



## The Fever Effect: Do Kids With Autism Do Better When They Use a Device To Warm Their Blood? Effects of a 6-week AVACEN Treatment Method on Autism Spectrum Disorder

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### Abstract

**Objective:** To evaluate the effects of the AVACEN Treatment Method (ATM) device on parent-reported language and sleep outcomes in children with autism spectrum disorder (ASD).

**Methods:** Thirteen children (ages 4.5 to 17.1 years) diagnosed with ASD were enrolled in a six-week, randomized, double-blind, placebo-controlled trial. Participants were randomly assigned to one of three experimental groups: (1) heat with negative pressure (n=4), (2) heat only (n=4), or (3) placebo (no heat or pressure) (n=5). Caregivers conducted two 20-minute sessions per day at home using the AVACEN - device. Observations on language use and sleep quality were collected at baseline, midpoint, and study conclusion through daily logbooks.

**Results:** Children in the active treatment group demonstrated the most consistent improvements across all measured sleep and language domains. In this group, 4 out of 4 participants were reported to have experienced longer, deeper sleep and greater expressive language use, including increased vocabulary and social engagement. Reported language and sleep improvements in the control groups were modest but varied.

**Discussion:** These preliminary findings suggest that the AVACEN device may offer a safe, non-invasive approach to improving core behavioral challenges in ASD, particularly in sleep and communication. Larger controlled trials using objective outcome measures are warranted to confirm efficacy and support potential clearance by the United States Food & Drug Administration (FDA) for use in pediatric populations with neurodevelopmental disorders.

### I. Introduction

Autism spectrum disorder (ASD) is a complex neurodevelopmental disorder marked by various degrees of impairment in communication, sleep, and social interaction, often accompanied by restricted and repetitive behaviors or interests.<sup>1</sup> The global prevalence of ASD has increased dramatically in recent decades.<sup>2</sup> In 2022, 1 out of 31 children aged 8 years old in the United States (US) carried a diagnosis of ASD.<sup>2</sup> Children with ASD often experience difficulties forming peer relationships and understanding social cues, conferring an increased risk of social isolation and comorbid mental health conditions, such as depression and anxiety.<sup>3</sup>

The burden of care in ASD frequently falls heavily on families. Studies indicate that families of children with ASD face significantly higher healthcare expenses, with average annual costs more than double those of families with an unaffected child, largely due to increased hospitalizations, therapy sessions, and other interventions.<sup>4</sup> Caregivers of children or adults with ASD often report elevated levels of stress and decreased quality of life due to the demands of managing ASD-related challenges.<sup>5</sup>

Despite the increasing availability of behavioral, educational, and therapeutic interventions, treatment options for ASD remain limited in scope and effectiveness.<sup>6</sup> Behavioral therapies are foundational but require significant cost, time, and access to trained professionals, which limits accessibility for many families.<sup>7</sup> Pharmacologic treatments may offer benefits for irritability and aggression but show limited efficacy in treating the core symptoms of ASD.<sup>8</sup> These are also associated with significant side effects such as weight gain, sedation, and metabolic disturbances.<sup>8</sup> Currently, there are no available therapies that directly target the core symptoms of ASD, particularly social communication deficits. These limitations represent a critical unmet need for novel, accessible, and well-tolerated therapeutic modalities that can meaningfully improve quality of life for children with ASD and their caregivers.

Among the most intriguing and unexplored phenomena in autism research is the “fever effect,” a temporary but marked improvement in core ASD symptoms during febrile episodes, which is defined as a period where a person’s body temperature is elevated above 99.5°F.<sup>9–11</sup> This phenomenon was first formally noted in 1980 when a viral outbreak occurred at a therapeutic nursery for children with autism at Bellevue Psychiatric Hospital in New York.<sup>10</sup> Clinicians observed that affected children became markedly more alert, social, and communicative while experiencing fever.<sup>10</sup> However, those improvements vanished soon after the fever subsided.

Since that early report, a growing body of observational data has documented similar patterns across diverse ASD populations. For example, one study found that 83% of children with ASD showed behavioral improvements during fever, including reductions in hyperactivity, repetitive behaviors, and irritability.<sup>9</sup> These behavioral changes were observed independently of fever-related lethargy, suggesting that the underlying mechanism might involve neurobiological changes rather than mere fatigue.

More recent analyses from large datasets, such as the Simons Simplex Collection, indicate that approximately 17% of children with ASD may exhibit the fever effect, particularly those with more pronounced repetitive behaviors and limited language skills.<sup>12</sup> While the exact pathophysiological mechanisms remain elusive, several hypotheses have been proposed. These include transient modulation of synaptic function, changes in neurotransmitter systems (e.g., glutamate, glutamine, and GABA), aberrant activation of the immune system, and induction of heat-shock proteins, which may transiently restore cellular homeostasis in neural circuits disrupted in ASD.<sup>13–15</sup>

The convergence of behavioral observations and plausible biological mechanisms has inspired interest in replicating the therapeutic effects of fever in a controlled, non-pathological way. In the present study, we attempt to replicate the fever effect using the AVACEN (Advanced Vascular Circulation Enhancement) device. This is a non-invasive, Food & Drug Administration (FDA)-cleared heat therapy system indicated for temporary relief of minor muscle and joint pain stiffness, joint pain associated with arthritis, muscle spasms, and minor strains and sprains.<sup>16</sup> The AVACEN device works by warming blood through the arteriovenous anastomoses (AVAs) located in the palm while applying negative pressure to increase blood flow.<sup>16</sup> The warmed, lower-viscosity blood is then rapidly distributed throughout the body, raising the core temperature by approximately 1°F, a deviation sufficient to trigger a thermoregulatory response from the hypothalamus.<sup>16</sup>

The hypothalamus, a key center for autonomic regulation, reacts to this thermal shift by activating a systemic vasodilatory cascade.<sup>17</sup> This includes enhanced perfusion, nitric oxide release from endothelial cells, and reduction in blood viscosity, leading to improved oxygen delivery and metabolic waste clearance.<sup>18</sup> Though modest in magnitude, this thermogenic response mimics the physiological changes associated with low-grade fever, and thus has the potential to replicate the beneficial behavioral effects seen in children with ASD during febrile episodes.<sup>16</sup>

Early anecdotal evidence and observational data have suggested the potential utility of the AVACEN device in improving core symptoms of ASD.<sup>11</sup> The improvements included enhanced attention, better academic performance, reduced anxiety, and increased verbal communication. In light of these observations, a pilot study was conducted to evaluate the safety and potential efficacy of AVACEN treatment in a pediatric population. The 6-week, double-blinded, placebo-controlled study enrolled children aged 4.5 to 17 years diagnosed with ASD and randomly assigned them to three groups with differing thermal and pressure parameters (active treatment and two control conditions). The study aimed to assess changes in social communication, sleep patterns, and parent-reported stress using qualitative methodology.

The rationale for this study rests on the hypothesis that sub-febrile thermal elevation via AVACEN treatment could elicit a beneficial neurophysiological response analogous to the fever effect, potentially improving behavioral and communicative outcomes in children with ASD.

## II. Methods and Materials

This study was a 6-week, double-blind, placebo-controlled pilot trial designed to evaluate the effects of a home-based AVACEN Treatment Method (ATM) on children diagnosed with ASD. Participants were randomly assigned to one of three conditions involving different combinations of thermal and vacuum stimulation using the AVACEN device. The study protocol was approved by the Institutional Review Board at Fielding Graduate University.

## *Participants*

Thirteen children with a confirmed diagnosis of ASD participated in this pilot study. Participants ranged in age from 4.5 to 17.1 years, with a mean age of 11.6 years (N=13). Nine out of thirteen participants were male, and four out of thirteen were female. The study population included a diverse sample in terms of age and functional profile, representing both verbal and minimally verbal children. Diagnostic confirmation of ASD was obtained through a parent report of a formal diagnosis from a licensed healthcare provider, in accordance with DSM-V criteria. Participants were recruited through autism clinics, parent advocacy networks, social media outreach, and word-of-mouth referrals. All caregivers provided written informed consent for participation, and consent was obtained from children when appropriate.

## *Experimental Design*

Participants were randomly assigned to one of three experimental groups: 1) active treatment (heat and vacuum) (n=4), 2) heat only (n=4), and 3) placebo control (n=5). The experimental design aimed to assess the impact of sub-febrile thermal elevation and negative pressure (vacuum) on core symptoms of ASD. Neither the caregivers nor the primary investigator conducting assessments were aware of the condition to which each child was assigned. Device programming and condition assignment were managed by a third-party engineer not involved in participant interaction or data analysis, ensuring blinding was maintained.

## *Experimental Conditions*

Three experimental conditions were configured as follows:

1. Active Treatment: Participants received both heat and negative pressure.
2. Heat only (sham heat): Participants received heat but no vacuum pressure. The warming pad was activated, but no seal was formed on the wrist cuff, allowing ambient air pressure.
3. Placebo control: Participants received neither heat nor vacuum. The device is still powered on, emitting normal operating sounds, but no thermal or pressure mechanisms are activated.

## *Materials*

The AVACEN device units were provided by the manufacturer, pre-configured to deliver the specific condition assigned to each participant. The device interface and internal parameters were visually identical across all three conditions, preserving the integrity of blinding. Participants also received a parental logbook to record daily observations and subjective impressions, specifically regarding language and sleep behaviors.

A standardized questionnaire was developed to capture parent-reported outcomes related to communication and sleep. Parents were instructed to complete this brief survey three times over the course of the study: at baseline (week 0), midpoint (week 3), and study conclusion (week 6). These qualitative observations were coded and analyzed for themes related to improvement or deterioration in expressive language, initiation of conversation, vocabulary use, sleep onset, duration, and continuity.

### *Procedures*

Prior to the study, families participated in an orientation session, either in person or via secure videoconferencing, during which the purpose of the study, device usage, and reporting protocols were explained in detail. Each family received a pre-configured AVACEN device, an instruction manual, and a parental log for home use.

Participants were instructed to use the device for two 20-minute sessions per day, in the morning and afternoon, for 6 consecutive weeks. The child's non-dominant hand was inserted into the device, and a wrist cuff ensured secure placement. During the session, children could engage in other passive activities that did not involve the use of other electronic devices. Parents monitored the session to ensure compliance and take note of any adverse reactions or behavioral changes.

Device adherence and functional status were checked weekly via caregiver phone check-ins. Caregivers were reminded to complete observational forms at the designated intervals and return them electronically or via mail at the conclusion of the study.

Following the 6-week intervention period, families returned the device and completed a final follow-up call with the research coordinator. Families who wished to continue with active treatment were enrolled in the open-label extension.

No adverse events were reported during the course of the study. Parents were instructed to contact the research team or discontinue use if they noticed any discomfort or unusual behavior during the sessions, but no such incidents occurred.

### III. Results

The present study evaluated parent-reported changes in language and sleep behavior in children with ASD following 6 weeks of at-home AVACEN treatment under one of three experimental conditions: active heat and vacuum, sham heat only (no vacuum), and placebo (no heat or vacuum). Outcomes were gathered through structured parent interviews conducted at baseline, midpoint, and study conclusion. The data shown in Tables 1 and 2 reflect the proportion of children whose caregivers reported affirmative changes in specific domains of language and sleep functioning by the end of the study.

## Language Outcomes

Table 1 shows the percentage of participants in each experimental condition whose caregivers reported affirmative changes in various aspects of expressive and pragmatic language.

Parents reported multiple areas of improvement in expressive language and pragmatic communication, particularly in the active treatment (heat and vacuum) group. All participants in the active treatment group were reported to have increased their vocabulary and were more willing to use words to initiate interaction (Table 1). This group also showed the highest levels of improvement across other domains, such as understanding verbal gestures, willingness to engage in conversations, and clarity of thought.

In contrast, the heat-only group demonstrated more modest gains. Only 25% of children in this condition were reported to produce lengthier responses or demonstrate improved vocal cadence (Table 1). The placebo group showed the least consistent improvements, though some changes were still reported.

Table 1. Parent-Reported Language Improvements (%) by Experimental Condition

Language Statements	Heat & Vacuum	Heat Only	No Heat & No Vacuum
Reported increased vocabulary to express themselves	100	75	40
Produced lengthier responses	50	25	40
More willingness to engage in conversations	100	25	20
More willingness to use words to engage others	100	50	60
Understanding other' non-verbal gestures	100	50	20
Responding to "why?" questions	75	25	40
Increased vocal cadence (e.g., softer, slower, inflection)	75	25	60
Fewer tangents	100	50	40
Responded to cues for extending narratives	75	50	60
Reported increased receptiveness, expression, and accuracy when communicating	100	50	60
Reported clarity of thought	75	50	20
Verbalizing disagreement and frustration	100	50	60

### *Sleep Outcomes*

Sleep disturbances are among the most commonly reported concerns for families of children with ASD. The present study tracked improvements in five sleep-related parameters: sleep onset, sleep depth, nighttime awakenings, ease of returning to sleep, and morning refreshment.

The percentages of participants showing improvement across five caregiver-reported sleep domains are listed for each experimental group in Table 2. All participants in the active treatment group reported improvement across all five domains. This uniform improvement was not reported in either of the control groups.

The heat-only group showed moderate improvement in sleep quality, with 75% of caregivers reporting longer sleep and fewer awakenings, and 50% noting easier sleep onset and improved ability to return to sleep after waking. Surprisingly, the placebo group exhibited unexpectedly high rates of improvement in certain domains, particularly for sleep onset and decreased nighttime waking. However, these outcomes were inconsistent across other measures.

Table 2. Parent-Reported Sleep Improvements (%) by Experimental Condition

Sleep Statements	Heat & Vacuum	Heat Only	No Heat & No Vacuum
Reported longer and deeper sleep	100	75	60
Easier falling asleep	100	50	100
Reported feeling refreshed in the morning	100	75	80
Reported decreased frequency of waking up at night	100	75	100
Reported going back to sleep easily again after waking up in the middle of the night	100	50	80

### IV. Discussion

This pilot study provides preliminary support for the safety, feasibility, and therapeutic potential of the AVACEN device in children with ASD. Notable findings emerged from parent-reported improvements in both language and sleep domains, particularly in participants receiving the full AVACEN Treatment Method protocol, incorporating both heat and negative pressure. These results align with the hypothesized link between thermoregulatory interventions and modulation in neurodevelopmental disorders, particularly in the context of the well-documented “fever effect” in autism.<sup>10,11</sup>

In the language domain, 4 out of 4 (100%) participants in the active treatment group were reported to have expanded their expressive vocabulary, improved conversational engagement, and demonstrated increased use of words to express their needs and emotions. These results suggest potential improvements in social-pragmatic language, a key area of impairment in ASD. Similarly, significant improvements were noted in parent-reported sleep patterns, including reductions in sleep latency and nighttime awakenings, with improvements reported across all measured sleep domains in the active group. These findings may be clinically meaningful given the pervasive impact of sleep disturbances on daytime functioning in children with ASD.<sup>19</sup>

The AVACEN device delivers dry heat therapy through the palm while simultaneously applying negative pressure to facilitate thermal exchange through AVAs. This mechanism has been shown in prior studies to enhance microvascular perfusion, modulate autonomic tone, and improve systemic thermoregulation.<sup>16</sup> These effects may be particularly relevant in ASD, where alterations in autonomic nervous system function and atypical sensory integration have been well documented.<sup>20</sup> The fever effect itself may stem from transient normalization of homeostatic functions during febrile states, potentially through the activation of heat-shock proteins, cytokine modulation, or transient fluctuations in synaptic plasticity.<sup>9,13,15,21</sup> The AVACEN device, by engaging similar thermoregulatory pathways without inducing systemic infection, may partially mimic these beneficial effects in a controlled and repeatable fashion.

The observed improvements in communication and sleep may also reflect downstream effects of enhanced cerebral perfusion and autonomic regulation. Increased vagal tone, reduced sympathetic arousal, and improved sleep architecture are all plausible mediators of cognitive and behavioral improvements, and each has been associated with improved outcomes in ASD.<sup>22-24</sup> Moreover, better sleep is independently linked to improvements in learning, emotional regulation, and social interaction, all of which are impacted in autism.<sup>25</sup>

While encouraging, these findings should still be interpreted with caution. The sample size used was small, including only four or five participants per experimental condition, and did not include any objective measures. While trends were strong in the active treatment group, significant improvements were seen in the control groups as well, which may limit the interpretation of between-group differences. Further, the lack of standardized behavioral assessments prevents firm conclusions about clinical efficacy.

Nevertheless, the results support the rationale for larger, controlled trials to further evaluate the AVACEN device as a novel, non-invasive intervention for children with ASD. Further studies should incorporate standardized outcome measures, non-parental blinded raters, and neurophysiological assessment, such as electroencephalogram (EEG) or heart rate variability (HRV), to explore potential underlying mechanisms. Given the unmet therapeutic needs in this population, as well as the favorable safety and usability profile of the AVACEN system, this line of research warrants rigorous follow-up.

If efficacy is confirmed in larger-scale randomized controlled trials, the AVACEN device could represent an innovative adjunctive therapy for managing core and associated symptoms of ASD. As a non-pharmacologic, home-based intervention, it may be especially appealing for families seeking low-risk and accessible treatment options that improve communication and behavioral regulation. The FDA approval of such a device could significantly broaden the toolkit available to clinicians treating autism, improving outcomes and quality of life for affected children and their caregivers.

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