Supplemental Information

Identifying Neural Signatures of Tobacco Retail Outlet Exposure: Preliminary Validation of a 'Community Neuroscience' Paradigm

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Additional Store Audit, Photography and Database Curation Procedures

Study County TROs. As noted in the manuscript, prior to initiating the human subjects portion of the study, a county-wide database of TROs and control outlets was compiled by the study team. Potential TROs were identified from databases of registered businesses and online search tools (e.g. Google Maps), ground searches, and an existing database obtained by members of the study team in previous years. All potential TROs were visited and formal store audits conducted to verify sale of tobacco products. Store exteriors were photographed during each visit. Photographs were taken from multiple angles, with effort to capture proximal landmarks that could serve as cues to specific store identity for chain stores with similar exterior branding. When possible, exterior store signs, branding and advertisements were also captured. GPS coordinates were obtained at the entrance to each store. Due to variability in the quality of GPS signals, these were later repositioned offline to fall directly over store entrances. For stores with multiple entrances, a separate coordinate was recorded for each entrance. The final database consisted of 270 separate entrances for 241 distinct TROs.

Study County Control Outlets. In addition to TROs, 100 control outlets were selected to serve as store-type controls. These retailers were selected from a database of all registered businesses in the study county. First, the list of businesses was narrowed to potentially suitable retail outlets based on their North American Industry Classification System (NAICS) category. We divided the database of TROs and potential control outlets into clusters based on 2010 census tract boundaries. The number of TROs within each tract was computed and a proportional number of control outlets were targeted for inclusion. Potential control outlets within each census tract were then randomly sorted and iteratively examined for final inclusion as a control outlet until the target number was reached. Inappropriate control outlets (i.e. stores that were not end-consumer retailers [wholesalers, manufacturers], did not sell physical products [service industries], and mall-based stores or stands with no exterior entrance to photograph) were discarded. Each control outlet was visited by the study team to obtain GPS coordinates and photographed using procedures identical to those for TROs. The full list of eligible categories and percent of each category present in the final database is available in Table S1. When NAICS were not readily available (typically new stores or small and potentially unlicensed corner stores) these were imputed based on the NAICS code of similar businesses.

Different County TROs and Control Outlets. A total of 12 TROs and 12 control outlets were selected for the Different County in proportion to the overall number of stores across the study county database. For TROs, this resulted in: (1) 7 Convenience Stores; (2) 2 Grocery Stores; (3) 1 Tobacco Shop; (4) 1 Pharmacy; and (5) 1 Discount Store. For control outlets, this included one of each of the following store types (based on NAICS descriptors): Automotive Parts and Accessories Stores; Cosmetics, Beauty Supplies and Perfume Stores; Department Stores; Florists; Furniture Stores; Hardware Stores; Office Supplies & Stationery Stores; Paint & Wallpaper Stores; Used Merchandise Stores; Women's Clothing Stores; All Other Home Furnishings Stores; All Other Misc Store Retailers. These stores were also photographed by the study team using identical procedures.

Table S1. NAICS Codes and Types for Study County Tobacco Retail and Control Outlets

Tobacco Retail Outlets (N = 240)			Control Outlets (N = 100)		
NAICS Code	**NAICS Description**	**% of Stores**	**NAICS Code**	**NAICS Description**	**% of Stores**
445110	Supermarkets and Other Grocery Stores	15.8%	441310	Automotive Parts and Accessories Stores	13.0%
445120	Convenience Stores	30.4%	442110	Furniture Stores	10.0%
445210	Meat Markets	0.4%	442299	All Other Home Furnishings Stores	3.0%
445230	Fruit and Vegetable Markets	0.8%	443141	Household Appliance Stores	1.0%
445310	Beer, Wine, and Liquor Stores	0.8%	443142	Electronics Stores	1.0%
446110	Pharmacies and Drug Stores (except CVS)	6.7%	444120	Paint and Wallpaper Stores	4.0%
447190	Other Gasoline Stations	26.3%	444130	Hardware Stores	3.0%
452111	Department Stores (WalMart only)	0.8%	446110	Pharmacies and Drug Stores (CVS only)	1.0%
452910	Superstores and Warehouse Clubs	0.8%	446120	Cosmetics, Beauty Supplies, and Perfume Stores	8.0%
452990	Dollar Stores (except Dollar Tree)	5.4%	448120	Women's Clothing Stores	5.0%
453991	Tobacco Stores	9.2%	448140	Family Clothing Stores	3.0%
517210	Cellular Telephone Stores	0.8%	448190	Other Clothing Stores	2.0%
522298	Pawnshops	0.4%	448210	Shoe Stores	2.0%
722511	Full-Service Restaurants	0.4%	448310	Jewelry Stores	2.0%
811111	General Automotive Repair	0.8%	451110	Sporting Goods Stores	2.0%
			451120	Hobby, Toy, and Game Stores	2.0%
			451130	Sewing, Needlework, and Piece Goods Stores	1.0%
			451140	Musical Instrument and Supplies Stores	1.0%
			451211	Book Stores	2.0%
			452210	Department Stores	7.0%
			452990	Dollar Stores (Dollar Tree only)	0.0%
			453110	Florists	6.0%
			453210	Office Supplies and Stationery Stores	2.0%
			453310	Used Merchandise Stores	11.0%
			453920	Art Dealers	1.0%
			453998	All Other Miscellaneous Store Retailers	5.0%

Additional Participant Exclusion Criteria

Additional exclusion criteria included an inability to attend sessions, having ever lived or worked in the different county, having made an attempt to quit smoking within the last 30 days, current use of NRT or other cessation treatments, use of psychoactive medications, use of smokeless tobacco more than 5 of the last 30 days, positive drug screen (except marijuana or medications for which a valid prescription was provided), positive pregnancy test, significant health problems, MRI contraindications, current pregnancy or efforts to become pregnant, currently breastfeeding or (for smokers) having another individual in the household who purchased cigarettes for them.

Enrollment and Attrition Information

A total of 62 individuals (42 smokers; 20 non-smokers) were screened for the study. Two non-smokers were screen-failed due to discomfort with the MRI (claustrophobia or obesity). A third non-smoker was withdrawn due to inability to complete the practice MRI task due to difficulties managing button boxes even after multiple attempts. Twelve smokers were deemed ineligible at screening (Recent Quit Attempt: 1; Uncomfortable with MRI due to size/claustrophobia: 4; CO too low: 4; Not buying own cigarettes: 1; Drug Screen: 1; use of psychoactive meds: 1). An additional 10 were withdrawn later in the study (Unable to abstain: 1; Problems with GPS: 4; Discovered concurrent enrollment in other studies: 1; Threatened staff: 1; Lost to contact: 1; Incarcerated: 1; No longer able to attend visits: 1). This resulted in the final sample of 20 smokers and 17 non-smokers who proceeded to the MRI portion of the session. Analyses examining attrition across sequential stages indicated smokers and non-smokers did not differ in the rate at which they passed the initial screening [X^2 (1) = 2.67, p = .102], completed GPS tracking [X^2 (1) = 2.62, p = .106], whether GPS tracks were of sufficient quality for inclusion [X^2 (1) = 3.05, p = .081], completed the MRI [X^2 (1) = 2.44, p = .118] or provided usable MRI data [X^2 (1) = 2.78, p = .096].

GPS Tracker Technical Difficulty Analyses

As noted in the manuscript footnote, it was discovered during post-study data quality checks that a subset of GPS trackers had a "smart tracking" feature enabled during the data collection period. When enabled, this feature caused periodic intensification of the sampling rate to 0.2 hertz (from $0.0\overline{3}$ hertz) during bouts of high activity. Given the primary purpose of GPS data in the present context was to characterize frequency of exposure to different stores within the same individual and the intensification was sporadic, this is unlikely to produce substantial bias in store selections. Nonetheless, some additional analyses were completed to determine the exact impact. To accomplish this, time differences between consecutive points in the raw GPS trace were computed and each point was assigned a "time duration" equal to the average of the time difference with the preceding and subsequent point. One non-smoker was excluded from these analyses because the time value was corrupted when exporting the data from their GPS tracker. Correlation of time-based metrics to raw point counts (across all participants) was then examined. The 12 stores to which participants reported the most exposure (or made tobacco purchases) were also re-computed using these time-based metrics for comparison.

Consistent with expectations, impact of this error on store exposure metrics was very minimal. For both TROs and control outlets, there was an extremely strong positive relationship between the time-based metric and raw point count across all stores (TROs: $r = .923$, $p < .0001$; Control Outlets: $r = .973$, $p < .0001$). This relationship remained strong when considering only those outlets shown during the MRI scan (TROs: $r = .923$, $p < .0001$; Control Outlets: $r = .999$, $p < .0001$). Of the 396 control stores that fell within the top 12 for a participant based on raw point counts and were therefore included in the MRI task, only 28 (7.1%) TROs and 20 (5.1%) Control Outlets fell outside the top 12 based on the duration metric. This occurred for no more than 3 TROs or 4 Control Outlets for any given participant. The average rank based on the duration metric for just impacted stores was 18.7 ($SD = 9.3$) for TROs and 16.7 ($SD = 4.0$) for controls. This indicates exposure to these stores was still substantially higher than to the majority of stores. Lastly, it is worth noting that if any effects on results were to occur we would expect inclusion of stores with less relative exposure within this "inside activity space" category would be expected to reduce the strength of the observed effects (i.e. produce false negatives rather than false positives). Given the findings we observed, we are confident our results are not driven by this issue.

Scanning Parameters

All scans were completed at the Brain Imaging and Analysis Center (BIAC) of Duke University. Scans used a 3T General Electric MR750 scanner (Milwaukee, WI, USA). An 8-channel head coil was used. Scanning began with a localizer series to identify the anterior and posterior commissures of a midsagittal slice. Afterwards, the following sequences were acquired in the order below:

Resting State: Data from the resting scan is not reported in the present manuscript.

TRO Viewing Task (x4): Gradient-recalled inward spiral pulse imaging with K-space trajectory. TR = 1500 ms; TE = 30 ms; Flip Angle = 60º; FOV = 240 mm^2; Matrix = 64 x 64 x 34; Voxel Size = 3.75 x 3.75 x 4.

T1-weighted Structural Scan: Axial Enhanced Fast Spoiled Gradient Echo (EFGRE3D – BRAVO); TR = 7.644 ms; TE = 2.936 ms; Flip Angle = 12º; FOV = 256 mm^2; Matrix = 256 x 256 x 162' Voxel Size = 1 mm x 1 mm x 1 mm.

Rationale, Details and Code for Primary ROIs (Spatial Perception, Memory and Self-Relevance)

General Rationale: In most cases, ROI boundaries were drawn from a previous study in our laboratory examining smoking and environmental cues.[1] The sole exception is the parahippocampal cortex which was not previously included and was drawn from an anatomical atlas for purposes of the present study. Given the novelty of the proposed paradigm, we felt this approach struck the best balance between being inclusion and rigor at the present stage of work, though further efforts to narrow this region are of importance.

A) **Parahippocampal Cortex:** Left and right regions were drawn directly from the Wake Forest University PickAtlas Automated Anatomical Labeling (AAL) Atlas. [2]
B) **Anterior and Posterior Hippocampus:** These ROIs were slightly modified from the method described by Chen & Etkin. [3] Using the Harvard-Oxford Subcortical Structural Atlas included with FSL, we extracted regions with a ≥ 60% probability of falling within the hippocampus. The hippocampus was then divided into three regions along the Anterior-Posterior axis. Due to slight hemispheric variation in the underlying atlas, these numbers differed between the left and right hippocampus. For the left hippocampus, these regions were as follows: Posterior -40 to -30; Central -28 to -18; Anterior -16 to -6. For the right hippocampus, these regions were: Posterior – 38 to -28; Central -26 to 18; Anterior – 16 to -6. Only the posterior and anterior portions were used in analyses. FSL syntax for generating these ROIs is as follows:

```
fslmaths LHipp.nii.gz -thr 60 LHipp_thr60.nii.gz
fslmaths RHipp.nii.gz -thr 60 RHipp_thr60.nii.gz
fslmaths LAmyg.nii.gz -thr 60 LAmyg_thr60.nii.gz
fslmaths RAmyg.nii.gz -thr 60 RAmyg_thr60.nii.gz
fslmaths MNI152_T1_2mm_brain -mul 0 -add 1 -roi 0 -1 43 6 0 -1 0 -1 left_posthippmask
fslmaths MNI152_T1_2mm_brain -mul 0 -add 1 -roi 0 -1 55 6 0 -1 0 -1 left_anthippmask
```

fslmaths $FSLDIR/data/standard/MNI152_T1_2mm_brain -mul 0 -add 1 -roi 0 -1 44 6 0 -1 0 -1 right_posthippmask
fslmaths $FSLDIR/data/standard/MNI152_T1_2mm_brain -mul 0 -add 1 -roi 0 -1 55 6 0 -1 0 -1 right_anthippmask
fslmaths LHipp_thr60.nii.gz -mul left_posthippmask -bin ROI_LHipp_Post_Final.nii.gz
fslmaths LHipp_thr60.nii.gz -mul left_anthippmask -bin ROI_LHipp_Ant_Final.nii.gz
fslmaths RHipp_thr60.nii.gz -mul right_posthippmask -bin ROI_RHipp_Post_Final.nii.gz
fslmaths RHipp_thr60.nii.gz -mul right_anthippmask -bin ROI_RHipp_Ant_Final.nii.gz

C) **Precuneus:** Left and right precuneus were created as a 5 x 5 x 10mm box centered on ±6, -60, 20. FSL syntax for generating these ROIs is as follows:
fslmaths MNI152_T1_2mm_brain -mul 0 -add 1 -roi 48 1 33 1 46 1 0 1 -kernel boxv3 5 5 10 -fmean -bin ROI_LPrecuneus_Final -odt float
fslmaths MNI152_T1_2mm_brain -mul 0 -add 1 -roi 42 1 33 1 46 1 0 1 -kernel boxv3 5 5 10 -fmean -bin ROI_RPrecuneus_Final -odt float

D) **Medial Prefrontal Cortex (mPFC):** Left and right mPFC (including rostral portions of the anterior cingulate gyrus) were created as a 5 x 10 x 10mm box centered on ±6, 40, 10. FSL syntax for generating these ROIs is as follows:
fslmaths MNI152_T1_2mm_brain -mul 0 -add 1 -roi 42 1 83 1 41 1 0 1 -kernel boxv3 5 10 10 -fmean -bin ROI_RmPFC_Final -odt float
fslmaths MNI152_T1_2mm_brain -mul 0 -add 1 -roi 48 1 83 1 41 1 0 1 -kernel boxv3 5 10 10 -fmean -bin ROI_LmPFC_Final -odt float

Rationale, Details and Code for Secondary ROIs (Smoking Cue Reactivity)

General Rationale: As for primary ROIs, boundaries were drawn from a previous study in our laboratory on a related topic or other cues in the area we felt represented the most rigorous efforts to date targeting relevant brain processes [1,4,5].

E) **Dorsal and Ventral Anterior Insula:** These ROIs were drawn from the Faillenot et al. probabilistic atlas of in the insula [6] using regions that have previously shown differential association between internally and externally-generated cigarette cravings [4].

F) **Amygdala:** This region was defined anatomically also using the Harvard-Oxford Subcortical Structural Atlas. We extracted regions with a ≥ 60% probability of falling within the amygdala. FSL syntax for generating these ROIs is as follows:
fslmaths LAmyg_thr60.nii.gz -bin ROI_LAmyg_Final.nii.gz
fslmaths RAmyg_thr60.nii.gz -bin ROI_RAmyg_Final.nii.gz
fslmaths RParaHippAnt_Final.nii.gz -add RParaHippPost_Final.nii.gz -bin ROI_RParaHipp_Final.nii.gz
fslmaths LParaHippAnt_Final.nii.gz -add LParaHippPost_Final.nii.gz -bin ROI_LParaHipp_Final.nii.gz

G) **Dorsal and Ventral Striatum:** These ROIs were also drawn from the Harvard-Oxford Subcortical Structural Atlas using the method described by Schacht et al. [5] ROIs consisted of a 6mm sphere centered near the points of maximum probability for the nucleus accumbens (ventral) and the anterior caudate (dorsal). Minor modifications were made to avoid overlap. FSL syntax for generating these ROIs is as follows:
fslmaths MNI152_T1_2mm_brain.nii.gz -mul 0 -add 1 -roi 51 1 70 1 33 1 0 1 -kernel sphere 6 -fmean -bin ROI_LvSTR_Final -odt float
fslmaths MNI152_T1_2mm_brain.nii.gz -mul 0 -add 1 -roi 51 1 71 1 39 1 0 1 -kernel sphere 6 -fmean -bin ROI_LdSTR_Final -odt float
fslmaths MNI152_T1_2mm_brain.nii.gz -mul 0 -add 1 -roi 39 1 70 1 33 1 0 1 -kernel sphere 6 -fmean -bin ROI_RvSTR_Final -odt float
fslmaths MNI152_T1_2mm_brain.nii.gz -mul 0 -add 1 -roi 39 1 71 1 39 1 0 1 -kernel sphere 6 -fmean -bin ROI_RdSTR_Final -odt float

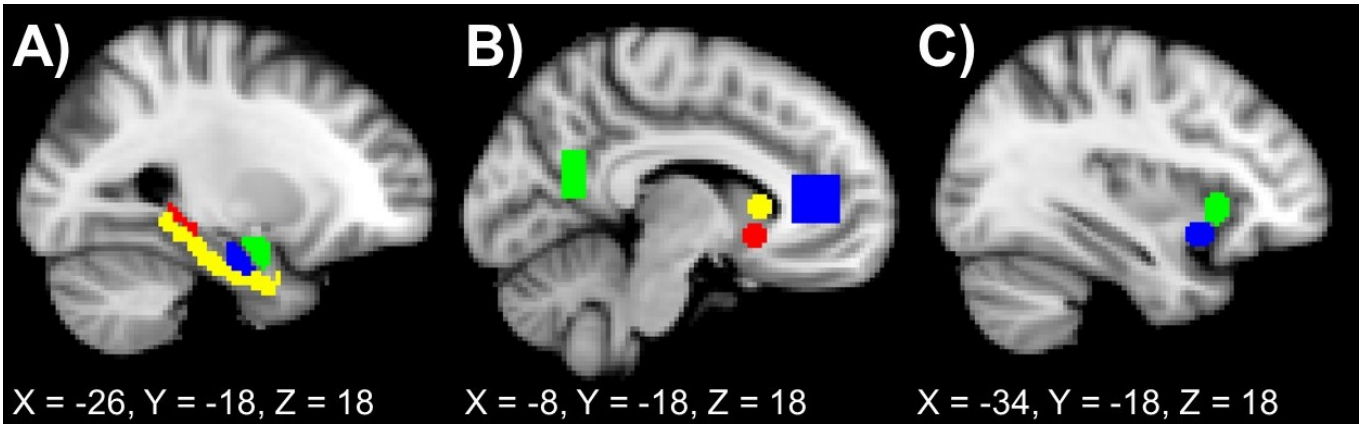


Figure S1. Regions of Interest. **A)** Amygdala (green), Anterior Hippocampus (blue), Posterior Hippocampus (red), Parahippocampus (yellow). **B)** Precuneus (green), Medial Prefrontal Cortex (blue), Ventral Striatum (red), Dorsal Striatum (yellow). **C)** Ventral Anterior Insula (green), Dorsal Anterior Insula (blue).

Familiarity Analyses Excluding Three Participants with > 10% Missing Trials

As noted in the manuscript, three participants failed to respond to > 10% of trials. 3.0% of responses were missing. No participant had more than 25% of trials missing overall or 33.3% of trials missing for any given trial type. Given the relatively short response window of 4 seconds and the potential for missing data to bias findings in the event responses are consistently slowed for familiar (or unfamiliar) stores, we repeated analyses excluding these participants with relatively higher amounts of missing data. Findings were entirely consistent with those results for the full sample of participants. Main effects were found for both Activity Space ($F = 20.2$, $p < .0001$) and Store Type ($F = 33.6$, $p < .0001$), as well as a Smoking Status x Store Type interaction ($F = 27.4$, $p < .0001$). Activity Space contrasts indicated no difference in familiarity ratings for Different County and Outside Activity Space stores ($p = .949$), but significantly higher familiarity ratings for Inside Activity Space stores relative to both Different County stores ($p < .0001$) and Outside Activity Space stores ($p < .0001$). Breakdown of the Smoking Status x Store Type interaction indicated smokers reported significantly greater familiarity with TROs relative to Control Outlets ($p < .0001$), whereas this effect was absent for non-smokers ($p = .615$). We are thus confident that the observed pattern of findings was not an artifact of missing trial-level data.

Table S2. Additional MRI Processing QA Information

Subject	Structural Scan BET FI Threshold	Functional Run 1 # Bad Vols	Functional Run 2 # Bad Vols	Functional Run 3 # Bad Vols	Functional Run 4 # Bad Vols
Smokers					
103	0.2	0	0	0	0
104	0.3	0	0	1	4
117	0.4	0	0	0	0
119	0.5	0	0	0	0
128	0.3	0	0	0	0
135	0.4	0	0	0	0
136	0.5	1	7	13	3
139	0.5	0	0	0	0
140	0.2	0	0	0	0
141	0.4	2	6	0	0
142	0.3	0	0	0	0
143	0.3	0	0	0	0
144	0.4	0	0	0	0
146	0.3	0	0	0	0
150	0.4	0	0	0	0
151	0.4	0	0	3	3
152	0.4	0	0	0	0
Non-Smokers					
201	0.2	0	0	1	0
202	0.3	0	0	1	0
203	0.5	12	12	5	9
204	0.3	0	0	1	0
205	0.3	0	0	0	0
207	0.3	1	0	1	0
208	0.3	0	0	0	0
209	0.4	0	0	0	0
211	0.3	0	0	0	0
213	0.4	0	0	0	0
218	0.4	0	0	1	5
220	0.3	0	2	0	1
221	0.4	0	1	4	1
222	0.4	0	0	0	0
223	0.4	0	0	1	1
224	0.3	0	0	0	0
148	0.4	0	0	0	0

BET FI = Brain Extraction Tool Fractional Intensity. A vertical gradient of 0.1 was also necessary for one participant (201). # Bad Vols reflects the number of volumes with DVARS [7] values ≥ 90 (~ 4 SDs above the grand mean) and therefore were addressed via voxelwise confound regressors.

Table S3. *Detailed Primary and Secondary ROI effects*

	Smoking Status		Activity Space		Store Type		Smoking Status x Activity Space		Smoking Status x Store Type		Activity Space x Store Type		Smoking Status x Activity Space x Store Type	
	F	***p-value***	***F***	***p-value***	***F***	***p-value***	***F***	***p-value***	***F***	***p-value***	***F***	***p-value***	***F***	***p-value***
Primary Brain Regions														
Left Anterior Hippocampus	0.15	.698	7.29	< .001	0.04	.837	0.43	.649	0.03	.864	0.31	.731	1.65	.195
Left Posterior Hippocampus	0.43	.517	10.74	< .001	13.06	< .001	1.68	.190	1.71	.193	0.25	.782	2.30	.104
Left Parahippocampus	0.07	.800	13.27	< .001	5.93	.016	0.43	.650	5.48	.020	0.48	.620	1.71	.184
Left Precuneus	1.06	.310	37.79	< .001	32.58	< .001	1.95	.146	14.80	< .001	0.69	.505	0.59	.553
Left medial Prefrontal Cortex	0.21	.649	7.52	< .001	0.40	.526	0.86	.426	1.28	.261	0.43	.653	2.10	.126
Right Anterior Hippocampus	0.07	.792	9.40	< .001	0.77	.382	0.46	.634	0.28	.597	0.06	.938	0.96	.385
Right Posterior Hippocampus	0.54	.469	3.24	.042	5.85	.017	0.50	.606	0.08	.779	1.14	.323	1.73	.180
Right Parahippocampus	0.05	.826	14.76	< .001	6.37	.013	0.58	.561	3.23	.074	0.42	.656	1.18	.309
Right Precuneus	0.06	.804	41.47	< .001	36.80	< .001	1.18	.310	10.39	.002	0.42	.658	1.15	.321
Right medial Prefrontal Cortex	0.41	.525	6.68	.002	0.60	.439	2.56	.081	0.93	.335	0.20	.816	4.10	.018
Secondary Brain Regions														
Left Amygdala	0.04	.852	9.22	< .001	0.10	.754	0.27	.766	0.08	.783	0.69	.505	0.47	.627
Left Dorsal Anterior Insula	5.41	.027	6.24	.002	11.59	< .001	1.65	.195	13.36	< .001	4.11	.018	0.54	.587
Left Ventral Anterior Insula	0.23	.638	4.71	.010	1.72	.192	2.31	.103	2.25	.136	2.26	.107	1.96	.145
Left Dorsal Striatum	1.21	.279	6.05	.003	0.06	.806	0.60	.552	2.82	.095	0.15	.862	1.37	.258
Left Ventral Striatum	0.52	.478	4.10	.018	1.09	.298	1.51	.225	1.53	.218	0.37	.694	2.66	.073
Right Amygdala	0.01	.942	6.97	.001	0.00	.948	1.21	.300	0.00	.967	0.13	.881	0.33	.718
Right Dorsal Anterior Insula	3.79	.060	2.48	.087	12.29	< .001	1.29	.277	12.32	< .001	0.98	.376	0.21	.813
Right Ventral Anterior Insula	0.02	.884	0.87	.420	3.75	.055	2.13	.123	3.06	.082	2.02	.135	1.89	.154
Right Dorsal Striatum	3.07	.089	5.95	.003	0.06	.805	0.01	.995	3.82	.052	0.03	.971	1.75	.177
Right Ventral Striatum	0.30	.589	4.47	.013	0.88	.351	0.13	.882	2.63	.107	0.23	.794	4.59	.012

Note. Significant values ($p < .05$ for primary brain regions, $p < .005$ for secondary brain regions) are highlighted in yellow.

Table S4. *Primary Brain Regions – Mean (SD) by Brain Region, Task Condition and Smoking Status*

Smoking Status:	***Non-Smoker***						***Smoker***					
Activity Space:	***DC***		***OAS***		***IAS***		***DC***		***OAS***		***IAS***	
Store Type:	***Control***	***TRO***	***Control***	***TRO***	***Control***	***TRO***	***Control***	***TRO***	***Control***	***TRO***	***Control***	***TRO***
L Anterior Hippocampus	0.00 (0.09)	-0.00 (0.12)	-0.02 (0.12)	0.16 (0.07)	0.04 (0.11)	0.02 (0.13)	0.01 (0.19)	0.00 (0.14)	0.03 (0.16)	0.12 (0.14)	0.04 (0.15)	0.07 (0.14)
L Posterior Hippocampus	0.08 (0.13)	0.09 (0.14)	0.07 (0.12)	0.09 (0.14)	0.10 (0.11)	0.11 (0.12)	0.08 (0.12)	0.11 (0.12)	0.10 (0.11)	0.11 (0.13)	0.12 (0.13)	0.17 (0.12)
L Parahippocampus	0.05 (0.20)	0.04 (0.23)	0.05 (0.20)	0.07 (0.22)	0.11 (0.19)	0.10 (0.23)	0.00 (0.20)	0.05 (0.16)	0.02 (0.16)	0.05 (0.14)	0.05 (0.18)	0.16 (0.12)
L Precuneus	-0.02 (0.17)	0.02 (0.24)	-0.02 (0.16)	0.05 (0.21)	0.14 (0.14)	0.12 (0.22)	-0.05 (0.23)	0.11 (0.26)	-0.01 (0.23)	0.16 (0.18)	0.16 (0.25)	0.32 (0.29)
L medial Prefrontal Cortex	-0.18 (0.07)	-0.18 (0.10)	-0.17 (0.11)	-0.18 (0.08)	-0.12 (0.10)	-0.14 (0.08)	-0.16 (0.18)	-0.16 (0.12)	-0.15 (0.11)	-0.15 (0.12)	-0.16 (0.13)	-0.11 (0.12)
R Anterior Hippocampus	0.01 (0.11)	0.02 (0.10)	0.01 (0.13)	0.03 (0.09)	0.06 (0.09)	0.04 (0.11)	-0.01 (0.18)	0.00 (0.14)	0.01 (0.16)	0.10 (0.17)	0.04 (0.17)	0.06 (0.17)
R Posterior Hippocampus	0.05 (0.10)	0.06 (0.12)	0.05 (0.12)	0.06 (0.11)	0.05 (0.10)	0.08 (0.11)	0.05 (0.11)	0.09 (0.11)	0.09 (0.11)	0.08 (0.12)	0.09 (0.11)	0.11 (0.12)
R Parahippocampus	0.04 (0.15)	0.05 (0.13)	0.05 (0.14)	0.06 (0.13)	0.09 (0.14)	0.09 (0.13)	0.00 (0.16)	0.04 (0.14)	0.03 (0.14)	0.05 (0.13)	0.06 (0.14)	0.13 (0.13)
R Precuneus	0.02 (0.24)	0.08 (0.28)	0.03 (0.20)	0.10 (0.25)	0.18 (0.20)	0.17 (0.26)	-0.02 (0.23)	0.11 (0.24)	0.02 (0.24)	0.14 (0.19)	0.15 (0.21)	0.30 (0.21)
R medial Prefrontal Cortex	-0.22 (0.10)	-0.20 (0.13)	-0.21 (0.13)	-0.21 (0.09)	-0.15 (0.12)	-0.17 (0.10)	-0.17 (0.17)	-0.18 (0.13)	-0.17 (0.11)	-0.17 (0.14)	-0.18 (0.14)	-0.13 (0.14)

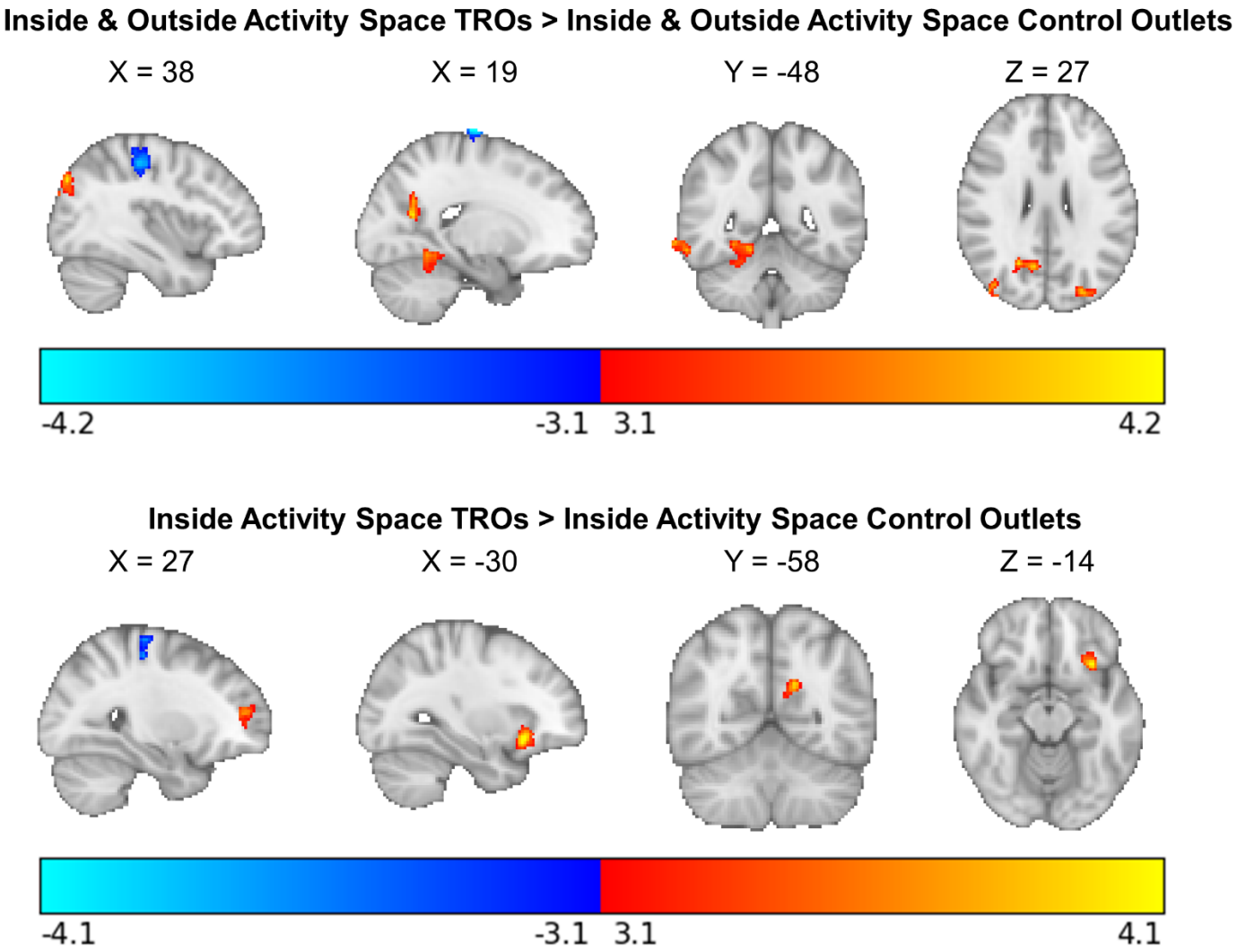
Note. TRO = Tobacco Retail Outlet. DC = Different County. OAS = Outside Activity Space. IAS = Inside Activity Space. L = Left. R = Right

Table S5. *Secondary Brain Regions - Mean (SD) by Brain Region, Task Condition and Smoking Status*

Smoking Status:	***Non-Smoker***						***Smoker***					
Activity Space:	***DC***		***OAS***		***DC***		***OAS***		***DC***		***OAS***	
Store Type:	***Control***	***TRO***	***Control***	***TRO***	***Control***	***TRO***	***Control***	***TRO***	***Control***	***TRO***	***Control***	***TRO***
L Amygdala	0.01 (0.15)	0.02 (0.21)	-0.00 (0.17)	0.01 (0.17)	0.05 (0.17)	0.06 (0.22)	0.01 (0.20)	-0.02 (0.13)	-0.01 (0.16)	-0.01 (0.14)	0.04 (0.20)	0.07 (0.17)
L Dorsal Anterior Insula	0.16 (0.10)	0.16 (0.12)	0.16 (0.10)	0.14 (0.12)	0.19 (0.12)	0.21 (0.14)	0.24 (0.23)	0.31 (0.20)	0.29 (0.22)	0.31 (0.21)	0.26 (0.21)	0.38 (0.19)
L Ventral Anterior Insula	-0.00 (0.13)	-0.00 (0.14)	-0.00 (0.11)	-0.01 (0.11)	0.04 (0.12)	0.04 (0.15)	0.01 (0.12)	0.03 (0.10)	0.04 (0.12)	0.02 (0.12)	0.00 (0.13)	0.07 (0.11)
L Dorsal Striatum	-0.04 (0.09)	-0.07 (0.08)	-0.07 (0.07)	-0.08 (0.06)	-0.03 (0.06)	-0.04 (0.08)	-0.05 (0.11)	-0.02 (0.13)	-0.03 (0.11)	-0.03 (0.11)	-0.01 (0.11)	-0.01 (0.11)
L Ventral Striatum	0.03 (0.13)	0.00 (0.14)	-0.00 (0.10)	0.01 (0.13)	0.06 (0.08)	0.06 (0.15)	0.02 (0.13)	0.07 (0.11)	0.06 (0.10)	0.04 (0.13)	0.04 (0.13)	0.08 (0.09)
R Amygdala	0.01 (0.12)	0.02 (0.14)	0.03 (0.15)	0.02 (0.12)	0.05 (0.14)	0.04 (0.15)	0.01 (0.22)	-0.01 (0.16)	0.00 (0.19)	0.02 (0.18)	0.06 (0.22)	0.07 (0.20)
R Dorsal Anterior Insula	0.21 (0.11)	0.22 (0.12)	0.21 (0.12)	0.20 (0.14)	0.23 (0.16)	0.24 (0.17)	0.24 (0.17)	0.32 (0.15)	0.29 (0.17)	0.33 (0.15)	0.27 (0.14)	0.37 (0.13)
R Ventral Anterior Insula	0.04 (0.12)	0.06 (0.17)	0.03 (0.16)	0.03 (0.17)	0.07 (0.14)	0.06 (0.18)	0.03 (0.13)	0.06 (0.17)	0.07 (0.18)	0.06 (0.16)	0.01 (0.18)	0.10 (0.13)
R Dorsal Striatum	-0.05 (0.14)	-0.09 (0.14)	-0.07 (0.09)	-0.07 (0.13)	-0.03 (0.10)	-0.05 (0.12)	-0.03 (0.10)	0.01 (0.11)	-0.01 (0.09)	-0.01 (0.12)	0.01 (0.12)	0.03 (0.09)
R Ventral Striatum	0.04 (0.12)	0.00 (0.18)	0.01 (0.11)	0.04 (0.13)	0.06 (0.09)	0.05 (0.15)	0.02 (0.14)	0.08 (0.12)	0.05 (0.12)	0.03 (0.12)	0.05 (0.12)	0.09 (0.11)

Note. TRO = Tobacco Retail Outlet. DC = Different County. OAS = Outside Activity Space. IAS = Inside Activity Space. L = Left. R = Right

Figure S2. *Exploratory whole-brain analyses depicting differences between smokers and non-smokers in BOLD activation for two different contrasts. Smoker > Non-Smoker differences are shown in red, while Non-Smoker > Smoker differences are shown in blue.*



Supplement References

H) 1 McClernon FJ, Conklin CA, Kozink RV, Adcock RA, Sweitzer MM, Addicott MA, et al. Hippocampal and insular response to smoking-related environments: neuroimaging evidence for drug-context effects in nicotine dependence. Neuropsychopharmacology. 2016;41(3):877.

I) 2 Tzourio-Mazoyer N, Landeau B, Papathanassiou D, Crivello F, Etard O, Delcroix N, et al. Automated anatomical labeling of activations in SPM using a macroscopic anatomical parcellation of the MNI MRI single-subject brain. Neuroimage. 2002;15(1):273-89.

J) 3 Chen AC, Etkin A. Hippocampal network connectivity and activation differentiates post-traumatic stress disorder from generalized anxiety disorder. Neuropsychopharmacology. 2013;38(10):1889-98.

K) 4 Janes AC, Krantz NL, Nickerson LD, Frederick BB, Lukas SE. Craving and Cue Reactivity in Nicotine-Dependent Tobacco Smokers Is Associated With Different Insula Networks. Biol Psychiatry Cogn Neurosci Neuroimaging. 2020;5(1):76-83.

L) 5 Schacht JP, Anton RF, Randall PK, Li X, Henderson S, Myrick H. Stability of fMRI striatal response to alcohol cues: a hierarchical linear modeling approach. Neuroimage. 2011;56(1):61-8.

M) 6 Faillenot I, Heckemann RA, Frot M, Hammers A. Macroanatomy and 3D probabilistic atlas of the human insula. Neuroimage. 2017;150:88-98.

N) 7 Power JD, Barnes KA, Snyder AZ, Schlaggar BL, Petersen SE. Spurious but systematic correlations in functional connectivity MRI networks arise from subject motion. Neuroimage. 2012;59(3):2142-54.