Itch in autism spectrum disorder: a scoping review of skin-barrier dysfunction and the skin-brain axis, and an agenda for itch-specific research

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Background

Chronic itch is a shared endpoint of skin-barrier dysfunction and dysregulated itch processing, yet its burden in autism spectrum disorder (ASD) is largely uncharacterized. A proposed "skin-brain axis," rooted in the common ectodermal origin of epidermis and neural tissue, links barrier integrity and cutaneous inflammation to neurodevelopmental conditions [1][2]. Itch is documented in ASD across behavioral, epidemiologic, and preclinical studies, but remains a scattered and heterogeneous endpoint. This scoping review maps evidence at the intersection of itch, skin-barrier dysfunction, and ASD and defines research priorities.

Objectives

(1) To characterize the extent, range, and nature of published evidence on itch and skin-barrier function in ASD; (2) to identify whether and how itch is measured in ASD cohorts; and (3) to construct an evidence-gap map across barrier markers, itch outcomes, and study population.

Methods

The review follows JBI scoping-review methodology and PRISMA-ScR reporting. MEDLINE,

Embase, PsycINFO, Web of Science, and the Cochrane Library are searched from inception without language restriction, using controlled vocabulary and free-text terms for ASD, itch/pruritus, and skin-barrier function. Eligible sources include original human and preclinical studies, reviews, and abstracts reporting itch and/or quantitative barrier data in ASD or validated ASD models. Two reviewers independently screen and chart data using a piloted form capturing population, barrier metrics, itch assessment, and findings; synthesis is by structured narrative and evidence-gap matrix.

Results

Pilot charting identifies four underconnected evidence domains. (1) *Skin-barrier biophysics:* autistic children (n=56) show lower stratum corneum hydration, higher TEWL, and elevated skin-surface pH versus controls (all $p<0.0001$) [3]; a smaller adolescent cohort (n=25) and a valproate mouse model show elevated but non-significant/preliminary TEWL [1]. (2) *Behavioral itch:* contagious itch is heightened 2–3 fold in children with ASD (large effect), with baseline itch scaling with symptom severity [4]. (3) *Dermatologic epidemiology:* pruritic dermatoses are overrepresented (dry skin, eczema, skin allergy all $p<0.0001$) [5], and two meta-analyses confirm the AD–ASD link (RR 1.34 [6]; OR 1.87 [7]), though the 2026 AAD guideline rates this association low-certainty [8]. (4) *Preclinical mechanism:* Shank3 mice display mechanical itch hypersensitivity (alloknesis) via C-low-threshold mechanoreceptor hyporesponsiveness [9]; valproate/propionate models show parallel Shank/BDNF and cutaneous changes [10]. Notably, no itch instrument is ASD-validated: pediatric self-report tools (PIQ-C, ItchyQuant) and caregiver observer-reported diaries (PRUCISION ObsRO) must be matched to developmental rather than chronological age [11][12][13]. The resulting evidence-gap matrix shows no cell

linking itch outcomes to barrier metrics, no human mechanistic data, and no study using itch as a primary endpoint.

Table 1. Evidence-gap matrix across four domains at the intersection of itch, skin-barrier dysfunction, and ASD.

Evidence domain	What was measured (outcome)	Evidence type	Population	Key finding	Residual gap
AD/eczema–ASD epidemiologic association	Prevalence/odds of eczema in ASD	Two meta-analyses	Children (Elgenidy 30 studies; Cheng 24 studies, >71M)	Eczema RR 1.34 [6]; ASD OR 1.87 [7]	Association only; AAD 2026 rates certainty low [8]; no itch endpoint
Skin-barrier physiology	Hydration, TEWL, surface pH	Case–control biophysical study	Autistic children (n=56; adolescent n=25)	Reduced hydration, elevated TEWL, altered pH (all $p<0.0001$) [3]	No linkage of barrier metrics to itch; no mechanistic pathway
Behavioral / contagious itch	Contagious & baseline itch response	Experimental behavioral study	Children with ASD	2–3× heightened contagious itch (large effect); baseline itch scales with severity [4]	Behavioral only; no barrier or neural correlate; not a clinical itch outcome
Preclinical mechanism	Mechanical itch, Shank/BDNF, cutaneous change	Animal models (Shank3; valproate/propionate)	Mice	Primary sensory neuron dysfunction → mechanical itch hypersensitivity; parallel Shank/BDNF & skin changes [9][10]	Animal-only; no human validation; no barrier–itch integration

Conclusions

Itch and skin-barrier dysfunction are each documented in ASD but have never been studied together or as primary endpoints. This review defines a discrete research niche and proposes a concrete agenda: itch-specific outcome measurement in ASD cohorts, communication-appropriate itch instruments matched to developmental level and paired with an ASD-validated

sensory measure (e.g., SEQ 3.0) [14], and integration of barrier biomarkers to move the field from mechanistic plausibility toward measurable clinical burden.

Keywords: pruritus; autism spectrum disorder; skin barrier; transepidermal water loss; skin-brain axis; scoping review

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