EÖTVÖS LORÁND UNIVERSITY

FACULTY OF EDUCATION AND PSYCHOLOGY



**Theses of the Doctoral Dissertation**

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**Methodological and theoretical advances in autism research**

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Budapest, 2023

## Publications in the dissertation:

Toth, O., Pesthy, O., Farkas, K., Guttengeber, A., Komoroczy, E., Réthelyi, J. M., ... & Németh, D. (2022). Intact fluency in autism? A comprehensive approach of verbal fluency task including word imageability and concreteness. *Autism Research*, *15*(4), 677-686.

Pesthy, O., Farkas, K., Sapey-Triomphe, L. A., Guttengéber, A., Komoróczy, E., Janacsek, K., ... & Németh, D. (2023). Intact predictive processing in autistic adults: evidence from statistical learning. *Scientific Reports*, *13*(1), 11873.

Zolnai, T., Dávid, D. R., Pesthy, O., Nemeth, M., Kiss, M., Nagy, M., ... & Ergul, A. (2022). Measuring statistical learning by eye-tracking. *Experimental Results*, *3*, e10.

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## Other publications:

Simor, P., Zavecz, Z., Horváth, K., Éltető, N., Török, C., Pesthy, O., ... & Nemeth, D. (2019). Deconstructing procedural memory: Different learning trajectories and consolidation of sequence and statistical learning. *Frontiers in Psychology*, *9*, 2708.

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# General Introduction

A great effort has been made to find a comprehensive framework to explain traits and behaviors typical of Autism Spectrum Disorder (ASD). ASD affects about 1% of the population (Zeidan et al., 2022) and individuals with this condition can exhibit a wide range of behaviours, making it challenging to develop a single framework to explain them all. Consequently, reducing noise in data by capturing underlying mechanisms is key in ASD research (Karmiloff-Smith, 1998; Thomas & Karmiloff-Smith, 2002). Using accurate measurement methods and combining different approaches could result in a better understanding of ASD. My dissertation aims to contribute to the understanding of ASD by exploring three frameworks that aim to explain ASD: the executive dysfunction hypothesis (Hill, 2004; Ozonoff et al., 2007; Pennington & Ozonoff, 1996), predictive processing framework of autism (Lawson et al., 2017; Palmer et al., 2017; Pellicano & Burr, 2012; van de Cruys et al., 2014), and amygdala theory (Baron-Cohen et al., 2000; Wang & Li, 2023), while also proposing methodological considerations to benefit the field.

## The executive dysfunction hypothesis

Executive function (EF) comprises top-down mental processes necessary for goal pursuit and is linked to the prefrontal cortex (Diamond, 2013). The three core EFs (inhibitory control, working memory, and cognitive flexibility) support higher-order EFs, including generativity, the ability to generate novel ideas (Miyake et al., 2000). Impaired EFs, especially cognitive flexibility, inhibition, and working memory, are relevant factors in explaining ASD symptoms but studies on generativity in ASD have produced mixed results (Hill, 2004).

Rigid, repetitive behaviours, and failures in the theory of mind and communication in ASD may be associated with failed EFs (Geurts et al., 2009; Mosconi et al., 2009; Schmitt et al., 2018). Generativity could play a role in impaired communication and social interactions in ASD (Hill, 2004; Turner, 1997). Study 1 aimed to measure generativity in autistic adults using the verbal fluency task and explore their use of concrete versus abstract words, which might shed light on their language generation strategies in real-life situations. The cognitive preference for concrete words appears to be more prominent in autistic individuals (Hillis & Caramazza, 1991; Paivio, 1979; Paivio et al., 1994; Schafer et al., 2013), but its impact on verbal fluency performance and communication in ASD has not been thoroughly investigated.

## The predictive processing framework of autism

The predictive processing framework posits that autistic individuals experience an impairment in predicting future events based on past experience and sensory input (Gregory, 1980; Lawson et al., 2017; Pellicano & Burr, 2012; Sinha et al., 2014; van de Cruys et al., 2014). This impairment is believed to explain most autistic traits and atypicalities: ASD individuals may struggle to generate accurate hypotheses about their environment, leading to uncertainty and anxiety, resulting in repetitive behaviours as they strive to create predictable surroundings; moreover, that social interactions and theory of mind are inherently prediction problems, and difficulties in predictive processing could account for social and communication symptoms of ASD (Cannon et al., 2021).

To better understand predictive processing in ASD, we used statistical learning, a long-neglected type of predictive processing. Statistical learning involves the brain's ability to pick up probability-based regularities in the environment without feedback or reward (Christiansen et al., 2012; Schapiro & Turk-Browne, 2015). Investigating statistical learning in ASD could offer valuable insights into a potential impairment in predictive processing. In Study 2, we used the Alternating Serial Reaction Time (ASRT) task (Howard & Howard, 1997), where participants were asked to react to flashing stimuli by pressing the button corresponding to the stimulus location, while they unconsciously learn the hidden sequence the order of the stimuli follow.

However, the field of ASD research could benefit of a version of this task where no button presses are required and where underlying cognitive processes are easier to track. One way to manage this is by exploring predictive processes through eye-tracking technology (Schwizer Ashkenazi et al., 2020; Tal & Vakil, 2020; Vakil et al., 2021). Developing an eye-tracking version of the ASRT task provides a solution to the disadvantages of using button presses in research. With eye-tracking, researchers can capture anticipatory eye movements, where participants look towards the expected location of the next stimulus before its actual occurrence (Vakil et al., 2017). This technology reduces the impact of motor impairments, providing less noisy data and enabling a more accurate measurement of cognitive components of statistical learning (Tal & Vakil, 2020). Thus, in Study 3, we developed the eye-tracking ASRT task on neurotypical participants, which can be a powerful tool to study predictive processing and learning in ASD in the future.

## The amygdala theory

The amygdala theory of autism proposes that abnormalities in the amygdala, a brain region involved in emotion processing and social behavior (Brothers, 1990; Todd & Anderson, 2009), may explain some of the symptoms observed in ASD (Baron-Cohen, 2000; Wang & Li, 2023). Studies have shown that ASD individuals may exhibit altered amygdala functioning (Baron-Cohen, 2000; Ibrahim et al., 2019; Janak & Tye, 2015; Tottenham et al., 2014), leading to difficulties in recognizing facial emotions (Janak & Tye, 2015; Tottenham et al., 2014), affective theory of mind (Schmitgen et al., 2016), and regulating interpersonal distance during social interactions (Kennedy et al., 2009; Kennedy & Adolphs, 2014; Wang & Li, 2023). The theory originated from neuropsychological studies of individuals with amygdala lesions, who displayed traits similar to those seen in ASD, such as impaired social reciprocity and altered emotional responses (Baron-Cohen et al., 2000).

Exploring physiological measures indicating the autonomous nervous system functioning, like heart rate variability (HRV), could shed further light on the amygdala theory. HRV reflects the balance between sympathetic and parasympathetic nervous system activity (Laborde et al., 2017). The amygdala is known to play a role in this balance (Buijs & Van Eden, 2000), and HRV can indirectly provide insights into its functioning. Research on HRV in autistic participants has shown reduced baseline HRV and lower HRV reactivity during social stress (Arora et al., 2021), indicating potential autonomic dysregulation. By combining HRV measurements with interpersonal distance regulation assessments in Study 4, we hoped to uncover connections between altered parasympathetic-sympathetic balance and social behaviours in ASD.

In Study 4, we aimed to examine interpersonal distance regulation in individuals with autism, taking into account additional factors that might influence it, such as eye contact and the ability to infer the preferred distance of others. Socially appropriate interpersonal distance relies on reciprocity, which may be challenging for autistic individuals due to difficulties in theory of mind skills (Baron-Cohen, 2000; Hamilton et al., 2016; Livingston et al., 2019). Investigating these factors could shed light on the complexities of social interactions in ASD and provide valuable insights into the role of the amygdala in shaping social behaviour. By combining behavioural assessments with physiological measures like HRV, researchers hope to gain a more comprehensive understanding of the underlying processes contributing to ASD symptoms and pave the way for more targeted interventions.

# Study 1

Tóth, O., **Pesthy, O.**, Farkas, K., Guttengéber, A., Komoróczy, E., Réthelyi, J. M., Szuromi, B., & Nemeth, D. (2022). Intact fluency in autism? A comprehensive approach of verbal fluency task including word imageability and concreteness. *Autism Research, 15*(4), 677-686.

## Introduction

Retrieving words in a given category given a limited time frame, that is, verbal fluency is a common way to measure generativity (Diamond, 2013; Miyake et al., 2000). The results on generativity in ASD show inconsistency: both impaired (Corbett et al., 2009; Czermainski et al., 2014; Kenworthy et al., 2008; Kleinhans et al., 2005) and intact (B. S. Baxter et al., 2016; Beacher et al., 2012; Borkowska, 2015) verbal fluency performance has been reported.

These inconsistencies may be a result of different underlying mechanisms. To explore this, we went beyond previous studies that concentrated on overall word productivity, errors, perseverations, clustering, or switching two ways. First, we used qualitative measures of the word types listed by the ASD and the neurotypical groups. Words that are concrete or more imageable are easier to retrieve, as their representations are richer than those of abstract or less imageable words (Kousta et al., 2011; Paivio, 1979; West & Holcomb, 2000). Previous studies suggest that it may be more pronounced in ASD (Schafer et al., 2013), but the effect of this has not been tested in the context of verbal fluency. Second, we assessed the performance in the first and the second half of the task, as Carmo et al. (Carmo et al., 2015, 2017) suggested that lower generativity in ASD may be due to an impairment of initiation.

We hypothesized that ASD participants underperform neurotypical peers on the classic fluency measures, they will list more concrete and imageable words than neurotypicals, and they will show a different qualitative pattern in the first and second half of the task.

## Materials and methods

We recruited 16 adults (12 male, 4 female) with autism spectrum disorder and 16 neurotypical controls matched by age, gender, and education. None of the participants had any intellectual disability or language impairment. To test generativity, we used phonemic and semantic fluency tests, where participants were asked to list as many words as they could on phonemic (sound ‘T’, sound ‘K’) and semantic category (‘animals’ and ‘groceries’) conditions, without repeating themselves. We used Paivio, Yuille & Madigan's ((PAIVIO et al., 1968)) 7-point scale to rate the words for concreteness and imageability. 69 independent raters were recruited to rate the words – each of them received 50 words to rate in an online questionnaire out of the pool of 669 words in total. Besides these measures, we calculated the total (correct) word count, errors, perseverations, and cluster numbers and switching for each participant by conditions. We ran a mixed-design analysis of variance (ANOVA) on the word count with the independent variables group (ASD/neurotypical) and condition (semantic average/phonemic average); independent t-tests or Mann-Whitney tests on the cluster numbers, errors, perseverations, imageability, and concreteness. We tested this latter two separately in the first and second half of the task performance using a mixed-design ANOVA with the independent variables group and time (first 30 sec/second 30 sec).

## Results

We found no significant group main effects [*F(1, 30) = 0.207, p = 0.652, η2p = 0.007*] or any group interactions [*F(1,30) = 0.052, p = 0.822, η2p = 0.002*] regarding the word count (see Figure 1).

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*Figure 1.* Average number of words produced by ASD and neurotypical (NTP) groups for phonemic and semantic fluency tasks. The top and the bottom of the box show the upper (Q3) and lower (Q1) quartiles, the line dividing the box represents the median, and notches show a 95% confidence interval around the median.

There were no significant group differences in the number of clusters [*U = 127.00, p = 0.985, d’ = 0.013*], cluster size [*t(30) = -0.448, p = 0.657, d’ = 0.158*], number of errors [*U = 120.000, p = 0.780, d’ = 0.107*], and perseverations [*U = 158.500, p = 0.254, d’ = 0.415*] either.

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*Figure 2.* Average number of words produced by ASD and NTP groups getting high (6 or above) or low (2 or below) imageability (Panel A) and concreteness (Panel B) scores. The top and the bottom of the box show the upper (Q3) and lower (Q1) quartiles, the line dividing the box represents the median, and notches show 95% confidence interval around the median.

We found no significant differences in the count of high imageability [*t(30) = 0.367, p = 0.716, d’ = 0.130*], high concreteness [*t(30) = -0.549, p = 0.587, d’ = -0.194*], low imageability [*U = 122.500, p = 0.834, d’ = 0.073*], or low concreteness [*t(30) = 0.358, p = 0.723, d’ = 0.127*] words either (see Figure 2).

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*Figure 3.* Proportion of words produced by ASD and NTP groups getting high (6 or above) concreteness (Panel A) and imageability (Panel B) scores during the first and second part of the task. The top and the bottom of the box show the upper (Q3) and lower (Q1) quartiles, the line dividing the box represents the median, and notches show 95% confidence interval around the median.

Lastly, no significant group x time interaction was found for high imageability [*F(1, 30) = 0.496, p = 0.487, η2p = 0.016*], low imageability [*F(1, 30) = 0.254, p = 0.618, η2p = 0.008*], high concreteness [*F(1, 30) < 0.001, p = 1.000, η2p < 0.001*], or low concreteness [*F(1, 30) = 1.357, p = 0.253, η2p = 0.043*] word counts (see Figure 3).

## Discussion

In this study, the objective was to compare the performance of autistic and neurotypical subjects in verbal fluency tasks, using a comprehensive approach: besides focusing on variables such as word count, clustering, switching, also assessing the abstractness/concreteness and imageability of the listed words. We hypothesized that the ASD group would exhibit differences in these measures, reflecting potential deficits in generativity. However, the results did not reveal any significant between-group differences, even when examining the first and second 30-second intervals separately. This finding contradicted some previous studies that reported impaired verbal fluency in ASD (Corbett et al., 2009; Czermainski et al., 2014; Kenworthy et al., 2008; Kleinhans et al., 2005). Our study, on the other hand, is in line with other research that reported no deficit in verbal fluency among autistic individuals (B. S. Baxter et al., 2016; Beacher et al., 2012; Borkowska, 2015). The absence of significant differences in word count, errors, perseverations, and the use of high or low concreteness and imageability words suggests that autistic adults without intellectual disability or language impairment can perform similarly to NTP individuals on verbal fluency tasks. A possible explanation to these null results is the presence of compensatory mechanisms or alternative brain networks utilized by ASD individuals to achieve comparable performance (Baxter et al., 2016). We recommend, however, that future studies use additional assessments, such as self-rating of words and graph analysis of speech patterns, to gain a more comprehensive understanding of the verbal fluency differences within and between groups. In conclusion, this study highlights the need for a comprehensive approach to assess verbal fluency in ASD research, contributing to a deeper understanding of this complex cognitive process in individuals with autism and other neurodevelopmental disorders.

# Study 2

Pesthy, O., Farkas, K., Sapey-Triomphe, L. A., Guttengéber, A., Komoróczy, E., Janacsek, K., ... & Németh, D. (2023). Intact predictive processing in autistic adults: evidence from statistical learning. *Scientific Reports, 13*(1), 11873.

## Introduction

One of the influential frameworks that emerged to explain ASD is the predictive processing framework, which posits that autistic behaviour may arise from an atypical ability to predict future events based on experience and sensory input, using the prediction error to update the representation of the environment (Gregory, 1980; Pellicano & Burr, 2012; Sinha et al., 2014). Within the predictive processing framework, various perspectives offer explanations for autistic traits by highlighting specific atypicalities in different components of the process. Atypical predictive processing may result from 1) high and inflexible prediction errors (van de Cruys et al., 2014); 2) relying more on incoming sensory data (bottom-up information) than their prior experiences (top-down processes or priors) (Pellicano & Burr, 2012); 3) overestimating how much the environmental regulatities change, that is, volatility (Lawson et al., 2017; Palmer et al., 2017).

We investigated statistical learning, a form of predictive processing that involves learning probability-based regularities in the environment (Christiansen et al., 2012; Schapiro & Turk-Browne, 2015). Despite its significance, statistical learning in ASD was long neglected in this line of literature. Studies on statistical learning in ASD often have used tasks where the regularities are predictable with a probability of one (deterministic tasks) (Larson & Mostofsky, 2008; Mostofsky et al., 2000; Müller et al., 2004; E. Sharer et al., 2015; E. A. Sharer et al., 2016; Travers et al., 2010, 2013). However, the results are mixed. Yet, when regularities can be predicted with a probability less than one (probabilistic tasks), no studies have found impaired statistical learning: on probabilistic tasks, autistic individuals have exhibited similar (Barnes et al., 2008; Brown et al., 2010; Nemeth et al., 2010) or even superior (Roser et al., 2015) statistical learning compared to neurotypical peers. One study suggested that superior statistical learning in autistic adults might be due to differences in local and global level processing (Frith & Happé, 1994; Roser et al., 2015). In their visuospatial task, participants benefitted from local-level processing, which potentially functions better in ASD. However, it is unclear whether the superior performance in this study resulted from better statistical learning or differences in processing style. In our study, we aimed to test autistic adults on a probabilistic statistical learning task to shed light on these questions.

## Materials and Methods

We recruited 42 participants, of whom 20 were neurotypical individuals and 22 had a diagnosis of ASD. Participants with intellectual disability, language impairment, or active psychosis were excluded from the study. The two groups (neurotypical and ASD) were matched in terms of age, gender distribution, and years of education. We employed the ASRT task (Howard & Howard, 1997) to measure statistical learning. In this task, participants had to press buttons corresponding to the location of a target stimulus on the screen. Unbeknownst to them, the serial order of the stimulus locations followed a specific structure, with some combinations occurring more frequently than others. The task structure allows us to measure statistical learning based on reaction times and accuracy differences between high-probability and low-probability triplets of elements (see Figure 4). Participants performed 40 one-minute-long block (that is, 8 epochs). We performed mixed-design ANOVAs with the dependent variable of reaction time or accuracy, and with the independent variables epoch (1-8), triplet type (high-probability/low-probability), and group (ASD/neurotypical). The study's data are publicly available.

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*Figure 4.* The task & design and an example sequence. (A) The blue rectangles represent the one-minute-long blocks. One block consisted of 85 trials and five blocks were merged into one unit of analysis (epoch). The stimulus appeared in one of the four locations. PATTERN and random stimuli alternated. (B) The design of the ASRT task. Participants performed for ~40 minutes in total, with a 15-minute break in the middle. (C) Example for the sequence. High-probability triplets can be formed by two PATTERN (P) elements and one random (r), or by two random and one pattern element. Low-probability triplets can only be formed occasionally, by two random and one pattern elements; thus, they occur less frequently.

## Results

On reaction time measures, based on nonsignificant Triplet x Group and Epoch x Triplet x Group interactions, the groups differed neither in the overall amount of learning [*F*(1,40) = 1.603, *p* = .213, *η²p* = 0.039, *BFexcl* = 2.828] nor in the dynamics of learning [*F*(7,280) = 0.720, *p* = .655, *η²p* = 0.018, *BFexcl* = 25.586], respectively. On accuracy measures we have found a similar pattern, both the overall learning [indicated by the Triplet x Group interaction: *F*(1,40) = 0.130, *p* = 0.721, *η²p* = 0.003, *BFexcl* = 3.606] and the dynamics of learning [indicated by the Epoch x Triplet x Group: *F*(7,280) = 0.898, *p* = .508, *η²p* = 0.022, *BFexcl* = 15.263] were similar in ASD and neurotypical groups. For the reaction time results, see Figure 5.

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*Figure 5.* A) Reaction time in the neurotypical (NTP, left figure) and ASD (right figure) groups, by the epochs. The brown color indicates the reaction time of high-probability triplets, and the green color the reaction time of low-probability triplets. The gap between these two lines indicates the magnitude of statistical learning. We found no significant differences between the groups. The dashed line indicates a 15-minute-long break. Error bands indicate the standard error of the mean (SEM). B) Statistical learning score on the reaction times, in the neurotypical (left figure) and ASD (right figure) groups, by the epochs. Learning scores indicate the reaction time differences between high- and low-probability triplets, i.e., show how many ms faster participants reacted to the high-probability vs. the low-probability triplets. The blue lines indicate the mean performance of the given group, and the gray lines represent the learning score of individual participants. The dashed line indicates a 15-minute long break. We found no significant differences between the groups. Error bands indicate the SEM in the group.

## Discussion

Our study aimed to investigate statistical learning in autistic adults within the framework of predictive processing. We examined both overall statistical learning and the dynamics of the learning process, which had not been previously explored in autistic adults. Our findings showed that autistic participants demonstrated intact learning performance and similar learning curves. These results seemingly contradict the predictive processing framework of ASD, which suggests impaired statistical learning in autistic individuals (Gordon & Stark, 2007; Mostofsky et al., 2000). However, they are consistent with previous literature that found no impairment in probabilistic statistical learning tasks in autistic children (Barnes et al., 2008; Brown et al., 2010; Nemeth et al., 2010). The contradictions in the literature highlight the possibility that predictive processing in autism may vary depending on the specific task used, and different components of predictive processing might be intact in ASD.

One explanation could be related to the general information processing style required by the task (Roser et al., 2015): perhaps the performance of ASD participants did not exceed that of the neurotypical ones on the ASRT task because it requires a higher level of global processing compared to the task used in Roser et al (Roser et al., 2015). Another factor could be the atypical use of prediction errors in ASD (van de Cruys et al., 2014): since their precision is high and inflexible in ASD, it may keep signalling them that the regularity in the environment is not yet fully learned, leading to a longer learning process. Additionally, the estimation of volatility, rather than the inherent noise in the task (Lawson et al., 2017), could be a factor influencing learning in ASD. This can account for the current results as no volatility was present in the ASRT task used here. The results contribute to the understanding of predictive processing in ASD and highlight the importance of considering task specificity and different aspects of predictive processing in future research. It suggests that predictive processing in ASD may not be entirely impaired and can result in intact (or even superior) performance under certain circumstances.

Overall, the findings suggest that predictive processing in ASD is a complex phenomenon, and further research is needed to fully understand the specific mechanisms involved. The implications of our study may be relevant for clinicians, who can use strength-based methods in therapy and education for autistic people, such as using probabilistic approaches or providing sufficient time for learning. These approaches could help them reach their best competencies and improve our understanding of predictive processing in autism.

# Study 3

Zolnai, T., Dávid, D. R., Pesthy, O., Nemeth, M., Kiss, M., Nagy, M., ... & Ergul, A. (2022). Measuring statistical learning by eye-tracking. *Experimental Results, 3*, e10.

## Introduction

Procedural learning is essential for developing perceptual and motor skills through extensive practice (Simor et al., 2019). Procedural learning, among other mechanisms, statistical learning (Nemeth et al., 2013). While statistical learning has been extensively researched, measuring it accurately faces challenges. Tasks often involve manual responses (Howard & Howard, 1997; Nissen & Bullemer, 1987), which can add noise to the measurements (Vakil et al., 2017), and this is especially problematic when studying certain populations like infants or patients with conditions like Parkinson's disease. Additionally, some widely used tasks do not allow for the separation of different mechanisms contributing to procedural learning, limiting the specificity of the measurements (Albouy et al., 2006; Bloch et al., 2020; Kinder et al., 2008; Koch et al., 2020; Lum, 2020; Tal et al., 2021; Tal & Vakil, 2020; Vakil et al., 2017, 2021).

To address these issues, we aimed to develop an eye-tracking version of the ASRT task used in Study 2. Using eye-tracking allows for a deeper understanding of predictive processing involved in statistical learning by measuring anticipatory eye movements, providing insights into the underlying cognitive processes (Vakil et al., 2017). It also enables the separation of perceptual/cognitive processes from motor components, which is essential in gaining more precise measurements (Vakil et al., 2017). The ASRT task (described in more details in Study 2) is widely used in procedural learning studies. A great advantage of it compared to other tasks such as the Serial Reaction Time task that it makes it more difficult for participants to gain explicit knowledge of the underlying structure, enables continuous measurement of the learning process, and offers a purer measurement of statistical learning by disentangling it from other subprocesses involved in procedural learning (Farkas et al., 2021; Nemeth et al., 2013). While many studies have used eye-tracking for the SRT task (e.g., Albouy et al., 2006; Bloch et al., 2020; Kinder et al., 2008; Koch et al., 2020; Lum, 2020; Tal et al., 2021; Tal & Vakil, 2020; Vakil et al., 2017, 2021), no study before has developed an eye-tracking version of the ASRT task. In summary, this study seeks to overcome the limitations of measuring procedural learning by developing an eye-tracking version of the ASRT task. This new approach provides unique insights into statistical learning and helps to separate perceptual/cognitive processes from motor components, making it a valuable tool for future research in this field.

## Materials and Methods

The study included 24 healthy young adults after excluding participants with eye-tracker calibration issues and outlier eye-tracking data. We the ASRT task, adapted to eye-tracker. Besides the reaction times, statistical learning was also measured by assessing the participants' anticipatory eye movements toward high-probability triplets compared to all anticipatory eye movements. The ASRT task was presented in blocks, with five epochs in the Learning phase and three in the Testing phase, separated by a 15-minute break. The Testing phase included trials with the original sequence (OS) and a different, previously unseen sequence (interference sequence, IS) to measure interference. Eye-tracking data was recorded using a Tobii Pro X3-120 eye-tracker (Tobii AB, 2017). Statistical analyses were conducted using repeated-measures ANOVAs. The effect of interference was assessed using paired-samples t-tests and Bayesian paired-samples t-tests to calculate Bayes Factors.

## Results

Considering the reaction times, in the Learning Phase, we have found significant Triplet main effect, indicating that statistical learning was significant overall the task [*F*(1, 23) = 11.59, *p* = .002, *η2p* = .33], while the significant Triplet x Epoch interaction [*F*(4, 92) = 5.25, *p* < .001, *η2p* = .19] showed an improvement of the performance, which reached significance in the 4-5th epochs (*pBonf*≤ .016). The analyses of the Testing phase revealed that, although overall statistical learning was significant, indicated by the Triplet main effect [*F*(1, 23) = 22.31, *p* < .001, *η2p* = .49], the significant Triplet x Epoch interaction [*F*(1.39, 31.93) = 5.80, *p* = .014, *η2p* = .20] showed that learning dropped in the 7th (interference) epoch (*pBonf* = 1.000), while it remained significant in the 6th and the 8th (*pBonf* ≤ .033). Further exploration of the interference epoch revealed that that despite the interference, the acquired statistical structure of the original sequence still affected the reaction time [difference between triplets that were high-probability only in the original sequence and those that were low-probability in both sequences: *t*(23) = -2.80, *p* = .010, *d* = -0.57, *BF10* = 4.75], moreover, participants also learned the statistical structure of the interference sequence to some extent [triplets that were high-probability only in the IS vs. triplets that were low-probability in both sequences: *Z* = 252.00, *p* = .003, *rrb* = .68, *BF10* = 28.32]. See Figure 6 for the reaction time results.

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*Figure 6.* Reaction times are presented as a function of high-probability (blue line with triangle symbols) and low-probability (orange line with square symbol) triplets throughout the epochs of the Learning phase (1-5) and the Testing phase (6-8). Note, that stimuli were presented randomly in the first epoch, and participants performed on an interference sequence in the seventh epoch, instead of the original sequence used in the rest of the epochs (2-4th, sixth and eighth epochs). The difference between high- and low-probability triplets represents statistical learning. In the Learning phase, the difference between triplet types reached significance in the fourth and remained significant in the fifth epoch. In the Testing phase, the seventh, interference epoch has a temporal negative effect on the reaction time differences, but when the OS was presented (sixth and eighth epoch), the learning was significant again. Error bars represent the SEM.

Learning-dependent anticipatory eye movements were able to show learning after only one sequential epoch in the Learning phase [*F*(4, 92) = 14.76, *p* < .001, *η2p* = .39, post hoc 1st vs 2nd epoch: *pBonf* < .001]. In the Testing phase, the ratio of learning-dependent anticipatory eye movements changed between epochs [*F*(2, 46) = 14.47, *p* < .001, *η2p* = .39]: it was higher in the 6th (*pBonf* < .001) and the 8th (*pBonf* = .004) than in the 7th (interference) epoch. No general skill learning was found in the Learning phase, as indicated by the nonsignificant Epoch main effect [*F*(2.20, 50.68) = 3.01, *p* = .054, *η2p* = .12], moreover, in the Testing phase, we observed a significant slow-down throughout the epochs [*F*(1.60, 36.91) = 6.01, *p* = .009, *η2p*= .21]. For results on anticipatory eye movements, see Figure 7.

Chart, diagram

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*Figure 7.* A) Percentage of learning-dependent anticipation (solid line) compared to all anticipatory eye movements (dashed line) during the ASRT task. The first, randomized epoch shows the smallest value. In the Learning phase, anticipatory eye movements of the sequential epochs (2-5th) are determined by the original sequence to a higher extent than in the first (random) epoch. The interference epoch leads to a temporal decrease in the learning-dependent anticipation ratio. Error bars represent the SEM. The dashed line indicates the chance level. B) The ratio of all anticipatory eye movements (green line) and learning-dependent anticipatory eye movements (black line) compared to all trials, epochwise. Error bars represent the SEM.

## Discussion

We aimed to develop an eye-tracking version of the ASRT task to measure statistical learning without manual responses. We have found that oculomotor reaction times reflected robust, interference-resistant statistical learning. Learning-dependent anticipatory eye movements indicated learning even earlier than reaction times, suggesting they may be a more sensitive measure of implicit statistical learning. However, no general skill learning was observed in average reaction times. This eye-tracking version of the ASRT task offers methodological and theoretical advantages, providing a non-manual alternative to measure the dynamics of statistical learning with greater precision.

Moreover, the eye-tracking allowed for better tracking of temporal dynamics compared to traditional oculomotor SRT tasks. Participants both kept their knowledge about the original sequence and acquired the interference sequence to some extent, showing the robustness of statistical learning, indicated by earlier studies as well (Kobor et al., 2017; Vékony et al., 2022). Learning-dependent anticipations demonstrated learning after only a short practice period, making them a valuable measure of statistical learning. The lack of general skill learning contradicts previous findings (Howard & Howard, 1997; Kinder et al., 2008; Vakil et al., 2021), possibly due to fatigue.

The study's implications extend to both basic and clinical research, offering a tool to study statistical learning with reduced motor components and fewer motion artifacts, making it compatible with imaging techniques. It is especially useful for special target groups, such as infants or individuals with motor disorders like Parkinson's or cerebellum disorders. Overall, this eye-tracking ASRT task contributes to the understanding of implicit statistical learning by providing a highly fine-grained measure of the learning process.

# Study 4

Farkas, K., Pesthy, O., Guttengéber, A., Weigl, A. S., Veres, A., Szekely, A., ... & Németh, D. (2023). Altered interpersonal distance regulation in autism spectrum disorder. *Plos one, 18*(3), e0283761.

## Introduction

ASD is characterized by difficulties in social communication and repetitive behaviours. One of the cornerstones of social interactions is finding the appropriate interpersonal distance. However, the interpersonal distance regulation in ASD has received less attention, although ASD individuals may show differences in maintaining appropriate interpersonal distance. Our study aimed to measure interpersonal distance and HRV during a task and examine how eye contact and self-attribution influence interpersonal distance in ASD. It also investigated autonomic functions in ASD and their potential connection to interpersonal distance regulation.

Previous research on interpersonal distance in ASD has shown inconsistent results, with some studies reporting atypical distance (Asada et al., 2016; Candini et al., 2017; Gessaroli et al., 2013; Ingram et al., 2007; Lough et al., 2015; Pedersen, 1997) and others showing no difference (Kennedy & Adolphs, 2014) compared to neurotypical individuals. To address the methodological challenges in measuring interpersonal distance, we used an experimental setting with personal presence to improve ecological validity. We utilized the Stop Distance Paradigm (Kennedy et al., 2009) to measure interpersonal distance regulation. Our aim was as well to test modulating factors like eye contact and attribution to understand their impact on interpersonal distance. The processing of facial expressions, particularly eye contact, plays a significant role in social behaviour, and it is altered in ASD (Black et al., 2017; Monteiro et al., 2017).

Autonomic functions, such as HRV, are believed to be altered in ASD, with reduced variability indicating imbalanced autonomic regulation (Arora et al., 2021). Thus, we examined the relationship between autonomic functions and interpersonal distance regulation. Our hypotheses were that ASD individuals show greater interpersonal distance and that eye contact and attribution modulate interpersonal distance. Furthermore, we expected reduced baseline HRV and HRV reactivity during the task in ASD, potentially influencing preferred interpersonal distance.

## Methods and Material

The study involved 43 participants, including 22 autistic and 21 control neurotypical participants. The participants underwent an interpersonal distance measurement task using a modified stop-distance paradigm (Kennedy et al., 2009), including eye contact and attribution as conditions. The task involved approaching each other while consciously maintaining a comfortable social distance. Participants repeated this procedure with and without eye contact. Heart rate variability (HRV) was measured during the task using wearable Polar H10 devices (Saario, 2019). We calculated the root mean square of successive inter-beat interval differences (RMSSD) both for baseline and during the stop-distance paradigm. Mixed-design ANOVAs were performed for 1) the preferred distance or HRV during the stop-distance paradigm as a dependent variable and eye contact (with/without), attribution (participant’s own preferred interpersonal distance/the interpersonal distance they thought the experimenter preferred), and group (ASD/neurotypical) as independent variables, 2) the HRV as the dependent variable and time (baseline/during the task) and group (ASD/neurotypical) as independent variables.

## Results

We have found that the ASD group preferred a greater interpersonal distance than the neurotypical one [*F*(1,41)=8.999, *p*=.005, *η2p*=0.180], but it was moderated by neither the Eye contact [*F*(1,41)group×eye =2.480, *p*=.123,*η 2p*=0.057] nor Attribution [*F*(1,41)group×attrib =1.378, *p*=.247,*η 2p*=0.033], see Figure 8.

Chart, box and whisker chart

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*Figure 8.* Interpersonal distance in cm.Dots represent the mean of distance data of eight conditions for each individual. The top and the bottom of the box show the upper (Q3) and lower (Q1) quartiles, the line dividing the box represents the median, and notches show a 95% confidence interval around the median. Asterisks indicate significant group differences. Orange: control participants (NTP), blue: ASD participants.

These interactions were not significant in the interpersonal HRV measures either [Eye contact x Group: *F*(1,32) = 0.817, *p* = .373, *η 2p* = 0.025; Attribution x Group: *F*(1,32) = 0.554, *p* = .462, *η 2p* = 0.017]. The HRV, however was significantly lower in the ASD group as indicated by the significant Group main effect [*F*(1,35)=3.470, *p*=.071, *η2p* =0.090], indicating a higher sympathetic nervous system activity. Moreover, the Group x Time interaction was significant too [*F*(1,35)=4.598, *p*=.039, *η 2p*  =0.116], that signals that the ASD group had a lower HRV reactivity than the neurotypical group, see Figure 9.

**Chart, line chart

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*Figure 9.* Heart rate and heart rate variability. Panel A: Baseline and reactive (interpersonal conditions) heart rate in beat per minute (bpm). Panel B: Baseline and reactive (interpersonal conditions) heart rate variability (RMSSD). Error bars: standard error of the mean. Asterix indicates significant group difference. Orange line: neurotypical participants, blue line: participants with ASD.

## Discussion

We aimed to investigate how autistic individuals regulate interpersonal distance and the underlying autonomic response. In our study, adult ASD participants and neurotypical controls underwent an interpersonal distance measurement task while we recorded their HRV to gain information about their autonomic regulation. The results revealed that ASD participants preferred significantly larger interpersonal distances compared to neurotypical controls. Despite our expectations, eye contact and attribution had no modulatory effect on interpersonal distance of the groups. Regarding HRV, the ASD group showed reduced baseline HRV and diminished HRV reactivity during the interpersonal distance task, indicating lower parasympathetic activity. This difference in HRV may contribute to the atypical interpersonal distance regulation.

The results on interpersonal distance regulation align with those studies who have found larger interpersonal distance in ASD compared to neurotypical peers (Candini et al., 2017, 2019; Gessaroli et al., 2013). However, it contradicts a Japanese study that has found smaller distance (Asada et al., 2016). The explanation may be that in this latter study, the distance ASD participants preferred is comparable to the distance we found in our ASD group. This might indicate that cultural norms affect ASD people less than neurotypical ones. Furthermore, our results contrast with the “eye avoidance” hypothesis (Tanaka & Sung, 2013; Tottenham et al., 2014), and studies that indicated difficulties of higher-order mentalization in ASD (Frith et al., 1991; Livingston et al., 2019). It is possible that the effect of these factors manifests only in more complex social situations.

Our experimental design combined interpersonal distance measurement with HRV registration. This approach shed light on how autistic individuals navigate social interactions and the physiological responses involved. However, the study had some limitations, such as a relatively small sample, due to the COVID-19 pandemics.

Overall, the findings suggest that interpersonal distance regulation and autonomic responses in ASD are complex processes involving both behavioural and physiological factors. This research may have implications for understanding social communication difficulties in ASD and potentially aid in developing biofeedback tools for social communication training for autistic individuals.

# General Discussion

My dissertation had a dual focus: first, to enhance the understanding of social and cognitive functioning in ASD, and second, to expand the methodological approaches used in the field. The studies aimed to complement existing frameworks of ASD, with Study 1 investigating generativity through a verbal fluency task within the executive dysfunction hypothesis framework. Study 2 explored statistical learning to extend the predictive processing framework of ASD. Study 3 developed an eye-tracking version of the statistical learning task to improve future ASD research. Study 4 linked atypical autonomic regulation and interpersonal distance regulation in ASD individuals. Surprisingly, we have found that verbal fluency and statistical learning performance was similar between autistic and neurotypical individuals, challenging previous expectations, while in Study 4 we found a greater preferred interpersonal distance in ASD, which, contrary to our hypothesis, was unaffected by eye contact or attribution.

To put our results into context, it is important to note that intact performance in neurodevelopmental disorders, such as ASD, can be achieved through different compensatory mechanisms and underlying brain functioning (L. C. Baxter et al., 2019; Karmiloff-Smith, 1998; Thomas & Karmiloff-Smith, 2002). The brain's plasticity allows for the emergence of these compensatory mechanisms, which can vary significantly among autistic people due to unique genetics and environmental factors, contributing to the considerable within-group variability in behaviour and cognition – as stated by the neuroconstructivist view of neurodevelopmental disorders (Karmiloff-Smith, 1998).

In the context of the four studies presented in my dissertation, the neuroconstructivist view challenges the interpretation of intact performance in verbal fluency and statistical learning in ASD. While Study 1 and Study 2 found no group differences in these tasks, this perspective suggests that the absence of differences might be due to compensatory mechanisms at play (B. S. Baxter et al., 2016; Müller et al., 2004). For instance, autistic participants may rely on individually different cognitive processes to achieve intact performance, thus masking potential group differences. These findings call for a deeper exploration of the underlying mechanisms at a lower level of measurement to better understand the true nature of cognitive functioning in ASD (Karmiloff-Smith, 1998; Thomas & Karmiloff-Smith, 2002).

This view also highlights the impact of task complexity and length on the results. In the case of verbal fluency, using more challenging categories or tasks might reveal differences between ASD individuals and neurotypical peers. Similarly, the length of a task, as in the case of predictive processing (Solomon et al., 2011), could affect learning curves and potentially lead to reversed U-shaped relationships between learning and ASD. Future studies should consider these factors to obtain a more comprehensive understanding of cognitive functioning in ASD.

Moreover, the neuroconstructivist view underscores the importance of inter-individual variability in ASD. It suggests that factors like language impairment or life history experiences may influence performance. Considering these complex sociocognitive profiles and employing path models involving multiple factors could provide a more nuanced understanding of how different functions interact and shape behaviour in ASD individuals. It is crucial to explore how compensatory mechanisms and unique developmental paths contribute to the observed behaviour and overall autistic experience.

Furthermore, it is important to establish connections among the three frameworks and the four studies to gain a more comprehensive insight into ASD. Exploring the results through different frameworks can provide valuable perspectives that individual frameworks might miss. For instance, in Study 2, where predictive processing was investigated without reward or feedback, the amygdala theory could shed light on the null results. Altered reward processing in ASD, indicated by reduced seeking or expecting rewards (Dziura et al., n.d.; Hsu et al., 2020; Keifer et al., 2021), might be linked to intact statistical learning in the absence of feedback, possibly due to lower amygdala involvement.

Additionally, examining the interplay between executive functions and predictive processing in ASD could offer new insights. While the group-level results showed intact performance on both verbal fluency and statistical learning, exploring the potential competition or balance between these processes (Poldrack & Packard, 2003; Virag et al., 2015) might unveil unique cognitive profiles in ASD individuals. Furthermore, understanding how atypical use of prior knowledge (Pellicano & Burr, 2012) influences interpersonal distance regulation in ASD can help us comprehend social behaviour through the lens of predictive processing. The altered preferred distance in autistic individuals might reflect reduced reliance on social norms, providing valuable insights into the experiences of autistic people in societal settings (Walsh et al., 2018). Moreover, the role of interpersonal distance in cognitive testing could be a clinical and methodological issue, contributing to inconsistencies in cognitive findings in ASD research. Considering and reporting the distance between experimenters and participants during tasks might help account for preserved performance observed in certain studies.

Taken together, my dissertation aimed to advance the understanding of social and cognitive functioning in ASD while broadening the methodological approaches used in the field. The neuroconstructivist view highlights the role of compensatory mechanisms and individual differences in ASD, suggesting that the absence of group differences in these tasks may be due to unique cognitive processes used by each individual. Moreover, the field of ASD could benefit from a more holistic point of view rather than separate, distinct theories that try to explain the symptoms.

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