

## **Abnormal Brain Activation in Excoriation (Skin Picking) Disorder: Evidence from an Executive Planning fMRI Study**

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## **ABSTRACT**

**Background:** Excoriation (Skin Picking) Disorder (SPD) is a relatively common psychiatric condition whose neurobiological basis is unknown.

**Aims:** We sought to probe the function of fronto-striatal circuitry in SPD.

**Methods:** Eighteen SPD subjects and 15 matched healthy controls undertook an executive planning task (Tower of London) during functional Magnetic Resonance Imaging (fMRI).

Activation during planning was compared between groups using region of interest and whole-brain permutation cluster approaches.

**Results:** For the contrast of task minus rest, SPD subjects exhibited significant functional under-activation in a cluster encompassing bilateral dorsal striatum (maximal in right caudate), bilateral anterior cingulate, and right medial frontal regions. These abnormalities were, for the most part, outside the usual dorsal planning network typically activated by executive planning tasks.

**Conclusions:** Abnormalities of neural regions involved in habit formation, action monitoring, and inhibition, appear to be involved in the pathophysiology of SPD. The findings have implications for understanding the brain basis of excessive grooming and the relationship of SPD with putative obsessive compulsive spectrum disorders.

### **Declaration of interest:**

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Excoriation (skin picking) disorder (SPD), also known as pathological skin picking, neurotic/psychogenic excoriation and dermatillomania, is a body-focused repetitive behavior (BFRB) characterized by compulsive picking of skin causing tissue damage (1). Due to the growing body of research and recognition of SPD as a clinically significant condition over the past approximately ten years, SPD is included in the 5<sup>th</sup> edition of the Diagnostic and Statistical Manual (DSM-5) under the name *Excoriation (Skin Picking) Disorder* as a full disorder for the first time.

SPD is associated with a significant degree of psychosocial dysfunction, poor quality of life, and medical complications (2-3) and appears to be a fairly common disorder in the general population. In recent years, prevalence studies have indicated rates of SPD between 1.2% and 5.4% in population samples (4-7).

From a phenomenological perspective, SPD appears similar to trichotillomania and onychophagia (compulsive nail-biting), in that it is characterized by repetitive and excessive maladaptive grooming habits that are difficult for individuals to suppress (1). Indeed, these different types of symptoms commonly co-occur within individuals, leading to the notion that they be considered body focused repetitive behaviors (BFRBs), which may share a common pathophysiological basis (8). Another somewhat complimentary perspective is that SPD be considered an Obsessive Compulsive “Spectrum” Disorder or disorder of the “Impulsive-Compulsive Spectrum” given the overlapping phenomenological and clinical characteristics of SPD and Obsessive Compulsive Disorder (OCD) and high rate of co-occurrence between the two disorders. In a study conducted in 901 patients with OCD, for example, 16.4% of the sample met criteria for concomitant SPD, while 4.9% met criteria for concomitant trichotillomania (9). Recent etiological research examining proposed genetic and environmental risk factors for the

development of the Obsessive Compulsive Spectrum Disorders found a high rate of overlap between these disorders, especially SPD and trichotillomania (10). Therefore, the relationship between SPD and OCD may be particularly pertinent in terms of such a conceptualization.

Little is known regarding the neurobiological mechanisms or constructs involved in the etiology of SPD. Recent structural imaging of SPD indicated reduced fractal anisotropy in tracts distributed bilaterally, which included white matter close to the anterior cingulate cortices, compared to controls (11). These regions were remarkably similar to those separately found to be abnormal in trichotillomania (12-13). For OCD, there exists a large body of literature, implicating dysregulation of the striatum (involved in habit generation) coupled with a lack of top-down input from cortical regions (including both medial and lateral prefrontal regions) responsible for various cognitive processes (14). Patients with OCD often show behavioral impairments in executive planning (e.g., 15-17). Such deficits extend into relatives of patients with OCD who are clinically asymptomatic, highlighting the centrality of this cognitive function and its implicated neural substrates in the pathophysiology – it may well represent an intermediate biological ‘vulnerability marker’ for OCD (18-19). As such, planning-related functional magnetic resonance imaging (fMRI) tasks represent a useful means of probing fronto-striatal integrity in OCD and related conditions, since they challenge salient distributed neural circuitry. Decreased responsiveness in the (mainly dorsolateral) prefrontal cortex and caudate nucleus was found during fMRI executive planning in people with OCD compared to controls (20).

The objective of this study was to probe the integrity of fronto-striatal circuitry in people with SPD compared to matched healthy controls using an fMRI executive planning paradigm. We hypothesized that SPD would be associated with under-activation during planning in the

striatum and (dorsolateral) prefrontal cortex versus controls, supporting a neurobiological relationship between SPD and OCD.

## **Method**

### ***Study Participants***

Men and women aged 18 to 54 with a primary diagnosis of SPD based on DSM-5 criteria and a structured clinical interview with a board certified psychiatrist with expertise in SPD and BFRBs were recruited by newspaper and poster advertisements. All subjects were recruited and underwent neuroimaging procedures at the University of Minnesota Medical Center.

Inclusion criteria included: 1) Subjects met DSM-5 criteria for SPD for at least the past 12 consecutive months: a) recurrent skin picking resulting in skin lesions; b) repeated attempts to decrease or stop skin picking; c) picking causes clinically significant distress or impairment in social, occupational, or other important areas of functioning; d) picking is not due to the direct physiological effects of a substance (e.g., [meth]amphetamine, cocaine) or a general medical condition (e.g., scabies); and e) skin picking is not restricted to the symptoms of another mental disorder (e.g., skin picking due to fixed beliefs about skin infestation in delusional disorder or parasitosis, preoccupation with appearance in body dysmorphic disorder); 2) a minimum score of >16 on the Yale Brown Obsessive Compulsive Scale modified for Neurotic Excoriation (NE-YBOCS; 21-22); and 3) picking behavior occurred daily for at least 30 minutes consistently over the past 12-months.

Exclusion criteria in those with SPD comprised: 1) unstable medical illness or clinically significant abnormalities on physical examination; 2) current pregnancy or lactation; 3) lifetime history of bipolar disorder type I or II, dementia, or any psychotic disorder; 4) any current (past

12 months) DSM-5 psychiatric disorder including OCD, body dysmorphic disorder, trichotillomania, gambling disorder, nicotine dependence and disruptive, impulse-control, and conduct disorders; 5) initiation of psychotherapy or pharmacotherapy within three months prior to study entry and, if taking medication, no dose changes for the preceding three months; 6) history of head injury or neurologic disorders; and 7) any contraindications to MRI based on safety screening and clinical history. In addition, no subjects had a history of hypertension or diabetes, conditions which may interfere with brain imaging.

After complete description of the study to the subjects, written informed consent was obtained. No secondary consents were allowed for the study (i.e., parent/guardian consent was not allowed). A full Institutional Review Board approved the consent procedures and all study procedures were carried out in accordance with the ethical principles for medical research involving human subjects established in the 2008 Declaration of Helsinki.

Age and gender matched healthy control subjects were recruited via word of mouth, poster and newspaper advertisements. All controls were free of any lifetime psychiatric disorder according to the Structured Clinical Interview for DSM-IV (SCID-I) (23) and DSM-5 criteria for SPD.

### *Assessments*

Subject interviews and scale administration were conducted by a board-certified psychiatrist with expertise in the assessment and treatment of BFRBs, OCD, and disorders of impulse control. Psychiatric comorbidity was assessed using the SCID-I (23). The severity of SPD was assessed using the Yale Brown Obsessive Compulsive Scale modified for Neurotic Excoriation (NE-

YBOCS) (21-22). All subjects underwent a safety screening for contraindication for MRI at study entry and at the scanning facility to ensure safety.

Functional imaging was completed within seven days of the intake assessment. Given the unfunded nature of this study, we decided to conduct one fMRI task which, based on the OCD and trichotillomania literature, would offer the best opportunity to examine striatal and frontal lobe integrity in SPD. As such, the *Tower of London (ToL)* task of frontal lobe integrity was chosen given that this paradigm had previously been found to be sensitive to brain dysfunction in those with pathological gambling (24-25), obsessive compulsive disorder (20), Parkinson's Disease patients (26-27), and National Football League (NFL) players with executive deficits (28). Given significant time and funding constraints, this task was chosen based on our hypotheses of executive function deficits in the SPD group and this previous research. The ToL has been validated in other clinical contexts but never before applied to SPD (27,29). The task lasted for approximately ten minutes, during which planning and subtracting problems were shown on a computer screen (inter-trial interval jittered 5-15 sec). For each trial, subjects were presented with two sets of tubes, with a random assortment of three colored balls inserted in the tubes. Subjects were prompted with a cue screen displaying the word "plan" or "subtract" before each new problem was presented. For "plan" trials, subjects were instructed to mentally determine the minimal number of ball moves required to make the top set of tubes match the bottom set of tubes. Subjects indicated their response using a button-box placed in their right hand by pressing one of four buttons numbered 1-4; as such, trial duration was response driven (for further details see 27). The task ran for 10 minutes in total. For "subtract" trials, subjects were instructed to count the number of balls in the top row and subtract them for the number of balls in the lower row. Again, responses were indicated using a button box. Both tasks used only



problems with correct responses of 2, 3, or 4. Subjects were not provided with feedback regarding the correctness of their responses in order to minimize any possible influence of error related feedback on brain activation. Task difficulty varied via a predefined pseudo-randomized sequence.

All subjects underwent a training session before scanning to ensure that they understood the rules of the task and were able to perform it adequately, and to minimize the risk of between-group behavioral differences in the scanner, which can represent major confounds in interpreting fMRI group differences.

All subjects were scanned at the University of Minnesota using a 3-Tesla Siemens (Munich, Germany) TIM Trio MRI scanner. Three-hundred and thirty T2-weighted echo-planar images depicting BOLD signal were acquired, with the first ten being discarded to avoid T1-equilibrium effects. fMRI sequence data was as follows: Acquisition time 2 s (per volume); Type: 2D; Slices: 32; Slice gap: 25%; Slice thickness: 3 mm; Slice order: Descending (32,31,...,1); FOV: 192 mm x 192 mm; Matrix: 64 x 64; Resolution: 3 mm x 3mm; TR: 2000 ms; TE: 30 ms; Flip angle: 78 deg; Bandwidth: 2232 Hz/Px; Echo spacing: 0.51 ms.

### *Data analysis*

Potential differences between the study groups on demographic and clinical measures of interest were explored using independent sample t-tests or alternative non-parametric tests as indicated, with significance defined as  $p < 0.05$  uncorrected for these purposes. Imaging data were pre-processed using the methods as previously reported (27). In brief, the scan data were motion-corrected, slice time acquisition corrected, co-registered to structural scans (standard MPRAGE),

and normalized to the standard Montreal Neurological Institute echo-planar imaging template. The resulting images were smoothed with a 8mm full-width at half-maximum Gaussian kernel.

We first examined whether the task activated the expected fronto-striatal planning network by conducting a whole brain analysis using SPM (version 5) for the plan minus subtract contrast, collapsing across all study participants ( $p < 0.05$  FDR corrected). The general linear model (GLM) included the onsets and durations of the task events convolved with the canonical Haemodynamic Response Function (HRF). It also included movement parameters and a constant term. There has been some debate in the neuroimaging field regarding the choice of FDR vs. the alternative family wise error (FWE) correction method for multiple comparisons (for discussion see e.g., 30). Our choice of FDR correction was in order to avoid the elevated risk of false positives if using FWE, and in order to maintain consistency of approach with prior work (e.g. 27-28).

In order to explore potential differences between the groups in terms of fMRI activation, we used the contrast of task minus rest (since this typically yields greater variance for detection of cross-group effects and is more easily interpretable for such analyses, as compared to the count minus subtract contrast). We used two complementary analysis approaches:

1. Select Region of Interest (ROI) analysis. Mean activation data were extracted from the activation clusters and compared cross-group using the MarsBaR Regions of Interest toolbox (random effects) (31). Regions of interest were defined as 10mm spheres based on peak activation co-ordinates derived from an independent healthy volunteer dataset [the first 50 healthy controls participating in (28)]; note that this dataset was entirely independent with no participants taking part in both studies. The ROI co-ordinates were:

dorsolateral prefrontal cortex left (DLPFC L) -22 14 56, DLPFC R 26 26 56, posterior parietal cortex left (PPC L) -36 -76 38, PPC R 44 -70 34, frontoparietal cortex right (FPC R) 28 50 2. MarsBaR is a particularly sensitive approach when there is a strong prior hypothesis, because it averages values from all voxels within the region of interest. This eschews the need to correct for many voxelwise comparisons and thereby increases the sensitivity for detecting positive effects, mitigating the risk of false negatives.

2. Whole-brain unconstrained analysis. Cross-group differences were examined using robust permutation modeling (Cambridge Brain Analysis Software, CamBA; random effects). To provide stringent control for multiple comparisons, cluster correction was applied such that the expected number of false positive clusters for the contrast of interest was less than one. Unlike parametric methods (e.g. those used in SPM), permutation modeling using CamBA is robust against outliers and non-normally distributed data. Moreover, CamBA offers a more advanced correction approach than SPM. More specifically, it uses cluster weights as opposed to extents and controls for multiple comparisons at the cluster level with permutation modeling.

We also examined correlations between clinical severity using the NE-YBOCS and (i) behavioral task measures; and (ii) extracted mean ROI and cluster values from the imaging analyses (Pearson's  $r$ , uncorrected  $p < 0.05$ ). Correlations were also conducted between age of symptom onset and these measures. Exploratory t-tests (uncorrected  $p < 0.05$ ) were used to explore possible moderating influence of medication status and lifetime history of other psychiatric disorders in the SPD individuals, with respect to disease severity, and any behavioral or brain activation measures that differed between groups.

## **Results**

### ***Sample Characteristics***

18 subjects (mean age  $29.9 \pm 9.7$ ; 100% female) with SPD and 15 age-matched control subjects (mean age  $32.9 \pm 14.7$ ; 86.7% female) met inclusion criteria and underwent the clinical assessment and functional neuroimaging. SPD subjects had a mean age of onset of  $11.3 \pm 4.1$  years and a mean duration of illness of  $18.6 \pm 9.1$  years (Table 1). A total of 9 (50%) subjects met DSM-5 criteria for another lifetime psychiatric condition:  $n=6$  major depressive disorder;  $n=2$  major depressive disorder and other specified anxiety disorder;  $n=1$  generalized anxiety disorder. Per our exclusion criterion, however, no subjects had a current psychiatric disorder. Five subjects were taking stable doses of psychotropic medications at the time of imaging: three were taking a selective serotonin reuptake inhibitor (SSRI), and two were taking a selective noradrenergic reuptake inhibitor (SNRI). Of the three subjects on an SSRI, one had citalopram augmented with aripiprazole while another had citalopram augmented with buspirone. Of the two subjects on an SNRI, one was augmented with bupropion and the other had augmentation with lamotrigine.

No significant demographic or clinical severity differences were found between subjects with a history of a lifetime psychiatric disorder and those without such a history (all  $p > 0.010$ ) (age:  $p=0.641$ ; age of onset:  $p=0.507$ ; NE-YBOCS:  $p=0.243$ ), or between those taking a psychotropic medication versus those not taking medication (age:  $p=0.108$ ; age of onset:  $p=0.510$ ; NE-YBOCS:  $p=0.569$ ).

\* TABLE 1 AROUND HERE PLEASE \*

### ***Imaging Results***

No individually clinically significant MRI structural abnormalities were identified. On the Tower of London task, SPD subjects did not differ significantly from controls in terms of response times [subtract trials mean (SD): patients 3.6 seconds (0.8), controls 4.9s (2.8);  $p=0.10$ ; plan trials: patients 8.4s (3.0), controls 8.7s (2.5);  $p=0.73$ ]. Similarly, SPD subjects and controls did not differ significantly in terms of percentage correct on the task [subtract trials: patients 82.5 (11.0), controls 71.7 (17.7);  $p=0.05$ ; plan trials: patients 74.9 (19.5), controls 70.2 (20.4);  $p=0.51$ ].

As expected, the Tower of London task activated a network of brain regions during executive planning, including frontal, parietal and striatal brain regions based on the plan minus subtract contrast. In close concordance with previous studies that have used this paradigm, subtracting trials from planning trials rendered a dorsal subset of these regions including dorsolateral prefrontal cortex and posterior parietal cortex (Table 2 and Figure 1).

\* TABLE 2 AND FIGURE 1 AROUND HERE PLEASE \*

In the region of interest (MarsBaR) analysis, no significant activation differences were evident between the two groups within the dorsal planning network (Table 2;  $p>0.05$  uncorrected; Figure 2).

\* TABLE 2 AND FIGURE 2 AROUND HERE PLEASE \*

Whole brain analysis indicated that SPD was associated with significant under-activation during the task versus controls in a single cluster (Table 4 and Figure 3). The cluster was

maximal in the right caudate nucleus [14, 24, -8], and included the bilateral caudate, right putamen, bilateral anterior cingulate cortices, bilateral olfactory lobes, and right frontal (superior-medial and middle-orbital) regions. In exploratory analyses, mean activation in the identified brain cluster did not differ significantly as a function of medication status ( $p=0.676$ ) nor as a function of past history of psychiatric comorbidities in the SPD group ( $p=0.702$ ).

No significant correlation was found between mean brain activation in the identified cluster and task behavioral measures ( $p=0.603$ ); nor between NE-YBOCS total scores and task behavioral measures ( $p=0.332$ ). Furthermore, no significant correlation was identified between mean brain activation in the identified cluster and NE-YBOCS total scores ( $p=0.211$ ) nor age of symptom onset ( $p=0.542$ ).

\* TABLE 4 AND FIGURE 3 AROUND HERE PLEASE \*

Since the control group contained two male participants while the patient group had none, supplementary analyses investigated possible gender influences over the activation in the identified cluster. Activation in the identified cluster was remarkably similar as a function of gender in controls, and the patient-control difference in activation remained highly significant even when the two male controls were excluded (Supplementary Online Figure 1).

## **Discussion**

This study comprises the first functional imaging study to be conducted in SPD, a fairly common disorder newly formalized in the DSM-5. Using a task of executive planning, no significant differences were found between the SPD and control group in terms of task performance or brain

activation within the neural network typically activated by this cognitive process, using a region-of-interest (ROI) approach (task minus rest contrast). Using unconstrained analysis across the whole brain (permutation cluster analysis with stringent correction for multiple comparisons, for the contrast of task minus rest), SPD was associated with significant under-activation in distributed neural circuitry including the bilateral dorsal striatum, bilateral anterior cingulate, and right frontal regions. These neural abnormalities appeared to be unrelated to symptom severity, or age of symptom onset.

Brain imaging has been helpful in furthering our understanding of the potential neurobiological mechanisms involved in other, similar compulsive behaviors such as OCD (e.g., 32). There is an ongoing search in psychiatry for models of the neurobiological circuitry implicated in given disorders. Greater understanding of such circuitry is likely to have ramifications for novel treatments and more appropriate diagnostic classification systems (33-34). Although caution is warranted when comparing findings across studies that have used somewhat different methodologies, it is interesting to contrast the intact planning performance we observed in SPD coupled with normal activation in the dorsal planning network according to the ROI analysis, to previous findings of deficient executive planning and hypoactivation in this network in OCD patients versus controls (20). Thus, viewed together, these results militate against a primary planning deficit in SPD. Rather, the data suggest that SPD is associated with abnormal function of neural regions outside the usual 'planning' network: specifically, as indicated by the permutation cluster analysis, hypoactivation of the dorsal striatum, anterior cingulate cortices, and right frontal regions. These regions are anatomically close to those found to be structurally abnormal in previous SPD but also trichotillomania research (11-13). Thus, it appears that SPD is associated not only with structural but also functional brain abnormalities in

regions involved in habit generation, action monitoring, and top-down inhibitory control processes (11). In OCD, dysfunction extends from medial to lateral prefrontal networks while in SPD, dysfunction may be more restricted to medial sectors of this circuitry.

These results suggest that cognitive fMRI tasks germane to other cognitive processes, such as motor inhibition and habit generation, may shed more light on the pathophysiology of SPD than executive planning tasks. In terms of the state versus trait nature of the currently identified neural abnormalities, we could not detect a significant correlation between activation and disease severity. The study may have been too small to detect such a relationship; alternatively, the hypoactivation could be ‘trait’ in nature: i.e. it may exist in people at risk of SPD even before symptoms develop. This lack of relationship between fMRI measures and disease severity could also theoretically be a consequence of the severity scale measure used. Since the NE-YBOCS (although the gold-standard for measuring symptom severity for this disorder) only assesses severity over the past seven days, it may not be a good reflection of more of a “trait” cognitive dysfunction that arguably underlies SPD. Future work could address this issue by utilizing an “endophenotyping” design in which patients are recruited along with clinically unaffected first-degree relatives.

The demographics, clinical characteristics, and severity of our SPD sample accord well with the characteristics of previously reported samples of patients with SPD (3), suggesting that our sample and findings may be representative of the female SPD population at large. However, several limitations to this current study should be considered. First, the relatively small sample size of both SPD patients and controls limits the power to make any definitive statements about neural processing in SPD. Due to the limited sample size, we opted for the dual complementary approaches of utilizing both an ROI analysis in conjunction with FDR correction (to maximize



power and minimize type-II error), and a separate whole brain permutation cluster analysis (to evaluate potential abnormalities in an unconstrained fashion, but at potential risk of diminished power). The cluster identified in the permutation analysis appeared to contain some white matter, a finding not uncommon in fMRI studies more broadly (see 35 for discussion). This could be due to imprecision in the localization of fMRI signal (particularly with gap slices) in that the regions could nonetheless represent grey matter activation differences; alternatively they may truly reflect abnormal activation associated with white matter, there being evidence elsewhere of structural white matter abnormalities in SPD (11). White matter findings using fMRI are, however, controversial and potentially problematic to interpret. Second, half of our sample had a lifetime psychiatric history and nearly one-third was taking a stable dose of a psychotropic medication at the time of imaging. This study was neither designed nor powered to address possible influences of medications and comorbidities on brain activation. Nonetheless, exploratory analyses showed that these variables did not significantly impact brain activation in the identified cluster in the SPD group. Future studies will need to formally address this issue with larger sample sizes before firm conclusions are drawn about the observed abnormal activation patterns being entirely attributable to disease rather than potential confounds. Given that subjects with SPD report high rates of psychiatric comorbidity (1,3), however, we felt that excluding these subjects would result in a less-generalizable sample to the SPD population at-large, as well as diminishing power for an already relatively small study for which funding is scarce. Finally, and as control subjects were for the most part recruited in advance of SPD subjects, by chance two control participants were male while no patients were male (and we had anticipated some males in the patient group). Analysis confirmed, however, that inclusion of these two male controls did not affect the imaging results, in that the patient-control difference in

activation in the identified cluster remained highly significant even when both male controls were excluded.

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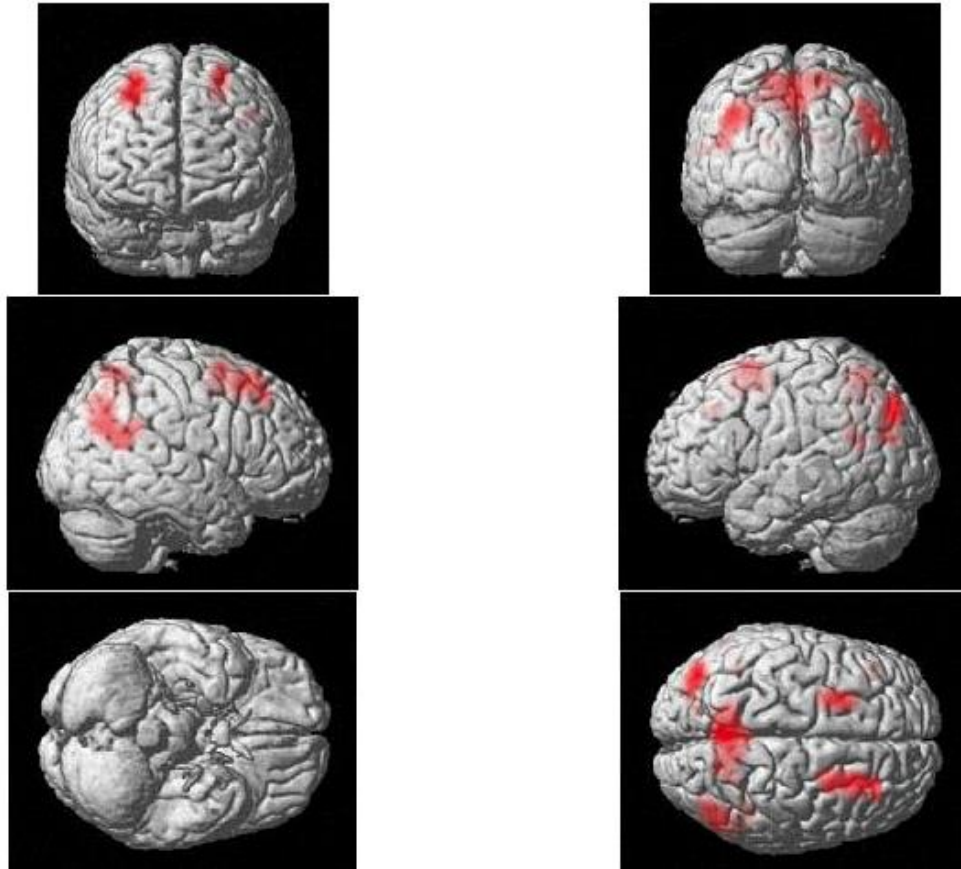
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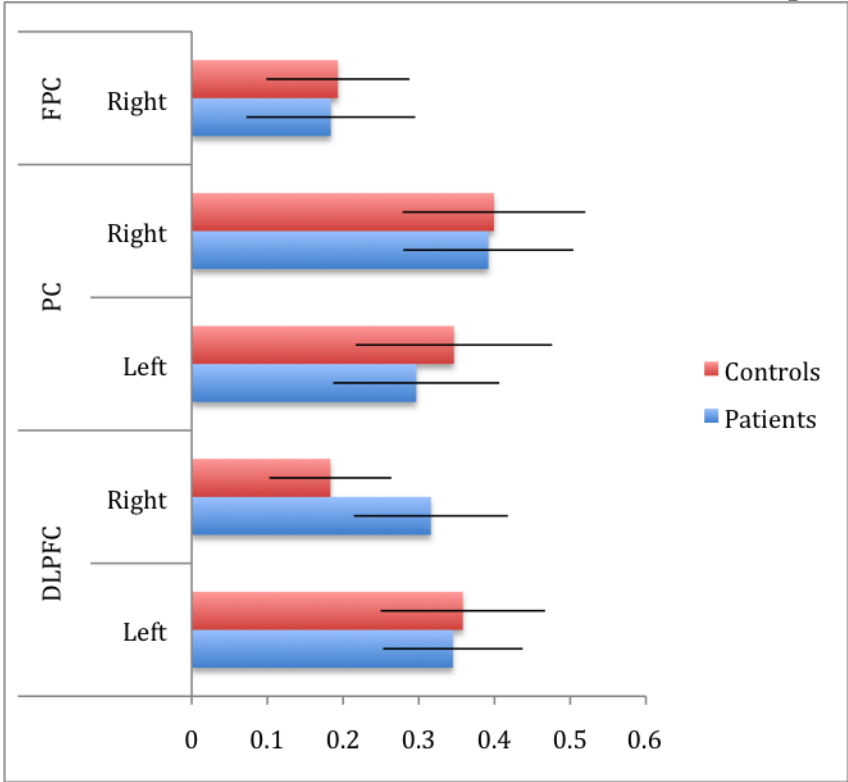
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**FIGURE 1. SPM whole brain analysis: Plan minus Subtract for all participants generated activation within the expected network**



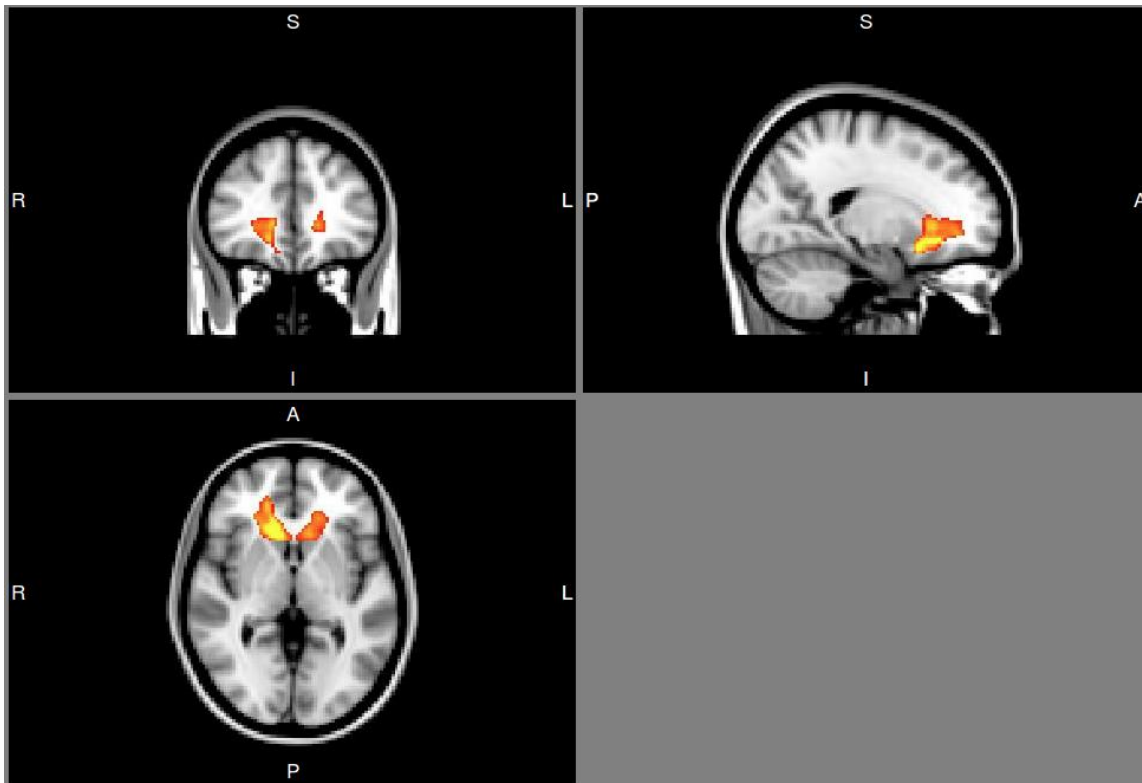
Note:  $p < 0.05$ , FDR corrected

**FIGURE 2. Tower of London task: Task minus Rest collapsed across difficulty level**



Abbreviations: FPC=frontoparietal cortex right; PC=parietal cortex; DLPFC=dorsallateral prefrontal cortex

**FIGURE 3. CamBA analysis: Regions of significant under-activation during the planning task in SPD versus controls (task minus rest)**



Note:  $p < 0.05$  uncorrected voxelwise then cluster corrected at  $p < 1$  false positive cluster across the whole brain mass



**TABLE 1. Characteristics of Skin Picking Disorder Subjects and Healthy Control Subjects**

Variable <sup>1</sup>	Baseline		Test <sup>2</sup>	p-value
	SPD (n=18)	Controls (n=15)		
Age, years	29.9 (9.7)	32.9 (14.7)	t=0.703	0.488
Sex, female, n (%)	18 (100)	13 (86.7)	f	0.199
White/Caucasian, n (%)	17 (94.4)	12 (80)	f	0.308
Single, n (%)	13 (72.2)	10 (66.7)	f	1.000
Education, n (%)				
Less than a college degree	7 (38.9)	3 (20)	f	0.283
College degree or higher	11 (61.1)	12 (80)		
Right Handedness, n (%)	15 (83.3)	13 (86.7)	f	1.000
Age of Onset, years	11.3 (4.1)			
Any Lifetime Psychiatric Comorbidity, n (%) meeting DSM-IV history	9 (50)			
NE-YBOCS, Total Score	21.9 (4.6)			

<sup>1</sup>Variables are mean ( $\pm$ SD) unless otherwise indicated

<sup>2</sup>t-test unless otherwise indicated (f=Fisher's Exact Test)

Abbreviations: NE-YBOCS = Yale Brown Obsessive Compulsive Scale Modified for Neurotic Excoriation

**TABLE 2. Significant activation across all subjects for plan minus subtract contrast, in dorsolateral prefrontal cortex and posterior parietal cortex**

cluster	cluster	peak	peak	peak	MNI co-ordinates
equivk	p(FWE-cor)	T	equivZ	p(FDR-cor)	x,y,z {mm}
800	<0.001	7.72	6.69	<0.001	0 -60 45
		5.31	4.92	<0.001	18 -54 21
		4.74	4.45	0.001	3 -60 30
175	0.002	6.62	5.92	<0.001	-36 -81 39
		3.82	3.66	0.007	-42 -75 21
		3.69	3.54	0.009	-21 -81 48
192	0.001	5.3	4.91	<0.001	-24 6 57
55	0.204	5.26	4.87	<0.001	-15 -57 21
362	<0.001	5.02	4.68	<0.001	42 -48 27
		4.76	4.46	0.001	48 -66 30
		4.74	4.45	0.001	51 -54 21
353	<0.001	4.91	4.59	<0.001	27 12 51
		4.8	4.5	0.001	24 3 57
		4.35	4.12	0.002	33 30 48

**TABLE 3. ROI approach (Marsbar): Comparison of activation between SPD subjects and controls within the fronto-parietal network, task minus rest contrast.**

<b>ROI</b>	<b>Contrast value</b>	<b>t statistic</b>	<b>Uncorrected p</b>
Left DLPFC [-22 14 56]	0.04	0.32	0.375
Right DLPFC [26 26 56]	-0.009	-0.67	0.746
Left PPC [-36 -76 38]	0.04	0.23	0.409
Right PPC [44 -70 34]	-0.03	-0.16	0.563
Right FPC [28 50 2]	0.05	0.36	0.359

**TABLE 4. CamBA approach, comparison of activation between SPD subjects and controls, task minus rest contrast**

Cluster 1, size 1607 voxels  
max -3.937232 at 14.00,24.00,-8.00 mm  
in Caudate\_R (72)  
Space outside regions (917 voxels)  
BA 6: Frontal\_Sup\_Orb\_R (17 voxels)  
BA21: Olfactory\_L (18 voxels)  
BA22: Olfactory\_R (69 voxels)  
BA24: Frontal\_Sup\_Medial\_R (6 voxels)  
BA26: Frontal\_Mid\_Orb\_R (39 voxels)  
BA28: Rectus\_R (83 voxels)  
BA31: Cingulum\_Ant\_L (9 voxels)  
BA32: Cingulum\_Ant\_R (38 voxels)  
BA71: Caudate\_L (123 voxels)  
BA72: Caudate\_R (256 voxels)  
BA74: Putamen\_R (32 voxels)