KINEMATIC SIGNATURES OF CHILDREN WITH ASD

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A dissertation submitted in partial fulfillment of the requirements for the Degree of Masters in Biomedical Research (Specialization Area: Neuroscience) at Faculdade de Ciências Médicas | NOVA Medical School of NOVA University Lisbon

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This work is dedicated to the memory of Professor Ilan Golani, a friend, and a teacher. His uncanny ability to integrate strict scientific methods with philosophy and art gave him a unique and holistic understanding of animal and human behavior and the way they move in this world. His work has motivated my first steps in research and will continue to inspire my work.

"...the animal's three-dimensional life-space is enacted dimension by dimension in morphogenesis, in reference to the physical vertical absolute (gravity), the life-space is embedded within physical space, enfolding its dimensionality, and thus disclosing the animal's (cognitive) understanding of it."

Golani, Ilan, in "On the Morphogenesis and Form of Animal Behavior", 2022

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Abstract

Autism Spectrum Disorder, ASD, is a lifelong neurodevelopmental disorder commonly known for persistent deficits in communication and social skills. Increasing evidence suggests that motor symptoms are pervasive among autistic children and are integral to the ASD phenotype. Yet, findings related to distinctive motor features in ASD are sparse: clumsiness, altered gait patterns, difficulties in handwriting, difficulties in performance of executive movements and excessive motor stereotypical movements are only some examples of motor symptoms related to ASD. Thus, though motor deficits are consistent in children with ASD, it remains unclear whether they share an underlying etiology with ASD core symptoms themselves or whether they constitute a distinct motor profile particular to some autistic children. Moreover, a preliminary association between motor, cognitive and social symptoms in ASD was found, but whether and how ASD symptoms from different domains are related to motor features remains mainly elusive. This is partially due to the challenge in designing feasible experimental conditions to study movement of children with neurodevelopmental disorders under multiple contexts.

The study presented here analyzed movement of children (both autistic and neurotypical) during free play using a tool previously developed for the analysis of rodent behavior in unsupervised settings. We created a semi-supervised design, where children's free play was recorded in two contexts: with and without a parent present in the room, thus assessing environmental effect related to the socio-emotional domain. We demonstrate that by analyzing similarity patterns of acceleration data recorded with a single accelerometer, we could identify an individualized behavioral repertoire distinguishing autistic children from peers. Moreover, our results support previous findings as we show that children with ASD move more often in lower acceleration levels and show fewer behaviors involving transitions between acceleration levels on the dorsa-ventral plane. Finally, our data suggests that parental presence led to increased variability within the ASD group while having little effect on the behavior of children from the control group. These results, once further validated, may contribute significantly to our understanding of the interaction between motor behavior and socio-emotional processing in autistic and neurotypical children, and lead to the development of a simple assessment tool that may be used in numerous study contexts.

Table of Contents

List of tables

List of figures

List of acronyms

ASD, Autism Spectrum Disorder

NT, Neuro-typical

ADOS-G, Autism Diagnostic Observation Schedule- Generic

DSM-V, Diagnostic and Statistical Manual of Mental Disorder, version V

IMU, Inertial Measurement Unit

X GA, X Gravity Acceleration, gravity component on x axis

Total BA, Total Body Acceleration

PDF, Probability Density Function

AP, Affinity Propagation (clustering)

RGB, Red Green Blue, pixels color codes in image processing

KLD, Kullback - Leibler Divergence

ms, milliseconds

fps, frames per second

1.Introduction

Autism spectrum disorder, ASD, is a complex neurodevelopmental condition characterized by social and communication deficits as well as restricted interests and repetitive behaviors [1]. Autism prevalence has reached a pandemic level and affects approximately one in 100 children worldwide, a number that may be underestimated as the prevalence of autism in many low- and middle-income countries is unknown [2].

ASD is a highly heterogeneous disorder in terms of etiology [3], [4], as well as in terms of clinical manifestations [1], [4], [5], and a distinctive biomarker for the condition is still missing. To date, diagnosis of ASD relies mainly on expert assessment based on standardized diagnostic criteria such as those defined in DSM-V [1], and observational tools such as the structured Autism Diagnostic Observational Schedule- Generic (ADOS-G) protocol [6]. Such assessments are costly and partially inaccessible to large parts of the population. Moreover, though autism may be formally diagnosed from the second year of life [7], and risk factors are distinguishable as early as the first months of life [8], [9], [10] many children are assessed and diagnosed only in late school years [11].

Indeed, identification of measurable objective markers for ASD is of extreme interest as it is crucial both to direct the development of cellular and animal models to fill the many persisting gaps in our understanding of ASD etiology, and to inform the establishment of a unified objective diagnostic method that may be widely available in the community and primary health care services.

Motor symptoms have been gradually recognized as part of ASD core symptoms [12]. The potential of finding an objective motor biomarker for ASD has led to tremendous scientific effort to identify motor features of patients with ASD. Though, traditionally, motor difficulties were mainly associated with the restricted and repetitive behavior domain, advancements in technological tools have allowed the identification of numerous motor symptoms distinctive of ASD. Importantly, clinical studies suggest that preschool and school aged children are especially prone to suffer from motor impairments that significantly interfere with their and their family quality of life [12].

Current knowledge of motor manifestation in children with ASD

Motor impairments are estimated to affect about 87% of children with ASD [13] and include a large variety of manifestations and motor domains such as fundamental movement skills [14], [15] and specifically, the display of unique gait features [16], [17], impaired coordination and balance [18], difficulties in fine motor skills [19] as well as in performance of executive movements and motor planning [20], altered kinematics, [21], [22] and repetitive motor behaviors [1].

Technological advancements enabled the development of several methodologies for quantification and analysis of high-resolution continuous data of motor traits to objectively compare movements of children with autism to neuro typical (NT) peers and children with other developmental disorders. For example, using smart tablets equipped with sensors and machine learning programs, gestures of children with ASD could be distinguished from those of controls [21]. In another study infants were fitted with wearable accelerometers allowing for continuous recording of their movements at home for an entire day. Analysis of movements' complexity revealed persistent reduced complexity in the movements of infants later diagnosed with ASD [23]. Yet another study that used high resolution sensors was able to establish a new kinematic metric, termed R, which measures randomness of speed peaks within motion cycles at millisecond time scale. Levels of R were shown to be significantly higher in patients with autism than those of controls [24].

Despite these advances, most reports need further validation in the population. Moreover, literature regarding motor symptoms in ASD remains highly sparse and it remains unclear whether there is a single motor signature to ASD or diverse motor profiles within ASD. The use of highly variable methodologies, different behavioral paradigms, and the fact that different studies give results in different metrics, challenge the possibility of finding a common ground between the various motor traits attributed to autism. Moreover, most studies are task- based and study goal-oriented actions with different complexity levels. It is necessary to show whether findings extrapolate to spontaneous daily behavior in naturalistic settings. Namely, it is difficult to conclude whether repetitive behavior is correlated with subtle kinematic changes, if modifications in movements complexity are relatable to a general delay in motor development, or if altered hand gestures captured during play on a touch screen reflect hand gestures in other contextual situations. Furthermore, it remains unclear whether the motor peculiarities that have been described in ASD are specific to this disorder, or rather a broader marker of neurodevelopmental conditions. For example, the marker R, previously described here, was found to discriminate not only behavior of patients with ASD from that of controls, but also behavior of NT children from that of NT adults.

Do motor features associate with other core symptoms of ASD?

Another crucial gap in the understanding of motor peculiarities in ASD regards the relation between motor traits and other core symptoms of the syndrome, as until recently symptoms from the different domains have been mostly studied independently. Nonetheless, accumulating large scale data sets have repeatedly pointed to a possible association between severity of motor impairments and severity of autistic symptoms from other domains [13], [25]. Furthermore, correlation between early motor a-typicalities and deficits in language development suggests that abnormalities in motor control that emerge at early stages of development may contribute critically to impaired acquisition of language and atypical development of cognitive and social skills in ASD [26], [27], [28].

It has been suggested that the development of motor and social deficits in autism might share a neurodevelopmental mechanism during early maturation of the central nervous system related to abnormal connectivity between lower and higher brain regions [29]. This is partially supported by the fact that neonates later diagnosed with ASD show abnormal growth in head circumference [30], and inefficiencies in functional networks are found in MRI studies in the first two years of life in autistic children [31]. Studies of older children and adults with ASD indicate that atypical motor behavior and altered kinematic profiles may have a direct negative impact on socio-cognitive perception in ASD, damaging the ability to not only understand motor actions of others, but also their intentions [32]. Though reviews have confirmed the correlation between motor and social, emotional and cognitive manifestations in autism, our understanding of the nature of this association remains mainly theoretical, and the current state of the art holds very little data-driven evidence. Altogether, this emphasizes the necessity of better understanding the source of motor impairments in ASD.

Parents effect on motor skills of children with ASD

There are many descriptions of dyadic interactions between parents and healthy children in studies of child motor skills and locomotor behavior in developmental psychology. Yet, literature regarding the effect of parents over motor behavior of their autistic children is negligible [33]. Nonetheless, a few studies demonstrate that parents actively influence their children´s play and motor behavior in motor skill tasks [34], [35]. Moreover, initial results show that parents also have a positive effect on motor skills of children with ASD in parent mediated interventions [36]. In another study, researchers investigated infants' movements in the presence of their stationary mothers [37]. They showed that in contrast to typically developing infants, infants later diagnosed with autism do not display structured exploration, do not seek their mother's physical proximity and tended to prolonged episodes of staying in place [37]. An important aspect of this study was the assessment of the effect of the mother's presence independently of her ad hock actions. When further explored, such paradigm may shed further light on the way environmental factors from emotional and social domains, interfere with autistic children´s management of their movements. Furthermore, in that research, the design was created in an analogy to the "home base" paradigm of animal exploration of novel space, a well-established paradigm in the field of animal behavior. The authors assumed that a mother serves as a secure point from which children initiate and terminate exploration episodes. They analyzed the structure of infants' movement in a reference system, comparable to that of animal models, hence their findings may not only help distinguish infants at developmental risk from NT peers, but also potentially serve as a translational marker.

In summary, motor peculiarities are pervasive and varied among children with ASD, and preliminary evidence suggests that they may correlate with symptoms in the socio-emotional and cognitive domains. Motor symptoms must be further understood within the complex manifestations of autism and within the neurodevelopmental process of ASD. Studying the prominent effect of parents on autistic children's motor behavior has immense potential in unveiling the interrelation between environmental cues related to social and emotional domains and autistic children's motor behavior. These together highlight the crucial need to establish robust methods that prove able to capture the motor peculiarities of ASD in various contexts, such as during social interaction, task performance, and spontaneous movements, to validate the presence of an integral motor signature in the movement repertoire of patients with ASD and how it relates to other core symptoms of this syndrome.

To answer this need, we adapted a method previously developed for the study of neuronal activity during unsupervised animal behavior [38]. This tool employs an algorithm that can recognize behavioral types based on acceleration patterns collected by a single device. In animal models, the suggested method proved able to capture and cluster a wide range of behaviors. The benefit of this tool lies in the ability to cluster and characterize behavior in a wide range of situations and capture meaningful motor characteristics of patients with ASD as elucidated in acceleration patterns. Moreover, the possibility to classify behavioral patterns based on a single lightweight device is of paramount importance in the study of children with neurodevelopmental conditions, who commonly have sensorimotor difficulties and suffer from hypersensitivity. In another recent publication, open field behavior of female and male mice was clustered and analyzed by quantifying similarities between the individual display of clusters by each subject [39]. The authors demonstrated that the dissimilarity between the behavioral repertoires of individual animals predicted mouse identity with superior power to estrous phase, suggesting that a behavioral signature may be identified within clustered behavioral repertoires.

Taking these together, we set out to test whether individual repertoires of clusters, as found by the unsupervised clustering algorithm developed by Klaus et al. [38], are distinctive between children with ASD and NT peers. In this study, we compared the behavioral repertoires of children on the autistic spectrum and NT peers in the presence and without the presence of their parents and assessed the acceleration levels of their movements in each condition.

This project is essentially a proof-of-concept study, aimed to investigate the feasibility and validity of the use of a single wearable accelerometer for the study of motor symptoms in developmental delays and specifically in ASD. Once validated, our method has the potential to not only provide a powerful means to investigate the existence of a unique motor signature characteristic of the behaviors of patients with ASD, but it may also one day offer a diagnostic and / or prognostic biomarker that could be used in any physician’s office and even at home.

2. Hypothesis and aims

This project was set up as an exploratory study, seeking to assess the potential of unsupervised clustering to find distinguishable features of motor behavior of children with ASD. The main goal was to establish a feasible and valid experimental scheme using the tool described above for assessing motor behavior of children with ASD in multiple environmental contexts.

Hypotheses

We followed three main hypotheses:

1. Behavioral repertoires, as captured by the clustering algorithm, are significantly different between children with ASD and NT children.
2. The differences in display of clusters between the groups will reflect differences in kinematic aspects of movement.
3. A parent's presence will increase the between-group difference in the representation of clusters.

Aims of the research

1. The first aim of this study was to adjust the unsupervised behavioral clustering algorithm, adapted to mouse behavior in the open field, to be suitable for studying children's movements during free play.
2. The second aim was to evaluate whether behavioral repertoires constructed from the output of the algorithm are distinctive between groups.
3. The third aim was to investigate whether the parent's presence will affect the between group difference and to which direction (increase or decrease).
4. Lastly, kinematic aspects are suspected to underlie many of motor symptoms in ASD. We aimed to assess whether the differences in cluster representation reflect a kinematic characteristic of the behavior.

3. Methods

3.1 Participants

This study comprised two study groups with children in the age range between 3-7. The first group included children on the autism spectrum, and the control group included neuro-typical children. All children were healthy with no known orthopaedic or motor difficulties caused by other conditions. The ASD group included five boys and the control group included four boys and one girl. Originally, we aimed to have participants from both genders in both groups, but it was not possible within the project's time frame and gender differences should be accounted for in future work. All participants in the study were attending a formal education system.

Table 1 presents the demographic details of participants.

Group	***subject code***	***age***	***ADOS***	***ADOS score***	***gender***	***medications***	***motor difficulties***
ASD	1	5	V	12/2 = 14	m	X	X
ASD	2	6	V	10/1 = 11	m	X	X
ASD	3	4	V	18/3 = 21	m	-	X
ASD	4	5	V	?	m	X	X
ASD	5	5	V	16/4 = 20	m	X	X
ctrl	6	4	-	-	m	X	X
ctrl	7	3	-	-	m	X	X
ctrl	8	7	-	-	m	X	X
ctrl	9	5	-	-	m	X	X
ctrl	10	7	-	-	f	X	X

Table 1. ***Summary of subjects' details***

3.1.1 Recruitment

Participants for the ASD group were recruited through CADIn – Neurodesenvolvimento e Inclusão, a private non-profit organization specialized in diagnosing and treating neurodevelopmental conditions across the lifespan. All members in the study group participated frequently in occupational therapy sessions at CADIn and were recruited by their respective therapists. Participants for the control group were recruited by the study team asking parents and children to volunteer for the study purposes. The recruitment process for all members included initial contact with parents where the study aims and protocol were explained, followed by the signing of a consent form by parents who were interested in collaborating. An example of the consent form is available in the annexes.

3.1.2 Inclusion and exclusion criteria

All participants included in the ASD group needed to have their diagnosis confirmed by the ADOS -G protocol. One child had a confirmed ASD diagnosis but the source-document with the scores was not available. The second inclusion criterion was for the children to be in the age range between 3-7 years old. This age range was selected based on the availability of participants in the intervention program and limited to avoid bias in results due to large difference in development and motor skills related to age. Exclusion criteria were having motor difficulties, limited movement, or motor conditions.

3.2 Study design

To achieve our study aims, we created a mixed model design including between-subject and within-subject analysis. The study included two groups, children on the autistic spectrum and NT children and two contexts, with and without a parent present in the room. Experiments took place in a gym especially designed for occupational therapy for children with developmental and motor disorders. Recordings of children from the ASD group took place in their ordinary therapy hours. Children from the control group arrived in a convenient time for them and their parents, based on the availability of the space and the therapist. The location for the experiments was chosen to maximise degrees of freedom of motor behaviour, allowing us to evaluate the capabilities of the algorithm to cluster a wide range of movements within a controlled environment. Importantly, a welcoming and appealing space was selected. The study protocol included 20 minutes of data collection, 10 minutes in the presence of a parent, and 10 minutes of play without a parent present in the room. Each 10 minutes were originally intended to include 5 minutes where children could voluntarily play without any guidance from the therapist and five minutes with structured motor tasks included in the occupational therapy program. In a pilot test conducted before data collection began, some children did not comply with the part dedicated to assessing unguided play, hence it was decided that the therapists would attempt to guide the session and include variable activities, so as to ensure that similar activities would be performed in the two environmental conditions, namely that activities done in the first part would be repeated in the second part. Therapists had prepared a list of suitable activities that could be used by them for that purpose. The protocol is attached in the annexes.

3.2.1 Experimental settings

3.2.1.1 The gym

All experiments took place in the gym of CADIn Cascais, a large room well provided with equipment for encouraging different gross and fine motor behaviours. This space is inviting and secure for children of all ages and suitable for the display of varied motor behaviours. Moreover, as autistic children often show difficulties in novel environments, the fact that the participants from the ASD group were well acquainted with the space contributed to a high extent to their comfort and voluntary participation in the activity.

3.2.1.1 Session guidance

All session were guided by certified and experienced occupational therapists from CADIn. The therapists had a well-established secure relationship with each participant from the ASD group, who were frequent visitors of the program. This was important for the secure feeling of parents and participants.

3.3 Data Collection

3.3.1 Apparatus and data recording

We used two types of Inertial Measurement Units, IMUs, in this study. Initially, data was collected with the MetaMotionR sensor produced by MbientLab (© Copyright 2021, MbientLab), a commercially available single unit device combining accelerometer, gyroscope, magnetometer, and thermometer. MbientLab offers an open-source app, MetaWear (© Copyright 2021, MbientLab.), for streaming data from the IMU directly to a smartphone via Bluetooth. Due to a malfunction in the device we had to replace our data collection method and data was further collected using the MTw Awinda xsens set, produced by Movella (© 2024 by Movella Inc.). MTw awinda xsens is a multiunit set for 3d tracking of human movements. For the purpose of our study, we used a single device from the set. Importantly, the same device was used for data collection in all experiments. The MTw awinda sensors stream data via a docking station connected physically to a computer by USB. Data is saved to the computer using the MT manager program, an adequate program free for download by the company. When using the xsens unit, a laptop connected to the docking station was placed in a corner of the room to minimise interference with the sessions and avoid children reaching to it. We recollected data using the MTw awinda for all children except one. Since our sample size was small, we did not discard this sample but ensured the data from the MetaMotionR was comparable with data collected by MTw awinda by equalizing data units, sampling rate, calibration, and normalization of samples.

Both IMU's used in this study were small and light, with relatively similar measurements:

MetaMotionR is 36 X 36 X 26 mm and weighs 85g.

MTw awinda is 148 X 104 X 31.9 mm and weighs 200g.

3.3.2 Attachment of the IMU to the children's body

For the purpose of the study, we manufactured a small lightweight stretch belt with an outer pocket for the placement of the IMU. A scotch band was sowed to the inner side of the pocket for securing the devices. MTw awinda is delivered with a scotch band, and as to the MetaMotionR, we glued a scotch piece to the outer surface of its case.

3.3.3 Video recording

All experiments were video recorded using a wide-angle security camera for the purpose of logging clusters to real-time occurrence of events. Yet, the gap between the acceleration data given in 100Hz and the video frame rate of 20fps led to a lag between clusters indices and calculated matching frames in the video, making it difficult to recognise transitions between clusters in the children's behaviour using the clusters indices given by the algorithm. In future work, an adequate program for logging data should be used, for a better comparison between acceleration data and video material.

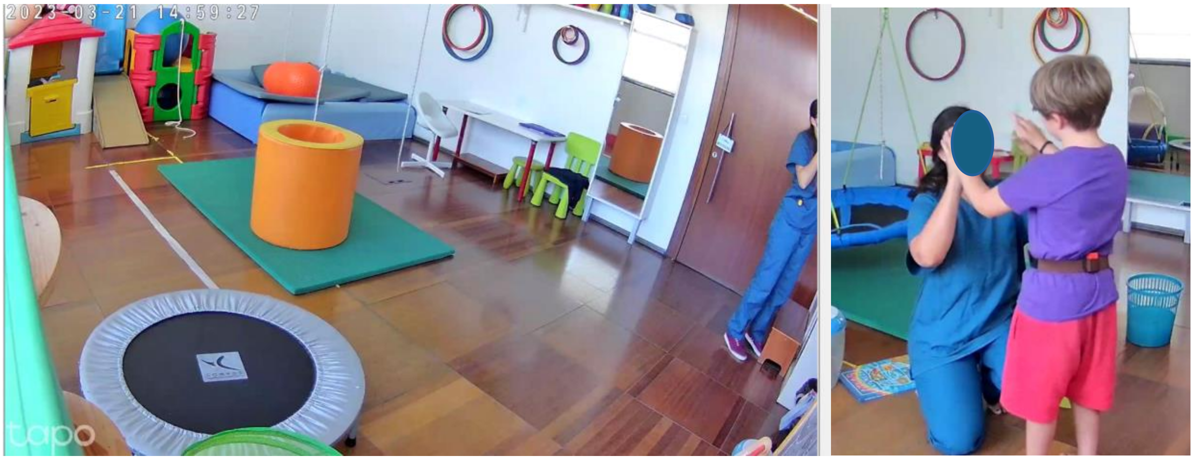

Figure 1 Overview on the study location and IMU attachment

Left: overview of the gym at CADIn Cascais. Right: an example of the placement of the IMU on the lower back of the child with the stretch belt designed for the study.

3.4 Data Pre-processing before Analysis

Data was loaded from the original csv documents (MetaMotionR) and text documents (xsens) using MATLAB. Before clustering, several pre-processing steps were taken:

3.4.1 Transformation to g units

The clustering algorithm expects data input to be in g (gravity) units. Data collected by xsens is given in acceleration units: m/s^2, and was transformed into g's by division by the conventional gravitation value 9.81.

3.4.2 Levelling the sample rate between data sets

MetaWear collects data in 200Hz while the maximal frequency of the xsens is 100Hz, hence, we down-sampled the raw data collected by the MetaMotionR using the built-in MATLAB function *downsample()*. Down-sampled data accurately followed the original data appoints, yet some extreme points were missed. In future work, it is important to ensure all data is collected in unified frequency to avoid data loss. All sessions recorded by the xsens were recorded in 100Hz.

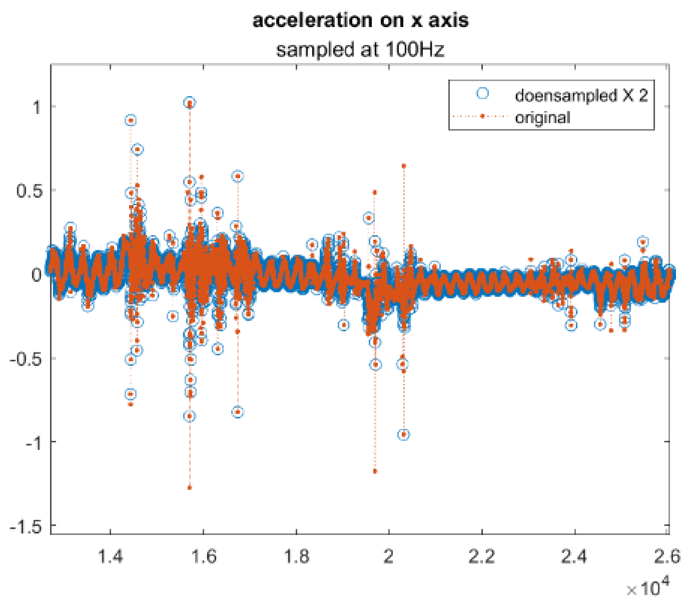

Figure 2 Example of data after sample rate reduction.

Example of original acceleration data on the x axis collected by the MetaMotionR in 200Hz and the equivalent data after sample rate reduction. The y axis shows acceleration values in g, and on the x- axis are the sample indices. Most data peaks were integrated within the down sampled points, yet some information was lost.

3.4.3 Calibration using Euler degrees

In all sessions, by protocol, the device should be placed with the x vector facing down, with the base value of 1g. In two cases, the device was placed upside-down on the child´s body, so the x axis vector was directing upwards when the child was standing, and data was aligned to -1g instead of 1g. We used a rotation matrix to rotate the data 180 degrees on the z axis (roll), with theta x set to 1, theta y to 0 and theta z to 0.

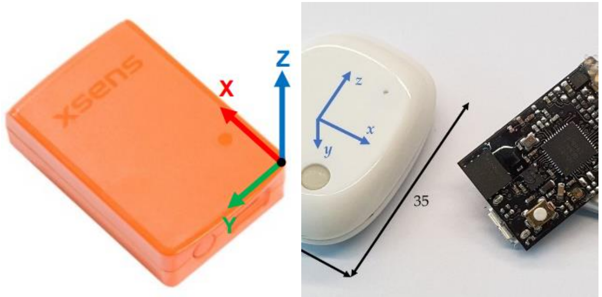

Figure 3. Apparatus.

Left: Coordinate system for the MTw Awinda. Right: Coordinate system for MetaMotionR. Pictures were taken ftom the respective websites of the comercial proveiders.

3.4.5 Extraction of body and gravity components

Acceleration measured by an accelerometer attached to a moving human (or animal) is composed by two components: acceleration caused by the force of gravity, termed Gravitational Acceleration, GA, and acceleration related to the force generated by body, i.e., the muscles, termed Body Acceleration, BA. The individual BA components for each axis were calculated by median-filtering the raw acceleration time series and by subsequent high-pass (0.5 Hz) filtering with a first-order Butterworth filter [38]. Gravitational acceleration, GA, was obtained for each axis by subtracting the BA component from total acceleration measured on each axis.

3.4.6 Setting start and end frame for each condition

The duration of data collection differed across subjects, particularly in the ASD group as in 3 cases data collection was paused before the completion of 20 minutes due to discomfort from the device in one case, and difficulty in following the activity protocol in two cases. Moreover, duration of the parent/ no parent condition varied among the subjects and especially within the ASD group. To ensure unbiased results in the analysis, we decide to use 12 minutes from each subject, based on the smallest sample for one condition of one participant and doubled it to create equal duration from the two conditions. The first 6 minutes and last 6 minutes of each session were taken from each subject´s full sample. We took these time points to ensure the presence and absence of a parent within the selected data of each subject as data collection always started in the presence of a parent and in all sessions no parent was present in the last 6 minutes.

3.4.7 Grouping data

The Clustering algorithm was run over the grouped data of all subjects. This was important to create identical conditions in clustering across subjects, validating that clusters were adequately represented (or not) in all subjects by these conditions. For that purpose, we joined the acceleration vectors from all subjects in a registered order.

3.4.8 Normalization

The acceleration distribution of subjects from the two groups, while varying within a relatively similar range, varied in the distribution centres. Therefore, data was normalized using z-scores before clustering to avoid plausible differences in acceleration values of specific subjects.

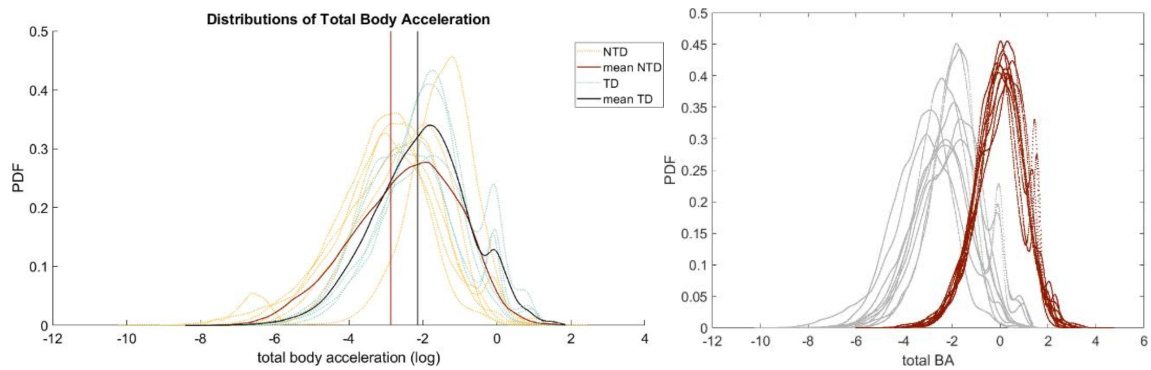

Figure 4 Normalization.

Left: PDFs of total Body Acceleration, total BA, for subjects from both groups, averaged distributions, and real average of total BA acceleration of each group. Right: PDFs of total BA for all subjects before normalization, in grey, and z-scores in crimson.

3.5 Data processing with the unsupervised behavioural clustering algorithm

The algorithm used for this analysis was adapted from Klaus et al., [38]. The algorithm computes similarities between acceleration levels in data collected by a single accelerometer and clusters the data based on these similarities. This method, accounts for the fact that the body and gravity components of acceleration measured over the three Cartesian axes may be used to represent unique behaviours if the accelerometer is attached to the body in a known position, thus the Cartesian axes represent the body planes. In this study, the accelerometer was placed on the lower back of children with the x vector representing the vertical axis, z the anterior posterior axis, and y was the right left axis.

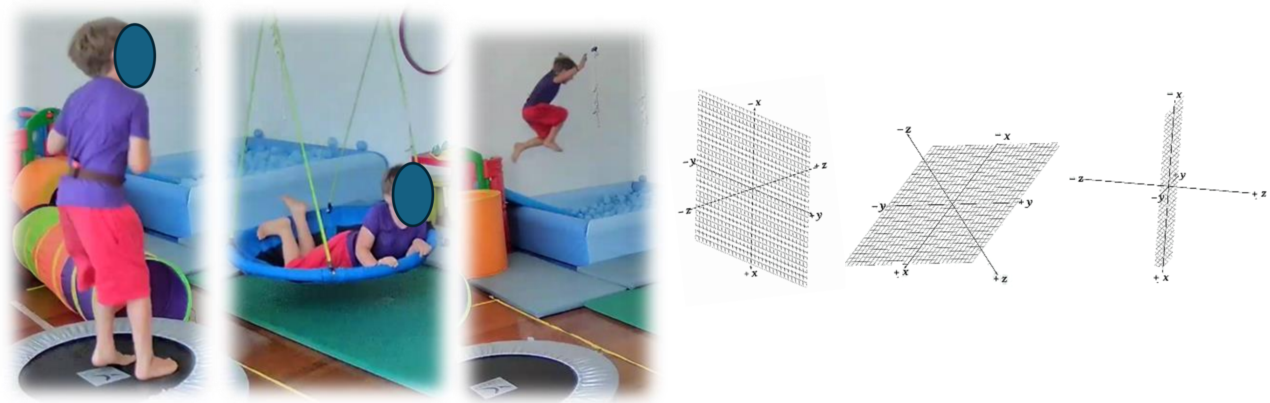

Figure 5 Example of changes in axes direction in relation to the body postural changes.
Left: Pictures taken from the video footage of one session. Right: illustration of potential changes in the direction of the axes on which acceleration is measured relative to the body position (the visualisations are for illustration purposes and were not taken from the real data points related to the pictures).

For example, in this set up; while standing completely still, it is expected to observe approximately 0 acceleration on the z axis and y axis and gravitational acceleration of 1g on the x axis. If the child walks, then ideally there will be small gravitational changes on the vertical axis and positive body acceleration on the dorsa- ventral axis. If the child is laying on his belly, the vertical axis becomes horizontal, and thus gravitational acceleration on it will circle around 0 and decreasing negative values of the body component will indicate progression. During jumping forward, there will be a pattern of decreasing negative gravitational and body acceleration followed by increasing negative values on the x axes and increasing then decreasing positive body and gravitational acceleration on z. From a human perspective, humans hardly move on the right left plane, yet acceleration on this axis is present in all movements.

3.5.1 Feature selection

For this work we used 3 acceleration vectors as the input data for the algorithm, henceforth termed features:

1) Gravitational acceleration measured on the vertical axis (in this case, the x axis). This feature was mainly used to assess postural changes, i.e., to differentiate between standing or sitting straight to bending or lying episodes. The simplified shortcut **x GA** will be further used for this feature.

2) Total body acceleration, calculated as the square root of the summation of the squared body acceleration component from each axis.

$$\text{Total BA} = \sqrt{BAx^2 + BAy^2 + BAz^2}$$

This feature is given in absolute values and limited by 0. As this feature sums the movement on all axes it emphasises small weight shifts and trunk movements and thus useful for detection of movement initiation and pause. We used this feature to distinguish periods of movement from staying still periods, as well as to determine the extent of the movement. It will be further termed as **total BA**.

3) Total acceleration (body and gravitation components) measures on the z axis. In this work, z is the anterior posterior axis, and positive values represent moving forward. This feature was valuable for two reasons: firstly, it allowed us to discriminate progression episodes from staying in place episodes, and secondly it allowed us to grasp postural changes too subtle to be identified with the more robust x GA feature. Here we will refer to this feature simply as **z**.

3.5.2 Setting thresholds to characterise acceleration levels of different behaviours

For each feature, thresholds were defined to distinguish between acceleration levels suitable for characterization of behaviour. The thresholds in this work were chosen in a data driven manner based on the shape of the distribution of each feature. First, histograms of each feature were plotted and local Maxima were identified using the *islocalmax()* built-in function in MATLAB. The conditions for a local maximum ware set to be with minimal prominence equal to 20% of the prominence of the highest peak and with distance of a least 5 bin edges to the next maximum. The number of thresholds was defined as number of local Maxima + 1, such that when there is one maximum there will be 2 thresholds etc. After setting the number of thresholds, thresholds were defined using the *multithresh()* function, a multilevel thresholding method based on Otsu´s method [40]. This function is available as part of the Image Processing Toolbox in MATLAB.
Briefly, Otsu’s method (named after it’s developer Nobuyuki Otsu) is a thresholding method developed for separating the foreground from the background in image processing. The method is based on the fact that contours have darker colours while

foreground elements tend to have brighter colours, and the thresholds are set based on the histogram of Red, Green Blue (RGB) levels of pixels. The algorithm iterates through the bins of the histogram and calculates the probability that the two classes of the histogram are separated by a threshold set in the specific bin n. It does so by multiplying the class probability (the sum of values in bins 1: n out of the entire sample) and the variance of each class. The threshold is chosen to be the value that maximizes the inter-class variance. Originally, the method was used for greyscale thresholding, assuming that colour intensity levels are distributed in a bimodal shape. To calculate more than one threshold, developments based on the original Otsu's method are recursively assessing the variation.

This method was especially relevant for our work as we aimed to find distinctive acceleration aspects of behaviour without a-priori assumptions on the type of activities displayed by the children.

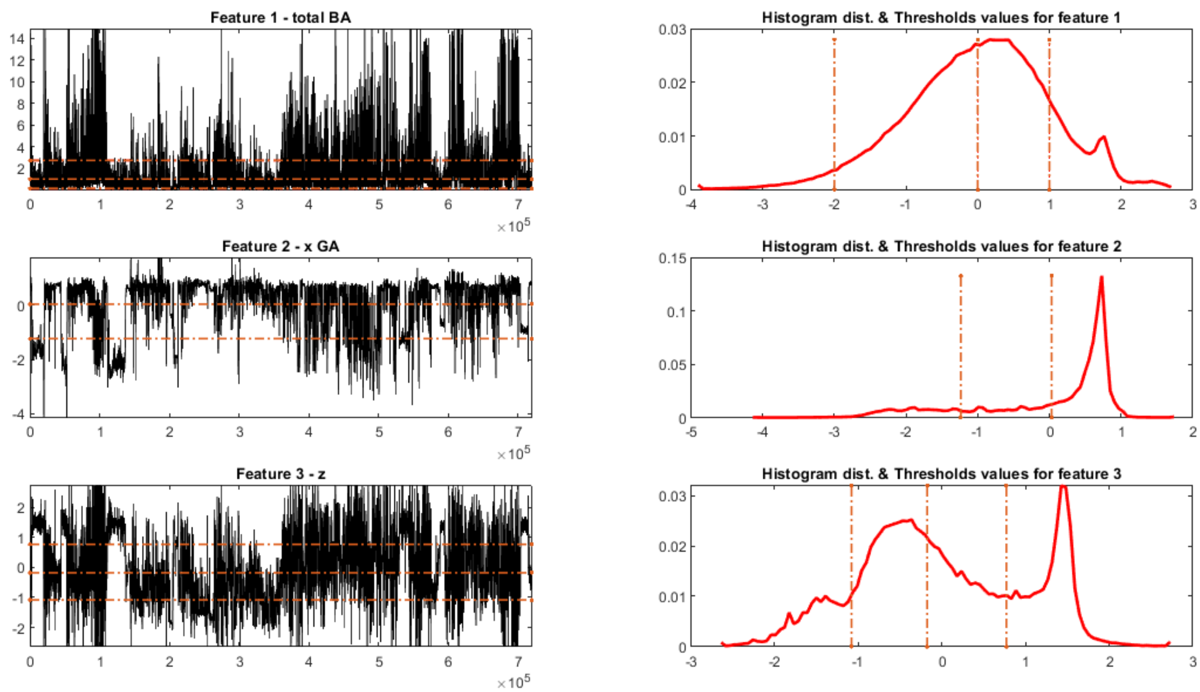

Figure 6: Features with Otsu based thresholds.
Left: the thresholds are plotted in red on the continuous normalised acceleration values across the entire sample. The x axis represents samples in Hz (sample rate of 100Hz). Values on the y axis are displayed as z scores of the original raw data. Right: distributions of the three features for the grouped normalised data, thresholds are marked as dashed vertical lines. The values on the x axis are acceleration levels after normalisation by z-score.

3.5.3 Computing similarities across the sample's time series

The defined thresholds are used by the algorithm to create discretised histograms which serve as the basic units for comparing data across the time sequence of the sample. Firstly, the data is divided into fixed size temporal bins with 30% overlap between them. For each bin 3 discretised histograms are created, one for each feature with edges defined by the thresholds. To compare between temporal bins, the similarity measure S is calculated using the Earth Movers Distance, EMD [41], a method for calculating the distance between distributions. EMD compares two histograms based on two factors: the "ground distance" and "flow". "Ground distance" takes into account the distance between the bin edges of the two histograms and the "flow" assesses the most efficient way to distribute the "weight", or the amount of data points which differentiate between the two distributions. For example, if the first histogram represents a temporal bin in which the child stands still, ideally the total BA is at zero and all data points will be within the first threshold in the first bar of the histogram. If the child starts walking slowly in the second temporal bin, then the histogram will hold more values in the second bar whereas if he starts running then some points will be within the third bar. As the EMD takes into account the distance between the bin edges of the histograms, transitioning from standing to running will have a higher EMD value than transitioning from standing to walking or walking to running. Thus, EMD is especially relevant to distinct between motor behaviours based on acceleration levels.

For each temporally paired bins, EMD is measured between the respective histograms of each feature. Then, the pairwise similarity S is set as the negative value for the square of the normalised sum of EMD of the 6 histograms:

$$S = -(EMD_{xGA} + EMD_{z} + EMD_{totalBA})/3)^2$$

Since we had 30 percent temporal overlap between the bins, for each data point the average distance between three sequential bins was used.

To further decide if two bins belong to the "same behaviour", the median EMD across all paired bins was used to distinguish "similar" from "dissimilar" histograms. Namely, If the EMD value between two bins was higher than the median, the first data point of the second bin was assigned as a "changing point", defining transitioning between different behaviours. In the next step the process is repeated using the “changing points” bins as the comparison units. Since the changing points bins have unequal sizes, the histograms were normalised to each bin’s size. Then, the EMD is calculated between every two changing points bins resulting in a large matrix in which every cell holds the similarity measure S between two changing points bins. This matrix was used for the clustering process.

3.5.4 Clustering

The clustering method used here was Affinity Propagation Clustering, AP Clustering, an unsupervised clustering method developed by Frey & Dueck [42]. AP groups data by finding ‘exemplars’, data points which are the most representative points for a group of samples. Exemplars are chosen in a iterative process assessing if a point k is suitable to serve as the exemplar of a point i, by two parameters: “responsibility”, reflecting how suitable point k is to serve as an exemplar for point i, taking into account how suitable were other data points to serve as the exemplar of i; “availability”, how suitable point k is to serve as an exemplar of point i, taking into account how suitable k is serving as an exemplar for other data points. As an unsupervised method, for each data point the “self-responsibility” and “self- availability” are updated with every iteration until “self-responsibility” and “self- availability” are equally indicative of a point as an exemplar and convergence is reached regarding the number of exemplars. Namely, each point is either chosen to be an exemplar or not, for a predefined number of iterations. AP clustering returns a vector of indices, labelling each data point, in our case, each changing point bin, by its exemplar. Exemplars can also be described as the cluster centroid.

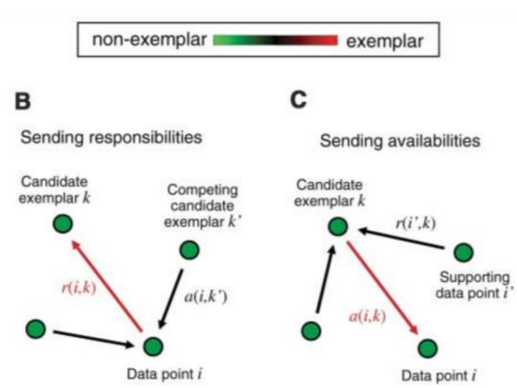

Figure 7. Affinity propagation clustering.
Adapted from Frey & Duebec., 2007. Representation of the messaging process in AP clustering.

To control the number of clusters, it is possible to give the AP clustering algorithm a preference distance, indicative of the preferred distance to the exemplar. To choose the preference distance we used the *Midcross()* function, available as part of the Signal Processing Tool Box in MATLAB. The MATLAB implementation is based on an histogram method developed for finding the mid-reference level of bi-level waves [43]. This method may be used for finding the Maximum Height Full Width, MHFH, of a distribution. We used *Midcross()* to find the 20% reference level, since it minimised the number of clusters compared to higher and lower reference levels. As seen in the plot below, this preference value is located at the tail of the histogram. Our data included mostly very similar values, to find distinctive clusters, we had to choose a high preference distance to not forego complex movements.

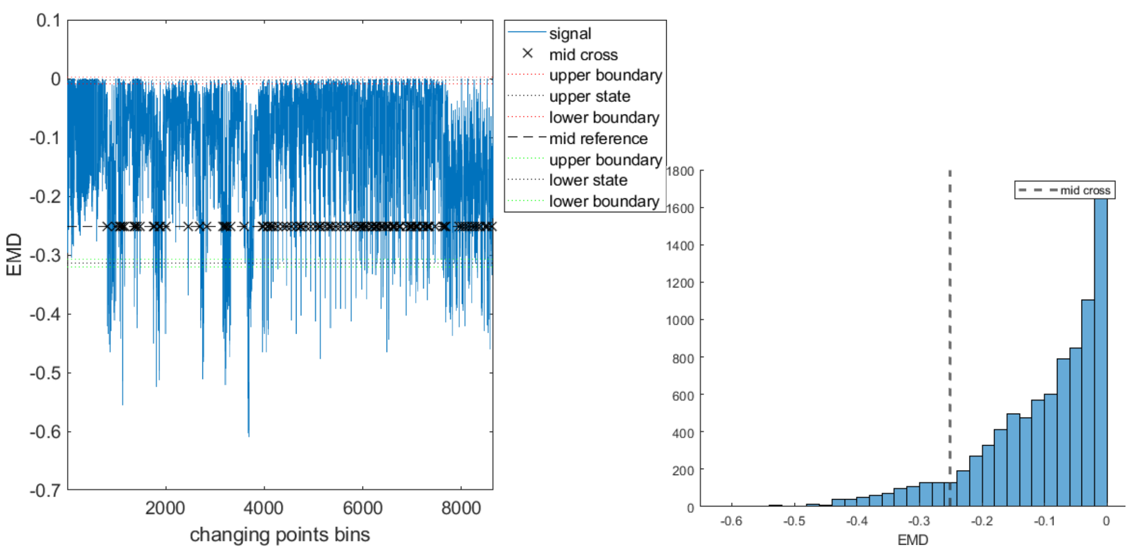

Figure 8. The "Midcross" reference level

The Midcross preference on: Left: an example set of EMD values between changing points bins. Right: on the histogram of EMD levels from the same example set.

3.5.5 Regression of clusters to the sample's original time series

After the clustering process is concluded, clusters are regressed to the original data points. The final output of the algorithm includes indices of the distinct clusters across the sample, indices of changing points, the EMD similarity matrix, as well as different statistical metrics such as standard deviation within thresholds, average similarity between points and average distances of points to cluster centroids for each cluster.

Graphical abstract

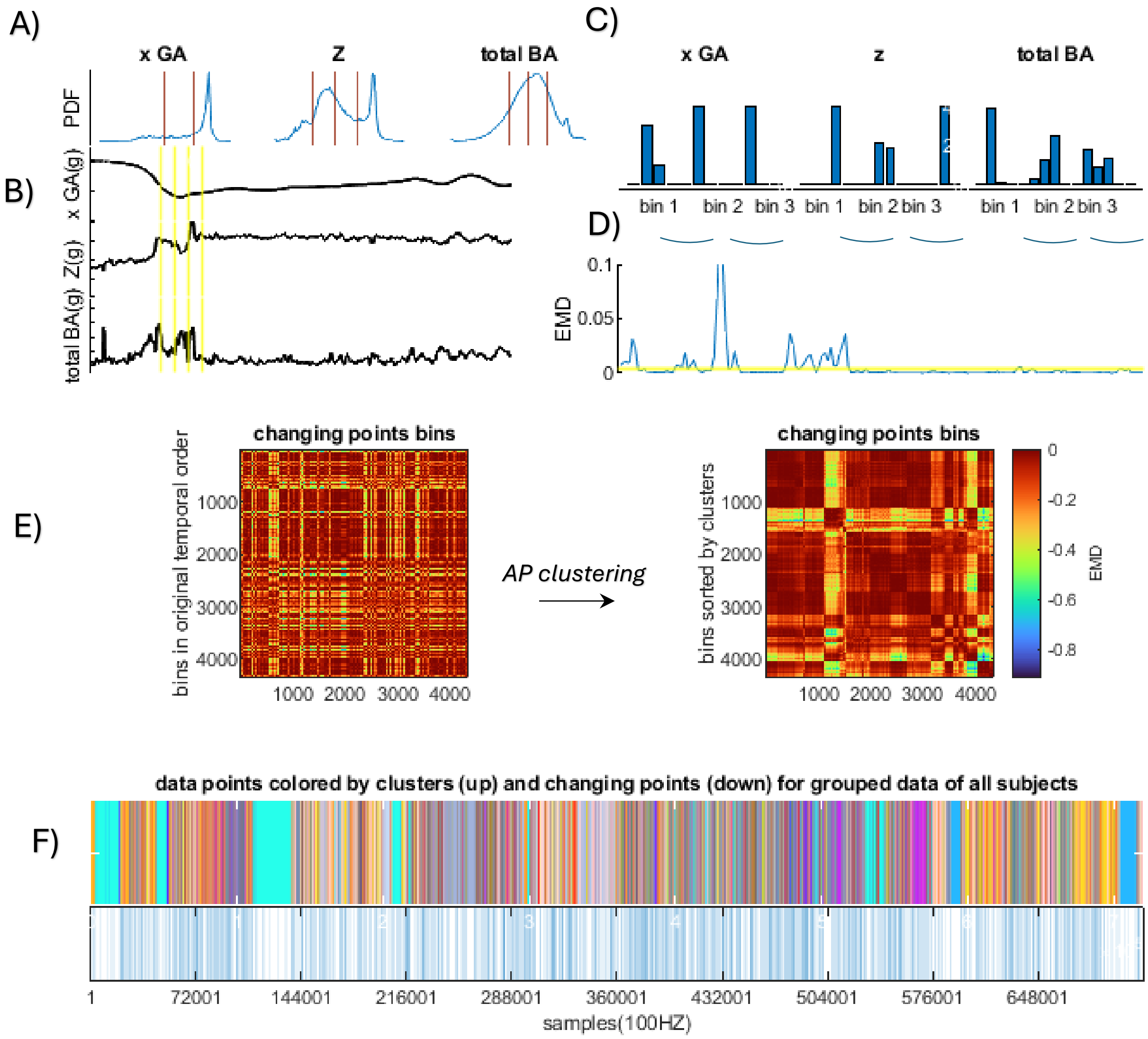

Figure 9. Graphical abstract of the clustering process.

A) The acceleration distribution on the 3 features used for analysis. Acceleration on each feature was divided by thresholds defined using a thresholding method based on Otsu's method. Thresholds are marked in crimson. B) Example of acceleration values on the three features. For each feature 2 minutes (1200 samples in100 HZ) are presented. The continuous acceleration data was divided into fixed size bins of 400 ms (40 samples) with 0.3 overlap. Bin edges are marked in yellow. For simplification of the visualisation the bins here are not overlapping. C) for each 400 ms bin, 3 discretised histograms were created based on the thresholds defined for each feature. 3 histograms for the 3 example bins on each feature are presented. Pairwise Earth Movers Distance, EMD, is calculated between following bins on each feature. The normalised summation of distance across features is used as the dissimilarity measure for each pair of bins. D) to decide if bins are related to the "same" movement we set a threshold equal to the median dissimilarity between bins. Points which are above the threshold are marked as "changing points". All samples between two changing points are then grouped into new bins, termed here as "changing point bins". E) The EMD is recalculated between the re-established bins creating the similarity matrix used for clustering. F) data points are relabelled by the identified clusters.

3.6 Details of specific adaptation made for the adjustment of the algorithm to the analysis of children´s free play.

The first aim of this project was to test the feasibility of unsupervised clustering based on data collected from a single IMU to assess children's spontaneous behaviour. Three main factors have been modified in order to obtain relevant clusters for our purpose.

3.6.1 Feature selection

In Klaus et al., 2017 [38] the authors use the 3 following features: total BA, which was used to distinguish arrest episodes from movement episodes; z GA, representing the dorsal-ventral axis of the mouse, and indicative of rearing, and phi, which was the rotational information calculated by the video material. We used the total BA feature in a similar manner to recapitulate information on movement and arrest episodes and x GA for posture in analogy to z GA in Klaus et al. We excluded the gyroscope information since it was very noisy in our sample, and the time frame of this project did not allow us to further improve filtering on this feature. Instead, we used z that gave informative input regarding the direction of the movement, small postural changes and importantly indicated if the child was laying on his back, information which is not present on the x axis.

3.6.2 Bin size and overlap

In Klaus et al., a 300 ms bin size is used as the primary bin size for pairwise comparison of similarities between acceleration levels, based on previous findings indicating 300 ms is the average time period between postural changes in mouse spontaneous behaviour in an open field arena [44]. To test the relevant time bin for our data we had to take into account the high variability presented in the children's behaviour. Some movements spread across half a second or even a second while others were about 100 ms. We took three measures to determine the bin size: 1) we calculated the average interval between acceleration peaks for the 3 features. The average peak interval across all features was 36 samples (360 ms); 2) we tested the effect of bin size and level of overlapping between bins over the number of output clusters; bin size reduces number of clusters in a roughly exponential model. Forty samples bin size is approximately the value before number of clusters becomes stable and after the sharp decrease in number of clusters for lower bins sizes. Overlaps 0.1 and 0.3 gave similar number of clusters and transitions. 3) we compared the time series of the clusters to video material. The combination of 40 sample (400 ms) and 0.3 overlap was found to most accurately identify transitions between behaviours as observed in the video. It was especially important for us to test transition between behaviours that involved high and low acceleration levels. For example, between jumping on the trampoline and standing.

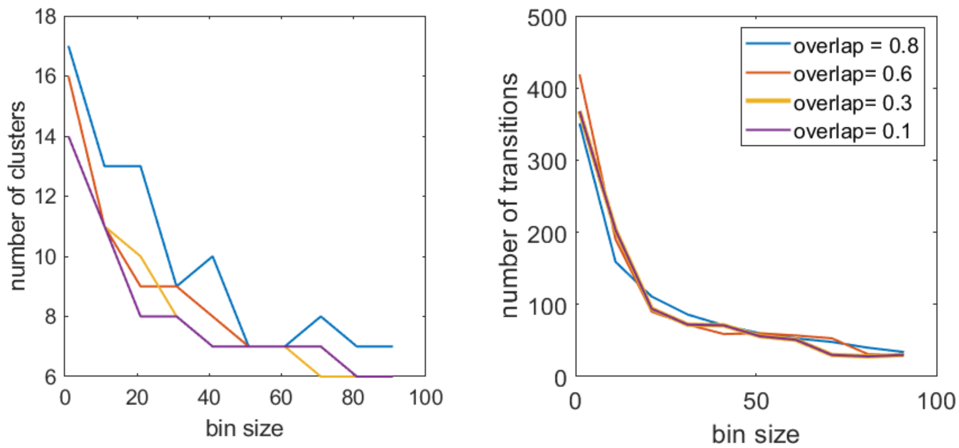

Figure 10. Effect of bin size and between bins overlap on clustering.

Decrease in number of cluster (left) and number of transitions between clusters (right) is shown as bin size increase. Overlap between bins has little effect on number of transitions, yet higher overlap leads to increase in number of clusters.

3.7 Analysis

3.7.1 t-SNE, a method for two-dimensional representation of multidimensional data

t- distributed Stochastic Neighbour Embedding, t-SNE, is a method for dimensionality reduction for visualization [45]. t-SNE calculates the probability of two points, x_i and x_j to be near each other in high dimensional space, p(j,i) by calculating the probability they would pick each other as neighbours if they were picked in proportion to their probability density under a Gaussian center point. It computes similarly the conditional probabilities for two points, y_i and y_j, q(i,j), in low dimensional space. If p(i,j) and q(i,j) are equal, then the low dimensional points are chosen as representatives of the high dimensional points. t-SNE only calculates conditional probabilities, therefore it cannot be used as a clustering algorithm as it only minimises the difference between the two calculated probabilities for adequate visual representation but does not evaluate the real distance between points. Yet, it may be used to evaluate how well the clusters distinguish the data.

We used t-SNE for representing the similarity matrix holding the EMD distances between changing points bins and refining values for input variables for the clustering process. The two-dimensional representation showed a certain overlap between the clusters found by the AP clustering algorithm.

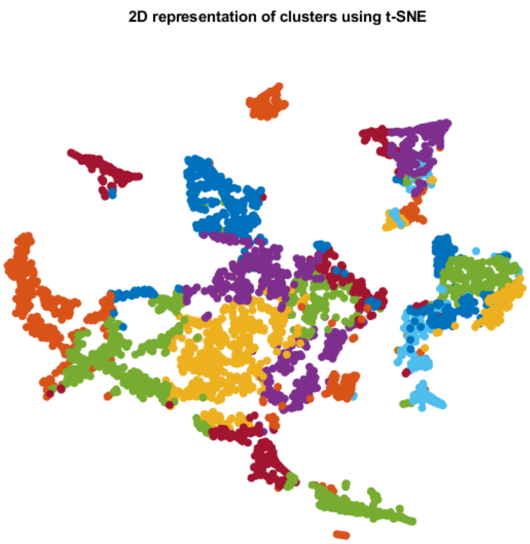

Figure 11. Two-Dimensional Representation of clusters obtained by t-SNE.

3.7.2 Kullback-Leibler Divergence

The Kullback-Leibler Divergence, KLD, also known as relative entropy measure, is a method used for quantifying dissimilarity between two probability distributions. It measures the difference, or direct divergence between the elements of the probability distributions *p*(**y**) and *p*(**x**) such that:

$$D_{\mathrm{KL}}(P \parallel Q) = \sum_{x \in \mathcal{X}} P(x) \log\left(\frac{P(x)}{Q(x)}\right),$$

When comparing two *n* elements distributions, a vector with *n* elements is returned, each cell containing the dissimilarity between every two paired elements.

The KLD measure gave us the means to explore how subjects changed their behavior in the presence and absence of their parents, i.e., the environmental effect of the parent presence, as well as to evaluate how different subjects, from the two-study groups, behaved in similar conditions. Following the analysis presented by Levy et al.,[39] we calculated a frequency distribution of clusters and normalized them to the duration of each condition (fraction of use) for each subject in the “with parent” and “without parent” conditions. These were attributed as the subject´s behavioral repertoire in each condition. The clusters in each distribution were organized by their frequency of appearance for all subjects, such that cluster in the first position appeared in the highest frequency in our entire sample. In practice, each subject had 2 distributions, vectors of 26 elements, each element held the value for the fraction of display of one cluster by the subject within a certain context.

Then the KLD was calculated between all possible paired combinations of subjects and conditions, namely the distribution of subject one in condition one was measured against the distributions of subject two in conditions one and two and similarly to the two distributions of all subjects and importantly, KLD was also calculated between the two distributions of each subject. For each KLD vector the average value was calculated and used as the dissimilarity measure between every two frequency of cluster usage distributions.

We used the averaged KLD values to perform three types of analysis:

a) <u>Within subject, between groups</u>: we used the KLD value of the comparison between distributions of each subject in the two conditions to test the change of the cluster repertoire in the presence and absence of parents. Then, we tested whether children in one of the groups had tendency to increased changes in their behavior due to the environmental effect.
b) <u>Within subject, within group:</u> to test how the variability within the group was affected by the parent presence and absence, we averaged the KLD values of each subject to peers from the same group in each condition, then tested whether the groups average was different between conditions.
c) <u>between subject, between groups</u>: to test how different were cluster repertoires of children from the two different groups, each subject received one KLD value which was the average KLD of his averaged “parent” KLD to all other subjects and averaged KLD “without parent” to all other subjects.

KLD was suitable for this specific analysis as it is an asymmetric measure which does not require any presumptions on the data. KLD was computed using the KLD function available in the “LaplacianDemon” package in R.

3.7.3 Statistics

For the statistical analysis of our results, we applied non-parametric tests suitable for the small sample size of our data and the lack of power for parametric analysis. The Wilcoxon signed rank test was used for paired comparisons, in within subject hypothesis testing. We used Mann- Whitney test (Wilcoxon sum-rank test) for between subject comparisons, and Friedman test for repetitive measures within subjects’ analysis. Friedman’s test analysis was combined with post hoc multiple comparisons. We did not consider correction for multiple comparisons as the study is merely exploratory, with a very small sample size.

All statistical analysis use done using the statistics Tool Box in MATLAB, version R2023b.

4. Results

In this project we asked to test the potential of unsupervised clustering of acceleration data collected with a single IMU, in semi-supervised settings to highlight distinct aspects of behaviour of children on the autistic spectrum when compared to neurotypical peers. We challenged our method by creating an experimental design permitting many degrees of freedom to the children's behavior. Processing the collected data with the unsupervised behavioral clustering algorithm (see methods), we identified 26 clusters that characterize the behavior of children from the two groups. We found that all clusters were displayed by at least 2 subjects from each group, with almost half the clusters shared by all subjects, and with more than half the subjects contributing to each of the clusters. Cluster characteristics are summarized in table 2 at the end of the results section.

We aimed to grasp global aspects of behavior rather than changes in specific behaviors, e.g., unique gait characteristics or speed of hand movements. We hypothesized that using our method we will find a distinctive signature represented by each individual. We further hypothesized that environmental effects related to socio-emotional stimuli such as the presence or absence of a parent would affect neurotypical and autistic kids differently. For that purpose, we quantified for each participant the frequency in which he or she used behavioral clusters obtained by the algorithm. The behavior of the subject was described by two behavioral repertoires, normalized frequency distributions of the clusters he or she displayed during the time the parent was present in the gym, and the time after the parent has left the gym. It is important to note that the clusters presented in this work are not equivalent to a set of behaviors recognized by a human observer in the way that two clusters or more may represent a single behavior, e.g., cluster 1 is "walking fast" and cluster 2 is "walking slowly", as well as the fact that clusters may represent aspects of movement related to acceleration changes that are undetectable by the human eye. In this work we chose to assess the obtained clusters in two contexts: a) within the global behavioral repertoire frame of each subject, comparing subjects' repertoires independently of any information regarding the specific nature of each cluster; b) by the kinematic aspects which were used for classification of clusters, e.g., the thresholding of acceleration over the features.

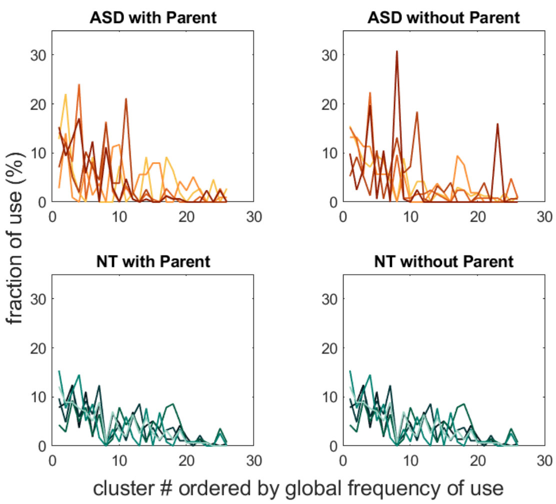

Figure 12. Behavioral repertoires of cluster usage. *The 4 panels represent the behavioral repertoires of children from the ASD and NT groups in the presence and in the absence of their parents. On the x axis the clusters are sorted in descending order from left to right by the global frequency of their use by all subjects. On the y axis the usage of cluster is drawn as a fraction of the total sample size for each individual within one context.*

4.1 Differences in frequency of usage of clusters, individual cluster repertoire

One of the leading goals of this study, was to determine whether clustering children´s free play will detect an individual behavioral signature presented in the clusters displayed by each individual, hypothesizing that such signature will be distinctive between children with ASD and NT peers. We calculated the normalized frequency of appearance of each cluster in each contextual time frame and created two frequency of usage distributions for each subject. These frequency distributions represented the behavioral repertoire of each child in each context. This analytical approach was inspired by the work of Levy et al., [39] who demonstrated that behavioral repertoires of mice in open field spontaneous behavior are highly distinctive between mice. Following Levy et al., we measured the similarity between the behavioral repertoires using the Kullback- Leibler Divergence, KLD, a method for calculating dissimilarity between two distributions.

We measured the KLD between all pair-wise combinations of the individual distributions, including between subjects (inter-subject) and wihin subject (intra-subject) combinations. Frequency distribution of each participant in the two contexts are presented in figure 16. Namely, the repertoires of subject 1 in the two contexts were compared, then the reprtoires of the same subject number 1 in contexts one and two were measured against the reptoires of subject 2 in contexts one and two and so forth. This resulted in two dissimilarity matrices presented in figure 12.

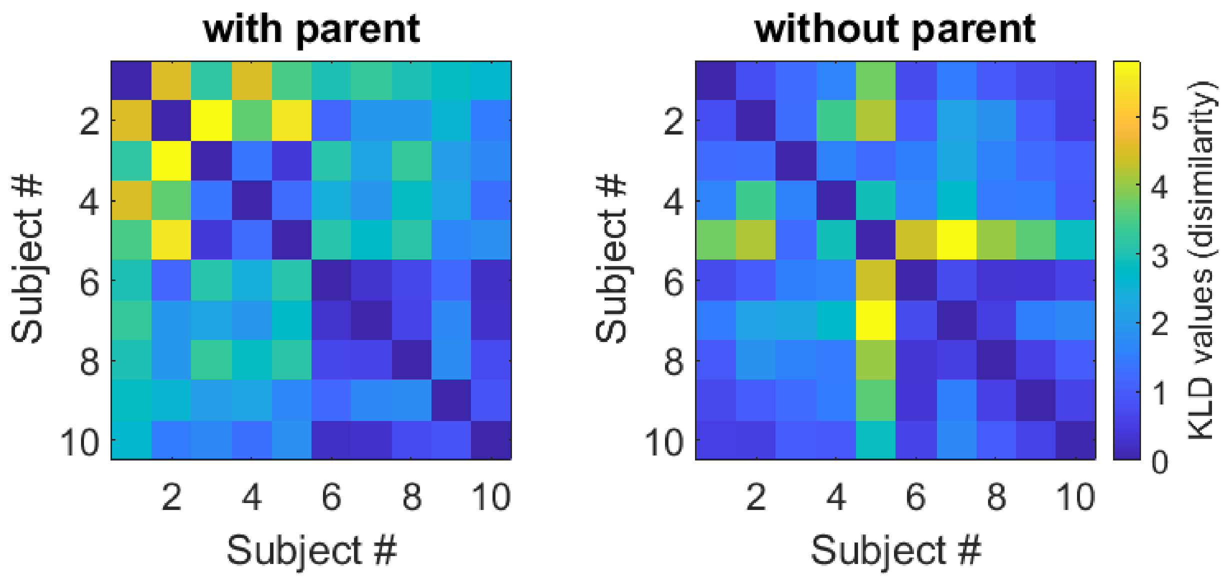

Figure 13. KLD values between subjects in the study contexts.

Dissimilarity matrices showing the paired KLD values between subjects in the two study contexts. Subjects 1 to 5 are the participants in the ASD group and subjects 6 to 10 are the controls from the NT group. The contrast between the high similairty within the NT group, as presented in the right lower square (rows 6 to 10 and colomns 6 to 10) and dissimilarity within the ASD group (upper square on the left, rows 1 to 5 and colomns 1 to 5) is outstanding. Moreover the similarity within the control group is stable acroos the two contexts while the KLD values within the ASD group are distinguishabel between the two pannels. Lastly, the KLD values between the subjects of the two groups seem higher in the context of the parent present.

For testing the hypothesis that the ASD children had distinctive repertoires and that the parent will affect their behavior in larger scale than the NT children we analysed this data in 3 conditions:

1. inter-subject, group level (figure 14): looking at the dissimilarity matrix presented in figure 12, it is obvious there is large difference between the groups in the similarity levels of the children to the rest of the sample. We tested the hypothesis the children in the ASD group are overall more different than the children in the NT group by denoting each child´s dissimilarity level as the average KLD value across the conditions. Using the Mann-Whitney test a significant between group difference was found with p= 0.0216, z = 2.297.

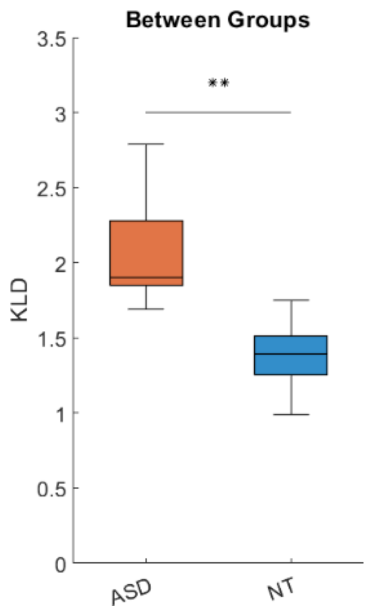

Figure 14. Between subject comparison of KLD values

Between group diffrence intotal KLD values measrues as the average KLD of each participant to the entire sampel.

2. Intra subject, within group (figure 13 upper left and upper right):
   Looking at the similarity matrix (figure 12) one of the most observable difrences is in the KLD values within the ASD group in the two conditions, suggesting that the variability within the group is higher in the presence of a parent. In contrast, the children from the control group demonstrate high similarity levels within the group in both conditions. To test the hypothesis that the parent's presence affect the within goup similarity level we took the average of the KLD values of each participants from his peers in the same group and tested whether the group average changed between the two conditions. No signifance level was reached in neither group. ASD, $p = 0.2249$, $z = 1.2136$. NT: $p=0.893$, $z= -0.1348$. However, it is noticeable from the similarity matrix in figure 12 that while the dissimilarity levels between participants one and two decreased in the parent's absence the behaviour of subjects 4 and 5 became more dissimilar to the rest of the group. It is also visually clear that the level of similarity within the control group is higher.

3. Intra-subject, between groups, (figure 13 down left=: the KLD value of the comparisons of each individual to him-, or herself was used to evaluate if there was a between group diffrence in the level of dissimilarity of children´s in the presence and absence of a parent. We used the Wilcoxon signed rank- test to compare this measure between the groups which was found to be non-significant. $p= 0.38$, $z= 1.4832$.

4. Inter-subject, between contexts, (figure 13 down right): To test whether the dissimilarity between groups was stable in the two contexts, we compared the paired KLD values of children from the two different groups in the parent presence and absence contexts. Using the Wilcoxon- signed rank test, no significant difference was found p= 0.372, z = 0.8925. Yet it seems that while mostly children from the ASD group behaved more similarly to those from the NT group in the parent's absence, one subject (number 5) behaved very differently from the remaining participants in this context, thus creating a bias in the median of the KLD values in the absence of a parent.

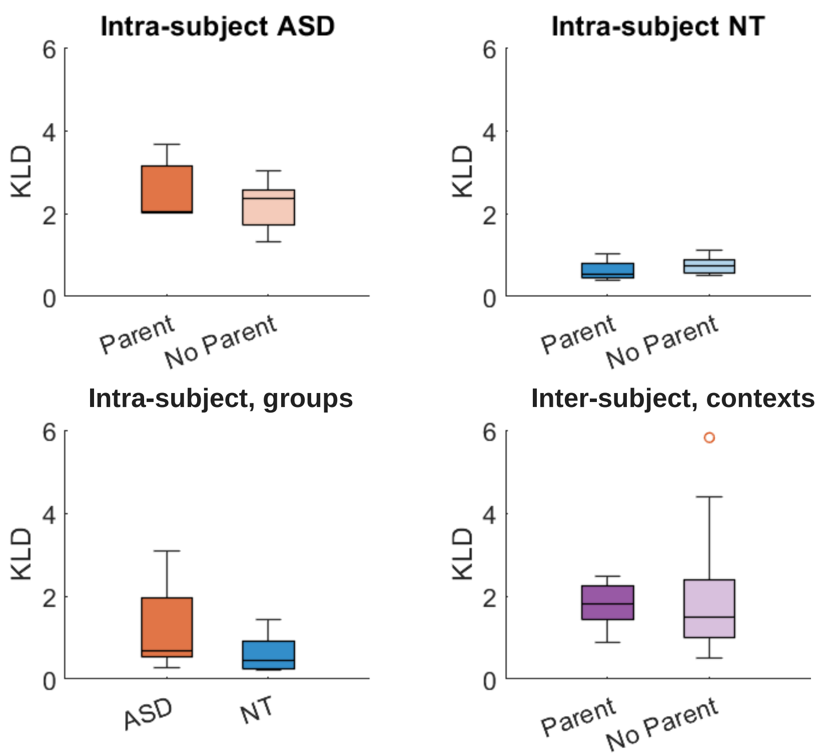

Figure 15. Comparison of KLD values.

Upper left: changes in KLD values within the ASD group between the parent presence and absence conditions. Upper right: changes in the KLD values within the NT group. Lower left: difference between the two groups in the KLD values of each subject between the two conditions. Lower right: dissimilarity of the behaviour of ASD children to NT children in each context. It is most notable from the four panel that the level of dissimilarity within the control group is significantly lower than in the ASD group and consistent between the two contexts.

In summary, by comprising individual behavioural repertoires using the 26 clusters identified by the algorithm we were able to find a distinctive between group difference which seem to be rooted in the high similarity in behaviour among NT children. Moreover, although not statistically significant, parental presence seems to have an effect on the behaviour of children with ASD although this effect is mixed. While some children increase their similarity level to the group, others reduce it. Moreover, it is notable that ASD children change their behaviour in comparison to themselves in the two contexts. These results should be further analysed in larger samples, using parametric tests and variance tests.

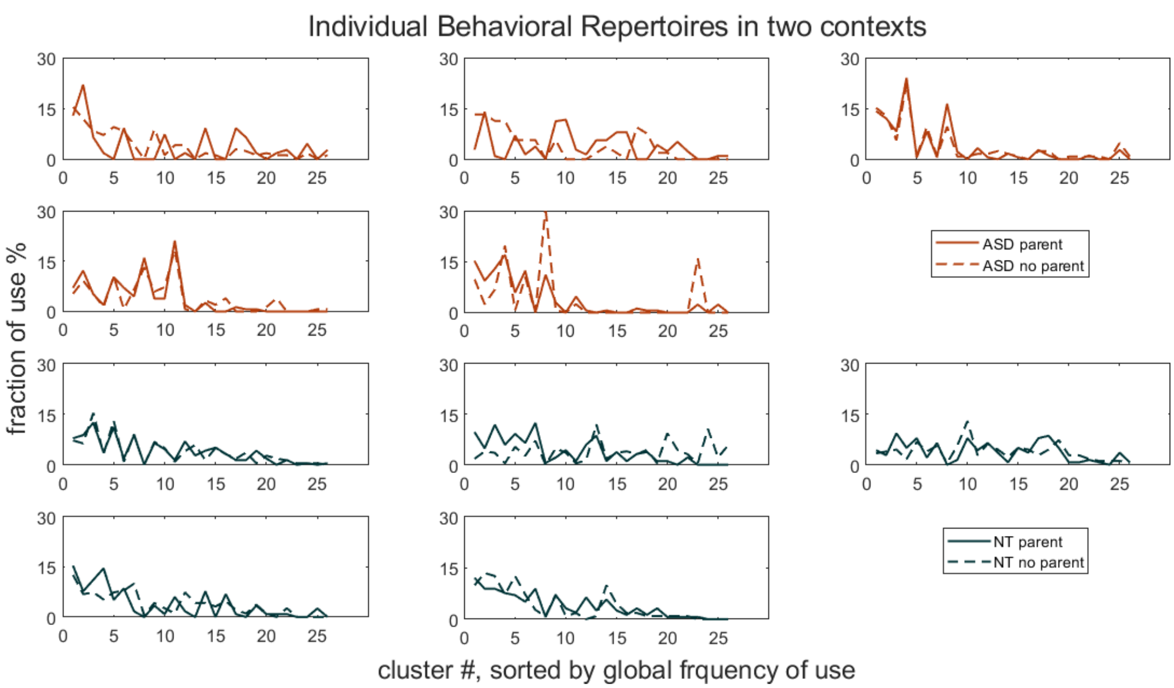

***Figure 16**. Individual behavioral repertoires of clusters' frequency of usage in the two contexts.*
Cluster usage in the presence of a parent is drawn by continuous lines and cluster usage in the absence of a parent by dashed lines. Each panel present the behaviour of one individual.

4.2. Children differ in the number of unique clusters displayed, but not in transitioning between clusters and distances to clusters centroids

To have an overview of the way the children used the clusters we tested three general parameters: number of clusters to which the subject contributed, the number of transitions each subject performed in each context and how well was his or her behaviour represented by the cluster by measuring the distance of data points to the clusters exemplars (centroids). We tested how each of these variables changed in the presence and absence of a parent contexts within each group as well as the global difference between subjects from the different groups.

4.2.1. Total number of clusters displayed by each subject.

Visualization of data, as seen in figure 12, and in further detail in figure 16, suggests that while the frequency of clusters usage in NT children is distributed in a relatively balanced way across all clusters, the autistic children displayed a more restricted repertoires and do not participate in all clusters. This restriction seemed to increase in some subjects in the parent's absence.

First, we asked to evaluate the difference at the group level. For that purpose, we used for each participant the average number of clusters displayed in the two contexts. Indeed, a significant difference was found when comparing the average number of clusters displayed by children from the two groups. $p = 0.0153$, $z=0$ -2.4244.

To evaluate the effect of a parent's presence on motor behavior flexibility of children with ASD and controls, we calculated the number of distinct clusters each child displayed in each context and compared it to children from the same group in the two contexts. However, number of clusters displayed by the children in the ASD group did not significantly change in the parents' presence and absence, $p= 0.885$, $z= -0.1414$, neither in children from the control group, $p= 0.153$, $z= -1.4142$. Interestingly, the parent absence seems to have a mixed effect within the ASD group as some children demonstrate higher behavioral flexibility while others have reduced flexibility in the presence of a parent.

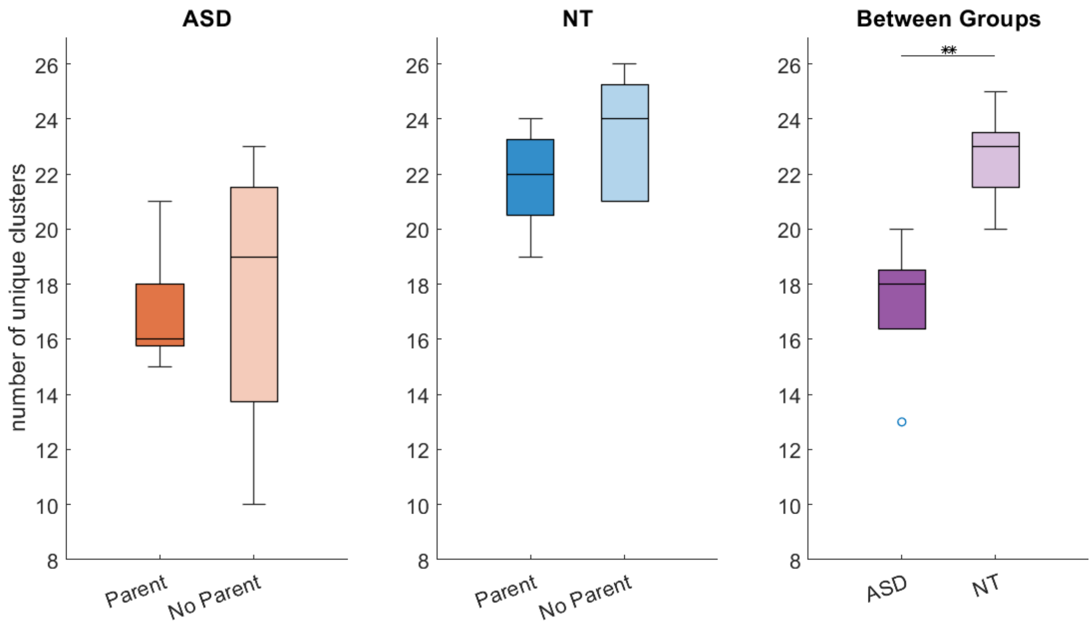

Figure 17. Changes in the number of unique behaviour (clusters) demonstrated by the study participants.

Left: comparison of the number of clusters displayed by the ASD children in the parent's presence and absence. Though no statistical difference was found, the within group variability is higher in the parent's absence. Middle: the number of clusters displayed by children form the NT group. children have a slight tendency to display higher number of clusters when the parent is absent which was not found significant. Right: between group difference in the average number of clusters displayed in the two contexts. Neurotypical children display significantly higher number of clusters.

4.2.2. Transitions between behaviours

To further use clusters to characterize the children's behavior we tested whether children from the two groups differed in the number of between cluster transitions, namely how often they transitioned from one type of behavior to another. We used a similar approach, assessing the difference in each group in each context, and the overall between group difference. The number of transitions did not statistically vary between the two groups. $p= 0.3452$, $z = -0.8381$, nor within each group in the two contexts. Comparing the change in number of transitions for the ASD group: $p= 0.4735$, $z= 0.9439$, and for the NT: $p= 0.4735$, $z= -0.9439$. Yet, there seems to be a considerable difference in the effect the parent absence has on children's behavior. In the ASD group there is a small tendency to decrease the number of transitions in the absence of the parent, while NT children, in the same situation, change more frequently between distinct clusters.

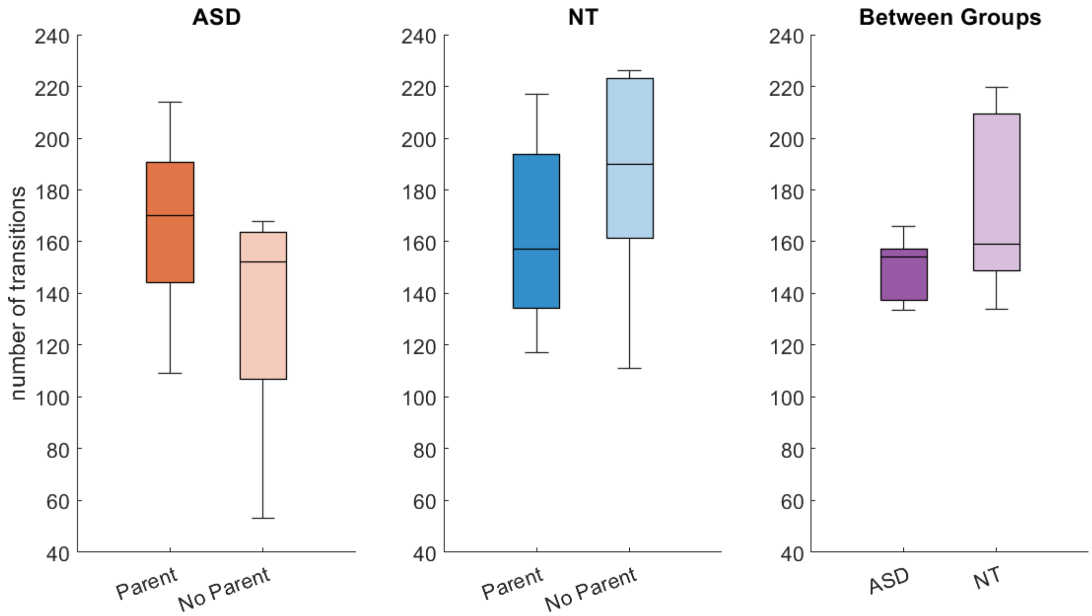

Figure 18. Between subject comparison of number transitions between behaviors.

Left: comparison of the number of transitions displayed by the ASD children in the parent's presence and absence. Seemingly, a parent has an effect to the number of transitions performed by some of the children of the ASD group. Middle: the number of transitions displayed by children form the NT group. Controls have a slight tendency to display higher number of transitions when the parent is absent which was not found significant. Right: between group difference in the number of transitioned displayed. Though no statistical significance was found, it seems that children from the NT group tend to perform higher number of transitions between behaviours.

4.2.3 Distance to centroid.

Lastly, we asked how well a cluster described individuals' behaviour. For that purpose, we used the average distance of data points belonging to each individual from the cluster centroids. Essentially, clusters, as classified by the Affinity Propagation, AP, clustering, are the grouping of data points around the exemplar, the most representative point of the group. The distance of each point to the exemplar is a measure of how well the cluster centroid serves as its reference point. If a subject is more distant from the centroid of a given cluster, this means that he or she has a more unique behavioral pattern within a certain cluster. To calculate points' distance to centroids, we used the EMD distance previously calculated between histograms. The average for each subject was calculated in each context and then the average between contexts.

In terms of distance to centroid, children from both groups retained similar distance to centroids. Mann-Whitney test did not reveal statistically significant difference at the group level overall: $p = 0.8341$, $z = -0.2089$. Using Wilcoxon signed-rank test, no statistical difference was found related to the parent presence for the ASD group: $p = 0.312$, $z = 1.2136$, nor for the NT group: $p = 0.89$, $z = -0.1348$.

It seems the parent's presence had small effect on this measure, yet this effect was opposing between the two groups. Children from the ASD group tended to decrease distance to centroid in parents' absence, while children from the NT group increased distance to centroid.

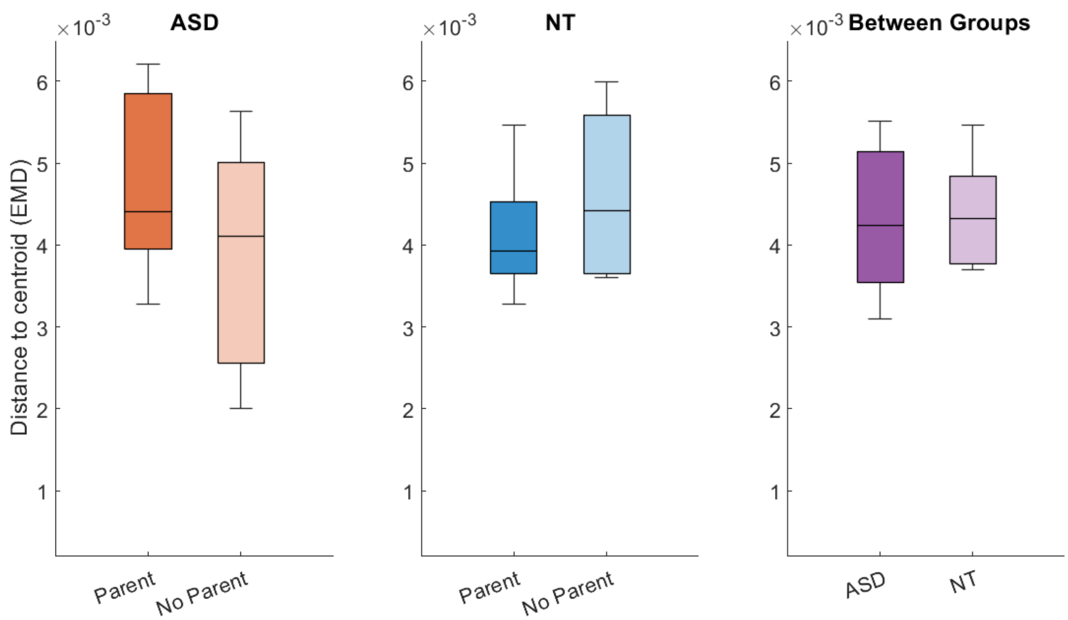

Figure 19. Between subject differences in distance to cluster centroids.

In all panels the y axis represents the average EMD values of bins displayed by individuals to cluster centroids. Left: comparison of the distance of points belonging to ASD children to cluster centroid in the parent's presence and absence. There is a slight decrease in distance to centroid when the parent is absent. Middle: comparison of the distance of points belonging to NT children to cluster centroid in the parent's presence and absence. There is a slight increase in the distance to centroid when the parent is absent. Right: between group difference in distance to centroids. Children from both groups had similar distance to centroids indicating that clusters represented the behaviour of children from both groups equally well.

In summary, we demonstrated in this section that while children from the two groups tend to transition in a similar frequency between behaviours, as well equally contribute to the within cluster variance (as represented by the distance to centroid), the number of behaviours display by individuals in the ASD group is smaller. This is aligned with the tendency to restricted behaviour common among children with ASD [1]. These findings suggest that in our analysis the most relevant feature are the specific characteristics of the clusters.

4.3 Kinematic representation within clusters

As a first step, we compared the behavioral repertoire displayed by each subject within our sample independently of investigating the clusters' characteristics. This was of importance as one of the study aims was to explore whether the methodology offered here is valid for future work when information over the child's behavior might be limited. We showed that the main distinguishing feature between groups was the cluster identity, which manifested both in terms of differences in frequency of use of clusters and in terms of number of clusters displayed. In contrast, transitions between clusters as well as quality of contribution to clusters, as measured by distance to centroid, were similar in both groups.

Next, we asked to explore the relevance of the thresholding scheme used for the clustering process in distinguishing between subject's motor behavior. We assumed that the differences found in the cluster´s repertoires are related to acceleration levels characteristics of each cluster, as previous findings indicate that kinematic aspects of movement may underlay many motor symptoms of children with ASD [21], [22], [24], [32]. The 3 features used for this study analysis were:

A) Gravitational acceleration on the vertical axis, X, x GA. x GA was divided by two thresholds into three acceleration levels. Acceleration values close to 1g indicated that the subject is standing or sitting in an angle of approximately 90 degrees to the floor. Values close to 0 indicated that the device is parallel to the floor, when the subject is laying or deeply bending the torso. The third level, the middle level, represented transitions between these two dichotomous states.

B) Total body acceleration, total BA, was divided by 3 thresholds into four levels and was used to assess the total extent of movements. Lower values indicated staying in place, middle values represented most movements, including walking crawling etc. Finally, high values may be indicative of one of the following conditions, a movement which has very high acceleration on one dimension, like jumping, or movements which involve acceleration on more the one axis resulting in an overall high summation of acceleration on the 3 axes.
C) Total acceleration on the z axis was divided by four thresholds into five acceleration levels. Since this feature holds the total acceleration on the backward forward plane including both gravitational and body components, increase and decrease in acceleration levels could be indicative of both movement on this plane as well as postural changes. In upright position the z axis is parallel to the floor thus values are mostly circling around zero. When the child bends deeply forward or lays on the stomach, values will be around one while negative values around minus one were indicative of laying on the back. This axis was used to distinguish progression from gross movements in place and to identify subtle postural changes that were not captured by the more robust x GA classification.

Using the division of clusters by thresholds into main acceleration levels, we asked how subject's behavior varied within the groups in the presence and in the absence of their respective parents as well as between the groups in each condition. We mapped clusters based on the proportion of time each of the acceleration levels contributed to the total cluster display and created for each feature three (or four for z), classes, "low", "medium" and "high". On the total BA feature, cases where two thresholds contributed to one cluster, we classified the cluster as "medium". For example, cluster A in figure 20 was classified as "low", since the second threshold included in low acceleration levels was the threshold most representative of it. We did so as we thought it was more appropriate to group it with cluster representing movement rather than cluster representing staying still episodes based on observations across the data in comparison to video material. On the z feature, the image was more complex hence we created a different mapping system adding a "*transitions*" class indicating transitions between acceleration levels within the cluster.

This class was used to describe clusters to which different acceleration levels contributed similar proportions of time. For example, see cluster B on the left panel in figure 20.

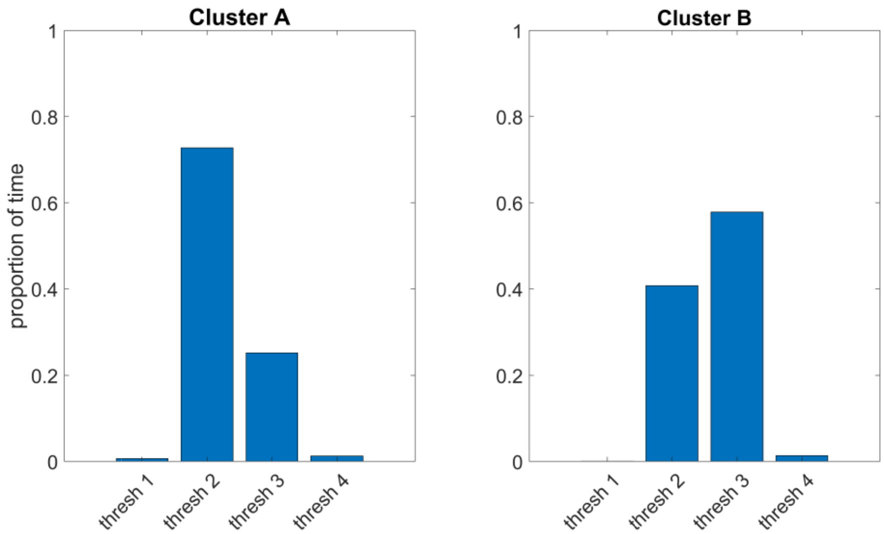

Figure 20 Histograms of proportion of time spent in acceleration levels within thresholds for two different clusters.

Left: Cluster "A" shows a distribution where most of the time children displayed movement characterized by acceleration within the second level. Right: Cluster "B" shows a more balanced distribution of proportion of time spent within acceleration levels.

In figure 21, clusters were mapped by the contribution of time spent within acceleration levels. Thresholding of x GA and total BA created a clear criterion for grouping, while acceleration levels on the z-axis present a more complex image and mostly more than one threshold contributes to each cluster.

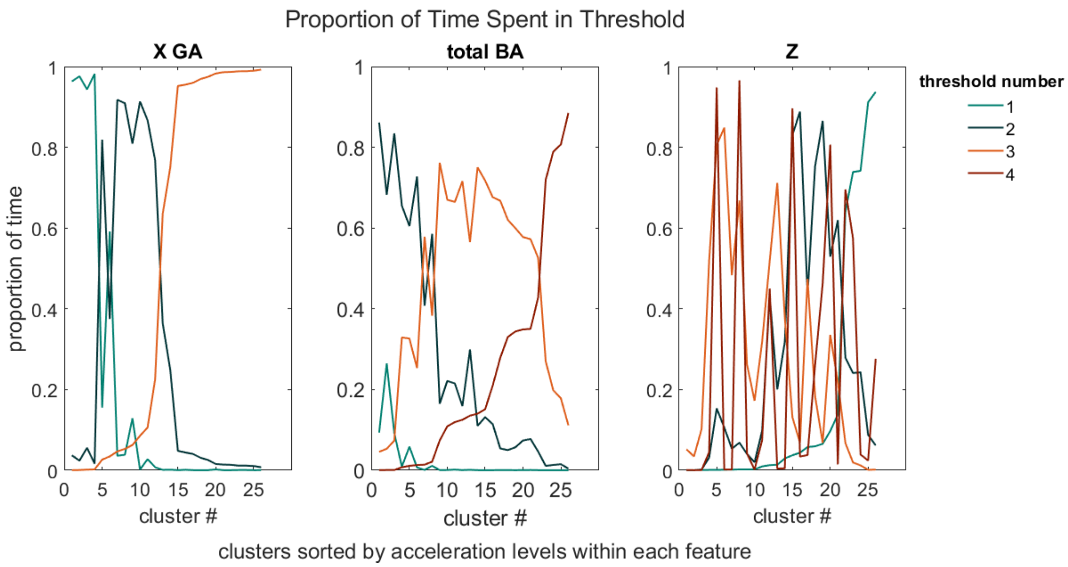

Figure 21. Division of acceleration levels within each cluster.
Left: cluster mapping on the x GA feature. Clusters are clearly distinguishable by acceleration level with minimal overlap. Middle: clusters mapping on the total BA feature. While clusters may be classified by total BA level, a certain overlap is seen between the medium level to both high and low levels within several clusters. Right: mapping of clusters across the z feature. It is notable that acceleration levels on the feature are complimentary within clusters giving a more complex image.

For analyzing the between subject differences, we calculated the proportion of time each subject spent in clusters belonging to each class.

For each feature we used two tests: 1) Friedman test, or Friedman's ANOVA, a non-parametric analysis of repetitive samples in dependent variables. This test was used to check the within group difference across the acceleration levels in the two contexts; 2) we used the Mann-Whitney test to assess the between group difference in specific acceleration levels which seemed more relevant for the analysis based on preliminary exploration of the data.

4.3.1 Between group comparison of acceleration levels on the Total BA feature

In both ASD and NT groups the proportion of time spent in *low* total body acceleration level differed from the *medium* and *high* acceleration levels in the parents' presence. For the ASD group: $p = 0.0011$, $X^2 = 13.54$., and for the NT group = 0.0005, $X^2 = 15.35$.

Based on prior exploration using data visualization, we wanted to explore if specific changes in proportion of time spent in the low and medium acceleration levels between the two contexts were distinctive between groups. Man- Whitney test showed no significant difference in the presence of a parent, p = 0.671, z= -0.4178. and no significant difference in the absence of a parent. P= 0.2963, z = -1.0445. Interestingly, the groups were not found to significantly differ in proportion of time spent in the *low* acceleration level in the presence of a parent p= 0.21, z= 0.1253, but did differ in the absence of a parent, p = 0.0367, z= 2.0889.

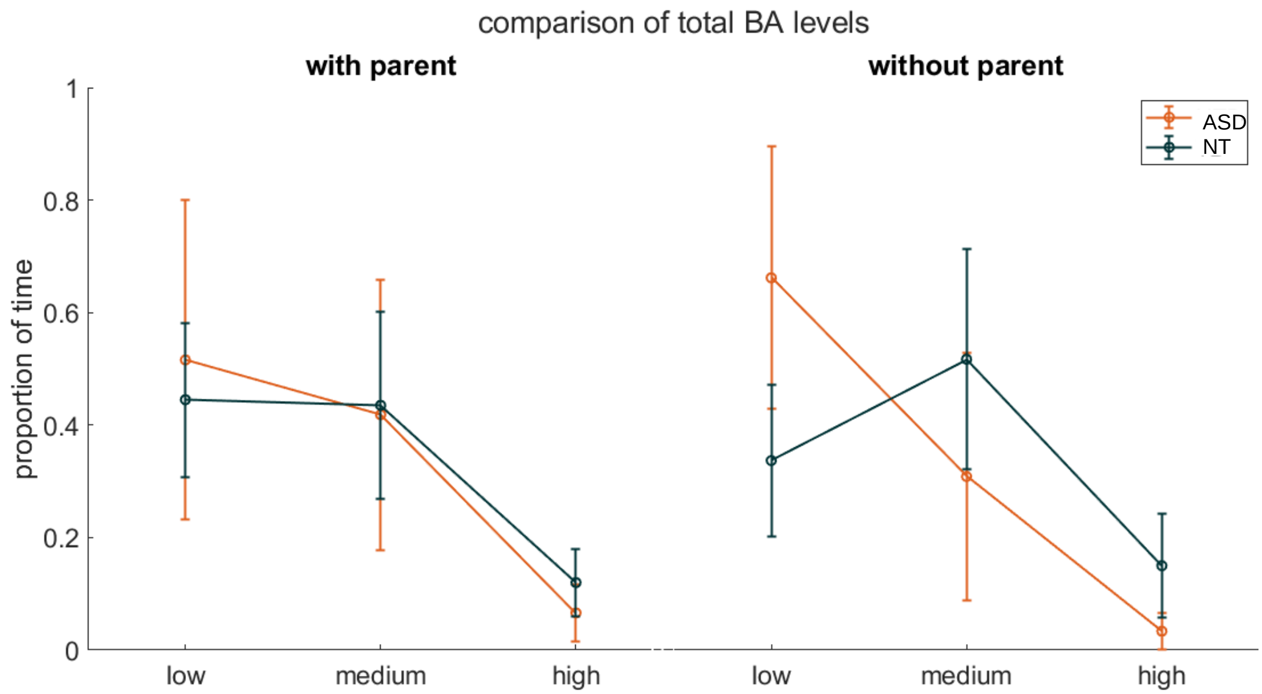

Figure 22. Proportion of time spent in acceleration levels on the total BA feature.

Proportion of time (y axis) spent in each of the acceleration levels, "classes" (x axis), on the feature total BA. While children from the ASD group increased the time spent in the low class and decreased the time spent in the medium class after the parent left, Children for the NT group demonstrate the opposite and increase the proportion of time spent in the medium class as the time in the low class was decreased.

4.3.2 between group comparison of acceleration levels on the X GA feature

Both groups showed a significant change in the proportion of time spent in clusters from the three acceleration level classes, the significance resulted from the difference of the *high* acceleration level from those of *medium* and *low* classes. For the ASD group, p= 0.0009, X^2= 13.94. For the NT, p= 0.0003 X^2= 16.17.

Data Visualization highlighted a possible between group difference in the medium acceleration levels of x GA which are mainly representing transitions between standing and laying or bending. To test if the two groups differ in that particular acceleration level and if that difference is consistent in the two contexts, we used the Man-Whitney test which revealed no significant difference in the presence of a parent, p=1, z = 0, and no significant difference in the absence of a parent, p= 0.143, z = -1.4623.

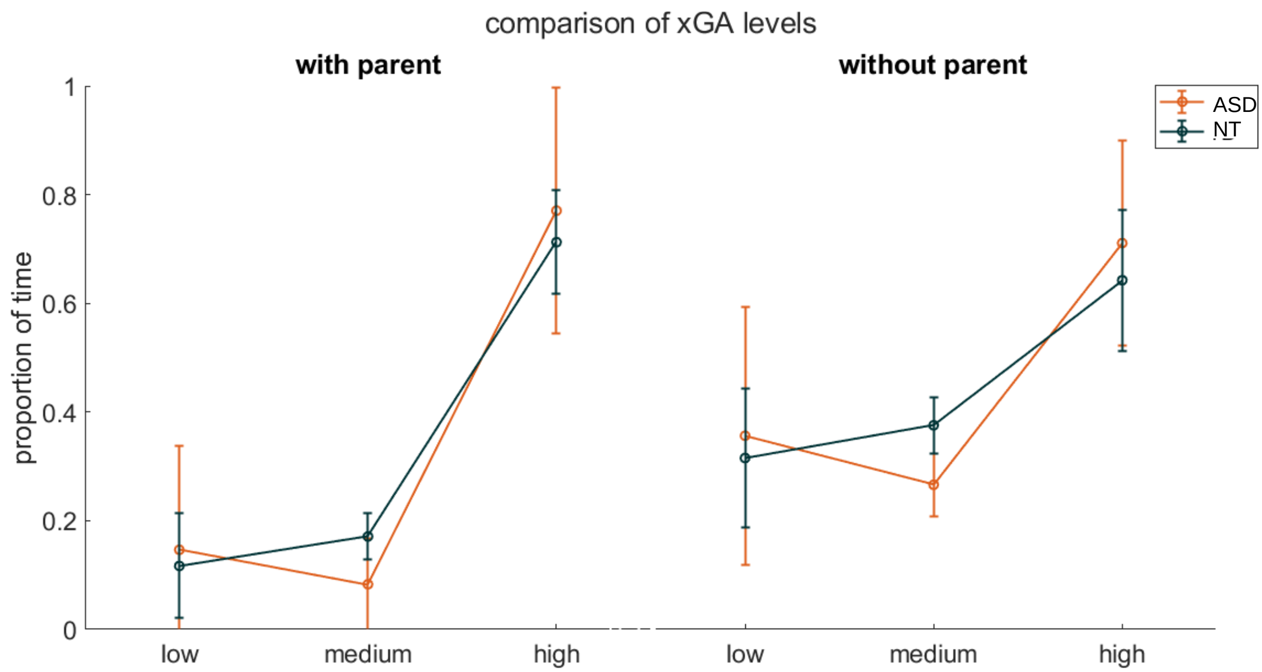

Figure 23. Proportion of time spent in acceleration levels on the x GA feature

Proportion of time (y axis) spent in each of the acceleration levels, "classes" (x axis), on the feature x GA as defined by the thresholding scheme used for clustering. Children in the two groups presented a relatively similar image of time spent across the classes.

4.3.3 Between group comparison of acceleration levels on the Z feature

On the z axis, subjects from the ASD group did not differ in proportion of time spent in particular level, p= 0.126, X^2 = 5.72. Yet, subjects from the NT group did, p= 0.001, X^2 = 20.43 and multiple comparison revealed that the median proportion of time spent in *low* acceleration level on z was significantly different from the median of the other classes. This finding was not very insightful as the *low* class of acceleration level on z specifically signifies behavior including laying on the back. We moved forward to evaluate particular between group differences in the *transitions* class as the between group differences seem to increase in the absence of a parent. Mann- Whitney test showed a marginally non/significant between group difference in the parents' presence, p = 0.061, z= -1.88. In the absence of a parent, differences in time spent in transitioning behavior as represented on the z axis was found significant between the groups, p= 0.035, z= -2.0889, being higher in the NT group.

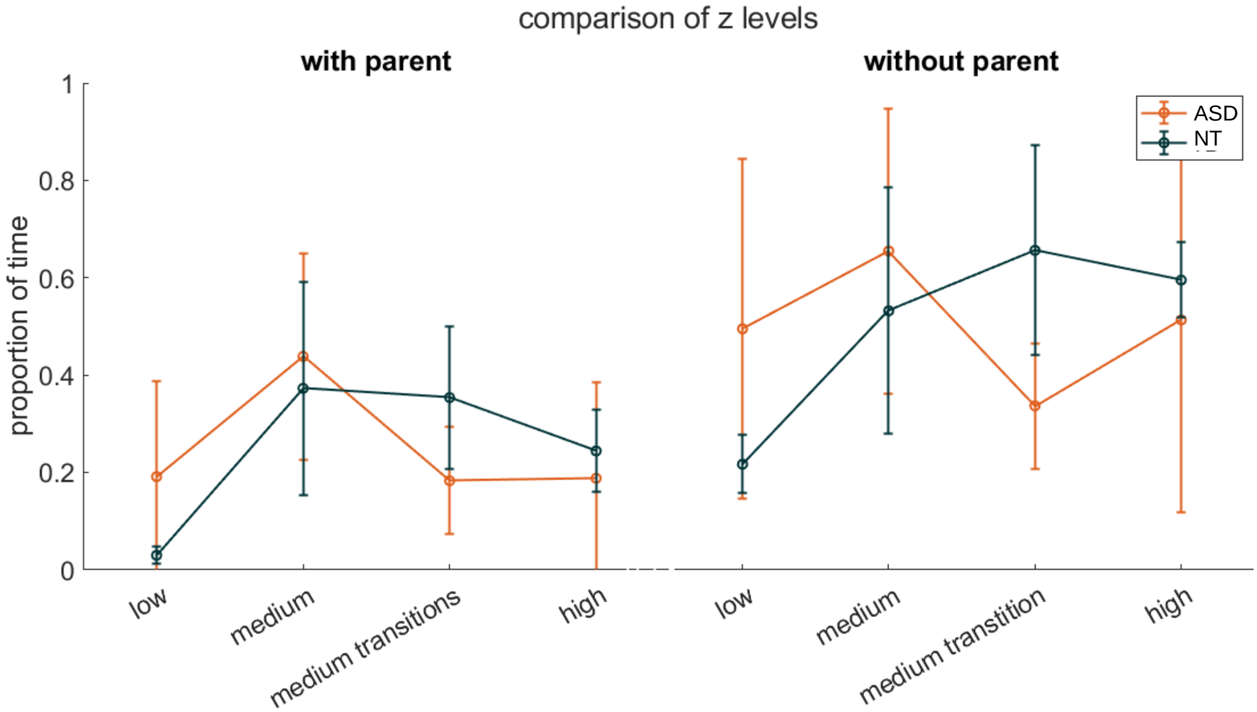

Figure 24. Proportion of time spent in acceleration levels on the z feature.

Proportion of time (y axis) spent in each of the acceleration levels, "classes" (x axis), on the feature Z. ZAs previously mentioned, the division across classes in the z feature was more complex. Adequately, it is shown that children from both groups display a more balanced time division between the different classes. The largest between group difference lays in the transitions class which was significant in the parent's absence.

In summary, in this section we found little evidence for between group differences as presented by the proportion of time spent in clusters which were attributed to a specific acceleration level. Nonetheless, most of the between group differences were particular to one of the contexts which may be indicative of the effect a parent has over the children's behavior. Moreover, data seem to indicate that children from the ASD group had higher tendency to lower acceleration level movements than the NT, and that the NT children showed higher flexibility on the z axis.

cluster #	*characteristic of group*	*participants*	*xGA level*	*BA level*	*z level*	*total appearance*	*average frequency*	*average dissimilarity*
1	Even	10	high	low	mid	36764	5.8	0.019
2	NTD	10	high	mid	mid	48664	9.22	0.9568
3	TD	10	high	high	mid	30632	3.35	0.017
4	Even	10	high	mid	mid	49896	9.42	1.2547
5	TD	8	low	mid	high	5852	1.3	0.0093
6	NTD	10	low	low	high	74570	2.24	0.1492
7	TD	10	mid	low	high	31360	2.52	0.0735
8	TD	4	low	mid	transitions	4956	0.98	0.1397
9	TD	7	low	mid	low	6692	0.72	0.0036
10	TD	9	high	high	transitions	16772	2.09	0.0458
11	Even	9	high	mid	transitions	17052	4.24	0.1645
12	Even	9	mid	mid	low	6636	1.41	0.0162
13	TD	10	high	mid	transitions	11900	3.1	0.0488
14	TD	10	high	low	transitions	62748	7.99	1.0125
15	Even	10	high	low	mid	85413	7.64	1.2697
16	Even	10	high	mid	transitions	20636	4.88	0.0511
17	TD	10	high	mid	transitions	32368	6.91	0.2661
18	TD	9	mid	mid	high	31080	5.03	0.4006
19	TD	9	mid	mid	transitions	8512	1.58	0.0463
20	NTD	10	high	mid	low	18536	4.09	1.227
21	TD	9	mid	mid	transitions	10724	2.81	0.0306
22	NTD	8	high	high	mid	8176	1.05	0.0066

23	TD	7	mid	high	high	10192	2.53	0.026
24	TD	7	low	mid	high	28336	2.92	0.5209
25	NTD	7	high	low	low	47796	5.07	0.5646
26	NTD	6	mid	low	low	13748	1.11	0.006

Table 2. Detailed characteristics of the 26 clusters identified by our algorithm*.*

The column characteristic of group represents the group which contributed more than 60% to cluster duration. the column participants indicated how many subjects participated in this cluster. The columns xGA level, BA level and z level, show which acceleration level was the main acceleration level for each feature in the cluster. In the column total appearance, the total number of samples described by the cluster is presented, i.e., the cluster size. Average frequency is the average frequency of use of the cluster by all subjects. Average dissimilarity indicates how differentially expressed was the cluster by the different subjects.

5. Discussion

Children with ASD tend to suffer from sensorimotor difficulties [46], hyper sensitivity [47], impaired adaptive behaviour [48], as well as communication deficits [1] which challenge the feasibility of many methods used for movement recordings to study movement of autistic children. Thus, though motor behaviour of children with ASD has been the subject of intense investigation in the last decade, literature is sparse, and we are yet to understand how various motor manifestations are contributing to the autism phenotype. Here, we tried to address this challenge by creating a simple experimental design tailored to the needs of children on the autistic spectrum as well as relevant for neurotypical children or children who suffer from other neurodevelopmental conditions. We were able to record high resolution acceleration data with minimal interference to the children's natural movement. The algorithm used in this work proved able to extract meaningful information regarding the children's patterns of behaviour and group them into behavioural clusters relevant for the representation of distinctive individual behavioural repertoires. Our analysis indicates that children with ASD use behavioural clusters differently from neurotypical children and, importantly, that they also have high behavioural variability within the group. To that end, the behavioural freedom given to the children, enabling us to study their movement during free play in semi- supervised conditions, seems highly valuable. Indeed, this work present high ecological potential contrasting with other studies previously discussed here, which involved mostly complex settings limiting the potential to study different motor feature within the same experimental scheme, the feasibility of data collection in larger proportion of the population as well as extrapolating findings to alternative environmental contexts. For example, to associate atypical gate to sensory-motor integration, Biffi et al., [49] had used advanced technology involving virtual reality with treadmills and motion capture systems. This equipment is costly, hard to move and requires a large space. Moreover, in these settings, children must be stabilised with belts making it irrelevant for children with hypersensitivity. In contrast, in our settings, once further developed, if the “walking” cluster is recognised, kinematic aspects of walking could be compared under various stimuli. On the other hand, more simple settings have focused the investigation of specific types of movements and developed specific metrics which are difficult to extrapolate to daily movements or to movements more relevant for animal models, e.g., reach an grasp or pointing tasks [24], [50]. In contrast, we were able to find both relevant metrics for translational studies in animal models as well as for comparison under multiple environmental contexts. Within our study scheme we could test the hypothesis that manifestation of motor features in ASD is influenced by environmental effect related to the core symptoms from social and emotional domains. Though significant conclusions could not be taken in this work, due to the small sample size, initial results indicate that a passive parent's presence has in fact an important effect on the behaviour of children with ASD and their underlying kinematic characterisation. In Frosting et al., [37] typically developing infants explored a novel space using their stationary mother as a "home base", a secure port from which to explore, while infants who later were diagnosed with a neurodevelopmental disorder did not. The importance of a mother as a secure subject, is well established in the revolutionary work of Marry Ainsworth and John Bowlby on attachment theory [52]. Ainsworth found that children with insecure attachment tended to stay in place and entangle in stereotypic behaviour in the presence of their caregivers. While this effect of a parent on an infant's behaviour is extensively described, very little is known on how a passive presence of a parent or care giver can affect the behaviour of older children. Here, we were able to highlight the importance and relevance of further investigation of the effect of such socio-emotional stimuli which may shed light on integrative mechanisms in movement planning and sensory motor integration speculated to be compromised in ASD [29].

Another important impact of this work lay in the fact our results are partially consistent with previous findings in animal behaviour studies which revealed that the individualised use of clustering has higher predictive power for the mouse identity than a global biological characterisation such as hormonal changes related to estrous phase [39]. Yet, the increased variability in the autistic children emphasises a plausible motor trait that is distinctive at the group level between individuals with autism and NT peers. In this pilot work we did not collect sufficient data for employing classification programs, but our initial results indicate that this may be highly relevant in future work. We found that NT children's behaviour is substantially similar within the group, yet it must be considered that KLD values presented in previous work are far lower than the KLD values found in this work.

Where in the study by Levy et al.[39], KLD values were generally lower than 1, similarly to the dissimilarity within the NT group of this study, KLD scores measured in the autistic group reached values as high as 5. Taking this into account, it is important to address in the future the predictive power of behavioural repertoires of identity of NT children which seemed negligible when compared to the large dissimilarity in the ASD group as well as its power to predict the identity of children with ASD which presented high variability within the group.

Finally, we sought to explore the possibility of identifying kinematic aspects of behaviour through the clustering map identified by the algorithm. To achieve this, we used a very general kinematic scheme which opened new perspectives for future work in this area. The findings of between group differences in terms of displayed acceleration levels on the z axis, may be related to small transitions of the torso or altered patterns of acceleration in movements forward. Both these directions should be further explored as they corroborate previous knowledge. Wu et al., [24] found that speed peaks of arm movements are more randomly distributed in patients with autism than in NT. Thus, our findings, showing mixed acceleration levels within clusters might be related to distribution of acceleration and speed peaks. Moreover, previous evidence indicates deficits in postural control in autism, and specifically in relation to sensory cues [51] thus postural related findings in our data emphasis the need for further analysis of the source of between group difference of use of acceleration levels on the z axis.

In conclusion, this work was an exploratory study with limited sample size. Yet, we were able to determine the viability of a method adapted from the study of animal behaviour to the study of behaviour of children with neurodevelopmental conditions. We found a significant difference in clusters usage as well as in time spent in acceleration levels determined by data driven automatic thresholds. The fact that these findings, with further investigation, may be used for translational studies of autism models is of high relevance for better understanding the association of motor symptoms and neuronal mechanisms in autism. Moreover, the feasibility of using this methodology for studying motor traits in ASD under various environmental stimuli holds opportunity for characterisation of the association between motor symptoms to symptoms from sensory, social and emotional domains.

7. Limitations

1. The main limitation of this study relates to the small sample size. All results should be taken with caution and further reproduced in a larger sample.
2. Another limitation related to participants is the lack of a control group of children with developmental delays other than autism as some autism related features are not exclusive to this syndrome, but rather a broader mar for developmental conditions.
3. Moreover, gender differences were not taken into account in this project and should be further explored.
4. The device position is always slightly inverted. Hence, we tried to calibrated data using a transformation matrix following the documentation in ”Tilt Sensing Using a Three-Axis Accelerometer”, by Mark Ped [53]. We used a 10 second sequence where the position of the accelerometer was known, i.e., when device was placed on the table such that the Z vector was facing down to earth and thus assuming Z values should be aligned to 1 g. Then we used two transformations matrices for pitch, rotating the data over the y axis, and roll, rotating the device on the x axis, to calibrate the device´s position.

$$\boldsymbol{R}_{yxz}\begin{pmatrix}0\\0\\1\end{pmatrix} = \boldsymbol{R}_y(\theta)\boldsymbol{R}_x(\phi)\boldsymbol{R}_z(\psi)\begin{pmatrix}0\\0\\1\end{pmatrix} = \begin{pmatrix}-\sin\theta\cos\phi\\ \sin\phi\\ \cos\theta\cos\phi\end{pmatrix}$$

   Unfortunately, the device was placed on the table while in the belt and poistion was never accuratly aligned. This resulted in lack of reference axes for correct calibration. In the future, data collection should include a clibration protocol with known position of the device inorder for calibration to be possible.
5. Logging acceleration data to video material. To signify the beginning of the protocol, therapists tapped the device 3 times after they attached it to the child´s body. Unfortunately, it was difficult to recognize the taps in the data since some children moved in parallel to the taps. In the lack of a direct mark indicative of the commencement of the protocol, we used the moment the therapist lifted the device from the table. Yet this made logging more difficult. Moreover, as video was recorded in 20 frames per second, and data collected in 100 Hz (100 samples per

second) there was always a small gap between events on the video recording to the acceleration and analyzed data. In this project video assisted analysis was limited and was only used to assess if there is a general acceptance between the clusters and events as observed by a human.

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9. Annexes

9.1 Protocol:

Before session:

1. Install camera in the chosen location
2. start recording (we will later delete parts recorded before and after data collection timeframe).
3. Configure accelerometer using metaBase app (validate battery is sufficiently charged, start new session with: accelerometer at 8g, 200hz, gyroscope at 100hz) Or using the MT manager for Xsens, connecting device and set to collect at 100Hz.

Session:

4. After taking shoes off dress the kid with the belt.
5. Tap the device 3 times in a visible spot to the camera.
6. 20 minutes recording:

   <u>With parents</u>

   5 min free play

   5 min of structured activity:

   - Trampoline
   - Puzzle or fitting pieces in the barrel and put them in the game after
   - Swing or hammock or the blue one- make baskets with the sandbags
   - Slide
   - Pilates ball

   <u>Without parents</u>

   5 min free play

   5 min of structured activity (same as above)
7. Tap the device three times
8. Take off belt

After session:

9. End metaBase session, name it and export

   Or end collection in the MT manager.

9.2 Informed Consent form

FOLHA DE INFORMAÇÕES E FORMULÁRIO DE CONSENTIMENTO INFORMADO

PARA A PARTICIPAÇÃO NO ESTUDO DE SUJEITOS MENORES

Título de estudo: Assinaturas cinemáticas de comportamento motor em crianças com Perturbação do Espectro do Autismo

(Título original em Inglês: Kinematic signatures of children with ASD)

Ao Participante e ao familiar que exerce a responsabilidade parental / representante legalmente reconhecido de:

________________________ ______

____

(nome do menor)

Exmo Sr. / Sra.

Pedimos a colaboração e disponibilidade de seu educando, para a participação no estudo "Assinaturas cinemáticas de comportamento motor em crianças com Perturbação do Espectro do Autismo", que será realizado no CADin - Centro de Apoio ao Desenvolvimento Infantil sob a responsabilidade da investigadora Hagar Ester Yulzari.

Antes de decidir se quer participar ou não neste estudo, por favor leia este documento cuidadosamente. Se necessitar de informações e esclarecimentos adicionais, entre em contacto com Hagar Ester Yulzari ou Dr. Helena Cunha (detalhes de contacto indicados no final deste documento).

Antecedentes e finalidade do estudo

Em crianças com perturbação do espectro do autismo (PEA), estão descritas dificuldades de motricidade grossa e fina que acompanham frequentemente as dificuldades de interação social e cognitiva. Estas dificuldades de motricidade grossa e fina podem ser detetadas pela primeira vez logo aos 12 meses de idade. Pensa-se hoje que os sintomas relacionados com as dificuldades de motricidade na PEA não são apenas comportamentais, mas que existe uma assinatura motora única que caracteriza a forma como as crianças com PEA se movem. O estabelecimento de um instrumento fiável para avaliar aspetos cinemáticos dos movimentos de crianças com perturbações do neuro desenvolvimento pode ajudar-nos a identificar um biomarcador objetivo da PEA.

Este estudo visa demonstrar a viabilidade e validade de um novo método de recolha e análise de dados cinemáticos de alta resolução para a investigação clínica de movimentos de crianças pequenas. Mais, pretendemos avaliar o efeito da interação social e capacidade cognitiva sobre os movimentos de crianças com perturbações do neuro desenvolvimento, avaliando a possível ligação entre os défices motores e os sintomas fundamentais da PEA. Os dados serão recolhidos durante as sessões semanais de terapia ocupacional, utilizando um acelerómetro, um pequeno dispositivo que fornece dados de alta resolução sobre aceleração corporal, com interferência mínima com o movimento da criança. O pequeno dispositivo será fixado às calças do seu educando, por si com a ajuda do terapeuta, ou por um membro da equipa do estudo, com um bolso externo e da forma minimamente intrusiva. Durante os primeiros 10 minutos da sessão pediremos a si/ou à pessoa que acompanha a criança à sessão de terapia ocupacional, que entre na sala de terapia. Este passo permitir-nos-á avaliar o efeito da presença de uma pessoa próxima sobre o movimento. A sessão de terapia irá então proceder normalmente, sem interrupção, para permitir que as crianças completem a sessão terapêutica num ambiente o mais familiar possível. Se nos der o seu consentimento para colher imagens de vídeo durante a sessão, os primeiros 20 minutos da sessão serão gravados em vídeo. Os vídeos serão utilizados exclusivamente para registar os dados de aceleração dos eventos que ocorrem durante a sessão.

Graças à participação do seu educando esperamos poder aprender mais sobre a relação entre os principais sintomas da PEA e características do comportamento motor e, de forma importante, evoluir no desenvolvimento de um método simples e preciso para identificar biomarcadores das perturbações do neuro desenvolvimento em crianças. para apoiar o conhecimento científico das PEA, os resultados deste estudo destinam-se a ser publicados numa revista científica revista por pares, bem como em conferências científicas.

Procedimentos do estudo

A recolha de dados terá lugar durante uma sessão normal de terapia ocupacional. Antes do início da sessão, irá encontrar-se com o terapeuta ou com um elemento da equipa de estudo que o ajudará a prender o acelerómetro à roupa do seu educando. Os dados serão recolhidos a partir do momento em que o dispositivo estiver ligado. Nos pediremos a si/ou à pessoa que acompanha a criança à sessão de terapia ocupacional, que entre na sala de terapia por os primeiros 10 minutos da sessão. A sessão progredirá como de costume, sem quaisquer modificações. Como mencionado acima, os primeiros 20 minutos da sessão serão gravados em vídeo com o objetivo de validar a nossa análise de dados. Outros dados pessoais para além da informação demográfica não serão utilizados na pesquisa e não serão registados. Todos os dados serão guardados de forma anónima.

O protocolo do presente estudo inclui, para além dos procedimentos já descritos, uma avaliação clínica dos sinais e sintomas de autismo utilizando o Programa de Observação de Diagnóstico do Autismo (ADOS), um teste de diagnóstico bem conhecido e padronizado. Se a criança já tiver completado esta avaliação como parte do seu acompanhamento clínico no CADIn ou noutro local, ser-lhe-á pedido que, caso concorde, disponibilize os resultados para efeitos do estudo e para evitar repetições desnecessárias de procedimentos de avaliação.

A análise dos dados de movimento será feita usando um algoritmo que pode detetar semelhanças entre padrões de aceleração. Usaremos o algoritmo para comparar os padrões de aceleração em vários intervalos de tempo no decurso da sessão. Por exemplo, compararemos os dados recolhidos dos movimentos da criança durante um período em que executa uma tarefa indicada pelo terapeuta com os dados recolhidos numa altura em que a criança brinca livremente. Igualmente, iremos comparar os padrões de aceleração em momentos em que a criança está com os pais, sublinhando uma relação social próxima, com um período de tempo em que a criança esteja apenas com o terapeuta, uma pessoa menos familiar.

Para responder aos nossos objetivos, compararemos os dados dentro de uma sessão, nomeadamente o efeito das alterações ambientais nos movimentos de cada criança e, posteriormente, entre as diferentes crianças. Além disso, os dados serão correlacionados com as características clínicas individuais de cada criança.

Possíveis benefícios

A participação no estudo não beneficiará diretamente a criança, dado que os resultados não terão no imediato uma aplicação clínica individual. Os benefícios serão eventualmente coletivos, na forma de um maior conhecimento científico sobre a fisiologia das PEA, e na eventual identificação de um método adicional de avaliação de características clínicas de crianças com PEA ou outras perturbações do neuro desenvolvimento.

Possíveis riscos ou inconveniências

As atividades do estudo não diferem das atividades desenvolvidas durante uma sessão terapêutica normal, pelo que não implica qualquer risco adicional. Pode suceder que a criança não tolere a presença do acelerómetro na roupa e nesse caso a participação no estudo será interrompida, sem qualquer prejuízo para a sessão de terapia ou para o acompanhamento em curso no CADIn. Os testes iniciais e posterior aplicação do protocolo serão realizados na presença e sob a orientação e supervisão de pessoal qualificado (técnicas superiores de reabilitação psicomotora) da equipa CADIn.

Participação no estudo

A participação é totalmente gratuita e voluntária.

Se concordar com a participação do seu educando, ser-lhe-á pedido que assine o Formulário de Consentimento Informado anexado a este documento antes que o seu educando comece os procedimentos de estudo.

O objetivo deste passo é garantir que tenha recebido informações completas sobre o projeto em desenvolvimento e, ao mesmo tempo, que seu consentimento represente a expressão completa de sua vontade em relação à participação da criança no estudo.

Esta assinatura não implica qualquer compromisso de continuar o estudo até ao fim, e não constitui uma obrigação contratual, nem representa uma renúncia aos direitos do participante.

Se decidir retirar o seu educando do estudo depois de ter aceitado inicialmente participar, pode cancelar a sua participação a qualquer momento, notificando o responsável do estudo sem ter de apresentar uma justificação. A escolha de não permitir que o seu educando participe, ou a decisão de retirar o consentimento após a aceitação inicial, não implica a exclusão ou limitação dos cuidados e assistência que a criança recebe ou irá receber no CADIn, nem qualquer alteração na relação com o pessoal técnico e clínico que o assiste.

Se forem conhecidos novos dados ou resultados que possam influenciar a participação no estudo, o responsável do estudo será imediatamente informado; além disso, o responsável do estudo poderá retirar a criança do estudo se considerar que esta decisão é do interesse da criança, informando o progenitor ou representante legal dessa decisão.

A participação no estudo não implica qualquer tipo de encargo ou despesa adicional para si. Além disso, não está prevista qualquer alteração ou suspensão do programa de cuidados regulares que a criança que representa recebe no CADIn.

Tratamento de dados pessoais

<u>Natureza dos dados recolhidos</u>

Neste estudo utilizam-se 3 fontes de dados: dados de aceleração dos movimentos da criança, recolhidos pelo acelerómetro; avaliação clínica representada pela pontuação dada pelo ADOS; e vídeos das crianças, que serão utilizados para validar a interpretação dos dados de aceleração. Não recolheremos informações pessoais sobre as crianças, exceto a idade e o gênero, e, se consentir, informações relativas aos défices motores conhecidos e à intervenção motora que a criança recebe.

Natureza dos dados, finalidades e métodos de tratamento

Os dados recolhidos neste estudo, incluindo dados de aceleração, pontuações de ADOS, serão guardados de forma anónima. Os detalhes pessoais, como a idade, o gênero e a avaliação clínica serão recolhidos e registados sem identificação pessoal da criança ou do progenitor ou representante legal.
Material de vídeo sera guardado sem identificação pessoal.

Todas as informações pessoais e clínicas sobre o seu educando, por si representado, recolhidas durante este estudo, são confidenciais e serão tratadas exclusivamente para fins de pesquisa científica de acordo com a legislação acima mencionada.

Os dados recolhidos serão processados por meios eletrónicos, mantidos entre os centros de investigação envolvidos neste projeto (CADIn e NOVA Medical School) até à obtenção dos resultados finais e serão eliminados após a conclusão do estudo. Caso seja efectuado um estudo de acompanhamento, será solicitada uma nova aprovação para a conservação do material de estudo. Os dados, incluindo dados de aceleração, pontuações de ADOS, poderão ser divulgados de forma estritamente anónima em reuniões, conferências e publicações científicas; em qualquer caso, o nome da criança ou da pessoa ou qualquer outro detalhe que a identifique nunca não será divulgado, pois os dados só poderão ser apresentados de forma agregada ou de forma que não torne identificáveis os sujeitos participantes do estudo. As imagens e os materiais de vídeo serão utilizados para efeitos de análise de dados, como explicado acima, e não serão publicados, exceto se der o seu consentimento explicito para a sua utilização para fins exclusivos de divulgação científica. Caso não consinta na sua divulgação para este fim os materiais de vídeo e as imagens serão eliminados após a conclusão do estudo.

O consentimento para o tratamento dos dados do seu educando é livre e revogável a qualquer momento, sem qualquer desvantagem ou prejuízo, no entanto, é essencial para a realização do estudo, pelo que a recusa de consentimento para o tratamento dos dados tornará impossível a participação no estudo da pessoa que representa.

Exercício de direitos

Em relação ao tratamento acima mencionado, lembramos-lhe que pode exercer os seus direitos ao abrigo do Regulamento da UE n.º 2018/1725, enviando um pedido ao responsável pelo tratamento de dados através de uma comunicação escrita.

Responsável

Hagar Ester Yulzari

Email: hagaryulzari@gmail.com

Tel: 913706668

Helena Cunha

Email: helena.cunha@cadin.net

Tel: 214 858 240 | 912 540 404 (via CADIn Caiscais)

Termo DE CONSENTIMENTO INFORMADO

Título de estudo: ***"*** Assinaturas cinemáticas de comportamento motor em crianças com Perturbação do Espectro do Autismo***".***

Eu, abaixo assinado: ____

Nome em maiúsculas do pai/mãe/do representante legalmente reconhecido.

como: ___________ _______ ____

Indicar a relação com a criança (pai, mãe, representante legalmente reconhecido).

de : ____

Nome em maiúsculas do menor

nascido, o..: ____________ _______ ____

Local e data de nascimento do menor

E (quando relevante)

Eu, abaixo assinado: ____

Nome em maiúsculas do menor

nascido, o..: ____________ ______ ____

Local e data de nascimento do menor

DECLARO O SEGUINTE:

1. Li e compreendi a ficha informativa, da qual este formulário é parte integrante;
2. Tive a oportunidade de fazer perguntas e pedir explicações a______________________________de quem recebi respostas satisfatórias;
3. Fui informado sobre a natureza, finalidade e duração do estudo, os procedimentos que serão seguidos, o tratamento dado aos participantes e o tipo de colaboração que será exigida deles;
4. Entendi que a participação do menor de quem sou o representante legal reconhecido é livre e voluntária e que a qualquer momento posso decidir interromper sua participação e retirá-lo da pesquisa sem ter que fornecer justificação e sem que ele seja privado de toda a assistência e cuidados necessários e sem que seus direitos e relação com os profissionais de saúde e técnicos sejam comprometidos;

5. de acordo com as leis de privacidade aplicáveis, eu concordo com o processamento dos dados pessoais da criança da qual eu sou o representante legal, recolhido como parte desta pesquisa, nos termos e da maneira aqui estabelecidos.

Dito isto, confirmo que concordo com a participação da criança, de quem sou representante legal, no estudo descrito neste documento.

Assinatura do representante legal (quando relevante) Assinatura do menor

[Identidade verificada]: *[Identidade verificada]:*

____

____

Local e data: _________________________

RECOLHA DAS IMAGENS E VÍDEOS

Eu, abaixo assinado: ____

Nome em maiúsculas do pai/mãe/do representante legalmente reconhecido.

como: ___________ ______
____
__

Indicar a relação com a criança (pai, mãe, representante legalmente reconhecido).

de :
____
___

Nome em maiúsculas do menor

nascido, o..: ____________ ______
____
_

Local e data de nascimento do menor

E (quando relevante)

Eu, abaixo assinado:
____
_

Nome em maiúsculas do menor

nascido, o..: ____________ ______
____
_

Local e data de nascimento do menor

1. Autorizo a recolha das imagens e vídeos do menor e dou autorização para a utilização dessas imagens para a finalidade do estudo, tal como descrito acima.

2. Autorizo / não autorizo a publicação das imagens e vídeos recolhidos no estudo para fins de divulgação científica, tais como artigos, conferências e apresentações científicas, ou provas académicas. As imagens e vídeos não serão utilizados ou publicados de qualquer outra forma que não para fins científicos.

Assinatura do representante legal (quando relevante) Assinatura do menor

[Identidade verificada]: *[Identidade verificada]:*

____

____

Local e data: _________________________

PARTE RESERVADA AO OPERADOR QUE APRESENTOU O DOCUMENTO:

Eu, abaixo assinado, _____________________________________*(nome em maiúsculas).*

Declaro:

a. que expliquei aos encarregados de educação a natureza e o objetivo da investigação e os procedimentos que serão adotados, bem como o tipo de colaboração que será necessária;

b. que não tentei influenciar ou coagir de qualquer forma as pessoas mencionadas acima para induzi-las a expressar seu consentimento para a participação da criança na pesquisa;

c. que entreguei ao encarregado de educação uma cópia assinada e datada deste formulário juntamente com a ficha de informação.

Local e data: ____________________________ Assinatura: ____________________________