total score for the number of correct switches made. Although the Inhibition/Switching condition could also potentially be used as an indicator for the shifting factor, previous work has found it to be involved in inhibition using the SEM framework (33).

The fluency indicators included the VF letter and category fluency scores, and the DF total composite score. The fluency indicators in the VF Test included the Letter Fluency Total Correct score and the Category Fluency Total correct scores. The fluency indicator from the DF test was the total unique designs drawn across the two DF trials.

The three-factor model including shifting, inhibition, and fluency was evaluated first for statistical fit, and one- and two-factor models were evaluated thereafter. The one-factor model included all indicators under one factor or a ‘common EF’. Three two-factor models were tested with three combinations of the latent factors (i.e., shifting with inhibition; shifting with fluency; inhibition with fluency). The proposed model is presented in **Figure 1** and the final model is presented in **Figure 4**.

## **Figure 1. Confirmatory Factor Analysis**

The proposed three-factor measurement model. VF, Verbal Fluency; TMT; Trail Making Test; DF, Design Fluency; CWIT, Color-Word Interference Test.

### *Structural Model*

The best fitting model from the confirmatory factor analysis was tested within the framework of structural equation modeling (SEM). The latent variable(s) in the model were the dependent variables in the SEMs. The use of structural equation models have been growing within the field of cognitive neuroscience (70) and brain dynamic analyses (71). First, BMI was tested as a moderator between each brain dynamic metric (DT, frequency of occurrence, and transitions) for each of the 5 CAPs and the latent variable (shifting, inhibition, or fluency). BMI and the brain dynamic metrics were mean centered to reduce multicollinearity (72). The interactions were tested separately to reduce effects of multicollinearity and negative impacts on parameter estimations (73). Accordingly, each latent factor outcome was tested while retaining all latent factors in the model due to best model fit, however, they were predicted one at a time as depicted in **Figure 2**. Variables without a significant interaction were tested for main effects using the SEM framework. Covariates included mean FD, age, and sex. For significant interactions, simple slope analyses were conducted using the Johnson-Neyman technique (74) at various standard deviations (i.e., +1/-1 SD from the mean) for BMI to provide regions of significance. To minimize type II error when performing a moderation in SEM, an alpha value of  $p < .10$  was selected as previously suggested (75).

## **Figure 2. Structural Equation Model**

Structural equation model linking co-activation patterns (CAPs) with executive function (shifting, inhibition, and fluency) moderated by body mass index (BMI).

## Results

### *Co-activation Patterns*

Five dynamically recurrent brain states were observed across the participants (**Figure 3**). CAP 1 was characterized by co-activation among the visual network. CAP 2 was characterized by co-activation among the L-FPN, M-FPN and limbic nodes. CAP 3 was characterized by co-activation among the M-FPN. CAP 4 was characterized by co-activation among the L-FPN, DAN, limbic, and M-CIN nodes. Lastly, CAP 5 was characterized by co-activation among the dorsal frontoparietal (D-FPN), M-CIN, somatosensory motor, and visual network nodes. See a graphical presentation of the CAPs in **Figure S3**. How frequently each CAP occurred can be seen in **Table S2**.

### **Figure 3. Recurring co-activation patterns**

Co-activation patterns (CAPs) showing brain regions activated together. The graphical depiction of each CAP is shown in the brain images on the left. L-FPN, lateral frontoparietal; M-FPN, medial frontoparietal, D-FPN, dorsal frontoparietal; M-CIN, mid cinguloinsular; SomMot, somatosensory motor.

### *Statistical Analyses*

Outliers were identified in BMI, however, the values represented physiologically obtainable values so they were retained. The average percentage of missing data was .1% and tests for normality indicated all variables approximated a normal distribution.

### *Confirmatory Factor Analysis*

Several models were tested including a three-factor model with shifting, inhibition, and fluency latent factors, a one-factor model including all indicators as one EF factor, and three two-factor models (shifting and inhibition, shifting and fluency, and inhibition and fluency). Examination of the three-factor model after the inclusion of residual covariances between indicators indicated good model fit,  $\chi^2 = 19.52$  ( $df = 19$ ,  $p = .424$ ), CFI = 1.00, SRMR = .03, and RMSEA = .01. The one-factor model indicated poor model fit,  $\chi^2 = 45.09$  ( $df = 22$ ,  $p = .003$ ), CFI = .96, SRMR = .05, and RMSEA = .07. Results of the two-factor models are in **Table 2**. All two-factor models indicated poorer model fit compared with the three-factor model thus confirming the apriori three-factor model (33).

The three-factor model included three latent factors of shift, inhibition, and fluency, and each factor had three indicators. The three-factor model was first tested without residual covariances. However, upon examination of the residual and modification indices, five residual covariances were identified (**Figure 4**). All the factor loadings were significant ( $p$ 's < .001; See **Figure 4**). Additionally, all standardized factor loading were  $> .5$ , except for the Tower indicator for Inhibition (.24). However, the Tower indicator was retained due to theoretical evidence supporting it as an indicator for inhibition (76). See **Table 3** for results of the three-factor measurement model.

The three-factor variables were significantly correlated with each other ( $p$ 's < .001; See **Figure 4**). Examination of the estimates of the correlations between pairs of residuals revealed various significant correlations ( $p$ 's < .01; **Figure 4**). Previous work suggests different EFs are correlated yet separable (22,33).

**Table 2. Summary of two-factor measurement models**

Model	$\chi^2$ (df)	$p$	CFI	SRMR	RMSEA
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1. Shifting/inhibition and fluency	37.29 (21)	.016	.97	.04	.06
2. Shifting/fluency and inhibition	25.18 (21)	.240*	.99	.03	.03
3. Inhibition/fluency and shifting	44.65 (21)	.002	.96	.05	.07

\*  $p > .05$

**Table 3. Summary of three-factor measurement model pathways**

	$\beta$	b	SE	p	95% CI
[lower 2.5%, upper 2.5%]					
<b>Shifting</b>					
1. TMT	.70	1.00	0.00	999	[1.00, 1.00]
2. DF Switch	.54	0.80	.12	< 0.001***	[0.57, 1.02]
3. VF Switch	.53	0.95	.14	< 0.001***	[0.68, 1.22]
<b>Inhibition</b>					
1. CWIT Inhibition	.85	1.00	0.00	999	[1.00, 1.00]
2. CWIT Inhibition/Switch	.82	1.01	.09	< 0.001***	[0.84, 1.18]
3. Tower	.24	0.23	.07	< 0.001***	[0.09, 0.36]
<b>Fluency</b>					
1. VF Letter	.53	1.00	0.00	999	[1.00, 1.00]
2. VF Category	.52	1.02	.16	< 0.001***	[0.71, 1.33]
3. DF Fluency	.68	1.00	.18	< 0.001***	[0.65, 1.35]

\* $p < .05$ . \*\* $p < .01$ . \*\*\* $p < .001$ .

#### **Figure 4. Final three-factor measurement model**

VF, Verbal Fluency; TMT; Trail Making Test; DF, Design Fluency; CWIT, Color-Word Interference Test.

#### *Structural Models*

Several structural models were conducted involving the interactions between BMI and the brain dynamic metrics for each CAP predicting shifting, inhibition, and fluency. The interactions were tested one at a time while predicting one latent factor at a time.

#### *Interactions*

Results from the moderation SEM models can be seen in **Table 5**. When the individual interactions predicted each latent factor, six significant interactions were present. First, there were significant interactions between BMI and CAP 2 (characterized by co-activation among the L-FPN, M-FPN and limbic nodes) DT predicting shifting,  $b = 0.05$ ,  $SE = 0.03$ ,  $p = .029$ , 95% CI [0.01, 0.23], and inhibition,  $b = -0.07$ ,  $SE = 0.03$ ,  $p = .041$ , 95% CI [-0.13, -0.003].

Next, there was a significant interaction between BMI and CAP 4 (characterized by co-activation among the L-FPN, DAN, limbic, and M-CIN nodes) DT predicting fluency, (DT)  $b = 0.05$ ,  $SE = 0.03$ ,  $p = .083$ , 95% CI [-0.01, 0.25].

There were also significant interactions between BMI and CAP 5 (characterized by co-activation among the DAN, M-CIN, somatosensory motor, and visual network nodes) DT predicting shifting,  $b = 0.06$ ,  $SE = 0.02$ ,  $p = .013$ , 95% CI [0.01, 0.11], and inhibition,  $b = -0.06$ ,  $SE = 0.03$ ,  $p = .063$ , 95% CI [-0.11, 0.003].

Lastly, there was a significant interaction between BMI and transitions predicting shift,  $b = -0.003$ ,  $SE = 0.002$ ,  $p = .099$ , 95% CI [-0.01, 0.001].

All interactions, except for the significant interaction predicting fluency, accounted for statistically significant proportions of variance in each latent factor (**Table 5**), respectively 6%, 5%, 6%, 5%, 2%, and 5%.

The interactions were further probed using the Johnson Neyman technique to generate regions of significance plots in Mplus (**Figure S4**). The results showed that for all significant BMI x CAP DT interactions predicting shifting and inhibition, significance was reached at average and high levels of BMI (0 to 5 z-scores). The BMI x transitions interaction predicting shifting revealed significance at all levels of BMI. Lastly, the BMI x CAP 4 DT predicting fluency revealed there were no regions of significance, suggesting this may not be a moderation. Further, at higher levels of BMI, an increase in CAP DTs and transitions was associated with an increase in shifting. The opposite relationship was shown in average and low BMI. However, for inhibition, at higher levels of BMI, an increase in CAP DTs was associated with a decrease in inhibition (**Table S1; Figure 5**). Overall, a high BMI was associated with an altered pattern between brain dynamics and executive functioning.

**Table 5. Summary of Interactions**

<i>Unstandardized</i>	$\beta$	<i>b</i>	<i>SE</i>	<i>p</i>	95% CI	$R^2$
[lower 2.5%, upper 2.5%]						
<b>Shifting</b>						
BMI x DT CAP 1	-.05	-0.03	0.03	.327	[-0.09, 0.03]	.05
BMI x DT CAP 2	.12	0.05	0.03	.029**	[0.01, 0.23]	.06
BMI x DT CAP 3	-.05	-0.03	0.03	.320	[-0.08, 0.03]	.05
BMI x DT CAP 4	.05	0.02	0.02	.412	[-0.03, 0.07]	.05
BMI x DT CAP 5	.14	0.06	0.02	.013**	[0.01, 0.11]	.06

BMI x F CAP 1	-.04	-0.35	0.50	.481	[-1.34, 0.63]	.05
BMI x F CAP 2	.08	0.67	0.47	.149	[-0.24, 1.59]	.05
BMI x F CAP 3	-.09	-0.74	0.45	.100	[-1.62, 0.14]	.04
BMI x F CAP 4	.01	0.11	0.50	.832	[-0.88, 1.09]	.04
BMI x F CAP 5	.05	0.43	0.48	.376	[-0.52, 1.37]	.05
BMI X Transitions	-.09	-0.003	0.002	.099*	[-0.01, 0.001]	.05

#### Inhibition

BMI x DT CAP 1	-.001	-0.001	0.04	.988	[-0.08, 0.07]	.04
BMI x DT CAP 2	-.12	-0.07	0.03	.041**	[-0.13, -0.003]	.05
BMI x DT CAP 3	.08	0.05	0.03	.157	[-0.02, 0.12]	.04
BMI x DT CAP 4	-.03	-0.02	0.03	.562	[-0.08, 0.04]	.04
BMI x DT CAP 5	-.11	-0.06	0.03	.063*	[-0.11, 0.003]	.05
BMI x F CAP 1	.06	0.72	0.64	.256	[-0.53, 1.97]	.04
BMI x F CAP 2	-.09	-0.89	0.59	.126	[-0.19, 0.25]	.04
BMI x F CAP 3	.09	0.89	0.57	.115	[-0.22, 2.01]	.05
BMI x F CAP 4	-.04	-0.46	0.65	.481	[-0.15, 0.07]	.04
BMI x F CAP 5	-.03	-0.36	0.62	.559	[-0.14, 0.08]	.04
BMI X Transitions	.07	0.003	0.002	.219	[-0.002, 0.01]	.04

#### Fluency

BMI x DT CAP 1	.08	0.04	0.04	.217	[-0.03, 0.11]	.01
BMI x DT CAP 2	-.04	-0.02	0.03	.524	[-0.07, 0.04]	.01
BMI x DT CAP 3	-.01	-0.004	0.03	.903	[-0.06, 0.06]	.01
BMI x DT CAP 4	.12	0.05	0.03	.083*	[-0.01, 0.25]	.02
BMI x DT CAP 5	-.07	-0.03	0.03	.309	[-0.07, 0.02]	.01
BMI x F CAP 1	-.02	-0.21	0.58	.711	[-1.35, 0.92]	.01

BMI x F CAP 2	-.06	-0.48	0.53	.366	[-1.51, 0.56]	.02
BMI x F CAP 3	.40	0.40	0.51	.433	[-0.60, 1.40]	.02
BMI x F CAP 4	.11	0.96	0.60	.110	[-0.22, 2.13]	.02
BMI x F CAP 5	-.08	-0.65	0.56	.243	[-1.75, 0.44]	.01
BMI X Transitions	-.02	-0.001	0.002	.730	[-0.01, 0.003]	.01

\* $p < .10$ . \*\* $p < .05$ . \*\*\* $p < .01$ .

CI, confidence interval; DT, dwell time; F, frequency; BMI, body mass index;

### Figure 5. Simple Slopes

The moderating effect of body mass index (BMI) on the relationship between co-activation pattern dynamics (dwell time (DT) and transitions) and EF (Inhibition, shifting, and fluency).

#### Main Effects

Non-significant interactions were followed up by testing for main effects. There was a main effect for BMI predicting shifting,  $b = 0.04$ ,  $SE = 0.02$ ,  $p = .046$ , 95% CI [0.001, 0.09], and inhibition,  $b = -0.06$ ,  $SE = 0.03$ ,  $p = .025$ , 95% CI [-0.12, -0.01]. There was additionally a main effect for DT of CAP 1 (characterized by co-activation among the visual network) predicting inhibition,  $b = -0.83$ ,  $SE = 0.41$ ,  $p = .044$ , 95% CI [-1.64, -0.02]. There were no other significant main effects as depicted in **Table 4**.

**Table 4. Summary of main effects**

	$\beta$	$b$	$SE$	$p$	95% CI
Shift					[lower 2.5%, upper 2.5%]

DT CAP 1	-.04	-.11	0.18	.548	[-0.45, 0.24]
DT CAP 3	.06	0.17	0.17	.319	[-0.17, 0.51]
DT CAP 4	-.02	-0.06	0.17	.708	[-0.39, 0.26]
F CAP 1	-.08	-3.90	2.77	.160	[-9.33, 1.53]
F CAP 2	-.002	-0.12	2.82	.967	[-5.65, 5.41]
F CAP 3	.06	2.97	3.00	.321	[-2.90, 8.85]
F CAP 4	.002	0.13	2.86	.965	[-5.48, 5.73]
F CAP 5	.03	1.46	2.89	.613	[-4.20, 7.12]
BMI	.13	0.04	0.02	.046*	[0.001, 0.09]
Age	-.07	-0.02	0.02	.210	[-.05, 0.01]
Mean FD	-.04	-0.95	1.49	.523	[-3.86, 1.96]
Sex	.18	0.72	0.23	.001**	[0.28, 1.16]
Inhibition					
DT CAP 1	-.24	-0.83	0.41	.044*	[-1.64, -0.02]
DT CAP 3	-.06	-0.24	0.43	.585	[-1.08, 0.61]
DT CAP 4	-.03	-0.09	0.44	.842	[-0.94, 0.77]
F CAP 1	.01	-0.54	3.52	.878	[-6.36, 7.44]
F CAP 2	-.01	-0.73	3.66	.841	[-7.91, 6.45]
F CAP 3	-.03	-1.82	3.92	.643	[-9.50, 5.87]
F CAP 4	.05	3.44	3.65	.345	[-3.71, 10.59]
F CAP 5	-.03	-1.69	3.63	.641	[-8.80, 5.41]
Transitions	-.17	-0.04	0.04	.264	[-0.11, 0.03]
BMI	-.15	-0.06	0.03	.025*	[-0.12, -0.01]
Age	.14	0.05	0.02	.013*	[0.01, 0.08]

Mean FD	-.03	-0.73	1.89	.699	[-4.43, 2.97]
Sex	-.07	-0.35	0.28	.211	[0.01, 0.08]
<b>Fluency</b>					
DT CAP 1	.003	0.01	0.36	.981	[-0.70, 0.71]
DT CAP 2	-.13	-0.30	0.28	.284	[-0.86, 0.25]
DT CAP 3	.03	0.08	0.39	.846	[-0.69, 0.84]
DT CAP 5	-.05	-0.13	0.33	.701	[-0.77, 0.52]
F CAP 1	-.01	-0.23	3.16	.942	[-6.43, 5.96]
F CAP 2	.09	4.24	3.25	.191	[-2.12, 10.60]
F CAP 3	-.09	-4.59	3.58	.200	[-11.61, 2.43]
F CAP 4	-.04	-2.07	3.24	.522	[-8.42, 4.27]
F CAP 5	.03	1.52	3.30	.646	[-4.96, 7.99]
Transitions	-.13	-0.02	0.04	.551	[-0.10, 0.05]
BMI	.01	0.004	0.03	.865	[-0.05, 0.05]
Age	-.02	-0.01	0.02	.746	[-0.04, 0.03]
Mean FD	.02	0.36	1.71	.835	[-2.99, 3.70]
Sex	-.06	0-0.22	0.26	.387	[-0.73, 0.28]

\* $p < .05$ . \*\* $p < .01$ . \*\*\* $p < .001$ .

CI, confidence interval; DT, dwell time; F, frequency; BMI, body mass index; Mean FD, mean framewise displacement;

## Discussion

Overweight/obesity is associated with far reaching negative impacts including health comorbidities (6), executive dysfunction (15), brain structural and functional alterations (77), and

poor mental health (28). However, it is unknown whether or not BMI moderates the relationship between brain network dynamics and executive function (EF).

The current study explored BMI as a moderator of whole brain network dynamics and EF using a dynamic CAP analysis. We first assessed a measurement model consisting of shifting, inhibition, and fluency latent factors and found a three-factor model best fit the data. Next, latent factors of EF were used as dependent measures within a moderation structural equation model (SEM). Latent factors as dependent variables reduce the task impurity problem and a latent variable is thought to be a purer measure of the target ability with reduced measurement error (31). We found BMI moderated the relationship between 1) DT of CAP 2 (L-FPN, M-FPN, and limbic) predicting shifting and inhibition, 2) DT of CAP 4 (L-FPN, D-FPN, M-CIN, and limbic) predicting fluency, 3) DT of CAP 5 (D-FPN, M-CIN, somatosensory motor, and visual) predicting both shifting and inhibition, and 4) transitions predicting shifting. In significant interactions predicting shifting and fluency, at higher levels of BMI, an increase in CAP DTs was associated with an increase (higher score) in shifting and fluency. The opposite, and expected relationship, was shown in average and low BMI. Conversely, the opposite relationships were seen among CAP DTs with inhibition, and transitions and shifting. Together, these findings suggest there is an altered relationship between brain network dynamics and EF in overweight/obesity.

Currently there is one study to our knowledge that has examined brain network dynamics across BMI (51). Few studies have assessed task fMRI brain activation and resting-state fMRI FC in overweight/obese individuals (37). The limited literature supports weight-related alterations in the M-CIN, M-FPN, and L-FPN (37). Overweight/obese individuals have been most commonly reported to have weakened connectivity among nodes within the L-FPN (39)

and enhanced connectivity among nodes within the M-CIN (78) and M-FPN (46,79). Consistent with this work, in all significant interactions between BMI and brain network dynamics, we found CAPs consisting of the L-FPN, M-FPN, and M-CIN. This suggests there are alterations among brain regions involved in executive functioning, internal thoughts, and salience processing (40) in individuals with a higher BMI.

Although there is limited information regarding the mechanisms surrounding executive dysfunction and brain alterations associated with an increased BMI (11), prior work suggests bi-directional relationships among BMI, cognition, and brain function (11,37). For example, weight loss has been shown to have positive impacts on cognition (80), and is associated with brain structural and functional changes (81,82). Additionally, there is evidence that functional differences associated with overweight/obesity among brain regions that support EF, notably among and within the L-FPN, M-FPN, and M-CIN, may contribute to executive dysfunctioning and potentially contribute to a higher BMI (37). Our results additionally suggest alterations among the L-FPN, M-FPN, and M-CIN may contribute to differences seen in EF in overweight/obesity, and extends prior work by revealing the relationship between brain dynamics and EF is moderated by BMI.

The literature also suggests brain alterations associated with a higher BMI are not only seen among the three large-scale brain networks but also with other regions important for sensory, emotional, and reward processing (44,46,83–86). Increased connectivity has also been shown in regions of the D-FPN in obese individuals (39), suggesting alterations are in top-down control of attention (87). Similarly, in the CAPs where the relationship predicting EF depended on BMI, co-activations also consisted of the limbic, D-FPN, somatomotor, and visual networks. Since the CAP relationships predicting EF were altered in a higher BMI, this suggests that top-

down and bottom-up processes are also altered, consistent with previous findings. However, this study extends prior research by assessing CAPs associated with EF and the moderating effect of BMI on those pathways. Together, alterations among the large-scale networks and visual, sensorimotor, D-FPN, and limbic networks associated with EF, may further perpetuate a higher weight in individuals with a higher BMI.

Previous work reports increasing age is associated with shorter dwell times (DT) (88), however, another study reported the relationship between DT and age changes at around 40 years of age (89). Cognitive decline does not begin until mid to late life (90). Thus, having a longer DT during younger ages suggests poorer cognition. Consistent with this notion, in most of the significant interactions between BMI and DT, we found at average and lower BMIs there was a negative relationship between the CAP DTs and shifting and fluency. This suggests as DT increases, EF worsens. However, the opposite relationship was observed for DT and inhibition. Opposite patterns among DT and shifting, inhibition, and fluency was also generally observed in individuals with a higher BMI compared to individuals with average and lower BMIs.

Previous literature reports similar brain regions are activated during inhibition and shifting tasks, notably those within the L-FPN (91–94). In the current study, both interactions predicting shifting and inhibition consisted of CAP 2 (L-FPN, M-FPN, and limbic) and CAP 5 (D-FPN, M-CIN, somatosensory motor, and visual). However, the dynamic relations of those CAPs with inhibition and shifting had opposite patterns. Previous work has also shown an antagonistic relationship between cognitive flexibility and inhibition (95), and other work has suggested that optimal cognition is reached when dynamic coupling between brain regions are both flexible and constrained depending on the cognitive and behavioral contexts (88,96). Our results therefore suggest that less time spent in certain states may be beneficial for cognitive

flexibility, whereas longer time spent in certain states may be beneficial for inhibition. Although this was consistent with individuals at an average and lower BMI, the opposite patterns were observed in individuals with a higher BMI, suggesting the neural mechanisms associated with EF is altered in overweight/obese individuals.

Greater brain variability has also been associated with cognitive ability, specifically, an increase in variability is associated with greater cognitive performance (88,89,97,98). Consistent with prior literature suggesting greater variability is associated with greater cognition, we found that in both low and average BMI, an increased number of transitions was associated with higher EF. However, in high BMI, the opposite relationship was seen. This suggests that for overweight/obese individuals, as transitions increase, EF worsens. Evidence supports that global brain network integration is needed for effective cognitive performance (99). A potential reason underlying the differences in individuals with a high BMI may be that although many transitions may occur, brain networks may not be well integrated, as supported by differences in FC (37–39,44,45), and therefore, associated with poorer EF. Overall, our findings support altered brain dynamic relationships with EF in individuals with a high BMI.

The mechanisms supporting brain related changes in overweight/obese individuals and the associated executive dysfunction remains elusive (11,37). There are various hypotheses that may contribute to our findings of altered brain dynamic relationships with EF in individuals with a high BMI. As previously mentioned, weight loss has been shown to be associated with changes in cognition and FC (37), suggesting weight is mechanistically linked with cognition and brain function. Potential hypotheses accounting for this mechanism have been suggested and include greater leptin levels (100) and resistance (101), higher levels of inflammatory markers (102,103), impaired insulin regulation (104), impaired blood brain barrier dysfunction (103), and elevated

triglycerides in overweight/obese individuals (11). For example, individuals with obesity have been found to be in a low-grade pro-inflammatory state (11). Certain inflammatory markers have been linked with cognitive decline (11,103,105,106), and sustained inflammation has been linked with neurodegeneration (107). Although these hypotheses reveal potential mechanisms to explain the relationships among BMI, brain dynamics, and EF, future work is needed to further explore these relationships in humans and longitudinally.

As previously noted (39), many neuropsychiatric disorders are characterized by alterations among the same networks as overweight/obese individuals, markedly the M-CIN, M-FPN, and L-FPN. For example, in autism spectrum disorder (ASD), there are mixed findings using FC that are often attributed to the heterogeneous nature of the disorder (108). Although that is an attributing factor, many studies have not controlled for BMI (61,62,109–112). Further, recent work suggests ASD should be studied in the context of heterogeneity but do not attribute BMI as a potential contributor (113), despite greater rates of overweight/obesity in ASD (114,115). In one study where BMI was accounted for while examining brain dynamic differences in ASD and neurotypical individuals, brain differences were seen in ASD individuals based on their BMI (Kupis et al., submitted). Our findings further support the notion that BMI may in part contribute to the differences seen between neurotypical populations and individuals with ASD. Therefore, BMI should be accounted for when exploring brain dynamic differences in heterogeneous, neuropsychiatric conditions.

Some limitations are important to note in this study. First, BMI is considered an acceptable measure to study weight related differences, however, it does not take into account adiposity or muscle leanness. Additionally, although the sample size included is one of the largest to assess brain relationships with BMI, future studies should continue to utilize larger

samples to increase generalizability of the results. Our sample also included fewer underweight individuals than healthy weight and overweight/obese individuals (Figure S1), and may account for the lack of significant results found in underweight individuals. Future studies should include a larger sample of underweight individuals. Further, not all tests were available as part of the D-KEFS for this particular sample. For example, a common shifting task is the Wisconsin Card Sorting Test (116), however, very few participants were given this test and therefore it was not included. Another consideration is the ‘Fluency’ latent factor that consisted of both verbal fluency and design fluency indicators. Therefore, the results for this factor may be more indicative of verbal ability rather than EF. Similarly, the CWIT Inhibition/Switching Condition was used as an inhibition indicator in the present study, however, this indicator may additionally recruit shifting abilities. The psychometric properties of the D-KEFS should be further explored. Lastly, the latent factors assessed were highly correlated. Although the measurement models tested indicated separable factors, there may still be overlap within the factors tested as previous work suggests EFs are correlated yet separable (22).

Future directions should be considered as a result of the findings from this study. In older age, having a higher BMI has been described as a ‘neuroprotective’ factor and the ‘obesity paradox’, where cognition is generally preserved (117), and life expectancy is increased (118). Moreover, there is evidence that being overweight in older adulthood (75-90 years) provides an advantage in episodic memory compared with normal-weight older adults (117), and this effect is potentially mediated by FC within the M-FPN. Future work is needed to explore the neuroprotective effect of a higher BMI in older adults and its relationship among brain dynamics and EF (i.e., cognitive flexibility, fluency/updating, and inhibition). To this end, future work is additionally needed to explore BMI longitudinally, and across the lifespan to gather further

evidence of the mechanisms underlying cognitive and neural changes associated with overweight/obesity.

In conclusion, we demonstrate BMI moderates the relationship between brain network dynamics among the M-CIN, M-FPN, L-FPN and lower processing regions of the visual, D-FPN, sensorimotor and limbic regions, and shifting, inhibition, and fluency. Specifically, a higher BMI was associated with an altered mechanism of brain network dynamics associated with EF. Our findings suggest brain network dynamics underlying EF depend on BMI, and that in future studies, BMI should be considered when studying brain network dynamics.

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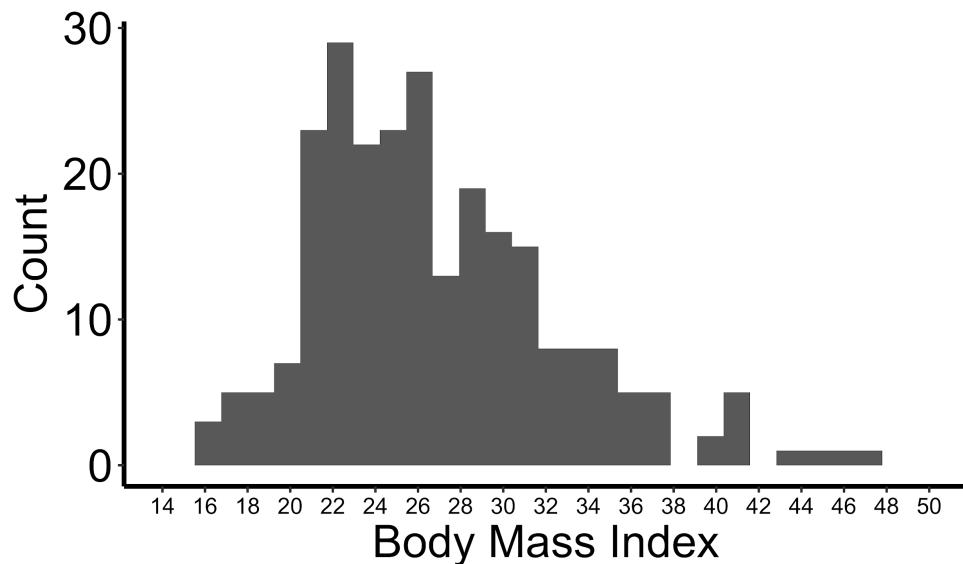
## Supplementary Materials

### *Global Signal*

Preprocessing was additionally conducted without global mean signal regression. The same analyses steps were taken to obtain the optimal *k*-value as done with global mean signal

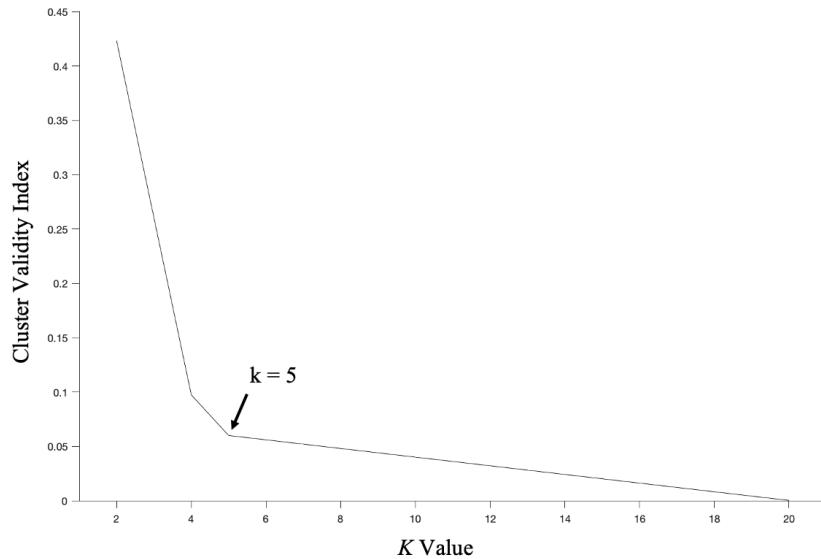
regression, resulting in 5 co-activation patterns (CAPs) (**Figure S5**). The resulting CAPs revealed the influence of the global signal, notably in CAPs 3 and 5. CAP 3 shows all nodes with activity and CAP 5 shows all nodes with inactivity representing the global signal across all nodes. Thus, this CAP analysis without global mean signal regression shows that when the global signal has a noticeable influence on a dynamic CAP analysis, it presents as network nodes in some CAPs being all active or inactive. Further, comparison of the whole-brain activation patterns further revealed the necessity to regress out the global signal in this dataset (**Figure S6**). Further, prior work suggests that whether or not the removal of the signal through GSR is good or bad depends on the scientific question and should be considered when interpreting the results (119). Additionally, the removal of the global signal as a preprocessing step significantly mitigates artifacts from a variety of sources (120,121). Although in some cases the global signal can represent neuronal signal (122,123), taking the above position, in this case removal of the global signal was beneficial to obtain CAPs associated with cognition.

**Figure S1**



**Figure S1. Distribution of Body Mass Index**

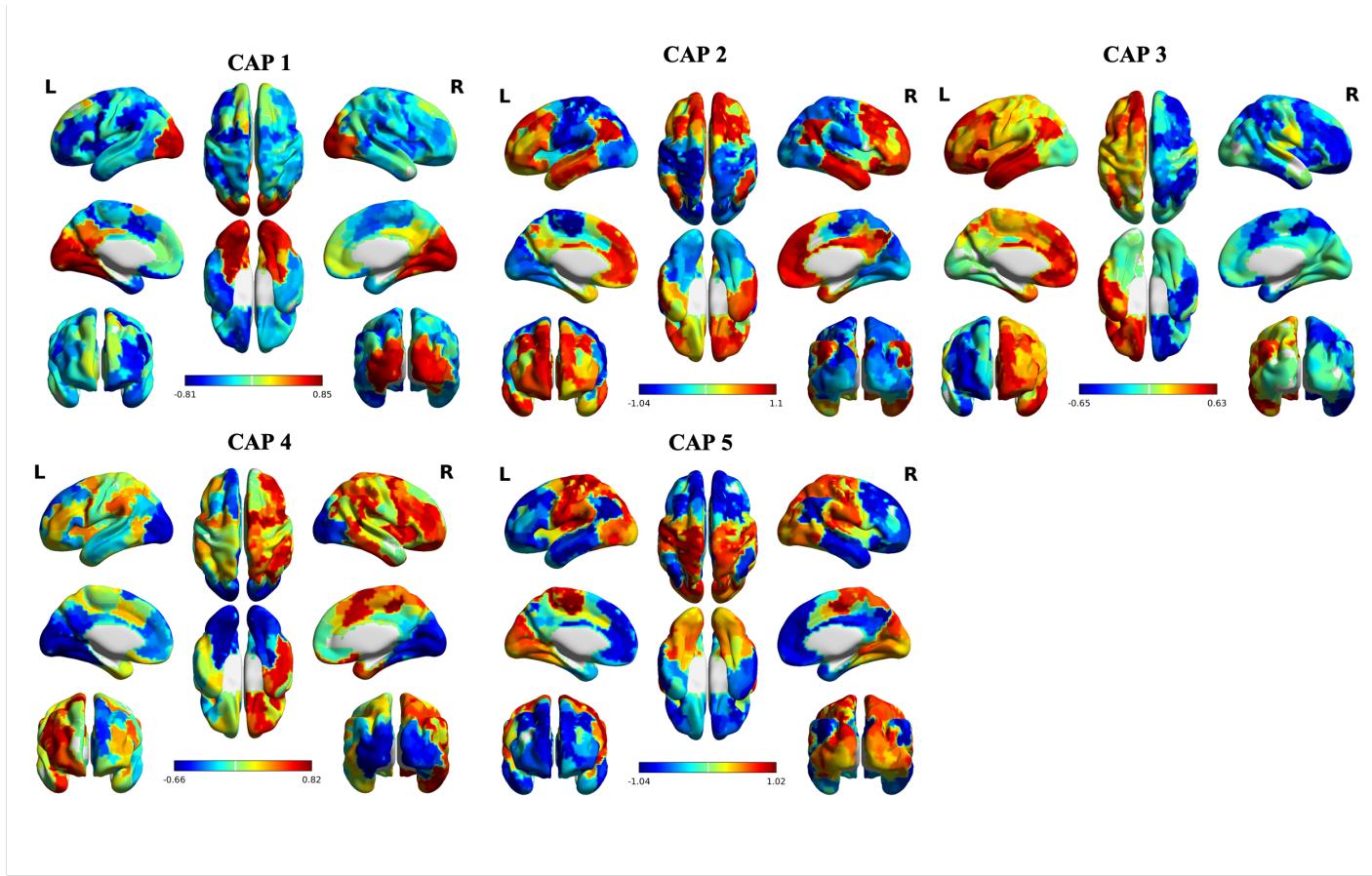
**Figure S2**



**Figure S2. Elbow Criterion**

The elbow criterion identifies  $k = 5$  clusters.

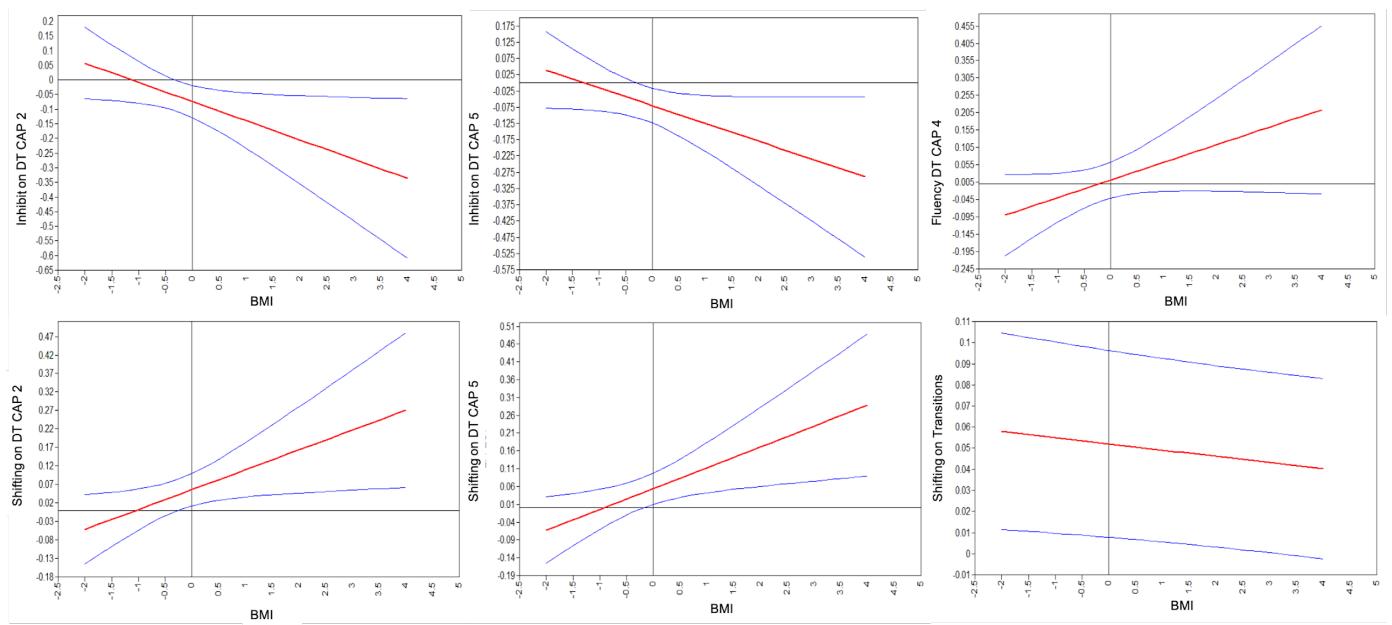
**Figure S3**



**Figure S3. Co-activation Patterns**

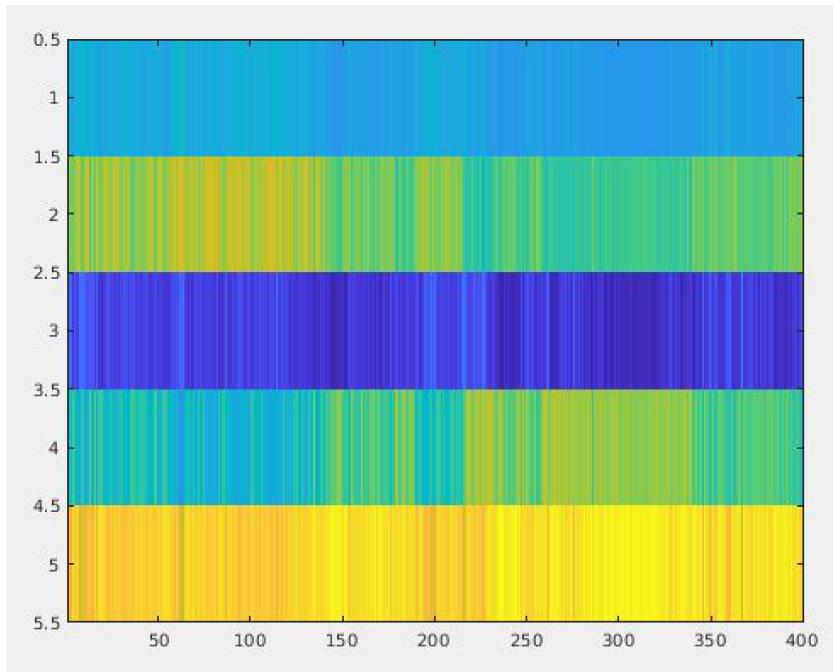
CAP 1 was characterized by co-activation among the visual network. CAP 2 was characterized by co-activation among the L-FPN, M-FPN and limbic nodes. CAP 3 was characterized by co-activation among the M-FPN. CAP 4 was characterized by co-activation among the L-FPN, DAN, limbic, and M-CIN nodes. Lastly, CAP 5 was characterized by co-activation among the dorsal frontoparietal (D-FPN), M-CIN, somatosensory motor, and visual network nodes.

**Figure S4**



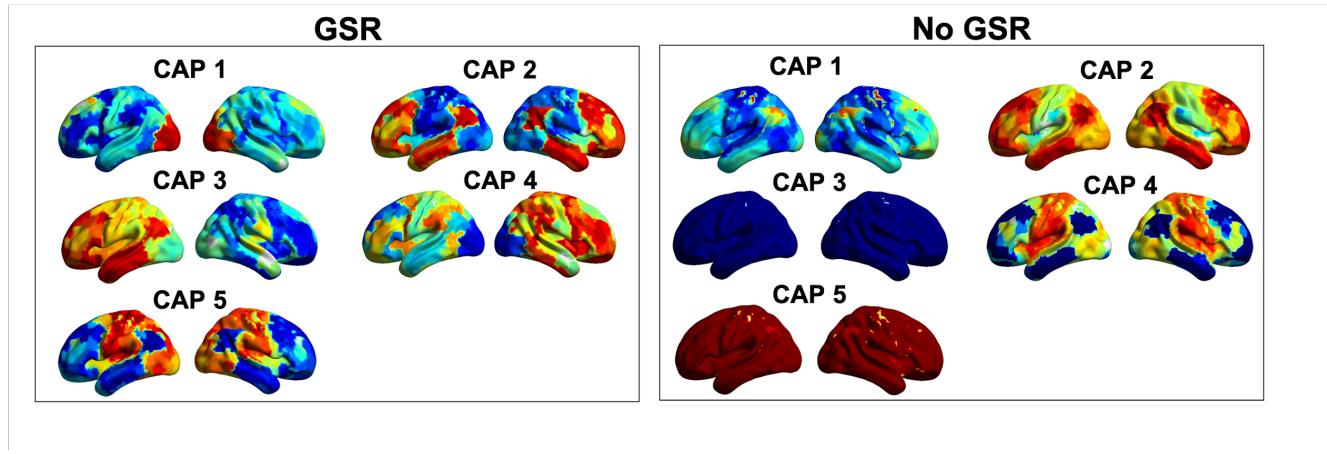
**Figure S4. Johnson-Neyman Plots**

**Figure S5**



**Figure S5. Co-activation pattern without global signal regression**

**Figure S6**



**Figure S6. Co-activation patterns with global signal regression (GSR) and without global signal regression**

**Table S1. Summary of Simple Slopes Analysis**

<i>Unstandardized</i>	<i>b</i>	<i>SE</i>
<b>Shifting</b>		
BMI x DT CAP 2 (-1 SD)	-0.04	0.15
BMI x DT CAP 2 (+1 SD)	0.06	0.15
BMI x DT CAP 2 (-2 SD)	-0.10	0.15
BMI x DT CAP 2 (+2 SD)	0.11	0.15
BMI x DT CAP 2 (-3 SD)	-0.16	0.16
BMI x DT CAP 2 (+ 3 SD)	0.17	0.16
BMI x DT CAP 5 (-1 SD)	-0.13	0.15
BMI x DT CAP 5 (+1 SD)	-0.02	0.14

BMI x DT CAP 5 (-2 SD)	-0.19	0.16
BMI x DT CAP 5 (+2 SD)	0.04	0.15
BMI x DT CAP 5 (-3 SD)	-0.25	0.17
BMI x DT CAP 5 (+ 3 SD)	0.10	0.15
BMI x Transitions (-1 SD)	0.01	0.01
BMI x Transitions (+1 SD)	0.001	0.01
BMI x Transitions (-2 SD)	0.01	0.01
BMI x Transitions (+2 SD)	-0.002	0.01
BMI x Transitions (-3 SD)	0.01	0.01
BMI x Transitions (+3 SD)	-0.01	0.01

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### Inhibition

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BMI x DT CAP 2 (-1 SD)	0.20	0.19
BMI x DT CAP 2 (+1 SD)	0.07	0.20
BMI x DT CAP 2 (-2 SD)	0.27	0.20
BMI x DT CAP 2 (+2 SD)	0.01	0.21
BMI x DT CAP 2 (-3 SD)	0.34	0.21
BMI x DT CAP 2 (+ 3 SD)	-0.06	0.22

BMI x DT CAP 5 (-1 SD)	0.10	0.19
BMI x DT CAP 5 (+1 SD)	-0.01	0.18
BMI x DT CAP 5 (-2 SD)	0.04	0.18
BMI x DT CAP 5 (+2 SD)	-0.07	0.19
BMI x DT CAP 5 (-3 SD)	0.21	0.21
BMI x DT CAP 5 (+ 3 SD)	-0.12	0.20
<hr/>		
Fluency		
<hr/>		
BMI x DT CAP 4 (-1 SD)	-0.15	0.19
BMI x DT CAP 4 (+1 SD)	-0.05	0.18
BMI x DT CAP 4 (-2 SD)	-0.26	0.21
BMI x DT CAP 4 (+2 SD)	0.05	0.19
BMI x DT CAP 4 (-3 SD)	-.26	0.21
BMI x DT CAP 4 (+ 3 SD)	0.05	0.19
<hr/>		

\* $p < .05$ . \*\* $p < .01$ . \*\*\* $p < .001$ .

**Table S2**

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Percentage % ( $SD$ )

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CAP 1	19.36 (0.04)
CAP 2	19.29 (0.04)
CAP 3	18.60 (0.04)
CAP 4	23.39 (0.04)
CAP 5	19.35 (0.04)

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**Table S2: Frequency of occurrence of each co-activation pattern (CAP)**