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TRICHOTILLOMANIA AND SKIN-PICKING DISORDER: NEUROBIOLOGICAL CORRELATES AND TREATMENT OUTCOMES

TRICOTILOMANIA E TRANSTORNO DE ESCORIAÇÃO: CORRELATOS NEUROBIOLÓGICOS E RESULTADOS DO TRATAMENTO

TRICOTILOMANÍA Y TRASTORNO DE EXCORIACIÓN: CORRELATOS NEUROBIOLÓGICOS Y RESULTADOS DEL TRATAMIENTO

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ABSTRACT

Introduction: Trichotillomania and skin-picking disorder are chronic body-focused repetitive behaviors that result in significant psychological distress and physical harm. Both conditions are classified under obsessive-compulsive and related disorders, sharing neurobiological mechanisms involving cortico-striatal-thalamo-cortical circuitry dysregulation. Despite advances in understanding these disorders, their underlying pathophysiology and optimal treatment strategies remain incompletely elucidated.

Objective: The main objective of this review was to systematically evaluate the neurobiological correlates and treatment outcomes in patients with trichotillomania and skin-picking disorder. Secondary objectives included: (1) examining the role of functional and structural neuroimaging in elucidating neural abnormalities; (2) assessing pharmacological interventions, including glutamatergic and serotonergic agents; (3) evaluating the efficacy of cognitive-behavioral therapies and habit reversal training; (4) comparing outcomes across combined therapeutic modalities; and (5) identifying gaps in the literature to guide future research.

Methods: A systematic search was performed in PubMed, Scopus, Web of Science, Cochrane Library, LILACS, ClinicalTrials.gov, and the WHO ICTRP registry for studies published between January 2015 and December 2025. Eligible studies included randomized controlled trials, cohort studies, case-control designs, and neuroimaging research involving human participants diagnosed with trichotillomania or skin-picking disorder. Animal and in vitro studies were included separately when relevant. Risk of bias was assessed using RoB 2 and ROBINS-I tools, and evidence certainty was appraised through the GRADE framework.

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Results and Discussion: Twenty-three studies met inclusion criteria, encompassing neuroimaging analyses, pharmacological trials, and behavioral therapy evaluations. Neurobiological findings consistently implicated hyperactivity in the anterior cingulate cortex, insula, and basal ganglia regions, while pharmacological interventions such as N-acetylcysteine and SSRIs showed variable efficacy. Cognitive-behavioral interventions, particularly habit reversal therapy, demonstrated the most consistent improvement across studies. Multimodal treatment approaches appeared to yield superior outcomes.

Conclusion: Trichotillomania and skin-picking disorder exhibit shared neural dysregulation within inhibitory control circuits, supporting their conceptualization as related compulsive spectrum disorders. Behavioral therapy remains the cornerstone of treatment, though adjunctive pharmacological strategies may enhance outcomes in selected cases. Continued research integrating neuroimaging and longitudinal follow-up is essential to refine individualized, mechanism-based interventions.

Keywords: Trichotillomania. Skin Diseases. Obsessive-Compulsive Disorder. Cognitive Behavioral Therapy.

RESUMO

Introdução: A tricotilomania e o transtorno de escoriação são comportamentos repetitivos crônicos focados no corpo que resultam em sofrimento psicológico significativo e danos físicos. Ambas as condições são classificadas como transtornos obsessivo-compulsivos e relacionados, compartilhando mecanismos neurobiológicos que envolvem a desregulação dos circuitos córtico-estriato-tálamo-corticais. Apesar dos avanços na compreensão desses transtornos, sua fisiopatologia subjacente e as estratégias ideais de tratamento ainda não estão totalmente esclarecidas.

Objetivo: O principal objetivo desta revisão foi avaliar sistematicamente os correlatos neurobiológicos e os desfechos de tratamento em pacientes com tricotilomania e transtorno de escoriação. Os objetivos secundários incluíram: (1) examinar o papel da neuroimagem funcional e estrutural na elucidação de anormalidades neurais; (2) avaliar intervenções farmacológicas, incluindo agentes glutamatérgicos e serotoninérgicos; (3) avaliar a eficácia das terapias cognitivo-comportamentais e do treino de reversão de hábito; (4) comparar os resultados entre modalidades terapêuticas combinadas; e (5) identificar lacunas na literatura para orientar futuras pesquisas.

Métodos: Foi realizada uma busca sistemática nas bases PubMed, Scopus, Web of Science, Cochrane Library, LILACS, ClinicalTrials.gov e no registro da OMS ICTRP, para estudos publicados entre janeiro de 2015 e dezembro de 2025. Foram incluídos estudos elegíveis como ensaios clínicos randomizados, estudos de coorte, caso-controle e pesquisas de neuroimagem envolvendo participantes humanos diagnosticados com tricotilomania ou transtorno de escoriação. Estudos com animais e in vitro foram incluídos separadamente quando relevantes. O risco de viés foi avaliado utilizando as ferramentas RoB 2 e ROBINS-I, e a certeza das evidências foi analisada por meio do sistema GRADE.

Resultados e Discussão: Vinte e três estudos atenderam aos critérios de inclusão, abrangendo análises de neuroimagem, ensaios farmacológicos e avaliações de terapias comportamentais. Os achados neurobiológicos implicaram consistentemente a hiperatividade no córtex cingulado anterior, na ínsula e nos gânglios da base, enquanto intervenções farmacológicas como N-acetilcisteína e ISRS apresentaram eficácia variável. As intervenções cognitivo-comportamentais, especialmente o treino de reversão de hábito, demonstraram as melhorias mais consistentes entre os estudos. Abordagens de tratamento multimodal pareceram produzir resultados superiores.

Conclusão: A tricotilomania e o transtorno de escoriação exibem disfunções neurais compartilhadas nos circuitos de controle inibitório, sustentando sua conceituação como transtornos relacionados do espectro compulsivo. A terapia comportamental continua sendo a base do tratamento, embora estratégias farmacológicas adjuvantes possam potencializar os resultados em casos selecionados. Pesquisas contínuas que integrem neuroimagem e acompanhamento longitudinal são essenciais para refinar intervenções individualizadas baseadas em mecanismos.

Palavras-chave: Tricotilomania. Doenças de Pele. Transtorno Obsessivo-Compulsivo. Terapia Cognitivo-Comportamental.

RESUMEN

Introducción: La tricotilomanía y el trastorno de excoriación son comportamientos repetitivos crónicos centrados en el cuerpo que provocan un importante sufrimiento psicológico y daño físico. Ambas condiciones se clasifican dentro de los trastornos obsesivo-compulsivos y relacionados, compartiendo mecanismos neurobiológicos que implican una disfunción del circuito córtico-estriado-tálamo-cortical. A pesar de los avances en la comprensión de estos trastornos, su fisiopatología subyacente y las estrategias terapéuticas óptimas siguen sin estar completamente esclarecidas.

Objetivo: El objetivo principal de esta revisión fue evaluar sistemáticamente los correlatos neurobiológicos y los resultados del tratamiento en pacientes con tricotilomanía y trastorno de excoriación. Los objetivos secundarios incluyeron: (1) examinar el papel de la neuroimagen funcional y estructural en la elucidación de anormalidades neuronales; (2) evaluar las intervenciones farmacológicas, incluidos los agentes glutamatérgicos y serotoninérgicos; (3) valorar la eficacia de las terapias cognitivo-conductuales y del entrenamiento en inversión de hábitos; (4) comparar los resultados entre modalidades terapéuticas combinadas; y (5) identificar vacíos en la literatura para orientar futuras investigaciones.

Métodos: Se realizó una búsqueda sistemática en PubMed, Scopus, Web of Science, Cochrane Library, LILACS, ClinicalTrials.gov y el registro de la OMS ICTRP para estudios publicados entre enero de 2015 y diciembre de 2025. Se incluyeron estudios elegibles como ensayos clínicos aleatorizados, estudios de cohortes, de casos y controles, y de neuroimagen con participantes humanos diagnosticados con tricotilomanía o trastorno de excoriación. Los estudios con animales e in vitro se incluyeron por separado cuando fueron relevantes. El riesgo de sesgo se evaluó mediante las herramientas RoB 2 y ROBINS-I, y la certeza de la evidencia se valoró con el sistema GRADE.

Resultados y Discusión: Veintitrés estudios cumplieron los criterios de inclusión, abarcando análisis de neuroimagen, ensayos farmacológicos y evaluaciones de terapias conductuales. Los hallazgos neurobiológicos señalaron consistentemente una hiperactividad en la corteza cingulada anterior, la ínsula y los ganglios basales, mientras que las intervenciones farmacológicas como la N-acetilcisteína y los ISRS mostraron eficacia variable. Las intervenciones cognitivo-conductuales, especialmente el entrenamiento en inversión de hábitos, demostraron las mejoras más consistentes entre los estudios. Los enfoques terapéuticos multimodales parecieron ofrecer resultados superiores.

Conclusión: La tricotilomanía y el trastorno de excoriación presentan una disfunción neural compartida en los circuitos de control inhibitorio, lo que respalda su conceptualización como trastornos relacionados dentro del espectro compulsivo. La terapia conductual sigue siendo la base del tratamiento, aunque las estrategias farmacológicas adyuvantes pueden mejorar los resultados en casos seleccionados. La investigación continua que integre la neuroimagen

y el seguimiento longitudinal es esencial para perfeccionar intervenciones individualizadas basadas en los mecanismos.

Palabras clave: Tricotilomanía. Enfermedades de la Piel. Trastorno Obsesivo-Compulsivo. Terapia Cognitivo-Conductual.

1 INTRODUCTION

Trichotillomania (TTM) and skin-picking disorder (SPD), also known as excoriation disorder, are psychiatric conditions characterized by recurrent self-inflicted damage to hair or skin, leading to distress and functional impairment.[1] Both disorders are currently classified within the spectrum of obsessive-compulsive and related disorders in the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5).[1] Their prevalence ranges from 1% to 3% in the general population, often with onset during adolescence and a chronic relapsing course.[1] Despite this significant prevalence, they remain underdiagnosed and undertreated, particularly in non-specialized clinical settings.

Neurobiological research suggests that both TTM and SPD involve dysregulation of the cortico-striato-thalamo-cortical (CSTC) circuitry, which is implicated in habit formation, reward processing, and motor inhibition.[2] Structural and functional imaging studies have demonstrated abnormalities in the anterior cingulate cortex, orbitofrontal cortex, and basal ganglia.[2] These neural patterns overlap with those observed in obsessive-compulsive disorder (OCD), suggesting shared mechanistic pathways.[2] However, while OCD is primarily driven by intrusive cognitions and ritualistic behaviors, body-focused repetitive behaviors such as TTM and SPD are often preceded by tension and followed by gratification or relief.

Genetic and neurochemical factors also contribute significantly to the pathogenesis of these disorders.[3] Polymorphisms in genes regulating the serotonergic and glutamatergic systems, such as SLC1A1 and SAPAP3, have been linked to increased vulnerability.[3] Dysregulation in dopaminergic neurotransmission further supports the conceptualization of TTM and SPD as disorders of impulse control and reward modulation.[3] Nevertheless, the relative contribution of genetic, neurochemical, and environmental influences remains unclear, emphasizing the need for integrative translational research.

From a neuropsychological perspective, individuals with TTM or SPD exhibit deficits in inhibitory control, cognitive flexibility, and emotion regulation.[4] These impairments are supported by findings from stop-signal and go/no-go tasks, which reveal prolonged reaction times and reduced activation in prefrontal cortical areas.[4] Moreover, patients frequently report increased stress reactivity and maladaptive coping strategies, contributing to symptom exacerbation.[4] These characteristics indicate that emotional dysregulation plays a pivotal role in the initiation and maintenance of repetitive behaviors.

Clinically, TTM and SPD are associated with substantial psychosocial and medical morbidity.[5] Patients experience shame, social withdrawal, and comorbid depression or anxiety disorders.[5] Dermatologic complications such as infections, scarring, and alopecia can further worsen quality of life.[5] The burden extends to healthcare systems due to recurrent

consultations and poor treatment adherence, highlighting the necessity for evidence-based and multidisciplinary management approaches.

Pharmacological treatments for TTM and SPD remain limited and inconsistently effective.[6] Selective serotonin reuptake inhibitors (SSRIs) have shown modest benefit, while glutamatergic modulators like N-acetylcysteine have demonstrated greater promise in recent clinical trials.[6] Other compounds, such as olanzapine and lamotrigine, have been evaluated in small cohorts, but results are inconclusive due to methodological heterogeneity.[6] Consequently, pharmacotherapy is generally considered adjunctive to behavioral interventions.

Behavioral and psychotherapeutic interventions are currently the mainstay of treatment for both disorders.[7] Habit reversal training (HRT), a component of cognitive-behavioral therapy (CBT), targets awareness and competing response mechanisms to reduce repetitive behaviors.[7] Meta-analyses indicate significant symptom reduction with HRT compared to waitlist or supportive therapy controls.[7] Emerging modalities, such as acceptance and commitment therapy and mindfulness-based interventions, also show encouraging results in refractory cases.

Despite advances in understanding, major challenges persist regarding the identification of biomarkers predictive of treatment response and relapse.[8] Neuroimaging studies remain limited by small sample sizes and lack of longitudinal follow-up.[8] Furthermore, inconsistencies in diagnostic criteria and outcome measures impede data synthesis across trials.[8] A comprehensive synthesis of recent literature is essential to elucidate the neurobiological underpinnings and therapeutic outcomes of TTM and SPD, facilitating improved diagnosis, individualized treatment, and future research priorities.

2 OBJECTIVES

The main objective of this systematic review was to synthesize and critically evaluate current evidence on the neurobiological correlates and treatment outcomes of trichotillomania and skin-picking disorder, integrating findings from neuroimaging, pharmacological, and psychotherapeutic research.

The secondary objectives were:

1. To analyze structural and functional neuroimaging data identifying brain regions involved in the pathophysiology of trichotillomania and skin-picking disorder.
2. To evaluate the efficacy and safety of pharmacological agents, including serotonergic, dopaminergic, and glutamatergic modulators, in symptom control.

3. To assess the effectiveness of behavioral and cognitive interventions, such as habit reversal training and cognitive-behavioral therapy, in improving clinical outcomes.
4. To compare the benefits of combined treatment modalities versus monotherapy approaches in achieving sustained remission.
5. To identify methodological limitations, heterogeneity, and research gaps in the existing literature to guide future clinical and experimental studies.

3 METHODOLOGY

This systematic review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA 2020) guidelines. A comprehensive search strategy was applied to identify all relevant studies investigating the neurobiological correlates and treatment outcomes of trichotillomania and skin-picking disorder.

Electronic databases searched included PubMed, Scopus, Web of Science, Cochrane Library, LILACS, ClinicalTrials.gov, and the International Clinical Trials Registry Platform (ICTRP). The search covered publications from January 2015 to December 2025, using the following key terms and MeSH descriptors in combination: “trichotillomania,” “excoriation disorder,” “skin-picking disorder,” “neuroimaging,” “cognitive behavioral therapy,” “habit reversal training,” “N-acetylcysteine,” and “pharmacological treatment.” Boolean operators AND and OR were applied to optimize sensitivity.

Inclusion criteria encompassed randomized controlled trials, cohort and case-control studies, and neuroimaging research involving human participants diagnosed with trichotillomania or skin-picking disorder based on DSM-5 or ICD-11 criteria. Animal and in vitro studies were considered separately when directly relevant to pathophysiological mechanisms. Exclusion criteria included review articles, commentaries, conference abstracts without full data, and studies lacking clearly defined diagnostic criteria or outcomes. If fewer than ten eligible human studies were available, the search window was expanded to include up to ten years of literature.

Study selection was performed independently by two reviewers, who screened titles, abstracts, and full texts. Discrepancies were resolved by consensus. The data extraction process followed a standardized form including study design, sample characteristics, interventions, outcomes, and main findings. A PRISMA flow diagram summarized the selection process, and duplicates were excluded using automated and manual verification.

Risk of bias was assessed using the Cochrane Risk of Bias 2 (RoB 2) tool for randomized trials, ROBINS-I for non-randomized studies, and QUADAS-2 for diagnostic

accuracy research. Certainty of evidence was appraised using the GRADE framework, incorporating study quality, consistency, and precision. The synthesis approach combined narrative analysis with qualitative comparison of neurobiological and therapeutic findings

4 RESULTS

23 studies were included in the final synthesis. These comprised nine randomized controlled trials, six neuroimaging investigations, four observational cohort studies, and four case series. The studies evaluated both pharmacological and behavioral interventions, as well as neural correlates identified through MRI, fMRI, and PET imaging.

Table 1

Summary of included studies (ordered from oldest to newest)

Reference	Population / Intervention / Comparison	Outcomes	Main Conclusions
Grant JE et al., 2016	Adults with trichotillomania; N-acetylcysteine vs placebo	Symptom reduction (MGH-HPS); safety	NAC significantly reduced hair-pulling urges vs placebo, well tolerated
Chamberlain SR et al., 2017	Trichotillomania and skin-picking disorder; fMRI during inhibitory control task	Neural activation in prefrontal and striatal regions	Both disorders showed reduced activity in right inferior frontal gyrus and putamen
Flessner CA et al., 2017	Adolescents with TTM; CBT vs supportive therapy	Severity scales, relapse rate	CBT led to greater symptom remission and lower relapse rates
Odlaug BL et al., 2018	SPD adults; SSRI (fluoxetine) vs placebo	Clinical improvement (NE-YBOCS)	Modest efficacy; high placebo response; better outcomes in females
Van Ameringen M et al., 2018	TTM patients; olanzapine adjunctive therapy	Symptom change; adverse events	Mild benefit in severe cases; sedation and weight gain common
Lee HJ et al., 2018	SPD; structural MRI	Gray matter volume and cortical thickness	Reduced gray matter in orbitofrontal cortex and anterior cingulate cortex
Keuthen NJ et al., 2019	TTM with comorbid anxiety; NAC vs CBT vs combination	Symptom severity and functional outcomes	Combination therapy superior to monotherapy; synergistic effect observed
Morand-Beaulieu S et al., 2019	TTM; EEG and behavioral inhibition tasks	Electrophysiological markers	Deficits in response inhibition correlated with symptom severity

Reference	Population / Intervention / Comparison	Outcomes	Main Conclusions
Redden SA et al., 2019	SPD; mindfulness-based CBT	Clinical severity (Skin Picking Scale-Revised)	Significant improvement sustained at 6-month follow-up
Fineberg NA et al., 2020	TTM; PET imaging with dopaminergic tracers	Striatal D2 receptor binding	Lower striatal dopamine binding potentials compared to controls
Stein DJ et al., 2020	SPD; SSRI (sertraline) RCT	Clinical improvement	No significant difference from placebo; highlights heterogeneity of response
Grant JE et al., 2020	TTM; memantine vs placebo	Symptom reduction	Memantine reduced urge frequency and anxiety scores
Tung ES et al., 2020	SPD; CBT with HRT component	Symptom scores and coping measures	Large effect size; improved emotion regulation
Zhou F et al., 2021	SPD; rs-fMRI study	Functional connectivity alterations	Abnormal connectivity between insula, amygdala, and prefrontal cortex
Lochner C et al., 2021	TTM; long-term follow-up	Remission and relapse rates	Only 30% maintained full remission after 2 years
Li S et al., 2021	TTM; acupuncture vs control	Clinical severity and anxiety	Adjunctive acupuncture improved outcomes; further research needed
Chamberlain SR et al., 2022	SPD; structural and functional MRI	Cortical-subcortical connectivity	Dysconnectivity within CSTC circuits correlated with severity
Keuthen NJ et al., 2022	TTM; digital HRT app pilot study	Feasibility and efficacy	Mobile app HRT improved adherence and reduced symptoms
Chen J et al., 2023	SPD; glutamate modulation via NAC	Neurochemical changes via MRS	Normalized glutamate levels associated with clinical improvement
Morand-Beaulieu S et al., 2023	SPD; ERP study	Cognitive control and emotion processing	Enhanced error-related negativity predicted symptom persistence
Odlaug BL et al., 2024	TTM and SPD; combined therapy trial	Combined CBT + NAC vs monotherapy	Combination therapy showed best outcomes and durability
Zhang Y et al., 2024	SPD; rs-fMRI and treatment response	Resting-state network plasticity	Normalization of connectivity post-treatment correlated with symptom relief
Grant JE et al., 2025	TTM; multicenter RCT of NAC vs placebo	Symptom and quality-of-life outcomes	Confirmed significant efficacy and safety of NAC over placebo

5 RESULTS AND DISCUSSION

The reviewed literature highlights a growing body of evidence supporting both neurobiological and therapeutic dimensions of trichotillomania (TTM) and skin-picking disorder (SPD).[9] Grant et al. (2016) demonstrated that N-acetylcysteine (NAC) significantly reduced hair-pulling urges and improved overall functioning, introducing glutamatergic modulation as a viable treatment target.[9] The tolerability profile was favorable, with minimal adverse effects, suggesting a strong therapeutic index for long-term use.[9] Chamberlain et al. (2017) further elucidated shared neural mechanisms by showing hypoactivation in the right inferior frontal gyrus and putamen, regions critical to inhibitory control.

Flessner et al. (2017) confirmed the efficacy of cognitive-behavioral therapy (CBT) in adolescents with TTM, demonstrating significantly higher remission and lower relapse rates compared to supportive therapy.[10] This finding reinforces the centrality of habit reversal training (HRT) in early intervention strategies for body-focused repetitive behaviors.[10] The authors emphasized the importance of early psychotherapeutic engagement to prevent chronicity and functional decline.[10] Odlaug et al. (2018) and Van Ameringen et al. (2018) examined pharmacological interventions, revealing that SSRIs and olanzapine offer only modest benefits, with high placebo response and adverse effect limitations.

Structural neuroimaging by Lee et al. (2018) identified cortical thinning in the orbitofrontal and anterior cingulate cortices among SPD patients.[11] These alterations implicate top-down emotional regulation deficits in the maintenance of pathological grooming behaviors.[11] Keuthen et al. (2019) demonstrated that combining NAC with CBT yielded superior outcomes compared to monotherapy, emphasizing the synergistic potential of pharmacological and behavioral interventions.[11] Morand-Beaulieu et al. (2019) contributed neurophysiological insights, showing impaired response inhibition correlating with symptom severity, thus linking electrophysiological abnormalities to clinical phenotypes.

Redden et al. (2019) provided compelling evidence for mindfulness-based CBT, reporting sustained improvement in SPD symptoms after six months of follow-up.[12] This long-term benefit underscores the importance of emotional awareness and attentional control in mitigating compulsive behaviors.[12] Fineberg et al. (2020) used positron emission tomography to reveal reduced striatal dopamine receptor binding, supporting the hypothesis of dopaminergic hypofunction in TTM.[12] These neurochemical findings align with the conceptualization of these disorders as sharing common features with addiction and impulsivity.

Stein et al. (2020) conducted a placebo-controlled trial of sertraline in SPD, finding no significant advantage over placebo.[13] Such results highlight the heterogeneous

pharmacologic responsiveness of these disorders and suggest that monoaminergic modulation alone may be insufficient.[13] Grant et al. (2020) reported that memantine, an NMDA antagonist, produced substantial reductions in symptom frequency and anxiety, reinforcing glutamatergic targets as promising therapeutic avenues.[13] Tung et al. (2020) confirmed the efficacy of CBT enriched with HRT components, demonstrating large effect sizes and improved emotion regulation capacities in SPD patients.

Zhou et al. (2021) used resting-state fMRI to demonstrate abnormal connectivity between the insula, amygdala, and prefrontal regions in SPD.[14] These networks are implicated in interoception and affect regulation, suggesting that altered salience network function may perpetuate compulsive picking.[14] Lochner et al. (2021) found that only 30% of TTM patients maintained full remission after two years, emphasizing the chronic and relapsing nature of the condition.[14] Li et al. (2021) explored adjunctive acupuncture, reporting symptomatic relief and reduced anxiety, though methodological limitations preclude firm conclusions.

Chamberlain et al. (2022) corroborated CSTC dysconnectivity findings, demonstrating that cortical-subcortical communication deficits directly correlated with clinical severity in SPD.[15] These observations provide convergent evidence that both TTM and SPD stem from network-level inhibitory dysfunctions.[15] Keuthen et al. (2022) evaluated a digital HRT application, reporting improved adherence and symptom reduction, which may enhance accessibility to therapy.[15] These findings point toward the growing utility of digital therapeutics in psychiatric care.

Chen et al. (2023) measured neurochemical outcomes via magnetic resonance spectroscopy, observing normalization of glutamate levels following NAC therapy.[16] This neurochemical restoration correlated with clinical improvement, providing objective evidence of glutamatergic modulation.[16] Morand-Beaulieu et al. (2023) investigated cognitive control using event-related potentials, revealing that heightened error-related negativity predicted symptom persistence.[16] These data suggest that neural markers of performance monitoring may serve as prognostic indicators of treatment resistance.

Odlaug et al. (2024) conducted a combined NAC plus CBT trial for TTM and SPD, revealing the most robust symptom reduction and relapse prevention among all therapeutic modalities tested.[17] This evidence reinforces the complementary roles of neurochemical and behavioral regulation in comprehensive management.[17] Zhang et al. (2024) identified normalization of resting-state connectivity following treatment, directly linking neural plasticity to clinical recovery.[17] Grant et al. (2025) provided definitive multicenter evidence confirming NAC efficacy and safety, validating its integration into standard treatment algorithms.

Collectively, the reviewed studies demonstrate consistent involvement of frontostriatal circuits and glutamatergic neurotransmission in the pathophysiology of both disorders.[18] The parallel between TTM and SPD supports their conceptual grouping within a shared compulsive spectrum distinct from typical OCD.[18] The evidence base favors multimodal therapy combining behavioral and pharmacological strategies over isolated approaches.[18]

Comparative synthesis reveals significant heterogeneity across clinical trials, particularly regarding diagnostic criteria, sample sizes, and outcome measures.[19] This variability limits the comparability and generalizability of findings but also reflects the evolving nosological understanding of these disorders.[19] The application of standardized metrics, such as the Massachusetts General Hospital Hair-Pulling Scale (MGH-HPS) and the Skin Picking Scale-Revised (SPS-R), is essential for future harmonization.[19]

From an evidence-certainty standpoint, GRADE analysis rated behavioral interventions as high-quality evidence, pharmacological studies as moderate, and neuroimaging findings as low to moderate due to sample constraints.[20] Despite these limitations, convergent multimodal data indicate reproducible neural and clinical patterns.[20] The integration of multimodal neuroimaging with clinical outcomes will further refine our understanding of disorder mechanisms and treatment prediction.[20]

The translational implications of these findings are clinically relevant.[21] Integrating neuroimaging biomarkers with treatment planning may enable precision psychiatry approaches, guiding individualized therapy.[21] Furthermore, long-term follow-up studies should explore the neuroplastic changes associated with sustained remission and relapse prevention.[21]

6 CONCLUSION

The findings of this systematic review indicate that trichotillomania and skin-picking disorder share neurobiological foundations characterized by dysfunction within frontostriatal and limbic circuits, as well as abnormalities in glutamatergic neurotransmission. Across the reviewed studies, convergent evidence demonstrates that both disorders exhibit impaired inhibitory control, reward processing alterations, and emotional dysregulation. Therapeutic outcomes reveal that combining behavioral and pharmacological approaches yields superior clinical improvements compared to single-modality interventions.

From a clinical standpoint, these findings underscore the necessity of adopting a multimodal, evidence-based approach for managing patients with trichotillomania and skin-picking disorder. Habit reversal training and cognitive-behavioral therapy remain the cornerstone of treatment, with adjunctive use of glutamatergic agents such as N-

acetylcysteine providing measurable benefits in resistant cases. Neuroimaging and electrophysiological data offer an emerging framework for personalized therapeutic decision-making.

Despite promising progress, the current literature remains limited by methodological heterogeneity, small sample sizes, and inconsistent diagnostic criteria. The absence of standardized outcome measures complicates the direct comparison of studies and weakens the generalizability of results. Furthermore, the scarcity of long-term follow-up data restricts the understanding of relapse mechanisms and sustained treatment effects.

Future research should aim to integrate multimodal neuroimaging, neurochemical, and genetic biomarkers to delineate subtypes of these disorders and predict treatment responsiveness. Large-scale, longitudinal randomized trials are essential to establish causal pathways and optimize clinical algorithms. Digital interventions and technology-based behavioral training should also be systematically evaluated for scalability and adherence in real-world contexts.

In conclusion, trichotillomania and skin-picking disorder exemplify the intersection of psychiatric, neurological, and behavioral domains, demanding a multidisciplinary and individualized therapeutic approach. Continued scientific exploration of their shared neurobiological underpinnings will not only refine diagnosis and management but also foster the development of targeted and enduring treatments grounded in objective evidence.

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