Abstract Book

2025 ANNUAL MEETING

Beer Sheva, Israel | March 3th

Azrieli National Center for Autism
And Neurodevelopment Research

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Lectures:

Session A: Risk Factors & Diagnosis

A1. Sex specific trajectories of autism: from pregnancy to adulthood including gender related camouflage

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Abstract: Autism diagnosis is skewed in terms of sex, being more often applied to males than females. Recent studies report changes in the ratio, from 4.5:1 males to females, to 3:1. Underlying etiological mechanisms that may occur in the prenatal stages of development can be used as a potential biomarker for later autism, which can lead for early detection and intervention. Early detection and intervention is hoped will improve long term outcomes for children and families of autistic people. In addition it is possible that current diagnostic tools are more suitable for autism diagnosis in males, and females may be underdiagnosed and may mask the symptoms. The term camouflage is used for hidden symptoms in females and different trajectories may be recognized earlier.
Aims: To explore the relationship between prenatal development growth trajectories and later development of autistic traits and autism in males versus females and to identify prenatal biomarkers that may be linked to a subsequent autism diagnosis.
Methods: A cohort of 572 pregnant mothers with singleton pregnancies (286 male; 286 female fetuses), were followed prospectively from mid-pregnancy until 24 months of child age. They underwent an ultrasound scan of anogenital distance (AGD), body size, brain and cerebellar measures.
Results: Post-natal follow-up was complete for 510 infants (257 males; 253 females). At 35 points level, the Quantitative Checklist for Autism in Toddlers (Q-CHAT) validity with ASD diagnosis had high specificity and sensitivity (0.99 and 0.80 respectively). Higher AGD index

prenatally was associated with both subsequent autism diagnosis (eta squared effect size of 0.074 ($p<0.003$)) and with number of autistic traits on the Q-CHAT. Fetal growth rates were also elevated in autistic children and significantly correlated with higher Q-CHAT scores.

Conclusion: This prospective study suggests that sex related prenatal findings are associated with the likelihood of a later autism diagnosis and prenatal trajectories emerge before birth.

A2. Evaluating the agreement across common measures of core autism symptoms

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Background: Different measures for autism symptoms are based on distinct sources of information and assessment procedures. The Autism Diagnostic Observation Schedule (ADOS) (Lord et al., 2012), measures symptoms in a specific, diagnostic situation where an individual interacts with an adult assessor. The Autism Diagnostic Interview-Revised (ADI-R) (Lord et al., 1994) measures symptoms through a structured parent interview administered by an assessor. The Social Responsiveness Scale (SRS) measures symptoms with a relatively short parent questionnaire. Many studies evaluating autism symptoms use one of these measures, often implicitly assuming that they measure the same construct. Recent reports, however, have shown modest correlations across their scores (Putnam et al., 2024; Ratto et al., 2018).

Objectives: To assess the agreement across autism symptom severity levels estimated by four measures listed below in the same children, while also separating severity scores for the social-communication and the restricted and repetitive behavior (RRB) domains. We also perform a factor analysis to determine whether a common factor for autism symptoms can be extracted across measures.

Methods: Seven-hundred and fifteen 2-to-5-year-old autistic children were evaluated from two cohorts: 1) the University of California, Davis MIND Institute Autism Phenome Project cohort, and 2) the Simons Simplex Collection cohort. Children were evaluated using four

measures: ADOS-2 (clinician observation), ADI-R (clinician-administered parent interview), SRS (Constantino, 2002) (parent questionnaire) and Repetitive Behaviors Scale-Revised (RBS-R) (Bodfish et al., 2000), (parent questionnaire). First, we evaluated correlations between pairs of measures to quantify their agreement in estimating symptom severity per child. Second, we conducted a Factor Analysis to evaluate if a common factor for autism symptoms exists across measures. We performed both analyses separately for overall, RRB, and social-communication severity.

Results: The correlations analysis showed that symptom severity levels assessed by measures based on parental interviews and questionnaires (ADI, SRS, and RBS) exhibited medium-to-medium-high associations (0.63>r>0.47) when examining the respective overall, RRB, and social-communication severity scores across measures (Figure 1). In contrast, ADOS scores showed considerably weaker associations with the three other (parent-report based) measures, especially with parent questionnaires (0.26>r>0.04). The factor analysis demonstrated that models with one latent factor that includes all measures showed the best fit to the data, for overall, RRB, and social-communication severity. Factor loadings, however, differed across measures (Table 1). Loadings for the ADI, SRS and RBS-R ranged from medium-to-high while loadings for the ADOS remained low across models. This demonstrated that most of the variance in ADOS scores cannot be explained by a common factor for autism symptoms.

Conclusions: Common measures for autism symptoms can yield different severity levels for the same child. Such gaps could result from methodological differences, i.e., relying on parent report / questionnaires vs clinician observation. Alternatively, they may capture real-world differences in how autism symptoms present (and measure) in various contexts, i.e., an assessment situation vs the home environment. It is essential to understand differences in the evaluation of autism symptoms using various standardized measures and how this impacts research and clinical work.

A3. Psychological Distress in Autistic and Non-Autistic Israeli Children Exposed to War and Terrorism

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Background: Exposure to war and terrorism is linked to psychological distress, impacting both those directly involved and their relatives. Children, who are especially vulnerable due

to their developing cognitive and emotional capacities, may be more gravely affected. However, there is a lack of research on the psychological effects of war and terrorism on autistic children.

Objectives: This study examined the psychological distress experienced by Israeli autistic children compared to non-autistic children following the October 7th, 2023, terrorism attack and subsequent war.

Methods: The study involved 228 parents of children aged 4-11 (134 autistic, 94 non-autistic) who completed online questionnaires regarding (1.) child's exposure to war events and experiences (CEE; e.g., missile attack sirens, injury or death of family members, home damage, evacuation) (2.) child's expose to war-related information (CEI; e.g., TV broadcast, public posters, adults conversations) and (3.) aggravation in their child's anxiety levels since the October 7th attacks (SCAS-A), based on the Spence Children's Anxiety Scale.

Results: Nearly all children (97.4%) were exposed to at least one potentially traumatic war-related event. While non-autistic children had higher CEE rates, CEI rates were similar between groups. Autistic children exhibited greater anxiety aggravation, particularly concerning fears of physical injury, panic attacks, and agoraphobia. Group moderated the association between exposure level and anxiety aggravation for both CEE and CEI.

Conclusions: These findings highlight the unique vulnerability of autistic children during severe traumatic events and emphasize the urgent need for early detection, diagnosis, and specialized treatment of trauma in autistic children in conflict-affected regions.

A4. Joint Contributions of Polygenic Risks for Autism and Schizophrenia to the Expression of Autistic and Psychotic Phenotypes

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Background: Psychotic experiences (PEs) and autistic traits (ATs) represent a complex interplay of genetic and environmental factors, often co-occurring in ways that suggest shared genetic pathways. Advances in genetic research have allowed the use of polygenic risk scores (PRS) to quantify genetic predispositions to complex traits and disorders, including autism and schizophrenia spectrum disorders (ASD and SSD, respectively). PRS

provide a cumulative measure of genetic liability across numerous risk alleles, enabling the exploration of additive and sub-additive genetic effects on related phenotypes. Clarifying these effects is crucial for disentangling the genetic relationship between ASD and SSD, two conditions with distinct, overlapping, and even diametric clinical features.

Objectives: To investigate the extent to which PRS for ASD and SSD independently and interactively influence the manifestation of ATs and positive PEs. By examining both additive and sub-additive effects, we aim to clarify the shared and unique genetic contributions to these phenotypes, potentially revealing novel insights into their etiological underpinnings.

Methods: Genome-wide association study (GWAS)-based PRS for ASD and SSD were estimated for 2320 neurotypical adolescents (M/F = 1138/1177; Mean Age= 13.97, SD = 0.53) from the IMAGEN study. Positive PEs were estimated using the positive subscale of the Community Assessment of Psychic Experiences (CAPE) and ATs using the Social Responsiveness Scale (SRS). The effect of PRS for ASD and SSD on the expression of positive
PEs and ATs were estimated using response surface analysis (RSA) while controlling for IQ, sex, social functioning, and study center.

Results: We observe a significant linear additive effect of the PRS for ASD and SSD on the expression of positive PEs, such that higher PRS for both ASD and SSD were associated with an increased likelihood and intensity of positive psychotic experiences. We also observed and significant linear sub-additive effect of the PRS of ASD and SSD on the expression of ATs,
such that higher levels of positive PEs relative to ATs were associated with a reduced expression of ATs, indicating an interaction where combined genetic risks result in moderated trait expression.

Conclusion: Our findings reveal distinct genetic influences on PEs and ATs, with both additive and sub-additive effects of PRS for ASD and SSD uniquely contributing to these phenotypes. These results underscore the complex interplay between ASD and SSD genetic risks, suggesting that shared and differential genetic pathways shape the manifestation of psychotic and autistic phenotypes. This study provides novel insights into the genetic architecture of these traits and emphasizes the importance of examining both additive and sub-additive effects to understand the etiological nuances of ASD and SSD.

A5. Characteristics of Minimally Verbal Children with Autism Spectrum Disorder Before and After Age Five

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Background: Language impairment is a common feature in children with autism spectrum disorder (ASD) and may be variable and characterized by significant differences- either delayed or atypical language use. Around 25-30% of young children diagnosed with ASD are diagnosed as minimally verbal (MV), presenting with no speech or producing less than 5-20 meaningful words used for specific communication intentions. In the past, >50% of children with autism were thought to remain MV, while more recent studies show that only 20% remain minimally verbal as adults; this evidence stems from research conducted among English-speaking families and has now been examined in other populations. MV ASD subgroup at high risk for permanent language impairment is underrepresented in autism research both in terms of characterization and interventions, likely due to assessment challenges and inconsistency on definitions of MV and nonverbal. Better characterization and prognostic factor mapping will enable more specific, effective interventions that may promote language development.

Goals and Objectives: The goal of this proposal is to characterize factors associated with MV in young children with autism (before age five) and to explore which factors predict whether a child with ASD may remain MV after age five, a condition that is generally considered permanent.

Methods: A retrospective study of data obtained from the National Autism Research Center (NARCI) at Ben Gurion University (BGU). A retrospective analysis examined data from 487 children (382 boys, 104 girls, one unknown) from NARCI. The sample was divided by age (under/over 5 years) and verbal ability (Verbal: ADOS Module 2/3 ; MV: ADOS Module). Comprehensive analyses included socio-demographic variables, cognitive measures, language scores, and autism severity measures. Statistical analyses encompassed logistic regression and Classification and Regression Tree (CART) analysis to identify predictive factors.

Results: The prevalence of MV children decreased substantially from 65.15% under age 5 to 17.5% above age 5. Logistic regression ($\chi 2(5)=60.22$, $p<0.001$) identified significant predictors: maternal education (OR=1.17), maternal age (OR=0.91), socio-economic status (OR=1.71), and birth order (OR=0.80). CART analysis revealed maternal education as the primary predictor, with children of mothers having >13 years of education showing only a

38.5% chance of MV status versus 58.7% for ≤13 years. Among higher-educated mothers, high socioeconomic status dramatically reduced MV likelihood to 6.5%. Cognitive scores differed significantly between verbal and MV groups across age categories (under 5: $t(21)=3.48$, $p=0.002$; over 5: $t(139)=5.60$, $p<0.001$). DSM severity ratings for both social communication and restricted/repetitive behaviors significantly predicted verbal ability, with restricted/repetitive behaviors emerging as the strongest predictor in CART analysis.

Conclusions: This comprehensive study reveals the complex interplay between socioeconomic factors and autism-specific characteristics in determining verbal outcomes. The findings highlight significant disparities in language development based on socioeconomic status and maternal education while also emphasizing the crucial role of autism severity measures. These results suggest the need for targeted early interventions considering both environmental and clinical factors, particularly for families with limited socioeconomic resources. Additionally, the study underscores the urgent need for developing more accurate assessment tools for minimally verbal children with ASD.

A6. Urine Metabolomic Profiling and Machine Learning in ASD Diagnosis: Toward Precision Treatment

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Background: Autism Spectrum Disorder (ASD) diagnosis traditionally relies on behavioral assessments, which can be subjective and lead to delayed identification. Recent advances in metabolomics and machine learning offer promising alternatives for more precise diagnostic approaches.

Objectives: This study aimed to investigate the potential of urine metabolomic profiling combined with machine learning techniques to differentiate between children with ASD and neurotypical controls, exploring both internal and external metabolites as potential diagnostic markers.

Methods: The study analyzed first-morning urine samples from 52 children (32 with ASD, 20 controls), aged 5.04±1.87 and 5.50±1.74 years, respectively. Using LC-MS, 293 polar metabolites were identified and categorized into 188 internal (endogenously produced) and 105 external (exposome-originated) metabolites. We compared the ability of different machines learning classifiers, (i.e. Random Forest, Logistic Regression, Random Tree, and Naïve Bayes), to differentiate between ASD and control groups using 10-fold cross-validation.

Results: When using all 293 metabolites, the Random Forest classifier achieved 85% accuracy and an Area Under the Curve (AUC) of 0.9. In which classification based on 189 internal metabolites seemed to drive the effect with the Random Forest classifier achieving 85% accuracy and an AUC of 0.86. In contrast, external metabolites alone provided lower classification performance, with an accuracy of 71% and AUC of 0.72.

Conclusions: This study demonstrates the potential of urine metabolomic profiling as a complementary diagnostic tool for ASD. The independent performance of internal metabolites suggests that the body's metabolic processing may be more informative than dietary metabolites in distinguishing ASD. The high classification accuracy implies the potential for developing an assistive diagnostic method, though further research is needed to correlate metabolite profiles with specific behavioral characteristics and ASD subtypes.

Session B: Behavior

B1. Sensory avoidance in less and more cognitively able children with autism

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Background: Sensory processing abnormalities are increasingly recognized as one of the core characteristics of Autism Spectrum Disorder (ASD: autism) and have been formally integrated into the diagnostic criteria that appear in the *Diagnostic and Statistical Manual of Mental Disorders*, Fifth Edition (DSM-5; APA, 2013). Research has revealed sensory subtypes within autism, delineating unique clustering of sensory patterns, which provide a framework for understanding the variability in sensory experiences. Two research groups have found sensory subtypes, including a group selectively elevated on hypersensitivity and avoiding (Ausderau et al., 2014; Simpson et al., 2019). A recent educational paper found that the elevated hypersensitive-avoiding group is correlated with better adaptive behaviour, for more cognitively able children with autism only.

Objectives: The objective of this research was to examine the relationship among sensory subgroups and autism symptomatology, behaviour profiles and adaptive behaviour in less and more cognitively able children with autism through cluster analysis of the four patterns of sensory processing according to Dunn' model (1997). Once the clusters were obtained, we focused on the subgroup with elevated avoiding patterns and its association with autism symptomatology, behaviour profiles and adaptive behaviour.

Methods: The study utilized the database of the Azrieli National Autism Center, comprising 1,170 participants with a diagnosis of autism. Those under 3 years of age and over 15 years of age were excluded, resulting in a final sample of 823 participants (614 boys/209 girls) with a mean age of 5.3 years (SD = 2.35). The variables were measured by the Autism Diagnostic Observation Schedule-2 (autism symptomatology), the Aberrant Behavior Checklist (behavior profiles), the Adaptive Behavior Assessment System (adaptive functioning) and the Sensory Profile-2 from which the sensory clusters were calculated. We divided the children, *a priori*, into less cognitively able (<70) and more cognitively able children (85+).

Results: Two groups emerged for the less cognitively able group, roughly comparable to Ausderau's et al., (2014) Mild and Extreme-Mixed groups, however in the more cognitively able
group, three clusters emerged: the same two as in the less able cognitive group, plus an intermediate group, which was characterized by more avoiding behaviors alongside fewer seeking behaviors. A robust correlation with less irritability and better adaptive functioning emerged for this group.

Conclusions: Finding this particular group in more cognitively able children with autism only confirmed the necessity of considering cognitive abilities when forming sensory subgroups. Specifically, there is an intermediate group which is associated with better

adaptive functioning despite being characterized by elevated avoiding pattern in their cluster. Avoiding may be used to support better self-regulation and enhance the ability to engage selectively in meaningful activities, fostering adaptive functioning. It is possible that if parents and teachers of less cognitively able children with autism can shield them from excessive sensory stimuli, it could result in better adaptive functioning for them as well. Further research is required to understand the implications of cognitive abilities in sensory subgroups.

B2. Risk of Injury in Children with Autism Spectrum Disorder With or Without Attention-Deficit/Hyperactivity Disorder - A Retrospective Cohort Study of Pediatric Emergency Department Visits in Israel

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Importance: Injuries are a major cause of morbidity and mortality among children with neurodevelopmental conditions. Identifying at-risk injuries for these children could inform specific actions for parents and caregivers to reduce the risk of these injuries in this vulnerable population.

Objective: To compare the injury risk among children with Autism Spectrum Disorder (ASD), Attention-Deficit/Hyperactivity Disorder (ADHD), co-existing ASD and ADHD (ASD+ADHD), and those with typical development (TD).

Design: An observational, retrospective, population-based cohort study involving 325,412 children born between 2005 and 2009, followed up until the end of 2021.

Setting: The study data were extracted from the database of Clalit Health Service (CHS), which contains comprehensive clinical and sociodemographic data on all members of CHS admitted to the emergency department (ED) in all hospitals in Israel during the study period.

Participants: All pediatric admissions to the ED of children up to 18 years of age (n= 1,072,980 visits) were included in the study . Participants were classified into four groups: ASD, ADHD, ASD+ADHD, and TD.

Main Outcomes and Measures: Negative binomial regression models were used to assess differences in incidence rate ratios (IRRs) of ED visits between the study groups. These models were adjusted for three covariates: year of birth, sector, and socio-economic status. Furthermore, IRRs between the study groups for specific injuries were also assessed. The statistical significance of each IRR was assessed using a 95% confidence interval.

Results: In this cohort, children with ASD, ADHD, or both were significantly more likely to visit an ED than TD children (1.48, 1.45 and 1.29 times more frequently, respectively, compared to the TD control group). However, when conducting a focused analysis of ED visits due to physical injuries, we found that children with ADHD were 1.18 times more susceptible to physical injuries than the TD group, while children with ASD were 0.91 times less susceptible compared to the TD group, and children with ASD+ADHD were 0.96 times less susceptible . An examination of the injury profiles revealed significant differences between the study groups: Children with ASD or comorbid ASD+ADHD were more prone to ingestion and inhalation injuries, while children with ASD alone were less prone to animal-inflicted injuries.

Conclusions and Relevance: Our findings suggest that children with ASD experience fewer injuries, potentially due to increased adult supervision.

B3. Early joint attention abilities measured by the ADOS-2 predict subsequent expressive language abilities in young autistic children

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Background: Most autistic children exhibit early language delays with 25-30% remaining minimally verbal (MV) throughout life. Hence, expressive language is a key area for early intervention that is critical for successful outcome. Previous studies have suggested that autistic children with better social communication and joint attention abilities early in development were more likely to successfully develop expressive language abilities later.

Objectives: To identify early predictors of expressive language development in MV 1-4-year-old autistic children using ADOS-2 and cognitive test variables at diagnosis.

Methods: We analyzed retrospective data from 101 children (83 boys), 13-50 months old at diagnosis (M=27.4, SD=7.20). All children completed two ADOS-2 assessments, one at diagnosis and another at follow up, 12–24 months later. We used the coding system developed by Visser et al., (2017) to create a common 8-point scale across ADOS-2 modules, thereby transforming A1 item scores into scores ranging from 0 (Children use sentences in a largely correct fashion) to 7 (No language production at all). All the selected children in the current study were classified as MV at diagnosis according to this scale. Children were divided into three groups based on their verbal ability at follow-up: MV (scores 6-7), one-word phase (scores 4-5), phrases (scores 2-3) and fluent speech (0-1). Joint attention (JA) was calculated according to the scale developed by Gotham et al. (2007), by summing the following 6 items from the different ADOS-2 modules: Pointing, Gesturing, Showing, Initiation of Joint Attention, Unusual Eye Contact, and Reaction to Joint Attention.

Results: Children who developed expressive language abilities at follow-up (scores of 0-5) had significantly higher ADOS-2 Social Affect (SA) Calibrated Severity Scores (CSS) at diagnosis ($F(2, 98)=5.531$, $p=0.005$). Logistic regression models revealed that both ADOS-2 SA-CSS (Estimated=0.46, SE=0.33, $p=0.007$, OR=2.44, 95% CI [1.33, 4.95]) and JA (Estimate=0.22, SE=0.31, $p=0.013$, OR=2.16, 95% CI [1.22, 4.19]) scores, at diagnosis, were significant predictors of expressive language abilities at follow-up. In contrast, cognitive scores and ADOS-2 Restricted and Repetitive Behaviors (RRB) CSS at diagnosis did not

differ significantly across children who remained MV or developed expressive language. Additionally, when analyzing changes in ADOS-2 SA-CSS, ADOS-2 RRB-CSS, and JA scores over time, only the changes in JA scores showed a significant difference between groups ($F(97, 2) = 9.65$, $p = 0.001$).

Conclusions: In line with previous studies, we demonstrate that early social abilities and primarily joint attention abilities are associated with better development of expressive language in preschool autistic children (i.e., “the rich get richer”). This demonstrates that JA scores extracted from the ADOS-2 represent a meaningful prognostic measure for estimating outcome, as proposed previously with more elaborate methods for assessing JA. Further studies examining these predictors in different intervention settings are highly warranted.

B4. Working Together: A Longitudinal Study Examining Differences in Adaptive Behavior and Social Communication Between Autistic and Neurotypical Employees

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Purpose: Adaptive behavior and social communication skills are essential for participation and obtaining employment. The present study compared these skills between cognitively able autistic vocational soldiers and their neurotypical counterparts, tracking their progress over two years of military service.

Methods: The study included 46 autistic and 41 neurotypical participants matched for age, sex and military profession. The autistic soldiers participated in a supportive program named "Roim Rachok" Program ('Looking Ahead' in Hebrew). Evaluations at T1 (upon entering the military unit), T2 (after one year in military service) and T3 (after two years of military service) included adaptive behavior (Adaptive Behavior Assessment Scale 2nd Edition [ABAS-II]) and communication skills (Faux Pas; Empathy Quotient [EQ] and Conversation task based on Yale in vivo Pragmatic Protocol [YiPP]).

Results: Emotional empathy predicted ABAS-II conceptual, social and practical adaptive behavior for autistics but not for neurotypicals. Social adaptive behavior was also predicted

by cognitive empathy among autistics. Autistic and neurotypical participants exhibited stability in adaptive and social functioning over two years of service. Consistent significant differences in adaptive behavior and social communication were found between the groups except in interpreting awkward social situations.

Conclusion: The study underscores the distinct differences between the two populations required to collaborate in the workforce and suggests strategies to bridge gaps in communication and adaptive behavior. Additionally, with adequate support, the majority of autistic young adults with cognitive abilities can maintain employment for at least two years despite disparities in crucial domains.

Implications of the study findings are discussed.

B5. Cognitive Abilities of Autistic Adults and Intellectual Disability in Relation to Age: Accelerated Development, Stable Progression, or Continued Age-Related Trajectories?

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Background: Research on long-term cognitive trajectories in autistic adults with intellectual disability (ID) remains limited, and their specific aging patterns are not well understood. This cross-sectional study examines cognitive changes from young to late adulthood, drawing on three neurocognitive disorder models: Accelerated Aging, Stable, and Continuous Trajectories. While cognitive stability is typical in the general population until decline begins at ages 50-60, individuals with ID tend to show continuous improvement in both verbal and non-verbal abilities until middle age (40-50), followed by stability, in line with the Compensation Age Theory. This study explores whether similar or distinct patterns emerge in autistic adults with ID.

Objectives: To assess age-related trajectories of nonverbal cognitive ability, receptive and expressive language, and adaptive behavior in three age cohorts of autistic adults with ID, in relation to the above three models of cognitive change with age.

Methods: Seventy-eight participants (24 females), aged 25.9 to 63.3 years (M=1.95/SD=9.91), previously diagnosed with autism based on medical records, and currently residing and working in sheltered environments for autistic adults with high

support needs, were enrolled in the study. All participants were assessed for adaptive skills using the Vineland Adaptive Behavior Scales (VABS) and for autism trait intensity with the Social Responsiveness Scale. They were divided into three age groups (25-35, 35-45, and 45+), which were equivalent in autism trait intensity. Nonverbal reasoning ability was evaluated using the Test of Nonverbal Intelligence (TONI), while verbal intelligence was assessed through the SHEMESH naming skills test and the Peabody Picture Vocabulary Test for language comprehension.

Results: Since the distribution of test scores deviated significantly from normality, non-parametric analyses were conducted. Kruskal-Wallis tests revealed significant differences between age groups for TONI ($p < .001$), PPVT ($p = .045$), and VABS ($p = .023$) scores, but not for SHEMESH scores ($p = .074$). Additional Mann-Whitney tests examining differences between the two groups indicated that TONI scores were significantly higher in the 35-45 cohort compared to the 25-35 cohort ($p < .001$) and remained stable in the 45+ cohort ($p = .498$). The 45+ cohort scored significantly lower on the PPVT compared to the 35-45 cohort ($p = .016$). Although SHEMESH scores did not differ overall, significant declines were observed in the 45+ cohort compared to the 35-45 cohort ($p =.036$). VABS scores also declined significantly in the 45+ cohort compared to the 35-45 cohort ($p =.009$).

Conclusions: The cognitive profile of participants revealed divergent age-related patterns: verbal test scores declined in late adulthood, while nonverbal test scores improved in young adulthood and remained stable in late adulthood. These findings suggest a decline in verbal abilities and an increase followed by stability in nonverbal abilities in late adulthood, consistent with the Continuous Trajectory Model for verbal decline and the Compensation Age Theory for nonverbal improvement. However, since only the TONI assessed nonverbal ability, these findings should be interpreted with caution. The overall findings suggest distinct cognitive aging trajectories, which could be crucial for developing targeted interventions aimed at enhancing functioning in older adults.

B6. Quality of Life and Mental Health in Families of Children with Autism Spectrum Disorder during Wartime

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Background: Children with autism spectrum disorder (ASD) tend to be particularly vulnerable to disasters, including war. Exposure to war often results in a pervasive loss of personal and social resources. Existing research has primarily focused on individual resource loss following war, overlooking the unique challenges and broader impacts faced by families caring for children with ASD.

Objectives: To (i) assess the family quality of life (FQoL) and mental health of primary caregivers (parents) of children with ASD during wartime; (ii) examine which child, parent, family, and environmental characteristics (including war-related stressors) are associated with FQoL attainment during wartime.

Methods: 236 parents (90% mothers) of children with ASD (mean age=8.8±4.4) completed questionnaires regarding their FQoL attainment (adapted from the FQOL survey; Brown et al., 2006) and Mental health 5-inventory (Veit & Ware, 1983) - related to the periods before and since the outbreak of war.

Results: A significant decrease was evident in all nine FQoL attainment domains during wartime, with effect sizes ranging from 1.32 in the leisure domain to 0.13 in the domain of support from others. Similarly, there was a significant decrease in parental mental health (Cohen's d = 1.73). Of the child characteristics examined, level of communication was positively associated with FQoL attainment. None of the parent characteristics were associated with FQoL attainment. Family income was positively associated with FQoL attainment. Finally, of the environmental stressors examined, proximity to the warzone and evacuation from home were associated with decreased FQoL attainment, while degree to which the educational framework operated 'as usual' was associated with increased FQoL attainment. Additionally, there was a positive association between wartime parental mental health and FQOL attainment. A multivariate model suggested that significant predictors of wartime FQoL attainment include higher family income, operation of educational frameworks and better parental mental health. The operation or lack of operation of educational frameworks contributed directly and indirectly to FQoL attainment during wartime, so that when the educational framework operated as usual, parental mental health was higher, which, in turn, was associated with higher FQoL attainment.

Conclusions: Caregivers of children with ASD face significant adverse effects on their mental health and FQoL during wartime. Families with limited resources are particularly vulnerable during mass trauma, such as war. This study shows that restricting educational frameworks - crucial but often inaccessible for children with disabilities - undermines family resources and exacerbates preexisting vulnerabilities. Restricted educational services directly diminish family resources, and indirectly affect FQoL by intensifying caregivers' mental health challenges. These findings underscore the compounded impact of war and parental mental health on family functioning.

Session c: Mechanism

C1. *Shank3* mutation impairs glutamate signaling and myelination in autism spectrum disorder models

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Background: Autism spectrum disorder (ASD) is characterized by social and neurocognitive impairments, with *SHANK3* mutations being a significant genetic contributor. While SHANK3's role in neurons has been extensively studied, its function in oligodendrocytes (OLs) and myelination remains poorly understood. Understanding this gap is critical for elucidating ASD pathophysiology.

Objectives: This study aimed to investigate the impact of *SHANK3* mutations on OL function, myelination processes, and their broader physiological and behavioral consequences in ASD.

Methods: We utilized the InsG3680 mouse model carrying a human-relevant *SHANK3* mutation and examined primary oligodendrocyte precursor cells (OPCs), mature OLs, and myelin *in vitro* and *in vivo*. Complementary studies were conducted on iPSC-derived OPCs from an individual with the same mutation. Restoration experiments were performed by reintroducing *SHANK3* to mutant OPCs. Data were analyzed using molecular, cellular, and electrophysiological approaches, supported by advanced imaging and statistical tests.

Results: Mutant OPCs exhibited reduced Shank3 expression, abnormal calcium signaling, and impaired differentiation. InsG3680 mice displayed significant myelin deficits, including reduced expression of myelination-related genes (*Mbp, Plp1*) and proteins, abnormal myelin ultrastructure, and decreased axonal conductivity. Restoration of SHANK3 expression in mutant OPCs significantly improved postsynaptic protein levels and cellular function. Similar deficits were observed in patient-derived iPSC OPCs.

Conclusions: *SHANK3* mutations disrupt OL function and myelination, contributing to ASD pathology. Restoration of SHANK3 offers a promising therapeutic avenue for addressing myelin-related deficits in ASD.

C2. A phenotype-based approach for prioritizing ASD genetic variants from whole-exome sequencing

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Background: Autism Spectrum Disorder (ASD) is a genetically and phenotypically heterogeneous condition, making the identification of causal genetic variants challenging. Current genetic diagnosis of ASD is mainly based on the American College of Medical Genetics (ACMG) guidelines and has a relatively low diagnostic yield (3%–28%). Thus, new approaches for detecting genetic variants contributing to ASD susceptibility are needed.

Objective: To develop a phenotype-driven approach for the identification and prioritization of ASD genetic variants.

Methods: We obtained comprehensive phenotypic and genetic (whole-exome sequencing [WES]) data from 102 children registered in the database of the Azrieli National Center for Autism and Neurodevelopment Research (ANCAN). We used the Human Phenotype Ontology (HPO) nomenclature to assign HPO terms to all phenotypes and to group them into broad phenotype categories. Then, we used these phenotype categories to characterize each participant with an Observed Phenotype Vector (OPV), and each gene in the HPO database with an Expected Phenotype Vector (EPV). Finally, we used our in-house bioinformatics pipeline to identify gene-disrupting variants (GDVs) in our sample and then assessed the concordance between each such variant's EPV and the corresponding OPV of its carrier.

Results: Overall, 228 HPO terms grouped into 40 broad phenotype categories were identified in our sample. Notably, high-confidence ASD genes (according to the SFARI gene database) had significantly higher counts of expected phenotypes compared to non-ASD genes (29.8 ± 16.57 vs. 12.05 ± 11.56, p = 1.5e-45), suggesting an association of the 40 broad phenotype categories with ASD genes. Of the 186 GDVs detected in the WES of our sample, 18 demonstrated a significant EPV-OPV concordance ($p < 0.05$). Of these, 3 variants were distributed in known ASD genes while the other variants resided in 15 potentially novel ASD genes.

Conclusion: Our findings underscore the value of a phenotype-driven approach in detecting potentially novel genetic variants associated with ASD. Future explorations are needed to confirm the clinical contribution of these novel variants to ASD susceptibility.

C3. Protective inherited and *de novo* pathological mutations in ADNP: essential for sex-dependent hippocampal gene expression regulating neurogenesis and cognition

Illana Gozes[1], Guy Shapira[1,2], Gidon Karmon[1], Gal Hacohen-Kleiman[1], Maram Ganaiem[1], Shula Shazman[3], Paschalis Theotokis[4], Nikolaos Grigoriadis[4], Noam Shomron[1,2], Elizer Giladi[1] and Joseph Levine[1,5]

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Activity-dependent neuroprotective protein (ADNP) is essential for neurodevelopment and *de novo* mutations in ADNP cause the autistic ADNP syndrome. Performing longitudinal assessments (Vinland questionnaire) on a cohort of 15 ADNP syndrome individuals indicated developmental delays/arrests, coupled with potential spurts of development at early ages. Severe outcomes correlated with the remaining heterozygous mutated ADNP length with STOP truncating mutations affecting communicative skills and driving premature aging with Alzheimer's disease like - tauopathy (Levine et al., J Mol Neurosci 2024 Jan 29;74(1):15). Results further implied a more severe male phenotype, and two phenotypes corresponding to haploinsufficiency and gain of toxic function. In contrast, a woman with inherited mutation, p. ADNP_Glu931Glyfs*12 (VB), showed above average Vineland performance. Bioinformatics/in silico protein modeling revealed that while ADNP contains four 14-3-3

protein interaction sites (instrumental for ADNP nuclear/cytoplasmic shuttling), ADNP_Glu931Glyfs*12 contains an additional fifth 14-3-3 interaction site, implicating stronger associations. Furthermore, the endogenous NAPVSIPQ (NAP, investigational drug, davunetide) site was involved in the ADNP and ADNP_Glu931Glyfs*12-14-3-3 interactions. These structural results suggest an explanation for the Vineland scores. HB, the eight-year-old VB's son, while carrying the same apparently protective inherited ADNP mutation, also presents a heterozygous pathogenic *de novo* mutation ADNP, p.Arg730Thrfs*5. However, in comparison to carriers of a similar mutation, HB exhibited overall better Vineland scores, implicating extended protective measure of the inherited ADNP_Glu931Glyfs*12 mutation (Gozes et al., Genom Psychiatry 2025; 1(2). Given the impact of ADNP on cognition, intimately involved with neurogenesis, we investigated mechanisms in mouse models of the ADNP syndrome. Using bromodeoxyuridine (BrdU) as a marker of neurogenesis, we identified two-fold higher labeling in the hippocampal sub-ventricular zone of ADNP-intact male versus female mice. *Adnp* haplo-insufficient (*Adnp*$^{+/-}$) mice or mice CRSIPR/Cas9-edited to present the most prevalent neurodevelopmental ADNP syndrome mutation, p.Tyr718* (Tyr) showed dramatic reductions in male BrdU incorporation, resulting in mutated females presenting higher labeling than males. Treatment with NAP (the investigational drug davunetide) compensated for the male reduction of BrdU labeling. Hippocampal RNAseq revealed male-specific Tyr down-regulation of endoplasmic reticulum unfolded protein response genes critical for sex-dependent organogenesis. Newly discovered mitochondrial accessibility of ADNP was inhibited by the Tyr718* mutation further revealing female-specific Tyr downregulation of *mitochondrialATP6*. NAP moderated much of the differential expression caused by p.Tyr718* (Shapira, Karmon et al. Molecular Psychiatry, December, 2024). In this respect, we have recently discovered that davunetide sex-dependently boosts memory in prodromal Alzheimer's disease (Gozes et al., Transl Psychiatry. 2024;14(1):412), now planned for development in the ADNP syndrome (Exonavis Therapeutics Ltd).

C4. Splicing Regulation by Wbp4 is Critical for Neurodevelopment and Autism Spectrum Disorder

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Background: Dysregulation of pre-mRNA splicing is increasingly recognized as a major contributor to autism spectrum disorder (ASD) and related neurodevelopmental conditions. The spliceosome, a dynamic RNA-protein complex, ensures the precise removal of introns and the joining of exons during mRNA processing, a critical step for gene expression. WBP4, a core spliceosome component, has emerged as a key regulator of neural development.

Objectives: To investigate the role of WBP4 in neurodevelopment and its contribution to ASD pathogenesis by integrating human and mouse studies.

Methods: We combined analyses from fibroblasts derived from WBP4-/- patients diagnosed with ASD, WBP4-/- patient-derived induced pluripotent stem cells (iPSCs) differentiated into neural progenitor cells (NPCs), and findings from our Wbp4 knockout (Wbp4-/-) mouse model.

Results: Our studies in humans and animal models have implicated WBP4 mutations in brain abnormalities and ASD, linking spliceosomal dysfunction to disrupted neuronal development and synaptic regulation. Human studies revealed that WBP4 mutations cause splicing dysregulation in genes critical for neuronal differentiation and synaptic function, many of which are linked to ASD. Aberrant splicing patterns were validated in NPCs derived from patient iPSCs, demonstrating consistent mis-splicing of ASD-associated genes. In parallel, Wbp4-/- mice exhibited embryonic lethality, as well as structural anomalies, such as cortical thinning. Through deep RNA sequencing and splicing analysis in the E15.5 forebrain, significant splicing deviations were found, including microexon retention. Importantly, shared splicing targets were identified across species, emphasizing WBP4's conserved role in regulating ASD-relevant pathways.

Conclusions: This study highlights WBP4's critical role in splicing regulation and its contribution to ASD pathogenesis. By integrating patient-derived and mouse model data, we have established a robust link between spliceosome dysfunction and ASD, offering new avenues for understanding and potentially targeting the molecular basis of this condition.

C5. The Role of Thioredoxin System in Autism Spectrum Disorder

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Autism spectrum disorders (ASDs) are neurodevelopmental disorders defined solely by behavioral diagnosis. Despite extensive research, the biochemical mechanisms underlying ASD remain unknown. Evidence suggests that ASD pathology may be linked to oxidative and nitrosative stress, accompanied by a compromised antioxidant system. Reduced antioxidant status, elevated nitric oxide (NO) levels, and abnormal S-nitrosylation (SNO) were obsereved in individuals with autism suggesting potential abnormalities in cellular antioxidant metabolism. We hypothesize that dysregulation of the Thioredoxin (Trx) system contributes to the redox imbalance observed in ASD.

To test this, we utilized the *Shank3*Δ4-22 Knockout (KO) mouse model, an established ASD model, and found significant reductions in antioxidant proteins such as Trx1, Trx2, and Thioredoxin reductase 1 (TrxR1), along with elevated oxidative and nitrosative stress markers including 3-nitrotyrosine (3-Ntyr), Peroxiredoxin 1 (Prdx1), and Peroxiredoxin 2 (Prdx2) in the cortex of KO mice compared to wildtype (WT) mice.

To investigate the potential role of Trx in ASD, we inhibited it in WT mice using PX-12, an irreversible Trx1 inhibitor. PX-12-treated WT mice exhibited ASD-like behaviors, including impaired social interaction, memory, and cognitive abilities, similar to those observed in *Shank3* KO mice. Molecular analysis revealed elevated levels of 3-nitrotyrosine (3-Ntyr), Prdx1, and Prdx2, indicating increased oxidative and nitrosative stress. Additionally, we observed altered expression of several synaptic proteins, including PSD95, synaptophysin (SYP), and Homer, which are involved in synaptic signaling and plasticity. Changes were also noted in key excitatory/inhibitory (E/I) markers, such as GAD1, which is involved in GABA synthesis, and VGAT, responsible for GABA transport, as well as NR1, a subunit of the NMDA receptor. These alterations in synaptic protein expression suggest potential disruptions in synaptic function and E/I balance, which may contribute to ASD pathology.

These results suggest that deficiencies in the Trx system may play a pivotal role in ASD pathology. Our preliminary findings highlight the potential involvement of antioxidant deficiencies and increased oxidative and nitrosative stress in autism, offering a foundation for future research into the underlying mechanisms. Further studies are required to decipher the specific processes involved.

C6. Distinct protein expression in umbilical cord blood of individuals with Autism Spectrum Disorder

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Background: Autism Spectrum Disorder (ASD) is a complex neurodevelopmental condition with high heritability. Genetic factors are associated with the autistic phenotype in 30–40% of children diagnosed with ASD. Despite substantial advances in genetic research, the precise cause of ASD remains unclear, suggesting that environmental factors may also play a crucial role. Stressors such as ischemia, maternal immune activation (MIA), and toxins have been linked to the development of ASD, either through direct effects on the brain or by inducing mitochondrial dysfunction and endoplasmic reticulum (ER) stress. These processes, in turn, are associated with perturbations in neuronal differentiation, potentially disrupting synaptic protein function and impairing neural circuit formation. Extracellular vesicles (EVs) are membrane-surrounded nanovesicles routinely excreted by cells, containing proteins, lipids, nucleic acids, and metabolites, and play a role in cell-to-cell communication. EVs mainly originate from the Golgi system, ER, or, to a lesser extent, direct exocytosis from cellular or mitochondrial membranes. The content of EVs extracted from plasma reflects physiological processes occurring in body tissues, including the brain. Thus, disrupted processes, in the brain, characteristic of ASD may be evident in their protein profiles.

Objectives: The aim of this study was to investigate the protein composition in children with ASD at birth and compare it to that of neurotypical (NT) children. We hypothesized that the protein profile in idiopathic ASD would reveal differences associated with MIA, mitochondrial dysfunction, and ER stress.

Methods: The study was conducted on 30 children with idiopathic ASD and 30 NT children. EVs were extracted from plasma collected from their cord blood, and mass spectrometry-based proteomic analysis was used to identify the protein content. Only proteins found in more than 21 children in each group were included in the analysis. Statistical analysis was performed using Python statistical packages.

Results: Mass spectrometry identified 2,924 proteins, with 565 proteins showing differential mean expression levels between the groups. A striking finding was the exceptionally lower variance in protein expression within the ASD group. STRING analysis classified the differing proteins into three major clusters: mitochondrial (aerobic respiration, ATP synthesis, and uncoupling proteins), ER stress, and neutrophil secretory proteins. Cytoscape analysis indicated that a substantial portion of the proteins (140/565) potentially originated from the brain. Based on the Human Protein Atlas, 13 proteins representing each cluster were predominantly expressed in the brain. Using machine learning algorithms, we identified 11 significant proteins capable of differentiating samples originating from ASD. These proteins, along with the most dominant brain proteins, are associated with mitochondrial and ER stress.

Conclusions: The findings suggest that mitochondrial dysfunction and ER stress are present in children with ASD at birth, processes that are associated with abnormal brain development, specifically synaptogenesis and myelination. Post-mortem studies of children diagnosed with ASD have found similar pathophysiological patterns. The distinct protein profile of children diagnosed with ASD and the homogeneity within the group raise the hypothesis that mitochondrial dysfunction and ER stress represent a common and potentially necessary pathway leading to abnormal brain microstructure and an increased susceptibility to developing ASD.

Session D: Treatment

D1. Examining the Effect of Parental Involvement on Child and Parent Outcomes in the PEERS for Preschoolers (P4P) Social Skills Intervention: A Randomized Controlled Trial

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Background: Research-supported social-skills training groups involving parents are considered the most effective treatment mode for autistic children (DeRosier et al., 2011). These interventions often rely on parental involvement as a key component, recognizing parents as facilitators of social learning opportunities and of the maintenance and

generalization of treatment gains (Siller et al., 2018). Parents also appear to benefit from participating in these interventions (Solomon et al. 2008). The Program for the Education and Enrichment of Relational Skills for Preschoolers (PEERS for Preschoolers; P4P, Laugeson et al., 2024) is an evidence-based, parent-assisted social-skills training program for young autistic children. In P4P, parents attend parallel sessions to their children, learning strategies to support skill practice and facilitate peer-interactions. Previous studies have demonstrated concurrent improvements in social and caregiving skills (Factor et al., 2022), which were maintained at follow-up (Antezana et al., 2022). However, these studies have not directly examined the role of parental involvement in intervention outcomes through a randomized controlled trial, nor the generalization of gains to other social settings.

Objectives: This study conducted a randomized controlled trial comparing the effects of the P4P program to those of a P4P program with minimal parent involvement (P4P-MPI) on intervention-related gains in child social-skills and generalization to school settings.

Methods: Sixty-nine participants (9 females) aged 4-7 (M=5.29, SD=0.98), diagnosed with ASD without intellectual disability, were randomly assigned to the standard P4P intervention (*n*=34) or the P4P-MPI (*n*=35). In the P4P-MPI condition, parents received handouts summarizing didactic lessons instead of attending parents group. Each intervention group included up to 10 children. Conditions were comparable in age, sex, cognitive abilities, and ADOS-2 scores. Participants were evaluated pre- and post-intervention using parent and teacher questionnaires: Social Skills Improvement System (SSIS; Gresham & Elliott, 2008) and Social Responsiveness Scale, 2nd ed. (SRS-2; Constantino & Gruber, 2012). Parents also filled out the Quality of Play Questionnaire (QPQ; Frankel & Mintz, 2011) and the Parenting Stress Index (PSI; Abidin, 2006).

Results: Parent reports indicated significant improvements in social-skills, self-control, and empathy (SSIS subscales) and reduced ASD symptoms (SSIS Autism-Spectrum subscale) only in the P4P condition. Additionally, only children in the P4P condition showed a marginally significant increase in play-date invitations (QPQ). Notably, both groups exhibited elevated parental stress across all three PSI subscales (Parental Distress, Difficult Child, and Parent-Child Dysfunctional Interaction), with a statistically significant increase observed only in the P4P-MPI condition.

Teacher reports presented a complex picture. While significant time effects were observed for all SSIS subscales, improvement patterns differed between conditions. The P4P condition showed significant improvements in communication, responsibility, and engagement, while the P4P-MPI condition improved significantly in empathy and self-control. Moreover, teachers reported significant improvements in SRS-2 total score and Social Communication and Interaction, Social Awareness, and Social Cognition subscales

only for the P4P condition. For the P4P-MPI condition, teacher reports indicated significant improvement in Social Communication and Restricted Interests and Repetitive Behavior subscales .

Conclusions: Results highlight the importance of parental involvement in social-skills interventions for autistic children and demonstrate improvement in various social abilities in young autistic children. Results indicate that participation in social-skills interventions increases parental stress. However, parental involvement appears to moderate this relationship. Furthermore, although effects differ between home and school settings, parental involvement appears to enhance the generalization of some learned skills to school settings. Finally, these results offer support for the cross-cultural effectiveness of P4P and provide the first evidence of its efficacy in a randomized controlled trial.

D2. Depression and Suicide Risk Among Autistic Adults

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Background: Autistic adults are at disproportionate risk for experiencing depression and suicidal thoughts and behaviors (STB) compared to the general population. Our talk will present two studies that explore the unique risk factors and potential mechanisms for depression and suicidality among autistic people. The first study examines the associations between social camouflaging of autistic traits and autistic burnout, as well as the interplay between them in predicting depression. The second study explores the rates of STB during lifetime and the past year, the disclosure of STB among autistic adults, and the potential role of autistic burnout as a risk factor for STB.
Method: The study was conducted according to participatory research principles, involving community experts throughout at every stage as part of long-running research group that brings together autistic and non-autistic researchers, clinicians, educators, social activists, family members. The studies used self-report questionnaires to measure camouflage (Camouflaging Autistic Traits Questionnaire - CAT-Q), depression (Patient Health Questionnaire 9 - PHQ-9), and burnout-exhaustion (an adapted version of the Parental Burnout Assessment - PBA). Study 1 and 2 included 92 and 144 autistic adults living in Israel, respectively.

Results: Study 1 found social camouflaging and autistic burnout positively correlated with depression, and autistic burnout partially mediated the association between camouflaging and depression (C'=1.39, CI: 0.16-3.38). Study 2 indicated higher rates of STB among participants. Burnout-exhaustion was found to be associated with STB, and it doubled the risk for suicidal ideation during the past year (OR = 2.09).
Conclusion:
Unique risk factors, such as social camouflaging of autistic traits and autistic burnout, seem to play a significant role in depression and suicide risk among autistic adults. Thus, it is important to evaluate them as part of the psycho-social suicide risk assessment, while also including relevant coping strategies as part of prevention efforts.

D3. Randomized controlled trial (RCT): The effectiveness of OT-ParentShip on parental resilience, self-determination and the functioning of autistic adolescents

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Parents of autistic adolescents are at risk for low parental competence and decreased sense of autonomy, facing challenges in parent-child relationships. *OT (Occupational Therapy(-ParentShip* an intervention program for these parents, employs a comprehensive multidimensional approach to address various factors affecting autistic adolescent functioning. The study aims to assess the effectiveness of *OT-ParentShip* in promoting parental resilience and enhancing adolescent participation.

Two group, randomized controlled trial. Thirty-nine participants were recruited, 21 were randomly assigned to *OT-ParentShip* intervention (research group) and 18 to an online psycho-educational intervention (control group). Results were analyzed before intervention (T0), immediately after (T1), and three months post intervention (T2), measuring perception of performance, parental resilience indicators and self-determination aspects (need satisfaction).

Significant improvement was found in performance and satisfaction at daily functioning from T0 to T1 for parents and adolescents in both groups, and a significant timeXgroup interaction effect was found indicating a greater improvement in the research group. The research group exhibited a significant improvement in parental resilience, in contrast to the control group where no significant change was observed. Additionally, a significant timeXgroup interaction effect was detected. The research group exhibited significant improvement in need satisfaction domains (autonomy, competence, relatedness) from T0 to T1 compared to the control group, along with a timeXgroup interaction effect in the competence index. Results were maintained three months post intervention (T2) in the research group.

Results validate *OT-ParentShip* intervention's effectiveness, demonstrating enhancement in parent and adolescent attainment of functional goals, improved parental resilience, and increased parental self-determination.

D4. Safety and effectiveness of risperidone and methylphenidate in children with autism spectrum disorder

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Background and objectives: Psychotropic drugs are commonly used to ameliorate co-occurring symptoms among children and adolescents with Autism Spectrum Disorder (ASD). However, their effectiveness and associated adverse events are highly variable in this population. In this study, we focused on two commonly prescribed drugs, risperidone and methylphenidate, and aimed to identify clinical and behavioral characteristics associated with their prescription, effectiveness and adverse effects in children with ASD.

Methods: We conducted a retrospective cohort study of 354 children with ASD, who were born on and after 01/2014, and were diagnosed and treated at the Preschool Psychiatry Unit at Soroka University Medical Center (SUMC). Medical information on these children was retrieved manually from physician's notes in the SUMC computerized medical charts. Additional information on sociodemographic, behavioral and clinical characteristics was obtained from the Azrieli National Center for Autism and Neurodevelopment Research (ANCAN) database. The effectiveness of psychotropic therapy was determined by documentation of partial or complete response in the child's medical chart. Adverse events

were defined as one or more reports of an adverse event attributed to pharmacological therapy. We used standard univariate statistics to assess the association between these children's characteristics and the utilization, effectiveness and safety of the psychotropic drugs in this sample.

Results: A total of 53 (15%) children were prescribed risperidone and 49 children (14%) had a prescription for methylphenidate.

Children with risperidone prescription, compared to those without prescription, were characterized by higher ASD severity (73% vs. 38% and 61% vs. 31% required substantial support according to DSM-5 A&B criteria respectively; p<0.001), lower IQ (57.0±11 vs. 75.5±20, p<0.001), worse sleep habits (mean CSHQ score 53.8±12 vs. 48.3±10, p=0.02), poorer language skills (mean PLS-4 score 62.3±22 vs. 72.3±21, p=0.026) and deficits in adaptive behavior (mean ABAS-GAC score 56.3±15 vs. 66.2±18, p=0.029). In addition, prescription of risperidone was associated with attention-deficit/hyperactivity disorder (ADHD) (15% vs. 4.3%, p=0.006) and intellectual disability (81% vs. 40%, p<0.001) co-occurrence. Furthermore, language delay was more prevalent among children who did not respond to risperidone treatment (47% vs. 14%, p=0.033), while children with reported adverse events had younger age at ASD diagnosis (37.6±15 vs. 50.3±21 months, p=0.046) and lower IQ scores (54.4±10 vs. 65.4±15, p=0.05).

Children with methylphenidate prescription, compared to those without prescription, had higher prevalence of ADHD co-occurrence (29% vs. 2.3%, p=0.03). The proportion of Bedouin children differed significantly between those prescribed with methylphenidate and those who were not (10% vs. 25%, p=0.03). In addition, methylphenidate ineffectiveness was associated with younger age at ASD diagnosis (39.7±15 vs 53.5±16 months, p=0.027).

Conclusion: These preliminary results highlight a range of clinical characteristics associated with the prescription, effectiveness and adverse effects of risperidone and methylphenidate. Further confirmation of these findings in larger prospective studies will help guide physicians on psychotropic therapy prescriptions in children with ASD.

D5. Family Accommodation as a Mechanism for RRB Expression in Autism: Associations with Child and Parent Characteristics

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Background: Repetitive and restrictive behaviors (RRBs) are underrepresented in research and intervention practices, despite their centrality to autism. Family accommodation (FA)—modifications caregivers make to reduce distress associated with a child's psychological or developmental conditions—has emerged as a potential mechanism for understanding the persistence and expression of RRBs. FA is associated with increased RRB severity, lower adaptive functioning, and elevated caregiver burden (e.g., Feldman et al., 2019; Matz Vaisman & Koller, under review). Additionally, RRB expression has been linked to emotion regulation (ER), particularly in the context of self-injurious behaviors and other maladaptive coping mechanisms (Martinez-Gonzalez et al., 2022). Understanding FA's role in shaping both RRBs and ER, and expanding the focus of this work to include teacher accommodation, can provide critical insights into how caregiver behaviors influence child developmental trajectories.

Objectives: This study investigates FA as a mechanism for understanding RRB expression in young autistic children, examining its associations with child ER, adaptive functioning, and caregiver characteristics. Additionally, we explore the longitudinal stability and variability of FA to elucidate its impact over time.

Methods: Participants included 133 children (94 males) age 2–4 years, with confirmed autism diagnosis. Gold-standard assessments measured development (Mullen; WPPSI), autism symptomatology (ADOS-2; RBS-R), and adaptive functioning (ABAS). Families completed questionnaires on RRBs, FA, and ER. Follow-up data collection took place 6 and 12 months after the initial diagnosis.

Results: At time of diagnosis over 75% of parents and teachers reported daily or weekly FA. Maternal FA showed a robust positive association with RRB severity ($r(85) = .487$, $p < .001$) and a negative association with adaptive functioning ($r(87) = -.253$, $p < .05$). Paternal FA also positively associated with RRB severity ($r(76) = .313$, $p < .01$), while maternal and paternal FA were interrelated ($r(77) = .369$, $p < .001$). FA correlated significantly with child negative affect ($r(82) = .41–.50$) and surgency ($r(82) = .24–.28$). Maternal FA was positively correlated with maternal expressive suppression ($r(43) = .37$, $p < .007$), suggesting that parental ER strategies may reinforce accommodation behaviors. Longitudinally, FA frequencies decreased slightly, but average accommodation scores increased, with correlations between maternal and paternal FA persisting ($r(47) = .572$, $p < .01$).

Conclusions: These findings position FA as a critical mechanism for understanding the expression and variability of RRBs in autistic children. FA reflects a dynamic interaction between caregiver behaviors and child characteristics, associating with adaptive functioning and ER. Longitudinal trends underscore the need for nuanced analyses of caregiver-specific accommodations and their impact on RRB trajectories. Interventions

that address FA as a modifiable mechanism may enhance adaptive functioning and foster developmental resilience, particularly when targeting maladaptive RRBs.

D6. Comparison of perceptions of autism and neurodiversity between autistic individuals their parents and child psychiatrists: A qualitative study

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Background: In recent years, the neurodiversity movement has gained popularity among autistic persons, advocating for a paradigm shift in how autism and other neurodevelopmental conditions are perceived. This approach frames autism as a natural neurological variation rather than a pathological condition, emphasizing that the challenges faced by autistic individuals often stem from societal expectations and stigma rather than intrinsic deficits. This change in the perception of autism among autistic persons could increase the gap in perception of autism between autistic persons, their parents and clinicians, and may lead to different expectations from treatment.

Objectives: To understand and compare perceptions on autism, neurodiversity, and treatment objectives, between autistic adolescents, their parents, and child and adolescent psychiatrists.

Methods: A total of 36 participants (12 from each group) are collected from two adolescent outpatient clinics were interviewed, with interviews conducted separately but following a uniform structure. The researchers conducting the interviewers and coding consisted of autistic and nonautistic researchers. Half of the interviews are conducted by a child psychiatrist, and the other half by an autistic researcher. This approach ensures a genuinely diverse and inclusive discussion, fostering a richer exploration and analysis of the topics.

Results and conclusions: We will present preliminary findings, using qualitative thematic analysis. Four main themes emerged: (1) the influence of autism diagnosis on the autistic

adolescent and their parents, (2) perspectives on neurodiversity, (3) perspectives on autism itself, and (4) treatment objectives.

Psychiatrists emphasized the importance of tailored interventions to balance independence, societal integration, and self-awareness, aiming to improve overall functioning. However, many expressed challenges with the "autistic spectrum" concept, finding it diagnostically limiting compared to the more defined categories in earlier DSM versions. They highlighted the value of fostering a sense of community among individuals with autism.

Parents viewed the diagnosis as a positive and organizing framework, appreciating its role in addressing practical and social challenges. Their focus was on improving daily functionality and reducing difficulties related to social and behavioral adaptation through treatment.

Autistic adolescents, on the other hand, expressed concerns about the "autistic spectrum" concept, criticizing it for creating disparities among individuals with varying support needs and perpetuating stigma. They prioritized therapies aimed at fostering self-acceptance, emotional well-being, and social skills, emphasizing the importance of understanding their own needs. They also discussed the phenomenon of masking as a reaction to treatments, highlighting how it can be exhausting, self-diminishing, and lead to significant stress.

These findings highlight significant differences in priorities and perspectives among the groups, underscoring the need for more nuanced and collaborative approaches to autism care.

Posters:

1. Aberrant Alternative Splicing in Autism Spectrum Disorder

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Background: Autism spectrum disorder (ASD) is a neurodevelopmental condition with a complex genetic basis involving hundreds of genes. Many of these genes regulate chromatin structure and function, crucial processes for gene expression. Additionally, genes related to precursor mRNA (pre-mRNA) splicing, a process carried out by the spliceosome, have also been associated with ASD. Splicing, particularly alternative splicing plays a key role in the generation of protein isoforms and is crucial for brain development. Disruptions in splicing, caused by mutations in splicing factors or spliceosome components, have been implicated in various diseases, including ASD. Recent transcriptomic studies revealed that splicing alterations are more prevalent than differential gene expression in ASD. However, whether these splicing changes drive or are the result of the disorder remains unclear.

Objectives: In this study, we aimed to investigate whether splicing is a driver of ASD by performing a meta-analysis of RNA-seq data. We focused on mutations in splicing factors and spliceosome components—NOVA2, RBFOX1, SRRM2, SART3, U2AF2, and WBP4—chosen for their known associations with autistic phenotypes and related neurodevelopmental disorders. Our goal was to identify shared splicing events among these mutations and compare them to splicing changes observed in ASD postmortem brain tissue, ultimately elucidating their contribution to ASD pathology.

Methods: RNA-seq data from mutant and control samples for NOVA2, RBFOX1, SRRM2, SART3, U2AF2, and WBP4, as well as ASD postmortem brain tissue, were analyzed. Quality control and alignment were conducted using FastQC and STAR. Differential splicing events were identified using rMATS with thresholds of FDR < 0.05, inclusion level difference ≥ |0.1|, and genes with TPM > 1 across samples. Gene ontology analysis was performed to determine enriched biological pathways, while splice site strength was calculated using MaxEntScan. Selected splicing events were validated using RT-PCR.

Results: We identified splicing changes across the different datasets. We identified 315 genes exhibiting splicing changes in four or more mutant splicing factor datasets and 233 of

these showed splicing changes in ASD as well ($P < 0.00001$). Pathway enrichment analysis revealed chromatin regulation as a recurrent mechanism in all datasets, particularly involving the SWI/SNF chromatin remodeler complex. Notably, 19 SWI/SNF genes showed splicing changes, including SMARCC2, a core component. Mutations in SMARCC2 are known to cause intellectual disability, developmental delay, and Coffin-Siris syndrome. RT-PCR validation confirmed significant splicing alterations in SMARCC2, highlighting its potential role in ASD pathology.

Conclusions: This study reveals a pivotal link between alternative splicing disruptions in splicing factors, spliceosome components, and ASD pathology. The enrichment of chromatin remodeler genes, particularly the SWI/SNF complex, highlights the intricate interplay between splicing and chromatin regulation in shaping neurodevelopment. Among these, SMARCC2 stands out as a key candidate for understanding ASD-related splicing changes and their contribution to neurodevelopmental disorders.

2. Personal Growth and Mental Health in the Transition to Parenthood among Siblings of autistic people

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The birth of a child with autism has far-reaching implications for siblings. The current study aimed to investigate the challenges encountered by siblings of individuals diagnosed with autism as they transition into parenthood. Using the Schaefer and Moos model (1992), we compared personal growth and mental health outcomes in siblings of autistic people to those of typically developing peers, examining the role of personal and environmental resources.

A cross-sectional quantitative research design was employed. 104 participants were included, all of them are parents of infants/toddlers aged four to 36 months: 52 siblings of autistic people, and 52 siblings of typically developing individuals. The groups were matched according to parent gender, age, and infant/toddler age.

The findings revealed significant differences between groups. Siblings of autistic people reported lower levels of parenting competence, social and family support, and mental health than members of the control group. Specifically, regarding the perceived social and family support scale, significant differences were found only for the subscales of family support and significant other support, with siblings of autistic people reporting lower levels of support in these areas. Furthermore, a relationship was found between social and family support and mental health. However, when examining the relationship between social and family support and personal growth, a significant positive correlation was found only between social support and personal growth among siblings of individuals with autism.

The study's findings extend the Schaefer and Moos model (1992) to intergenerational aspects and highlight the unique (differential) contributions of different types of support for young parents from diverse family backgrounds. The findings point to a greater need for emotional support among siblings of individuals with autism during the transition to parenthood. It is recommended to develop therapeutic interventions for siblings of individuals with autism and their parents both during childhood and during the transition to parenthood.

3. Identification of novel genes and pathways essential for neural development

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Abstract

Neurodevelopmental disorders (NDDs) result from disruptions in brain development, yet the pathways involved remain incompletely understood. Here, we employed a genome-wide knockout screen to identify over 300 genes essential for neural differentiation. While showing enrichment with known NDD genes, over 80% of identified genes are novel. NDD genes with dominant inheritance were enriched with transcriptional regulators, while recessive genes were linked to metabolism. We characterized mice with mutations in eight genes (*Eml1, Dusp26*, *Dynlrb2*, *Mta3*, *Peds1, Sgms1*, *Slitrk4* and *Vamp3*), seven not previously linked to NDDs, and found severe neuroanatomical phenotypes, with half causing microcephaly. Investigation of *PEDS1*, involved in plasmalogen biosynthesis, led to the discovery of biallelic loss-of-function variants in affected individuals with microcephaly, global developmental delay and congenital cataracts. Our comprehensive study revealed essential pathways for neural differentiation and provides a new genetic platform to identify dominant and recessive genes implicated in neurodevelopmental disorders.

4. Effects of Medical Cannabis Treatment for Autistic Children on Anxiety and Restricted and Repetitive Behaviors and Interests

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Background: The literature supports the of medical cannabis's benefits for core and comorbid symptoms in autistic individuals and anxiety-related symptoms in individuals without autism. However, no study has specifically investigated how CBD-rich cannabis affects anxiety subtypes in autistic children or its relationship with restricted and repetitive behaviors and interests (RRBI). Understanding the effects of CBD-rich cannabis treatment on anxiety subtypes and RRBI could offer more precise treatment approaches to managing anxiety symptoms and reducing RRBI frequency in autistic children.
Objectives: To examine (1) the impact of CBD-rich cannabis treatment on autistic children's (1a) anxiety levels and subtypes and (1b) RRBI and subtypes and (2) whether changes in anxiety explain changes in RRBI following cannabis treatment.
Method: In this open-label study, we analyzed data from 65 autistic children (5–12 years) who had participated in research on the effects of CBD-rich cannabis on children with autism. Their parents completed the Repetitive Behavior Scale-revised (RBS-R) to assess the frequency and severity of six subgroups of their children's recurrent behaviors and the Screen for Child Anxiety-Related Emotional Disorders (SCARED) for symptoms related to five types of anxiety disorders. They completed these assessments at three time points: (T1) before treatment, (T2) after 3 months, and (T3) after 6 months of treatment.
Results: The results indicated reduced RRBI and symptoms related to various anxiety subtypes in autistic children following 6 months of CBD-rich cannabis treatment. Specifically, we observed significant differences in the autistic children's overall anxiety and in some anxiety subtypes (i.e., general, social, panic, and separation anxieties). Significant improvements were observed in RRBI, including the total score, and specifically in compulsive, ritualistic, and sameness behaviors. Our findings revealed that reduced anxiety, particularly within the panic- and separation-related subtypes, predicted a subsequent decrease in RRBI, specifically sameness behaviors, following cannabis treatment.
Conclusions: The findings of the cannabis treatment's potential benefits for alleviating anxiety symptoms, leading to reduced RRBI, may provide evidence for the meaningful

relationship between these variables and for the potential benefits of cannabis treatment for autistic children.

5. Reduced Outcome-irrelevant learning tendencies in Autism Spectrum Disorder

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Autism Spectrum Disorder (ASD) is increasingly seen through the lens of cognitive diversity rather than solely as a deficit. This study explores the claim that individuals with ASD exhibit strengths in logical reasoning and reduced cognitive biases. Specifically, we examined whether individuals with ASD demonstrate reduced outcome-irrelevant learning—a tendency commonly observed in neurotypicals to assign credit to action features irrelevant to outcome prediction. In a pre-registered online study, 75 autistic adults and 79 controls were recruited. Participants completed a reinforcement learning task, which allowed us to use computational modeling to estimate the extent of outcome-irrelevant learning. We found that individuals with ASD adjusted their reliance on action features based on their predictive value more effectively, demonstrating a superior ability to disregard irrelevant information compared to typically developing individuals. These findings highlight often overlooked strengths in ASD and provide valuable insights into their decision-making processes.

6. Vocational Assessment for autistic adults: Cognitive Ability Test Achievements and Behavioral Tendencies

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Background: Growing research in autism and employment highlights both the challenges autistic individuals may encounter when entering the job market and the potential advantages and unique strengths they may bring. Studies on autism-specific employment abilities are often based on self-identified strengths, employer impressions, or lab-based performance measurements rather than real-world employment contexts (Griffiths et al., 2024). Employment aptitude tests, such as Cognitive Ability Tests (CAT) and personality

assessments, provide objective psychometric measures commonly used in recruitment and vocational guidance.

Vocational counseling aims to support informed career choices and establish optimal career paths but remains under-researched in the field of autism. In Israel, vocational assessment and counseling are key components of rehabilitation services supported by the National Insurance Institute, including evaluations of cognitive abilities, skills, and personality traits through computerized and manual tools. Data on the characteristics of autistic individuals accessing these services and their achievements could offer valuable insights.

Objectives: To evaluate the socio-demographic characteristics of autistic individuals who underwent vocational counseling at 'Gal College, a central vocational service provider', and to examine their CAT results and personality dimensions in comparison to the general population.

Method: The study analyzed 130 vocational counseling reports from 'Gal College' (2021–2023), which included socio-demographic data, CAT results, and Big Five personality assessments. A general population sample completing the same measures for vocational counselling purposes was used for comparison. Statistical analyses employed single-sample t-tests, with Cohen's d effect sizes calculated to evaluate differences.

Results: Participants had an average age of 23.5 years (Range - 18-50, SD = 4.72), with 77% male. A little more than half attended regular secondary education (with/without aid), 22% studied in small classrooms, and 21% in special education. After high school, 68% volunteered for national/military service, 10% were fully recruited, and 22% did not serve or volunteer. Sixty-eight percent held a high school 'Bagrut,' and 16% completed tertiary education. Sixty-eight percent had little to no employment experience.

In CAT results (see Table 1), no significant differences were observed in Vocabulary, Arithmetic Series Completion, Letter and Digit Comparisons, and English Comprehension, indicating comparable performance to the general population. However, autistic participants scored lower on tasks involving verbal reasoning, arithmetic, Following Instructions and visual-spatial processing, with small effect sizes. The largest difference, with a medium effect size, was in Shape Identification, reflecting significant challenges in attention and concentration.

In personality assessments, autistic participants scored lower in Extraversion, Agreeableness, and Conscientiousness and higher in Neuroticism (see Table 2). Low Social Desirability scores suggest potential self-perception biases.

Conclusions: The variability in scores suggests that domain-specific abilities are intertwined with working memory and processing speed. Overarching autism-specific strengths may oversimplify these complexities, as scores reflect the interplay of domain-specific abilities and executive functions. Tailored career guidance is crucial to support diverse career paths rather than relying on generalized assumptions. Additionally, low social desirability scores suggest low self-perception, influencing vocational assessments, recruitment, and work integration. Self-compassion interventions (Galvin & Richards, 2023) could enhance resilience, well-being, and positive self-perception in vocational programs.

Table 1. Cognitive Ability Test Results

Factor	test	N	Mean (SD), Autistic Group	Mean (SD), General Population	t-value (df)	p-value	Cohen's d	95% Confidence Interval
Verbal	**Vocabulary**	122	19.11 (7.46)	18.51 (8.55)	0.883 (121)	0.379	0.08	[17.77, 20.44]
	Verbal Analogies	118	23.6 (6.38)	25.98 (5.67)	-4.047 (117)	<0.001	-0.37	[22.44, 24.77]
	Following Instructions	129	22.22 (8.34)	25.48 (6.97)	-4.458 (128)	<0.001	-0.39	[20.76, 23.67]
	English Comprehension	63	11.00 (5.66)	10.68 (5.33)	0.449 (62)	0.655	0.06	[9.57, 12.43]
Numerical	**Arithmetic Ability**	121	8.86 (5.28)	10.03 (4.69)	-2.439 (120)	0.016	-0.22	[7.91, 9.81]
	Arithmetic Series Completion	125	10.15 (4.46)	10.66 (4.46)	-1.107 (124)	0.27	-0.1	[9.22, 11.07]
Analytical Reasoning	**Matrices**	130	16.74 (6.33)	17.99 (5.00)	-2.254 (129)	0.026	-0.2	[15.64, 17.84]
Attention	**Letter and Digit Comparisons**	111	97.89 (21.33)	97.85 (19.31)	0.019 (110)	0.985	0	[93.88, 101.90]
	Shape Identification	107	35.15 (6.12)	38.8 (6.83)	-6.169 (106)	<0.001	-0.6	[33.98, 36.32]
Visual-Spatial	**Hidden Shape Counting**	89	11.66 (7.39)	14.76 (6.80)	-3.956 (88)	<0.001	-0.42	[10.11, 13.22]
	Cubes	90	18.08 (7.85)	21.71 (7.13)	-4.393 (89)	<0.001	-0.46	[16.43, 19.72]

Table 2. Personality Dimensions (Big Five and Social Desirability, N=108)

Dimension	Mean (SD), Autistic Group	Mean (SD), General Population	t-value (df)	p-value	Cohen's d	95% Confidence Interval
Extraversion	188.71 (39.68)	210.07 (34.76)	-5.594 (107)	<0.001	-0.54	[181.14, 196.28]
Agreeableness	225.58 (27.81)	239.98 (28.21)	-5.382 (107)	<0.001	-0.52	[220.28, 230.89]
Conscientiousness	224.13 (34.73)	232.57 (31.67)	-2.525 (107)	0.013	-0.24	[217.50, 230.76]
Neuroticism	206.67 (41.19)	184.69 (28.97)	5.544 (107)	<0.001	0.53	[198.81, 214.52]
Openness	219.24 (30.40)	223.50 (29.14)	-1.469 (107)	0.145	-0.14	[213.44, 225.04]
Social Desirability*	-108.56 (75.20)	-61.13 (58.35)	-6.556 (107)	<0.001	-0.63	[-122.91, -94.22]

*Reverse scale

7. Behavioral modulation in*Shank3* mice with autism spectrum disorder through skin ultraviolet exposure

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Abstract: Chronic exposure to low-dose UV radiation has been shown to significantly enhance social behaviors and reduce anxiety, effects mediated through the skin, as demonstrated in our work and others. Given that autism spectrum disorder (ASD) is characterized by social deficits, anxiety-related behaviors, and repetitive behavior patterns, we reasoned that UV exposure may affect these core symptoms. Here, we found that chronic low-dose UVB radiation significantly increased social preference in *Shank3* mutant mice bearing the InsG3680$^{(+/+)}$ human mutation, restoring their behavior to levels typical of wild-type mice. Additionally, UVB exposure rescued anxiety-related behaviors, returning them to wild-type levels when compared with mock-irradiated mutant mice. Proteomic analyses of the brain, skin, and immune organs revealed molecular insights into the mechanisms underlying the effects of UV exposure on ASD-related phenotypes. Taken together, our findings present a novel model for uncovering regulators of ASD-associated behaviors and suggest a potential pathway through which solar radiation could be used as a modulator of neuropsychiatric conditions.

8. Anxiety Profiles in Girls and Boys with Autism

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Background: Anxiety is a common co-occurring condition in autism which has a co-interaction with sensory and emotional processing (South & Rodgers, 2017). Additionally, previous research has posited a relationship between anxiety and sex in typically developing children. This study addresses the associations among sensory processing and the prevalence of anxiety symptoms and sex in preschool and school-aged children with autism. The inclusion of younger children was one of the innovations of this research in order to examine the developmental aspects of autism and co-occurring anxiety in girls and boys with autism.

Objectives: The objective of the current study was to explore parent-reported anxiety symptoms in girls and boys with autism. The study addresses some of the limitations of previous research by matching the girls and boys with autism by chronological and mental ages, allowing for the comparison of the study variables at different ages.

Methods: Parents of 45 girls and 45 boys with autism completed the Spence Children's Anxiety Scale (SCAS; Spence, 2001). The boys and the girls with autism were matched on age and IQ (mean age = 7.84 years; mean IQ = 82.76). The preschool or the school aged questionnaire was used according to the children's age.

Results: The girls and boys were divided into four groups according to age, with 24 preschool and 26 school-aged girls, and 21 preschool boys and 19 school-aged boys, in order to assess the expression of anxiety at differing ages. No group differences emerged in IQ or age between the preschool or the school-aged girls and boys with autism. While the preschool girls had significantly more parent-reported anxiety than the boys on all the SCAS subscales except social anxiety in which no differences emerged, the difference between school-aged girls and boys anxiety profile was more nuanced. No differences between the girls' and boys' anxiety emerged on OCD, separation anxiety, and general anxiety, whereas the girls revealed significantly more social anxiety, panic and physical fear than the boys did at this age.
Conclusions: This study addressed sex differences in anxiety among children with autism. Similar to typically developing children, a relationship between sex and anxiety emerged but by looking at younger and older children a differentiated profile emerged. It appears that in younger children the girls revealed more anxiety on all the subscales except for social anxiety which could be eclipsed into the social impairments of autism criteria. As the children grow, this profile reveals some differences in anxiety presentation. Specifically, because no sex differences in OCD, social anxiety and separation anxiety subscales emerged, it is important to understand that anxiety in autism may be different because of the underlying social difficulties inherent in autism. Thus, the profiles of anxiety in girls and boys with autism may differ from those reported in typically developing children and may indicate a separate pattern of anxiety symptoms on children with ASD. Further investigation is needed in this area.

9. Identity, Resilience, and Collective Trauma: A Comparative Analysis of Autistic and Non-Autistic Students During Iron Swords war

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On October 7, 2023, the "Iron Swords" war broke out in Israel, exposing civilians and security forces to terrorist attacks, resulting in widespread collective trauma. This event highlighted the need to examine resilience factors and trauma risk among various populations, particularly those diagnosed with Autism Spectrum Disorder (ASD). Clinical evidence indicates that individuals with ASD face elevated risks of traumatic events compared to the general population. This increased vulnerability is attributed to significant

difficulties in understanding social interactions, including misinterpretation of others' intentions and challenges in identifying dangerous situations. Additionally, heightened rumination tendencies can impair effective processing of traumatic experiences. Recent research has emphasized the importance of diagnosis-related self-identity, recognizing its impact on psychological development, social interactions, and overall well-being. The concept of illness-identity describes the extent to which a diagnosis or chronic condition becomes integrated into one's sense of self-identity. This construct is defined by a theoretical model comprising four distinct patterns of self-identity: acceptance (acknowledging the condition as part of oneself), enrichment (viewing the condition as adding value to life), rejection (refusing to acknowledge the condition as part of identity), and engulfment (allowing the condition to overwhelm one's identity).For individuals with ASD, self-discovery and diagnosis acceptance represent crucial stages in building a stable personal identity, often leading to improved self-image and psychological well-being. The aim of this study was to compare personal and community resilience between autistic and non-autistic students during the first months of the Iron Swords war and examine relationships between positive and negative autistic identity and resilience.

This cross-sectional study included students (N=87) in higher education, among them autistic students (n=44) and non-autistic students (n=33). Data was collected through validated questionnaires including Life Orientation Test, U.C.L.A Resilience Scale, Conjoint Community Resilience Assessment, Conor-Davidson Resilience Scale, Self-Efficacy, Harris Surveys of Community, Positive and Negative Affect Scale, Post-Traumatic Growth Index, Academic Support, and Autism Identity Scale.

Research findings were mixed, revealing that students in both groups demonstrated similar levels of self-efficacy ($t_{(81,2)}$=0.58, p=0.57), personal resilience ($t_{(81,2)}$=1.13, p=0.29), and affect in dealing with collective trauma ($t_{(81,2)}$=-1.67, p=0.12). Students with autism spectrum disorder felt significantly less lonely ($t_{(81,2)}$=1.85, p=0.06) and experienced the academic program more supportively ($t_{(81,2)}$=-5.11, p<0.001). However, they showed significantly lower post-traumatic growth ($t_{(81,2)}$=2.35, p=0.02) and felt less optimistic ($t_{(81,2)}$=2.97, p=0.004). Positive autism identity correlated significantly with post-traumatic growth (r=0.60, p<0.001), self-efficacy (r=0.27, p=0.04), and community resilience (r=0.29, p=0.03). Conversely, negative autism identity showed inverse correlations with optimism (r=-0.44, p<0.001) and personal resilience (r=-0.43, p<0.001).

This study demonstrates the complex interplay between autism identity and resilience during collective trauma. While autistic students showed comparable resilience to their non-autistic peers in several domains, their identity profiles significantly influenced their adaptation to trauma. Positive autism identity emerged as a potential protective factor, associated with enhanced post-traumatic growth and resilience. These findings highlight the importance of fostering positive autism identity in higher education support programs

and suggest that targeted interventions should consider identity-related factors in promoting resilience among autistic students during crisis situations.

10. Perturb-seq reveals divergent and convergent pathways in autism associated genes through early cortical differentiation

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Autism Spectrum Disorder (ASD) is a group of symptomatically heterogeneous neurodevelopmental disorders. ASD is known to have a strong genetic basis; however, its genetic architecture is very complex. The heterogeneity of the symptoms may stem, at least partially, from genetic heterogeneity. In this study, we employ a combined approach of CRISPR screening and single-cell RNA sequencing (Perturb-seq) to examine the effects of mutations in 39 high confidence ASD-associated transcription regulators on early in-vitro cortical differentiation of human embryonic stem cells. Our findings reveal that mutants tend to exhibit premature differentiation towards either neuronal cells or oligodendrocyte (OD)-like cells, correlating with known human phenotypes of the same genes. For example, perturbations that increase OD-like cells are more likely to be associated with microcephaly, while perturbations that decrease OD-like cells and increase neuronal cells are more likely to be associated with macrocephaly. Additionally, integrating cell-type composition changes with gene expression data enhances the distinction between genes predominantly associated with ASD and those predominantly associated with developmental delay. Our results advance the understanding of the genotype-phenotype relationship in ASD, potentially aiding in the identification of genetic subgroups within ASD and the development of targeted treatments.

Key Words: Autism Spectrum Disorder (ASD); Transcriptional regulation; Chromatin; Perturb-seq; Neuronal differentiation; Neuronal development; Neurodevelopmental disorders

11. The Role of Emotion Regulation in Suicidal Ideation of Autistic and Nonautistic Adults

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Background: Autism is characterized by high rates of psychiatric comorbidity, including suicidality. Autistic adults report higher suicidal ideation and behavior compared to non-autistic adults. However, the mechanisms behind those differences are still unclear.

Objectives: The current study examined the role of emotion regulation as mediator between having autism and suicidal ideation. We suggest the higher level of suicidal ideation shown in autistic (compared to nonautistic) adults may be related to greater difficulties regulating their emotions.

Methods: Fifty-one autistic adults (15 females) with no intellectual disability, and 71 comparable non-autistic adults (29 female) self-reported their suicidal ideation using items from the Brief Symptoms Inventory (BSI) and their emotion dysregulation using the Difficulties in Emotion Regulation Scale (DERS). The DERS measures several dimensions of emotion regulation, including clarity, strategies, impulse control, acceptance, awareness, and goal-directed behaviors.

Results: Autistic adults reported higher levels of suicidal ideation ($F(1, 120) = 4.17$, $p < .05$, $\eta^2 = .03$) and greater difficulties in emotion regulation ($F(1, 120) = 27.11$, $p < .001$, $\eta^2 = .18$) compared to their non-autistic peers. Specifically, autistic adults had higher scores in DERS subscales for Clarity ($F(1, 120) = 10.42$, $p < .01$, $\eta^2 = .08$), Strategies ($F(1, 120) = 27.24$, $p < .001$, $\eta^2 = .18$), Impulse ($F(1, 120) = 36.41$, $p < .001$, $\eta^2 = .23$), Nonacceptance ($F(1,120) = 4.96$, $p > 0.05$, $\eta^2 = .04$), and Goals ($F(1,120) = 26.13$, $p > 0.05$, $\eta^2 = .18$). Suicidal ideation was positively correlated with the total DERS score ($r = 0.45$, $p < .001$) and with all subscales (Awareness: $r = .36$; Clarity: $r = .46$; Strategies: $r = .36$; Impulse: $r = .39$; Nonacceptance: $r = .29$; Goals: $r = .21$; all $p < .001$). Mediation analysis for the association between having autism and suicidal ideation with DERS-Total as the mediator (controlling for age and sex), indicated full mediation (direct effect: $b = -.04$, $se = .36$, $t = -.12$, $p = .89$; mediation effect: $b = .77$, $se = .30$, CI [0.16, 0.65]). Subscale mediation analyses further highlighted the role of emotional clarity (direct effect: $b= .23$, $se= .33$, $t= 0.68$, $p= 0.49$; mediation effect: $b = .5$, $se = .23$, CI [0.12, 1.03]) and emotion regulation strategies (direct effect: $b= .13$, $se= .37$, $t= .36$, $p= .71$; mediation effect: $b = .59$, $se = .27$, CI [0.14, 1.19]) as full mediators. Other models yield no significant results.

Conclusions: These results suggest that the emotion regulation difficulties of autistic adults may play a mechanistic role in their increased suicidal ideation. The lack of emotional clarity and limited access to emotion regulation strategies are key regulatory factors contributing to suicidal ideation in autistic adults. Interventions targeting emotion regulation strategies and emotional clarity may assist in alleviating suicidal ideation in autistic adults.

12. Autism Spectrum Disorder and Selective Mutism in Girls

Selective Mutism and Autism Spectrum Disorder in Girls Diagnosed After Age 6: A Diagnostic Challenge

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Numerous studies indicate that autism is diagnosed in females at a later age compared to males, particularly when the diagnosis occurs beyond preschool years. This phenomenon often arises because autism in girls is masked by other psychiatric diagnoses or because certain mental health conditions obscure the diagnosis of autism spectrum disorder (ASD). Consequently, girls with selective mutism and communication difficulties may reach adolescence without accurate recognition or appropriate treatment.
Cook et al. (2023) noted that mental health conditions can either mask the diagnosis of autism or vice versa. In the work of Steffenburg et al. (2018), it was suggested that autism spectrum disorder may co-occur with selective mutism, but contemporary literature on this topic remains sparse. A literature review from 2024 identified only two studies addressing the relationship between autism and selective mutism in girls.
The present article highlights five case studies of girls aged 6–18 with typical cognitive development, all attending mainstream education, who were diagnosed with selective mutism at a young age and autism spectrum disorder at a later age. All participants met the diagnostic criteria for autism using established diagnostic tools, contradicting earlier reports in the scientific literature.
The findings suggest that young girls with selective mutism may experience significant distress, leading to a later autism diagnosis and meeting the threshold for ASD diagnosis using standard evaluation tools. This article raises questions about the diagnostic process for autism in girls and emphasizes the need for further research to explore larger samples,

the relationship between early selective mutism and autism diagnosis, and the unique manifestations of these conditions in girls.

13. Late Autism Diagnosis- New insights from Mirrors Autism Center 2022 cohort

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Background: One out of a 36 children is diagnosed with ASD . What is the path leading to a late ASD diagnosis?
Objectives: We set out to explore this question in a sample of 91 children reffered for an ASD evaluation after age 6.
Methods: The mean age of first time concern was 5.14, SD=2.90. 73 children were boys (80.2%) and 18 were girls (19.8%), and age when arrived at the clinic ranged from six to eighteen (Mean=11.67, SD=3.40). The empirical analyses of the data included two parts: a preliminary part that showed frequencies of major children's characteristics compared between boys and girls by the χ 2 test. Similarly, a set of gender comparisons of continuous scales, mainly, indicators of age when first concerns arose and other relevant score measures using the two-independent t-test. The second part included analyses of possible explanation for the children's diagnosis, using the generalized linear model (GLM) framework with the robust standard error option, where the outcome was a binary diagnosis (yes=1), complemented by a division between neurologists and psychologists to assess predicted probabilities for a child to affiliate with one of the four affiliation options: without autism , with autism , suspicion, group observation, all of which were predictors of the final binary diagnosis.
Results: 1. We found that the total Social Affect score of the Ados was associated with an increasing probability of positive diagnosis (b=0.37, p=.001, ODDs=1.44). 2. We found that higher age of first parental concerns, was associated with a higher probability of positive diagnosis (b=0.17, p=.055, ODDs=1.19). 3. Language difficulties indicated a lower probability of positive diagnosis (b=-1.24, p=.054, ODDs=0.29), which suggested that earlier concerns were in fact related to the language difficulties. 4. Other indicators were positively associated with the probability of positive diagnosis, e.g., RRB, Overall SA +RRB, comparison score, and ADOS classification, while group evaluation was found to associate with lower probability of positive diagnosis (b=-0.98, p=.034, ODDs=0.38)

Conclusions: The findings indicate that higher Social Affect scores significantly correlate with increased probabilities of receiving a positive autism diagnosis, showing the importance of assessing social communication deficits in determining ASD. Interestingly, language difficulties inferred from the data highlight a nuanced relationship with diagnosis—suggesting that earlier language challenges may hinder the likelihood of receiving an ASD diagnosis, an observation supported by research linking language delays to earlier parental concerns. The results also point out that certain behavioral indicators, such as restricted and repetitive behaviors (RRB), significantly boost the likelihood of diagnosis. The observation regarding group evaluation's negative impact on diagnosis probabilities highlights the multifaceted diagnostic challenges, echoing concerns about the complexity of diagnosing ASD amidst overlapping symptoms with other disorders. These results highlight the interplay between developmental parameters, age of first time parental concerns, co morbid conditions and current limits of diagnostic tools .

14. A behavioral and eye-tracking study in visual perceptual processing among minimally verbal children with Autism

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Background: During typical development, basic visual object recognition, unrelated to social interactions, begins to emerge within the first year of life. Shape processing involves both low-level visual cues, such as color and orientation, and more advanced mechanisms that rely on prior knowledge and inferences. However, little is known about basic, non-social, visual perceptual processing in minimally verbal children with autism (mvASD).

Objective: We set out to investigate basic, non-social, visual perceptual processing in older children with mvASD

Method: We studied pointing and eye-gaze in twenty older children with mvASD during low and mid-level visual processing tasks. In the oddball paradigm they pointed to an odd target among an array of distractors of varied difficulty and complexity consisting of low (e.g., color) and midlevel visual stimuli (e.g., 3D shapes). In the contour detection task, a circular contour was embedded among an increasing number of Gabor elements. In a third task a Kanizsa triangle was presented as well as modulated versions accentuating illusory triangle (e.g a central dot). Spontaneous pointing and eye gaze were recorded as distance from oddball target and Kanizsa center. Finally, during a computerized "Kanizsa dragging game" participants were dragging shape to correct Kanizsa.

Results: Our results suggest that children with mvASD are not a homogeneous group. While all children detected the odd target in the easiest condition of faint distractors, about half successfully detected it based on *all* low-level features. Importantly, some of these "high performers" deteriorated on mid-level visual tasks with higher stimulus. Furthermore, some 'high performers' correctly detected the Kanizsa oddball but unlike TDs pointed to local inducers rather than Kanizsa center. Strikingly, participants who failed lowest level of visual oddball tasks performed significantly better and above chance, when detecting the oddball through eye -gaze compared to pointing ($t(8)=3.19$, $p = 0.013$ with a large effect size ($d=1.05d$) and good discriminatory ability (AUC=0.77). For the single Kanizsa, pointing and eye gaze were at the local elements, but shifted towards the center in modulated versions. 'High performers' successfully dragged shape to correct Kanizsa.

Conclusions: Participants could do the tasks, with performance sensitive to distractor saliency and stimulus complexity, but the group was not homogeneous. Results could not be explained by lack of cooperation or task comprehension. This suggests early visual processing differences among children with mvASD, and visual perception based on low-level representations with attenuated inference-based processing. However, eye gaze superior to pointing, shifting of pointing and gaze for the single Kanizsa, to the center, with minor modulations, as well as successful matching of shape to Kanizsa, indicate more complex perceptual representations *do* exist. It seems that among children with mvASD, performance does not solely rely on *what* they perceive, but also on *how* they use the visual signal to drive their behavior. **They 'see the point, but do not (always) point to what they see'.**

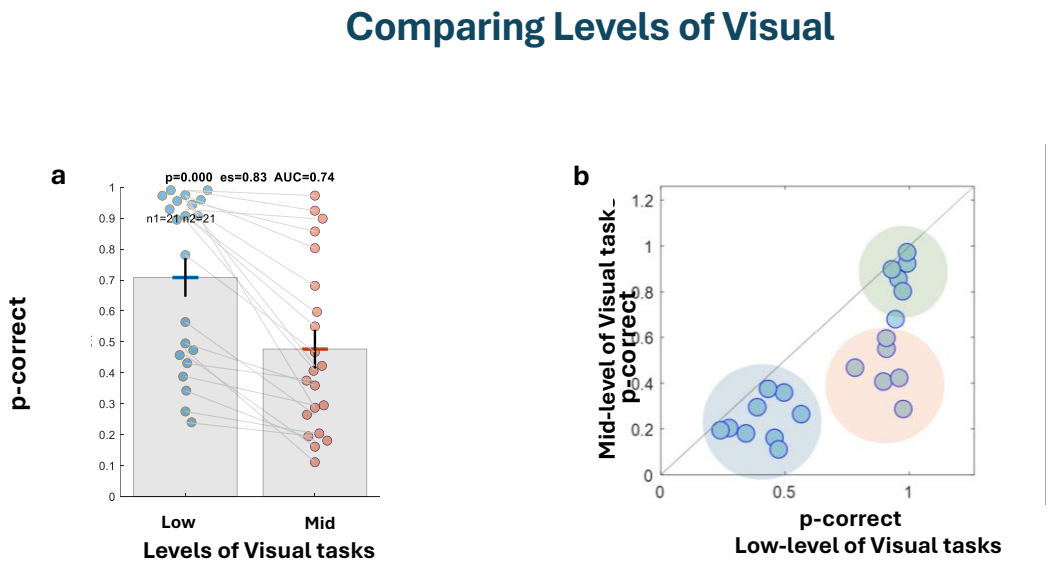

Figure 2. Performance comparison during all low and all mid-level visual tasks (by pointing). (a) *Bee-swarm, where each pair of circles connected by a grey line represents one mvASD participant's performance during visual tasks;* ***(b)*** *diagonal scatterplot, where each circle represents performance of one mvASD participant. The color circles mark three clusters obtained via K-means cluster analysis for K=3.* ***Note, complexity modulates performance and mvASD is not a***

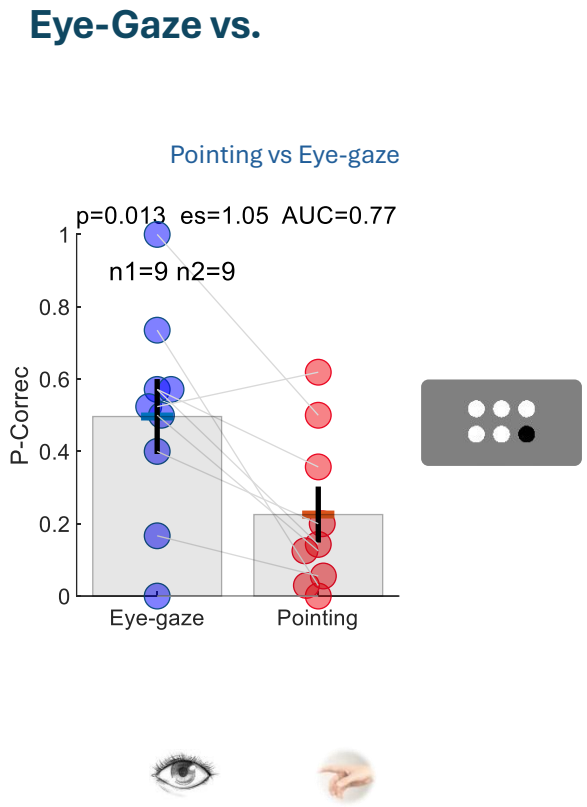

Figure 1. Eye-gaze vs pointing among 'low' performers. *Each pair of circles connected by a grey line represents one mvASD participant's eye-gaze and pointing performance respectively for the black/white oddball task.* ***Note, the superiority of eye-gaze performance over pointing.***

15. Bridging the Emotional Gap: A Teacher-Led Computerized Program for Improving Emotional Skills in Children with ASD

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Children with Autism Spectrum Disorder (ASD) face substantial challenges in understanding emotions, including difficulty in recognizing emotions through nonverbal cues, interpreting social context, and developing emotional vocabulary. This study evaluated the effectiveness of a research-backed, computerized intervention, which was adapted for teacher facilitation in special education classes, aimed at enhancing emotional skills in children with ASD.

The study included 116 children with ASD (17 girls), ages 7-10 (*M*=8.26, *SD* = .76), who were randomly assigned at the classroom level to either an intervention group (n=59) or a control group (n=57). The intervention group received two lessons per week for 22 weeks, while the control group continued their standard special education curriculum. Key outcomes measures included the ability to recognize emotions from nonverbal cues across multiple modalities (facial expressions, body language and tone of voice), understand emotions within social contexts and the use of emotional language. Additionally, the intervention's feasibility and accessibility were evaluated through teacher rating and interviews.

Multi-Level Modeling (MLM) analyses, accounting for the nested data structure with children nested within classrooms and controlled for background variables, revealed significant improvements in the intervention group across all targeted areas compared to the control group. Participants demonstrated an ability to generalize the learned material to new contexts involving different people and activities. However, these improvements were confined to emotions directly addressed by the program and did not extend to untrained emotional concepts. In addition, Teachers provided highly positive feedback on the program's feasibility, highlighting its practicality, ease of integration, alignment with developmental goals, and high levels of student engagement.

This study underscores the effectiveness and feasibility of a teacher-led, computerized intervention in improving emotional skills among children with ASD within a school setting, offering a scalable and accessible approach to enhancing social-emotional development in this population.

Keywords: autism, emotional skills, technological intervention.

16. Narrative abilities in multilingual children with ASD: Comparison of non-interactive and naturalistic acquisition

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Introduction: Some children with Autism Spectrum Disorder (ASD) grow up in multilingual environments, acquiring languages through naturalistic exposure, similar to their non-autistic peers. However, case studies have reported unexpected foreign language acquisition among autistic individuals through non-interactive exposure, such as TV and YouTube (e.g., Dumont et al., 2024; Kissine et al., 2019; Riedel et al., 2020; Smith & Tsimpli, 1995; Vulchanova et al., 2012; Zhukova, 2021).

Methodology: This study compares narrative abilities of English-Hebrew multilinguals aged 4;5-12 across three groups (n=54): ASD-Nat (multilingual children with ASD who learned English naturalistically), ASD-NI (multilingual children with ASD who acquired English non-interactively), and TLD-Nat (multilingual children with typical language development who acquired English naturalistically). All participants acquired Hebrew naturalistically.

Narrative production was assessed in English and Hebrew using the "Multilingual Assessment Instrument for Narratives" (MAIN), designed for children acquiring multiple languages from birth or early childhood (Gagarina et al., 2012). Narratives were transcribed and analyzed for verbosity, type-token ratio, errors, code-switching, and referential choice (e.g., full lexical phrases vs. pronouns, overt vs. null pronouns, ambiguous vs. non-ambiguous, definiteness marking). Pragmatic relevance in context, which influences the choice of linguistic expressions, poses challenges for individuals with ASD (e.g., Arnold, Bennetto & Diehl, 2009). Furthermore, the two languages, spoken by children in the study, differ in referential encoding; English is [-pro-drop], while Hebrew is a partial [+pro-drop] language.

Baseline assessments included non-verbal IQ using Raven's Colored Progressive Matrices (Raven, 1998), ASD severity via ADOS-2 (Lord & Rutter, 2012), morphosyntactic abilities using LITMUS sentence repetition tasks in English and Hebrew (Marinis & Armon-Lotem, 2015), and Theory of Mind (Wellman & Liu, 2004).

Results: The results show that multilingual children can produce simple narratives in both languages, regardless of acquisition mode (interactive vs. non-interactive) and clinical status (ASD vs. non-ASD). All children exhibited notable variability in verbosity, type-token ratio, and error count across English and Hebrew, reflecting uneven linguistic abilities between their

languages, consistent with previous findings among multilinguals (Kohnert, 2010). Differences in referential expression use were observed between autistic and non-autistic children, with autistic children producing more ambiguous expressions; however, no significant differences were found between the ASD groups. Cross-linguistic influence was evident in referential choices, such as pronoun omissions in English subordinate clauses, reflecting a transfer of the [+pro-drop] feature from Hebrew (e.g., "*The boy is crying because hurt*").

Discussion and Conclusions: Autistic children who acquire English through non-interactive sources, such as TV or YouTube, can exhibit linguistic tendencies similar to those of children who learn through natural interactions. However, children with ASD still display distinct qualitative differences compared to their non-autistic peers. These findings have significant clinical and theoretical implications, which will be further discussed.

17. Performance monitoring and reward processing in ASD: ERP and perceptual correlates

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Background: One of the key executive functions essential for seamless cognitive, affective, and motor processes – performance monitoring – appears to be impaired in individuals with autism spectrum disorder (ASD). A promising avenue for analyzing the characteristics of performance monitoring in ASD lies in its EEG-based biomarker, Feedback-Related Negativity (FRN), an event-related brain potential associated with error-processing mechanisms. However, the current literature on FRN in ASD is inconclusive (Hüpen et al., 2016), with studies reporting both the presence (Bellebaum et al. 2014; Stavropoulos & Carver, 2014) and absence (Larsson et al. 2011; McPartland et al., 2012; Clawson et al., 2014) of differences in FRN between ASD and neurotypicals.

Objectives: Following our lab's recent findings on reduced sensitivity to both internal and external feedback signals in individuals with ASD, we analyzed whether increasing the perceptual and motivational salience of feedback could enhance performance monitoring in individuals with ASD.

Methods: In Study 1, EEG was recorded in 26 ASD and 26 matched neurotypical (NT) participants during a two-tone discrimination task during standard visual feedback (Correct/Incorrect) and with same feedback with increased perceptual salience. Study 2 (20 ASD and 22 NT) introduced monetary motivation, where financial balance increased (Correct) or decreased (Incorrect) after each trial.

Results & Conclusions: 1 – Increasing perceptual salience of feedback may have limited value for ASD individuals. Although individuals with ASD exhibited a significant PES effect and a notable increase in FRN, the disappearance of intergroup differences in FRN was primarily due to a decrease in FRN among NT individuals rather than an increase among those with ASD.

2 – Monetary motivation may significantly increase FRN in individuals with ASD – but this is driven by reward processing rather than error processing. In the third experimental paradigm, where motivational salience was enhanced through monetary feedback, a significant increase in FRN magnitude was observed in the ASD group, with no changes in NT participants. However, this increase in FRN does not appear to reflect improved performance monitoring in ASD, as indicated by the following observations: (1) With clear monetary incentive, NTs exhibited a statistically significant improvement in accuracy, and a notable post-error slowing effect, as well as demonstrated an integrated assurance effect, showing higher performance on trials following Hard and Correct trials compared to Easy-Correct trials or trials with Incorrect responses at both difficulty levels. Conversely, ASD participants, despite reporting greater motivation – supported by behavioral observations and self-reports – failed to improve their accuracy or demonstrate post-error slowing or integrated assurance effect. (2) The increase in FRN magnitude in ASD under the Monetary protocol was primarily driven by enhanced ERP amplitudes for Correct feedback, with no significant changes for Incorrect. Notably, Correct feedback-evoked P300 amplitudes – associated with motivational salience – were significantly higher in ASD compared to NT participants, suggesting that reward processing mechanisms, rather than typical performance monitoring processes, may underlie the observed FRN changes in ASD.

18. The importance of a multifaceted longitudinal examination of anthropometric measures in studying the association between head growth during infancy and risk of autism spectrum disorder

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Background: Mounting evidence suggests a link between abnormal head size during infancy and autism spectrum disorder (ASD). These include reports of relatively small head circumference that normalizes within the first year of life among newborns later diagnosed with ASD. In addition, higher proportions of both macrocephaly and microcephaly have been consistently reported among children with ASD. However, the specific head growth trajectories during infancy associated with ASD and their relationship with the overall body growth of these children remain inadequately explored.
Objectives: To investigate the associations of head growth trajectories during infancy and the subsequent likelihood of ASD.
Methods: We conducted a retrospective case-control study including 262 children diagnosed with ASD and 560 controls without ASD or any other developmental disorders that were matched by age, sex, and ethnicity. Growth measures at the ages of 1, 2, 4, 6, 9, and 12 months were obtained from government-funded mother-child health clinics in southern Israel that regularly monitor the growth and development of all children in this region. First, we used the standardized infant growth charts to determine the HC and weight quartiles of participants at different ages. Then, we divided the sample into seven clusters based on their head growth trajectories and used conditional logistic regression models to assess the independent association of these clusters with ASD.
Results: The study sample comprised 78.2% males and 76.8% Jewish children. HC and weight were significantly correlated throughout the study period (Pearson Correlation r = 0.45-0.59, $p < 0.001$), and notably stronger in autism (r = 0.55-0.69) than in controls (r = 0.36-0.55). Children with small and large heads throughout infancy had the highest likelihood of developing ASD compared to children with normal head size (adjusted odds ratio [aOR] = 3.76, 95%CI = 2.29-5.73; and aOR = 3.34, 95%CI = 2.00-6.26, respectively). Further stratification of these lower and upper quartiles revealed that the strongest associations with ASD were seen among children in the most extreme (0-5th and 95-100th) percentiles (aOR = 4.57, 95%CI = 1.99-8.88; aOR = 11.87, 95%CI = 2.77-55.47, respectively). Interestingly, the associations between head growth trajectories and ASD were mainly driven by children having similar body weight trajectories (aOR = 6.23, 95%CI = 3.00-11.39; and aOR = 10.56, 95%CI = 3.88-28.54, respectively).
Conclusions: Our findings suggest that the reported association between atypical head size during infancy and ASD is not restricted to the head growth, but rather a characteristic of a broader physical growth anomaly. This conclusion highlights the importance of a multifaceted longitudinal examination of such anthropometric measures in studies of child development.

19. ToM^2: Parent's Perceptions of Their Autistic Child's Theory of Mind

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Background: Theory of Mind (ToM) - the ability to understand others' mental states - has been extensively studied in autism, with research documenting various patterns in its development. While children's ToM abilities are well-researched, we know surprisingly little about parents' understanding of their children's ToM capabilities, particularly in autism. Understanding this aspect is crucial, as research has shown that parents of autistic children often display challenges in understanding social cues and intentions, referred to as the broader autism phenotype (BAP). Family accommodation, wherein parents modify their behaviors to reduce their child's distress, has emerged as a significant factor in autism, potentially influencing parent-child understanding and interactions.

Objectives: This study proposes a new term: ToM^2 - referring to parents' ability to assess their child's social understanding. We investigated this construct in the context of parents of autistic child, and assess how child autism symptom expression, parents' BAP traits, and family accommodation behaviors relate to ToM^2 accuracy.

Methods: Initially, 49 parent-child dyads were recruited, with 33 included in the final analysis due to missing data. All children had confirmed autism diagnoses (mean age = 4.3 years) and completed the ADOS-2 assessment. Inclusion criteria required receptive language and visual reception abilities within or above average range (T scores > 40 on Mullen/WPPSI). Both parents and children completed a modified ToM scale designed for individuals with limited language capacity. Parents completed the scale as they believed their child would respond, allowing assessment of ToM^2 accuracy through match scores between parent predictions and child performance. Parents also completed measures of BAP (BAPQ) and accommodation (FAS-RRB).

Results: ToM^2 accuracy in the current sample showed that parents accurately predicted their child's performance in approximately one-third of the cases, with a slight tendency to overestimate their child's abilities. Moreover, higher family accommodation (FAS-RRB) was significantly associated with lower ToM^2 accuracy (OR = 0.66, p = 0.014). Although not statistically significant, a trend emerged showing that higher autism severity (ADOS) was associated with lower ToM^2 accuracy (OR = 0.72, p = 0.059). No significant relationship was found between parental BAP characteristics and ToM^2 accuracy.

Conclusions: These findings suggest that excessive accommodation might interfere with parents' understanding of their child's abilities, and that understanding social cognition may be more challenging in children with more severe symptomatology. Future research with larger sample sizes is needed to validate these findings.

Figure 1. Family Accommodation and ToM² Accuracy

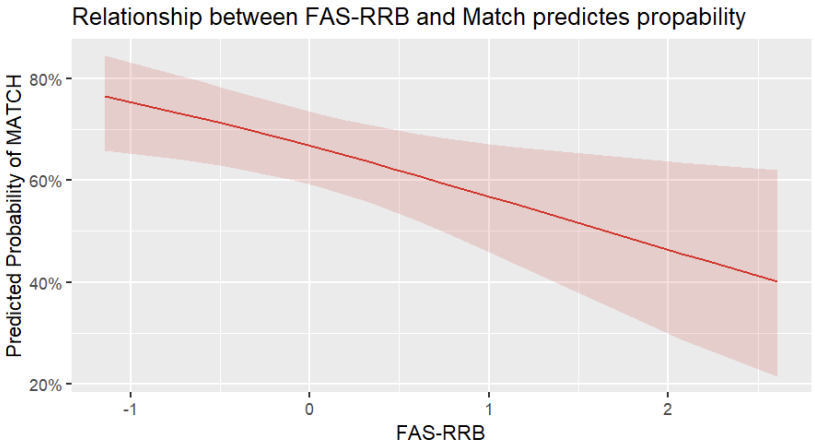
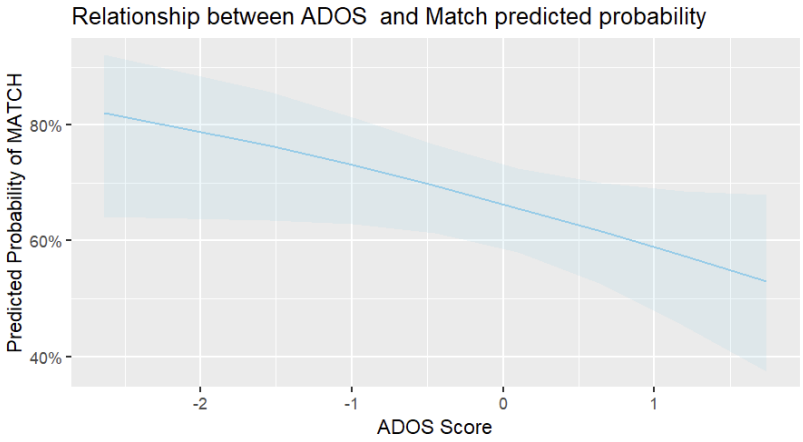


Figure 2. Autism Severity and ToM² Accuracy



20. Facial Mimicry Predicts Children's Autistic Symptoms

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Background: Facial mimicry, the proclivity to imitate other's facial expressions, is essential for social interaction and understanding other's emotional states. This ability is often impaired in individuals with autism and hinders their social interaction.
Objectives: The goal of this study was to examine the relations between facial mimicry and autistic symptoms among young autistic children.

Methods: Participants completed a mimicry task, where they imitated facial expressions from videos of adult and child models. Mimicry was analyzed using neural network-based frame analysis and lagged cross-correlation to derive two complementary measures: accuracy, reflecting the precision of the facial expressions' mimicry, and response lag, indicating the timing of mimicry. To measure autism symptoms, the Social Communication Questionnaire (SCQ) Lifetime form, was completed by the participants parents.
Results: Preliminary results from 8 participants (mean age = 7.63±0.86) indicated a possible association between slower mimicry responses and higher SCQ scores in the Reciprocal Social Interaction ($r = .710$, $p = .048$) and Communication ($r = .670$, $p = .069$, trending towards significance) domains. These results may reflect a relationship between slower mimicry capabilities and greater social and communication difficulties. Similarly, mimicry accuracy showed a negative correlation with SCQ Reciprocal Social Interaction Domain scores ($r = -0.655$, $p = .078$, trending towards significance), suggesting a potential link between greater social difficulties and lower mimicry accuracy. These findings require cautious interpretation due to the small sample size.
Conclusions; The present study's findings highlight the potential of automatic mimicry-based measures as predictors of social and communication symptoms in children with autism. By extending this work to include typically developing children, we aim to establish these measures as a reliable tool to aid in autism screening. Furthermore, these measures may serve as a sensitive tool for tracking symptom changes and evaluating the impact of therapeutic interventions. [3] Sagol School for Neuroscience, Tel Aviv University.

21. The role of Gsk3β-mediated synaptic and behavioral dysfunctions in the Cntnap2$^{-/-}$ mouse model of autism

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Abstract : Core behavioral deficits of autism spectrum disorder (ASD) have been reported in humans with CNTNAP2 mutation. This gene encodes a neuronal transmembrane protein member of the neurexin superfamily, which is involved in neuron-glia interactions and clustering of K^+ channels in myelinated axons. The Cntnap2 knockout mice (Cntnap2$^{-/-}$) exhibit core ASD-like behavioral phenotypes. This study aims to decipher the molecular mechanisms that underlie the cellular and behavioral deficits observed in the Cntnap2$^{-/-}$ mice. We hypothesize that a mutation in the Cntnap2 gene leads to a reprogramming of the protein expression and kinase signaling which could lead to synaptic and behavioral dysfunctions. Using our phospho-proteome platform, we observed a significant reduction in the phosphorylation levels of Gsk3β at serine 9 in the cortex of

the Cntnap2$^{-/-}$ mice. This site correlates with the inhibition of its kinase activity. Gsk3β is a serine/threonine kinase that plays a key role in synaptic function and plasticity and acts as the main negative regulator of the WNT/β-catenin signaling pathway. We, therefore, suggest that aberrant overactivation of Gsk3β in the cortex of the Cntnap2-/- mice may play a crucial role the synaptic and behavioral deficits. Based on our preliminary findings, we observed that Gsk3β phosphorylated β-catenin at three sites (serine 33,37 and Threonine 41), resulting in its subsequent ubiquitination and degradation, indicating downregulation of the WNT/β-catenin signaling pathway in the brains of Cntnap2-/- mice. Treatment with a selective inhibitor of Gsk3β, HU-50, improved certain ASD-like behavioral phenotypes, including sociability deficits and anxiety. These effects were accompanied by an increase in the dendritic spine densities in the cortex of the mutant mice. To decipher the molecular underpinnings of these observed effects, we explored the role of Gsk3β at both inhibitory and excitatory synapses. We found that Gsk3β phosphorylates the inhibitory scaffold protein gephyrin at serine 270, triggering its full-length cleavage. This cleavage event may disrupt the anchoring of GABAA receptor subunits to the synaptic plasma membrane, potentially leading to a reduction in inhibitory inputs within the cortex of mutant mice. Taken together, these results suggest that targeting Gsk3β could be a promising therapeutic approach for treating ASD-like phenotypes associated with CNTNAP2 mutation.

Keywords: autism spectrum disorder, phosphor-proteomics, Gsk3β, behavioral deficits, GABAergic dysfunction, synaptic plasticity.

22. Exploring Disfluency Patterns in Bilingual and Monolingual Children with and without Autism: A Pragmatic Perspective

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Background: Previous research on disfluency production in monolingual autistic children, compared to their non-autistic peers, has reported a reduced use of filled pauses (e.g., "uh," "um") and additive connectives (e.g., "and"). This pattern may indicate challenges in the interactional aspects of communication (Heeman et al., 2010) or a reduced use of listener-oriented disfluencies that enhance comprehension (Lake et al., 2011). Few studies have explored disfluencies in bilingual clinical groups. For instance, bilingual children with developmental language disorder (DLD) are reported to use more long pauses (Fichman &

Altman, 2024). However, no research has examined disfluency production in autistic bilingual children relative to their monolingual and bilingual non-autistic peers.
Objectives: This study is the first to examine both the independent effects of Clinical Status (autistic vs. non-autistic) and Language Status (monolingual vs. bilingual), as well as their interaction, on the production of disfluencies and connectives.
Methods: Participants included bilingual Russian-Hebrew autistic (n = 20) and non-autistic children (n = 27), monolingual Hebrew-speaking autistic (n = 20) and non-autistic children (n = 22), all aged 5–9 years. Narratives were elicited in Hebrew using the LITMUS-MAIN picture task (Gagarina & Lindgren, 2020). The disfluency analysis included intra- and inter-utterance silent pauses, broken words, filled pauses, prolongations, repetitions (whole-word, phrase, and part-word), self-corrections (whole-word and phrase), and phonological fragments. Connectives analyzed included "and," "and so," and "and then".
Results: Autism and bilingualism independently did not significantly affect overall disfluency rates, but their combination shaped specific patterns. Autistic monolingual children used fewer filled pauses but more phonological fragments and between-utterance long silent pauses than their non-autistic peers. Bilingual autistic children produced the connective "and" more frequently than non-autistic bilinguals, while all bilinguals exhibited more long intra-utterance silent pauses than monolinguals.
Conclusions: These findings suggest that the reduction in listener-oriented disfluencies, such as filled pauses, observed in Hebrew-speaking monolingual children is consistent with previous research. Furthermore, bilingualism appears to foster adaptive communication in autistic children by enhancing pragmatic skills, such as the use of connectives, which improve discourse cohesiveness. This highlights the role of bilingualism in pragmatic development in autism and challenges traditional distinctions between speaker- and listener-oriented disfluencies.

23. A Cross-Cultural Examination of the Comprehensive Autistic Trait Inventory (CATI) in Two General Population Samples

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Background: The Comprehensive Autistic Trait Inventory (CATI) is a self-report measure of autistic traits in the general population (English et al., 2021). It comprises six subscales: Social Interactions (SOC), Communication (COM), Social Camouflage (CAM), Repetitive

Behaviours (REP), Cognitive Rigidity (RIG), and Sensory Sensitivity (SEN). Previous research has indicated cultural differences in the expression and interpretation of autistic traits (Freeth et al., 2013). Additionally, sex differences in autistic traits have been widely reported, with males generally showing higher levels of autistic characteristics (See for example, Greenberg et al., 2018). However, recent research suggests that these may vary across different domains of autistic traits (Mahendiran et al., 2019; Siracusano et al., 2021).
Objectives: This study aimed to compare CATI scores between an English-speaking sample (mostly from Australia and the UK), and a Hebrew speaking24/ Israeli sample, to examine associations between subscales across cultural groups, and to investigate sex differences and age effects on CATI scores.
Method: 1997 individuals (995 English-speakers, 1002 Israeli) completed the CATI. Correlational analyses and a mixed-design ANOVA were conducted, with subscale as a within-subjects factor, cultural background and sex as between-subjects factors, and age as a covariate.
Results: Correlational analyses revealed varying subscale correlation strength across culture ($r = .29$ to $.44$, all $p<.001$), whereas Total CATI scores were strongly correlated cross-culturally ($r = .73$, $p<.001$), supporting the need for further analysis. The ANOVA revealed significant main effects for subscale ($F(5,1988)=167.24$, $p<.001$), with RIG showing the highest mean score ($M = 22.24$, $SD=7.76$) and COM the lowest ($M=13.90$, $SD=4.87$); for cultural background ($F(1,1992) = 61.208$, $p <.001$) with English-speakers scoring higher than Israeli participants; and for sex ($F(1, 1992)=6.34$, $p=.012$) with males ($M=18.52$, $SE=.14$) scoring higher than females ($M=18.04$, $SE=.14$).
In addition, significant interactions were found between subscale and cultural background ($F(5,1988)=39.23$, $p<.001$) and between subscale and sex ($F(5,1988)=37.76$, $p<.001$) (Figures 1&2). These interactions suggest that the pattern of scores across subscales differed by cultural background and by sex. Post-hoc analyses revealed that English-speaking participants scored significantly higher than Israeli participants on SOC (Mean Difference (MD) = 4.47, $SE=.34$, $p < .001$), COM ($MD=1.35$, $SE=.22$, $p<.001$), REP ($MD=1.21$, $SE=.29$, $p<.001$), and RIG ($MD=1.34$, $SE=.27$, $p<.001$) subscales. Regarding sex differences, males scored higher on COM ($MD=1.94$, $SE=.21$, $p<.001$), CAM ($MD=0.75$,$SE=.27$, $p=.005$), REP ($MD=1.36$, $SE=.28$, $p<.001$), and RIG ($MD=.54$, $SE=.26$, $p=.034$), while females scored higher on SEN ($MD=1.72$, $SE=.29$, $p<.001$).
Age significantly effected CATI scores ($F(1,1992)=77.49$, $p<.001$), with a general trend of increasing scores with age across most subscales, particularly the REP, CAM and RIG subscales.
Conclusions: The CATI demonstrates cross-cultural differences in autistic trait profiles, with English-speaking participants generally scoring higher than Hebrew speakers. Sex differences were observed across subscales, highlighting the importance of considering sex in autistic trait assessment. Age influences CATI scores, suggesting a need for age-specific norms. The CATI shows promise as a cross-cultural measure, though culture-specific

cutoffs may be required for screening purposes. These findings contribute to our understanding of the broader autism phenotype across cultures and emphasize the importance of cultural considerations in autistic trait assessment.

24. Peer Interaction in Peer Interaction in Late Diagnosed Autistic Adolescents' Boys and Girls.

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Background. Sex differences can be informative with regards to personalization of social intervention to facilitate peer interaction which is consider as a core deficit in autism-but due to lack of observational tools that allow a comprehensive assessment of social-communicative abilities, during spontaneous peer- interaction situation-it is hard to discern those informative sex differences.

Objective. The current study set out to close the gap in the literature and examine sex differences in the social-communication behavior and personality characteristics (externalizing, internalizing) of autistic adolescents who diagnosed late (during adolescence) boys versus girls (12-18 years), during natural peer interaction situation. We also examined the link between observed peer interactive behaviors and parental report of their children's social deficit, adaptive skills, and personality characteristics (externalizing, internalizing) with relations to sex differences.

Method. Participants included sixty-one adolescents with autism, (*n*=31 boys, CA=179.10 months, IQ=104.94;*n*= 30 girls, CA=184.97 months, IQ=103.30). The social-communicative abilities assessed using the Autism Peer Interaction Observation Scale-Adolescence (APIOS-A) which was adapted and validated for the present study, based on the APIOS-Young for preschoolers (Bauminger-Zviley & Shefer, 2020). The APIOS-A included 7 social communication categories (non-verbal communication, social and prosocial behaviors, discourse skills, general interaction quality indicators, shared enjoyment, and negative interaction) that were coded during a free play situation. The APIOS-A is mapping the core areas of the social disability of boys and girls with autism and enables the creation of a hierarchical profile of their social and communication difficulties severity on a scale ranging from 1-typical behavior to 4-atypical behavior. In addition, we used standardized questionnaires to assess social and communicative behavior (SRS-2, Constantino, 2013

and ABAS-II; Lopata et al., 2012), and personality characteristics -externalizing and internalizing behaviors (CBCL, Achenbach, 1991).

Results. Surprisingly, boys and girls showed similar level of social deficit according to the various APIOS-A interactive behaviours (see Figure 1). The most challenging behaviours for both groups were non-verbal communication followed by prosocial behaviors and lastly discourse skill was the least severely affected interactive behaviours for boys and girls. The examination of the link between the APIOS-A, SRS-2, ABAS and CBCL with relation to sex differences revealed important information that validated the APIOS-A as a valid observation scale to tap socio-communicative deficit in boys and girls with autism. For example, among boys, less severe disability of the APIOS-A's behaviours (e.g., understanding and use of humor, discourse skills, the ability for mental flexibility and the quality of their initiative references) were correlated with higher social and adaptive ability according to ABAS-II and less of social deficit's severity according to the SRS-2. Among girls, higher severity of internalizing behaviors was correlated with more deficient social sharing abilities according to the APIOS-A.

Conclusion: The integration of the information obtained from the APIOS-A on adolescent's boys and girls with autism, together with the information obtained from the standard tools accepted in the field, helps characterize the difficulties and strengths of adolescents with autism and may help determine targeted goal and objectives in the construction of social intervention.

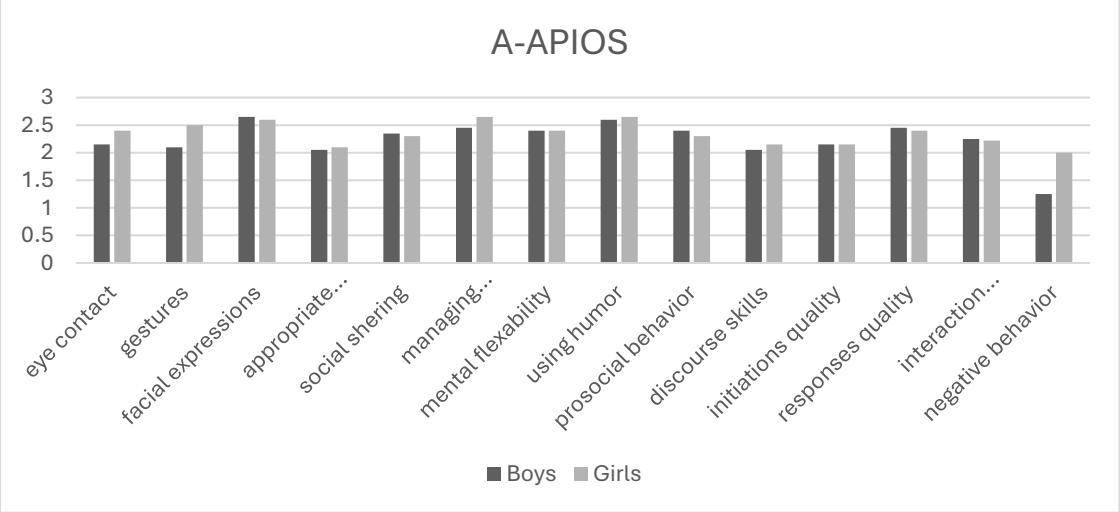

Figure -1: APIOS-A hierarchical socio-communicative profile for boys and girls with autism

25. Understanding the Purpose of Treatments: Perspectives of Children with Autism

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Introduction: While parents' and professionals' perspectives on children with autism spectrum disorder (ASD) have been extensively studied, limited data exist on the views of children with ASD regarding their needs and the objectives of the interventions they experience.
Methods: Nineteen children and adolescents (ages 5.7–14.2 years) formally diagnosed with ASD, with borderline to high intelligence (range 70–140), and able to converse verbally were interviewed in person at a child development clinic. A qualitative approach was used to capture children's perceptions of their understanding of a novel ASD treatment. The interview included direct and projective open-ended questions on each topic. Interpretive content analysis was used to evaluate the children's answers. Medical data were extracted from medical records. The children's parents completed questionnaires on their children's disability levels, awareness of ASD diagnosis, and sociodemographic details.
Findings: The study identified four themes: (1) comprehension of the therapeutic intervention, (2) understanding the therapeutic framework, (3) understanding the practical requirements and considerations, and (4) engagement in the healthcare dialogue. Children exhibited varying levels of understanding regarding the educational and therapeutic goals established for them. Notably, only one boy explicitly identified his diagnosis, actively participated in goal setting, and was encouraged to express his preferences.
Discussion and conclusions: Children with ASD are frequently excluded from the process of patient information provision and lack an understanding of the goals of interventions. Findings suggest the need to explore developmentally and emotionally adaptive ways to involve children with ASD in discussions of their condition and possible interventions.

26. Are preschool children with autism more likely to be placed in special education if they exhibit aberrant behaviors?

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Background: In many western countries autistic children can be placed in either special or mainstream preschool educational settings. These settings often differ dramatically in their cost, exposure to typically developing children, expertise and size of the educational staff, and their ability to incorporate structured autism intervention. Surprisingly little research has examined how placement decisions are made or what child characteristics predict placement in one setting versus the other. Previous studies have reported that children with lower cogni-tive abilities were more likely to be placed in special rather than mainstream preschool set-tings.
Objective: To identify the strongest predictors of first year preschool educational placement in special versus mainstream education in Israel.

Methods: We recruited 165 children with autism as they entered their first year of kindergarten, at an average age of 37.86 (SD=4.4) months (i.e, 3-4-years-old). Of these children, 120 (73%) were placed in special education and 45 (27%) in mainstream education. All children completed the Autism Diagnostic Observation Schedule (ADOS-2), and most completed as-sessment of cognitive abilities with the Bayley or Mullen (n = 114), adaptive behaviors with the Adaptive Behavior Rating Scale 3rd edition (ABAS-3) (n = 113), and aberrant behaviors with the Aberrant Behavior Checklist (ABC) (n = 126). We used t-tests to compare children placed in mainstream versus special education settings and multiple logistic regression to de-termine the relative contribution of assessment scores in predicting educational placement. We also performed the same comparison across educational settings only with children with-out intellectual disability (NID, cognitive scores > 80).
Results: Children placed in special education exhibited significantly lower cognitive scores [80.8 vs 68.7; p=0.014], were diagnosed at an earlier age [33.8 vs 30.2; p=0.014] and their

mothers had fewer years of education [14.7 vs 13.6; p=0.04]. There were no significant differences across settings in ADOS-2 Calibrated Severity Scores (CSS), ADOS-2 social affect (SA) CSS, ADOS-2 restricted and repetitive behaviors (RRB) CSS, ABAS-3 general score and all 5 subscales of the ABC. However, when isolating the analysis to NID children, those placed in special education exhibited significantly higher ABC: Irritability scores [7.29 vs 14.2; p=0.012]. A logistic regression analysis revealed that ADOS RRB-CSS (OR = 10.98, p = 0.009) and ABC: Irritability scores (OR = 7.01, p = 0.013) were both significant predictors of placement.

Conclusions: These findings suggest that early placement decisions for children with ASD entering kindergarten are primarily influenced by cognitive abilities. However, for children without intellectual disability, severity of repetitive behaviors and irritability are predictors of placement. In contrast the severity of core autism social symptoms does not seem to be a sig-nificant factor in placement decisions.

27. Language, Theory of Mind, and non-verbal Cognitive Measures in Arabic-speaking children with autism: Evidence from Network and Clusters Analyses

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Background: Autism spectrum disorder (ASD) is characterized by impairments in social interactions, communication, and repetitive, stereotyped behaviors[1] . While language difficulties are not core symptoms of ASD, they frequently co-occur. Language profiles in autistic children range from minimally verbal to fluent speakers with impaired or age-appropriate skills[2] . Theory of mind (ToM) deficits, which involve difficulties in understanding others' mental states, are common in ASD[3,4] , and challenges in non-verbal cognitive abilities, including executive function (EF) challenges such as inhibition, flexibility[5] , and central coherence processing (local vs. global)[6] . These deficits impact daily functioning and learning. Research has reported mixed findings on the relationships between language (phonology, morphosyntax, lexicon, pragmatics), ToM, EF, and central coherence in autistic children[7] . This study aims to contribute to this debate by providing evidence from Arabic-speaking children—an understudied group.

Objectives: This study investigates the language profiles of Palestinian-Arabic-speaking children with and without ASD, focusing on the relationship between language, background variables (age and ASD severity), ToM, and non-verbal cognitive skills. It explores the interrelatedness and independence of these skills through network analysis. Furthermore,

we examine language profiles in children with ASD using cluster analysis, linking these profiles to ToM and cognitive abilities.
Methods: The sample included 163 Palestinian-Arabic-speaking children aged 4 to 12, comprising children with ASD and those with typical language development (TLD). Language assessments covered phonology (indexed by non-word repetition), morphosyntax (measured by sentence repetition), lexicon (evaluated through vocabulary tasks), and pragmatics (assessed using speech acts and narrative tasks). Additional evaluations encompassed verbal and non-verbal ToM tasks, non-verbal IQ, as well as measures of inhibition, flexibility, and central coherence.
Results: Group-level results showed that children with ASD underperformed their TLD peers across all measures. Network analysis revealed robust interconnections between language, ToM, and cognitive skills in both groups. In autistic children, language was a central node, with pragmatics prevailing over morphosyntax and lexicon, while age was central in the TLD group. Cluster analysis identified four language clusters within the ASD group, demonstrating dissociations between language domains: (1) high performance across all domains, (2) moderate performance in phonology and morphosyntax with low pragmatic abilities, (3) moderate performance in phonology and lexicon with low morphosyntax and pragmatics, and (4) moderate phonology and lexicon with extremely poor morphosyntax and pragmatics— autistic children with enhanced language abilities performed better in verbal and non-verbal ToM and EF tasks.
Conclusions: The findings underscore the variability and dissociations within and between language domains in children with ASD. These results provide valuable insights into the interplay between language, cognitive abilities, and ToM, offering implications for personalized interventions targeting specific language and cognitive profiles.

28. Ecological momentary assessment: A novel tool for assessing RRBs and their relationship with adaptive functioning

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Background: Restricted and repetitive behaviors (RRBs) represent a heterogeneous group of behaviors, ranging from repetitive motor movements and speech to persistent rituals and preoccupation with intense and fixed interests. These vary from person to person and their presentation can change within individuals across time and contexts (Lombardo et al., 2019). The literature shows inconsistent findings regarding the relationship between RRBs and adaptive functioning, partially due to our inability to accurately assess these traits. Researchers and autistic self-advocates have long expressed concerns regarding the state of assessment of autistic traits, including challenges related to content and ecological

validity (e.g., Sturm et al., 2017). RRBs have proven particularly difficult to reliably and validly measure (e.g., Uljarević, 2021). Most studies rely on observational measures of autism symptomatology, which largely skew toward criterion A of the DSM, impairment in social communication and interaction. Such measures (e.g., ADOS) produce a single score intended to capture all RRBs, ignoring the variable nature of this symptom class (Ozonoff et al., 2005). An ecological momentary assessment (EMA) of RRBs could serve to capture the multidimensionality of RRBs and more accurately characterize the way in which they manifest in different contexts in the child's daily life. This framework would allow to examine how specific RRBs associate with functional outcomes in the context of a specific child and his/her environment, allowing for the differentiation of adaptive from maladaptive RRBs in a subjective fashion.

Objectives: (1) To establish the feasibility of the EMA of RRBs. (2) To examine the association between RRB subtypes, as measured through EMA, and adaptive functioning in a subjective manner.

Methods: Participants are parents of autistic children aged 3-6. Through a novel mobile EMA platform developed by the Computerized Neuroscience Laboratory at the Hebrew University (Yitzhak et al., 2023; Nahum et al., 2023), participants will report on the frequency of six subtypes of RRBs twice daily for a period of two weeks. Participants will also report on child adaptive functioning (ABAS-3; Harrison & Oakland, 2015). Hierarchical linear modeling will be used to examine patterns of association between RRB subtypes and adaptive functioning.

Results: Preliminary analyses from 8 participants (2 females; mean age = 50±9.7 months) show feasibility for the EMA tool, pointing to high completion rates (mean = 86.5% ± 24.3, range = 50- 100%) and time efficiency (mean time to complete per EMA entry = 3.8 min). The EMA data reveals a unique RRB profile for each child, and comparison of EMA data to retrospective parent-report measure (i.e., RBS-R; Bodfish et al., 1999) shows that EMA provides a distinct perspective on RRB expression (see Figures below). Data collection is ongoing and future analyses with a larger sample will examine associations of RRB subtypes and adaptive functioning.

Conclusions: EMA is a feasible framework for measuring RRBs, which may more accurately depict naturalistic RRB phenotypes than single timepoint retrospective reporting. Through this framework, we can examine how specific RRBs associate with functional outcomes in the context of a specific child, operationalizing a way to distinguish adaptive from maladaptive RRBs.

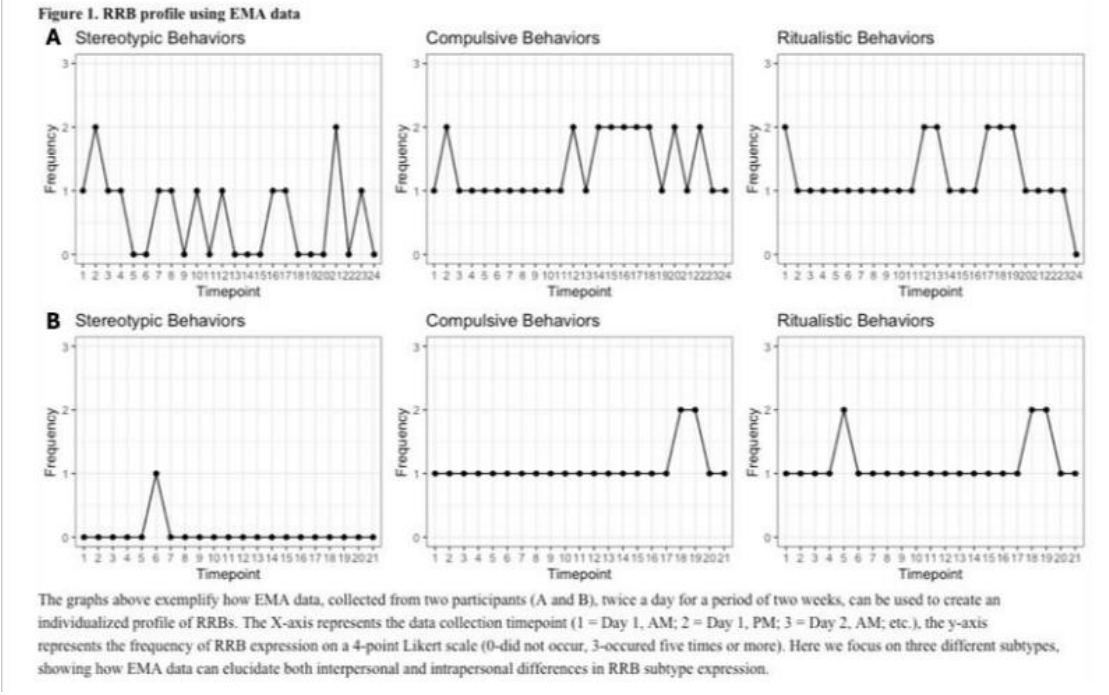

Figure 1. RRB profile using EMA data

The graphs above exemplify how EMA data, collected from two participants (A and B), twice a day for a period of two weeks, can be used to create an individualized profile of RRBs. The X-axis represents the data collection timepoint (1 = Day 1, AM; 2 = Day 1, PM; 3 = Day 2, AM; etc.), the y-axis represents the frequency of RRB expression on a 4-point Likert scale (0-did not occur, 3-occured five times or more). Here we focus on three different subtypes, showing how EMA data can elucidate both interpersonal and intrapersonal differences in RRB subtype expression.

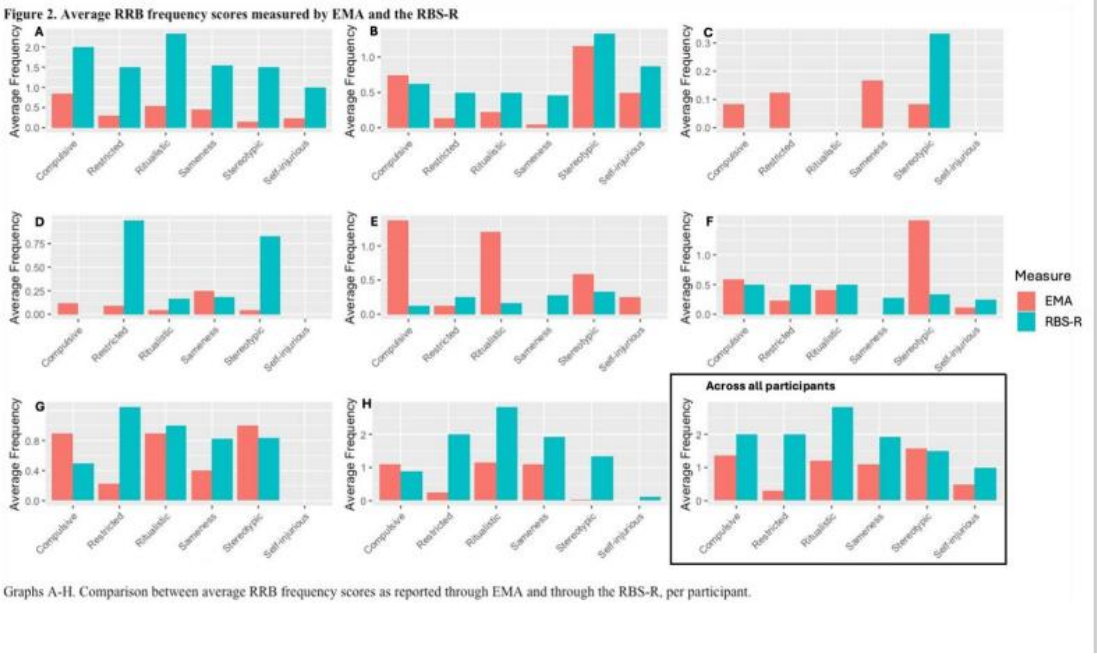

Figure 2. Average RRB frequency scores measured by EMA and the RBS-R

Graphs A-H. Comparison between average RRB frequency scores as reported through EMA and through the RBS-R, per participant.

29. Cognitive Control and Broad Autism Phenotype among Parents of Autistic Children

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Background: Autism symptomatology is normally distributed in the population, with elevated symptom expression equating an autism diagnosis and milder, subclinical cases as capturing the Broad Autism Phenotype (BAP). BAP is associated with real-world functional challenges across multiple domains. Its relationship with cognitive control (CC), defined as the capacity to regulate, coordinate, and direct cognitive processes such as attention, memory, and problem-solving to achieve goal-directed behavior, remains unclear due to inconsistent findings.
Methods: Within the context of a larger study examining CC and BAP, including experimental assessment of parental CC, and measures of family accommodation and child's symptom expression, the current study focuses on the association between parent self-report of CC (ADEXI) and BAP (BAPQ). The sample consists of 78 parents of 2-4-year-old children (44 autistic; 34 non-autistic).
Results: Results revealed, across all parents, significant correlations between the pragmatic language index from the BAPQ and all ADEXI indices: working memory ($r(76)=.35$, $p=.001$), inhibition ($r(76)=.28$, $p=.009$), and total ADEXI scores ($r(76)=.35$, $p=.001$). Parents of autistic children exhibited higher CC impairments ($M = 34.93$) than parents of non-autistic children ($M=27.53$), $t(75.51)=3.90$, $p <.001$.
Conclusions: This study contributes to our understanding of cognitive mechanisms underlying parenting in autism, linking CC with BAP, particularly regarding pragmatic language. It also identifies differences in CC abilities between parents of autistic and non-autistic children. The inclusion of experimental data and additional parent and child variables measures will deepen insights into how cognitive and behavioral dynamics interact within families and may inform targeted interventions to support parents of autistic children.

30. Effects of the October 7th Attacks and the Ensuing War on Autistic Children in Israel and Their Parents

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Introduction: The October 7th attacks, the ensuing war, and consequent upheaval in daily life in Israel present unique challenges to autistic children, who rely on routine and predictability. This is the first ever study of the experience of autistic children and their parents in the context of war.
Methods: Study 1 is a one-year longitudinal study in which parent-report of child trauma (CATS) and parental negative emotional states (DASS) has been collected on autistic (n=57; 32 males; mean age = 7.02 years, SD=3.7) and non-autistic (n=35; 16 males; mean age = 7.12 years, SD=3.65) children every two months beginning October 2024. Data from an independent study before October 7th (N=55; 43 males; mean age = 4.5 years, SD=1.02) allowed for comparison of DASS scores across pre/post-war cohorts of autistic children. Study 2 is a complementary cross-sectional, mixed-methods study (n=72). Parent-report measures and interviews assessed the above constructs as well as parental trauma (PCL-5) and parental resilience (BRS).
Preliminary Results: In Study 1, parents of autistic and non-autistic children report trauma above the cut-off for PTSD, with autistic children (M=34.7, SD=12.5) scoring significantly higher than their non-autistic peers (M=28.5, SD=9.95), $t_{(75.43)} = 2.47$, $p < 0.05$, $d = 0.54$. Parents of autistic children reported elevated levels of stress ($t_{(df)} = x$; $p < 0.05$, d=0.56) and anxiety ($t_{(df)} = x$; $p < 0.001$, d=0.84) compared to parents of non-autistic children. Final analyses will be conducted in November 2025 upon completion of data collection. Parental negative emotional states in parents of autistic children were 2-4 times higher in the month following October 7th than in the independent, pre-war sample ($p <$ 0.001, d=2.62-2.77).
In Study 2, parental trauma, together with higher anxiety levels, accounted for 43.8% of the explained variance of child trauma ($R^2 = 0.438$). Quantitative and qualitative analyses are ongoing.
Conclusion: Parent-reported levels of trauma in autistic and non-autistic children post-October 7th are strikingly high, as are negative emotional states in parents. Autistic children and their parents appear to experience even more pronounced distress. It is essential to consider these findings in supporting children and families affected by war.

31. A Pilot Trial of the Social ABCs in Israel

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Background: Studies have demonstrated that autistic children can exhibit delay in language development and social-communication skills (Brian et al., 2015). The Social ABCs, a parent-mediated intervention for toddlers originally developed in Canada (Brian et al., 2016), targets early functional verbal communication and positive affect sharing in the context of play and caregiving activities.
Objectives: The aim of the current pilot study was to evaluate the impact of the intervention in Israel on various child and parent variables, using both standardized tools and questionnaires.
Methods: Participants were 17 autistic children aged 19-39 months (M=26.4, SD = 5.61; 94.1% male) who participated in the Social ABCs in two sites in Israel. The current study followed the group Social ABCs protocol, which includes 6 online parent group sessions, and 9 frontal coaching parent-child sessions. Children were administered a gold-standard evaluation prior to the intervention and 6 weeks after completion of the protocol. Relevant measures included assessments of autism symptom severity (ADOS-2); developmental screening (Communication and Symbolic Behavior Scales Developmental Profile; CSBS-DP), lexical capacity, (Hebrew Communicative Development Inventory (HCDI); parenting stress (PSI-SR), and aberrant behaviors (ABC).
Results: Of 25 families who met inclusion criteria, 20 (80%) elected to participate in the intervention program, and 17 completed the intervention. Parents rated the intervention as highly satisfactory (M=33.13, SD =2.78, of a maximum score of 35). Children's vocabulary increased significantly from pre- to post-intervention both for expressive ($t(14)=-4.11$, $p=0.001$) and receptive vocabulary ($t(14)=-3.94$, $p=0.002$) with large effect sizes ($d>1.0$). We found no statistical change in the ADOS Social Affect Calibrated-Severity-Score, but significant gains were observed both for the social ($t(14)=-2.90$, $p=0.012$) and speech composites ($t(14)=-2.20$, $p=0.045$) of the CSBS-DP. A significant decrease in parenting stress scores occurred in the Parent-Child Dysfunctional Interaction (PCDI) subscale ($t(16)=3.25$, $p=0.005$), indicating lower stress during parent-child interaction. ABC scores showed a significant decrease in the Social Withdrawal subscale ($t(16)=2.42$, $p=0.028$), indicating increased social involvement of the child.
Conclusions: This study provides evidence that the Social ABCs is feasible, acceptable, and satisfactory in Israel. In the current pilot study, improvement was noted in child social functioning and language development, and reduced reported dysfunctionality in parent-child interactions.

32. Cortical Sound Processing Alterations in Autism Spectrum Disorder

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Autism spectrum disorder (ASD) is often associated with altered sensory processing. One of the main sensory-related symptoms in individuals with ASD is auditory hypersensitivity. We used a combination of in-vivo two-photon imaging and rodent behavior to understand how sound processing and loudness perception are modulated in ASD. When examining cortical activity in ASD mice, we found increased spontaneous and sound-evoked activity as well as an increase in the percentage of sound-responsive cells when compared to WT mice. To test if these cortical changes affect sound perception, we trained mice in a 2AFC loudness perception task. We found that intermediate tone intensities (44-65 dB SPL) sounds, categorized as soft by WT mice, were more frequently reported as loud by ASD mice. Together these findings suggest a possible mechanism underlying increased loudness perception in ASD.

33. Empowering Diagnosis: Uncovering the Impact of Wechsler Test Repetitive Behavioral Data in ASD Assessment.

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Introduction: Autism Spectrum Disorder (ASD) is a complex neurodevelopmental disorder. Early diagnosis of ASD is essential to provide comprehensive treatment to individuals with ASD and their families. The ADOS and ADI are widely used clinical tools for diagnosing ASD. The Wechsler Intelligence Scale for Children (WISC) is widely used to assess cognitive ability among children but not to evaluate the autistic features. We hypothesis that repetitive behaviors during the WISC cognitive test can provide information about the risk of autism and therefore serve as a screening tool for ASD diagnosis.

Methods: A prospective study was conducted on children age 6-18 years who were examined at the Autism Diagnosis Clinic at Bnai Zion Medical Center. A thorough evaluation using the WISC, ADOS and ADI tests was conducted. A unique scale for repetitive behaviors during the conduction of the WISC (WISC-RRB's) was used to evaluate autistic behaviors.

Results: Fifty children (70% males) participated in the study. No significant difference was found in IQ, age, and score in diagnostic tests between males and females. Older children with ASD had significantly higher IQ. A significant correlation was found between WISC-RRB's and Autism diagnosis compared to children without ASD. A negative correlation was found between IQ and stereotypical behaviors in the Wechsler test (WISC-RRB's).
Conclusions: Stereotypical behaviors observed during the WISC test were in correlation with the diagnosis of ASD. Thus, the WISC, which is widely used for evaluation of cognition might be useful as a screening tool for ASD.

34. Behavioral differences in autism across different tasks and behavioral domains

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Autism is characterized by behavioral differences that can vary widely among individuals, often making diagnosis and assessment challenging. This study investigated the variability in behavior across different tasks and behavioral domains during the Autism Diagnostic Observation Schedule (ADOS) assessment. We analyzed three specific ADOS tasks—Emotional Questions (EMO), Storytelling (STO), and Tooth brushing (TB) under three behavioral domains: gaze, facial expressions, and vocal characteristics. Behavioral features were extracted using Computer Vision and Speech analysis tools and analyzed through machine learning classifiers. Several machine learning models were trained independently using different combinations of tasks and domains to distinguish autistic from nonautistic individuals. Two forms of analysis were conducted, first-order features (individual task-domain features) were used to asses' difference in behavior within tasks and domains and secondorder features (differences in feature values between tasks) were used to analyze the difference between autistic and nonautistic in the changes of behaviors between tasks. Results showed distinct patterns of behavior across tasks, highlighting the differential importance of domains. For example, smile-related features were most predictive in the EMO task, while gaze features proved significant in TB. Combining domains and tasks improved classification accuracy, achieving a baseline of 86% in distinguishing autistic from nonautistic individuals. Second-order analyses revealed differences in how participants adapt their behavior across tasks, with nonautistic individuals showing greater variability compared to autistic individuals. This study sheds light on the intricate relationships between tasks, domain, and behavioral adaptations in autism. These findings emphasize the need for multi-domain and multi-task approaches in autism assessments to capture the behavioral diversity and improve diagnostic insights.

35. Identifying Needs and Challenging Environments to Design a Virtual Reality Environment for Intervention for Adolescents with Autism Spectrum Disorder (ASD)

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Background: Individuals with Autism Spectrum Disorder (ASD) face significant challenges in social skills and executive functions that significantly impact their daily lives. These domains are correlated, where improvement in one may facilitate progress in the other. However, existing interventions often demonstrate limited effectiveness and poor generalization to real-world scenarios. Adolescents frequently experience intervention fatigue, highlighting the need for engaging, age-appropriate solutions. Virtual Reality (VR) provides a promising platform, offering structured activities, personalization, and reduced distraction- characteristics particularly appealing to adolescents with ASD who prefer technology-based interventions.
Objectives:(1) explore adolescents with ASD's perspectives on social skills and executive function challenges by mapping challenging environments, difficulties, and needs. (2) compare these perspectives with those of parents and healthcare professionals to inform the design of a Virtual Reality (VR) intervention.
Methods: The study included 40 adolescents with ASD (34 males, six females; mean age 15.3), 36 parents (20 males, 15 females, one non-binary; mean age 47.1), and 36 healthcare/education professionals. Participants completed a special questionnaire designed by the research team, assessing challenging environments, difficulties, and environmental factors affecting functioning. The questionnaire examined five central aspects: rating the importance of different environments, VR practice preferences, identifying challenging areas, assessing difficulties in social and executive function, and rating disruptive environmental factors on a Likert scale (rating 1- low to 3- very important)
Results: A Mixed two-factor ANOVA revealed significant group [$F(2,109)=12.06$, $p<.001$], and environment type [$F(8,872)=16.61$, $p<.001$] main effects, and group x environment interaction [$F(16,872)=3.91$, $p<.001$, $\eta 2p=0.67$]. Adolescents mostly rated challenges lower than parents and professionals across all domains. Social media, schools, and shopping malls were ranked highest by adolescents, while parents and professionals agreed on school and emphasized public transportation and supermarkets. The school playground during recess emerged as particularly challenging, with parents and adolescents rating it significantly higher than other areas. Primary challenges included self-explanation,

initiating contact with unfamiliar people, and maintaining conversations. All groups identified crowding, noise, and the presence of many people as the most disruptive environmental factors, with less structured environments consistently rated as more challenging than structured ones.
Discussion: There is a significant discrepancy between adolescents' self-assessments and evaluations by parents and professionals, emphasizing the importance of incorporating multiple perspectives into intervention design. However, there was consensus among all participants (adolescents, parents, and therapists) regarding challenging environments (particularly unstructured school settings, playgrounds, and cafeterias) and sensory factors (notably noise levels and crowding). Identifying specific challenging settings, such as school playgrounds during recess and mall food courts, offers concrete targets for VR environment and intervention design, prioritizing skills such as self-explanation, responding to new situations, and maintaining conversations incorporating gradually increasing levels of sensory stimuli and social complexity.
Conclusions: The findings reveal important insights into the complex nature of assessing and planning age-appropriate interventions for adolescents with ASD. Including the perspective of adolescents and stakeholders is essential to enhance engagement while facilitating skill generalization to daily situations.

36. Smart Glasses for Remote Assistance: Analyzing Usability and Optimal User Characteristics Among Young Adults With and Without Autism

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Background: Young adults with autism spectrum disorder (ASD) often face challenges in achieving functional independence, particularly in areas like employment, education, and autonomy, necessitating substantial intervention support during their transition to adulthood. Technology-driven interventions such as smart glasses have demonstrated effectiveness in enhancing various skills and there are encouraging findings regarding the positive effect of integrating smart glasses as an assistive technology in intervention processes among adults with ASD. However, there is still insufficient evidence on using smart glasses as a tool for remote support.
Objectives: The aims of the current study were to assess the usability of smart glasses for remote support during daily tasks among young adults with and without ASD; to explore the correlations between the usability ratings and users' sensory, cognitive, and emotional characteristics; and to explore new clusters of potential users for remote support using smart glasses.

Methods: 44 young adults were recruited in this study aged (20–34 years) with (n = 22) and without (n = 22) ASD. Assessments, before task, included demographics, Adolescent/Adult Sensory Profile (AASP), Behavior Rating Inventory of Executive Function-Adult (BRIEF-A), and Depression and Anxiety Stress Scale (DASS) and, post task, the Usefulness, Satisfaction, and Ease-of-Use (USE) and Post-Study System Usability Questionnaire (PSSUQ).
Results: Findings showed good usability for both groups (PSSUQ M = 2.82; USE M = 5.29; SD = .81). The ASD group showed more difficulty in the ease-of-use category. Sensory characteristic correlations were found between the USE usability score and low registration ($r = -.40$, $p = .01$) and between the PSSUQ and low registration ($r = .34$, $p < .05$), seeking ($r = -.35$, $p < .05$), and sensitivity ($r = .35$, $p < .05$). Correlations were found between PSSUQ and BRIEFA for cognitive ($r = .36$, $p < .05$) and PSSUQ and DASS for emotional ($r = .30$, $p = .05$) characteristics. Cluster analysis identified a subgroup (n = 19; 43.2%) more suited for using smart glasses, with higher seeking behaviors and executive functions, lower sensitivities and negative emotional states.
Conclusions: Findings demonstrate the high usability of smart glasses among young adults with and without ASD for remote support while performing daily tasks. We managed to identify optimal user characteristics and their relationship with usability ratings, highlighting the potential of smart glasses as a promising tool for therapists. As technology evolves, we anticipate a broader use of such devices across diverse populations and therapeutic interventions. However, to optimize their effectiveness, it is crucial to consider individual's sensory, cognitive, and emotional characteristics, not just their diagnostic features, when designing and implementing smart glasses in therapy interventions. Future research should further explore and deepen our understanding of smart glasses' role as a remote support tool across a wider range of populations that target our therapy to enhance their independence and personalize their interventions according to their special needs.
Keywords: autism spectrum disorder, young adult, smart glasses, usability, remote support

37. Motor Profile Differences Between Autistic and Non-autistic Children Across Age-Groups

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Background. Significant motor functioning differences between autistic and non-autistic children, are well documented, with autistics demonstrating greater challenges in executing fine (e.g., cutting, writing) and gross (e.g., walking, jumping) motor tasks compared to their neurotypical peers. However, these differences are usually not compared across a broad developmental age-range. Moreover, no study so far presented a within hierarchical motor profile, from simplest to the most complex motor skills in autism and typical development.

Objectives. This study investigated group (autistic, non-autistic) and age (early-childhood, preadolescence, adolescence) differences in motor functioning. We predicted better motor functioning in the non-autistic group and among older participants. Moreover, we examined within-group differences in fine and gross motor functioning to identify each study-group's hierarchical motor profile. Predicting this profile was difficult due to the limited prior research.

Method. This study included 84 autistic children ages 6-16 years, and 64 non-autistic children matched by age, sex, IQ, and mother education across three age groups (early-childhood, 6-8.5 years, preadolescents, 8.5-12 years, adolescents, 12-16 years). The participants' gross (e.g., catching a ball, hopping) and fine (e.g., Curved-line cutting and nailing) motor skills were assessed using the Individual Motoric Observation Scale (IMOS), yielding scores for each motor behavior, gross and fine motor categories, and overall motor functioning. The IMOS score reflected the percentages of success in each task according to proficiency and quality for various appearance and accuracy components.

Results. Group (autistic/non-autistic) and age (early-childhood/preadolescence/adolescence) differences in motor abilities were computed by a series of multivariate and univariate analyses of variance (MANOVAs, follow-up ANOVAs). One-way ANOVAs were conducted for the IMOS total score. Overall, non-autistic showed more advanced fine and gross-motor abilities than their autistic counterparts. The adolescents age-group outperformed early-childhood participants on most motor tasks (see Table 1). However, the overall motor performance of non-autistic early-childhood participants was similar to that of autistic adolescents. To explore hierarchical motor profiles differences within each study-groups we compared IMOS components' scores using repeated-measure ANOVA for each group.. Post-hoc pairwise comparisons used Bonferroni correction to signify the scale of difficulty from the easiest (a) to the complexed (e) motor task in each group. The non-autistic group exhibited a more homogeneous developmental motor profile, with only two levels of difficulty (a,b). Curved-line cutting and ball catching were more challenging than other motor tasks. In contrast, the autistic group displayed a broader range of motor difficulties, thus hopping was the easiest task (a) and ball catching was the most complexed (e) (see Figure 1).

Conclusions. Findings align with previous studies depicting motor abilities differences between autistic and non-autistic children. Our investigation of the motor development continuum across three developmental age-groups within the autistic group, despite their motor difficulties, is novel, suggesting their potential motor skills advancement. The variation in the motor profile within each study-group, particularly in the sequence of skill acquisition and the range of task difficulties, enhances our understanding and lead to the development of motor intervention programs focusing on more complex motor tasks that present greater challenges for autistic youth.

Table 1

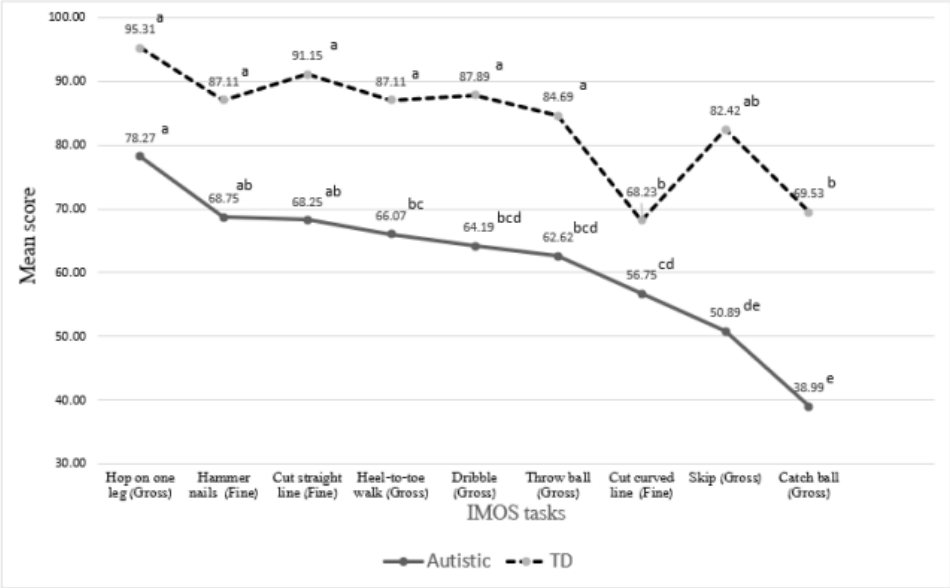
Univariate and Multivariate F Values and η_p^2 for Main Effects, Group x Age Interactions, and Post Hoc Analyses for IMOS Components (N=148)

Individual Motor Observation Scale (IMOS) tasks		Group	*p*	η_p^2	Age	*p*	η_p^2	Between-age differences	Group x Age	*P*	η_p^2	Within-group differences
		F(1,142)			*F*(2,142)				*F*(2,142)			
Gross-motor	Throw ball	**47.23**	.000	.25	**5.21**	.007	.07	1<2,3	**3.45**	.035	.05	$1_{autism}<2,3_{autism}$
	Catch ball	**39.09**	.000	.21	**16.78**	.000	.19	1<2,3	0.71	.492	.01	
	Dribble	**64.24**	.000	.31	**29.16**	.000	.29	1<2<3	1.60	.207	.02	
	Hop	**21.41**	.000	.13	2.52	.084	.03		.74	.479	.01	
	Heel-to-toe walk	**36.05**	.000	.20	**8.91**	.000	.11	1,2<3	.24	.789	.00	
	Skip	**27.32**	.000	.16	**7.01**	.001	.09	1<2,3	1.70	.186	.02	
	MANOVA	*F*(6,137) **21.35**	.000	.48	*F*(12,274) **6.68**	.000	.27		*F*(12,274) 1.52	.118	.06	
		F(1,142)			*F*(1,142)				*F*(1,142)			
Fine-motor	Cut straight line	**41.81**	.000	.23	**15.00**	.000	.17	1<2<3	2.12	.123	.03	
	Cut curved line	**11.38**	.001	.07	**20.66**	.000	.23	1<2,3	2.15	.120	.03	
	Hammer nails	**24.03**	.000	.15	**7.70**	.001	.10	1,2<3	.32	.726	.00	
	MANOVA	*F*(3,140) **16.12**	.000	.26	*F*(6,280) **8.66**	.000	.16		*F*(6,280) **2.93**	.009	.06	
IMOS Total		*F*(1,142) **125.53**	.000	.47	*F*(1,142) **37.99**	.000	.35	1<2<3	*F*(1,142) .23	.794	.00	

Note. Age 1= Early-childhood, Age 2= Preadolescence, Age 3= Adolescence. Values in bold are significant.

Figure 1

Within-Group Hierarchical Profile of Difficulty on IMOS Motor Tasks



Note. The letters denote within-group differences (a-easiest throw e-hardest) – significant pairwise comparisons at the level of at least $p<0.05$ according to Bonferroni correction.

38. Visual Search and ASD: Basic vs. Superordinate Category Search

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Abstract: Visual search has been classified as easy feature search, with rapid target detection and little set-size dependence, versus slower difficult search, with focused attention and set-size-dependent speed. Reverse Hierarchy Theory attributes these classes to rapid high-cortical-level "vision at a glance" versus return-to-low-level "vision with scrutiny," attributing easy search to high-level representations. Accordingly, faces tend to "pop out" of heterogeneous object photographs. Individuals with Autism Spectrum Disorder (ASD) have difficulties recognizing faces, and yet we found this disability doesn't disturb face search.

We now explore visual categorization abilities in individuals with ASD, focusing on differences between basic-level and superordinate-level tasks. In the basic-level task, participants were asked to detect specific items within a category, such as "dogs" or "apples." In contrast, the superordinate-level task required them to categorize objects into broader groups, such as "animals" or "food." For each task, we presented a set of 4 –64 images, with participants instructed to touch the image that matched the target category as quickly as possible. The test was structured to observe how reaction times (RT) changed as the number of items in the set increased, allowing us to analyze the relationship between set size and RT.

We find that individuals with ASD encounter greater challenges when performing superordinate categorization compared to basic categorization. For basic-level categorization, participants showed faster reaction times and less variability across set sizes. This suggests that recognizing objects at a basic level requires less cognitive effort and is a more automatic process. In contrast, when tasked with superordinate-level categorization, which involved broader categories, participants experienced greater challenges. Superordinate-level search showed a significantly stronger set-size effect, with RTs increasing by (92 ms/item), compared to (50 ms/item) for basic-level search. These results suggest that superordinate-level categorization involves higher cognitive challenges and more effortful, deliberate processing, which can be more challenging for individuals with ASD.

Furthermore, the increased variability in performance, particularly at the superordinate level, indicates that different individuals with ASD may face varying levels of difficulty depending on their cognitive processing abilities. This pattern aligns with previous findings that basic-level categorization is typically faster and more efficient, as it relies on

distinguishing specific, easily identifiable features, whereas superordinate categorization requires a broader, more generalized conceptual understanding.

39. Predicting the Attainment of an ASD Diagnosis: A Classification Tree Analysis of an Israeli Tertiary Sample

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Background: The last two decades have seen a significant increase in the prevalence of ASD. While many autistic children are diagnosed as toddlers, diagnosing older children and adolescents with intact intelligence with ASD is more complex. The clinical profiles of these individuals, based on socio-demographic factors and on social communication (SC) and restricted repetitive behavior (RRB) scores on standardized diagnostic measures have received little empirical attention.
Objectives: To examine how children's socio-demographic factors and children's performance on standardized diagnostic measures, predict the attainment of an ASD diagnosis.
Methods: Data were collected from records of children and adolescents who were referred to "Bayit Echad" ASD tertiary centers between the years 2013-2018, with a question of an ASD diagnosis. Records of 466 Israeli children and adolescents (84.1% boys), aged 4–18 years (M = 11.14, SD = 3.59) were included. Assessments were made by clinical psychologists, according to DSM-5 criteria, based on ADOS-2 and ADI-R assessments. 55.6% of cases had a previous diagnosis of ADHD and 15.7% had a previous diagnosis of an anxiety disorder.
A classification tree analysis (CTA) was employed to evaluate how combinations of background factors and diagnostic tools' scores can be used to anticipate the binary diagnostic result. We used the chi-squared automatic interaction detector (CHAID) growth method and set the minimum parent nodes to 60 and the child nodes to 30.
Results: The dependent variable in the CTA was ASD diagnosis (Y/N) with 66.7% meeting the diagnosis criteria. Overall prediction accuracy was good .82. The algorithm classified those with a diagnosis of ASD with an accuracy rate of .88 (i.e., sensitivity), and those without a diagnosis of ASD with an accuracy rate of .70 (i.e., specificity).
The most predictive variable of ASD was ADOS-SA. The algorithm partialed the ADOS-SA range into four categories. The first category included 17% of the participants with ADOS-SA lower or equal to 3. These participants were mostly and correctly classified as not meeting the ASD cut-off. This classification of children as having no ASD was further improved if they previously had an ADHD diagnosis.

The second category (15.5%) included participants with ADOS-SA values ranging from 3 to 5 whose accurate classification was improved with the aid of ADI-Social Interaction and Communication scores.
The third category (17.6%) included participants with mid-high ADOS-SA values ranging from 5 to 7.1 whose accurate classification was improved with the inclusion of ADOS-RRB. The fourth and last ADOS-SA range included 50% of the sample and was characterized by high ADOS-SA values (> 7.1). For participants in this category, ASD was correctly predicted in 88.4%, but the inclusion of ADI-RRB further improved its accuracy. Classification improved even more when participants were 12 or younger. Figure 1 illustrates the CTA.
Conclusions: Combining scores from clinical diagnostic measures examining child behavior and parent review of the child's development increase diagnostic accuracy, especially in pre-adolescence. This integrated picture distinguishes well between children who have ASD and children with other neurodevelopmental conditions, such as ADHD.

40. Maternal influenza vaccination during pregnancy and risk of ASD in the offspring

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Background: Autism Spectrum Disorder (ASD) is a developmental neurological disorder affecting 2.2% of the global population, characterized by persistent social communication challenges and repetitive behavioral patterns. While its etiology is multifactorial, involving genetic and environmental factors, maternal infections during pregnancy have been recognized as potential contributors. Influenza vaccination during pregnancy is widely recommended to reduce maternal and fetal complications, but its association with ASD risk remains understudied. Few large-scale studies have examined this relationship, leaving a critical gap on the safety of influenza vaccination during pregnancy.
Objectives: This study aimed to investigate the association between maternal influenza vaccination during pregnancy and the risk of ASD in offspring. A secondary objective was to evaluate whether the timing of vaccination during specific pregnancy trimesters influenced ASD risk.
Methods: A retrospective cohort study was conducted using data from the Clalit Health Organization, encompassing 145,956 live births between January 2016 and December 2020. Inclusion criteria included all singleton live births where the mother and child were

continuously enrolled in the health system throughout the study period. Exclusion criteria included mothers diagnosed with influenza, febrile illnesses, or COVID-19 during pregnancy, as well as children with developmental delays of known genetic origin (e.g., Fragile X syndrome). Kaplan-Meier survival curves and Cox proportional hazards models were applied to compare ASD incidence between exposed (vaccinated) and unexposed (unvaccinated) groups, with adjustments made for sociodemographic, maternal, and prenatal confounders.

Results: Among the cohort, 37,203 (25.5%) offspring were exposed to influenza vaccination during pregnancy, while 108,753 (74.5%) were unexposed. During a median follow-up of 6.03 years, ASD diagnoses occurred in 1,049 (2.82%) exposed offspring and 2,456 (3.02%) unexposed offspring. Adjusted analyses revealed no significant association between maternal vaccination and ASD risk (aHR = 0.98, 95% CI: 0.91-1.06). When stratified by trimester, adjusted hazard ratios were 1.04 (95% CI: 0.93- 1.18) for the first trimester, 0.92 (95% CI: 0.81-1.05) for the second trimester, and 0.98 (95% CI: 0.88- 1.08) for the third trimester. These findings demonstrate no significant increase in ASD risk, irrespective of the timing of vaccination.

Conclusions: This study, one of the largest and most comprehensive to date, found no evidence that influenza vaccination during pregnancy increases the risk of ASD in offspring. The findings support the safety of maternal influenza vaccination as a preventive health measure and align with prior studies. By addressing public concerns and filling a critical gap in evidence, this study provides reassurance for public health policies promoting influenza vaccination during pregnancy to reduce maternal and fetal complications.

41. Multilingual Exposure and its Impact on Language and Communication in Minimally Verbal Children with ASD: Preliminary Findings from Multiple Case Studies

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Background: Recent research highlights that verbal multilingual children with Autism Spectrum Disorder (ASD) exhibit language abilities comparable to, or even surpassing, their monolingual peers, with no observed delays or adverse effects (Meir & Novogrodsky, 2020; Prévost & Tuller, 2022). Interestingly, caregiver reports have increasingly documented cases of verbal autistic children acquiring high proficiency in languages not spoken in their immediate environment through passive exposure to screen-based media, such as TV and

online content—a phenomenon termed non-interactive bilingualism (Hindi & Meir, 2025). Despite these promising findings, the impact of multilingualism on minimally verbal (MV) children with ASD remains unexplored in the scientific literature.

Objectives: Given the rise in both autism and multilingualism, it is therefore the goal of this study to categorize the language profiles of MV children with ASD, assess differences in lexical production and comprehension in monolingually versus multilingually-raised children, and explore factors that explain language dominance differences, and the role of home language exposure in verbal outcomes.
Methods: Participants included MV children with ASD aged 5-12 years old raised in monolingual and multilingual families. Parents filled out online questionnaires regarding language use and exposure (the Bilingual Parent Questionnaire (BIPAQ); Abubtbul-Oz & Armon-Lotem, 2022), and functioning and behavioral questions (sociodemographic and ABAS questionnaire; Harrison & Oakland, 2003). Parents also filled out the Social Communication Questionnaire (SCQ; Rutter et al., 2003) to obtain a measure of autism risk severity. To evaluate language development, MacArthur-Bates Communicative Development Inventory (CDI) (Fenson *et al.*, 1993) was used. The children in this study were all diagnosed with ASD prior to their participation. Data collection is currently ongoing, and we will present findings from multiple case studies (n=9).
Preliminary Results: Our sample consisted of nine minimally verbal (MV) children, including two children raised in multilingual families. Among the monolingually raised children (n=7) with minimal exposure to other languages, we observed cases of non-interactive bilingualism (n=4) as previously reported in verbal autistic children. These children produced words in English despite having no naturalistic exposure to the language in their environment, relying instead on non-interactive sources such as YouTube. For instance, a 9-year-old child raised in a monolingual Hebrew-speaking environment produced 20 words in Hebrew and 10 in English. Notably, despite the child's mother addressing them exclusively in Hebrew, the child responded in English 75% of the time. In the bilingually exposed group (n=2), we documented a case of a 7-year-old child producing significantly more words in Hebrew—nearly five times more—compared to their home language, Russian. This pattern aligns with parental reports indicating societal pressure to prioritize Hebrew and discourage exposure to other languages.
Conclusions: This study aims to deepen our understanding of the language profiles of MV children with ASD. Preliminary findings indicate that a comprehensive evaluation of language abilities in these children should include all languages to which they are exposed, both through naturalistic interactions and non-interactive means, to capture a holistic view of their linguistic competence.

42. Autism Spectrum Disorder Guilt and Maternal Depression Among Married and Single Mothers: A Moderated Moderation Model.

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Raising children with Autism Spectrum Disorder (ASD) presents unique challenges for parents, especially mothers, who often experience heightened levels of depression. The present study examined the associations between ASD, maternal guilt, and depression in single and married mothers.

Hypotheses

1. Mothers of children with ASD, regardless of their marital status, will demonstrate higher prevalence of depressive symptoms compared to mothers of TD children.
2. Interpersonal guilt over loneliness and marital status will have a double moderating effect on the association between child diagnosis and maternal depression: Interpersonal guilt augments the negative effect of parenting a child with ASD on maternal depression, more for married mothers than single mothers.

A moderated moderation model was tested, examining how perceived guilt in intimate relationships and marital status influence maternal depression in mothers of children with ASD compared to mothers of typically developing (TD) children.

Procedure: The study included 85 mothers (54 married, 31 single) who completed measures of depression (DASS-21) and relationship-related loneliness (LIRS).

Results: To describe the three-way interaction, we performed two moderation analyses (Model 1) separately for married and single mothers. The models included child diagnosis (ASD/TD) as independent variable, perceived guilt in close relationships as moderator and maternal depression as dependent variable. The interaction term for child diagnosis and guilt in close relationships was found significant only for the married mother's group (b = 0.37, t = 2.80, p = .007, 95%CI: 0.10, 0.64), and not for the single mothers group (b = -0.12, t = -0.60, p = .55, 95%CI: -0.53, 0.29). The Johnson-Neyman method analysis found that the confidence interval of the simple slope did not contain zero for levels of guilt of 1.70 and above, indicating that, only for married women, the effect of autism on maternal depression is stronger for higher levels of perceived guilt in close relationships

Discussion: our results indicated that the presence of guilt in close relationships significantly exacerbates depression in married mothers of children with ASD, highlighting the importance of emotional support in marital relationships. Maternal depression was significantly higher for mothers of children with ASD but was not explained by marital status alone. This study underscores the need for targeted interventions that address emotional distress and guilt among mothers raising children with ASD.

43. A Crosstalk between nitric oxide and mTOR signaling pathway in autism spectrum disorder (ASD) pathology.

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Background: Nitric oxide (NO) is a multifunctional signaling molecule that plays a crucial role in synaptic transmission and neuronal function. However, little is known about the role of NO signaling and S-nitrosylation (SNO, the NO-mediated posttranslational modification) in neurodevelopmental disorders (NDDs), including ASD. One of the important pathways implicated in physiological and pathological conditions is the mammalian target of rapamycin (mTOR)
Objectives: This study aimed to investigate the role of nitric oxide (NO) and the mTOR signaling pathway in the pathology of autism spectrum disorder (ASD). We examined the effects of excessive NO levels in mice carrying Shank3 and Cntnap2 mutations on nitrosative stress, S-nitrosylation (SNO) of synaptic proteins, and mTOR signaling. Additionally, the study aimed to evaluate the effects of pharmacological inhibition of NO using 7-NI .
Methods: The biochemical experiments were conducted in vivo and in vitro to test for nitrosative stress and SNO of synaptic proteins. The effects of 7-NI, a pharmacological inhibitor of NO, were also examined .
Results: The study showed that mutant mice exhibited decreased levels of synaptic proteins, accompanied by increased phosphorylation of mTOR and RPS6. The expression of NR1 and GAD1 were also altered. Treatment with 7-NI reversed these changes, protecting against excessive NO production. These findings indicated that excessive NO production induced by Shank3 and Cntnap2 mutations resulted in abnormal mTOR signaling and disrupted synaptic neurotransmission. Statistical analysis was performed using GraphPad Prism Software, v. 9.3 (San Diego, CA, USA). Data are presented as mean ± SEM. A one-way ANOVA followed by Tukey's multiple comparison test was used for the group comparisons. The differences between the groups were considered statistically significant at $P<0.05$.
Conclusions: These findings suggest that targeting NO production could be a potential therapeutic approach for ASD, with implications for restoring normal synaptic function and alleviating symptoms associated with the disorder.

44. The role of nitric oxide-mediated glutamatergic alterations in the Shank3$^{\Delta 4\text{-}22}$ mouse model of autism

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Abstract: SHANK3 gene is mutated in 1% of autism spectrum disorder (ASD) cases. SHANK3 codes for a major scaffolding protein in glutamatergic neurons having central role in post-synaptic density structure and stability. The Shank3Δ4-22 mouse model exhibits the major behavioral phenotype of ASD and is used in this work. Previously we showed that nitric oxide (NO) signaling is impaired in ASD mouse models and patients carrying the mutation, however the mechanism causing excessive NO is unknown.
Purpose: Our goal is to decipher the mechanism causing the NO overproduction. We hypothesize that a mutation in SHANK3 gene causes imbalance in the glutamatergic system which could potentially lead to the ASD-related behavioral deficits.
Methods: We preformed biochemical and pharmacological experiments using Shank3 mouse model and SH-SY5Y cell line to test our hypothesis.
Results: We discovered dysregulation of the NMDA and AMPA receptors expression in brain of mutant mice. Selective nNOS inhibitor, reversed the glutamatergic alterations in the mutant mice. To understand how exactly NO affects different proteins, we focused on PSD-95 protein, which may be affected by NO levels. Immunoprecipitation assay showed that in the KO mice, there is over-ubiquitination of PSD-95, reversed by nNOS inhibition, suggesting that NO causes poly-ubiquitination and excessive protein degradation. Using SH-SY5Y cells with SHANK3 deletion, we showed that a selective antagonist to specific NMDA receptors inhibits nNOS activity and NO production.
Conclusion: we deciphered a novel crosstalk mechanism between NO and the glutamatergic system, which may lead to the discovery of novel drug targets for ASD.

45. The spliceosome component WBP4 is vital for neurodevelopment

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Background: Autism spectrum disorder (ASD) is a developmental condition characterized by social and communication deficits. ASD can be accompanied by other conditions including intellectual disability (ID) and developmental delay, as well as physical abnormalities in cases of syndromic ASD. Despite advancements in research, the cellular processes contributing to ASD remain largely unidentified. Recent research suggests that

disruptions in the splicing process may contribute to ASD, a finding supported by our discovery of mutations in the spliceosome component WBP4 as a cause of syndromic ASD. Objective To generate a Wbp4 knockout mouse model and use this model to investigate how aberrant splicing contributes to ASD, exploring the link between splicing regulation and neurodevelopment.

Methods: The mouse model was generated using CRISPR-Cas9 genome editing to knockout Wbp4. The phenotypes of Wbp4-/- mice were characterized, including embryonic lethality, brain size, and structural abnormalities. To identify splicing alterations and gene expression patterns, RNA-seq analysis was performed on E15.5 forebrain samples from wild-type and Wbp4-/- embryos. Additionally, induced pluripotent stem cells (iPSCs) from a WBP4-/- patient and the patient's parents were differentiated into neural progenitor cells (NPCs) to validate the conservation of WBP4-regulated splicing targets across species.

Results: Wbp4-/- mice exhibited embryonic and perinatal lethality, reduced body and brain size, and structural brain abnormalities. On the molecular level, RNA-seq analysis revealed 2,075 splicing events across 1,610 genes that were significantly altered in Wbp4-/- embryos. These splicing changes were enriched in genes critical for development, particularly those associated with preweaning lethality and central nervous system abnormalities. Differential gene expression analysis identified 1,417 genes with altered expression in Wbp4-/- mice, with significant enrichment for neuronal function-related phenotypes. Cellular deconvolution analysis suggested disruptions in neuronal development and oligodendrocyte maturation in Wbp4-/- forebrains. Comparing RNA-seq data from the mouse forebrain with human WBP4-/- fibroblasts revealed 112 mutual genes with altered splicing. This set of genes significantly overlapped with SFARI genes associated with ASD ($P < 0.005$, Fisher's exact test). The conservation of WBP4-regulated splicing targets, specifically ones associated with NDD and ASD, was confirmed in human NPCs derived from the WBP4-/- patient.

Conclusions: Our research reveals that similar to humans, loss of WBP4 leads to brain abnormalities in mice, highlighting its crucial role in neurodevelopment. As behavioral testing in mice is used to assess ASD, we planned to use such tests to investigate the potential link between aberrant splicing and ASD observed in WBP4-deficient human patients. However, embryonic lethality in the mouse model prevents such studies. Future research employing conditional knockouts of WBP4 in mice brains could provide valuable insights into this connection. Notably, the significant overlap between conserved WBP4-regulated splicing targets and known ASDassociated genes suggests that WBP4 has a fundamental role in brain development, leading to neurodevelopmental phenotypes when missing. These findings illuminate the potential link between splicing dysregulation and ASD pathogenesis, laying the groundwork for further investigations into the molecular mechanisms underlying ASD.

46. Genetic Insights into Autism Spectrum Disorder: Unveiling the Role of Intrinsically Disordered Regions in Proteins

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Background: Autism Spectrum Disorder (ASD) affects approximately 1 in 36 children globally, creating significant public health challenges for healthcare systems, educational institutions, and families. Early identification and intervention are crucial for improving outcomes, but genetic screening tools remain limited. While genetic influences in ASD are well-documented, the complex relationship between genetic markers, particularly intrinsically disordered regions (IDRs) in proteins, and ASD expression requires further investigation to develop effective public health screening strategies.

Methods: This study utilized genetic data from the SFARI Gene database. 643 ASD-associated genes were selected from the SFARI database. Additionally, a control list of 277 genes was curated from a previous study. Machine learning methods, including artificial neural networks, were used to analyze genetic patterns, focusing on IDRs in proteins. A novel classification based clustering approach to classify ASD- associated genes, which could inform targeted public health interventions, has been developed. The model's performance was evaluated using area under the curve (AUC) metrics.

Results: The machine learning approach achieved an initial AUC of 0.6 in distinguishing ASD-associated genes. After implementing a preliminary clustering step, the AUC improved to 0.8, demonstrating enhanced predictive capability. The analysis revealed two distinct clusters of ASD-associated genes, characterized by differences in IDR percentage, IDR length, and protein hydrophobicity. These findings suggest potential population-level screening strategies and opportunities for tailored early intervention programs. Furthermore, using gene ontology for analyzing the function of ASD-associated proteins with a high IDR percentage (>=49%) revealed that their function is enriched with behavior and cognition, while the ASD-associated proteins with low IDR percentages (<= 11%) were enriched with cognition.

Conclusions: This study provides valuable insights for public health professionals and policymakers in developing more effective ASD screening programs. The identification of distinct genetic clusters could lead to more targeted public health interventions and resource allocation. The findings highlight that incorporating genetic subtyping into public health screening protocols could enhance early detection and improve intervention outcomes at the population level.

47. Comparison of empathy indices in autism spectrum disorder and social anxiety

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Introduction: Autism Spectrum Disorder (ASD) and Social Anxiety Disorder (SAD) share significant social challenges, despite being distinct conditions. ASD involves deficits in social communication and repetitive behaviors, while SAD is marked by fear and avoidance of social situations. These overlapping difficulties often complicate differential diagnosis. Empathy, a key factor in social functioning, includes cognitive empathy (understanding others' emotions) and emotional empathy (sharing others' emotions). This study aimed to compare cognitive and emotional empathy in young adults with ASD, those with heightened social anxiety (SA) symptoms but no ASD, and controls. Additionally, it sought to identify empathy-based predictors of group affiliation.
Method: A total of 105 participants (86 males, 19 females; mean age = 24.22, SD = 2.78) were included, divided into three groups: 34 students with ASD (ASD group), 38 students with significant SA symptoms (SA group) and 33 controls with no ASD and low SA symptoms (control group). Autism severity was measured using the Social Responsiveness Scale-II (SRS-II), and social anxiety symptoms were assessed using the Liebowitz Social Anxiety Scale (LSAS). Empathy was evaluated through the Interpersonal Reactivity Index (IRI), Theory of Mind Inventory - Self-Report Adults (TOMI-SRA), and Reading the Mind in the Eyes Task (RMET). These instruments measured trait empathy (long-term tendencies) and state empathy (empathic reactions in specific situations).
Results: The ASD group showed reduced cognitive empathy, especially on the IRIperspective-taking subscale compared to controls. They also scored lower on TOMISRA and IRI-empathic concern compared to the SA and control groups. Both ASD and SA groups displayed higher IRI-personal distress scores compared to controls, indicating more emotional distress in response to others' emotions. The personal distress to empathic concern ratio (PD/EC) was higher in the ASD group than in the SA and control groups and positively correlated with autism severity. Logistic regression analysis for the ASD and SA groups demonstrated that the PD/EC ratio significantly predicted autism diagnosis (B = 0.275, SE = 0.132, p = .036, Exp(B) = 1.317), meaning that each one-unit increase in the PD/EC ratio increased the odds of an autism diagnosis by a factor of 1.32. A ROC analysis identified a PD/EC ratio cutoff of 0.83, offering good sensitivity and medium specificity for distinguishing ASD from high SA symptoms. No differences between the groups were noted for the RMET test representing state empathy.
Conclusions: This study uncovered distinct empathy profiles in individuals with ASD and those with high SA symptoms. The ASD group had significant deficits in cognitive empathy and empathic concern, often reacting with personal distress rather than typical empathetic

responses. Conversely, participants with high SA symptoms maintained relatively intact empathic abilities despite experiencing elevated distress. The PD/EC ratio emerged as a useful tool for differentiating between ASD and high SA symptoms. Clinically, the IRI questionnaire, along with empathy measures, could aid in improving diagnostic accuracy between these conditions. These insights provide a foundation for developing tailored treatment plans that address the specific empathy challenges in each population, potentially improving treatment outcomes

48. Maternal Covid-19 Vaccination During Pregnancy and Risk of early diagnosis of Autism Spectrum Disorder in the offspring

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Background: The novel RNA vaccine that was developed against the Covid-19 virus has been proved effective and safe, leading to recommendations for use during pregnancy. However, the long-term effect of this vaccination on the developing offspring has not been tested yet. Therefore, the aim of this study was to examine the association between Covid-19 vaccination during pregnancy and a subsequent diagnosis of autism spectrum disorder (ASD) in the offspring.

Methods: We conducted a retrospective cohort study including all pregnancies of singleton live births between March 25, 2020, and January 31, 2022, where both the mother and child were members of Clalit Health Services (CHS), and the delivery occurred in CHS-affiliated hospitals. The follow-up period continued until data extraction on May 6, 2024. We excluded pregnancies where the mother was infected with Covid-19 during pregnancy or children who were diagnosed with ASD with a known genetic cause. Kaplan-Meier survival curves and Cox proportional hazards models were applied to compare ASD incidence between exposed (vaccinated) and unexposed (unvaccinated) groups, with adjustments made for sociodemographic, maternal, and prenatal confounders.

Results: The study encompassed a total of 46,111 children (51.5% males), with 37% (17,094) born to mothers who received a Covid-19 vaccine during pregnancy. Significant sociodemographic differences were seen between exposure groups whereby 39% of the unvaccinated women were southern Arabs compared to only 9% of vaccinated women. By the end of the follow-up period, 412 children (0.9%) were diagnosed with ASD with no significant differences between the exposure groups (HR=1.13, 95% CI=0.93-1.39). However, after adjusting to the sociodemographic differences between the groups, a significantly lower risk of ASD was observed among pregnancies of vaccinated women (aHR=0.76, 95%CI=0.62-0.94). Interestingly, this reduced risk of ASD was seen only among pregnancies of women who received two doses of the vaccine (aHR 0.74, 95% CI 0.59–0.91)

but not among those who received only one dose (aHR 1.04, 95% CI 0.65–1.61), suggesting a potential dose-response relationship.
Conclusions: This pioneering study suggests that Covid-19 vaccination during pregnancy does not increase the risk of early diagnosis of ASD in offspring. A potential association with a reduced risk was observed, but this may be confounded by sociodemographic factors. Further research is needed to confirm these findings and explore the long-term effect of Covid-19 vaccination during pregnancy and ASD diagnosis in the offspring at older ages.

49. Personalized Nutrient-based Care in Autism Spectrum Disorders: Building a Pipeline for a Clinician Assistant Tool as a safe, low-risk, first-line treatment.

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Background: Nutrients are critical in brain development, synaptic structure, and neuronal function. They act as cofactors in enzymatic processes, aid vesicle packaging, and support functional connectivity. Autism Spectrum Disorder (ASD) is a biologically and phenotypically diverse condition, with up to 70% of affected children exhibiting nutrient imbalances and eating-related symptoms. These complexities contribute to inconsistent outcomes of nutrient supplementation, particularly with a one-size-fits-all approach.
Objectives: To develop an automated, scalable system capable of identifying and addressing individual nutrient needs in children with ASD, accounting for population heterogeneity.
Methods: Phenotypic data from over 800 questionnaires were integrated with urine metabolomic profiles (n=149) analyzed using targeted and untargeted methods. A pipeline processed diverse data inputs, linking symptom profiles and dietary habits to metabolomic predictors of nutrient imbalances. Machine learning models, principal component analysis (PCA), correlation analyses, and regression models uncovered associations between symptoms and biological correlates. These associations informed a heuristic recommendation system generating personalized dietary and supplementation plans. Effectiveness was evaluated using Autism Treatment Evaluation Checklist (ATEC) subscales after 8 weeks of algorithm-guided supplementation.

Results: The system generated tailored dietary and supplement recommendations based on symptoms, diet, and metabolomic data. Preliminary results demonstrated an improvement of up to 40% in ATEC subscales after 8 weeks.
Conclusions: While further validation studies are needed, these findings highlight the system's potential as a scalable clinician's tool for precision nutrition. By addressing the individualized nutritional needs of children with ASD, the system supports personalized interventions, improves symptom management, and informs broader applications in ASD care.

50. Motor and Socio-Cognitive Mechanisms Explaining Peers' Synchronization of Joint Action Across Development in Autistic and Non-Autistic Children

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Background. Partners coordinating their movement in time and space to reach a goal engage in joint action (JA), a fundamental component of everyday social interaction. This process relies on both motor skills and socio-cognitive abilities (e.g., Theory of Mind, ToM)). Autistic children often exhibit difficulties in executing fine and gross motor tasks, inferring or predicting others' actions and intentions on the basis of their behavior (ToM), and mirroring and complementing others' movements (JA). Despite JA's importance for peer interaction, the shared contribution of motor and socio-cognitive mechanisms (ToM) to its formation is insufficiently explained.
Objectives. The current study's aim was to explore motor skills and ToM abilities' joint contribution to JA performance with a peer partner. Mediation model assumes that the link between the dependent variable (JA) to the independent variable (Group) is better explained by indirect mechanisms that mediate this link and contribute to its more comprehensive understanding. Since theoretically motor and socio-cognitive mechanisms underlie JA constitution, we assumed that these mechanisms would jointly mediate autistic and non-autistic children's JA performance.
Method. This study included 84 autistic children ages 6-16 years, and 64 non-autistic children matched by age, sex, IQ, and mother education across three developmental-age groups (early childhood,6-8.5 years, preadolescents, 8.5-12, adolescents, 12-16 years). Group differences on age and IQ were non-significant. The participants' composite score of gross and fine motor skills was assessed using the Individual Motoric Observation Scale (IMOS), while their early, basic, advanced and composite ToM scores, as rated by parents, were evaluated using the ToM Inventory (TOMI). Children also completed four-dyadic-JA

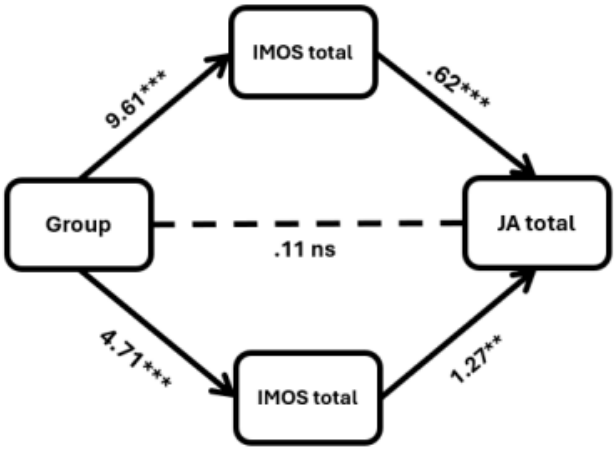
tasks (side-by-side walking, face-to-face movement, imaginary-football, and crossing a narrow corridor), yielding a total JAcoordination score.

Results. To examine possible mediation effects (indirect effects) of motor skills and ToM abilities, as parallel mediators between group and JA and to explore their joint contribution to JA performance, we used SPSS PROCESS mediation model 4. Our mediation analysis revealed a significant indirect effect of group (autism/ Non-autistic) on the total JA score through the IMOS total score, as well as a significant indirect effect of group on the total JA score through the TOMI composite score (see Figure 1).

Conclusions. Together, motor and socio-cognitive underlying mechanisms significantly contributed to JA performance beyond the participant's diagnostic-group affiliation, elucidating the relationship between these three capabilities. This offers a novel theoretical and therapeutic perspective on autistic and non-autistic children's everyday social-motor interaction. Consequently, improving motor skills and ToM abilities can enhance JA performance, thereby positively influencing autistic children's social participation throughout their school years.

Figure 1

Direct and Indirect Effects of Group (non-autistic/autistic), Motor Abilities (IMOS), and ToM (TOMI) on Joint Action (JA) Abilities



Indirect effect(s) of X on Y:

TOMI composite	BootLLCI: 2.2527	BootULCI: 10.1057
IMOS total	BootLLCI: 2.8745	BootULCI: 9.3480

51. PathoBiocheModelling to manage Unknowns in Neurodevelopmental Cofactor Disorders

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Background. In adults, the brain represents～2% of body weight and consumes～20% of body energy. In children <5 years, the metabolic rate is 1.5 times higher showing that neurodevelopment demands energy. The pathogenesis of neurodevelopmental delay (NDD) is incomplete but onethought is clear: metabolism is involved. It refers them as neurometabolic disorders. The metabolism is shaped by genetic and epigenetic environmental factors and is regulated by cofactors.In most cases we can do nothing with genetics but we can try to manage epigenetics. Some factors are known but unknown ones prevail. How can we manage it?

Objectives. We model a patient's neurometabolism through illustrating links between symptoms and lab tests via reported biochemical pathways. This approach can help to suspect genetic and/or epigenetic issues in metabolism.
Methods. Primarily, every issue should be treated as epigenetic because we can reverse it. If a cofactor is described, we use it, otherwise we consider findings with similar molecular patterns described in scientific reports and suggest relevant therapy. Patients A, B and C are 4 to 5 year old boys from different families and towns with similar symptoms of NDD. We modelled their molecular pathogenesis in order to normalize their metabolism through personalized biomedical interventions such as dietary modifications, nutritional supplements, and lifestyle adjustments.
Results. We found explicit and implicit cofactor disorders – unknowns. A model of Patient A predicted vitamin B12 deficiency which was confirmed by low blood level. Patient B had decreased activity of several enzymes with similar cofactors. Vitamin levels were normal. However, techniques were not available to measure -lipoic acid. Yet, we administered it based on reports. α Patient C had notable decreased activity of FAD-dependent Isovaleryl-CoA dehydrogenase (IVD). Since the vitamin levels including FAD were normal, a genetic cause was suspected. Moreover, we also found decreased activity of some other FAD-dependent enzymes such as Aconitase. These findings suggested an epigenetic cause. Indeed, we focused on patient's high blood Mn2+ levels ,which can destabilize FAD-dependent enzymes disrupting Fe-S clusters that mediate the electron transfer from FAD.

Based on these, we made an analogy to a similar pattern of IVD cofactor regulation which is also Fe-S-dependent. The significant neurological and metabolical improvement of all 3 patients on directed therapy validate the rationale of this approach.
Conclusion. PathoBiocheModelling helps to suspect unknown neurodevelopmental cofactor disorders and propose solutions when data is limited.

52. Co-occurrence of Epilepsy and Autism – Two Sides of the Same Coin?

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Background: Autism Spectrum Disorder (ASD) is often accompanied by co-occurring conditions encompassing psychiatric, neurologic, and physical aspects. Among these, epilepsy emerges as a particularly intriguing co-occurring condition with a prevalence among individuals with ASD between 2.4% to 46%, notably elevated compared to the general population. The pathophysiology of both ASD and epilepsy is characterized by disrupted neural networks and altered neuronal connectivity, suggesting shared underlying mechanisms. Considering the significant co-occurrence and the shared pathophysiology of these two conditions it is likely that people with both ASD and epilepsy will exhibit unique characteristics compared to those with each of the conditions alone.
Objective: The study objective was to identify distinct characteristics associated with co-occurring ASD and epilepsy.
Methods: To address this goal, we conducted a cross-sectional study among all children born in Israel between 2010 and 2020 who were members of Clalit Health Services (CHS). We identified all children in this cohort who had a diagnosis of ASD or epilepsy and divided them into three groups: co-occurring ASD and epilepsy, ASD only, and epilepsy only. Data was extracted from the CHS electronic database combined with data from the Azrieli National Center for Autism and Neurodevelopment Research (ANCAN) database. Annual prevalence rates, age at first diagnosis, and condition precedence in co-occurring cases were assessed and sociodemographic, clinical, maternal, obstetrical, and labor characteristics were compared between study groups using standard univariate statistics.

Results: The study cohort included 1,465,958 live births. Of these, 34,277 children (2.34%) were diagnosed with either ASD or epilepsy with opposite trends in the prevalence of ASD and epilepsy during the study period. While ASD prevalence has more than doubled (from 1.02% for children born in 2010 to a peak of 2.26% for children born in 2018), the prevalence of epilepsy has constantly declined (from 0.84% to 0.44% in the same years) and the prevalence of children with co-occurring ASD+epilepsy remained relatively stable. Furthermore, the ratio between epilepsy and ASD as the primary diagnosis among children with both of these conditions remained ~1. Interestingly, children with co-occurring ASD+epilepsy were more similar to children with only ASD than children with only epilepsy in their sociodemographic and obstetrics characteristics. However, they had significantly higher rates of intellectual disability, ADHD, gastrointestinal problems and motor coordination problems than children with either epilepsy or ASD alone ($p<0.001$). Finally, higher rates of specific epilepsy types were seen among children with only epilepsy than in children with epilepsy+ASD (21.5% vs. 16.6%; $p<0.001$), whereas no significant differences in the severity of ASD symptoms were seen between the two ASD groups.
Conclusions: The findings from this study suggest that the co-occurrence of epilepsy and ASD is not a distinct, homogeneous condition but rather a mixture of both conditions. Elucidating the pathophysiological mechanisms underlying the co-occurrence of these conditions may shed brighter light on this intriguing phenomenon.

53. Evaluating Participation Improvements in Children with Autism Spectrum Disorder in Special Education: Insights from Parents and Therapists

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Background: Early educational settings are crucial for children with ASD, as these children exhibit greater developmental progress with intensive preschool interventions. Enhancing participation and performance skills are key goals of these settings. Participation is influenced by the interaction between health conditions and contextual factors, making it essential to explore individual treatments (one-on-one sessions) and ecological treatments (contextual, functional purpose sessions). Participation at home and in the community is also vital for children's development and well-being, so educational settings should aim to improve participation beyond the classroom.

Objectives: To evaluate changes in participation and performance skills among children with ASD in special education settings, as perceived by parents and therapists, and to identify key predictors of improved participation.
Methods: Sixty-seven preschoolers with ASD from 14 special educational settings participated. Parents and therapists completed the Children Participation Questionnaire (CPQ) to assess participation (diversity, frequency, independence, enjoyment, and caregivers' satisfaction) and the Performance Skills Questionnaire (PSQ) to assess motor, process, and communication skills. Parents also reported family socio-demographic information, and therapists recorded each child's intervention program. At the end of the year, parents and therapists repeated the CPQ and PSQ. Differences were analyzed using paired t-tests, and linear regression identified predictors of participation improvement.
Results: Significant differences were found between parents' and therapists' perspectives. Both groups noted significant improvements in participation (independence, enjoyment, and caregivers' satisfaction) with small to medium effect sizes (Cohen's d = 0.4-0.6) and in performance skills with medium effect sizes (Cohen's d = 0.5). Performance skills, individual and ecological treatment sessions, and years in special education explained 65% of the variance in parental satisfaction improvement. Individual treatment sessions explained 30% of the improvement in enjoyment, while performance skills and ecological sessions explained 21% of the improvement in independence. The most significant participation improvements occurred in the first year, especially for children with low-functioning autism.
Conclusions: Special education settings with individualized and ecological treatments led by multidisciplinary teams enhance performance skills and participation over a year. However, there are discrepancies between parents' and therapists' perceptions. Further research is needed to understand these differences and to identify factors influencing ASD children's participation, particularly those related to the characteristics of interventions.

54. Significant clinical improvement of severe autism spectrum disorder symptoms following mesenchymal stromal cell treatments: case report

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Background: Autism spectrum disorder (ASD) is associated with significant lifelong challenges for severely affected children and their families. Despite the rise in the prevalence of ASD and the flurry of research being conducted to improve diagnostics and therapeutics, currently no highly effective therapeutic options exist. Studies have linked hallmark ASD traits with dysfunctional innate and adaptive immune responses. There has

been anecdotal reporting of the positive impact of mesenchymal stem cell therapies (MSCT) in children with ASD.

Objectives: To assess the outcome of MSCT in a minimally communicative boy with severe classical symptoms of ASD, intractable seizures, a pathological electroencephalogram (EEG), gastrointestinal symptoms and an extensive family history of autoimmune diseases.

Methods: Between the ages of 5.75 years and 9 years, the child underwent five intravenous MSCTs from allogeneic placenta and umbilical cord tissue. Throughout the treatment period, the child continued with the same schedule of occupational and communication therapies. The Autism Treatment Evaluation Checklist (ATEC) and Social Responsiveness Scale-2nd edition (SRS-2) scales were used to assess treatment effects. In addition, parental observations were recorded at each follow-up visit.

Results: Significant and continuous clinical responses were observed following each MSCT, including immediate disappearance of seizures, normalization of the EEG and clinical improvements of gastrointestinal symptoms, alongside progressive improvements in ASD symptoms, social, verbal and cognitive skills, and emotional expression. By the end of treatment, the child was more relaxed and less aggressive, communicated and engaged with other children, initiated conversations, communicated with long sentences, had improved his pronunciation and was seizure-free. He also exhibited sensorimotor improvements, crystallized thinking skills and more mature and rational decision-making. He clearly expressed his feelings, and was able to read books aloud.

Conclusions: Allogeneic MSCT might offer an attractive innovative modality for some children with ASD. It may also prove a promising therapy for children with seizure disorders. Clinical research directions to develop these innovative treatments and design future research will be presented.