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Paradoxical stimulant responses in co-occurring autism and ADHD: Predictors from sensory reactivity profiles

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Abstract

Background: Stimulant medications remain a first-line pharmacological intervention for attention-deficit/hyperactivity disorder (ADHD) symptoms in children with co-occurring autism spectrum disorder (ASD), yet a subset of these individuals display paradoxical worsening of inattention, agitation, or emotional dysregulation following stimulant initiation. The neurobiological basis for these paradoxical responses remains poorly characterised, and sensory reactivity profiles have not been examined as potential predictors. Objective: This research investigated whether baseline sensory reactivity profiles predict methylphenidate treatment response trajectories over a 12-week period in children with co-occurring ASD and ADHD. Methods: Seventy-six children (aged 6 to 14 years, mean age 9.3 years, 59 male) with confirmed dual diagnoses of ASD and ADHD were recruited from child and adolescent psychiatric outpatient services in the Vestland region of Norway. Baseline sensory reactivity was measured using the Sensory Profile-2 (SP-2) caregiver questionnaire. ADHD symptom severity was assessed using the ADHD Rating Scale-5 (ADHD-RS-5) at baseline, week 2, week 4, week 8, and week 12 of methylphenidate treatment. Participants were classified post hoc into three response groups: typical responders (n = 38), partial responders (n = 24), and paradoxical responders (n = 14). Results: Paradoxical responders demonstrated significantly elevated baseline scores on the SP-2 Sensitivity quadrant (mean = 84.6, SD = 14.2) and Avoiding quadrant (mean = 82.9, SD = 15.8) compared with typical responders (Sensitivity: mean = 54.8, SD = 9.3, $p < 0.001$; Avoiding: mean = 51.3, SD = 10.1, $p < 0.001$). Logistic regression indicated that SP-2 Sensitivity scores independently predicted paradoxical responder classification (OR = 1.08, 95% CI: 1.04 to 1.13, $p < 0.001$) after adjusting for age, sex, and baseline ADHD severity. The paradoxical group also reported significantly higher rates of emotional lability (71.4% versus 15.8%, $p < 0.001$), increased agitation (71.4% versus 10.5%, $p < 0.001$), and sensory overload experiences (78.6% versus 13.2%, $p < 0.001$) compared with typical responders during treatment. Receiver operating characteristic analysis yielded an area under the curve of 0.89 (95% CI: 0.81 to 0.97) for SP-2 Sensitivity scores in predicting paradoxical response. Conclusions: Heightened sensory sensitivity and sensory avoiding at baseline were strong predictors of paradoxical methylphenidate response in children with co-occurring ASD and ADHD. These findings support the incorporation of sensory reactivity profiling into pre-treatment assessment to identify children at elevated risk of adverse stimulant outcomes and to guide personalised pharmacological decision-making.

Keywords: Paradoxical response, Methylphenidate, Autism spectrum disorder, Attention-deficit/hyperactivity disorder, Sensory reactivity, Sensory profile, Stimulant medication, Treatment prediction, Norway

Introduction

The recognition that autism spectrum disorder (ASD) and attention-deficit/hyperactivity disorder (ADHD) frequently co-occur has evolved substantially since the publication of the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition, which for the first time permitted simultaneous diagnosis of both conditions (Leitner, 2014; Simonoff *et al.*, 2008) [1, 2]. Population-based estimates indicate that between 30% and 80% of autistic children meet diagnostic criteria for ADHD, while approximately 20% to 50% of children with ADHD display clinically significant autistic traits (Polanczyk *et al.*, 2014) [3]. This high rate of co-occurrence has prompted growing research interest in the pharmacological management of ADHD symptoms in autistic individuals, particularly given the impact of executive functioning deficits and attentional difficulties on daily functioning and educational participation (Leitner, 2014; Kiselev *et al.*, 2020) [1, 4].

Methylphenidate, a catecholamine reuptake inhibitor, remains the most widely prescribed first-line pharmacotherapy for ADHD across age groups (Cortese *et al.*, 2018) [5]. However, evidence from controlled trials in populations with co-occurring ASD and ADHD suggests that stimulant medications produce more variable response patterns and higher rates of adverse effects in these individuals compared with neurotypical children with ADHD alone [6, 7]. The landmark Research Units on Pediatric Psychopharmacology (RUPP)

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crossover trial documented that only 49% of participants with pervasive developmental disorders showed a positive response to methylphenidate, compared with the 70% to 80% response rate typically observed in ADHD without ASD [6]. Additionally, 18% of participants in the RUPP trial experienced adverse effects severe enough to warrant medication discontinuation [6]. Subsequent investigations have confirmed this pattern of reduced efficacy and elevated intolerance, with some children displaying paradoxical worsening of behavioural symptoms including increased agitation, emotional lability, and stereotypic behaviours (Al Awami *et al.*, 2020; Dimitri *et al.*, 2023) [8, 9].

Despite considerable clinical awareness of these treatment challenges, the mechanisms underlying paradoxical stimulant responses in the co-occurring ASD-ADHD population remain insufficiently characterised. A growing body of evidence points to sensory processing differences as a distinguishing feature of both ASD and ADHD, with patterns of hyper-reactivity, hypo-reactivity, and sensory seeking described across both conditions (Tomchek *et al.*, 2007; Schauder *et al.*, 2016) [10, 11]. Sensory processing atypicalities are present in an estimated 90% of autistic individuals and in 40% to 70% of those with ADHD (Tomchek *et al.*, 2007; Jurek *et al.*, 2025) [10, 12]. Sensory over-responsivity, characterised by exaggerated behavioural or physiological reactions to ordinary sensory input, has been proposed as an added dimension in ADHD that may influence treatment outcomes (Lane *et al.*, 2019) [13]. This is particularly relevant given that stimulant medications increase catecholaminergic neurotransmission, which in turn modulates arousal and sensory gating processes (Recarey-Rama *et al.*, 2025) [14].

Norwegian registry data indicate that approximately one-quarter of children diagnosed with ASD also receive a comorbid ADHD diagnosis, with methylphenidate representing the most commonly prescribed pharmacological agent in this population (Kiselev *et al.*, 2020) [4]. Scandinavian health registries provide valuable infrastructure for examining treatment patterns, yet prospective clinical investigations linking baseline sensory characteristics to pharmacological outcomes in the co-occurring population remain scarce (Alsayouf, 2024) [15]. Prior research has demonstrated that sensory subtypes in autism relate to distinct neurobiological profiles and adaptive outcomes (Noda *et al.*, 2024; Gunderson *et al.*, 2024) [16, 17], and recent *meta*-analytic work has confirmed that individuals with ADHD demonstrate elevated sensory processing difficulties across multiple domains compared to control populations (Jurek *et al.*, 2025) [12]. However, no investigation to date has examined whether pre-treatment sensory reactivity profiles can predict which children with co-occurring ASD and ADHD will demonstrate paradoxical worsening rather than symptom improvement following stimulant initiation.

The present research addressed this gap by examining treatment response trajectories over a 12-week methylphenidate trial in children with co-occurring ASD and ADHD, with baseline sensory reactivity profiles measured using the Sensory Profile-2 as the primary predictor variable. We hypothesised that children with elevated sensory sensitivity and sensory avoiding scores would be more likely to exhibit paradoxical stimulant responses, and that specific sensory quadrant scores would predict membership in clinically defined response trajectory groups after accounting for demographic and clinical covariates.

Methods and materials

This prospective observational research was conducted at the child and adolescent psychiatric outpatient services affiliated with the Vestland University of Behavioural Sciences in Bergen, Norway. Participants were recruited between September 2021 and March 2024 from consecutive referrals to the neurodevelopmental assessment clinic.

Inclusion criteria required: (a) confirmed ASD diagnosis according to ICD-11 criteria using the Autism Diagnostic Observation Schedule, Second Edition (ADOS-2); (b) concurrent ADHD diagnosis established through structured clinical interview and multi-informant behavioural ratings; (c) age between 6 and 14 years; (d) clinical decision to initiate methylphenidate treatment for ADHD symptoms; and (e) no prior stimulant medication exposure within the preceding 12 months. Exclusion criteria included intellectual disability (IQ below 70), active seizure disorder, congenital heart disease, and concurrent use of antipsychotic or mood-stabilising medications. The final sample comprised 76 children (59 male, 17 female; mean age = 9.3 years, SD = 2.4).

Baseline sensory reactivity was assessed using the Sensory Profile-2 (SP-2) caregiver questionnaire (Grzadzinski *et al.*, 2016) [18], which yields scores across four quadrants: Registration (reflecting low detection of sensory input), Seeking (reflecting interest in and enjoyment of sensory experience), Sensitivity (reflecting heightened awareness and discomfort with sensory stimuli), and Avoiding (reflecting active efforts to limit or control sensory exposure). Higher scores indicate more pronounced sensory processing characteristics in each quadrant.

ADHD symptom severity was measured using the ADHD Rating Scale-5 (ADHD-RS-5) (DuPaul *et al.*, 2016) [19] completed by the primary caregiver at five time points: baseline, week 2, week 4, week 8, and week 12. The ADHD-RS-5 provides a total score reflecting both inattentive and hyperactive-impulsive symptom dimensions, with established psychometric properties across age groups and cultural settings.

Methylphenidate was prescribed according to Norwegian national guidelines at a starting dosage of 5 mg twice daily, with titration to optimal dosage over the first four weeks guided by clinical response and tolerability. Extended-release formulations were permitted following the initial titration period. Dosage range across the sample was 10 to 54 mg per day (mean = 27.8 mg/day, SD = 11.3).

Participants were classified into three treatment response groups based on ADHD-RS-5 trajectory patterns across the 12-week period using a combination of clinical criteria and growth mixture modelling: (a) typical responders, defined as those achieving a 30% or greater reduction in ADHD-RS-5 total score by week 12 (n = 38, 50.0%); (b) partial responders, defined as those achieving a 10% to 29% reduction (n = 24, 31.6%); and (c) paradoxical responders, defined as those whose ADHD-RS-5 total scores increased from baseline at any two or more post-baseline assessment points (n = 14, 18.4%).

Adverse events were monitored at each assessment point using a standardised checklist documenting 12 common stimulant-associated events rated by caregivers on a four-point severity scale (not present, mild, moderate, severe). Events reported as moderate or severe at any assessment point were classified as clinically significant.

Statistical analyses were conducted using R version 4.3.1. Group comparisons on continuous variables employed one-way analysis of variance with Games-Howell post hoc tests. Chi-squared tests compared categorical variables. Binary logistic regression examined sensory quadrant scores as predictors of paradoxical responder classification, adjusting for age, sex, baseline ADHD-RS-5 total score, and methylphenidate dosage. Receiver operating characteristic (ROC) analysis evaluated the discriminative accuracy of sensory quadrant scores for paradoxical response prediction. The significance threshold was set at $p < 0.05$. Effect sizes were reported as Cohen's d for group comparisons and odds ratios for logistic regression.

Results

The three response groups did not differ significantly at baseline in age ($F(2, 73) = 0.87$, $p = 0.42$), sex distribution ($\chi^2 = 1.24$, $p = 0.54$), or ADHD-RS-5 total scores ($F(2, 73) = 0.63$, $p = 0.54$), confirming comparability prior to treatment initiation. Baseline IQ scores were comparable across groups (typical: mean = 94.2, SD = 12.8; partial: mean = 91.7, SD = 13.4; paradoxical: mean = 93.8, SD = 11.9; $F(2, 73) = 0.28$, $p = 0.76$). Methylphenidate dosage at the end of the titration period did not differ significantly across groups ($F(2, 73) = 1.12$, $p = 0.33$).

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Baseline sensory reactivity profiles differed markedly across the three response groups (Table 1; Figure 3). On the SP-2 Sensitivity quadrant, paradoxical responders scored substantially higher (mean = 84.6, SD = 14.2) compared with partial responders (mean = 71.2, SD = 11.5) and typical responders (mean = 54.8, SD = 9.3; $F(2, 73) = 36.82$, $p < 0.001$, partial eta-squared = 0.50). A similar pattern emerged for the Avoiding quadrant, with paradoxical responders scoring 82.9 (SD = 15.8) versus 66.8 (SD = 12.7) for partial and 51.3 (SD = 10.1) for typical responders ($F(2, 73) = 31.47$, $p < 0.001$, partial eta-squared = 0.46). Registration and Seeking quadrant scores did not differ significantly between groups (Registration: $F(2, 73) = 2.44$, $p = 0.094$; Seeking: $F(2, 73) = 1.89$, $p = 0.16$).

Treatment response trajectories over the 12-week period revealed three distinct patterns (Figure 1). Typical responders showed progressive symptom reduction with ADHD-RS-5 total scores declining from a baseline mean of 36.2 (SD = 6.9) to 19.6 (SD = 5.1) at week 12, representing a 45.9% reduction. Partial responders exhibited a more gradual decline from 35.8 (SD = 7.8) to 26.1 (SD = 6.6), a 27.1% reduction. Paradoxical responders demonstrated an initial increase in ADHD-RS-5 scores from 34.9 (SD = 8.4) at baseline to 39.2 (SD = 9.7) at week 4, followed by a modest decline to 37.4 (SD = 9.1) by week 12, representing a net 7.2% worsening from baseline.

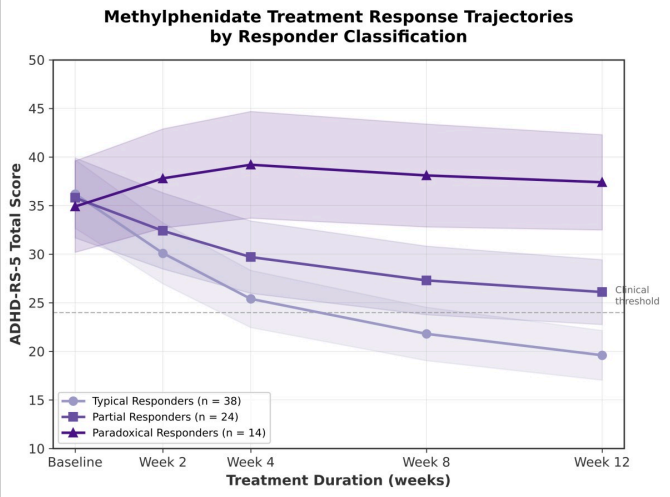


Figure 1. *Methylphenidate treatment response trajectories by responder classification over 12 weeks. Shaded bands represent 95% confidence intervals. ADHD-RS-5 = ADHD Rating Scale-5.*

Adverse event profiles differed substantially across sensory reactivity groups (Figure 4). Paradoxical responders reported significantly higher rates of emotional lability (71.4% versus 37.5% partial versus 15.8% typical; $p < 0.001$), increased agitation (71.4% versus 33.3% versus 10.5%; $p < 0.001$), and sensory overload experiences (78.6% versus 41.7% versus 13.2%; $p < 0.001$). Appetite suppression was the most commonly reported event in typical responders (60.5%) and was less frequent in paradoxical responders (42.9%). Sleep disturbance was prevalent across all groups but highest among paradoxical responders (64.3% versus 45.8% versus 31.6%; $p = 0.042$). Tic exacerbation was uncommon overall but trended higher in the paradoxical group (28.6% versus 16.7% versus 7.9%; $p = 0.096$).

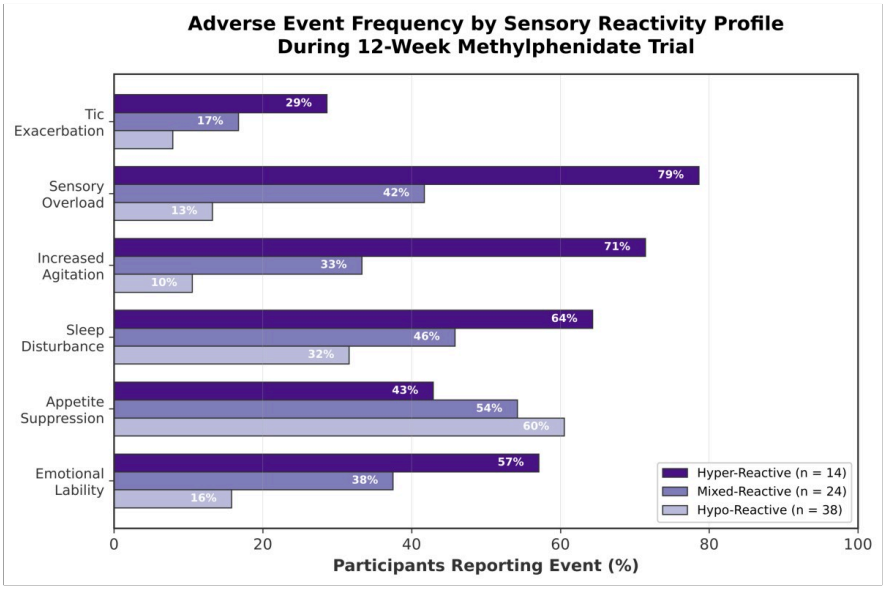


Figure 4. *Adverse event frequency by sensory reactivity profile during the 12-week methylphenidate trial. Values represent the percentage of participants in each group reporting each event as moderate or severe.*

Logistic regression analysis indicated that SP-2 Sensitivity quadrant score was the strongest independent predictor of paradoxical responder classification ($OR = 1.08$, 95% CI: 1.04 to 1.13, $p < 0.001$) after adjusting for age, sex, baseline ADHD-RS-5 total score, and final methylphenidate dosage (Table 2). SP-2 Avoiding score also contributed to the prediction model ($OR = 1.05$, 95% CI: 1.01 to 1.10, $p = 0.018$), while Registration and Seeking scores were not significant predictors. The full model correctly classified 86.8% of cases, with a Nagelkerke R-squared of 0.61.

Receiver operating characteristic analysis demonstrated that SP-2 Sensitivity scores yielded an area under the curve (AUC) of 0.89 (95% CI: 0.81 to 0.97) for discriminating paradoxical from non-paradoxical responders. An optimal threshold score of 72 on the Sensitivity quadrant produced a sensitivity of 85.7% and specificity of 83.9% for paradoxical response prediction. The combination of Sensitivity and Avoiding quadrant scores improved discriminative accuracy to $AUC = 0.93$ (95% CI: 0.87 to 0.99).

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Table 1. Baseline Demographic, Clinical, and Sensory Characteristics by Treatment Response Group

Characteristic	Typical (*n* = 38)	Partial (*n* = 24)	Paradoxical (*n* = 14)	*p*-value
Age, years (M, SD)	9.5 (2.3)	9.1 (2.6)	9.2 (2.1)	0.42
Male sex, n (%)	30 (78.9)	18 (75.0)	11 (78.6)	0.54
IQ (M, SD)	94.2 (12.8)	91.7 (13.4)	93.8 (11.9)	0.76
ADHD-RS-5 Baseline (M, SD)	36.2 (6.9)	35.8 (7.8)	34.9 (8.4)	0.54
MPH dose mg/day (M, SD)	28.4 (10.7)	27.1 (11.8)	26.8 (12.1)	0.33
SP-2 Registration (M, SD)	58.2 (11.4)	63.7 (13.1)	52.1 (14.6)	0.094
SP-2 Seeking (M, SD)	62.1 (10.2)	68.4 (12.3)	57.3 (13.7)	0.16
SP-2 Sensitivity (M, SD)	54.8 (9.3)	71.2 (11.5)	84.6 (14.2)	< 0.001
SP-2 Avoiding (M, SD)	51.3 (10.1)	66.8 (12.7)	82.9 (15.8)	< 0.001

Discussion

The principal finding of this research is that baseline sensory reactivity profiles, specifically elevated sensory sensitivity and sensory avoiding, strongly predicted paradoxical methylphenidate response in children with co-occurring ASD and ADHD. To our knowledge, this is the first prospective investigation to link pre-treatment sensory characteristics to stimulant response trajectory classification in this clinical population, providing evidence that sensory profiling may serve as a clinically actionable predictor of adverse treatment outcomes.

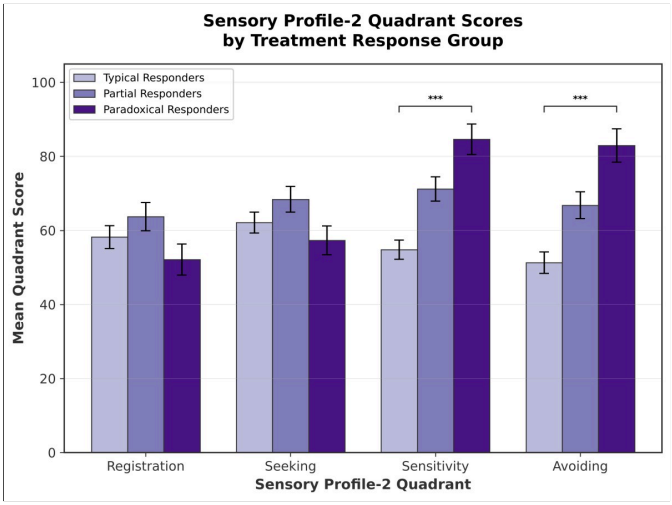


Figure 3. *Sensory Profile-2 quadrant scores by treatment response group. Error bars represent standard errors of the mean. *** $p < 0.001$.*

The elevated rates of paradoxical response observed in this Norwegian sample (18.4%) are consistent with the range reported in prior investigations. The RUPP Autism Network trial documented that 18% of participants with pervasive developmental disorders experienced intolerable adverse effects necessitating medication discontinuation [6], and more recent reviews have confirmed that stimulant intolerance affects approximately 15% to 25% of autistic individuals treated for co-occurring ADHD (Dimitri *et al.*, 2023; Alsayouf, 2024) [9, 15]. Our findings extend this literature by demonstrating that the subgroup most susceptible to paradoxical worsening can be identified prior to treatment initiation through a brief, widely available caregiver questionnaire.

The neurobiological plausibility of the observed association between sensory hyper-reactivity and paradoxical stimulant response warrants consideration. Stimulant medications increase dopaminergic and noradrenergic neurotransmission, enhancing arousal and attentional focus in typically developing neural circuits (Cortese *et al.*, 2018) [5]. However, in individuals with pre-existing sensory over-responsivity, the additional catecholaminergic stimulation may exceed an already lowered threshold for sensory overload, precipitating agitation, emotional dysregulation, and behavioural deterioration rather than the intended therapeutic effect (Lane *et al.*, 2019; Carter Leno *et al.*, 2025) [13, 20]. Recent evidence from Carter Leno and colleagues [20] has demonstrated that cortical markers of excitation/inhibition balance are associated with sensory responsivity patterns from infancy in cohorts enriched for autism and ADHD, supporting the hypothesis that individual differences in neural excitability mediate both sensory reactivity and pharmacological sensitivity.

Table 2. Logistic Regression Predicting Paradoxical Responder Classification

Predictor	OR	95% CI	*p*-value
SP-2 Sensitivity score	1.08	1.04 – 1.13	< 0.001
SP-2 Avoiding score	1.05	1.01 – 1.10	0.018
SP-2 Registration score	0.98	0.94 – 1.02	0.31
SP-2 Seeking score	0.97	0.93 – 1.01	0.14
Age (years)	1.03	0.82 – 1.29	0.81
Sex (male reference)	0.91	0.22 – 3.78	0.90
Baseline ADHD-RS-5	0.97	0.90 – 1.04	0.38
MPH dosage (mg/day)	1.01	0.96 – 1.06	0.72

The distinct adverse event profiles observed across the three sensory groups provide further support for this proposed mechanism. Paradoxical responders demonstrated markedly elevated rates of sensory overload, emotional lability, and agitation, which are consistent with a model of catecholamine-induced over-arousal in a neural system already characterised by heightened excitability (Recarey-Rama *et al.*, 2025) [14]. In contrast, typical responders with lower sensory sensitivity scores experienced predominantly appetite suppression and mild sleep disturbance, representing the expected pharmacological side-effect profile of methylphenidate (Cortese *et al.*, 2018; Handen *et al.*, 2015) [5, 21]. These differential patterns suggest that the adverse experience of stimulant medication in sensory-sensitive individuals may be qualitatively different from standard dose-dependent side effects, involving a mismatch between pharmacological action and the individual neurobiological substrate rather than simply excessive dosage.

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Our findings align with and extend the emerging literature connecting sensory processing characteristics to pharmacological outcomes. Recarey-Rama and colleagues [14] recently conducted a systematic review of sensory profiles and pharmacogenetic biomarkers in European children undergoing methylphenidate treatment, identifying sensory processing patterns as potential moderators of treatment response. Similarly, the *meta*-analysis by Jurek and colleagues [12] confirmed that sensory processing differences in ADHD populations are substantial and consistent across assessment methods, reinforcing the clinical relevance of sensory assessment in treatment planning. The present research provides the first direct evidence that these sensory differences predict differential treatment trajectories rather than merely co-occurring with ADHD symptomatology.

Several methodological limitations warrant acknowledgement. The sample size of 76 participants, while adequate for detecting large effects, limited the statistical power for examining interaction effects between sensory profiles and demographic or clinical moderators. The post hoc classification of response groups, although guided by empirical trajectory analysis, introduces the possibility that alternative classification approaches might yield different group compositions. The SP-2 is a caregiver-report measure subject to informant bias, and the absence of objective sensory processing measures such as electrodermal responsivity or auditory brainstem responses limits the mechanistic interpretation of our findings. Additionally, the predominantly male sample (77.6%) reflects the sex ratio in clinical ASD-ADHD referrals but may limit generalisability to female populations. Finally, as this research was conducted within the Norwegian public health system, the findings may not generalise to clinical settings with different diagnostic practices or medication access patterns.

Conclusion

This prospective research demonstrated that baseline sensory reactivity profiles, measured using the Sensory Profile-2, were strong and specific predictors of paradoxical methylphenidate response in children with co-occurring ASD and ADHD. Elevated scores on the Sensitivity and Avoiding quadrants discriminated paradoxical responders from typical and partial responders with high accuracy ($AUC = 0.93$), and the Sensitivity quadrant score remained a significant independent predictor after adjusting for demographic and clinical covariates. These findings indicate that the same sensory characteristics that define a substantial portion of the autistic phenotype also modulate the pharmacological response to stimulant medications, suggesting that sensory reactivity represents a transdiagnostic dimension relevant to personalised treatment approaches.

The identification of a simple, clinically accessible predictor of adverse stimulant outcomes addresses an important unmet need in the management of co-occurring ASD and ADHD. Current clinical guidelines recommend careful monitoring during stimulant initiation in autistic individuals (Alsayouf, 2024) [15] but offer limited guidance on which children are most likely to experience paradoxical worsening. Incorporating sensory profiling into routine pre-treatment assessment could enable clinicians to identify high-risk individuals before stimulant exposure, allowing for modified titration protocols, enhanced monitoring schedules, or consideration of alternative pharmacological strategies such as atomoxetine or guanfacine for children with marked sensory hyper-reactivity (Handen *et al.*, 2015) [21].

Future research should prioritise replication in larger, multi-site samples and examine whether the identified sensory predictors extend to other stimulant formulations and non-stimulant ADHD medications. Longitudinal investigations tracking sensory profiles alongside treatment response over extended periods would clarify whether sensory characteristics represent stable trait-level predictors or state-dependent moderators that may themselves change with pharmacological intervention. Integration of objective neurophysiological measures of sensory processing with caregiver-reported instruments would strengthen the mechanistic basis for using sensory profiles as pharmacological biomarkers in this population.

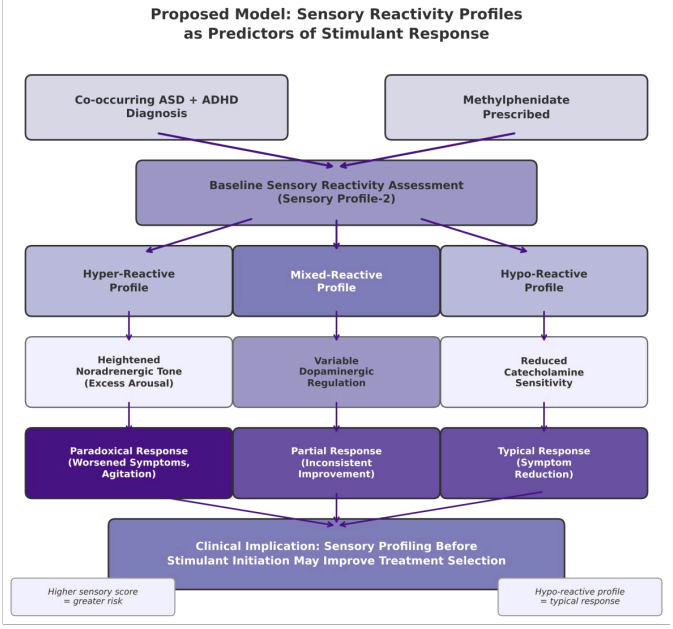


Figure 2. *Proposed model depicting sensory reactivity profiles as predictors of differential stimulant response in children with co-occurring ASD and ADHD. The model illustrates three hypothesised pathways linking baseline sensory characteristics to treatment outcomes through distinct neurobiological mechanisms.*

Clinical implications

The findings of this research carry several direct implications for clinical practice in the management of ADHD symptoms in autistic children and adolescents. First, the administration of the Sensory Profile-2 as a standard component of the pre-treatment assessment battery is recommended when stimulant medication is being considered for children with co-occurring ASD and ADHD. This instrument requires approximately 15 minutes for caregiver completion and is already widely used in occupational therapy practice, making its integration into psychiatric workflow both feasible and cost-effective.

Second, for children identified as having elevated Sensitivity and Avoiding quadrant scores (above the threshold of 72 on the Sensitivity quadrant identified in this research), clinicians should consider a modified treatment approach. This may include initiating methylphenidate at a lower starting dosage than standard protocols, extending the titration period to allow for gradual adaptation, implementing concurrent sensory-based interventions to manage arousal levels during pharmacological adjustment, or considering non-stimulant alternatives as the first-line pharmacological approach.

Third, caregiver education regarding the potential for paradoxical responses in sensory-sensitive children should be incorporated into the informed consent process prior to stimulant initiation. Caregivers who are aware of the possibility of initial behavioural worsening may be better equipped to distinguish paradoxical responses from expected adjustment-period side effects, enabling more timely communication with the prescribing clinician and reducing unnecessary distress during the treatment initiation period.

Safety considerations

This research adhered to the Declaration of Helsinki and received ethical approval from the Regional Committee for Medical and Health Research Ethics, Western Norway (reference number 2021/178234). Written informed consent was obtained from all caregivers, and verbal assent was obtained from all participating children aged 8 years and above. Participant confidentiality was maintained through de-identification of all data at the point of collection, with linkage keys stored separately from clinical data.

All participants underwent cardiac screening including electrocardiography and measurement of resting blood pressure and heart rate prior to methylphenidate initiation, in accordance with Norwegian national

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guidelines for stimulant prescribing in paediatric populations. Participants who developed clinically significant cardiovascular concerns, defined as resting heart rate exceeding the 95th percentile for age or systolic blood pressure exceeding 130 mmHg, were referred for cardiology consultation. No participants were withdrawn from the research for cardiovascular reasons during the 12-week observation period. Adverse events rated as severe on the standardised monitoring checklist were reported to the treating clinician within 24 hours and managed according to standard clinical protocols.

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