Supplemental Text

Data preprocessing

Initial preprocessing of the brain imaging data was performed using fMRIPrep 1.4.1rc1 (Esteban, Markiewicz, et al., 2018; Esteban, Blair, et al.. 2018; RRID:SCR_016216), which is based on Nipype 1.2.0 (Gorgolewski et al., 2011; Gorgolewski et al., 2018; RRID:SCR_002502). The T1w anatomical image was corrected for intensity non-uniformity (INU) with N4BiasFieldCorrection (Tustison et al., 2010), distributed with ANTs 2.2.0 (Avants et al. 2008, RRID:SCR_004757), and used as T1w-reference throughout the workflow. The T1w-reference was then 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, Brady, & Smith 2001). Brain surfaces were reconstructed using recon-all (FreeSurfer 6.0.1, RRID:SCR_001847, Dale, Fischl, & Sereno 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 ICBM 152 Nonlinear Asymmetrical template version 2009c [Fonov et al., 2009, RRID:SCR_008796; TemplateFlow ID: MNI152NLin2009cAsym] 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 preprocessing steps were performed using fMRIPrep for each run of functional data. First, a reference volume and its skull-stripped version were generated using a custom methodology of fMRIPrep. 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). Then, runs were slice-time corrected using 3dTshift from AFNI 20160207 (Cox & Hyde, 1997, RRID:SCR_005927). Functional runs were resampled into MNI152NLin2009cAsym standard space, and several confounding time-series were calculated based on the preprocessed data: framewise displacement (FD), DVARS, and three region-wise global signals. FD and DVARS are calculated for each functional run, both using their implementations in Nipype (following the definitions by Power et al., 2014). The three global signals are extracted within the CSF, the WM, and the whole-brain masks. Additionally, a set of physiological regressors were extracted to allow for component-based noise correction (*CompCor*; Behzadi et al., 2007). Principal components are estimated after high-pass filtering the *preprocessed BOLD* time-series (using a discrete cosine filter with 128s cut-off) for the two *CompCor* variants: temporal (tCompCor) and anatomical (aCompCor). tCompCor components are then calculated from the top 5% variable voxels within a mask covering the subcortical regions. This subcortical mask is obtained by heavily eroding the brain mask, which ensures it does not include cortical gray matter regions. For aCompCor, components are calculated within the intersection of the aforementioned mask and the union of cerebrospinal fluid and white matter masks calculated in T1w space, after their projection to the native space of each functional run, using the inverse BOLD-to-T1w transformation. Components are also calculated separately within the white matter and cerebrospinal fluid masks. For each CompCor decomposition, the k components with the largest singular values are retained, such that the retained components' time series are sufficient to explain 50 percent of variance across the nuisance mask (CSF, WM, combined, or temporal). The remaining components are dropped from consideration. The head-motion estimates calculated in the correction step were also placed within the corresponding confounds file. The confound time series derived from head motion estimates and global signals were expanded with the inclusion of temporal derivatives and quadratic terms for each (Satterthwaite et al., 2013). Frames that exceeded a threshold of 0.5 mm FD or 1.5 standardised DVARS were annotated as motion outliers. All resamplings can be performed with *a single interpolation step* by composing all the pertinent transformations (i.e. head-motion transform matrices, susceptibility distortion correction when available, and co-registrations to anatomical and output spaces). Gridded (volumetric) resamplings were performed using antsApplyTransforms (ANTs), configured with Lanczos interpolation to minimize the smoothing effects of other kernels (Lanczos, 1964). Non-gridded (also known as surface) resamplings were performed using mri_vol2surf (FreeSurfer).

Additional Analyses

We undertook additional analyses to examine the specificity of results to the segregation measure used in the main manuscript.

Alternative system segregation measures. We ran two additional models similar to the model specified in equation 3 with the default mode system segregation measure (equation 1) and the frontoparietal system segregation measure as predictors in place of the default mode and frontoparietal system segregation measure. These models allowed us to examine if any particular components of the default mode and frontoparietal system segregation measure were particularly important in explaining associations between system segregation and lapse behavior.

Components of the system segregation measure and lapse behavior. The segregation measure consists of three components: within-system connectivity of the default mode system, within-system connectivity of the frontoparietal system, and between-system connectivity of the default mode and frontoparietal systems. In additional analyses we used these three components as predictors in a model similar to the model specified in equation 3 to examine independent associations between these three components and lapse behavior.

Salience system. Previous work has implicated a role for the salience network in substance use (Moradi et al., 2020) and smoking abstinence specifically (Lerman et al., 2014). The salience network has two primary functions (Uddin, 2015; Kelly et al., 2008). One function relates to salience detection and the second relates to the facilitation of access to cognitive control resources (e.g., attention, working memory) following the detection of salient stimuli. The access to cognitive control is facilitated by signaling the engagement of the FPN while suppressing DMN activity (Bonnelle et al., 2012; Sridharan et al., 2008). To examine the role of the salience system in decisions to leave the scanner, we created a resource allocation index designed to measure the interrelationship between salience, frontoparietal, and default mode systems by computing the difference of the correlation coefficients between the salience and frontoparietal systems and the salience network and the default mode systems for each participant. The RAI is positive if connectivity between the salience network and the frontoparietal network is larger than connectivity between the salience network and the default mode network.

Additional Results

Here we present results from the additional analyses.

Alternative system segregation measures. Results were similar to those in the main manuscript when considering default mode system segregation (see equation 1; Table S10). The extent of default mode system segregation in the scanning block preceding the decision to stay or leave the scanner was associated with the choice to leave the scanner in order to smoke a cigarette, β_2=-0.73, p=0.04. With one standard deviation increase in the segregation variable, participants were 0.48 times (HR=0.48) as likely, or 52% less likely (percent change = 100 x [0.48- 1.00]=-52%), to choose to leave the scanner in order to smoke a cigarette.

Results did not extend to the case of frontoparietal system segregation (Table S11). The extent of frontoparietal system segregation in the scanning block preceding the decision to stay or leave the scanner was not associated with the choice to leave the scanner in order to smoke a cigarette, β_2=-0.34, p=0.26.

Components of the segregation measure and smoking lapse behavior. Examining the independent associations between the components that make up the default mode and frontoparietal system segregation measure revealed that none of the individual connectivity metrics were independently associated with decisions to leave the scanner (Table S12).

Salience system. The resource allocation index showed no evidence of being associated with decisions to leave the scanner β=-0.20, p=0.50 (Table S13).

Table S1.

Additional characterization of study participants

Measure	**Mean (*SD*)**
Positive Affect (PANAS)	26.18 (*6.10*)
Negative Affect (PANAS)	13.41 (*3.84*)
Smoking Urge (QSU-Brief)	42.71 (*15.18*)
Desire to Smoke (QSU-Brief Subscale)	27.65 (*8.13*)
Anticipation of Relief (QSU-Brief Subscale)	15.06 (*8.14*)
Anger (WSWS)	2.86 (*1.10*)
Anxiety (WSWS)	2.59 (*0.78*)
Concentration (WSWS)	2.06 (*0.96*)
Craving (WSWS)	3.54 (*0.80*)
Hunger (WSWS)	2.89 (*0.52*)
Sadness (WSWS)	1.22 (*0.81*)
Sleep (WSWS)	1.52 (*1.08*)

Notes: *N*=17; PANAS=Positive and Negative Affect Schedule; WSWS = Wisconsin Smoking Withdrawal Scale; QSU= Questionnaire of Smoking Urges.

Table S2.

Cox regression results testing association between default mode and frontoparietal system segregation and age on hazard of choosing to leave the scanner to smoke controlling for age, motion, and cigarettes per day

Predictor	**Estimate**	**Standard Error**	***p***	**Hazard Ratio**	**95% Confidence Interval of Hazard Ratio**
System segregation	-0.89	0.90	0.02	0.41	0.19 – 0.87
Age	-1.22	0.67	0.07	0.30	0.08 – 1.10
Motion	-0.20	0.47	0.68	0.82	0.33 – 2.08
Cigarettes Per Day	-0.44	0.37	0.23	0.64	0.31 – 1.33
-2 Log Likelihood	37.39				
AIC	45.39				

Note: AIC= Akaike Information Criteria. *N* = 17 persons. Likelihood ratio test: $\chi^2(4)=8.84$, $p=0.07$.

Table S3.

Cox regression results testing association between default mode and frontoparietal system segregation and age on hazard of choosing to leave the scanner to smoke controlling for age, motion, and FTCD

Predictor	**Estimate**	**Standard Error**	***p***	**Hazard Ratio**	**95% Confidence Interval of Hazard Ratio**
System segregation	-0.79	0.37	0.03	0.45	0.22 – 0.93
Age	-1.07	0.60	0.08	0.34	0.11 – 1.12
Motion	-0.39	0.43	0.36	0.68	0.29 – 1.57
FTCD	-0.28	0.40	0.50	0.76	0.34 – 1.68
-2 Log Likelihood	37.39				
AIC	45.39				

Note: AIC= Akaike Information Criteria. *N* = 17 persons. Likelihood ratio test: $\chi^2(4)=7.78$, $p=0.10$.

Table S4.

Cox regression results testing association between system segregation and age on hazard of choosing to leave the scanner to smoke controlling for self-reports of urge, affect, arousal, and resistance

Predictor	**Estimate**	**Standard Error**	***p***	**Hazard Ratio**	**95% Confidence Interval of Hazard Ratio**
System segregation	-1.11	0.51	0.03	0.33	0.12 - 0.90
Age	-0.59	0.66	0.38	0.56	0.15 – 2.05
Urge	2.07	1.54	0.18	7.89	0.39 – 160.81
Affect	0.89	0.73	0.22	2.44	0.58 – 10.23
Resist*	0.48	0.77	0.38	0.54	0.36 – 7.33
Arousal	0.11	0.49	081	1.12	0.43 – 2.91
Cigarettes Per Day	-0.47	0.52	0.36	0.63	0.23 – 1.72
Motion	0.62	1.09	0.57	1.86	0.22 – 15.74
-2 Log Likelihood	25.95				
AIC	42.28				

Note: AIC= Akaike Information Criteria. N = 16 persons. *One participant did not have data on this variable. Likelihood ratio test: $\chi^2(8)$=16.33, p=0.04.

Table S5

Cox regression results testing association between system segregation and urge to smoke on hazard of choosing to leave the scanner to smoke controlling for urge

Predictor	**Estimate**	**Standard Error**	***p***	**Hazard Ratio**	**95% Confidence Interval of Hazard Ratio**
System segregation	-1.15	0.50	0.02	0.32	0.12 – 0.84
Age	-0.40	0.60	0.51	0.67	0.21 – 2.18
Urge	1.68	0.79	0.03	5.36	1.13 – 25.41
Cigarettes Per Day	-0.39	0.44	0.38	0.68	0.28 – 1.62
Motion	0.22	0.76	0.77	1.24	0.28 – 5.48
-2 Log Likelihood	29.79				
AIC	39.79				

Note: AIC= Akaike Information Criteria. *N* = 17 persons. Likelihood ratio test: $\chi^2(5)$=15.38, *p*=0.01.

Table S6

Cox regression results testing association between system segregation and affect on hazard of choosing to leave the scanner to smoke controlling for affect

Predictor	**Estimate**	**Standard Error**	***p***	**Hazard Ratio**	**95% Confidence Interval of Hazard Ratio**
System segregation	-0.97	0.39	0.01	0.38	0.18 – 0.81
Age	-1.41	0.65	0.03	0.24	0.07 – 0.87
Affect	0.58	0.55	0.29	1.79	0.61 – 5.25
Cigarettes Per Day	-0.49	0.38	0.20	0.61	0.29 – 1.29
Motion	-0.002	0.49	0.99	0.99	0.38 – 2.61
-2 Log Likelihood	35.12				
AIC	45.12				

Note: AIC= Akaike Information Criteria. *N* = 17 persons. Likelihood ratio test: $\chi^2(5)=10.05$, p=0.07.

Table S7

Cox regression results testing association between system segregation and arousal on hazard of choosing to leave the scanner to smoke controlling for arousal

Predictor	**Estimate**	**Standard Error**	***p***	**Hazard Ratio**	**95% Confidence Interval of Hazard Ratio**
System segregation	-0.90	0.39	0.02	0.41	0.19 – 0.87
Age	-1.10	0.66	0.09	0.33	0.09 – 1.20
Arousal	0.52	0.38	0.17	1.68	0.80 – 3.55
Cigarettes Per Day	-0.62	0.41	0.14	0.54	0.24 – 1.21
Motion	-0.04	0.50	0.94	0.96	0.36 – 2.57
-2 Log Likelihood	34.50				
AIC	44.50				

Note: AIC= Akaike Information Criteria. *N* = 17 persons. Likelihood ratio test: $\chi^2(5)=10.67, p=0.06$.

Table S8

Cox regression results testing association between system segregation and efforts to resist the urge to smoke on hazard of choosing to leave the scanner to smoke controlling for resistance

Predictor	**Estimate**	**Standard Error**	***p***	**Hazard Ratio**	**95% Confidence Interval of Hazard Ratio**
System segregation	-0.98	0.45	0.03	0.38	0.16 – 0.91
Age	-0.62	0.56	0.27	0.54	0.18 – 1.61
Resist*	1.17	0.56	0.04	3.23	1.07 – 9.70
Cigarettes Per Day	-0.31	0.45	0.50	0.74	0.30 – 1.79
Motion	-0.26	0.85	0.76	0.77	0.15 – 4.08
-2 Log Likelihood	29.46				
AIC	39.46				

Note: AIC= Akaike Information Criteria. *N* = 16 persons. *One participant did not have data on this variable Likelihood ratio test: $\chi^2(5)=12.82, p=0.03$.

Table S9.

Cox regression results testing association between time-invariant default mode and frontoparietal system segregation and age on hazard of choosing to leave the scanner to smoke

Predictor	**Estimate**	**Standard Error**	***p***	**Hazard Ratio**	**95% Confidence Interval of Hazard Ratio**
Time-invariant system segregation	-0.61	0.43	0.15	0.54	0.24 – 1.25
Age	-1.33	0.93	0.15	0.26	0.04 – 1.65
Cigarettes Per Day	-0.40	0.37	0.28	0.67	0.33 – 1.38
Motion	-0.15	0.44	0.73	0.86	0.36 – 2.03
-2 Log Likelihood	40.36				
AIC	48.36				

Note: AIC= Akaike Information Criteria. N = 17 persons. Likelihood ratio test: $\chi^2(4)=4.82$, $p=0.31$.

Table S10.

Cox regression results testing association between default mode system segregation and age on hazard of choosing to leave the scanner to smoke

Predictor	**Estimate**	**Standard Error**	***p***	**Hazard Ratio**	**95% Confidence Interval of Hazard Ratio**
Default mod system segregation	-0.73	0.35	0.04	0.48	0.24 – 0.96
Age	-1.02	0.57	0.07	0.36	0.12 – 1.1
-2 Log Likelihood	38.35				
AIC	42.35				

Note: AIC= Akaike Information Criteria. *N* = 17 persons. Likelihood ratio test: $\chi^2(2)=6.82$, $p=0.03$.

Table S11.

Cox regression results testing association between frontoparietal system segregation and age on hazard of choosing to leave the scanner to smoke

Predictor	**Estimate**	**Standard Error**	***p***	**Hazard Ratio**	**95% Confidence Interval of Hazard Ratio**
Frontoparietal system segregation	-0.34	0.30	0.26	0.71	0.40 – 1.28
Age	-0.67	0.55	0.22	0.51	0.18 – 1.49
-2 Log Likelihood	42.19				
AIC	46.19				

Note: AIC= Akaike Information Criteria. N = 17 persons. Likelihood ratio test: $\chi^2(2)=2.98$, $p=0.23$.

Table S12.

Cox regression results testing association between system segregation components and age on hazard of choosing to leave the scanner to smoke

Predictor	**Estimate**	**Standard Error**	***p***	**Hazard Ratio**	**95% Confidence Interval of Hazard Ratio**
FPN-DMN	0.71	0.38	0.06	2.03	0.96 – 4.27
FPNwn	-0.34	0.34	0.31	0.71	0.37 – 1.37
DMNwn	-0.69	0.40	0.08	0.50	0.23 – 1.09
Age	-0.13	0.08	0.08	0.88	0.76 – 1.02
-2 Log Likelihood	37.66				
AIC	45.66				

Note: AIC= Akaike Information Criteria; FPN-DMN = frontoparietal and default mode between-system connectivity; FPNwn = within-system connectivity of the frontoparietal system; DMNwn – within-system connectivity of the default mode system; $N = 17$ persons. Likelihood ratio test: $\chi^2(4)=7.51, p=0.11$.

Table S13.

Cox regression results testing association between resource allocation index and age on hazard of choosing to leave the scanner to smoke

Predictor	**Estimate**	**Standard Error**	***p***	**Hazard Ratio**	**95% Confidence Interval of Hazard Ratio**
Resource allocation index	-0.20	0.30	0.50	0.82	0.46 – 1.47
Age	-0.62	0.48	0.19	0.54	0.21 – 1.37
Cigarettes Per Day	-0.25	0.36	0.48	0.78	0.38 – 1.57
Motion	-0.13	0.42	0.76	0.88	0.39 – 1.99
-2 Log Likelihood	42.41				
AIC	50.41				

Note: AIC= Akaike Information Criteria. N = 17 persons. Likelihood ratio test: $\chi^2(4)=2.76$, p=0.60.