Autism spectrum disorder (ASD) is a prevalent neurodevelopmental condition characterized by difficulties in social communication, as well as restricted, repetitive and sensorimotor behaviors [1]. Globally affecting ~78 million individuals [2], early diagnosis and intervention —ideally by 24 months— are critical to capitalize on heightened neuroplasticity during childhood [3]. However, current research on ASD highlights its significant overlap with attention deficit hyperactivity disorder (ADHD), particularly in shared behavioral traits [4]. The frequent co-occurrence of these two diagnostic categories poses a major challenge in tailoring optimal and effective intervention strategies, especially given the unique repertoire of behavioral complexities exhibited by children with both diagnoses [5].

Previous evidence shows that toddlers subsequently diagnosed with both ASD and ADHD exhibit greater internalizing and externalizing symptoms, more severe autism-related behaviors, and higher requirements in terms of parental support [6] . Nevertheless, the reliance of these findings in the current diagnostic framework may conceal the broader spectrum of these conditions, potentially limiting the effectiveness of early targeted interventions. Both ASD and ADHD are highly heterogeneous conditions, with a wild range of phenotypic manifestations. Consequently, the use of rigid diagnostic categories might not fully capture this diversity, particularly in young children whose developmental profiles are still emerging [7]. Furthermore, the exclusive reliance on behavioral observations to differentiate between ASD and ADHD has become increasingly problematic, since many behavioral traits are shared across the two disorders, such as persistent difficulties with social communication, deficits in executive function, inattention and impulsivity [8]. Consequently, studies structured around these predefined categories may miss subtler, yet clinically relevant, deviations in neurodevelopmental trajectories that do not fit traditional diagnostic criteria.

Advancing beyond the established diagnostic categories in research on neurodevelopmental conditions poses a major challenge, but also offers considerable potential. Data-driven grouping and dimensional objective measures are two alternatives that merit exploration, although they both require large, representative samples and extensive mapping of observable traits and behaviors. In this context, eye-tracking (ET) is a safe, affordable and well-tolerated technology that provides an early detectable signature of differences in visual attention by the quantification of low-level behaviors such as eye movements [9]. Several studies have provided compelling evidence of disparities in the way autistic children process visual information compared to children with typical development, such as lower time observing social stimuli [10], reduced gaze fixation to faces and eyes [11], [12], a preference for nonsocial (e.g. geometrical) cues [13] and longer latencies to disengage [14]. Furthermore, the convergent validity of ET indices of social attention has been corroborated by their robust association with caregiver ratings on clinical measures assessing social

communication [15]. The extensive use of ET as an early diagnostic and detection instrument in autism finds no parallel in its use to provide a neurobehavioral biomarker that helps to distinguish comorbid developmental trajectories. A recent proof-of-concept study revealed that compared with ASD, children with ADHD and ADHD+ASD demonstrated weaker vergence responses to the eyes, perhaps underlying the inability to pay attention to these cues for emotion detection [16]. Another study presented a classification framework for ASD and ADHD diagnoses, in which reduced average pupil diameters of the participants with ADHD had a higher classification power than behavioral features [17].

The aim of the present project proposal is to explore whether ET holds promise as a noninvasive, quantitative and objective outcome measure to provide an early an effective distinction between ASD, ADHD and comorbid neurodevelopmental trajectories in preschool children. With its ability to capture subtle gaze and attentional patterns in young children [18], ET has the potential to facilitate the robust identification of early behavioral differences linked with ASD, ADHD and their comorbidity, in particular because distinctive patterns of eye movements already emerge in toddlers at risk of autism long before behavioral symptoms become apparent [19], [20]. In addition, tracking developmental trajectories longitudinally to identify early indicators and understand how symptoms evolve is of paramount importance.

By enhancing our capacity to identify young children with comorbid ASD and ADHD at an earlier stage, we can more effectively adapt and customize interventions to address their specific developmental requirements. This research thus serves as a fundamental basis for subsequent investigations and offers immediate practical applications in clinical practice.

REFERENCE

[1] American Psychiatric Association, *Diagnostic and Statistical Manual of Mental Disorders*, DSM-5-TR. American Psychiatric Association Publishing, 2022. doi: [10.1176/appi.books.9780890425787](https://doi.org/10.1176/appi.books.9780890425787). Available: <https://psychiatryonline.org/doi/book/10.1176/appi.books.9780890425787>. [Accessed: Mar. 11, 2025]

[2] C. Lord *et al.*, “The Lancet Commission on the future of care and clinical research in autism,” *Lancet (London, England)*, vol. 399, no. 10321, pp. 271–334, Jan. 2022, doi: [10.1016/S0140-6736(21)01541-5](https://doi.org/10.1016/S0140-6736(21)01541-5)

[3] G. Dawson, “Early behavioral intervention, brain plasticity, and the prevention of autism spectrum disorder,” *Development and Psychopathology*, vol. 20, no. 3, pp. 775–803, 2008, doi: [10.1017/S0954579408000370](https://doi.org/10.1017/S0954579408000370)

[4] K. M. Antshel and N. Russo, “Autism Spectrum Disorders and ADHD: Overlapping Phenomenology, Diagnostic Issues, and Treatment Considerations,” *Current Psychiatry Reports*, vol. 21, no. 5, p. 34, Mar. 2019, doi: [10.1007/s11920-019-1020-5](https://doi.org/10.1007/s11920-019-1020-5). Available: <https://doi.org/10.1007/s11920-019-1020-5>. [Accessed: Mar. 11, 2025]

[5] J. M. J. van der Meer *et al.*, “Are Autism Spectrum Disorder and Attention-Deficit/Hyperactivity Disorder Different Manifestations of One Overarching Disorder? Cognitive and Symptom Evidence From a Clinical and Population-Based Sample,” *Journal of the American Academy of Child & Adolescent Psychiatry*, vol. 51, no. 11, pp. 1160–1172.e3, Nov. 2012, doi: [10.1016/j.jaac.2012.08.024](https://doi.org/10.1016/j.jaac.2012.08.024). Available: <https://www.sciencedirect.com/science/article/pii/S0890856712006491>. [Accessed: Mar. 11, 2025]

[6] A. Carta, E. Fucà, S. Guerrera, E. Napoli, G. Valeri, and S. Vicari, “Characterization of Clinical Manifestations in the Co-occurring Phenotype of Attention Deficit/Hyperactivity Disorder and Autism Spectrum Disorder,” *Frontiers in Psychology*, vol. 11, May 2020, doi: [10.3389/fpsyg.2020.00861](https://doi.org/10.3389/fpsyg.2020.00861). Available: <https://www.frontiersin.org/journals/psychology/articles/10.3389/fpsyg.2020.00861/full>. [Accessed: Mar. 11, 2025]

[7] F. Salazar *et al.*, “Co-occurring Psychiatric Disorders in Preschool and Elementary School-Aged Children with Autism Spectrum Disorder,” *Journal of Autism and Developmental Disorders*, vol. 45, no. 8, pp. 2283–2294, Aug. 2015, doi: [10.1007/s10803-015-2361-5](https://doi.org/10.1007/s10803-015-2361-5). Available: <https://doi.org/10.1007/s10803-015-2361-5>. [Accessed: Mar. 11, 2025]

[8] Y. Leitner, “The Co-Occurrence of Autism and Attention Deficit Hyperactivity Disorder in Children – What Do We Know?” *Frontiers in Human Neuroscience*, vol. 8, Apr. 2014, doi: [10.3389/fnhum.2014.00268](https://doi.org/10.3389/fnhum.2014.00268). Available: <https://www.frontiersin.org/journals/human-neuroscience/articles/10.3389/fnhum.2014.00268/full>. [Accessed: Mar. 11, 2025]

[9] M. Chita-Tegmark, “Social attention in ASD: A review and meta-analysis of eye-tracking studies,” *Research in Developmental Disabilities*, vol. 48, pp. 79–93, Jan. 2016, doi: [10.1016/j.ridd.2015.10.011](https://doi.org/10.1016/j.ridd.2015.10.011). Available: <https://www.sciencedirect.com/science/article/pii/S0891422215001821>. [Accessed: Mar. 11, 2025]

[10] F. Shic *et al.*, “The Selective Social Attention Task in Children with ASD: Results from the Autism Biomarkers Consortium for Clinical Trials (ABC-CT) Feasibility Study,” *Autism research : official journal of the International Society for Autism Research*, vol. 16, no. 11, pp. 2150–2159, Nov. 2023, doi: [10.1002/aur.3026](https://doi.org/10.1002/aur.3026). Available: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC11003770/>. [Accessed: Mar. 11, 2025]

[11] T. W. Frazier *et al.*, “A Meta-Analysis of Gaze Differences to Social and Nonsocial Information Between Individuals With and Without Autism,” *Journal of the American Academy of Child & Adolescent Psychiatry*, vol. 56, no. 7, pp. 546–555, Jul. 2017, doi: [10.1016/j.jaac.2017.05.005](https://doi.org/10.1016/j.jaac.2017.05.005). Available: <https://www.sciencedirect.com/science/article/pii/S0890856717302071>. [Accessed: Mar. 11, 2025]

[12] A. Klin, W. Jones, R. Schultz, F. Volkmar, and D. Cohen, “Visual Fixation Patterns During Viewing of Naturalistic Social Situations as Predictors of Social Competence in Individuals With Autism,” *Archives of General Psychiatry*, vol. 59, no. 9, pp. 809–816, Sep. 2002, doi: [10.1001/archpsyc.59.9.809](https://doi.org/10.1001/archpsyc.59.9.809). Available: <https://doi.org/10.1001/archpsyc.59.9.809>. [Accessed: Mar. 11, 2025]

[13] K. Pierce, S. Marinero, R. Hazin, B. McKenna, C. C. Barnes, and A. Malige, “Eye Tracking Reveals Abnormal Visual Preference for Geometric Images as an Early Biomarker of an Autism Spectrum Disorder Subtype Associated With Increased Symptom Severity,” *Biological Psychiatry*, vol. 79, no. 8, pp. 657–666, Apr. 2016, doi: [10.1016/j.biopsych.2015.03.032](https://doi.org/10.1016/j.biopsych.2015.03.032)

[14] M. Elsabbagh, J. Fernandes, S. Jane Webb, G. Dawson, T. Charman, and M. H. Johnson, “Disengagement of Visual Attention in Infancy is Associated with Emerging Autism in Toddlerhood,” *Biological Psychiatry*, vol. 74, no. 3, pp. 189–194, Aug. 2013, doi: [10.1016/j.biopsych.2012.11.030](https://doi.org/10.1016/j.biopsych.2012.11.030). Available: <https://www.sciencedirect.com/science/article/pii/S0006322312010864>. [Accessed: Mar. 11, 2025]

[15] M. Murias *et al.*, “Validation of eye-tracking measures of social attention as a potential biomarker for autism clinical trials,” *Autism Research: Official Journal of the International Society for Autism Research*, vol. 11, no. 1, pp. 166–174, Jan. 2018, doi: [10.1002/aur.1894](https://doi.org/10.1002/aur.1894)

[16] P. Bustos-Valenzuela *et al.*, “Atypical cognitive vergence responses in children with attention deficit hyperactivity disorder but not with autism spectrum disorder in a facial emotion recognition task,” *Psychiatry Research Communications*, vol. 2, no. 2, p. 100045, Jun. 2022, doi: [10.1016/j.psycom.2022.100045](https://doi.org/10.1016/j.psycom.2022.100045). Available: <https://www.sciencedirect.com/science/article/pii/S2772598722000265>. [Accessed: Mar. 11, 2025]

[17] M. Ozturk *et al.*, “Statistical Analysis and Multimodal Classification on Noisy Eye Tracker and Application Log Data of Children with Autism and ADHD,” *Intelligent Automation & Soft Computing*, vol. 24, no. 4, pp. 891–905, 2018, doi: [10.31209/2018.100000058](https://doi.org/10.31209/2018.100000058). Available: <https://www.techscience.com/iasc/v24n4/39813>. [Accessed: Mar. 11, 2025]

[18] F. Shic *et al.*, “The Autism Biomarkers Consortium for Clinical Trials: Evaluation of a battery of candidate eye-tracking biomarkers for use in autism clinical trials,” *Molecular Autism*, vol. 13, no. 1, p. 15, Mar. 2022, doi: [10.1186/s13229-021-00482-2](https://doi.org/10.1186/s13229-021-00482-2). Available: <https://doi.org/10.1186/s13229-021-00482-2>. [Accessed: Mar. 11, 2025]

[19] W. Hou, Y. Jiang, Y. Yang, L. Zhu, and J. Li, “Evaluating the validity of eye-tracking tasks and stimuli in detecting high-risk infants later diagnosed with autism: A meta-analysis,” *Clinical Psychology Review*, vol. 112, p. 102466, Aug. 2024, doi: [10.1016/j.cpr.2024.102466](https://doi.org/10.1016/j.cpr.2024.102466). Available: <https://www.sciencedirect.com/science/article/pii/S0272735824000874>. [Accessed: Mar. 11, 2025]

[20] W. Jones and A. Klin, “Attention to Eyes is Present But in Decline in 2–6 Month-Olds Later Diagnosed with Autism,” *Nature*, vol. 504, no. 7480, pp. 427–431, Dec. 2013, doi: [10.1038/nature12715](https://doi.org/10.1038/nature12715). Available: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4035120/>. [Accessed: Mar. 11, 2025]