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Theses of the Doctoral Dissertation

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LEARNING AND CONSOLIDATION OF SKILLS IN TYPICAL AND ATYPICAL DEVELOPMENT

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I. General introduction

Acquiring and executing skills occurs regularly in everyday life. During the human lifespan, we learn several skills, especially at a young age. How we learn, consolidate, and retrieve such skills is highly relevant not only in typical development, but in atypical development as well. In my dissertation, I will focus on these questions and aim to provide a deeper understanding of skill learning, more precisely, of procedural memory, by investigating these processes in typically developing children and adolescents, in a neurodevelopmental disorder as well as across the lifespan.

Multiple memory systems and phases of memory

Memory is not a unified construct; considering long-term memory, the traditional taxonomy differentiates between declarative and non-declarative memory systems (Squire, 1994; Squire & Wixted, 2011). Non-declarative memory consists of several different memory types, such as priming, classical conditioning, emotional and perceptual learning, and procedural memory (Squire & Wixted, 2011). Procedural memory is involved in the acquisition of skills and habits (Frith & Frith, 2012; Kaufman et al., 2010; Ullman, 2004) and this memory system is the main focus of the dissertation.

When investigating human memory, we have to consider the different phases of memory. The first phase is learning, followed by consolidation, when the fragile memory representations became more stable and less susceptible to future interferences, ensuring that the memory representations can be retrieved later (Walker, 2005). In procedural memory, successful consolidation can manifest as retention, which refers to similar performance at the end of learning and during subsequent testing or as offline gains, which refers to better performance during testing than learning (termed offline learning, Robertson, Pascual-Leone, & Miall, 2004). The present dissertation investigates both learning and consolidation within procedural memory.

Different regularities within procedural memory

Procedural memory gives us the ability to detect and extract many types of regularities from the environment, enabling adaptation. Humans are capable of extracting several different kinds of regularities, from quite simple, deterministic ones to more complex, probabilistic ones (Batterink, Paller, & Reber, 2019; Conway, 2020; Siegelman, Bogaerts, Christiansen, & Frost, 2017). Most of the prior studies investigated only one regularity at a time. In my dissertation, I will focus on two kinds of regularities, namely statistical and serial order-based regularities and examine them simultaneously within one paradigm. In the present framework, *statistical regularities* refer to shorter-range relations between stimuli based primarily on probabilistic information. The statistical information is typically learned relatively rapidly and in an incidental manner. The acquisition of *serial order-based regularities* refers to the learning a series of repeating elements which occur in the same order, typically with embedded noise between them.

To measure the different kind of regularities within procedural memory, we employed the two versions of Alternating Serial Reaction Time (ASRT) task (Howard & Howard, 1997; Nemeth, Janacsek, & Fiser, 2013), which is a visuo-motor four-choice reaction time task. The stimuli follow an 8-element alternating sequence, where pattern and random elements alternate with each other and due to the alternating sequence, some runs of three consecutive trials (termed triplets in the present studies) occur with a higher probability than others. Learning is quantified as faster reaction times and higher accuracy to high-probability triplets compared to low-probability ones (e.g., Howard & Howard, 1997; Nemeth, Janacsek, & Fiser, 2013; Song, Howard, & Howard, 2007a, 2007b). In the original ASRT task, statistical and serial-order

information are intermixed, hence, we used a modified version of the task to separate these regularities in one learning session.

Procedural memory in Tourette Syndrome

Investigating procedural memory is highly relevant both in typical and atypical development. Considering the latter, in my dissertation, I will focus on a childhood-onset neurodevelopmental disorder, namely Tourette Syndrome (TS). TS is characterized by recurrent, abrupt, semi-voluntary movements and vocalizations, called tics (APA, 2013) and by structural and functional alterations in the basal ganglia, in the related frontal regions and in the cortico-basal ganglia-thalamo-cortical (CBGTC) circuits (Albin & Mink, 2006). Prior studies suggested a potential link between tics and habits (Conceição, Dias, Farinha, & Maia, 2017; Goodman, Marsh, Peterson, & Packard, 2014; Maia & Conceição, 2017) as tics and habits show an overlap both on the behavioral and neural levels. Both tics and habits are automatically executed, inflexible responses to stimuli that are hard to inhibit; and just as tics, procedural memory has been linked to the basal ganglia and CBGTC circuits (Doyon et al., 2009; Janacsek et al., 2020; Poldrack & Packard, 2003). Prior studies proposed that the neural alterations in TS lead to a hyperfunctioning of the cognitive functions related to the altered brain regions (Clinical Extension Hypothesis, Dye, Walenski, Mostofsky, & Ullman, 2016), and one candidate for possible enhancement is procedural functions (Dye et al., 2016; Shephard, Groom, & Jackson, 2019; Takács et al., 2018; Walenski, Mostofsky, & Ullman, 2007). In Study 1 and 2, I will focus on the possible alteration of procedural memory in TS.

Procedural memory in typical development

Investigating procedural memory, especially the stabilization of procedural memory representations, is highly relevant not only in Tourette syndrome but across the lifespan as well, in neurotypical populations. The developmental trajectory of procedural learning has been described with three different models (for a review, see Zwart, Vissers, Kessels, & Maes, 2019), and two out of the three models proposed an age-variant trajectory (Janacsek, Fiser, & Nemeth, 2012; Lukács & Kemény, 2015). To the best of our knowledge, no theoretical model has been proposed for the developmental trajectory of procedural memory consolidation. Considering the developmental curves for procedural learning, different trajectories can be proposed for the consolidation of procedural knowledge. The age-variant trajectories for procedural learning raises the question whether the consolidation of such knowledge might follow an age-variant curve as well. Hence, in Study 3 and 4, we concentrated on the consolidation of procedural knowledge in typical development.

Research questions

To better understand procedural memory in typical and atypical development, we aimed to answer the following questions:

Study 1: Is the learning of statistical and serial order-based regularities enhanced in *Tourette syndrome?*

Study 2: Is the consolidation of statistical and serial order-based regularities robust in Tourette syndrome?

Study 3: Is the one-year consolidation of statistical and serial order-based regularities successful in typically developing children and adolescents?

Study 4: Does the consolidation of procedural knowledge follow an age-variant trajectory across the lifespan?

II. Study 1: Dissociation between two aspects of procedural learning in Tourette syndrome: Enhanced statistical and impaired sequence learning

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Introduction

Tourette syndrome (TS) can be marked by altered cognitive functions, including both impairments and enhancements and one of the areas where such enhancement has been found is procedural memory (Delorme et al., 2016; Dye et al., 2016; Palminteri et al., 2011; Takács et al., 2018; Walenski et al., 2007). It has been suggested that alterations in the fronto-striatal regions and improper procedural learning mechanisms can explain the hyperkinetic profile of TS (Albin & Mink, 2006). Here, we investigated two regularities within the procedural memory system, namely statistical and serial order-based regularities and we tested whether these regularities contribute to the procedural hyperfunctioning proposed by previous studies.

Materials and methods

Participants – Twenty-seven children diagnosed with TS between the age of 10 and 15 participated in the study. We excluded six participants due to comorbid diagnoses and medication and data of 21 children with TS (18 boys and three girls) were analyzed. In this final sample, three children met the criteria for comorbid ADHD and one child was diagnosed with comorbid OCD and ADHD. Ninety-nine typically developing (TD) children participated in the study. From the TD group, we matched 21 children one-to-one to the TS children based on sex and age. The individuals in the pairs did not differ more than six months in age and were in the same school grade.

Procedure – The experiment composed of two sessions on the same day with a 5-hour delay between them. In this study, we report only the first part of the experiment analyzing the learning phase of the procedural learning task.

Task – Learning was measured by the cued version of the Alternating Serial Reaction Time (ASRT) task (Nemeth, Janacsek, & Fiser, 2013).

Data analysis – The 20 blocks of the ASRT task were collapsed into four epochs, each containing five blocks, and these were used in the analyses. Reaction times (RTs) were calculated for the three different trial types present in the task: for high-probability pattern trials, for high-probability random trials and for low-probability random trials. To examine the learning of the two regularities, RT data were analyzed in a mixed design ANOVA across the four epochs. Learning of statistical regularities was quantified with a mixed-design ANOVA with FREQUENCY (high-probability random vs. low-probability random triplets) and EPOCH (1-4) as within-subjects factors and GROUP (TS and TD) as a between-subjects factor. Learning of serial order-based regularities was quantified with a mixed-design ANOVA with ORDER (high-probability pattern vs. high-probability random triplets) and EPOCH (1-4) as within-subjects factors and GROUP (TS and TD) as a between-subjects factor.

Results

The ANOVA for statistical regularities indicated that the time course of statistical learning was different between the groups (FREQUENCY*EPOCH*GROUP interaction, F(3, 120) = 2.96, p = .035, $\eta^2_p = 0.07$, Fig. 2.1.). Follow-up analysis revealed a difference in the first epoch between the groups: The TS group showed higher learning than the TD group (TS: M = 27.38 ms, SD = 31.45 ms; TD: M = -0.79 ms, SD = 28.91 ms; p = .004). There was no difference in learning in the remaining epochs (all ps > .203).



Figure 2.1. Statistical learning in the TD (A) and TS group (B). Dashed lines represent the TD group, continuous lines represent the TS group. Blue lines with square symbols indicate the reaction time (ms) on the low-probability random triplets, gold lines with triangle symbols indicate the reaction time (ms) on the high-probability random triplets. Statistical learning is indicated by the distance between the blue and gold lines. Error bars denote standard error of mean.

The ANOVA for serial order-based regularities suggested that the two groups differed in the RT difference between the triplets (ORDER*GROUP interaction, F(1, 40) = 4.93, p = .032, $\eta_p^2 = 0.11$). Follow-up analysis showed that the TD group learned to differentiate between high-probability pattern and high-probability random trials, but the TS group showed similar RTs on both trials (TD: M = 38.46 ms, SD = 66.11 ms; TS: M = 5.04 ms, SD = 19.71 ms) (see Fig. 2.2).



Figure 2.2. Sequence learning in the TD (A) and TS group (B). Dashed lines represent the TD group, continuous lines represent the TS group. Red lines with circle symbols indicate the reaction time (ms) on the high-probability pattern triplets, gold lines with triangle symbols indicate the reaction time (ms) on the high-probability random triplets. Sequence learning is indicated by the distance between the red and gold lines. Error bars denote standard error of mean.

Discussion

Children with TS showed enhanced sensitivity to statistical information. This result is in line with previous studies showing speeded processing on tasks tapping into procedural learning and memory (Dye et al., 2016; Shephard et al., 2019; Takács et al., 2018; Walenski et al., 2007). Here, the enhanced sensitivity to statistical information was more prominent at the beginning of the task. Prior studies on neurotypical population showed that statistical learning reach a plateau early, hence, probabilistic information is learned rapidly and then remains stable (Kóbor et al., 2018; Simor et al., 2019). Our results showed the same pattern in both groups, however, it happened faster in the TS than in the TD group. Furthermore, our results indicate impaired learning of serial-order regularities in TS. Similar alterations have been demonstrated in previous studies of motor learning in TS (Avanzino et al., 2011; Palminteri et al., 2011; Stebbins et al., 1995). The present study supports the notion of multifactorial procedural learning, as we found a dissociation between two aspects of learning in the clinical group. It is possible that the two aspects of learning compete with one another in TS. Therefore, having enhanced processing on one of them results in having a disadvantage on the other. Future studies are warranted to test this possibility.

III. Study 2: Access to procedural memories after one year: evidence for robust memory consolidation in Tourette syndrome

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Introduction

Based on the previous studies showing enhanced procedural learning in TS (Dye et al., 2016; Shephard et al., 2019; Takács et al., 2018; Tóth-Fáber, Tárnok, et al., 2021), an important question emerges: does procedural hyperfunctioning in TS lead to persistent changes? Processing information does not stop at the end of a learning session, and long-term memory performance is based on the stabilization of encoded information, that is, on the consolidation of information (McGaugh, 2000; Walker, 2005). However, little is known about whether procedural hyperfunctioning persists over the consolidation periods and whether consolidation of procedural information differs in TS and neurotypical controls. In the present study, we focused on this question and investigated the short-term (five-hour) and long-term (one-year) consolidation of two regularities within procedural memory, namely statistical and serial order-based regularities in children with TS.

Materials and methods

Participants – Twenty children diagnosed with TS between the ages of 10 and 15 participated in our study. One participant had to be excluded from the analyses as they consistently showed extremely low average accuracy on the procedural memory task (more than 3 times the interquartile range from the quartiles; Tukey, 1977). Therefore, the final TS sample consisted of 19 children (16 boys and three girls, $M_{age} = 11.95$ years, $SD_{age} = 1.27$ years). Three children had comorbid attention deficit hyperactivity disorder (ADHD) and one child had comorbid ADHD and obsessive-compulsive disorder. Participants did not have any other psychiatric or neurodevelopmental disorders. Three children were taking medication during either time of testing. A subgroup of the TS children had been examined in the study of Tóth-Fáber, Tárnok, et al. (2021) (the overlap between the two samples is 81%), however, a new control group had been recruited due to difficulties in assessing the original control group one year later.

Seventy-eight typically developing (TD) children were recruited from local schools. From this group, we matched 19 children one-to-one to the TS participants based on age and gender (16 boys and three girls, $M_{age} = 11.79$ years, $SD_{age} = 1.48$ years). The pairs had an age gap maximum of six months and were in the same school grade. None of the matched controls had any psychiatric, neurological, or neurodevelopmental disorders based on parental reports. *Tasks* – The cued version of the Alternating Serial Reaction Time (ASRT) task (Howard & Howard, 1997; Nemeth, Janacsek, & Fiser, 2013) was employed to measure the extraction of statistical and serial-order regularities. Tic severity was assessed with the Yale Global Tic Severity Scale (Leckman et al., 1989), which rates the number, frequency, complexity, intensity, and interference of tics. Tic severity scores represent values from the week prior to the experiment.

Procedure – The study consisted of three sessions. The first two sessions took place on the same day with a 5-hour-long offline period between them. The third session was administered ca. one year later ($M_{delay} = 53.78$ weeks, $SD_{delay} = 3.11$ weeks, between 47.95 and 60.57 weeks). Participants were assessed on the ASRT task in all three sessions. After the first testing day, participants were not informed that the ASRT task would be administered again one year later. The design of the experiment can be seen in Fig. 3.1.



Figure 3.1. The design of the experiment. The experiment consisted of three sessions. The Learning Phase and Testing Phase were administered on the same day with a 5-hour offline period between them. The Learning Phase was composed of four epochs (one epoch contained 5 blocks, and each block consisted of 85 stimuli) and the Testing Phase was composed of two epochs. The four-epoch-long Retesting Phase was administered ca. one year later. Figure 1 is adapted from Kóbor, Janacsek, Takács, and Nemeth (2017).

Statistical analyses – The ASRT task was presented in blocks. During the statistical analyses, blocks were collapsed into epochs, with each epoch containing five blocks. Reaction times (RTs) were calculated for the three different trial types present in the task: for high-probability pattern trials, for high-probability random trials and for low-probability random trials. Learning of probability-based regularities is defined as the difference in RT between high-probability random and low-probability random low trials. Learning of serial-order regularities was quantified as the RT difference between high-probability pattern and high-probability random high trials. Hence, higher scores indicate better learning/memory. We also calculated an offline change score separately for knowledge of statistical and serial-order regularities. The shortterm offline change score was calculated by subtracting the memory score in Epoch 4 from the memory score in Epoch 5, and the long-term offline change score was calculated by subtracting the memory score in Epoch 6 from the memory score in Epoch 7. In both cases, negative scores show forgetting and positive scores indicate offline learning. To assess learning and the retention of knowledge, repeated-measures ANOVAs and paired-samples t-tests were conducted on RT data, separately for statistical and serial-order based regularities. Concurrently with the frequentist analyses, Bayesian paired samples *t*-tests and independent samples *t*-tests were performed, and Bayes Factors (BF) were calculated for the relevant comparisons.

Results

Prerequisite of memory consolidation – Significant learning preceding the offline period is a prerequisite of assessing memory consolidation (Kóbor et al., 2017; Robertson, 2009). Thus, at first, we tested whether significant learning of statistical and/or serial-order regularities occurred in both the TS and TD groups. Considering statistical regularities, we found successful learning in both groups which ensure that the analyses of short-term and long-term consolidation of statistical regularities across groups are justified. Regarding serial order-based regularities, the results suggested that the groups did not successfully acquire the serial-order information during the Learning Phase, therefore, the prerequisite of assessing memory consolidation was not fulfilled. The lack of significant learning calls into question the applicability of retention analyses concerning serial-order regularities. Hence, from this point on, we focus on consolidation of statistical information.

Short-term (five-hour) consolidation of knowledge of statistical regularities – To examine the five-hour consolidation of knowledge of statistical regularities, we conducted a mixed-design ANOVA on RT with GROUP (TS vs TD) as between-subjects factor and PROBABILITY (high-probability random vs low-probability random) and EPOCH (4 vs 5) as within-subject factors. The ANOVA revealed, that over groups, the memory scores did not change in the five-hour offline period (non-significant PROBABILITY × EPOCH interaction, F(1, 36) = 0.25, p = .62, $BF_{01} = 5.08$), with similar memory scores in the 4th (M = 21.80 ms) and in the 5th (M = 23.86 ms) epochs. Importantly, the groups did not differ in retention (non-significant GROUP × PROBABILITY × EPOCH interaction, F(1, 36) = 0.14, p = .71, Fig. 3.2.A.; Bayesian

independent samples *t*-tests conducted on the short-term offline change score $BF_{01} = 3.004$, short-term offline change scores: $M_{\text{TS}} = 3.58 \text{ ms}$, $M_{\text{TD}} = 0.53 \text{ ms}$).

Long-term (one-year) consolidation of knowledge of statistical regularities – To investigate the one-year consolidation of knowledge of statistical regularities, we run a mixed-design ANOVA on RT with GROUP (TS vs TD) as between-subjects factor and PROBABILITY (high-probability random vs low-probability random) and EPOCH (6 vs 7) as within-subject factors. The ANOVA revealed retained memory of statistical regularities after the one-year delay (non-significant PROBABILITY × EPOCH interaction, F(1, 36) = 0.496, p = .49, BF_{01} = 4.53), memory scores were similar in the 6th (M = 26.85 ms) and in the 7th (M = 22.34 ms) epochs. Importantly, memory scores were similar in the TS and TD groups (non-significant GROUP × PROBABILITY × EPOCH interaction, F(1, 36) = 0.64, p = .43, Fig. 3.2.B.; Bayesian independent samples *t*-tests conducted on the long-term offline change score $BF_{01} =$ 2.47, long-term offline change scores: $M_{TS} = -9.63$ ms, $M_{TD} = 0.61$ ms).



Figure 3.2. Five-hour (A) and one-year (B) retention of knowledge of statistical regularities in the TD and TS groups. For the five-hour retention, memory scores were measured by RT values for the last epoch of the Learning Phase (Epoch 4) and the first epoch of the Testing Phase (Epoch 5). For the one-year retention, memory scores were measured by RT values for the last epoch of the Testing Phase (Epoch 6) and the first epoch of the Retesting Phase (Epoch 7). Error bars denote the standard error of mean.

The relation of tic severity and consolidation of knowledge of statistical regularities – In the TS group, we measured the severity of present tics on the first testing day as well as one year later, on the second testing day. Neither severity of the present tics on the first testing day, nor the change in tic severity over the one-year period correlated with memory retention.

Discussion

The present study showed retained knowledge of statistical information: participants acquired the statistical regularities, then successfully retained them both after the five-hour and one-year offline period. Children with TS and matched typically developing controls showed comparable retention of knowledge of statistical regularities. These results were supported by Bayesian statistics as well, strengthening the evidence for successful five-hour and one-year retention in both groups. These results are in line with the findings of Takács et al. (2018), where intact retention of statistical regularities was shown in TS. The present study replicates and goes beyond the results of Takács et al. (2018): (1) our results also showed comparable short-term (five-hour) consolidation, and (2) we showed intact one-year retention of knowledge of statistical regularities, the prerequisite of assessing

memory consolidation was not fulfilled as the groups did not acquire the serial-order information. Hence, consolidation of serial-order information could not be reliably tested here.

Long-term stability of procedural memories has potential educational implications. Procedural memory underlies the acquisition of cognitive, motor and social skills, such as language learning or sports (Frith & Frith, 2012; Kaufman et al., 2010) and is related to habits as well (Goodman et al., 2014; Takacs, Münchau, Nemeth, Roessner, & Beste, 2021). Importantly, a one-year long offline period that has been used in the current study can resemble real-word observations. Namely, learning a new skill or developing a habit happens over a longer stretch of time than a timescale of a lab visit. Our results suggest that children with TS have stable memory representations of procedural knowledge without additional practice during a long time interval and their performance is comparable with TD children. These robust memory representations of procedural knowledge could manifest in everyday settings in the following way: children with TS might be better in learning a new skill (as suggested by prior studies on procedural learning, Takács et al., 2018; Tóth-Fáber, Tárnok, et al., 2021) and they can be also successful in maintaining and remembering those skills, as the current study suggests.

IV. Study 3: Statistical and sequence learning lead to persistent memory in children after a one-year offline period

Publication: Tóth-Fáber, E., Janacsek, K. & Nemeth, D. (2021). Statistical and sequence learning lead to persistent memory in children after a one-year offline period. *Scientific Reports, 11*, 12418. <u>https://doi.org/10.1038/s41598-021-90560-5</u>

Introduction

Ample studies investigated the consolidation of regularities within procedural memory and skills with a one-minute, one-hour, four-hour, 12-hour, 24-hour or one-week delay (Arciuli & Simpson, 2012; Fanuel et al., 2020; Meier & Cock, 2014; Nemeth & Janacsek, 2011; Nemeth et al., 2010; Press, Casement, Pascual-Leone, & Robertson, 2005; Simor et al., 2019; Song et al., 2007b; Walker, Brakefield, Hobson, & Stickgold, 2003). Although everyday experiences suggest that the representation of the acquired regularities and skills is persistent even for a more extended period (months or years), it has been rarely tested empirically, especially from a developmental perspective. Only a few studies investigated the effect of month- or year-long offline periods: Romano, Howard, and Howard (2010) and Kóbor et al. (2017) both showed persistent representation of regularities after a one-year offline period in neurotypical adults. In the present study, we aim to investigate the long-term (one-year) consolidation of two types of regularities, that is, statistical and serial order-based regularities in neurotypical children between the ages of 9 and 15 years.

Materials and methods

Participants – The final sample consisted of 70 participants ($M_{age} = 11.99$ years, $SD_{age} = 1.61$ years; 37 boys, 33 girls). None of the participants in the final sample had any neurological, psychiatric, or neurodevelopmental disorders according to parental reports.

Task – The detection and extraction of statistical and serial order-based regularities was measured by the cued version of the Alternating Serial Reaction Time (ASRT) task (Howard & Howard, 1997; Nemeth, Janacsek, & Fiser, 2013).

Procedure – The experiment was composed of three sessions. The first two sessions were administered on the same day with a 5-hour delay between them, while the third session was administered ca. one year later ($M_{delay} = 53.08$ weeks, $SD_{delay} = 2.39$ weeks, between 47.95 and 60.24 weeks). The ASRT task was administered in all three sessions. At the end of the first day (i.e., after the Learning and Testing Phases), participants were not informed that they would perform the task one year later.

Statistical analyses – The ASRT task was presented in blocks. During the statistical analyses, we collapsed the blocks of the task into epochs, with each epoch consisting of five blocks. Reaction times (RTs) were calculated for the three different trial types present in the task: for high-probability pattern trials, for high-probability random trials and for low-probability random trials, separately for each participants and each epoch. To control for the effect of baseline RT differences related to age on learning and consolidation of knowledge, we transformed the data in the following way. We divided each participants' raw RT values of each trial type and each epoch by their own average performance (i.e., baseline RT) in the first epoch of the task (Horvath, Torok, Pesthy, Nemeth, & Janacsek, 2020; Nitsche et al., 2003). We conducted all analyses on standardized RT data. Learning of statistical regularities was quantified as the difference between high-probability random and low-probability random trial types. Learning of serial order-based regularities was calculated as the difference between highprobability pattern and high-probability random trial types. Higher scores indicate larger statistical or sequence learning/memory. To assess learning and the retention of knowledge, repeated-measures ANOVAs and paired-samples t-tests were conducted on standardized RT data, separately for statistical and sequence learning. In conjunction with the frequentist analyses, we performed Bayesian paired-samples *t*-tests and calculated the Bayes Factor (BF) for the relevant comparisons as well.

Results

Prerequisite of memory consolidation – To assess memory consolidation, significant learning has to occur preceding the offline period. Significant learning was found concerning both statistical and serial order-based regularities.

Do children retain regularities after a one-year offline period? – To test one-year consolidation of statistical knowledge, we conducted a two-way repeated-measures ANOVA on standardized RT with PROBABILITY (high-probability random vs. low-probability random) and EPOCH (6 vs. 7) as within-subject factors. The ANOVA revealed evidence for retained statistical memory after the one-year delay (non-significant PROBABILITY × EPOCH interaction, F(1, 69) = 0.03, p = .86, BF₀₁ = 7.50; Fig. 4.1.A.), with similar memory scores in the 6th (M = 0.049) and in the 7th (M = 0.048) epochs.

To investigate one-year consolidation of serial-order knowledge, we also run a two-way repeated-measures ANOVA on standardized RT with ORDER (high-probability pattern vs. high-probability random) and EPOCH (6 vs. 7) as within-subject factors. The ANOVA revealed retained serial-order knowledge (non-significant ORDER × EPOCH interaction, F(1, 69) = 0.18, p = .67, BF₀₁ = 6.97; Fig. 4.1.B), memory scores were similar in the Testing and Retesting Phases (6th epoch: M = 0.05, 7th epoch: M = 0.045).



Figure 4.1. Retention of (A) statistical and (B) serial-order knowledge. Memory scores measured by standardized RT values for the last epoch of the Testing Phase (Epoch 6) and the first epoch of the Retesting Phase (Epoch 7). Error bars denote the standard error of mean.

Does age affect the one-year retention of statistical and serial-order regularities? – To check the possible association between age and retention, we conducted Pearson's correlation between the offline change scores and age. No significant correlation was found (statistical knowledge: r(68) = .06, p = .62, BF₀₁ = 5.92; serial-order knowledge: r(67) = -.06, p = .62, BF₀₁ = 5.91).

Discussion

The present study showed retained knowledge of both statistical and serial order-based information after the one-year offline period in typical development; participants successfully learnt and stabilized the regularities, and the acquired knowledge was resistant to forgetting over a long period of time. Our results are supported by Bayesian statistics as well, further strengthening the evidence for successful one-year retention. The finding are in line with the studies of Romano et al. (2010) and Kóbor et al. (2017) showing retained statistical knowledge following a one-year offline period in neurotypical adults. Thus, our study offers indirect evidence of comparable consolidation of statistical and serial order-based information in childhood and adulthood, supporting developmental invariance in consolidation. The lack of association between retention and age in our sample also promotes the developmental invariance model.

V. Study 4: Lifespan developmental invariance in memory consolidation: evidence from procedural memory

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Introduction

The developmental trajectory of statistical learning has been described with different models (Zwart et al., 2019) and it is mostly likely varies as a function of age (Janacsek et al., 2012; Lukács & Kemény, 2015). Despite the ample investigation on the lifespan trajectory of statistical learning, the *consolidation* of such knowledge did not receive much attention. The age-variant trajectories of statistical learning raise the question whether we can expect that the consolidation of such knowledge will also follow an age-variant trajectory.

Since statistical learning requires repeated exposure to the same regularities (Conway, 2020), during this period of repeated exposure (i.e., in the learning phase), other learning processes are also engaged that could confound the measures and interpretation of statistical learning as well as its consolidation. One such learning process is called general skill learning, which refers to the faster processing of and responding to stimuli and improved visuomotor coordination as a result of practice, independent of the regularities embedded in the stimulus stream (Hallgato, Győri-Dani, Pekár, Janacsek, & Nemeth, 2013; Juhasz, Nemeth, & Janacsek, 2019).

To the best of our knowledge, no study has tested consolidation of statistical and/or general skill knowledge with the same experimental design across the lifespan so far. The present study fills this gap using a learning task that enables us to tease apart consolidation processes specific to statistical knowledge vs. general skill knowledge in a large sample of participants aged between 7 and 76 years.

Materials and methods

Participants – The final sample of the present study consisted of 255 participants aged between 7 and 76 years (Table 5.1.). None of the participants had any neurological, psychiatric, or neurodevelopmental disorder.

 Table 5.1. Demographic data (mean and standard deviation for age, and gender ratio) for all age groups.

Group	Age	Gender
7-8-year-old (n=26)	7.92 (0.27)	13 M / 13 F
9-10-year-old (n=28)	9.79 (0.42)	13 M / 15 F
11-13-year-old (n=30)	12.10 (0.61)	13 M / 17 F
14-15-year-old (n=30)	14.55 (0.57)	13 M / 17 F
16-17-year-old (n=30)	16.56 (0.54)	13 M / 17 F
18-29-year-old (n=30)	21.64 (2.93)	12 M / 18 F
30-44-year-old (n=30)	36.67 (3.81)	12 M / 18 F
45-60-year-old (n=26)	51.65 (4.46)	6 M / 20 F
61-76-year-old (n=25)	65.28 (4.47)	5 M / 20 F

Task – Statistical learning and consolidation was measured by the original version of the Alternating Serial Reaction Time (ASRT) task (Howard & Howard, 1997). The ASRT task enables us to separate statistical learning from general skill improvements. Statistical learning is defined as faster and more accurate responses to high-probability elements than to low-probability ones (Howard & Howard, 1997). In contrast, general skill improvements refer to

average speed-up and changes in accuracy that are independent of the probabilities of events. These improvements reflect more efficient visuomotor and motor-motor coordination due to practice (Hallgato et al., 2013; Juhasz et al., 2019).

Procedure – The ASRT task was presented in blocks. One block consisted of 85 trials: each block started with five random practice trials followed by the eight-element sequence repeated 10 times. The ASRT task was administered in two sessions with a 24-hour delay between them. **Statistical analysis** – To facilitate data processing, epochs of five blocks were analyzed instead of single blocks (e.g., Blocks 1-5 corresponded to Epoch 1, Blocks 6-10 to Epoch 2, and so on). The Learning Phase consisted of four epochs, while the Testing Phase consisted of one epoch. We calculated mean accuracy and median RTs (for correct responses) for each participant and each epoch, separately for high- and low-probability triplets. Statistical learning scores were calculated as the difference in RTs between high- and low-probability triplets (i.e., RTs for low-probability triplets minus RTs for high-probability triplets). Higher scores indicated better learning/memory performance. General skill knowledge was defined as a general decrease in median RTs during practice (i.e., participants became faster throughout the task), irrespective of triplet types. Median RTs were calculated separately for each epoch in each phase.

As children and older adults are typically respond with slower RTs overall (e.g., Juhasz et al., 2019), we conducted additional ANOVAs on standardized RTs. To control for the effect of average RT differences across age groups on learning and consolidation of knowledge, we employed two different ways of standardization: (1) ratio scores and (2) log-transformed RT data. For calculating ratio scores, we divided each participants' raw RT values of each trial type and each epoch by their own median RT in the first epoch of the task (for a similar approach, see Horvath et al., 2020; Juhasz et al., 2019; Nitsche et al., 2003; Tóth-Fáber, Janacsek, & Németh, 2021). We then calculated standardized learning and memory scores by subtracting standardized RTs for high-probability triplets from standardized RTs for low-probability triplets. Higher standardized scores indicated better learning/memory. General skill knowledge scores were standardized in an identical way. For log-transformed RT data, we applied a logN transformation on the trial-based raw RT data. Then, we computed the mean of log-transformed RTs for each trial type and each epoch, separately for each participant. In conjunction with the frequentist analyses, we performed Bayesian mixed-design ANOVAs and Bayesian paired-samples *t*-tests for the relevant comparisons.

Results

Are there age-related differences in the consolidation of statistical knowledge? - To test 24hour consolidation of the acquired statistical knowledge, we contrasted statistical learning scores computed for the last epoch of the Learning Phase (Epoch 4) with the learning scores computed for the first of the Testing Phase (Epoch 5) and submitted these scores to a mixeddesign ANOVA with EPOCH (Epoch 4 vs Epoch 5) as a within-subject factor and AGE GROUP as a between-subjects factor. The ANOVA revealed overall significant statistical knowledge (main effect of INTERCEPT: F(1, 246) = 309.24, p < 0.001, $\eta_p^2 = 0.56$) and significant differences in overall learning across age groups (main effect of AGE GROUP: F(8,246) = 2.91, p = 0.004, $\eta_p^2 = 0.09$). Importantly, statistical knowledge appears to be retained over the 24-hour delay period with no significant change between the end of the Learning Phase and the Testing Phase (main effect of EPOCH: F(1, 246) = 0.39, p = 0.53, $\eta_p^2 = 0.002$). Moreover, no age group differences emerged in the retention of the statistical knowledge (nonsignificant EPOCH x AGE GROUP interaction: F(8, 246) = 0.14, p = 0.997, $\eta_0^2 = 0.005$; all ps > 0.52): this suggests that all age groups retained the acquired knowledge over the 24-hour delay period (Fig. 5.1.). The analysis of effects of the Bayesian mixed-design ANOVA corroborated the findings of the frequentist ANOVA. Moreover, both frequentist and Bayesian analyses on the standardized RT data showed identical results.



Figure 5.1. Consolidation of statistical knowledge over the 24-hour offline period across age groups. RT statistical learning scores for the last epoch of the Learning Phase (Epoch 4, light gray bars) were contrasted with those for the first epoch of the Testing Phase (Epoch 5, dark gray bars). BF_{01} values were obtained by paired-samples *t*-tests for this contrast separately for each age group. All reported BF_{01} values indicate substantial evidence for the null-hypothesis ($BF_{01} > 3$), providing evidence for comparable knowledge in Epoch 4 and Epoch 5 in each age group. Error bars denote the standard error of mean (SEM).

Are there age-related differences in the consolidation of general skill knowledge? – We tested the consolidation of general skill knowledge (defined as median RTs changes) over the delay period with a mixed-design ANOVA on median RTs (i.e., RTs irrespective of the probabilities of events) with EPOCH (Epoch 4 vs Epoch 5) as a within-subject factor and AGE GROUP as a between-subjects factor. Our analysis found that the median RTs significantly decreased over the 24-hour delay (main effect of EPOCH: F(1, 246) = 107.92, p < 0.001, $\eta_p^2 = 0.31$): participants responded faster in the Testing Phase compared to the end of the Learning Phase (significant speed-up in all age groups: all ps < 0.014, except for the 14-15-year-old group, where p = 0.080, Fig. 5.2.). The amount of speed-up over the delay period, however, was not uniform across the age groups (EPOCH x AGE GROUP interaction: F(8, 246) = 2.26, p = 0.02, $n_{\rm D}^2 = 0.07$). A follow-up ANOVA on the offline change score (i.e., RTs in Epoch 4 minus RTs in Epoch 5) showed that the 7-8-year-olds exhibited the greatest speed-up over the delay, significantly differing from the speed-up of almost all other age groups (ps < 0.026; 7-8-yearold vs 9-10-year-old groups: p = 0.068). The other age groups' median RT changes over the delay period were not significantly different from one another (all ps > 0.062). Bayesian mixeddesign ANOVA supported these results. Analyses on the standardized RT data revealed a significant RT speed-up over the delay period, however, in contrast to the ANOVA on raw RT scores, the age groups did not differ from each other in the amount of speed-up. The Bayesian mixed-design ANOVAs on standardized RT scores also supported this results. These results suggest that the group differences observed in the raw average RT analyses above were largely driven by some age groups being on average slower in the task than other groups; controlling for this confound eliminated the group differences in the consolidation of general skill knowledge over the delay period.



Figure 5.2. Consolidation of general skill knowledge over the 24-hour offline period across age groups. Average RT values for the last epoch of the Learning Phase (Epoch 4, light gray bars) were contrasted with those for the first epoch of the Testing Phase (Epoch 5, dark gray bars). BF_{01} values were obtained by paired-samples *t*-tests for this contrast separately for each age group. BF_{01} values for all age groups except for the 61-76-year-olds indicate substantial evidence for the alternative hypothesis ($BF_{01} < 0.33$) providing evidence for offline learning over the 24-hour delay. BF_{01} value obtained for the 61-76-year-olds could not provide evidence for either the null or the alternative hypotheses. Error bars denote the SEM.

Discussion

The present study examined the 24-hour consolidation of statistical and general skill knowledge in a large sample of participants between the age of 7 and 76 years using the same experimental design across the sample. Based on statistical learning scores computed from raw RT data, we showed retained statistical knowledge in all age groups. Analyses on standardized RT data and Bayesian analyses (both on raw RTs and standardized RTs) further corroborated these results. As for general skill knowledge, while the analyses on raw RT data suggested offline improvement that was the greatest in the 7-8-year-olds, results on standardized RT data revealed offline gains in all age groups with a uniform speed-up across the sample. Bayesian analyses of general skill consolidation also confirmed this uniform speed-up.

A considerable amount of research has focused on the changes of different cognitive functions across the lifespan. The lifespan trajectory of several cognitive functions has been described as an inverted U-shape: these functions continuously mature through childhood and adolescence, then peak in young or middle adulthood and decline over the course of aging (e.g., Alloway & Alloway, 2013; Zelazo, Craik, & Booth, 2004). Some functions peak in childhood and starts to decline as soon as adolescence or young adulthood (e.g., Janacsek et al., 2012; Johnson & Newport, 1989; Juhasz et al., 2019), whereas some functions remain intact in late adulthood as well (e.g., Ikier, Yang, & Hasher, 2008). The consolidation of statistical regularities seems to follow a different, age-invariant trajectory: the acquired statistical knowledge is comparably retained in all age groups from the age of 7 to 76 years. Consolidation of general skill knowledge also seems to follow an age-invariant trajectory: in this case, the offline improvement over the delay period is comparable across all age groups. Since the oldest adult in our study was 76 years old, future studies could provide further insights into how aging affects consolidation by involving individuals beyond this age as well.

VI. General discussion

Conclusions regarding atypical development

In Study 1, we examined how statistical and serial order-based regularities within the procedural memory system are affected in TS and whether they contribute to the possible procedural hyperfunctioning proposed by previous studies (Dye et al., 2016; Shephard et al., 2019; Takács et al., 2018; Walenski et al., 2007). Considering statistical regularities, we found enhanced sensitivity in TS: children with TS extracted these regularities faster than their typically developing peers. The acquisition of serial order-based regularities was impaired in TS: children with TS did not learn these regularities, whereas typically developing participants did.

The goal of Study 2 was to examine the consolidation of statistical and serial orderbased regularities over a short-term (five-hour) and long-term (one-year) offline delay in children with TS and typically developing peers. Both groups showed successful retention of statistical regularities following the offline periods and retention performance was comparable between the groups. The retention of serial order-based regularities could not be investigated in this study as children with TS did not acquire these regularities, therefore, their consolidation could not be reliable tested here.

Conclusions regarding typical development

To discover any potential developmental impact on procedural memory consolidation processes, Study 3 and 4 focused on typical development. These findings could help develop a theoretical model for age-related changes in procedural memory consolidation. Study 3 examined the one-year consolidation of statistical as well as serial order-based regularities in a sample of children and adolescents aged 9-15 years. Retained knowledge of both regularities has been shown: participants successfully acquired the regularities, which then were resistant to forgetting over a one-year delay. Our results are in line with prior studies showing successful one-year consolidation in healthy young adults (Kóbor et al., 2017; Romano et al., 2010), suggesting that retention is comparable in childhood and adulthood in typical development. Moreover, the lack of correlation between age and retention in our sample also points towards the direction of developmental invariance in procedural memory consolidation. Nonetheless, the results of Study 3 and prior studies can only provide indirect evidence. Hence, studies are needed which directly investigate this question using the same experimental design across age groups, as we aimed to do so in Study 4.

In Study 4, we tested the 24-hour consolidation of statistical and general skill knowledge in a cross-sectional design with participants between the ages of 7 and 76 years. Considering statistical knowledge, both raw and standardized RT data showed retained knowledge in all age groups, using both frequentist and Bayesian analyses. Regarding general skill knowledge, the analyses on raw RT data showed offline learning in all age groups, however, offline gain was significantly higher in the 7-8-year-olds than in the other age groups. Results on standardized RT data also suggested offline learning in all age groups, however, contrast to raw RT data, the offline gain was similar across the age groups. The uniform speed-up was corroborated by Bayesian analyses as well. Comparable retention of statistical knowledge across the age groups is in line with the results of Study 3 and with prior studies finding successful retention across various offline delays from childhood to old adulthood (e.g., Arciuli & Simpson, 2012; Hedenius, Lum, & Bölte, 2021; Kóbor et al., 2017; Nemeth, Janacsek, Király, et al., 2013).

Overall conclusions

To summarize the findings of the four studies, we can conclude that changes in the frontostriatal networks might influence learning as shown by age-variant statistical learning across the lifespan (Janacsek et al., 2012) and by enhanced statistical learning in TS (Study 1). In contrast, retention of the acquired knowledge might not be influenced by changes in the frontostriatal networks as consolidation is not altered in TS (Study 2) and age-invariant across the lifespan (Study 3 and 4).

VII. References

- Albin, R., & Mink, J. W. (2006). Recent advances in Tourette syndrome research. *Trends in Neurosciences*, 29(3), 175-183.
- Alloway, T. P., & Alloway, R. G. (2013). Working memory across the lifespan: A crosssectional approach. *Journal of Cognitive Psychology*, 25(1), 84-93.
- APA. (2013). *Diagnostic and statistical manual of mental disorders (DSM-5*®): American Psychiatric Pub.
- Arciuli, J., & Simpson, I. C. (2012). Statistical learning is lasting and consistent over time. *Neuroscience Letters*, 517(2), 133-135.
- Avanzino, L., Martino, D., Bove, M., De Grandis, E., Tacchino, A., Pelosin, E., . . . Abbruzzese, G. J. M. D. (2011). Movement lateralization and bimanual coordination in children with Tourette syndrome. 26(11), 2114-2118.
- Batterink, L. J., Paller, K. A., & Reber, P. J. (2019). Understanding the neural bases of implicit and statistical learning. *Topics in cognitive science*, *11*(3), 482-503.
- Conceição, V. A., Dias, Â., Farinha, A. C., & Maia, T. V. (2017). Premonitory urges and tics in Tourette syndrome: computational mechanisms and neural correlates. *Current Opinion in Neurobiology*, *46*, 187-199.
- Conway, C. M. (2020). How does the brain learn environmental structure? Ten core principles for understanding the neurocognitive mechanisms of statistical learning. *Neuroscience and Biobehavioral Reviews*, *112*, 279-299.
- Delorme, C., Salvador, A., Valabregue, R., Roze, E., Palminteri, S., Vidailhet, M., . . . Worbe, Y. (2016). Enhanced habit formation in Gilles de la Tourette syndrome. *Brain*, *139*(2), 605-615.
- Doyon, J., Bellec, P., Amsel, R., Penhune, V., Monchi, O., Carrier, J., . . . Benali, H. (2009). Contributions of the basal ganglia and functionally related brain structures to motor learning. *Behavioral Brain Research*, *199*(1), 61-75.
- Dye, C. D., Walenski, M., Mostofsky, S. H., & Ullman, M. T. (2016). A verbal strength in children with Tourette syndrome? Evidence from a non-word repetition task. *Brain and Language*, *160*, 61-70.
- Fanuel, L., Pleche, C., Vekony, T., Quentin, R., Janacsek, K., & Nemeth, D. (2020). The longer the better? General skill but not probabilistic learning improves with the duration of short rest periods. *bioRxiv*, 2020.2005.2012.090886. doi:10.1101/2020.05.12.090886
- Frith, C. D., & Frith, U. (2012). Mechanisms of social cognition. *Annual Review of Psychology*, 63, 287-313.
- Goodman, J., Marsh, R., Peterson, B. S., & Packard, M. G. (2014). Annual research review: the neurobehavioral development of multiple memory systems–implications for childhood and adolescent psychiatric disorders. *Journal of child psychology and psychiatry*, 55(6), 582-610.
- Hallgato, E., Győri-Dani, D., Pekár, J., Janacsek, K., & Nemeth, D. (2013). The differential consolidation of perceptual and motor learning in skill acquisition. *Cortex*, 49(4), 1073-1081.
- Hedenius, M., Lum, J. A., & Bölte, S. (2021). Alterations of procedural memory consolidation in children with developmental dyslexia. *Neuropsychology*, *35*(2), 185.
- Horvath, K., Torok, C., Pesthy, O., Nemeth, D., & Janacsek, K. (2020). Divided attention does not affect the acquisition and consolidation of transitional probabilities. *Scientific Reports*. doi:10.1038/s41598-020-79232-yda129685-49a7-438c-85e0-20e6384f29e9
- Howard, J. H., Jr., & Howard, D. V. (1997). Age differences in implicit learning of higherorder dependencies in serial patterns. *Psychology and Aging*, 12(4), 634-656.
- Ikier, S., Yang, L., & Hasher, L. (2008). Implicit proactive interference, age, and automatic versus controlled retrieval strategies. *Psychological Science*, 19(5), 456-461.

- Janacsek, K., Fiser, J., & Nemeth, D. (2012). The best time to acquire new skills: age-related differences in implicit sequence learning across the human lifespan. *Developmental science*, *15*(4), 496-505.
- Janacsek, K., Shattuck, K., Tagarelli, K., Lum, J., Turkeltaub, P., & Ullman, M. T. (2020). Sequence learning in the human brain: A functional neuroanatomical meta-analysis of serial reaction time studies. *Neuroimage*, 207, 116387.
- Johnson, J. S., & Newport, E. L. (1989). Critical period effects in second language learning: The influence of maturational state on the acquisition of English as a second language. *Cognitive Psychology*, 21(1), 60-99.
- Juhasz, D., Nemeth, D., & Janacsek, K. (2019). Is there more room to improve? The lifespan trajectory of procedural learning and its relationship to the between- and within-group differences in average response times. *PloS One*, 14(7), e0215116. doi:10.1371/journal.pone.0215116
- Kaufman, S. B., Deyoung, C. G., Gray, J. R., Jimenez, L., Brown, J., & Mackintosh, N. (2010). Implicit learning as an ability. *Cognition*, 116(3), 321-340. doi:10.1016/j.cognition.2010.05.011
- Kóbor, A., Janacsek, K., Takács, Á., & Nemeth, D. (2017). Statistical learning leads to persistent memory: Evidence for one-year consolidation. *Scientific Reports*, 7(1), 760. doi:10.1038/s41598-017-00807-3
- Kóbor, A., Takács, Á., Kardos, Z., Janacsek, K., Horváth, K., Csépe, V., & Nemeth, D. (2018). ERPs differentiate the sensitivity to statistical probabilities and the learning of sequential structures during procedural learning. *Biological Psychology*, 135, 180-193.
- Leckman, J. F., Riddle, M. A., Hardin, M. T., Ort, S. I., Swartz, K. L., Stevenson, J., & Cohen, D. J. (1989). The Yale Global Tic Severity Scale: initial testing of a clinician-rated scale of tic severity. *Journal of the American Academy of Child and Adolescent Psychiatry*, 28(4), 566-573.
- Lukács, Á., & Kemény, F. (2015). Development of different forms of skill learning throughout the lifespan. *Cognitive Science*, *39*(2), 383-404.
- Maia, T. V., & Conceição, V. A. J. B. p. (2017). The roles of phasic and tonic dopamine in tic learning and expression. 82(6), 401-412.
- McGaugh, J. L. (2000). Memory--A century of consolidation. Science, 287(5451), 248-251.
- Meier, B., & Cock, J. (2014). Offline consolidation in implicit sequence learning. *Cortex*, 57, 156-166.
- Nemeth, D., & Janacsek, K. (2011). The dynamics of implicit skill consolidation in young and elderly adults. *Journal of Gerontology Psychological Science*, *66*(1), 15-22.
- Nemeth, D., Janacsek, K., & Fiser, J. (2013). Age-dependent and coordinated shift in performance between implicit and explicit skill learning. *Frontiers in Computational Neuroscience*, 7. doi:10.3389/fncom.2013.00147
- Nemeth, D., Janacsek, K., Király, K., Londe, Z., Németh, K., Fazekas, K., ... Csányi, A. (2013). Probabilistic sequence learning in mild cognitive impairment. *Frontiers in Human Neuroscience*, 7, 318. doi:10.3389/fnhum.2013.00318
- Nemeth, D., Janacsek, K., Londe, Z., Ullman, M. T., Howard, D. V., & Howard, J. H., Jr. (2010). Sleep has no critical role in implicit motor sequence learning in young and old adults. *Experimental Brain Research*, 201(2), 351-358. doi:10.1007/s00221-009-2024x
- Nitsche, M. A., Schauenburg, A., Lang, N., Liebetanz, D., Exner, C., Paulus, W., & Tergau, F. (2003). Facilitation of implicit motor learning by weak transcranial direct current stimulation of the primary motor cortex in the human. *Journal of Cognitive Neuroscience*, 15(4), 619-626.

- Palminteri, S., Lebreton, M., Worbe, Y., Hartmann, A., Lehéricy, S., Vidailhet, M., . . . Pessiglione, M. (2011). Dopamine-dependent reinforcement of motor skill learning: evidence from Gilles de la Tourette syndrome. *Brain*, 134(8), 2287-2301.
- Poldrack, R. A., & Packard, M. G. (2003). Competition among multiple memory systems: converging evidence from animal and human brain studies. *Neuropsychologia*, 41(3), 245-251.
- Press, D. Z., Casement, M. D., Pascual-Leone, A., & Robertson, E. M. (2005). The time course of off-line motor sequence learning. *Cognitive Brain Research*, 25(1), 375-378.
- Robertson, E. M. (2009). From creation to consolidation: A novel framework for memory processing. *PLoS Biology*, 7(1), e1000019.
- Robertson, E. M., Pascual-Leone, A., & Miall, R. C. (2004). Current concepts in procedural consolidation. *Nature Reviews Neuroscience*, 5(7), 576-582.
- Romano, J. C., Howard, J. H., Jr., & Howard, D. V. (2010). One-year retention of general and sequence-specific skills in a probabilistic, serial reaction time task. *Memory*, 18(4), 427-441. doi:10.1080/09658211003742680
- Shephard, E., Groom, M. J., & Jackson, G. M. (2019). Implicit sequence learning in young people with Tourette syndrome with and without co-occurring attention-deficit/hyperactivity disorder. *Journal of Neuropsychology*, *13*(3), 529-549.
- Siegelman, N., Bogaerts, L., Christiansen, M. H., & Frost, R. (2017). Towards a theory of individual differences in statistical learning. *Phil. Trans. R. Soc. B*, 372(1711), 20160059.
- Simor, P., Zavecz, Z., Horvath, K., Elteto, 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.
- Song, S., Howard, J. H., Jr., & Howard, D. V. (2007a). Implicit probabilistic sequence learning is independent of explicit awareness. *Learning and Memory*, *14*, 167–176.
- Song, S., Howard, J. H., Jr., & Howard, D. V. (2007b). Sleep does not benefit probabilistic motor sequence learning. *Journal of Neuroscience*, 27(46), 12475-12483. doi:10.1523/jneurosci.2062-07.2007
- Squire, L. R. (1994). Declarative and Nondeclarative Memory: Multiple Brain Systems Supporting Learning and Memory. In D. L. Schacter & E. Tulving (Eds.), *Memory* Systems 1994 (pp. 407). Cambridge: The MIT Press.
- Squire, L. R., & Wixted, J. T. (2011). The cognitive neuroscience of human memory since H.M. Annual Review of Neuroscience, 34, 259-288.
- Stebbins, G. T., Singh, J., Weiner, J., Wilson, R. S., Goetz, C., & Gabrieli, J. D. E. (1995). Selective impairments of memory functioning in unmedicated adults with Gilles de la Tourette's syndrome. *Neuropsychology*, 9(3), 329-337.
- Takács, Á., Kóbor, A., Chezan, J., Éltető, N., Tárnok, Z., Nemeth, D., . . . Janacsek, K. (2018). Is procedural memory enhanced in Tourette syndrome? Evidence from a sequence learning task. *Cortex*, 100, 84-94.
- Takacs, A., Münchau, A., Nemeth, D., Roessner, V., & Beste, C. (2021). Lower-level associations in Gilles de la Tourette syndrome: convergence between hyperbinding of stimulus and response features and procedural hyperfunctioning theories. *European Journal of Neuroscience*.
- Tóth-Fáber, E., Janacsek, K., & Németh, D. (2021). Statistical and sequence learning lead to persistent memory in children after a one-year offline period. *Scientific Reports*, in press.
- Tóth-Fáber, E., Tárnok, Z., Janacsek, K., Kóbor, A., Nagy, P., Farkas, B. C., . . . Nemeth, D. (2021). Dissociation between two aspects of procedural learning in Tourette syndrome: Enhanced statistical and impaired sequence learning. *Child Neuropsychology*, 1-23.

Tukey, J. W. (1977). Exploratory data analysis. Reading, MA: Addison-Wesley.

- Ullman, M. T. (2004). Contributions of memory circuits to language: The declarative/procedural model. *Cognition*, 92(1-2), 231-270.
- Walenski, M., Mostofsky, S. H., & Ullman, M. T. (2007). Speeded processing of grammar and tool knowledge in Tourette's syndrome. *Neuropsychologia*, 45, 2447–2460.
- Walker, M. P. (2005). A refined model of sleep and the time course of memory formation. *Behavioral and Brain Sciences*, 28(1), 51-104.
- Walker, M. P., Brakefield, T., Hobson, J. A., & Stickgold, R. (2003). Dissociable stages of human memory consolidation and reconsolidation. *Nature*, 425(6958), 616-620.
- Zelazo, P. D., Craik, F. I. M., & Booth, L. (2004). Executive function across the life span. *Acta Psychologica*, 115, 167-183.
- Zwart, F. S., Vissers, C. T. W., Kessels, R. P., & Maes, J. H. (2019). Procedural learning across the lifespan: A systematic review with implications for atypical development. *Journal of Neuropsychology*, *13*(2), 149-182.

VIII. List of publications included in the dissertation

Tóth-Fáber, E., Tárnok, Z., Janacsek, K., Kóbor, A., Nagy, P., Farkas, B. C., Oláh, Sz., Merkl, D., Hegedűs, O., Nemeth, D., & Takács, Á. (2021). Dissociation between two aspects of procedural learning in Tourette syndrome: Enhanced statistical and impaired sequence learning. *Child Neuropsychology*, 27(6) 799-821.

https://doi.org/10.1080/09297049.2021.1894110

- Tóth-Fáber, E., Tárnok, Z., Takács, Á., Janacsek, K., & Nemeth, D. (2021). Access to procedural memories after one year: evidence for robust memory consolidation in Tourette syndrome. *Frontiers in Human Neuroscience*, 458. https://doi.org/10.3389/fnhum.2021.715254
- Tóth-Fáber, E., Janacsek, K. & Nemeth, D. (2021). Statistical and sequence learning lead to persistent memory in children after a one-year offline period. *Scientific Reports, 11*,
- 12418. <u>https://doi.org/10.1038/s41598-021-90560-5</u> **Tóth-Fáber, E.,** Nemeth, D. & Janacsek, K. (2023). Lifespan developmental invariance in memory consolidation: evidence from procedural memory. *PNAS Nexus*, pgad037. https://doi.org/10.1093/pnasnexus/pgad037

Total impact factor of the published studies: 10.79

Note: Each co-author has granted permission for the given publication to be included in the current dissertation.

IX. List of publications not included in the dissertation

Peer-reviewed scientific papers

International

- Wendiggensen, P., Paulus, T., Bluschke, A., Takacs, A., Tóth-Fáber, E., Weissbach, A., ... & Beste, C. (2023). Theta activity dynamics during embedded response plan processing in tourette syndrome. *Biomedicines*, 11(2), 393.
- Kóbor, A., Tóth-Fáber, E., Kardos, Z., Takács, Á., Éltető, N., Janacsek, K., ... & Nemeth, D. (2023). Deterministic and probabilistic regularities underlying risky choices are acquired in a changing decision context. *Scientific Reports*, 13(1), 1127.
- Tóth-Fáber, E., Janacsek, K., Szőllősi, Á., Kéri, Sz., & Nemeth, D. (2021). Regularity detection under stress: Faster extraction of probability-based regularities. *PloS ONE*, 16(6), e0253123.
- Farkas, B. Cs., Tóth-Fáber, E., Janacsek, K., & Nemeth, D. (2021). A Process-Oriented View of Procedural Memory Can Help Better Understand Tourette's Syndrome. *Frontiers in Human Neuroscience*, 15, 683885.
- Adelhöfer, N., Paulus, T., Mückschel, M., Bäumer, T., Bluschke, A., Takacs, A., Tóth-Fáber, E., Tarnok, Z., Roessner, V., Weissbach, A., Münchau, A., & Beste, C. (2021). Increased scale-free and aperiod activity during sensorimotor integration a novel facet in Tourette Syndrome. *Brain Commun*, 3, fcab250.
- Kóbor, A, Kardos, Z., Takács, Á., Éltető, N., Janacsek, K., Tóth-Fáber, E., Csépe, V., Nemeth, D. (2021). Adaptation to recent outcomes attenuates the lasting effect of initial experience on risky decisions. *Scientific Reports*, 11, 10132.
- Dilcher, R., Beste, C., Takacs, A., Bluschke, A., Tóth-Fáber, E., Kleimaker, M., Münchau, A., & Li, SC. (2021). Perception-action integration in young age - a cross-sectional EEG study. *Dev Cogn Neurosci*, 50, 100977.
- Beste, C., Mückschel, M., Rauch, J., Bluschke, A., Takacs, A., Dilcher, R., Tóth-Fáber, E., Bäumer, T., Roessner, V., Li, SC., & Münchau, A. (2021). Distinct brain-oscillatory neuroanatomical architecture of perception-action integration in adolescents with Tourette Syndrome. *Biol Psychiatry GOS*
- Dilcher, R., Jamous, R., Takacs, A., Tóth-Fáber, E., Münchau, A., Li, SC., & Beste, C. (2021). Neurophysiology of embedded response plans: age effects in action execution but not in feature integration from pre-adolescence to adulthood. *J Neurophysiol*, 125, 1382-1395.
- Éltető, N., Janacsek, K., Kóbor, A., Takács, Á., **Tóth-Fáber, E.,** & Nemeth, D. (2019). Do adolescents take more risks? Not when facing a novel uncertain situation. *Cognitive Development*, 50, 105-117.
- Tóth-Király, I., Bőthe, B., **Tóth-Fáber, E.,** Hága, Gy., & Orosz, G. (2017). Connected to TV series: Quantifying series watching engagement. *Journal of Behavioral Addictions*, 6(4), 472-489.

Hungarian

Tóth-Fáber, E., Takacs, A., Tarnok, Zs., Janacsek, K., & Nemeth, D. (2020). Cognitive advantage in atypical development: outstanding procedural learning in Tourette's syndrome. *Psychiatria Hungarica*, *35*(4), 484-492.

Conference presentations and posters

International

- **Tóth-Fáber, E.,** Tárnok, Zs., Takács, Á., Janacsek, K., & Németh, D. (2022 September). *Enhanced procedural functions in Tourette syndrome*. Poster presented, 22nd Conference of the European Society for Cognitive Psychology, Lille, France.
- Kóbor, A., **Tóth-Fáber, E.,** Éltető, N., Kardos, Zs., Bárány, D., & Németh, D. (2022 September). *Sensitivity to unexpected uncertainty is reflected by ERPs during risky decisions.* Poster presented, 22nd Conference of the European Society for Cognitive Psychology, Lille, France.
- **Tóth-Fáber, E.,** Janacsek, K., & Németh, D. (2022, May). *Age-invariant retention of statistical knowledge across the lifespan.* Poster presented, Interdisciplinary Advances in Statistical Learning, San Sebastian, Spain.
- Tóth-Fáber, E., Tarnok, Z., Takacs, A., Janacsek, K., & Nemeth, D. (2022, January). *Skill* consolidation in typical development and Tourette syndrome: Evidence for one-year retention. Poster presented, Budapest CEU Conference on Cognitive Development, online.
- Kovács, L.Á., Tóth-Fáber, E., Mikula, B., Simor, P., Janacsek, K., Zavecz, Zs., & Németh, D. (2021 June). Associations of sleep parameters with cognitive performance and behavioral problems in a pediatric sleepdisordered population. Poster presented, 5th international conference of the European Society for Cognitive and Affective Neuroscience, Budapest, Hungary.
- Tóth-Fáber, E., Janacsek, K., Szőllősi, Á., Kéri, Sz. & Németh, D. (2019, September). Dissociation within procedural learning under stress: boosted statistical learning but unaffected sequence learning. Poster presented, 21st Conference of the European Society for Cognitive Psychology, Tenerife, Spain.
- **Tóth-Fáber, E.,** Janacsek, K., Szőllősi, Á., Kéri, Sz. & Németh, D. (2019, March). *Stress Boosts Statistical Learning but Not Sequence Learning*. Poster presented, International Convention of Psychological Science, Paris, France.
- Farkas, B. Cs., Tóth-Fáber, E., Tárnok, Zs., Kóbor, A., Janacsek, K., Rádosi, A., Szabó, E. D., Merkl, D., Oláh, Sz., Hegedűs, O., Nagy, P., Vidomusz, R., Takács, Á., & Németh, D. (2019, March). *Executive Functions and Procedural Learning in Tourette Syndrome*. Poster presented, International Convention of Psychological Science, Paris, France.
- Tárnok, Zs., Tóth-Fáber, E., Kóbor, A., Janacsek, K., Rádosi, A., Szabó, E. D., Merkl, D., Oláh, Sz., Hegedűs, O., Nagy, P., Vidomusz, R., Németh, D., & Takács, Á. (2018, June). Enhanced procedural learning in Tourette syndrome and its relation to premonitory urges. Poster presented, 11th Conference on Tourette Syndrome and Tic Disorders, Copenhagen, Denmark.
- Tóth-Fáber, E., Tárnok, Zs., Kóbor, A., Janacsek, K., Rádosi, A., Szabó, E. D., Merkl, D., Oláh, Sz., Hegedűs, O., Nagy, P., Vidomusz, R., Németh, D., & Takács, Á. (2018, March). *Explicit probabilistic sequence learning in Tourette syndrome*. Poster presented, 25th Annual Meeting of the Cognitive Neuroscience Society, Boston, United States of America.
- Tóth-Fáber, E., Tárnok, Zs., Kóbor, A., Janacsek, K., Rádosi, A., Szabó, E. D., Merkl, D., Oláh, Sz., Hegedűs, O., Nagy, P., Vidomusz, R., Németh, D., & Takács, Á. (2018, January). *Implicit and explicit sequence learning in Tourette syndrome*. Poster presented, Budapest CEU Conference on Cognitive Development, Budapest, Hungary.
- Tóth-Fáber, E., Kóbor, A., Takács, Á., Kardos, Zs., Janacsek, K., Éltető, N., Csépe, V., & Nemeth, D. (2017, September). *The influence of initial experience on subsequent risk-*

taking behavior. Poster presented, 20th Conference of the European Society for Cognitive Psychology, Potsdam, Germany.

Tóth-Király, I., Bőthe, B., Tóth-Fáber, E., Hága, Gy., & Orosz, G. (2017, July). Connected to TV series: Quantifying Series Watching Engagement. Poster presented, 18th General Meeting of The European Association of Social Psychology. Granada, Spain.

Hungarian

- Tárnok, Zs., Tóth-Fáber, E., Janacsek, K., Kóbor, A., Nagy, P., Farkas, B. Cs., Oláh, Sz., Merkl, D., Hegedűs, O., Nemeth, D., & Takacs, A. (2021, May). Procedural hyperfunctioning in Tourette syndrome. Oral presentation, 44th Congress of the Hungarian Association of Child and Adolescent Psychiatry and Allied Professions, online.
- Mikula, B., Zavecz Zs., Tóth-Fáber, E., Kassai, R., Benedek, P., Németh, D. (2019, May). The relationship between declarative memory and sleep parameters in children with sleep disorders. Oral presentation, Hungarian Psychological Association's 28th National Scientific Session, Debrecen, Hungary.
- Farkas, B.Cs., Tóth-Fáber, E., Tárnok, Zs., Janacsek, K., Kóbor, A., Nagy, P., Németh, D., Takács, Á. (2019, May). *Learning processes in Tourette syndrome*. Oral presentation, Hungarian Psychological Association's 28th National Scientific Session, Debrecen, Hungary.
- Berta, K., Madura, Zs., Tass, A., Tóth-Fáber, E., Szőllősi, Á., Kéri, Sz., Janacsek, K., & Németh, D. (2019, May). *The effect of acute stress on procedural learning*. Oral presentation, Hungarian Psychological Association's 28th National Scientific Session, Debrecen, Hungary.
- Nagy, P., Hajnal, M., Tóth-Fáber, E., Bognár, E., Merkl, D., Vidomusz, R., Hegedűs, O., & Tárnok, Zs. (2019, May). Sensory phenomena in Tourette syndrome. Szenzoros jelenségek Tourette-szindrómában. Oral presentation, 43rd Congress of the Hungarian Association of Child and Adolescent Psychiatry and Allied Professions, Gyula, Hungary.
- **Tóth-Fáber, E.** (2018, November). *Implicit learning in childhood typical and atypical development*. Oral presentation, "Metszéspontok" V. Professional Conference, Szeged, Hungary.
- Tóth-Fáber, E., Tárnok, Zs., Kóbor, A., Janacsek, K., Rádosi, A., Szabó, E. D., Merkl, D., Oláh, Sz., Hegedűs, O., Nagy, P., Vidomusz, R., Németh, D., & Takács, Á. (2018, May). Statistical and sequence learning in Tourette Syndrome. Oral presentation, Hungarian Psychological Association's 27th National Scientific Session, Budapest, Hungary.