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Resting-state functional connectivity of supplementary motor area associated with skin-picking symptom severity

Ashley A. Huggins[a], Ashleigh M. Harvey[a], Tara A. Miskovich[b], Han-Joo Lee[a], Christine L. Larson[a,*]

[a] University of Wisconsin-Milwaukee, Department of Psychology, PO Box 413, Milwaukee, WI, 53201, USA
[b] VA Northern California Health Care System, Martinez, CA, USA

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ABSTRACT

Pathological skin picking (excoriation) is a relatively common disorder. Although it has been hypothesized to share a similar pathophysiological basis as other obsessive-compulsive (OC) spectrum disorders, to date, little work has specifically examined the precise neurobiological mechanisms involved in excoriation. Disruption in functional circuits involving the right inferior frontal gyrus (rIFG) and supplementary motor area (SMA) may be particularly relevant to skin-picking pathology as these regions have been implicated in other OC-spectrum disorders for their roles in response inhibition and voluntary motor action, respectively. To this end, the present study examined the associations between skin-picking symptom severity and resting-state functional connectivity of the rIFG and bilateral SMA. Participants endorsing elevated symptoms of excoriation completed a self-report measure of symptom severity and resting-state functional magnetic resonance imaging scan. Results indicated that symptom severity was associated with weaker connectivity between the SMA and clusters within the orbitofrontal cortex and angular gyrus. Contrary to hypotheses, there were no effects of symptom severity on functional connectivity of the rIFG. Overall, these findings suggest that skin-picking symptom severity may be associated with disruption in higher-order motor networks contributing to deficits in top-down regulation of motor behavior.

1. Introduction

Excoriation disorder is characterized by excessive skin picking that results in tissue damage, accompanied by significant distress and/or functional impairment (American Psychiatric Association [APA], 2013). For instance, individuals struggling with skin picking may experience medical complications (e.g., infections, scarring) from lesions and spend up to several hours a day on picking behavior. Pathological skin picking is a relatively common disorder, with lifetime prevalence estimates ranging from 1.4 to 5.4% (Grant, Odlaug, Chamberlain, et al., 2012; Keuthen, Koran, Aboujaoude, Large, & Serpe, 2010), and is more common in women than men (APA, 2013). The negative health consequences and prevalence of this disorder highlight a need to better understand its pathophysiology; however, as a relatively new addition to the DSM, the precise neurobiological underpinnings of pathological skin picking have been largely understudied. The compulsive nature of skin-picking behavior, though, has led to its classification as an obsessive-compulsive spectrum disorder (APA, 2013). Disorders within this taxonomical classification – including obsessive-compulsive disorder (OCD) and trichotillomania – are thought to be functionally and mechanistically similar and may therefore share a common pathophysiological basis.

As such, hypotheses regarding the neurobiological substrates of pathological skin picking have largely been informed by a rich history of research that has elucidated the neural systems implicated in OCD. Dysfunction within orbitofrontal-striatal circuitry has received strong support as a neural model for OCD (Maltby, Tolin, Worhunsky, O'Keefe, & Kiehl, 2005; Menzies et al., 2008; Saxena, Brody, Schwartz, & Baxter, 2018). Specifically, this model suggests that symptoms of OCD are related to disrupted feedback loops between affective, cognitive, and sensorimotor systems, resulting in deficits in exerting top-down control over behavior. Core regions within this system include the right inferior frontal gyrus (rIFG), which has been extensively implicated in response inhibition (Chambers, Garavan, & Bellgrove, 2009; Rubia, Smith, Brammer, & Taylor, 2003), and the orbitofrontal cortex (OFC), which is critical in mediating goal-directed behavior (Hollerman, Tremblay, & Schultz, 2000; Torregrossa, Quinn, & Taylor, 2008). As repetitive behaviors characterize the compulsive features of obsessive-compulsive

* Corresponding author.
E-mail addresses: huggins@uwm.edu (A.A. Huggins), harveyam@uwm.edu (A.M. Harvey), leehj@uwm.edu (H.-J. Lee), larsoncl@uwm.edu (C.L. Larson).

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spectrum disorders, there is also support for dysfunction within core motor regions in OCD (de Vries et al., 2014; de Wit et al., 2012; Fitzgerald et al., 2005). For instance, the supplementary motor area (SMA), particularly the pre-SMA, may be of particular interest in obsessive-compulsive pathology given its role in directing voluntary motor action (Goldberg, 2010; Nachev, Wydell, O'Neill, Husain, & Kennard, 2007; 2008). Extant research has supported abnormalities in this frontostriatal circuitry in OCD, such as hypoactive rIFG recruitment during response inhibition (Roth et al., 2007; Woolley et al., 2018) and hyperactivation of frontostriatal regions (e.g., OFC, caudate, thalamus; Maltby et al., 2005; Saxena et al., 2018).

Although limited neuroimaging work has focused specifically on excoriation, emerging evidence has suggested that pathological skin-picking may, indeed, share some of the same neurobiological features as other obsessive-compulsive spectrum disorders. Several structural differences between patients and healthy controls have been identified, including increased volume of the ventral striatum (Roos, Grant, Fouche, Stein, & Lochner, 2015), decreased cortical thickness within the right frontal hemisphere and lateral occipital cortex (Blum et al., 2018; Roos et al., 2015), and decreased white matter integrity in tracts important for the generation and suppression of motor responses (Grant, Odlaug, Hampshire, et al., 2012). Functionally, skin-picking patients demonstrate deficient activation of regions involved in inhibitory control, action monitoring, and habit generation, including the OFC, right frontal regions, anterior cingulate cortex (ACC), and striatum (Odlaug, Hampshire, Chamberlain, & Grant, 2016; Schienle, Übel, & Wabnegger, 2017; Schienle, Übel, & Wabnegger, 2018). Structural and functional abnormalities in core affective regions, such as the amygdala and insula, also appear to differentiate skin-picking patients and healthy controls (Harries et al., 2017; Schienle, Übel, et al., 2018; Wabnegger, Übel, Suchar, & Schienle, 2018).

Nevertheless, research on the neural substrates of pathological skin-picking remains relatively limited, and, thus, further work is warranted to better characterize the disorder's etiology. For instance, despite the strong motor component involved in skin-picking behavior, most neuroimaging research has not targeted core motor regions as a focus of interest. One recent study identified structural and functional differences between skin-picking patients and healthy controls in the cerebellum, a region critical for motor control (Stoodley & Schmahmann, 2010; Thach, Goodkin, & Keating, 1992; Wabnegger & Schienle, 2018). Such findings suggest examination of core motor regions in skin-picking pathology is likely to be useful to clarify our understanding of precise neurobiological mechanisms characterizing the disorder. Moreover, it may be particularly important to examine motor areas closely integrated with frontal, executive systems, such as the SMA, as, clinically, pathological skin-picking is defined by impairment in exerting willful control over behavior (i.e., pronounced difficulty in stopping picking of skin). Overall, theoretical models, clinical observations, and developing neuroimaging research implicate neural networks relevant to both top-down inhibitory control and motor behavior in skin-picking pathology. However, a better understanding of precisely how these networks are disrupted and interact in pathological skin picking may help to elucidate the disorder's mechanistic underpinnings and inform targeted treatment strategies.

To this end, the goal of the current study was to examine how skin-picking symptom severity is related to differences in resting-state functional connectivity of regions associated with top-down inhibitory control and motor behavior. Importantly, a resting-state design allows for the examination of whether symptoms relate to possible underlying dysfunction within the distributed neural circuits that support these complex cognitive and motor processes. A community sample of adults endorsing elevated symptoms of excoriation was recruited to complete a resting-state fMRI scan and self-report measure of skin-picking symptom severity. We examined the effects of symptom severity on whole-brain functional connectivity of two seed regions - the rIFG and bilateral pre-SMA/SMA - hypothesizing that greater symptoms would be associated with decreased functional connectivity to prefrontal regions critical for executive control and inhibiting motor behavior.

2. Method

2.1. Participants and procedure

Twenty participants endorsing elevated excoriation symptoms were recruited from a larger intervention study for individuals with symptoms of obsessive-compulsive spectrum disorders. Participants were recruited from advertisements (newspaper, Craigslist, university research subject pool) in the community. To assess initial eligibility, participants completed an online pre-screen. Participants were eligible if they were aged between 18 and 60 and met at a score of at least 7 on a self-report measure of skin-picking symptom severity (i.e., Skin Picking Scale-Revised [SPS-R]). A cutoff score of 7 on the SPS has been demonstrated as an optimal score for sensitivity and specificity for differentiating self-injurious and non-self-injurious skin-pickers (Keuthen, Wilhelm, & Deckersbach, 2001). Exclusion criteria included contraindications to magnetic resonance imaging (e.g., irremovable metal in body, pregnancy), current substance use disorder, severe attention and/or hyperactivity symptoms, or a history of significant head trauma, neurological disorder, bipolar disorder, or psychotic disorder. Participants provided written informed consent after reviewing study procedures. Study participation included completion of self-report measures and a resting-state functional magnetic resonance imaging (fMRI) scan. All procedures were approved by the University of Wisconsin-Milwaukee and Medical College of Wisconsin Institutional Review Boards. Participants were compensated with cash payment for participation.

2.2. Measures

2.2.1. Symptom severity

Skin picking symptom severity was assessed using the Skin Picking Scale-Revised (SPS-R; Snorrason et al., 2012). The SPS-R consists of eight self-report items to assess symptom severity and impairment over the past week. Total SPS-R score was used for the primary analyses in order to characterize connectivity differences on a continuum of severity. The SPS-R consists of two subscales. The Severity scale assesses frequency and intensity of urges, time spent on picking, and control over the picking behavior. The Impairment scale assesses avoidance, emotional distress, interference, and picking-induced damage in skin. Items are rated on a 0–4 Likert scale. The SPS-R has been demonstrated to have good psychometric properties (Snorrason et al., 2012). In the current sample, the SPS-R demonstrated high internal consistency (Cronbach's $\alpha = .922$).

General obsessive-compulsive symptoms exist along a continuum and frequently co-occur with pathologic skin-picking (Çalikuşu, Yücel, Polat, & Baykal, 2003; Lochner & Stein, 2010). The Obsessive-Compulsive Inventory-Revised (OCI-R; Foa et al., 2002) was administered in order to control analyses for obsessive-compulsive symptoms and better assess whether skin-picking symptoms, specifically, are associated with functional connectivity. The OCI-R is an 18-item self-report measure that assesses common features of OCD (e.g., obsessing, checking). Items are rated on a 5-point Likert scale (possible range 0-72), with scores at or above 21 indicating likely presence of OCD.

2.2.2. MRI data acquisition

For the resting-state scan, functional T2*-weighted echoplanar images (EPI) were collected on a 3.0 T short bore GE Signa Excite MRI system using a 32-channel head coil at the Medical College of Wisconsin. Images were acquired in a sagittal orientation with the following parameters: repetition time (TR)/echo time (TE) = 2000/25 ms; FOV = 22.4 mm; matrix = 64 × 64; flip angle = 77°; slice thickness = 3.5 mm; voxel size 3.5 × 3.5 × 3.5 mm; ascending

interleaved acquisition. Scan duration was 8 min. Participants were instructed to remain still with their eyes open. They were not instructed to think about anything in particular.

High resolution spoiled gradient recalled (SPGR) structural images were acquired for coregistration of the functional data: TR/TE = 8.2/3.2 ms; FOV = 240 mm; matrix = 256 × 224; flip angle = 12°; thickness = 1 mm; voxel size 0.9375 × 0.9375 × 1 mm.

2.2.3. MRI data analysis

The CONN toolbox for functional connectivity was used to analyze resting-state fMRI data (Whitfield-Gabrieli & Nieto-Castanon, 2012). Standard preprocessing steps were applied to the data, including slice-time correction to adjust for non-simultaneous slice acquisition within each volume, six-parameter (rigid body) linear transformation to correct for head movement, and spatial smoothing (FWHM = 6 mm) to minimize effects of anatomical variability. Images were transformed to Montreal Neurological Institute space (MNI 152). To reduce confounding effects of motion, frame-wise displacement (FD) was calculated, and volumes with FD > 0.3 were "scrubbed," or excluded from further analyses. Participants for whom more than 20% of volumes were scrubbed were to be excluded from further analysis. No participants were excluded from analyses due to excessive motion (mean volumes scrubbed = 13.90, SD = 12.48). White matter signal, cerebrospinal fluid signal, and head motion parameters (and their first order derivatives) were regressed out as nuisance covariates (Cole, Smith, & Beckmann, 2010). Linear detrending and temporal bandpass (0.01-0.1 Hz) filtering were performed to remove low-frequency drifts and high-frequency physiological noise (Cordes, Haughton, & Arfanakis, 2001; Fox, Corbetta, Snyder, Vincent, & Raichle, 2006).

The rIFG and bilateral SMA were selected as seed regions in whole brain seed-to-voxel functional connectivity analyses. Seeds were derived from the Harvard-Oxford atlas. In this atlas, the SMA is referred to as the juxtapositional lobule cortex and comprises the pre-SMA and SMA proper. Mean bold time series were extracted from these ROIs and correlated with the time course of every other voxel in the brain to produce three-dimensional correlation coefficient (r) maps for each subject and each seed. Normalized Fisher-transformed correlation maps were used in group analyses. Subject connectivity maps were entered into a second-level general linear model in order to examine the association between skin picking symptom severity (SPS-R) and functional connectivity of the rIFG and bilateral SMA. Sex, age, handedness, and OCD symptoms (total OCI-R) were included as covariates in the model. Non-parametric statistical procedures were used to correct for multiple voxel-wise comparisons across the whole brain using 5,000 permutations. The height threshold was set at $p < .001$ (uncorrected) with a corrected cluster alpha = .05.

To inform a better understanding of how specific components of skin-picking pathology may relate to disruption within rIFG and SMA seeded functional circuits, we also conducted a series of exploratory analyses examining the effects of the SPS-R subscales (severity, impairment) and item-level responses.

3. Results

3.1. Participant characteristics

Participant characteristics are provided in Table 1. The sample was primarily female and right-handed. Average SPS-R was 12.80 (95% bootstrapped CI 10.54-15.06). No significant differences in symptom severity were observed between any of the demographic variables.

3.2. Functional connectivity results

After adjusting for sex, age, handedness, and total OCI-R, there was a significant main effect of the SPS-R total score on functional connectivity of the bilateral SMA. Specifically, more severe skin-picking symptoms were associated with weaker functional connectivity between the SMA and clusters within the medial frontal gyrus/OFC (6, 56, -18; cluster size $k = 296$; Fig. 1), left angular gyrus (-34, -78, 42; $k = 210$; Fig. 2), left inferior temporal gyrus (-52, -42, -12; $k = 105$), and right angular gyrus (50, -68, 40; $k = 56$). Results are reported in Table 2. There were no significant effects of the SPS-R on functional connectivity of the rIFG.

Table 1
Sample characteristics (n = 20); SPS-R, Skin Picking Scale-Revised; OCI-R, Obsessive-Compulsive Inventory-Revised.

	Mean (SD) or %
Sex	
Female	90%
Male	10%
Age	27.00 (9.80)
Handedness	
Right	80%
Left	20%
SPS-R Total	12.80 (4.83)
OCI-R Total	17.05 (11.43)

Exploratory analyses indicated that the SPS-R severity subscale was associated with weaker functional coupling between the SMA and left inferior temporal gyrus (-54, -50, -16; $k = 198$; $p_{corr} = .006$), left angular gyrus (-36, -54, 36; $k = 132$; $p_{corr} = .01$), and OFC (-10, 44, -18; $k = 59$; $p_{corr} = .04$). Item-level responses indicated that weaker SMA-OFC connectivity was associated with greater urge frequency (-8, 50, -20; $k = 88$, $p_{corr} = .02$). Greater urge intensity was also associated with weaker connectivity between the SMA and precuneus (4, -42, 8; $k = 446$; $p_{corr} = .003$), OFC/anterior cingulate gyrus (4, 54, -18; $k = 314$; $p_{corr} = .003$), and superior parietal lobe (-26, -46, 56; $k = 92$; $p_{corr} = .02$). Time spent picking was associated with decreased connectivity between the SMA and left inferior temporal gyrus (-52, -44, 16; $k = 205$; $p_{corr} = .01$) and left angular gyrus (-44, -54, 44; $k = 100$; $p_{corr} = .03$). Tissue damage due to picking was associated with decreased SMA-precentral gyrus connectivity (-34, -20, 60; $k = 217$; $p_{corr} < .001$).

4. Discussion

The current study sought to examine effects of skin-picking symptom severity on resting-state functional connectivity of the rIFG and bilateral SMA in an adult, community sample. Results revealed functional coupling of the SMA with the medial frontal gyrus/OFC, angular gyrus, and inferior temporal gyrus while at rest was negatively associated with symptom severity. Contrary to hypotheses that skin-picking severity would be related to weaker functional connectivity within circuits contributing to inhibitory control and planning, there were no effects on functional connectivity of the rIFG.

Consistent with a priori hypotheses, results revealed that weaker connectivity between the SMA and prefrontal regions - including the medial frontal gyrus and OFC - was associated with greater symptom severity. Exploratory item-level analyses also indicated that urge intensity and frequency, in particular, were associated with decreased functional coupling of the SMA and OFC. The OFC has been established as a core hub for executive functions such as decision-making and planning and thus plays a critical role in mediating goal-directed behavior (Hollerman et al., 2000; Torregrossa et al., 2008). Disrupted function of the OFC is a hallmark neurobiological feature of OCD (Chamberlain et al., 2008; Maltby et al., 2005), and the current findings implicate the OFC in skin-picking, as well. This is consistent with other preliminary neuroimaging work that has indicated OFC abnormalities in excoriation disorder, such as reduced grey matter volume (Schienle, Potthoff, & Wabnegger, 2018). Interestingly, abnormal OFC

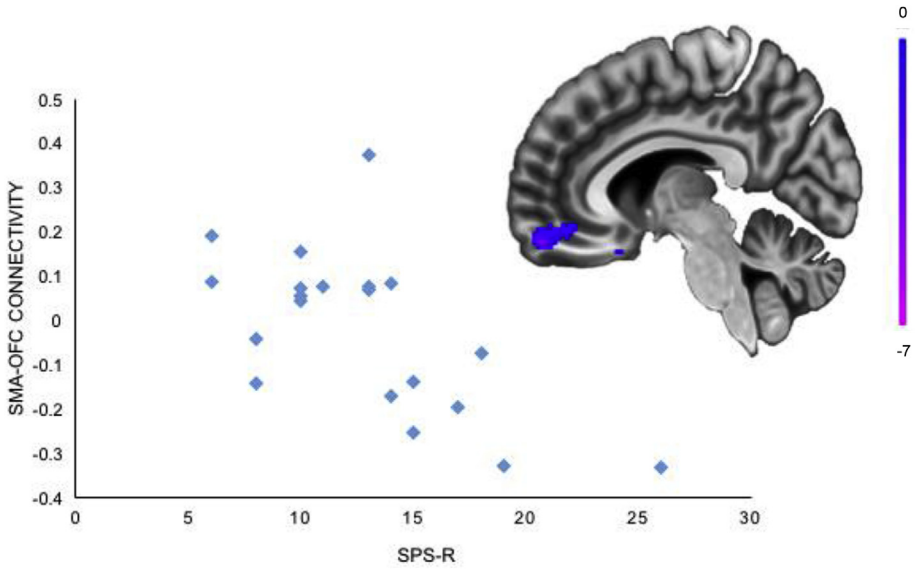

Fig. 1. Scatterplot depicts significant negative effect of skin-picking symptom severity (SPS-R total score, adjusted for sex, age, handedness, and obsessive-compulsive symptoms) on connectivity (r-to-z) of bilateral supplementary motor area (SMA) seed with the medial frontal gyrus/orbitofrontal cortex (6, 56, -18; k = 296; $p_{\text{-corr}}$ = .003).

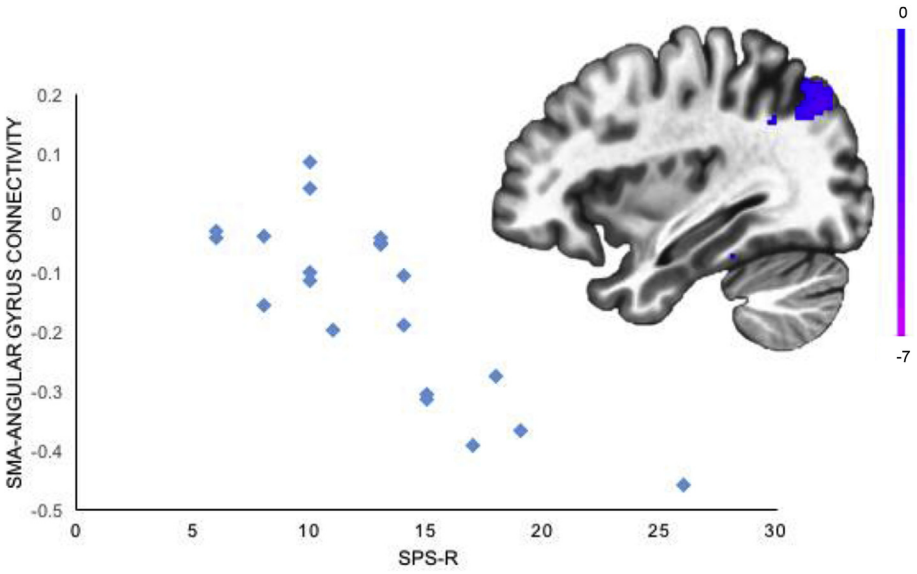

Fig. 2. Scatterplot depicts significant negative effect of skin-picking symptom severity (SPS-R total score, adjusted for sex, age, handedness, and obsessive-compulsive symptoms) on connectivity (r-to-z) of bilateral supplementary motor area (SMA) seed with the left anguar gyrus/inferior parietal lobe (-34, -78, 42; k = 210; $p_{\text{-corr}}$ = .004).

Table 2
Functional connectivity results.

Region	k	$t_{(14)}$	$p_{\text{-corrected}}$	Peak coordinates (MNI)		
				x	y	z
Bilateral SMA seed						
Medial frontal gyrus/OFC	296	6.66	.003	6	56	-18
Angular gyrus/inferior parietal lobe (L)	210	6.45	.004	-34	-78	42
Inferior temporal gyrus (L)	105	5.78	.01	-52	-42	-12
Angular gyrus/inferior parietal lobe (R)	56	5.77	.02	50	-68	40

responsivity corresponding with urge intensity has been observed across other disorders characterized by impulsive or compulsive behavior (e.g., substance use disorders, pathological gambling; (Potenza et al., 2003; Volkow & Fowler, 2000), consistent with our item-level connectivity findings for skin-picking pathology. Such findings suggest that urge intensity may be proportionally related to the metabolic activity of the OFC, which may then have consequences on its regulatory capacity via functional connections to other important regions (e.g., SMA). Given this research, it appears the OFC, particularly in the context of strong urges to pick, may not be effectively planning goal-directed behavior and consequently fails to exert top-down regulation of skin-picking behavior.

The finding that weaker SMA-angular gyrus connectivity was associated with skin-picking symptom severity was somewhat unexpected. While research has shown the angular gyrus to be involved in a variety of processes, many have focused on its role in language (e.g., semantic processing, word reading, comprehension, verbal abstraction) and memory (e.g., retrieval) functions (Binder, Desai, Graves, & Conant, 2009; Ciaramelli, Grady, & Moscovitch, 2008; Seghier, 2013). The broader picture of angular gyrus function, however, purports that the region serves as a cross-modal hub where multisensory information converges and is integrated to support higher-order functions and comprehension (Seghier, 2013). As such, in the case of skin-picking, the angular gyrus may be important for being able to relate sensory (e.g., tactile) information with motor action during picking behavior. The angular gyrus has been shown to play a role in response inhibition, particularly reactive inhibition, or stopping an action in response to a salient stimulus or signal (Nee, Wager, & Jonides, 2007; van Belle, Vink, Durston, & Zandbelt, 2014; Wager et al., 2005). Stimulation of the right

angular gyrus has also been shown to induce dissociative, out-of-body experiences (Blanke, Ortigue, Landis, & Seeck, 2002), suggesting it plays a role in sensory awareness. Importantly, the angular gyrus has also been implicated in action-awareness representations, with neural signal in this region tracking discrepancies between intent and consequence of motor behavior and relating to awareness of action authorship (Farrer et al., 2008). Taken together, these findings support a role for the angular gyrus in pathological skin-picking. Specifically, it may be that the SMA receives insufficient information from the angular gyrus to appropriately modulate willful motor activity and stop picking behavior. Given the associations with action awareness, disruptions within this circuit may be particularly relevant for automatic, rather than focused, skin-picking, wherein the individual engages in picking without particular conscious intent or awareness.

Analysis of the SPS-R subscales indicated that symptom severity, rather than impairment, was associated with weaker SMA-OFC and SMA-angular gyrus functional connectivity. These findings suggest that disruptions within neural circuitry modulating cognitive and motor control may relate to the actual presence of skin-picking symptoms, rather than being a consequence of the disorder itself. However, clinically, skin-picking symptoms can result in significant functional impairment and medical complications (e.g., infection, disfigurement). Results from exploratory item-level analyses indicated that decreased connectivity between the SMA and precentral gyrus was uniquely associated with self-reported tissue damage as a result of picking. The precentral gyrus comprises the primary motor cortex and has substantial anatomical and functional connections with the SMA (Vergani et al., 2014). Although exploratory, taken together, these findings suggest a higher-order motor network recruiting both core motor areas and regions critical for exerting top-down executive control on motor behavior may relate to the severity of symptoms (e.g., urge intensity, perceived control); given the obvious motor component to the disorder, aspects of impairment (e.g., tissue damage) may be more directly grounded in core motor circuitry. Future work would benefit from continuing to disentangle how the complexities of the excoriation phenotype are reflected in functional neural circuitry.

Contrary to hypotheses, no effects of skin-picking symptom severity on functional connectivity of the rIFG were observed in the current study. The rIFG has been established as a critical region for response inhibition (Chambers et al., 2009; Rubia et al., 2003), and abnormalities in this region have been observed in other obsessive-compulsive spectrum disorders (Roth et al., 2007; Woolley et al., 2018). In addition, extant literature suggests skin-picking patients demonstrate impaired inhibitory control during cognitive tasks, such as the stop-signal task, shown to rely on neural circuitry including the rIFG (Grant, Odlaug, & Chamberlain, 2011; Odlaug, Chamberlain, & Grant, 2010). The current study focused on a resting-state design, which may be one explanation for this lack of findings. Specifically, it may be that the neural circuits critical for inhibitory control appear functionally intact while at rest but struggle to effectively communicate when actively trying to suppress motor action. Indeed, previous work has shown the rIFG's role in inhibition is specifically to direct stopping or pausing of a response in action (Aron, Robbins, & Poldrack, 2014); thus, a resting-state state design may not appropriately capture the whether the rIFG is adequately engaging this “brake.” On the other hand, complex interactions within higher-order motor networks may be a more defining feature of pathological skin picking, with preserved function of the rIFG differentiating the disorder from other obsessive-compulsive spectrum disorders. As the neurobiological correlates of skin picking are only just beginning to be understood, future work should continue to examine the rIFG – both in connectivity and function – and how it relates to skin-picking symptom presentation.

The current study is limited in several ways. First, the sample was relatively small and included a number of individuals with mild, subclinical symptoms. Participants were not required to meet DSM-5 criteria to be included in the study. As such, the study may have been underpowered to detect certain effects which may be more robust in larger, more symptomatic samples. Additionally, the study used a self-report questionnaire measure to assess symptoms; clinician-administered diagnostic inventories may be better able to characterize symptom severity and can be used to derive clinical diagnoses. Furthermore, although the current study offers insight into the effects of skin-picking symptoms on neural circuitry, the lack of a control group limits the ability to draw conclusions about how these circuits are disrupted relative to healthy individuals. The current study is also limited in that it is uncertain whether participants engaged in any skin-picking behavior during the fMRI scan. Participants were instructed to lie still during the scan and had relatively little head motion; however, visual monitoring and/or a self-report assessment of skin-picking behavior and urges during the scan would support our conclusions that these circuits are disrupted at rest, rather than during active skin-picking behavior. The inclusion of left-handed individuals is also a limitation. Motor behavior is contralaterized, such that motor cortices of one neural hemisphere direct action on the opposite side of the body (Kim et al., 1993). Moreover, handedness has been shown to have pronounced effects on neural organization (Hécaen, De Agostini, & Monzon-Montes, 1981; Knecht, 2000). While handedness was statistically controlled for, future work would certainly benefit from a solely right-handed sample, or a sample large enough to facilitate comparison of left- and right-handed individuals.

Overall, the current findings point to disruption within higher-order motor networks in pathological skin-picking and contribute to a promising line of research aiming to delineate the neurobiological underpinnings of this disorder. The results demonstrate that skin-picking symptom severity is associated with decreased functional coupling between the SMA and OFC and angular gyrus. As such, individuals who engage in skin picking may struggle to integrate awareness of their behavior with voluntary motor action, contributing to deficits in ability to stop picking. As the current study assessed functional connectivity while at rest, it would be beneficial for future research to investigate whether similar abnormalities are seen during inhibitory control tasks (e.g., stop-signal) and symptom provocation. Additionally, future work would benefit from further breaking down pathological skin-picking into various sub components to better understand competing theoretical models of the disorder. For instance, while many have characterized skin-picking primarily as an inhibitory control disorder (Grant, Odlaug, Chamberlain, et al., 2012; Smári & Ólafsson, 2011), other models attribute the pathology to maladaptive emotion regulation (Roberts, O'Connor, & Bélanger, 2013; 2015) or have conceptualized it as a disgust-based grooming disorder (Bienvenu et al., 2000; Grant, Menard, & Phillips, 2006). Disentangling features of excoriation disorder – such as automatic versus focused picking – and systematically examining potentially relevant constructs – such as emotion regulation strategies, disgust sensitivity, reward sensitivity – is likely to aid in our understanding of how these theoretical models fit together. Broad, refined research in these domains will also help inform understanding of the skin-picking phenotype and potentially indicate clinically-useful subtypes of the disorder.

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Contributors

HL and CL designed the larger intervention study and the neuroimaging sub-study, respectively. AAH, AMH, and TM collected study data. AAH conducted the neuroimaging and statistical analyses and drafted the manuscript. All authors contributed to the revision of the

manuscript and approved it in its final form.

Declaration of competing interest

All authors declare no conflicts of interest.

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