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FACULTEIT GENEESKUNDE EN LEVENSWETENSCHAPPEN
master in de revalidatiewetenschappen en de kinesitherapie

Masterproef

Multilimb coordination in adults with Autism Spectrum Disorder

Promotor :
Prof. dr. Marleen VANVUCHELEN

Copromotor :
dr. Koen CUYPERS

Lise Custers , Caroline Kleinmann

Scriptie ingediend tot het behalen van de graad van master in de revalidatiewetenschappen en de kinesitherapie

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Furthermore, we would like to thank dr. Caroline Beelen for the all the received data. Dr. Beelen carried out the data acquisition, wrote the research protocol, organized the recruitment of the participants and performed the actual testing of the participants.

Finally, our thankfulness goes to Cindy Leten and Jes Leysen who helped to optimize this master thesis, based on their advanced experience.

Diest, 2017 Lise Custers

Antwerpen, 2017 Caroline Kleinmann

Table of content

Research context

This observational explorative research compares individuals with Autism Spectrum Disorder (ASD) to Neurotypical Adults (NTA), concerning multi-limb coordination. While ASD is particularly well researched within a pediatric population it lacks research within an adult population, hence this study.

Individuals with ASD experience different symptoms in early childhood and possible findings of this study could help them manage their disorder from a younger age. It is known that an early diagnosis can help individuals with ASD in daily life. Specific impairments found in this study can be detected in an earlier age and be improved with an individual rehabilitation program.

The conducted multi-limb coordination test consists of different combinations of limb recruitment. When offered a visual cue, the participants had to lift corresponding limbs within a 1.5s time span. Results of this test can be used in further management of individuals with ASD.

We received the data of the multi-limb coordination test in 2016, but the data acquisition was done by dr. Caroline Beelen in 2015. She wrote the protocol of the study, organized the recruitment of the participants and the actual testing of the participants.

This duo-thesis was co-written by Lise Custers and Caroline Kleinmann with the help of Prof. dr. Marleen Vanvuchelen and dr. Koen Cuypers. After receiving the data, we divided the thesis into two parts, making this a 50-50 division in workload. The introduction and methods were written by Lise Custers whereas the data-analysis, the presentation and discussion of results were elaborated by Caroline Kleinmann.

Abstract

Background: Within Autism Spectrum Disorder (ASD) research, little is known concerning motor coordination tasks. Whereas results are inconclusive concerning reaction time of a performed task in comparison to a neurotypical control group, there is evidence of impairments concerning interpretation of visual information. Several hypotheses on the underlying mechanisms of motor limitations in individuals have been suggested but no consensus has been reached yet.

Objectives: Investigate the difference in multi-limb coordination between individuals with Autism Spectrum Disorder (ASD) and Neurotypical Adults (NTA).

Participants: 47 participants: 22 individuals with ASD and 25 NTA. All between 17-29 years of age, received at least 12 years of general education and individuals of the ASD-group were diagnosed by the DSM-V criteria.

Measurements: Primary outcome measures: reaction time (evaluated between the groups and per combination) and errors made (evaluated between the groups and per combination). Furthermore, limb, number of limbs, extremities, left/right side, SRS-A and AQ-score were analyzed in function of RT, error 1, error 2 and error total.

Results: The reaction time of the multi-limb test was similar for the ASD- and NTA-group in almost all different variables. A significant difference could be observed between both groups in error 1 in 3 combinations with 3 limbs. This significant difference regarding error 1 was also found in the different limbs, the two extremities, the two sides and when the number of limbs were 2 or 3. Regarding error 2 the difference between groups was not as outspoken as in error 1. The results for error total were similar to the results of error 1 except for a non-significant difference in combinations where the number of limbs was 2.

Conclusion: Individuals with ASD have a similar RT compared to Neurotypical Adults during the multi-limb coordination test. The ASD-group had more difficulties to perform the combinations without errors.

Keywords: Multi-limb, Coordination, Autism Spectrum Disorder, ASD, Pervasive Developmental Disorders

1 Introduction

Autism Spectrum Disorder is a multifactorial neurodevelopmental disorder defined by five major criteria that are classified in the Diagnostic and Statistical Manual of Mental disorder DSM-5. Criteria are as follows: (a) continuous impairment in interaction and communication that are reciprocal and social in nature; (b) patterns of activities, interests, and behaviors that are restricted and repetitive; (c) symptoms that are persistent from early childhood; (d) symptoms that interfere with everyday functioning; and (e) these disturbances are not better explained by intellectual disability (intellectual developmental disorder) or global developmental delay (Lobar 2016) (Appendix 1).

Previously, the DSM-IV criteria subdivided pervasive developmental disorders into Autistic Disorder (AD), Pervasive Developmental Disorder- not otherwise specified (PDD-NOS), Asperger's Disorder (AS), Rett's Disorder and Childhood Disintegrative Disorder (CDD), whereas the DSM-V criteria now encompass those four categories into a single entity Autism Spectrum Disorder (ASD) (Association 2013) (Appendix 2). The severity of ASD is indicated by three severity levels: requiring very substantial support, requiring substantial support and requiring support (Association 2013) (Appendix 3).

Since the prevalence rate of ASD continues increasing, with an estimated worldwide prevalence of 7.6% in 2014, ASD is a notable topic of research (Chmielewski and Beste 2015).

Within ASD-research most articles report on the most salient features of the disorder: deficits in social interaction and communication. For example, concerning social interactions: impairment of joint attention, ability to respond to gaze direction, imitate or initiate a shared focus with another individual could be indicators of future social deficits whereas dysfunctions in the mirror neuron system are considered to cause impairments in social interaction (Chmielewski and Beste 2015). When assessing literature about communication, a key factor is the lack of understanding non-literal language (Wang, Lee et al. 2006).

Another feature within this spectrum disorder is the deficit for motor coordination. In literature, the distinction between executive and visuo-motor function is commonly made. An 'executive function' (EF) refers to a variety of higher cognitive functions used to accomplish goals in a changing environment such as planning, inhibition, working memory, cognitive flexibility and initiation of action (Sachse, Schlitt et al. 2013).

Deficits in EF have been frequently reported in individuals with ASD and have been proposed to underlie stereotyped and repetitive behavior; one of the five main criteria for the diagnose of Autism Spectrum Disorder (Bölte, Westerwald et al. 2011). More specifically, ASD-individuals showed an impaired spatial working memory whereas planning, pure movement execution and inhibition was intact (Sachse, Schlitt et al. 2013).

Focusing on the visual part of motor performance it is known that, although individuals with ASD have no problems with their sight, they do have impaired interpretation of visual information. Bertone et al. demonstrated that individuals with ASD process motion stimuli that require additional neural processing (for example: stimulus-response tasks) less efficiently than a neurotypical comparison group. The cause of this impairment is possibly due to the diminished integrative function of neural mechanism at the perceptual level (Bertone, Mottron et al. 2003).

Regarding an ASD-population it is known that visual-perceptual processing is characterized by a superior performance while executing static spatial tasks, in big contrast to the performance registered during dynamic tasks (Bertone, Mottron et al. 2005). This phenomenon can be accounted for by the visual processing which takes place in the cortex of the brain. The ventral stream transmits information from the primary visual cortex to the temporal and frontal lobe and is used to recognize faces and objects. The dorsal stream goes from the primary visual cortex to the parietal and frontal lobes. In this stream the information is organized so it can be used for spatial control of actions. The functions that are related to the dorsal stream are tasks involving reaching, grasping, processing of motion, navigation, spatial memory, attention and executive functions. It is the dorsal stream that is more vulnerable in ASD (Braddick, Atkinson et al. 2003).

Within the domain of visuomotor performance, there is very little agreement between research groups. For example, Nebel et al. found that the connectivity of the visuo-motor function is interrupted in children with ASD. They also found that there is an incongruity between the visual and the motoric systems which causes a reduced integration between the visual input and the motoric output (Nebel, Eloyan et al. 2016). Whereas Gowen is convinced that deficits in motor performance are related to sensory misprocessing. This can be either caused by poor integration of information, which leads to less efficient motor planning or by increased variability in basic sensory inputs and motor output (Gowen and Hamilton 2013).

Conducting our experiment, a multi-limb coordination task, we will reflect on previous literature as well as implementing new information. Is reaction time linked with pathology, based on the assumptions of Bertone (Bertone, Mottron et al. 2005)? Are certain combinations more difficult to perform within an ASD-population because of planning difficulties, in contrary to what Sasche (Sachse, Schlitt et al. 2013) reported? Is there a link between ASD-severity, based on scores from screening instruments and motor performance?

We hope to enrich current literature with the answers to these fundamental questions and implement these finding as a base for contemporary revalidation.

2 Methods

2.1 Participants

Forty-seven subjects participated in this explorative research: 22 individuals with Autism Spectrum Disorder (ASD: 15 male, 7 female) and 25 Neurotypical Adults (NTA: 14 male, 11 female). All participants were aged between 17 and 29 years old (ASD: mean age = 21 years; NTA: mean age = 22 years). All participants had at least 12 years of general education.

The in- and exclusion criteria were as follows. Inclusion: 17-30 years old; ASD-diagnosis according to the DSM-V criteria; perfect knowledge of the Dutch language. Exclusion: visual deficits that are not corrected by lenses; history of seizure or head trauma; neurologic, chromosomal, psychiatric and medical disorders; psychotropic medication.

Participants were recruited on a voluntary basis after communication regarding this experiment by distribution of flyers, e-mail or via an ASD-website.

This study was approved by the ethics committees of Hasselt University and the University Hospitals of Louvain (Flanders, Belgium) before the collection of data. The experiment was performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki. All subjects gave their informed consent prior to their inclusion in the study.

2.2 Diagnosis

The diagnosis of ASD was based on the DSM-V diagnostic criteria and was confirmed by medical records. In addition, the Social Responsiveness Scale in self-report form (SRS-A) and Autism Spectrum Quotient (AQ-10) were presented to all participants.

Social Responsiveness Scale (SRS) (Constantino, Davis et al. 2003) is a 64-itemed quantitative measure of autistic traits. This questionnaire is developed for children between 4 and 18 years old and should be completed by a parent/teacher. Bölte reported good psychometric properties and cross-cultural validity of the scale for Autism Spectrum Disorder (ASD) (Bolte, Poustka et al. 2008)

Within this observational research based on an adult population, a revised form of the SRS was used. The Social Responsiveness Scale for Adults (SRS-A) also contains 64 items, scored on a 4-point Likert scale, concerning the past 6 months but is modified to address the social responsiveness in adulthood (Appendix 4). Completion of the questionnaire takes approximately 15-20 minutes.

Bölte reported on the good intern consistency (NTA: α=.71; ASD: α=.83), sensitivity (.85) and specificity (.83) of the SRS-A (Bolte 2012). This questionnaire was translated in Dutch by Roeyers et al. but no explicit validity or reliability research has been performed (Roeyers 2011).

Furthermore, subjects completed the AQ-10 questionnaire. This scale is a derivative of the Autism Spectrum Quotient which consists of 50 items, assessing personal preferences and habits. Those 50 items were theoretically divided into five subscales: social skill; communication; imagination; attention to detail; and attention switching. Participants rate to what extent they agree or disagree by using a 4-point Likert scale. A high total score indicates a high autistic load, close to the autistic end of the autism spectrum (Baron-Cohen, Wheelwright et al. 2001).

Booth et al. evaluated the ability of the AQ-10 (Appendix 5) to correctly classify individuals as suffering or not suffering from ASD. The results indicated the potential usefulness of the questionnaire as a brief screening instrument for ASD (Booth, Murray et al. 2013).

Concerning the Dutch version of the AQ-10 (Appendix 6) no validity or reliability research is documented yet whereas Hoekstra et al. evaluated the Dutch translation of the full AQ (AQ-50) as a reliable instrument to assess autism spectrum conditions (Hoekstra, Bartels et al. 2008).

2.3 Procedures

Within this observational explorative research a visual gross motor task was performed. All participants were seated at a desk behind a computer screen with their hands and feet placed on sensors. The four sensors were represented by four squares visible on the screen (Figure 1).

After the participants took place at the desk, the process of the multi-limb coordination task was explained through standardized instructions on the screen (PowerPoint presentation) (Appendix 7).

First, the subjects were informed about an exercise session prior to the actual experiment and were asked to perform both tasks to the best of their abilities: as accurately and quickly as possible. Subsequently, the starting position for both the exercise session and the experiment were described: four grey squares, representing both hands and feet were visible on the screen. When the limbs were placed correctly the squares colored white (Figure 1).

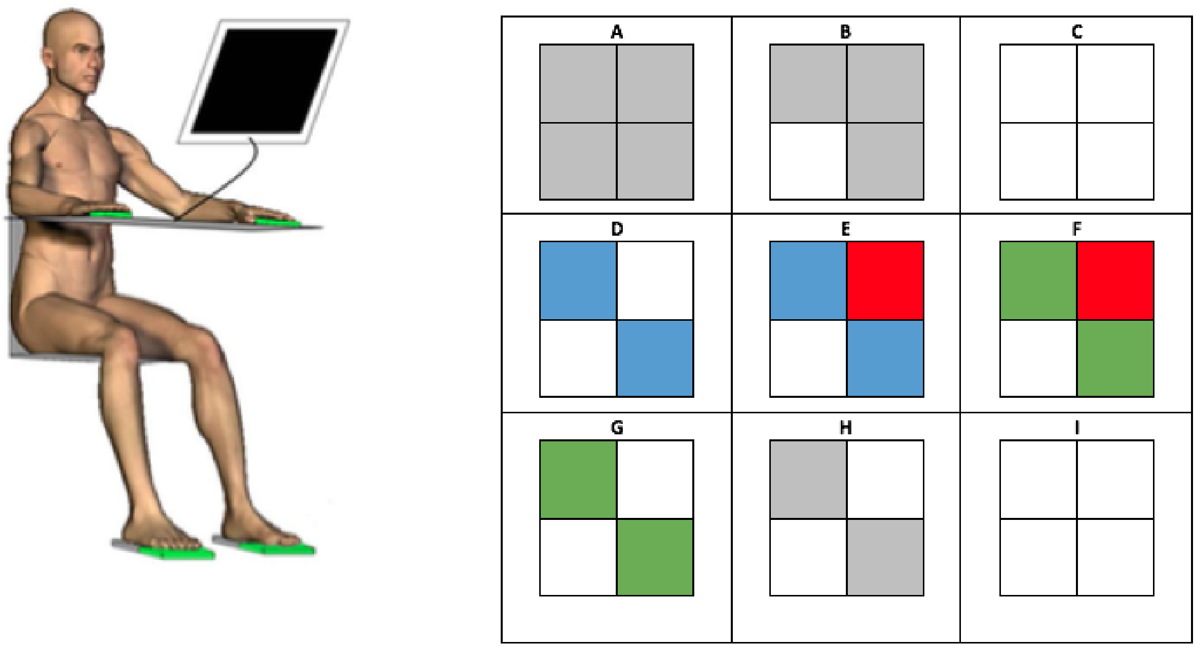


Figure 1 – Position of the multi-limb coordination test: 2 hands and 2 feet resting on 4 sensors. A: start screen, limbs are not yet in contact with the sensors, B: left foot is already in contact with the sensor, the 3 other limbs are not, C: all limbs are on the sensors, from this moment on the trial can start, D: the blue squares indicate which limbs need to be lifted, E: when the participants remove the wrong limb(s) the square will turn red, F: when the right limb(s) are removed the squares will turn green, G: only when there are no red squares (wrongfully removed limb) the trail can be validated, H: when the trial is validated the squares will turn back to grey meaning the participants need to replace the removed limbs back on the sensor, I: a new trial can start. The green and red feedback will only be given during the practice trial.

In the next slide, instructions were given on the three-minute exercise session: as multiple squares turned blue, the participants needed to lift their corresponding limbs as quickly and as synchronized as possible. Afterwards the limbs had to be repositioned rapidly on the sensors. The trial consisted of eleven different combinations. During the exercise session, the participants received feedback after each sequence. When performed correctly, the square of the corresponding limb turned green; when performed incorrectly, the square colored red. If the action was completed at a slow rate or the limb was not repositioned well, the square turned grey (Figure 1).

Finally, the participants were instructed that the exercise session was followed by a ten-minutes experimental session. The session consisted of the same eleven different combinations as during the exercise session, each randomly recurring six times. During this experimental session both the length of the trial was adapted (three vs ten minutes) and the right-or-wrong (green-or-red) feedback was omitted. When performed too slowly or repositioned inaccurately, the square turned grey as it did in the exercise session. At the end of the introduction additional time was allotted for questions.

From this experiment following factors can be derived: reaction time, group, combination, limbs, number of used limbs, extremities, left- of right-hand side, error (error 1/2/total), SRS-A +/- score and AQ + /– score (Table 1).

Table 1 – Definitions regarding outcome measures

Definitions regarding outcome measures	
Reaction time	Time between the visual stimulus and a detectable movement of the limbs
Groups	NTA-group: Neurotypical Adults ASD-group: Autism Spectrum Disorders
Limbs	Left hand (LH), Right hand (RH), Left foot (LF), Right foot (RF)
Number of limbs	2, 3, 4 limbs used per combination
Extremities	Hands or feet
Sides	Left or right
Combinations	Performed sequences: 11 possibilities (Table 10)
Error 1	Inability to lift all corresponding limbs in time/removing the wrong limb within time
Error 2	Inability to react within 1.5 second time limit
Error total	Error 1 + error 2
SRS- A +	Score of ≥ 60
SRS- A -	Score of < 60
AQ-10 +	Score of ≥ 6
AQ-10 -	Score of < 6

Primary outcome measures are:

- reaction time x group: RT compared between the different groups
- reaction time x combination: RT measured per combination
- error total x group: error total compared between the different groups
- error total x combination: error total measured per combination

Secondary outcome measures include:

- limb, number of limbs, extremities, left/right hand side, SRS-A and AQ-score which are analyzed in function of RT, error 1, error 2 and error total.

Afterwards, all secondary outcome measures were analyzed to check for differences between the groups (ASD-group vs NTA).

Not all the ASD-participants and NTA had a positive or negative result on the SRS-A or AQ-10, respectively and therefore, we divided the study population per SRS-A and AQ-score. Per scale, the participants were redistributed based on the test scores.

2.4 Data-analysis

Following testings were used to analyze the data: Wilcoxon non-parametric test (for all analysis with RT as outcome measure and differences between group distribution), Fisher exact two-tailed test, Pearson Chi-square test (error total, error 1 or error 2 as outcome measure) and Steel-Dwass all pairs comparison (comparison of RT between different combination and RT between different limbs used). The significance level was set on a p-value of $\alpha \leq 0.05$

Analysis of the data was performed with JMP, version Pro 12.2.0 (64-bit).

3 Results

3.1 Sample characteristics

Information regarding age, gender, AQ-10 and SRS-A score can be found in Table 2. Age ranged from 17 to 29, with a mean age of 21 (±2.68) in the ASD-group and 22 (±2.22) in the NTA-group, with no significant difference between groups, *Z = 1.88, p= 0.0592* .

With respect to gender, the ASD-group was predominantly male (15/22) but no significant difference, X^2 *(1, n= 47) = 0.735, p= 0.3913* could be found when compared to the NTA-group (14/25).

Table 2 – Sample characteristics. Age: in years, Mean, ± SD, Gender: Number, percentage, SRS-A: social responsiveness scale for adults: Mean, ± SD, AQ-10: Autism Quotient in 10 questions , Mean, ±SD, ASD: Autism Spectrum Disorders, NTA: Neurotypical Adults, * significant results: p< 0.05

	ASD	NTA	P-value
Age	21 ±2.68	22 ±2.22	0.0578
Gender (male)	15 68.18%	14 56.00%	0.3193
SRS-A positive	13 59.09%	2 8.00%	0.0002*
AQ-10 positive	11 52.38%	3 12.50%	0.0039*

The two screening tests were both significantly different between groups. The level of significance for AQ-10 was X^2 *(1, n= 45) = 8.312, p= 0.0039*, and for the SRS-A score X^2 *(1, n= 47) = 14.057, p= 0.0002*.

As suspected, the ASD-group did have the most positive scores of the SRS-A (13/22) and AQ-10 (11/21), one person did not take the test. The NTA-group however had also 2 positive scores on the SRS-A screening and 3 on the AQ-10 screening, one person did not take the AQ-10 test.

3.2 Reaction time

No significant difference was found between both groups regarding Mean Reaction Time (MRT), *Z= 0.15, p= 0.8846,* both groups even had an identical MRT of 792ms (Figure 2).

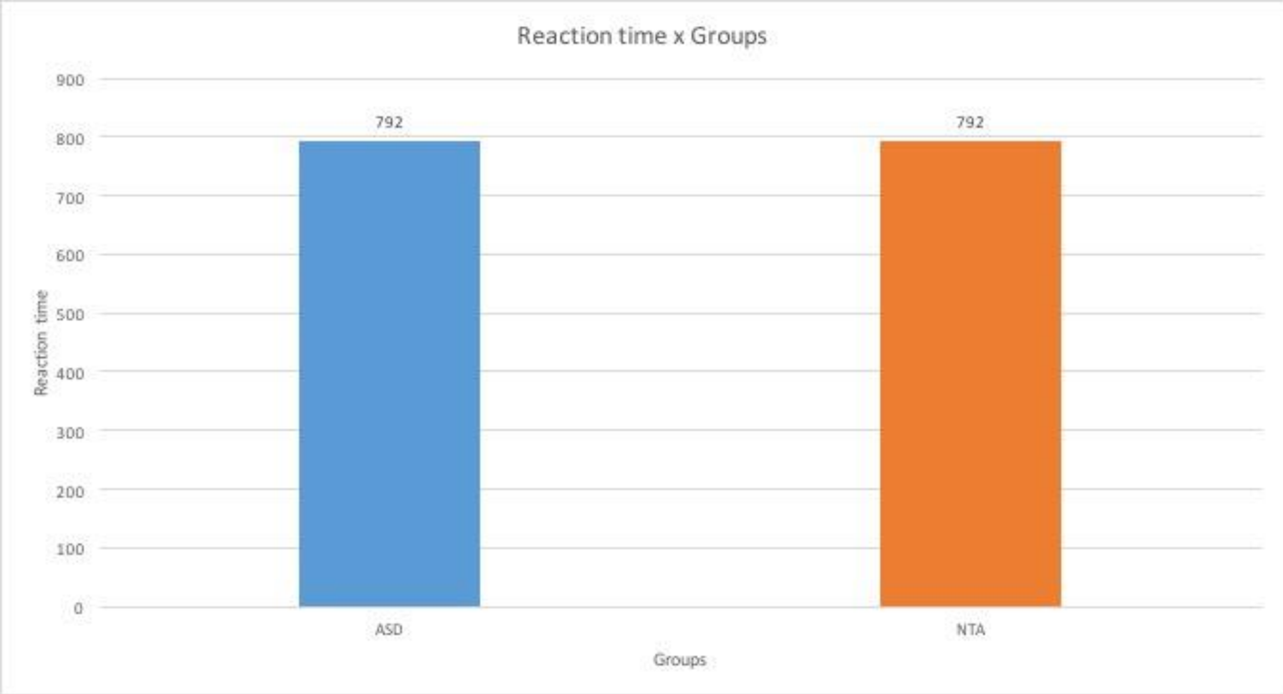
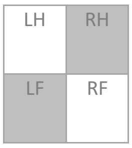
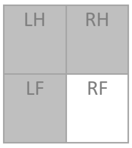
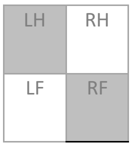
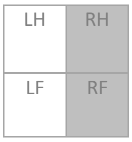
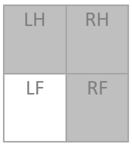
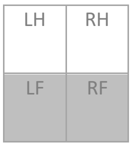
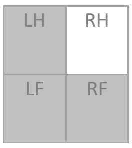


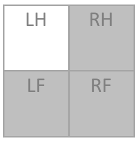
Figure 2 – Mean reaction time (ms) of both groups, ASD: Autism Spectrum Disorders, NTA: Neurotypical Adults

Looking at the MRT split in the different combinations, results showed that the NTA-group was only significantly faster in combination 3, *Z= 2.16, p= 0.0309* (Table 3).

Table 3 – Reaction time and accuracy of both groups and all participants together in 11 different combinations. Reaction time: mean in milliseconds, ± SD, Error: mean, total percentage, * significant results: p< 0.05, ** fisher exact test was used, cell count was <5

Combination		**ASD**	**NTA**	**P-value**	**All participants**
3	*Mean reaction time (ms)*	666.842 ±130.287	631.263 ±106.453	0.0309*	647.88 ±119.278
LH RH / LF RF	*Error 1*	9 6.82%	3 2.00%	0.0550	12 4.26%
	Error 2	3 2.27%	10 6.67%	0.0953	13 4.61%
	Total Error rate	12 9.09%	13 8.67%	0.9005	25 8.87%
5	*Mean reaction time*	737.215 ±139.789	712.867 ±145.373	0.1024	724.46 ±142.999
LH RH / LF RF	*Error 1***	1 0.76%	1 0.67%	1.0000	2 0.71%
	*Error 2***	1 0.76%	6 4.00%	0.1257	7 2.48%
	*Total Error rate***	2 1.52%	7 4.67%	0.1808	9 3.19%

6	*Mean reaction time*	882.867 ±202.121	855.409 ±153.523	0.5146	866.54 ±174.505
	*Error 1*	43 32.58%	23 15.33%	0.0015*	66 23.40%
	Error 2	44 33.33%	61 40.67%	0.8387	105 37.23%
	Total Error rate	87 65.91%	84 56.00%	0.0892	171 60.64%
7	*Mean reaction time*	935.016 ±181.129	885.000 ±193.659	0.1994	900.47 ±189.360
	*Error 1*	30 22.73%	17 11.33%	0.0022*	47 16.67%
	Error 2	39 29.55%	33 22.00%	0.0269*	72 25.53%
	Total Error rate	69 52.27%	50 33.33%	0.0013*	119 42.20%
9	*Mean reaction time*	855.933 ±210.492	931.280 ±153.997	0.0990	903.03 ±179.781
	*Error 1*	52 39.39%	33 22.00%	0.0024*	85 30.14%
	Error 2	50 37.88%	67 44.67%	0.4625	117 41.49%
	Total Error rate	102 77.27%	100 66.67%	0.0487*	202 71.63%
10	*Mean reaction time*	719.059 ±137.180	694.775 ±123.935	0.1166	706.02 ±130.542
	*Error 1*	8 6.06%	7 4.67%	0.5958	15 5.32%
	*Error 2***	5 3.79%	5 3.55%	1.0000	10 3.55%
	Total Error rate	13 9.85%	12 8.00%	0.5858	25 8.87%
11	*Mean reaction time*	885.222 ±171.391	892.383 ±166.672	0.8120	889.28 ±168.257
	*Error 1*	26 19.70%	21 14.00%	0.1469	47 16.67%
	Error 2	34 25.76%	35 23.33%	0.4076	69 24.47%
	Total Error rate	60 45.45%	56 37.33%	0.1667	116 41.13
12	*Mean reaction time*	704.762 ±125.055	708.440 ±129.346	0.8568	706.73 ±127.145
	*Error 1*	7 5.30%	4 2.67%	0.2615	11 3.90%
	*Error 2***	3 2.27%	5 3.33%	0.7292	8 2.84%
	Total Error rate	10 7.58%	9 6.00%	0.5984	19 6.74%
13	*Mean reaction time*	1021.55 ±191.406	987.17 ±179.584	0.2140	1000.77 ±184.438
	*Error 1*	31 23.48%	25 16.67%	0.0445*	56 19.86%
	Error 2	46 34.85%	41 27.33%	0.0503	87 30.85%
	Total Error rate	77 58.33%	66 44.00%	0.0163*	143 50.71%

14 	*Mean reaction time*	956.190 ±211.075	965.020 ±194.007	0.6638	961.78 ±199.818
	Error 1	42 31.82%	26 17.33%	0.0005*	68 24.11%
	Error 2	32 24.25%	24 16.00%	0.0078*	56 19.86%
	Total Error rate	74 56.06%	50 33.33%	<0.0001*	124 43.97%
15 	*Mean reaction time*	776.794 ±166.981	758.329 ±130.977	0.8083	766.98 ±148.928
	*Error 1***	3 2.27%	6 4.00%	0.5111	9 3.19%
	*Error 2**	3 2.27%	1 0.67%	0.3468	4 1.42%
	*Total Error rate***	6 4.55%	7 4.67%	1.0000	13 4.61%

The combinations as a whole have a strong effect on RT in both groups, *Z= 692.40, p< 0.001*. As shown in Figure 3; both groups performed slowest in combination 13 (ASD: 1022ms, NTA: 987ms) and fastest in combination 3 (ASD: 667ms, NTA: 631ms).

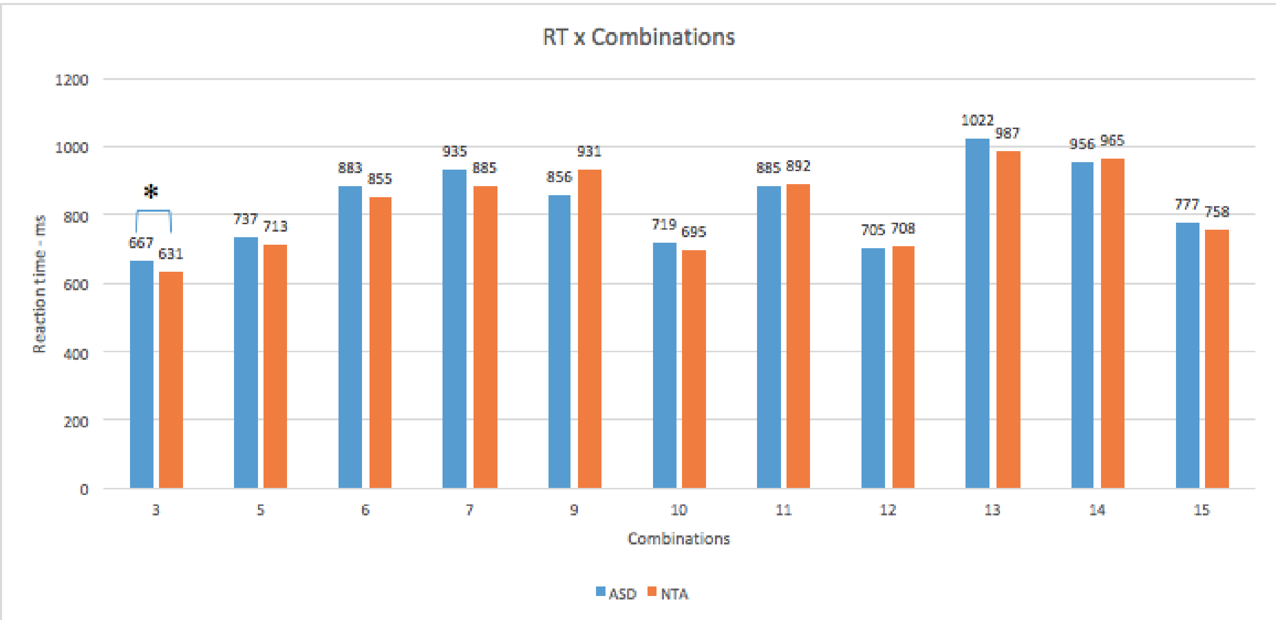


Figure 3 – Reaction time (ms) of both groups in 11 combinations, * significant results: p< 0.05, ASD: Autism Spectrum Disorder, NTA: Neurotypical Adults. There was a strong main effect of the combinations as a whole on the RT (p< 0.001)

The main observations to be made in Table 4 are: the most substantial differences between both groups were found between combination 14-3 (173ms), 13-3 (172ms), 13-12 (158ms), 11-3 (157ms), 13-10 (156ms). The combinations with 3 limbs were performed the slowest and the combinations with 2 limbs were carried out the fastest, especially combination 3 (hand-hand) was significantly faster than all combinations with 3 limbs.

Table 4 – Multiple comparison between different combinations using steel-dwass multiple comparison. Reaction time: mean difference in milliseconds, ± Std Err Dif, * significant results: p< 0.05

Combi-nations	3	5	6	7	9	10	11	12	13	14
5	86.188 ±13.31009 p <0.0001*									
6	127.498 ±12.08199 p <0.0001*	92.347 ±12.49468 p <0.0001*								
7	152.451 ±12.15449 p <0.0001*	116.758 ±12.47266 p <0.0001*	14.894 ±9.75141 p 0.9110							
9	124.670 ±12.47334 p <0.0001*	99.653 ±12.97346 p <0.0001*	13.798 ±8.10738 p 0.8351	2.730 ±9.59546 p 1.0000						
10	69.914 ±13.10201 p <0.0001*	18.821 ±13.31009 p 0.9453	97.924 ±12.08197 p <0.0001*	124.227 ±12.15446 p < 0.0001*	103.927 ±12.47328 p <0.0001*					
11	157.106 ±12.17331 p <0.0001*	119.142 ±12.48711 p <0.0001*	11.297 ±9.82180 p 0.9874	5.453 ±10.48843 p 1.0000	8.095 ±9.68474 p 0.9991	12.,568 ±12.17329 p <0.0001*				
12	74.014 ±13.17900 p <0.0001*	16.147 ±13.38131 p 0.9819	100.652 ±12.23638 p <0.0001*	125.681 ±12.27320 p < 0.0001*	105.508 ±12.66064 p <0.0001*	3.704 ±13.17900 p 1.0000	128.318 ±12.29039 p <0.0001*			
13	171.695 ±12.05099 p <0.0001*	153.673 ±12.40768 p <0.0001*	50.975 ±9.20480 p <0.0001*	45.406 ±10.08170 p 0.0003*	32.584 ±8.89217 p 0.0112*	155.721 ±12.05097 p <0.0001*	53.217 ±10.13921 p <0.0001*	158.152 ±16.26024 p <0.0001*		
14	172.695 ±12.12468 p <0.0001*	143.122 ±12.45134 p <0.0001*	35.462 ±9.63495 p 0.0106*	25.396 ±10.36135 p 0.3340	16.937 ±9.44728 p 0.7848	149.541 ±12.12566 p <0.0001*	31.834 ±10.41140 p 0.0802	151.236 ±12.24723 p <0.0001*	20.272 ±9.98698 p 0.6279	
15	127.667 ±13.25725 p <0.0001*	43.578 ±13.45388 p 0.0470*	67.253 ±12.39121 p< 0.0001*	92.110 ±12.39264 p < 0.0001*	80.260 ±12.84823 p <0.0001*	65.186 ±13.25723 p <0.0001*	92.486 ±12.40818 p <0.0001*	61.955 ±13.32989 p 0.0002*	135.987 ±12.31812 p <0.0001*	121.051 ±12.36948 p <0.0001*

The difference in RT between all different limbs is displayed in Table 5. A significant difference was found between all different limbs except within the same extremity (hand-hand, foot-foot), this analysis was done using the data of all participants. Figure 4 illustrates the same findings.

Table 5 – Multiple comparison between different limbs using steel-dwass multiple comparison. Reaction time: mean in milliseconds, ± SD, * significant results: p< 0.05

	Right hand	Left hand	Right foot
Left hand	7.631 ±30.16293 p 0.9943		
Right foot	206.411 ±30.08251 p <0.0001*	212.829 ±29.88906 p <0.0001*	
Left foot	203.786 ±30.32049 p <0.0001*	209.897 ±30.13467 p <0.0001*	6.297 ±30.05385 p 0.9967

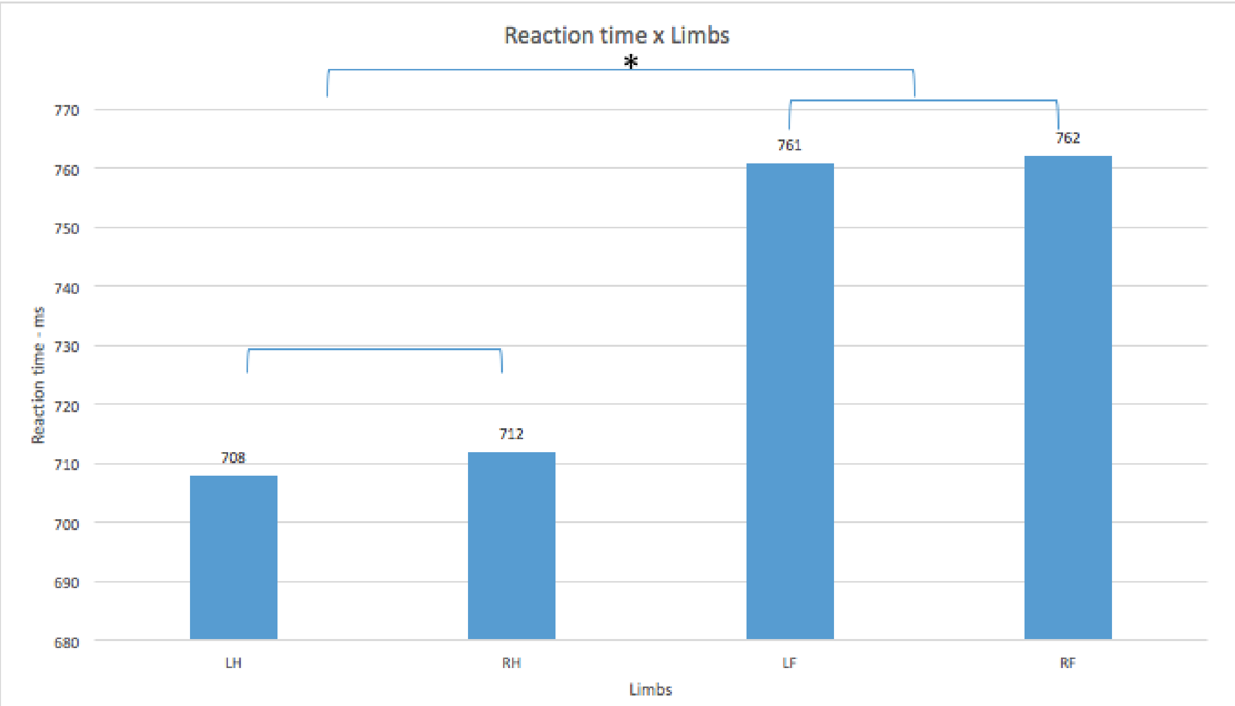


Figure 4 – Reaction time (ms) of different limbs, LH: left hand, RH: right hand, LF: left foot, RF: right foot, * significant results: p< 0.05

Analyzing reaction time of both groups for the four different limbs, no significant difference was found. When comparing both groups in the different extremities, both hands, *Z= 1.23, p = 0.2181*, nor feet, *Z= 1.87, p= 0.0615* were significantly different. This similarity between groups was also found for the number of limbs and the different sides involved (Table 6).

Table 6 - Reaction time regarding different limbs in both groups and all participants, extremities, sides and number of limbs.
Reaction time: mean in ms, ± SD, ASD: Autism Spectrum Disorder, NTA: Neurotypical Adults, * significant results: p< 0.05

	Reaction time			
	ASD	**NTA**	**P-value**	**All participants**
Right hand	715.575 ±182.472	708.414 ±169.552	0.3021	711.541 ±175.282
Left hand	714.836 ±168.557	702.570 ±181.852	0.4710	707.997 ±176.135
Hands total	715.208 ±175.620	705.543 ±175.668	0.2181	709.791 ±175.680
Right foot	754.811 ±198.190	767.185 ±189.120	0.1466	761.779 ±193.159
Left foot	754.255 ±184.977	766.457 ±185.803	0.2315	761.145 ±185.475
Feet total	754.529 ±191.521	766.815 ±187.378	0.0615	761.457 ±189.259
Left side	809.167 ±195.555	807.190 ±191.728	0.9951	808.057 ±193.384
Right side	802.657 ±193.982	805.123 ±189.859	0.6100	804.046 ±191.639
Number of limbs = 2	729.355 ±156.514	721.797 ±155.585	0.3253	725.244 ±155.992
Number of limbs = 3	942.161 ±193.492	930.709 ±188.755	0.4958	935.246 ±190.574
Number of limbs = 4	776,794 ±166,981	758.329 ±130.977	0.8083	766.978 ±148.928

When dividing all our participants in two groups according to their SRS-A score, the RT was not found to be significantly different between the SRS-A positive and negative group, *Z= 1.46, p= 0.15*. When redistributing the participants according to their AQ-10 score a similar result could be found, *Z= 0.22, p= 0.85* (Table 7).

Table 7 – Reaction time and error total was compared in both positive as negative SRS-1 and AQ-10 groups. Reaction time: mean difference in milliseconds, ± Std Err Dif, SRS-1: social responsiveness scale for adults, AQ-10, Autism questionnaire with 10 questions, * significant results: p< 0.05

	SRS-A			***AQ-10***		
	SRS-A +	**SRS-A -**	**P-value**	**AQ +**	**AQ -**	**P-value**
Total error rate	314 31.72%	652 30.87%	0.6353	351 35.41%	575 29.04%	0.0004*
Reaction time	783.775 ±188.616	795.875 ±191.096	0.1452	795.599 ±192.179	791.915 ±190.512	0.8252

3.3 Accuracy

Two types of error could be made. Type 1: inability to lift all corresponding limbs in time or removing the wrong limb within time. Type 2: inability to react within 1.5s time limit. Error total is a combination of both types.

3.3.1 Error total

There was a significant difference in total error rate between the ASD- and the NTA-group. The ASD-group had a higher error rate, X^2 *(1, n= 3102) = 21.614, p < 0.0001* (Figure 5).

Figure 5 – Number of error 1, error 2 and error total compared in both groups, ASD: Autism Spectrum Disorder, NTA: Neurotypical Adults, * significant results: p< 0.05

The combinations 7, 9, 13, 14 were significantly different between both groups (Table 3).

When dividing the participants based on their SRS-A score, no significant difference in total error rate could be determined between the participants with a score ≥60 and the ones with a lower score, X^2 *(1, n= 3102) = 0.225, p = 0.6353*. The AQ-10 score however had a significant association with error, X^2 *(1, n= 2970) = 12.654, p = 0.0004* (Table 7).

There was a significant effect of the combinations in total on the number of errors, X^2 *(10, n= 3102) = 835.376, p < 0.0001*.

There was a significant difference in total error rate between both groups regarding all the limbs, the extremities, and the sides. The values are presented in Table 8. In addition, results showed that the ASD-group made more errors in the combinations with 3 limbs, X^2 *(1, n= 1128) = 29.221, p <0.0001*, but not when the number of limbs was 2 or 4.

Table 8 - Error total of both groups and all participants regarding the different limbs, extremities, sides and number of limbs. Error: total, percentage, ASD: Autism Spectrum Disorder, NTA: Neurotypical Adults, * significant results: p< 0.05

	Error total			
	ASD	**NTA**	**P-value**	**All participants**
Right hand	321 34.74%	272 25.90%	<0.0001*	593 30.04%
Left hand	328 35.50%	299 28.48%	0.0008*	627 31.76%
Hands total	649 35.12%	571 27.19%	<0.0001*	1220 30.90%
Right foot	342 37.01%	300 28.57%	<0.0001*	642 32.52%
Left foot	325 35.17%	273 26.00%	<0.0001*	598 30.29%
Feet total	667 36.09%	573 27.29%	<0.0001*	1240 31.41%
Left side	653 35.34%	572 27.24%	<0.0001*	1225 31.03%
Right side	663 35.88%	572 27.24%	<0.0001*	1235 31.28%
Number of limbs = 2	226 28.54%	225 25.00%	0.1008	451 26.65%
Number of limbs = 3	280 53.03%	222 37.00%	<0.0001*	502 44.50%
Number of limbs = 4	6 4.55%	7 4.67	0.9614	13 4.61%

3.3.2 Error 1 and error 2

Looking separately at error 1 in Figure 5, there can be reported that the ASD-group made significantly more type 1 errors in comparison to the NTA-group, X^2 *(1, n= 2554) = 37.225, p <0.0001*. The type 2 errors were not significantly different between both groups, X^2 *(1, n= 2684) = 2.0850, p= 0.1488*. The results for the differences between both groups in the different combinations are summarized in Table 2.

No difference can be reported in the various limbs except for the left foot X^2 *(1, n= 1715) = 3.995, p= 0.0456* when looking at the error 2 rate. There was however a significant difference in both sides, both extremities and when the number of limbs was 3 (Table 9).

For the type 1 errors all variables were significantly different between both groups except for the combinations when the number of limbs was 4, *p= 0.5111 two tailed Fisher exact test* (Table 9).

Table 9 - Error 1 and error 2 of both groups and all participants regarding the different limbs, extremities, sides and number of limbs. Error: total, percentage, ASD: Autism Spectrum Disorder, NTA: Neurotypical Adults, * significant results: p< 0.05, ** fisher exact test was used, cell count was <5

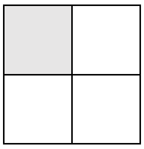
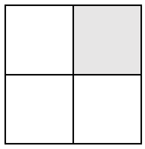
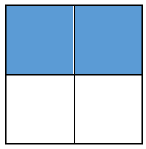
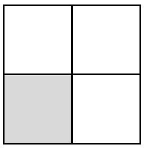
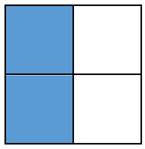
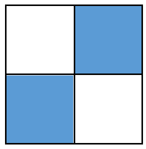
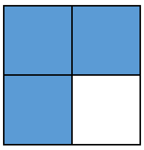
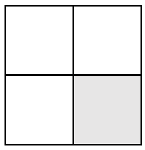
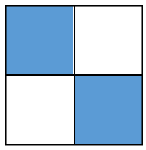
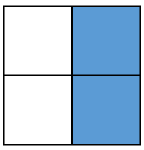
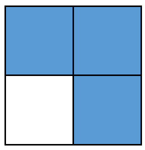
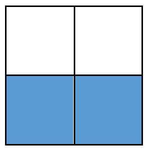
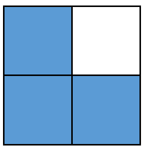
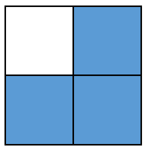
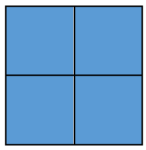
	Error 1				***Error 2***			
	ASD	**NTA**	**P-value**	**All Participants**	**ASD**	**NTA**	**P-value**	**All Participants**
Right hand	161 17.42%	102 9.81%	<0.0001*	264 16.05%	160 17.32%	169 16.10%	0.1033	329 19.24%
Left hand	152 16.45%	106 10.10%	<0.0001*	258 16.07%	176 19.05%	193 18.38%	0.2379	369 21.50%
Hands total	313 20.70%	209 12.03%	<0.0001*	522 16.06%	336 21.89%	362 19.14%	0.0472*	698 20.37%
Right foot	169 18.29%	122 11.62%	<0.0001*	291 17.93%	173 18.72%	178 16.95%	0.0608	351 20.86%
Left foot	157 16.99%	102 9.71%	<0.0001*	259 15.84%	168 18.18%	171 16.29%	0.0456*	339 19.77%
Feet total	326 21.63%	224 12.79%	<0.0001*	550 16.88%	341 22.40%	349 18.60%	0.0062*	690 20.31%
Left side	309 16.72%	208 9.90%	<0.0001*	517 15.96%	344 18.61%	364 17.33%	0.0250*	708 20.64%
Right side	330 17.86%	225 10.71%	<0.0001*	555 16.98%	333 18.02%	347 16.52%	0.0131*	680 20.04%
Number of limbs = 2	120 15.15%	71 7.89%	<0.0001*	191 11.29%	106 13.38%	154 17.11%	0.1536	260 15.37%
Number of limbs = 3	129 24.43%	89 14.83%	<0.0001*	218 19.33%	151 28.60%	133 22.17%	0.0001*	284 25.18%
Number of limbs = 4 **	3 2.27%	6 4.00%	0.5111	9 3.19%	3 2.27%	1 0.67%	0.3468	4 1.42%

4 Discussion

This study is, to our knowledge, the first to research the multi-limb coordination of both hands and feet, using a reaction time test in individuals with ASD.

The participants were evaluated using the multi-limb coordination test consisting of 15 combinations using 1 to 4 limbs. Since we are testing multi-limb coordination we only used 11 out of 15 combinations: the four combinations involving 1 limb were excluded (Table 10).

Table 10 - 15 combinations with 11 combinations used during our multi-limb test. Combinations 1,2,4 and 8 were excluded

1		**2**		**3**	
4		5		6	
7		8		9	
10		11		12	
13		14		15	

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In this study was tested if ASD has any influence on the coordination between the limbs, and if any impairment in execution or speed could be found when the ASD-participants are compared to Neurotypical Adults.

The reaction time (RT) and the accuracy were examined in correlation with these 11 combinations: the four different limbs, two extremities, the number of limbs, and the different sides (Table 1). To gain a better insight in the impairments found during this study, the movements were subdivided into three types of movements. A homologous movement could be described as a hand-hand or foot-foot combination, ipsilateral movements when two limbs of the same side (left-right) were requested, and diagonal when two diagonal limbs were recruited. The combinations with 3 limbs were categorized as diagonal movement.

Participants started with a practice trial of 11 combinations, this trial was conducted to limit the learning effect during the actual test. This study did not examine the results of this practice trial, only the data of the actual test are analyzed and discussed.

4.1 Reaction time

The aim of the study was to investigate the difference in multi-limb coordination between Neurotypical Adults (n= 22) and a group of participants with ASD (n= 21) (Table 2).

When looking at the MRT (Figure 2), no difference was found between both groups. This is the first time a multi-limb coordination test using reaction time is used for participants with ASD, therefore no comparison could be made with earlier studies.

When comparing the groups within each of the 11 combinations, only combination 3 resulted in a significant difference between both groups with a difference of only 35ms. This homogenous combination had the fastest MRT regarding all participants, making it the simplest combination within the multi-limb tasks. This combination can be compared to a simple reaction time task, consisting of a single hand or finger response on a visual cue. When looking at previous research, results were inconclusive when comparing individuals with ASD- to a NTA-group (Glazebrook, Elliott et al. 2006, Todd, Mills et al. 2009, Xiao, Xiao et al. 2012). Because of the small difference between groups, this result needs to be examined with some caution.

The 11 combinations as a whole had a significant impact on the RT in both groups. The combinations with 3 limbs were performed the slowest, followed by those with 4 limbs, and the combinations using 2 limbs had the fastest RT. This is in line with the research by Boisgontier. He proposes a model of coupling/decoupling interactions where there is an easy excitatory interaction and inhibition between homologous movements, a more difficult interaction between ipsilateral movements and the most difficult between diagonal limbs. The only difference between the results of Boisgontier and the results derived from the data of our experiment is that Boisgontier did not find a significant difference in RT between 3 and 4 limbs (Boisgontier, Wittenberg et al. 2014). No inhibition is needed during the combination with 4 limbs making it less complicated than those with 3 limbs. This could explain why a faster RT was found during our research.

A significant influence was determined regarding the extremities: the RT of the feet was 52ms slower compared to the RT of the hands (Table 4). This was also confirmed in the article of Boisgontier (Boisgontier, Wittenberg et al. 2014). In his study Boisgontier suggests that the difference can be explained by the longer nerve pathways to the feet, and additionally takes into consideration that the weight to lift a foot is higher than the weight to lift a hand.

When comparing the RT of the different limbs, data showed that on a homogenous level the reaction times were very similar (Figure 4). These results are confirmed in other literature (Rabbitt 1966, Miller 2012). With the use of electromyography a more prominent neural spread has been found in the homologous limb compared to the ipsilateral one (Davis 1942). Complementary results have been found by Hess, using transcranial stimulation of the motor cortex. He determined a facilitated response of a limb by activation the homologous limb (Hess 1986). Both of these studies explain an improved recruitment of the homologous limb compared to ipsilateral and diagonal movements were a significant difference could be found between the different limbs (Table 5).

No difference in RT between groups was found regarding: limbs, extremities, sides or number of limbs (Table 6).

Given the fact that the SRS-A and AQ-10 score did not predict correctly who belonged in the ASD-group or the NTA-group, all participants were redistributed in a SRS-A and AQ-10 positive and negative group. No difference in RT was found between the positive and negative SRS-A and AQ-10 groups (Table 7).

The only difference in RT between groups was found in combination 3 were the difference in RT was only 35ms (Table 3). Since RT can be seen as an indication of the speed and efficiency of central processing managed by the brain (Jensen 1993), we could carefully conclude that the central processing speed in the ASD-group is not affected compared to the NTA-group during the multi-limb coordination task, nor could a positive score on the SRS-A and AQ-10 have an influence on the RT.

4.2 Accuracy

Errors made during the coordination task were divided into three categories. Error 1 is the inability to lift all corresponding limbs in time or removing the wrong limb in time. Error 2 is the inability to react within the 1.5s time limit. Error total is the combination of both.

The difference between groups regarding the error 1 was 7.3% in comparison to the error 2, where the difference was only 0.46% (Figure 5). The ASD-group performed significantly more error 1 in all different limbs, sides, extremities and number of limbs, except for the combination with 4 limbs (Table 9). Also, the combinations with a diagonal aspect, except for combination 13, were significantly different between groups. This means that participants with ASD made significantly more errors regarding lifting the wrong limbs or not lifting all the limbs necessary for the combination asked. They had trouble with the inhibition of the wrong limbs.

All individuals demonstrate more mirror movements during childhood (-10 years) compared to adulthood (Koerte, Eftimov et al. 2010). These are unconscious movements of the homologous limb during a difficult motor task. The mirror movements disappear when the myelination of the corpus callosum starts (Mayston 1999). The corpus callosum is now able to use interhemispheric inhibition, this is an important mechanism for blocking mirror movements. Previous research tells us that the carpus callosum has a decreased size in individuals with ASD (Boger-Megiddo, Shaw et al. 2006) and a disturbed myelination process (Frazier, Keshavan et al. 2012). This is known to cause dysfunctions in fine motor movements and executive functions (Frazier and Hardan 2009). One of these executive functions is inhibition. This could be the explanation why error 1 is determined significantly more in individuals with ASD during the diagonal combinations.

Because an error 2 occurs when participants do not react within a 1.5s time limit, error 2 could be linked to the RT. This could be based on the assumption that the slower the participants were, the more chance they had ending up making a type 2 error. This theory was confirmed in the main results, where no difference could be found between ASD-individuals and NTA (Figure 5).

This is similar with the results between groups regarding RT. It leads to the conclusion that the ASD-participants had no delay in processing information compared to the NTA-group. When looking at the different combinations, it is clear that the homologous and ipsilateral combinations are the fastest regarding the RT and that the least error 2 occur in the same homologous and ipsilateral combinations (Table 3).

In RT no difference was found between both groups looking at all variables. Based on our previous theory that RT and error 2 are supposedly linked, we would expect this to be confirmed in all different variables. However, when looking at the results of both extremities, a significant difference is observed between the groups. This significant difference is also found between both groups in some of the combinations with 3 limbs: i.e. 7, 14, and there was a trend to significance in combination 13. When looking at the different limbs, the only significant difference found was regarding the left feet (Table 9). The ASD-group made 3.3% more faults compared to the NTA-group.

When examining error total, the ASD-group made a mistake in 35.26% of the combinations whereas the NTA-group only failed in 27.52% of the performed actions (Figure 5). This significant difference did not confirm the results found in several studies, where no significant difference could be found between the groups (Rinehart, Bradshaw et al. 2001, Glazebrook, Elliott et al. 2006, Todd, Mills et al. 2009). A possible explanation is the difficulty in the tasks that had to be performed. The tasks in our research were more complex than the tasks described in the articles. They used a simple reaction time task performed with only 1 limb at the same time, whereas our test was always performed with at least 2 limbs at the same time. In other words, the significant difference between both groups could be attributed to the difficulty of the multi-limb test. Liao et all. came to the same conclusion. More errors were made in the ASD-group when the task became more difficult (Xiao, Xiao et al. 2012).

The significant influence of difficulty in the tasks could be determined in the total error rate in the different number of limbs, whereas the ASD-group only scored lower in the combinations with 3 limbs involved (Table 8).

The total error rate was also significantly different between both groups for all different limbs, sides, extremities and in the combinations 7, 9, 13 and 14 (Tables 3 and 8). These four combinations involve a diagonal aspect. All participants had a bigger total error rate in these combinations in comparison to the homogenous and ipsilateral ones.

Since no significant difference could be found between both groups in error 2 we can assume that the significant difference was reached because of the amount of error 1 in the ASD-group. This means that the difference found between groups in the diagonal combinations could also be explained by the reduced interhemispheric inhibition in the corpus callosum.

4.3 Strengths, weaknesses and further investigations

The primary strength of this study is that it is a pioneer in investigating a multi-limb coordination task within an ASD-population. Previous research has been done regarding coordination (Fournier, Hass et al. 2010), but most of that research only used testings on activity level. Being the first study is a strength but also a weakness, since this is a new set-up: no validation nor reliability tests have been done yet. To make future results more valuable, examining the validation and reliability could be beneficial.

This article could be a first step in further investigation regarding multi-limb coordination. A bigger scale research is needed to increase our understanding of the mechanisms used during coordination tasks in participants with ASD.

Another strength in our study was the use of two trials. This minimalized the learning effect, which would have given us biased results.

The fact that the two screening tests were taken (SRS-A and AQ-10) was positive, but the results of those tests were not. Only 59.09% of the ASD-group had a positive score on the SRS-A and only 57.14% on the AQ-10. A total of 10 out of the 22 ASD-patients had a positive score on both tests. Hence, a note could be made on the reliability of the screenings. On the one hand one would expect more participants within the ASD-group to have a positive score on both screenings, on the other hand one would expect all the screenings of the NTA-group to be negative. Unfortunately, these screenings were carried out by an external researcher.

A possible bias that could have been overseen is the large chance of comorbidities in ASD (Lai and Baron-Cohen 2015). An example would be Developmental Coordination Disorder (DCD). DCD is a common comorbidity in participants with ASD (Caçola, Miller et al. 2017). Because of the disturbed coordination in individuals with DCD, some results could be contributed to the wrong pathology. Having comorbidities was an exclusion criterion, however this cannot entirely be excluded. There is chance that individuals have comorbidities without knowing it or having it properly diagnosed.

All different types of Pervasive Developmental Disorders are now encompassed in one DSM-V criteria. This must be taken into consideration when interpreting these results. ASD comes in many different forms, and not all encounter the same problems to the same extent. But this does not mean that the multi-limb coordination test has no value for persons with ASD. Participants with a bad score could be redirected to a physiotherapist to practice his coordination, and this could help him in daily life activities.

The data collection was done by one external researcher, this is a weakness because of our inability to verify if any mistakes happened during this part of the study. Since not all participants with ASD scored positive on the SRS-A and AQ-10 we wonder how strictly the recruitment selection was. The data-analysis was also done by one person, making it more likely that mistakes were not noticed during the analysis.

Another item this study did not explore was age, this because of the small age-range between all participants. 21 years old was the mean age in the ASD-group (17-29 years) and in the NTA-group it was 22 years old (18-25). The difference in age between groups almost reached a significance level, this could have been a possible bias when age would have been used as a variable.

The amount of participants should make us treat our results with caution. Only 22 individuals with ASD and 25 Neurotypical Adults participated in this study. A larger sample size gives a better prediction for all individuals with ASD in Belgium.

Additionally, it would be interesting to see if intelligence or gender has any influence on the multi-limb coordination task. This was not measured in this study but could potentially have a great influence on the results when looking at previous research (Glazebrook, Elliott et al. 2006).

Further research could find the underlying mechanism resulting in some of the impairments seen in individuals with ASD. This can help them reduce or cope with some of the difficulties in their daily life and can give them a better life value.

5 Conclusion

To summarize, we can conclude that no significant difference could be found in reaction time between individuals with Autism Spectrum Disorder and Neurotypical Adults. There was however a difference in the error rate between both groups: the ASD-group made more mistakes regarding the inability to lift all corresponding limbs in time or removing the wrong limb within time.

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Appendix

Appendix 1 - ASD-criteria

ASD-criteria		
A	Persistent deficits in social communication and social interaction across multiple contexts (as manifested by the following, currently or by history)	1. Deficits in social-emotional reciprocity, ranging, for example, from abnormal social approach and failure of normal back-and-forth conversation; to reduced sharing of interests, emotions, or affect; to failure to initiate or respond to social interactions. 2. Deficits in nonverbal communicative behaviors used for social interaction, ranging, for example, from poorly integrated verbal and nonverbal communication; to abnormalities in eye contact and body language or deficits in understanding and use of gestures; to a total lack of facial expressions and nonverbal communication. 3. Deficits in developing, maintaining, and understanding relationships, ranging, for example, from difficulties adjusting behavior to suit various social contexts; to difficulties in sharing imaginative play or in making friends; to absence of interest in peers. Specify current severity: severity is based on social communication impairments and restricted repetitive patterns of behavior (see Table 3).
B	Restricted, repetitive patterns of behavior, interests, or activities (as manifested by at least two of the following, currently or by history)	1. Stereotyped or repetitive motor movements, use of objects, or speech (e.g., simple motor stereotypies, lining up toys or flipping objects, echolalia, idiosyncratic phrases). 2. Insistence on sameness, inflexible adherence to routines, or ritualized patterns or verbal nonverbal behavior (e.g., extreme distress at small changes, difficulties with transitions, rigid thinking patterns, greeting rituals, need to take same route or eat food every day). 3. Highly restricted, fixated interests that are abnormal in intensity or focus (e.g., strong attachment to or preoccupation with unusual objects, excessively circumscribed or perseverative interest). 4. Hyper- or hyporeactivity to sensory input or unusual interests in sensory aspects of the environment (e.g., apparent indifference to pain/temperature, adverse response to specific sounds or textures, excessive smelling or touching of objects, visual fascination with lights or movement). Specify current severity: Severity is based on social communication impairments and restricted, repetitive patterns of behavior (see Table 3).
C	Symptoms must be present in the early developmental period (but may not become fully manifest until social demands exceed limited capacities, or may be masked by learned strategies in later life).	
D	Symptoms cause clinically significant impairment in social, occupational, or other important areas of current functioning.	
E	These disturbances are not better explained by intellectual disability (intellectual developmental disorder) or global developmental delay.	

Table 1 – characteristics of ASD
APA American Psychiatric Association. (2013). Neurodevelopmental disorders. Autism spectrum disorder. In: Diagnostic and statistical manual of mental disorders (5th ed.). Arlington, VA: American Psychiatric Association

Appendix 2 - Definitions

Definitions	
Autism spectrum disorder (ASD)	ASD is a neurodevelopmental disorder that is characterized by limitations in social interactions and communication, restricted interest, and stereotyped or repetitive behaviors. There is a continuum of behaviors represented within the ASD-diagnosis.
Pervasive developmental disorder (PDD)	The PDD diagnosis includes impaired social interaction and communication skills or the presence of stereotyped behaviors or restricted interests that are not congruent with developmental or cognitive ages. PDD encompasses several disorders including autistic disorder, Rett's disorder, childhood disintegrative disorder, Asperger's disorder, and PDD not otherwise specified.
Autism disorder	The diagnosis of autistic disorder is based on impaired social interaction and communication and the presence of repetitive or stereotyped behavior. There must also have been a delay in social interaction, social or communicative language, and play prior to the age of 3 years.
Asperger syndrome	The diagnosis of Asperger syndrome is based on impaired social interaction and restricted or stereotyped interests that interfere with daily functioning. There is no delay in language, cognitive development, or adaptive behaviors and activities of daily living skills.
Pervasive developmental disorder—not otherwise specified (PDD-NOS)	The diagnosis of PDD-NOS is used when there is impairment in social interaction that is associated with communication skills or is present with stereotyped behavior and restricted interest. These symptoms should not be accounted for by PDD, schizophrenia, schizotypical personality disorder, or avoidant personality disorder. PDD-NOS includes "atypical autism" (when the criteria have not been met for autism disorder).

Table 2 – Definitions
Adapted from the *Diagnostic and Statistical Manual of Mental Disorders–Fourth Edition* (*DSM-IV*).
Based on proposed revisions of the *DSM*, these currently used diagnoses may be incorporated into one diagnosis (ASD) when the fifth edition is published.

Appendix 3 - Level of severity

Severity level	Social communication	Restricted, repetitive behaviors
Level 3 "Requiring very substantial support”	Severe deficits in verbal and nonverbal social communication skills cause severe impairments in functioning, very limited initiation of social interactions, and minimal response to social overtures from others. For example, a person with few words of intelligible speech who rarely initiates interaction and, when he or she does, makes unusual approaches to meet needs only and responds to only very direct social approaches.	Inflexibility of behavior, extreme difficulty coping with change, or other restricted/repetitive behaviors markedly interfere with functioning in all spheres. Great distress/difficulty changing focus or action.
Level 2 "Requiring substantial support”	Marked deficits in verbal and nonverbal social communication skills; social impairments apparent even with supports in place; limited initiation of social interactions; and reduced or abnormal responses to social overtures from others. For example, a person who speaks simple sentences, whose interaction is limited to narrow special interests, and how has markedly odd nonverbal communication	Inflexibility of behavior, difficulty coping with change, or other restricted/repetitive behaviors appear frequently enough to be obvious to the casual observer and interfere with functioning in a variety of contexts. Distress and/or difficulty changing focus or action.
Level 1 "Requiring support”	Without supports in place, deficits in social communication cause noticeable impairments. Difficulty initiating social interactions, and clear examples of atypical or unsuccessful response to social overtures of others. May appear to have decreased interest in social interactions. For example, a person who is able to speak in full sentences and engages in communication but whose conversation with others fails, and whose attempts to make friends are odd and typically unsuccessful.	Inflexibility of behavior causes significant interference with functioning in one or more contexts. Difficulty switching between activities. Problems of organization and planning hamper independence

Table 3 – Severity of ASD

APA American Psychiatric Association. (2013). Neurodevelopmental disorders. Autism spectrum disorder. In: Diagnostic and statistical manual of mental disorders (5th ed.). Arlington, VA: American Psychiatric Association

Appendix 4 – Dutch translation of SRS-A

Social Responsiveness Scale for Adults (SRS-A					
Duid slechts één antwoord aan per vraag:		Niet waar	Soms waar	Vaak waar	Bijna altijd waar
1	Ik voel me veel minder op mijn gemak in sociale situaties dan wanneer ik alleen ben				
2	Mijn gelaatsexpressies komen niet overeen met wat ik zeg				
3	Ik voel me zelfverzekerd in de omgang met anderen				
4	Op stressvolle momenten vertoon ik rigide of weinig flexibele gedragspatronen die eigenaardig lijken				
5	Ik besef niet wanneer anderen misbruik van mij maken				
6	Ik ben liever alleen dan samen met anderen				
7	Ik ben mij bewust van wat anderen denken of voelen				
8	Ik gedraag mij op een manier die vreemd of bizar overkomt				
9	Ik ben te afhankelijk van hulp van anderen om mijzelf in mijn basisbehoeften te voorzien				
10	Ik neem dingen te letterlijk en vind het moeilijk de eigenlijke betekenis van een gesprek te vatten				
11	Ik heb een goed zelfvertrouwen				
12	Ik ben in staat mijn gevoelens naar anderen te communiceren				
13	Ik ben onhandig in wederzijdse interacties met anderen (bijv. ik vind het moeilijk om in een gesprek te antwoorden op de vragen)				
14	Ik heb geen goede coördinatie				
15	Ik herken veranderingen in intonatie en gelaatsexpressies van anderen en reageer hier adequaat op				
16	Ik vermijd oogcontact of maak ongewoon oogcontact				
17	Ik zie in wanneer iets onrechtvaardig is				
18	Ik maak moeilijk vrienden, zelfs wanneer ik erg mijn best doe				
19	Ik raak gefrustreerd als ik probeer mijn ideeën over te brengen in gesprekken				
20	Ik vertoon ongewone zintuigelijke interesses (bijv. ik ruik vaak aan mijn vingers) of ik hanteer rare gebruiken				
21	Ik ben in staat handelingen en de manier van doen van anderen te imiteren wanneer het sociaal gepast is				
22	Ik ga gepast om met andere volwassenen				
23	Ik neem niet deel aan groepsactiviteiten of sociale evenementen tenzij ik daartoe gedwongen word				
24	Ik heb het moeilijker dan anderen met veranderingen in mijn routines				
25	Ik bied troost aan anderen wanneer zij verdrietig zijn				
26	Ik vermijd het aangaan van sociale interacties met andere volwassenen				
27	Ik denk of praat telkens weer over hetzelfde				
28	Anderen vinden mij eigenaardig of raar				

29	Ik raak overstuur in situaties waarin veel dingen gaande zijn				
30	Ik kan mijn gedachten niet van iets afbrengen als ik er eenmaal over begin te denken				
31	Ik heb een goede persoonlijke hygiëne				
32	Ik ben sociaal onhandig, zelfs als ik beleefd probeer te zijn				
33	Ik vermijd mensen die een emotionele band met mij willen				
34	Ik heb moeite met het verloop van een gewoon gesprek te volgen				
35	Ik heb moeite om voeling te krijgen met familieleden				
36	Ik heb moeite om voeling te krijgen met andere volwassenen				
37	Ik reageer gepast op stemmingsveranderingen van anderen (bijv. wanneer de stemming van een vriend verandert, heb ik dit niet door)				
38	Ik heb een ongewoon beperkt interessegebied				
39	Ik ben fantasierijk zonder voeling met de werkelijkheid te verliezen				
40	Ik dwaal doelloos van de ene activiteit naar de andere				
41	Ik ben overgevoelig voor geluiden, texturen of geuren				
42	Ik vind het fijn 'over koetjes en kalfjes' te praten en ben hier goed in (kletsen met anderen)				
43	Ik begrijp niet goed hoe verschillende gebeurtenissen met elkaar verband houden (oorzaak en gevolg)				
44	Ik toon gewoonlijk interesse in datgene waaraan anderen aandacht schenken				
45	Mijn gelaatsuitdrukking is overdreven ernstig				
46	Ik lach op ongepaste momenten				
47	Ik heb een gevoel voor humor, begrijp grappen				
48	Ik ben extreem goed in sommige intellectuele taken of rekenkundige bewerkingen, maar doe het niet vaak				
49	Ik vertoon repetitieve, eigenaardige gedragingen				
50	Ik heb moeite om vragen rechtstreeks te beantwoorden en eindig met om het onderwerp heen te praten				
51	Ik weet wanneer ik te luid praat of te veel lawaai maak				
52	Ik praat tegen mensen op een ongewone toon (bijv. ik praat als een robot)				
53	Ik reageer op mensen alsof ze voorwerpen zijn				
54	Ik weet wanneer ik te dicht in de buurt ben bij iemand of iemands persoonlijke ruimte binnendring				
55	Ik loop tussen twee mensen door die met elkaar aan het praten zijn				
56	Ik heb de neiging mij te isoleren, mijn huis niet te verlaten				
57	Ik concentreer mij teveel op deelaspecten van dingen, eerder dan het geheel te zien				
58	Ik ben overdreven achterdochtig				
59	Ik ben emotioneel afstandelijk, toon mijn gevoelens niet				
60	Ik ben niet flexibel, heb moeite om van mening te veranderen				

61	Anderen vinden de redenen die ik geef voor wat ik doe ongewoon of onlogisch				
62	Ik raak anderen op een ongewone manier aan, groet anderen op een ongewone manier				
63	Ik ben te gespannen in sociale situaties				
64	Ik staar of mijn blik dwaalt af in het niets				

Table 4 – Dutch translation of SRS-A used during the experiment

Appendix 5 – AQ-10

Autism Spectrum Quotient (AQ-10)					
Please tick one option per question only:		Definitely agree	Slightly agree	Slightly disagree	Definitely disagree
1	I often notice small sounds when others do not				
2	I usually concentrate more on the whole picture, rather than the small details				
3	I find it easy to do more than one thing at once				
4	If there is an interruption, I can switch back to what I **was** doing very quickly				
5	I find it easy to 'read between the lines' when someone is talking to me				
6	I know how to tell if someone listening to me is getting bored				
7	When I'm reading a story I find it difficult to work out the characters' intentions				
8	I like to collect information about categories of things (e.g. types of car, types of bird, types of train, types of plant etc.)				
9	I find it easy to work out what someone is thinking or feeling just by looking at their face				
10	I find it difficult to work out people's intentions				

Table 5 – Original AQ-10, used as a base for the Dutch version

Appendix 6 – Dutch translation of AQ-10

Autism Spectrum Quotient (AQ-10)					
Duid slechts één antwoord aan per vraag:		Volledig akkoord	Min/meer akkoord	Min/meer niet akkoord	Volledig niet akkoord
1	Ik hoor vaak kleine geluidjes als anderen niets horen				
2	Ik richt mij meer op het totaalplaatje dan op de details				
3	Meerdere dingen tegelijk doen gaat me makkelijk af				
4	Als ik onderbroken word, kan ik makkelijk verder gaan waar ik gebleven was.				
5	Ik vind het makkelijk om 'tussen de regels door te lezen' als iemand tegen me praat				
6	Ik merk het als mensen die naar me luisteren zich gaan vervelen				
7	Als ik een verhaal aan het lezen ben, vind ik het moeilijk om te achterhalen waarom de personages...				
8	Ik verzamel graag informatie over specifieke onderwerpen (bv. automerken, vogels, treinen, planten)				
9	Door naar iemands gezicht te kijken weet ik wat iemand denkt of voelt				
10	Ik vind het moeilijk om erachter te komen wat mensen willen				

Table 6 – Dutch translation of AQ-10, used during the experiment.

Appendix 7 - Instructions multi-limb coordination task in Dutch

MULTI-LIMB TAAK

Alvorens de aanvang van de taak, werd er aan de participanten een PowerPointpresentatie getoond waarin de set-up en uitvoering van het experiment werd verduidelijkt. Deze wordt hieronder weergegeven.

Beste deelnemers,
het volgende experiment bestaat uit twee delen:

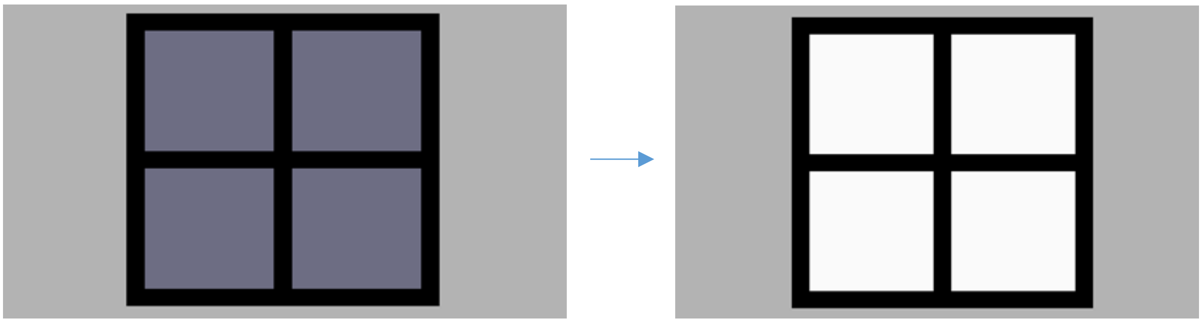
1. De oefensessie om aan de taak te wennen
2. De eigenlijke sessie

Het is steeds de bedoeling dat je de opdracht op je best uitvoert.
Dit betekent zo juist en zo snel mogelijk.

Uitgangshouding

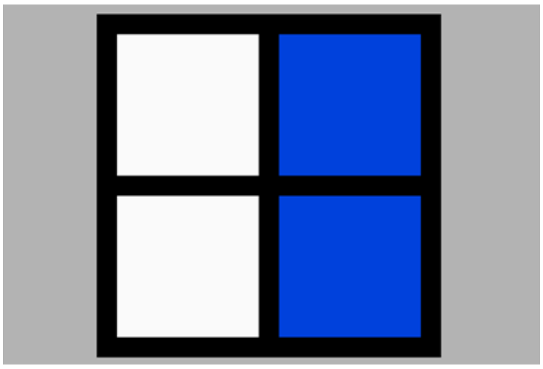
Leg je handen op beide plaatjes op de tafel.
Plaats je voeten op beide plaatjes onder de tafel.

Je ziet de bijbehorende vier grijze vakjes dan wit worden.



Oefensessie (3 minuten)

Wat zie je?
Twee of meer witte vlakken worden tegelijkertijd blauw.

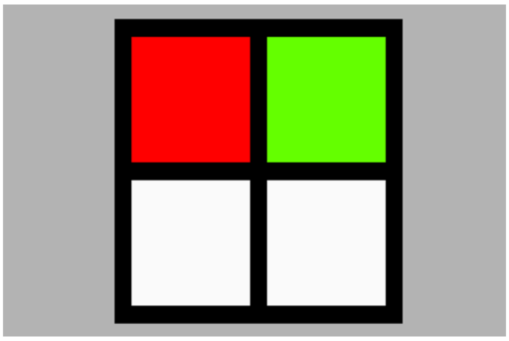


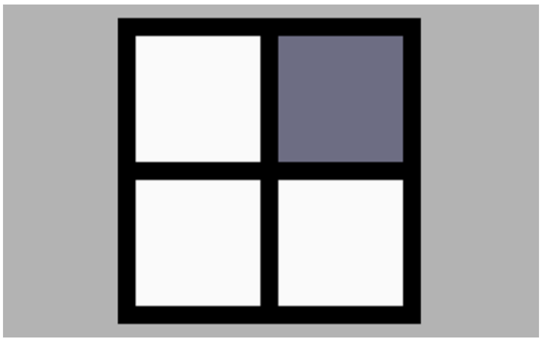
Wat moet je doen?

1. Hef de bijbehorende ledematen (handen en/of voeten) volledig op
   → in het voorbeeld dus rechterhand en rechtervoet

2. Doe dit zo snel en gelijktijdig mogelijk.
3. Plaats je handen/voeten daarna snel terug op de plaatjes

Feedback
Wat betekenen de kleuren?





Groen = de *correcte plaats*

Rood = de *foute plaats*

Grijs = te *traag* of onvoldoende *contact* bij terugplaatsen hand/voet

Voorbeeld 1:
- Rechterhand juist opgeheven
- Linkerhand had niet opgeheven moeten worden

Voorbeeld 2:
- Rechterhand te traag opgeheven

Heb je nog vragen? Is het duidelijk?

Echte sessie (10 minuten)

Wat moet je doen?

Hetzelfde als in de oefensessie:

1. Hef de bijbehorende ledematen (handen en/of voeten) volledig op
2. Doe dit zo snel en gelijktijdig mogelijk.
3. Plaats je handen/voeten daarna snel terug op de plaatjes

Maar: zonder feedback (juist/fout), wel grijze feedback.

Heb je nog vragen? Is het duidelijk?

Doe je best! ☺

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Richting: **master in de revalidatiewetenschappen en de kinesitherapie-revalidatiewetenschappen en kinesitherapie bij neurologische aandoeningen**
Jaar: **2017**

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Datum: **5/06/2017**