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Motor inhibition and cognitive flexibility in pathologic skin picking ☆

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ABSTRACT

Background: Individuals with pathologic skin picking (PSP) often report significant difficulty resisting the urges and drive to engage in picking behavior. Studies have shown significant inhibitory deficiencies (i.e. increased impulsivity) in subjects with other putative obsessive–compulsive spectrum disorders, such as trichotillomania, using objective tests. This study sought to assess motor inhibitory control and aspects of cognitive flexibility in a sample of individuals with PSP.
Method: Twenty subjects with PSP (mean age 33.1 ± 14.3 years; 85% female) and 20 healthy controls (mean age 31.6 ± 9.1 years; 85% female) underwent cognitive assessments using the Stop-signal and Intra-dimensional/Extra-dimensional (ID/ED) set-shift tasks. Groups were matched for age, gender, and education.
Results: PSP was associated with significantly impaired stop-signal reaction times but intact ID/ED cognitive flexibility compared to controls. Measures of disease severity in the PSP subjects did not covary significantly with stop-signal performance.
Conclusion: The finding of impaired inhibitory control but intact set-shift cognitive flexibility draws remarkable parallels with findings in trichotillomania but differs from obsessive compulsive disorder. These findings have important implications for understanding potential neurobiological dysfunction in PSP, how the disorder should be classified, and suggest new potential treatment directions.
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1. Introduction

Pathologic skin picking (PSP) is characterized by repetitive and compulsive picking of skin which causes tissue damage. Although there have been no population-wide epidemiological studies of PSP, it has an estimated prevalence rates of 2.0%–5.4% in the general population (Keuthen et al., 2000; Hayes et al., 2009). Individuals with PSP report that picking behavior causes scarring and infections, impairment in daily functioning, and significant distress stemming from their inability to control the behavior (Gupta et al., 1986; Arnold et al., 1998; Odlaug and Grant, 2008a,b).

The compulsive and repetitive behaviors seen in PSP and other grooming behaviors such as trichotillomania (TTM) have led to the hypothesis that they be classified as disorders of the obsessive–compulsive spectrum (Stein and Hollander, 1995). The often overwhelming urges to pick or pull coupled with a sense of relief or calm after engaging in the behavior reported by those with PSP and TTM are very similar to the urges to engage in compulsive acts reported by those with obsessive compulsive disorder (OCD). Studies have also shown significant clinical similarities between PSP and TTM such as age of onset, gender ratio, psychosocial functioning, and clinical severity (Cohen et al., 1995; Odlaug and Grant, 2008a). Furthermore, the body-focused, repetitive nature of PSP shares similarities to the compulsive acts seen in disorders such as OCD (Stein et al., 2006, 2008). Due to these phenomenological connections, tests of neurocognitive functioning have been examined in trichotillomania and OCD (Rettew et al., 1991; Keuthen et al., 1996; Coetzer and Stein, 1999; Bohne et al., 2005; Chamberlain et al., 2006). Chamberlain et al. (2006) measured motor inhibition (impulsivity) and aspects of cognitive flexibility in a group of 17 trichotillomania subjects, 20 OCD subjects, and 20 healthy controls (Chamberlain et al., 2006). Significant deficits of motor inhibition (Stop-signal task) were noted in both the trichotillomania and OCD groups but only the OCD group showed deficits in extra-dimensional set-shifting (assessed using the CANTAB intra-dimensional/extra-dimensional, ID/ED set-shift task). While set-shifting appears to be intact in trichotillomania, other aspects of cognitive flexibility may be impaired in this disorder. Bohne et al. (2005) reported impaired performance in trichotillomania subjects on the Object Alternation Test, while Stanley et al. (1997) showed impaired performance on Trails B test.

Despite the above research into other putative OC spectrum conditions, there have—to the knowledge of the authors—been no

Abbreviations: ADHD, Attention Deficit Hyperactivity Disorder; CGI, clinical global impression; HARS, Hamilton Anxiety Rating Scale; HC, healthy control; HDRS, Hamilton Depression Rating Scale; IDED, intra-dimensional extra-dimensional; OCD, obsessive compulsive disorder; PSP, pathological skin picking; SCID, Structured Clinical Interview for DSM-IV; SP-SAS, Skin Picking Symptom Assessment Scale; SP-YBOCS, Yale Brown Obsessive Compulsive Scale Modified for Skin Picking; SSRT, stop-signal reaction times; TTM, trichotillomania.

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studies of cognitive dysfunction in patients with PSP. Due to the clinical similarities of PSP to other disorders such as trichotillomania, this study sought to examine impulsivity and aspects of cognitive flexibility in a group of subjects with PSP. We hypothesized that significant deficits in motor inhibition would be found in the PSP population but that no deficits of ID/ED cognitive flexibility would be identified.

2. Materials and methods

2.1. Patient population

Patient participants were 20 adults aged ≥18 years who met full-diagnostic criteria for current PSP (Arnold et al., 2001): 1) Recurrent picking at or otherwise manipulating the skin that results in noticeable damage to the skin; 2) an increasing sense of tension, or an unpleasant emotional or physical state, immediately before picking the skin, or when trying to resist picking; 3) pleasure, gratification or relief at the time of picking; 4) clinically significant distress or impairment in social, occupational, or other important areas of function; 5) the skin picking is not due to a substance or a general medical condition; and 6) the skin picking is not better accounted for by another mental disorder (e.g., body dysmorphic disorder, obsessive compulsive disorder, delusion disorder, substance use disorder). All subjects were required to have picked their skin during the week prior to enrollment and to have picked on average at least once per week for the past 3 months. Although many studies have identified PSP as simply picking with result in significant distress, (Keuthen et al., in press), this study sought to identify more severe skin picking meeting full-proposed diagnostic criteria. PSP subjects were recruited via newspaper advertisements.

Exclusion criteria included: 1) use of psychotropic medication; 2) any thoughts of suicide; 3) current Axis I disorder determined by the Structured Clinical Interview of DSM-IV (SCID) and by SCID-compatible modules for impulse control disorders; 4) lifetime history of bipolar disorder type I or II, dementia, schizophrenia, or any psychotic disorder determined by SCID; 5) past 3 months DSM-IV substance abuse or dependence; 6) positive urine drug screen; and 7) initiation of psychotherapy or behavior therapy within 3 months prior to study entry.

Healthy control participants (HC) were also recruited for this study. Healthy volunteers were recruited via fliers and word of mouth. Inclusion criteria for HC subjects included no current (past 12 month) history of Axis I psychiatric disorders and no use of psychotropic medications.

The institutional review board for the University of Minnesota approved the study. This study was carried out in accordance with the Declaration of Helsinki. After complete description of the study to the subjects, written informed consent was obtained.

2.2. Clinical assessment

Subjects underwent a semi-structured interview assessing the clinical features of skin picking (e.g., time spent picking, triggers to behavior). Subjects were also evaluated using the Structured Clinical Interview for DSM-IV (SCID) (First et al., 2000) and SCID-compatible modules for impulse control disorders (Grant et al., 2005). Medical history and physical examination were performed.

In addition, skin picking symptoms were assessed using the clinician-administered Yale Brown Obsessive Compulsive Scale Modified for Skin Picking (SP-YBOCS) (Arnold et al., 1999; Grant et al., 2007) and the self-rated Skin Picking Symptom Assessment Scale (SP-SAS) (Grant et al., 2007). The Clinical Global Impression- Severity scale (CGI) (Guy, 1976) assessed severity in clinical symptoms. Anxiety symptoms were rated with the Hamilton Anxiety Rating Scale (HARS) (Hamilton, 1959), and depressive symptoms were assessed using the Hamilton Depression Rating Scale (HDRS) (Hamilton, 1960).

2.3. Cognitive testing

Cognitive testing was conducted using two previously validated tests taken from CANTABeclipse software (Cambridge Cognition Ltd., 2006). All testing was conducted in the same controlled environment to minimize confounding variables across subjects.

The stop-signal task was used to assess motor inhibition (impulsivity) (Logan et al., 1984; Aron et al., 2004). On this test, subjects were instructed to respond to a left- or right-facing arrow which appeared on a computer screen in a rapid fashion. Corresponding motor responses were measured as were the subjects' ability to inhibit responses when an auditory "beep" (stop-signal) sound occurred on a subset of trials. Through an algorithm, the time taken to internally suppress prepotent motor responses was measured, i.e. Stop-Signal Reaction Times (SSRT). Key outcome variables were SSRT, mean reaction time on 'go' trials, and the total number of directional errors made. This task has been shown to be dependent on distributed neural circuitry including the right inferior frontal gyrus (Aron et al., 2003a, 2005, 2007; Aron and Poldrack, 2006).

Aspects of cognitive flexibility relating to set-shifting were measured using the Intra-dimensional/Extra-dimensional Shift Task (ID/ED task), developed from the Wisconsin Card Sorting Test assessing frontal lobe integrity (Lezak et al., 2004). This test involved nine stages using multidimensional stimuli presented as a visual discrimination task. On the task, subjects were presented with two stimuli on-screen for each trial, and attempted to learn an underlying 'rule' about which stimulus was correct. After each choice, the task provided the subject with feedback (right/wrong). Thus, through experience, volunteers attempted to learn the underlying rule. After meeting learning criterion (6 consecutive correct choices), the rule was changed by the computer. Key outcome variables were the number of errors made on the Intra-dimensional (ID) and Extra-dimensional (ED) stages of the task.

2.4. Statistical analysis

A power calculation based on previous findings in patients with trichotillomania compared to healthy volunteers (Chamberlain et al., 2006), indicated that a sample size of $n = 20$ per group would provide >90% power to detect a significant group difference on stop-signal reaction times, assuming a similar magnitude of deficit, and an alpha of 0.01 http://www.dssresearch.com/toolkit/spcalc/power_a2.asp).

Demographic and neurocognitive indices were compared between the two study groups using independent *t*-tests, with the significance threshold set a priori at $p<0.05$. For significant pair-wise differences, effect sizes were calculated (Cohen's *D*). For variables where normality was violated, data were transformed to improve suitability for parametric statistics (Cardinal and Aitken, 2006). Where significant cognitive deficits were identified in PSP subjects, the relationships between these deficits and disease severity were explored via correlational analyses (Spearman's *r*).

3. Results

Demographic results for the two study groups are presented in Table 1. A total of 24 people reporting significant skin picking problems were screened and of these subjects, 20 met full PSP criteria and were included in this sample. A total of 20 subjects with PSP (mean age 33.1 ± 14.3 years; 85% female) and 20 healthy controls (mean age 31.6 ± 9.1 years; 85% female) underwent cognitive testing. The two groups were well-matched in terms of age, gender, and educational level (Table 1).

Mean age at onset of skin picking was 14.1 ± 11.7 (range 4–58) years. 10 subjects (50%) reported picking primarily at the face or head, 7 (35%) at the feet or hands, 2 (10%) at the arms or legs, and 1 (5%) at their torso. Fifteen (85%) subjects were aware of beginning their

Table 1
Demographic variables in 20 individuals with pathologic skin picking (PSP) and 20 healthy controls (mean, SD).

Variable	PSP ($n=20$)	Controls ($n=20$)	t	p
Age, yrs				
Mean (SD)	31.75 (14.11)	31.6 (9.05)	0.040	0.968
Female, n (%)	16 (80)	16 (80)		ns
Race/ethnicity, n (%)				
Caucasian	19 (95)	17 (85)		
Other	1 (5)	3 (15)	f	0.605
Marital status, n (%)				
Single	13 (65)	11 (55)		
Married	6 (30)	7 (35)		
Widow/separated/divorced	1 (5)	2 (10)	f	0.612
Education, n (%)				
High school grad or less	1 (5)	0 (0)		
Some college	7 (35)	7 (35)		
College graduate	12 (60)	13 (65)	f	0.741

f—Fisher's Exact test.
PSP = Pathologic Skin Picking.
Independent t-tests, $df=1,38$.

picking behavior at least 50% of the time, whereas 5 (15%) were aware of picking less than 50% of the time and therefore were picking "automatically" most of the time.

PSP subjects were generally quite ill, reporting a mean of 154.5 ± 107.19 min spent picking each day, with some subjects spending 6–8 h each day. Mean scores on the SP-YBOCS, SP-SAS, and CGI were 19.1 ± 4.1 (range 11–25), 27.4 ± 6.12 (12–36), and 4.2 ± 0.62 (3–5), respectively, equating to moderate severity of picking (Grant et al., 2007). Depressive mood and anxiety scores (HDRS and HARS scores) in the PSP patients were low and subclinical (4.1 ± 3.0 [range 0–9] and 3.9 ± 2.71 [range 0–7]) respectively.

On the Stop-signal test, patients with PSP exhibited significantly lengthened stop-signal reaction times (Cohen's $D=0.89$), and made significantly more directional errors (Cohen's $D=0.69$), compared to the healthy controls (Table 2). The two groups did not differ significantly in terms of mean reaction times for 'go' trials on the Stop-signal task. On the ID/ED task, the performance of PSP subjects did not differ from that of healthy volunteers.

There were no significant correlations between stop-signal reaction times and disease severity (SP-YBOCS, SP-SAS, CGI-Severity); nor between the number of directional errors and disease severity, in the PSP subjects (all $p>0.10$).

4. Discussion

This is the first study to assess cognitive function in Pathological Skin Picking (PSP), a debilitating yet under-researched and often overlooked psychiatric condition. The key finding was that subjects with PSP exhibited impaired inhibitory control on the stop-signal task but intact cognitive flexibility on the IDED task. This profile is remarkably akin to that previously reported in patients with trichotillomania (Chamberlain et al., 2006), a disorder with clinical, phenomenological, and possible biological and genetic links to PSP (Stein et al., 2006; Odlaug and Grant, 2008a,b). Significantly longer motor inhibitory response times have also been documented in other disorders characterized by problems suppressing inappropriate behavior, including methamphetamine abuse (Monterosso et al., 2005) and Attention Deficit Hyperactivity Disorder (ADHD) (Aron et al., 2003b; Lijffijt et al., 2005; Chamberlain et al., 2007a). Importantly, inhibitory deficits identified in PSP herein occurred in the absence of clinically significant anxiety or depressive mood, as indexed by HAM-A and HAM-D.

Stop-signal performance is dependent on a right lateralized fronto-striatal neural network including the right inferior frontal and bilateral anterior cingulate cortices. Patients with neurosurgical lesions to the right inferior frontal gyrus show impaired inhibitory control the magnitude of which is proportional to the volume of damage (Aron et al., 2003a). Multiple neuroimaging studies indicate that inhibitory control activates these regions. In translational studies, administration of the selective noradrenaline reuptake inhibitor atomoxetine has been shown to improve stop-signal inhibitory control, while serotonin manipulations had no effect (for reviews see Chamberlain et al., 2007b; Chamberlain and Sahakian, 2007). The finding of markedly impaired stop-signal performance in patients with PSP (large effect size) may implicate dysfunction of right frontal and bilateral cingulate cortices in its pathophysiology. Furthermore, these data suggest that it would be valuable to explore the clinical utility of pharmacological agents known to augment inhibitory control in the treatment of PSP in appropriately controlled trials. It would also be interesting to study whether inhibitory control in patients can be improved through neurocognitive training or adapted psychotherapies emphasizing this ability. Effective behavioral treatments (e.g., habit reversal and acceptance and commitment therapy) for PSP have been published (Teng et al., 2006; Twohig et al., 2006) and should be considered in conjunction with pharmacotherapies, since they often focus on improving individuals' inhibitory control over habits.

4.1. Conclusions—Future directions and limitations

Although this is the first ever published assessment of cognition in PSP, several limitations should be considered. The study had ample power to explore our primary hypothesis (that individuals with PSP would demonstrate impaired SSRT), but the overall sample size was relatively small, and this may have limited power to detect correlations between cognitive dysfunction and disease severity. It is noteworthy, however, that a sample size of ~20 was sufficient to detect a correlation between Stop-signal deficit and disease severity in trichotillomania patients previously (Chamberlain et al., 2006). We did not collect information regarding Axis-II disorders in the sample, nor did we collect anxiety/depression scores in the healthy volunteers. PSP subjects were mostly free from co-morbidities, and this may limit the generalizability of the findings. This study was neither designed nor powered to assess possible subtypes of PSP, such as patients with 'automatic' versus 'non-automatic' picking. In particular, previous work has suggested that focused hair-pulling, versus non focused hair-pulling, tends to be associated with, and to some extent driven by, anxiety and depressive mood. In the current paper, we found that patients with PSP—largely with focused symptoms—exhibited low levels of anxiety and dysphoria, as indexed by clinical instruments. It may be that the instruments used by the current study did not fully capture the contribution of these factors during acute episodes of picking; that there are differences between PSP and TTM; or some combination of these factors. Future studies should incorporate a

Table 2
Cognitive measures in 20 individuals with pathologic skin picking (PSP) and 20 healthy controls (mean, SD).

Cognitive variables	PSP ($n=20$)	Controls ($n=20$)	t	p
SST median correct RT on GO trials	463.63 (152.11)	492.71 (99.13)	−0.716	0.478
SST SSRT (last half)	207.20 (98.99)	139.89 (40.17)	2.818	0.008**
SST direction errors on stop and go trials	6.50 (10.65)	1.20 (1.64)	2.200	0.034*
IED total errors (adjusted)	17.05 (15.57)	12.00 (8.34)	1.278	0.209
Errors, ID shift	0.25 (0.55)	0.40 (0.5)	−0.900	0.374
Errors, ED shift	6.30 (7.85)	4.95 (5.91)	0.615	0.542

PSP = pathologic skin picking.
Independent t-tests, $df=1,38$.
* $p<0.05$.
** $p<0.01$.

larger sample size of subjects, and assess a broader range of neurocognitive domains in patients with PSP and the functional impact of any deficits identified. Furthermore, neuroimaging could be used to probe the correlates of any cognitive deficits identified in patients.

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