REVIEW ARTICLE

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Sleep Efficiency and Neurocognitive Decline in Atopic Dermatitis: A Systematic Review

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Atopic dermatitis is often accompanied by a lack of sleep efficiency, which may impact neurocognitive functions. This review assesses the association between sleep quality in atopic dermatitis patients and neurocognitive decline. Databases searched included PubMed, Scopus, and Web of Science from inception to 8 January 2024, adhering to PRISMA guidelines. Cross-sectional and longitudinal studies were included. Records were screened and assessed for eligibility, with 13 studies included in the final analysis. From an initial pool of 4,529 records, 13 studies involving 272,868 participants met the inclusion criteria. The review identified a consistent pattern of sleep disruption in individuals with atopic dermatitis, which was associated with various short-term neurocognitive challenges such as impaired focus, decreased sleep efficiency, and lower IQ. Limited evidence was found for potential long-term cognitive decline associated with chronic atopic dermatitis. Lower sleep quality in atopic dermatitis is associated with neurocognitive deficits. While immediate effects are evident, further research is needed to understand potential long-term consequences. Integrating sleep management into atopic dermatitis care is imperative.

Key words: atopic dermatitis; sleep; neurology; neurocognitive decline.

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SIGNIFICANCE

This study confirms that atopic dermatitis often disrupts sleep, leading to cognitive issues like poor focus and lower IQ. Hypothetically addressing sleep problems in atopic dermatitis patients could significantly improve their cognitive function and overall quality of life. Additionally, the study hints at potential long-term cognitive decline, emphasizing the urgent need to integrate sleep management into atopic dermatitis treatment to safeguard cognitive health in the long run.

Atopic dermatitis (AD), a prevalent chronic inflammatory skin disorder, has traditionally been characterized by its dermatological manifestations, such as intense itching and eczematous lesions (1). However, recent advancements in dermatological and neuroscientific research have shifted the focus towards a more systemic perspective on AD, particularly its impact on sleep and subsequent neurocognitive functions (2–4). The intense pruritus associated with AD, often worsening at night, disrupts sleep patterns, leading to frequent awakenings, prolonged sleep latency, and reduced sleep quality (5, 6). The nocturnal predominance of these symptoms exacerbates the impact on sleep, highlighting a critical area of concern for AD patients. Polysomnography studies in AD patients reinforce this connection, revealing altered sleep architecture characterized by reduced sleep efficiency, increased sleep onset latency, and disrupted rapid eye movement (REM) sleep (7–9). Chronic sleep disruption, a common feature in AD, poses a risk to cognitive health, potentially leading to deficits in memory, attention, and executive function (10). This association is particularly concerning considering the chronic and often lifelong course of AD, raising questions about the long-term neurocognitive outcomes in these patients.

Recent research proposes that melatonin might play a role in increasing the comfort of nightly regeneration, given its diverse impacts on sleep, immunomodulation, and antioxidant capabilities (11). This shift in understanding is pivotal, as AD is more than a mere skin condition, revealing its potential as a contributor to broader systemic disturbances, notably sleep disruption, and potential neurocognitive decline. The present systematic review aims to synthesize the current evidence on the association between atopic dermatitis, sleep efficiency, and neurocognitive function. We evaluate the impact of AD on sleep quality across age groups, analyse the relationship between AD-related sleep disturbances and neurocognitive outcomes, and assess evidence for both short-term and long-term neurocognitive effects. This review aims to reveal the interplay between AD, sleep, and cognitive function, potentially informing future research directions and clinical management strategies.

METHODS

Search strategy and selection criteria

We developed a study protocol, which was not published, prior to initiating this systematic review. The protocol included predefined tables for data abstraction. In compliance with the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) guidelines (12), we conducted a comprehensive literature search across databases including PubMed, Scopus, and Web of Science,

spanning from the earliest records up to 8 January 2024. We included studies only in the English language and included grey literature in our search. The search strategy used for all databases was as follows: ("atopic dermatitis" OR "eczema" OR "atopic eczema") AND ("sleep" OR "insomnia" OR "sleep disturbance" OR "sleep quality" OR "sleep efficiency") AND ("neurocognitive" OR "cognitive" OR "cognition" OR "memory" OR "attention" OR "executive function" OR "IQ" OR "academic performance" OR "ADHD" OR "hyperactivity"). This search aimed to find the relationship between atopic dermatitis, sleep disturbances, and neurocognitive decline across various life stages. To be included in this systematic review, studies needed to meet the following criteria: first, studies should be either cohort (retrospective or prospective), case-control studies, randomized controlled trials (RCTs), or cross-sectional studies, thereby capturing a wide range of evidence from high-quality experiments to observational studies that provide insights into real-world associations. Second, studies must examine the link between atopic dermatitis and cognitive dysfunction, incorporating a diverse range of cognitive outcomes including attention deficits, reduced stress resilience, lower IQ, and academic performance, as well as specific neurocognitive deficits such as impaired focus, delayed cognitive processing, and verbal comprehension. This inclusion reflects the complexity of cognitive development and decline across paediatric, adolescent, adult, middle-aged, and elderly populations. Third, these studies needed to employ various scales for assessing sleep quality, such as the Athens Insomnia Scale, Pittsburgh Sleep Quality Index, and the Insomnia Severity Index. Additionally, studies using the SCORing Atopic Dermatitis (SCORAD) index to assess AD severity were included if they also addressed sleep-related outcomes. Fourth, studies needed to present quantifiable data on cognitive function using diverse methodologies and scales, including outcomes related to academic performance, IQ measurements, attention and hyperactivity assessments, and self-reported cognitive and mood disturbances. Last, the inclusion of control groups without atopic dermatitis in the studies was considered crucial for drawing clearer comparisons and conclusions concerning the specific impacts of atopic dermatitis on sleep quality and cognitive function. Studies were excluded from this review if they focused on outcomes unrelated to the risk of cognitive dysfunction, were redundant, case reports, or review articles, utilized animal models, or were *in vitro* studies. In the initial phase, 2 authors, namely AK and JG, conducted an independent screening of titles and abstracts. Subsequently, they assessed full-text articles to confirm their alignment with the specified inclusion criteria. In instances where discrepancies arose between AK and JG, resolution was achieved through the involvement of a third author, WB.

Quality assessment and publication bias. We utilized the Strength of Recommendation Taxonomy (SORT) (13), which was chosen for its applicability to various study designs and its focus on patient-oriented outcomes. This taxonomy allows for the evaluation of individual studies and the body of evidence as a whole where evidence is categorized into 3 levels to assess its quality. Level 1 represents the highest quality (well-conducted randomized controlled trials or strong observational studies), Level 2 comprises lower-quality randomized trials or observational studies, and Level 3 comprises case series and expert opinions. Evaluation for publication bias included a thorough literature search and statistical analysis to identify any skewness in the reported results. WB independently carried out data extraction and quality evaluation. Any disagreements during this process were resolved through constructive discussions between authors.

RESULTS

Our systematic search initially identified 4,529 records across databases. After deduplication and automated screening, we reviewed 110 articles, excluding 73 for irrelevance or insufficient outcome data. Of the 37 full-text articles assessed, 24 were further excluded, resulting in 13 studies meeting our inclusion criteria (**Fig. 1**). These 13 studies, involving 272,868 participants (summarized in **Table I**), examined the link between lower sleep efficiency in individuals with atopic dermatitis (AD) and the risk of neurocognitive decline across various age groups. The review consistently found that individuals with AD experienced sleep disruptions associated with short-term neurocognitive challenges. In studies focusing on children and adolescents, Fishbein et al. (14) and Kruse et al. (15) found that those with moderate-to-severe AD had more frequent sleep disturbances than healthy controls, linked to impaired focus and decreased sleep efficiency. Vittrup et al. (16) reported that severe AD in children was associated with poorer school performance and lower IQ in young adults. In adult populations, Silverberg et al. (17) reported that AD severity was linked to cognitive impairment, particularly in focus and cognitive processing speed. Kaaz et al. (18) demonstrated a strong link between AD-related itch, insomnia, and poor sleep quality, associated with daytime sleepiness and cognitive impacts in adults. Smirnova et al. (19) suggested that Swedish males with AD in late adolescence showed reduced stress resilience, though no significant decline in cognitive function or education was observed. While most studies focused on immediate or short-term cognitive effects, Jackson-Cowan et al. (20) provided insights into potential long-term effects, reporting a pattern between itch severity and cognition over time in adults. Their 12-month follow-up suggested that persistent moderate to severe itch correlated with cognitive impairment.

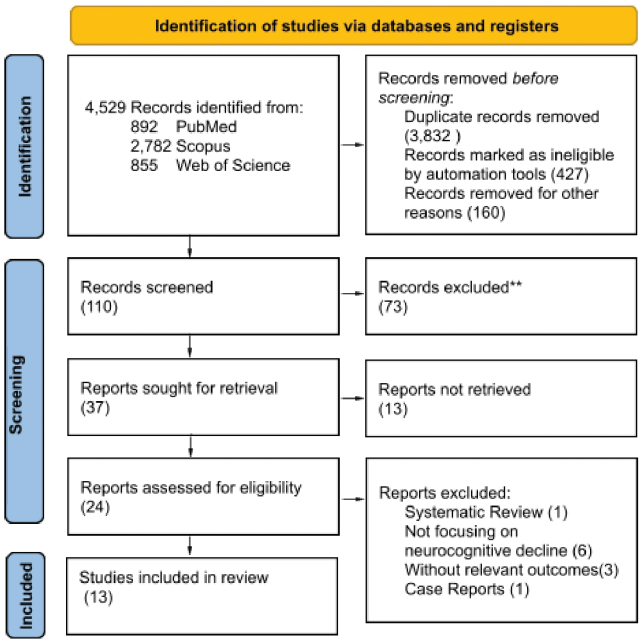

Fig. 1. Flowchart illustrating selection of studies included in this review.

Table I. Summary of studies investigating the association between atopic dermatitis (AD), sleep quality, and neurocognitive function

Study	Level of evidence*	Study design	Sample size, *n*	Age range	Sex (% female)	Country	Year	Participation rate (%)	AD assessment	Sleep assessment tool	Cognitive outcomes	Reported neurocognitive findings
Yu et al. (31)	2	Cross-sectional study	6	7–17 years	66.7%	USA	2023	Not reported	EASI	Patient-reported outcomes and quality of life	Self-perceived cognition, executive function	Worse self-perceived cognition in patients with more severe AD
Jackson-Cowan et al. (20)	1	Prospective cohort	192	≥18 years	66.7%	USA	2023	Not reported	Patient-Oriented Eczema Measure, NRS, EASI	PROMIS	Cognitive function	Decline in cognition over time in patients with persistent moderate-to-severe itch
Vittrup et al. (16)	1	Cross-sectional study	22,937	3–18 years	Not reported	Denmark	2022	Not reported	Hospital diagnosis of AD	Not used	IQ, school performance	Lower IQ and poorer academic performance in severe AD
Fishbein et al. (40)	2	Cross-sectional survey	180	5–17 years	45.5%	USA	2021	Not reported	POEM	Patient-Reported Outcome Measurement Information System	Depression, anxiety, attention-related issues	Long-term depression, anxiety, and attention-related issues in AD patients
Mann et al. (41)	2	Prospective Cohort	61	18–77 years	67.2%	Germany	2020	Not reported	EASI	Insomnia Severity Index	Sleep quality	Poor sleep during acute episodes of AD
Silverberg et al. (17)	2	Prospective cohort	386	Adults (≥ 18 years)	Not reported	USA	2020	Not reported	SCORAD, EASI, POEM, NRS for itch and pain	POEM	General cognitive dysfunction	Impaired focus and delayed cognitive processing in severe AD
Smirnova et al. (19)	1	Prospective Cohort	234,715	17–20 years	0% (all male)	Sweden	2019	Not reported	Hospital diagnosis of AD	Not used	Stress resilience	Reduced stress resilience in males with AD
Atefi et al. (39)	2	Cross-sectional study	95	4–18 years	47.4%	Iran	2019	Not reported	Not reported	Pittsburgh Sleep Quality Questionnaire	ADHD symptoms	Possible association of ADHD in people with AD
Ramirez et al. (42)	2	Prospective Cohort	13,988	2–16 years	48.4%	UK	2019	Not reported	UK Working Party criteria	Standardized questions	Sleep quality	Lower sleep efficiency in children with AD
Kaaz et al. (18)	1	Randomized controlled trial (RCT)	250	18–80 years	42%	Poland	2019	83.3%	SCORAD	Athens Insomnia Scale, Pittsburgh Sleep Quality Index	Daytime sleepiness	Negative impact on habitual sleep efficiency causing daytime sleepiness
Kruse et al. (15)	2	Retrospective cohort	18	6–17 years	50%	USA	2018	Not reported	SCORAD	Not reported	ADHD symptoms	Increased neurocognitive symptoms in children with moderate-to-severe AD
Fishbein A et al. (14)	2	Retrospective cohort	19	6–17 years	47.4%	USA	2018	Not reported	SCORAD	CDLQI	Sleep efficiency	Lower sleep efficiency in moderate-to-severe AD
Camfferman et al. (2)	2	Cross-sectional study	21	6–16 years	Not reported	Australia	2013	Not reported	SCORAD	Not reported	Neurocognitive performance	Short-term neurocognitive deficits, particularly in verbal comprehension and perceptual reasoning

*Level of evidence: 1=highest quality (well-conducted randomized controlled trials or strong observational studies), 2=lower-quality randomized trials or observational studies, Level 3=case series and expert opinions
ADHD: attention deficit hyperactivity disorder; SCORAD: SCORing atopic dermatitis; CDLQI- Children's Dermatology Life Quality Index sleep questionnaire; EASI: Eczema Area and Severity Index; IQ: intelligence quotient; POEM: Patient-Oriented Eczema Measure; NRS: numeric rating scale; PROMIS: Patient-Reported Outcomes Measurement Information System.

These findings highlight the varied impact of AD on sleep and cognition across different age groups, emphasizing the need for age-specific considerations in both research and clinical management of AD-related cognitive issues.

DISCUSSION

This systematic review reveals an intricate relationship between atopic dermatitis (AD), lower sleep quality, and neurocognitive function. The data suggest that the impact of AD on sleep is not a mere consequence of nocturnal pruritus but may also involve complex immunological and neurochemical pathways that predispose to cognitive alterations. For instance, the persistent inflammatory state in moderate-to-severe AD, as reflected in higher wake-after-sleep onset (WASP) and reduced sleep efficiency, could implicate systemic cytokine disturbances affecting neurocognitive pathways (21, 22). Several studies, such as those by Fishbein et al. (14) and Silverberg et al. (17), consistently point toward an association between AD severity and cognitive impairment. This relationship may be mediated by sleep, but the direct impact of AD on cognitive function cannot be discounted.

Neurocognitive decline: acute versus chronic manifestations

This review distinguishes between the short-term and potential long-term consequences of sleep disruption in AD. While most studies focus on immediate cognitive deficits, such as impaired focus and lower IQ, few provide a long-term perspective. The work of Jackson-Cowan et al. (20) is pivotal in this regard, suggesting a progressive cognitive decline correlated with chronic AD symptoms. This raises the question of whether chronic

sleep interruption may lead to lasting neurocognitive damage or whether AD's systemic effects play a more significant role over time.

Sleep quality as a potential therapeutic target

The evidence from our review underscores the importance of sleep quality in the context of AD and its associated cognitive impacts. While our study did not directly assess specific sleep interventions, the consistent association between sleep disturbances and cognitive outcomes in AD patients suggests that sleep-focused treatments could be beneficial. Various treatment strategies have been proposed to manage sleep disturbances in patients with AD. These include optimizing the treatment of AD itself with topical corticosteroids (23), topical calcineurin inhibitors (24), and topical phosphodiesterase-4 inhibitors (e.g., crisaborole) (25). Additionally, sleep aids such as melatonin (26) and first-generation antihistamines (27) have been suggested. Non-pharmacological approaches have also been explored, including cognitive-behavioural therapy (28), biofeedback techniques like progressive muscle relaxation (29), sleep hygiene practices (e.g., blue light therapy, altering bedtime routines) (30), and acupuncture (31). However, it is important to note that the last 4 methods have limited evidence specifically in AD. Insomnia is the most frequent sleep issue linked to AD. While various non-drug treatments for insomnia have been proposed, including hypnosis, biofeedback, acupuncture, meditation, and relaxation techniques, their effectiveness has not been consistently demonstrated. Among these approaches, cognitive behavioural therapy for Insomnia (CBT-I) has shown the most promise, alongside sedative-hypnotic medications (32). Future research should explore the efficacy of these various sleep improvement strategies in AD patients, to determine their impact on sleep quality and cognitive outcomes. This could lead to more comprehensive and effective AD management strategies that address dermatological symptoms and sleep-related issues.

Role of comorbidities and environmental factors

Understanding the complex relationships between atopic dermatitis (AD), sleep quality, and neurocognitive outcomes is essential for effective AD management. AD not only disrupts skin health but also significantly impacts sleep quality and cognitive functions through biological, psychological, and environmental mechanisms (8). Longitudinal studies underscore the links between AD and mental health issues, such as anxiety and depression, which both exacerbate and are exacerbated by AD symptoms (20). These psychological conditions further contribute to sleep disturbances – a common comorbidity in AD patients. Sleep disorders, including insomnia, restless legs syndrome, and sleep-related respiratory disorders, share inflammatory pathways with AD, suggesting a common mechanism that could exacerbate AD symptoms and, in turn, worsen sleep quality (5). Poor sleep quality associated with AD can lead to a decline in neurocognitive functions, such as memory, attention, and executive functioning, due to the systemic inflammation and stress associated with both poor sleep and AD (16, 18). Environmental and psychological stressors not only trigger AD flare-ups but also impair sleep quality, creating a cycle that potentially worsens cognitive impairments (33, 34). Moreover, the chronic inflammatory state in AD may directly impact cognitive function. Inflammatory mediators associated with AD can cross the blood–brain barrier, potentially affecting neural processes and contributing to cognitive impairments (17). This systemic inflammation adds another layer of complexity to the relationship between AD, sleep disturbances, and cognitive function, highlighting the need for a more holistic approach to AD management that considers these interconnected factors (35–38).

Limitations and future directions

Despite the strengths of the included studies, limitations exist, such as the variance in study design, sample sizes, and the measures of lower sleep efficiency and neurocognitive decline. Future research should aim to disentangle the bidirectional relationships and underlying mechanisms connecting AD, sleep disruption, and cognitive impairment. Longitudinal studies with larger cohorts and standardized cognitive assessments are necessary to confirm these findings and guide therapeutic strategies (39–43).

Conclusions

In summary, the systematic review elucidates a complex association between atopic dermatitis, disrupted sleep, and neurocognitive decline. The findings advocate for a holistic approach to AD management, emphasizing the need for multidisciplinary strategies that address not only skin symptoms but also sleep disturbances and potential cognitive impacts. Future research should prioritize longitudinal designs to further clarify the relationships among AD, sleep quality, and cognitive function, and support the development of targeted therapies. By addressing these interrelated aspects, we may be able to improve the overall management of AD and potentially mitigate its impact on cognitive function.

The authors have no conflict of interest to declare.

REFERENCES

1. Weidinger S, Novak N. Atopic dermatitis. Lancet 2016; 387: 1109–1122. https://doi.org/10.1016/S0140-6736(15)00149-X
2. Camfferman D, Kennedy JD, Gold M, Simpson C, Lushington K. Sleep and neurocognitive functioning in children with eczema. Int J Psychophysiol 2013; 89: 265–272. https://

doi.org/10.1016/j.ijpsycho.2013.01.006
3. Podder I, Mondal H, Kroumpouzos G. Nocturnal pruritus and sleep disturbance associated with dermatologic disorders in adult patients. Int J Womens Dermatol 2021; 7: 403–410. https://doi.org/10.1016/j.ijwd.2021.02.010
4. Jeon C, Yan D, Nakamura M, Sekhon S, Bhutani T, Berger T, et al. Frequency and management of sleep disturbance in adults with atopic dermatitis: a systematic review. Dermatol Ther 2017; 7: 349–364. https://doi.org/10.1007/s13555-017-0192-3
5. Bawany F, Northcott CA, Beck LA, Pigeon WR. Sleep disturbances and atopic dermatitis: relationships, methods for assessment, and therapies. J Allergy Clin Immunol Pract 2021; 9: 1488–1500. https://doi.org/10.1016/j.jaip.2020.12.007
6. Trier AM, Kim BS. Cytokine modulation of atopic itch. Curr Opin Immunol 2018; 54: 7–12. https://doi.org/10.1016/j.coi.2018.05.005
7. Guo M, Su J, Zheng S, Chen B. Objective sleep in atopic dermatitis: a meta-analysis. Dermatitis 2023; 34: 145–150. https://doi.org/10.1089/derm.2022.29005.mgu
8. Cameron S, Donnelly A, Broderick C, Arichi T, Bartsch U, Dazzan P, et al. Mind and skin: exploring the links between inflammation, sleep disturbance and neurocognitive function in patients with atopic dermatitis. Allergy 2023; 78: 2769–2783.
9. Piontek K, Arnold A, Ewert R, Stubbe B, Bremert T, Krüger M, et al. Polysomnographic characteristics of sleep in adults with and without physician-diagnosed atopic dermatitis: results from the Study of Health in Pomerania. Sleep Breath 2023; 27: 2123–2132. https://doi.org/10.1007/s11325-023-02937-7
10. Alhola P, Polo-Kantola P. Sleep deprivation: impact on cognitive performance. Neuropsychiatr Dis Treat 2007; 3: 553–567.
11. Chang YS, Chiang BL. Mechanism of sleep disturbance in children with atopic dermatitis and the role of the circadian rhythm and melatonin. Int J Mol Sci 2016; 17: 462. https://doi.org/10.3390/ijms17040462
12. Moher D, Liberati A, Tetzlaff J, Altman DG. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. PLoS Med 2009; 6: e1000097. https://doi.org/10.1371/journal.pmed.1000097
13. Ebell MH, Siwek J, Weiss BD, Woolf SH, Susman J, Ewigman B, et al. Strength of recommendation taxonomy (SORT): a patient-centered approach to grading evidence in the medical literature. J Am Board Fam Pract 2004; 17: 59–67. https://doi.org/10.3122/jabfm.17.1.59
14. Fishbein AB, Mueller K, Kruse L, Boor P, Sheldon S, Zee P, et al. Sleep disturbance in children with moderate/severe atopic dermatitis: a case-control study. J Am Acad Dermatol 2018; 78: 336–341. https://doi.org/10.1016/j.jaad.2017.08.043
15. Kruse L, Cices A, Fishbein AB, Paller AS. Neurocognitive function in moderate–severe pediatric atopic dermatitis: a case-control study. Pediatr Dermatol 2019; 36: 110–114. https://doi.org/10.1111/pde.13710
16. Vittrup I, Andersen YMF, Skov L, Wu JJ, Agner T, Thomsen SF, et al. The association between atopic dermatitis, cognitive function and school performance in children and young adults. Br J Dermatol 2023; 188: 341–349. https://doi.org/10.1093/bjd/ljac058
17. Silverberg JI, Lei D, Yousaf M, Janmohamed SR, Vakharia PP, Chopra R, et al. Association of atopic dermatitis severity with cognitive function in adults. J Am Acad Dermatol 2020; 83: 1349–1359. https://doi.org/10.1016/j.jaad.2020.05.041
18. Kaaz K, Szepietowski JC, Matusiak Ł. Influence of itch and pain on sleep quality in atopic dermatitis and psoriasis. Acta Derm Venereol 2019; 99: 175–180. https://doi.org/10.2340/00015555-3065
19. Smirnova J, von Kobyletzki LB, Lindberg M, Svensson Å, Langan SM, Montgomery S. Atopic dermatitis, educational attainment and psychological functioning: a national cohort study. Br J Dermatol 2019; 180: 559–564. https://doi.org/10.1111/bjd.17330
20. Jackson-Cowan L, Silverberg JI. Longitudinal course of cognitive impairment in patients with atopic dermatitis. Arch Dermatol Res 2023; 315: 1553–1560. https://doi.org/10.1007/s00403-023-02536-2
21. Gonzalez-Lopez G, Ceballos-Rodriguez RM, Gonzalez-Lopez JJ, Feito Rodriguez M, Herranz-Pinto P. Efficacy and safety of wet wrap therapy for patients with atopic dermatitis: a systematic review and meta-analysis. Br J Dermatol 2017; 177: 688–695. https://doi.org/10.1111/bjd.15165
22. Doss N, Kamoun MR, Dubertret L, Cambazard F, Remitz A, Lahfa M, et al. Efficacy of tacrolimus 0.03% ointment as second-line treatment for children with moderate-to-severe atopic dermatitis: evidence from a randomized, double-blind non-inferiority trial vs. fluticasone 0.005% ointment. Pediatr Allergy Immunol 2010; 21: 321–329. https://doi.org/10.1111/j.1399-3038.2009.00895.x
23. Simpson EL, Paller AS, Boguniewicz M, Eichenfield LF, Feldman SR, Silverberg JI, et al. Crisaborole ointment improves quality of life of patients with mild to moderate atopic dermatitis and their families. Dermatol Ther (Heidelb) 2018; 8: 605–619. https://doi.org/10.1007/s13555-018-0263-0
24. Chang YS, Lin MH, Lee JH, Lee PL, Dai YS, Chu KH, et al. Melatonin supplementation for children with atopic dermatitis and sleep disturbance: a randomized clinical trial. JAMA Pediatr 2016; 170: 35–42. https://doi.org/10.1001/jamapediatrics.2015.3092
25. Kelsay K. Management of sleep disturbance associated with atopic dermatitis. J Allergy Clin Immunol 2006; 118: 198–201. https://doi.org/10.1016/j.jaci.2006.04.038
26. Hedman-Lagerlof E, Bergman A, Lindefors N, Bradley M. Exposure-based cognitive behavior therapy for atopic dermatitis: an open trial. Cogn Behav Ther 2019; 48: 300–310. https://doi.org/10.1080/16506073.2018.1504320
27. Bae BG, Oh SH, Park CO, Noh S, Noh JY, Kim KR, et al. Progressive muscle relaxation therapy for atopic dermatitis: objective assessment of efficacy. Acta Derm Venereol 2012; 92: 57–61. https://doi.org/10.2340/00015555-1189
28. LeBovidge JS, Elverson W, Timmons KG, Hawryluk EB, Rea C, Lee M, et al. Multidisciplinary interventions in the management of atopic dermatitis. J Allergy Clin Immunol 2016; 138: 325–334. https://doi.org/10.1016/j.jaci.2016.04.003
29. Tan HY, Lenon GB, Zhang AL, Xue CC. Efficacy of acupuncture in the management of atopic dermatitis: a systematic review. Clin Exp Dermatol 2015; 40: 711–716. https://doi.org/10.1111/ced.12732
30. Mesjasz A, Zawadzka M, Chałubiński M, Trzeciak M. Is atopic dermatitis only a skin disease? Int J Mol Sci 2023; 24: 837. https://doi.org/10.3390/ijms24010837
31. Yu K, Seegan P, Lattanzio K, Chang H, Wan J. Cognitive functioning in children with atopic dermatitis: pilot observations. Pediatr Dermatol 2023; 40: 483–488. https://doi.org/10.1111/pde.15287
32. Bilsborough J, Leung DY, Maurer M, Howell M, Boguniewicz M, Yao L, et al. IL-31 is associated with cutaneous lymphocyte antigen-positive skin homing T cells in patients with atopic dermatitis. J Allergy Clin Immunol 2006; 117: 418–425. https://doi.org/10.1016/j.jaci.2005.10.046
33. Sandilands A, Sutherland C, Irvine AD, McLean WH. Filaggrin in the frontline: role in skin barrier function and disease. J Cell Sci 2009; 122: 1285–1294. https://doi.org/10.1242/jcs.033969
34. David Boothe W, Tarbox JA, Tarbox MB. Atopic dermatitis: pathophysiology. Adv Exp Med Biol 2017; 1027: 21–37. https://doi.org/10.1007/978-3-319-64804-0_3
35. Frazier W, Bhardwaj N. Atopic dermatitis: diagnosis and treatment. Am Fam Physician 2020; 101: 590–598.
36. Ring J, Alomar A, Bieber T, Deleuran M, Fink-Wagner A, Gelmetti C, et al. Guidelines for treatment of atopic eczema (atopic dermatitis) Part II. J Eur Acad Dermatol Venereol 2012; 26: 1176–1193. https://doi.org/10.1111/j.1468-3083.2012.04636.x
37. Chrostowska-Plak D, Reich A, Szepietowski JC. Relationship between itch and psychological status of patients with atopic dermatitis. J Eur Acad Dermatol Venereol 2013; 27: e239–e242. https://doi.org/10.1111/j.1468-3083.2012.04578.x
38. Kim J, Kim BE, Leung DYM. Pathophysiology of atopic dermatitis: clinical implications. Allergy Asthma Proc 2019; 40: 84–92. https://doi.org/10.2500/aap.2019.40.4202

39. Atefi N, Rohaninasab M, Shooshtari M, Behrangi E, Mehran G, Goodarzi A, et al. The association between attention-deficit/hyperactivity disorder and atopic dermatitis: a study among Iranian children. Indian J Dermatol 2019; 64: 451–455. https://doi.org/10.4103/ijd.IJD_458_18
40. Fishbein AB, Cheng BT, Tilley CC, Begolka WS, Carle AC, Forrest CB, et al. Sleep disturbance in school-aged children with atopic dermatitis: prevalence and severity in a cross-sectional sample. J Allergy Clin Immunol Pract 2021; 9: 3120–3129.e3. https://doi.org/10.1016/j.jaip.2021.04.064
41. Mann C, Dreher M, Weeß HG, Staubach P. Sleep disturbance in patients with urticaria and atopic dermatitis: an underestimated burden. Acta Derm Venereol 2020; 100: adv00073. https://doi.org/10.2340/00015555-3416
42. Ramirez FD, Chen S, Langan SM, Prather AA, McCulloch CE, Kidd SA, et al. Association of atopic dermatitis with sleep quality in children. JAMA Pediatr 2019; 173: e190025. https://doi.org/10.1001/jamapediatrics.2019.0025
43. Zhou Q, Yang D, Xiong C, Li X. Atopic dermatitis and cognitive dysfunction in middle-aged and older adults: a systematic review and meta-analysis. PLoS One 2023; 18: e0292987. https://doi.org/10.1371/journal.pone.0292987