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A Learning Tracker using Digital Biomarkers for Autistic Preschoolers
– Practice Track –

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Abstract

Preschool children, when diagnosed with Autism Spectrum Disorder (ASD), often experience a long and painful journey on their way to self-advocacy. Access to standard of care is poor, with long waiting times and the feeling of stigmatization in many social settings. Early interventions in ASD have been found to deliver promising results, but have a high cost for all stakeholders. Some recent studies have suggested that digital biomarkers (e.g., eye gaze), tracked using affordable wearable devices such as smartphones or tablets, could play a role in identifying children with special needs. In this paper, we discuss the possibility of supporting neurodiverse children with technologies based on digital biomarkers which can help to a) monitor the performance of children diagnosed with ASD and b) predict those who would benefit most from early interventions. We describe an ongoing feasibility study that uses the "DREAM dataset", stemming from a clinical study with 61 pre-school children diagnosed with ASD, to identify digital biomarkers informative for the child's progression on tasks such as imitation of gestures. We describe our vision of a tool that will use these prediction models and that ASD pre-schoolers could use to train certain social skills at home. Our discussion includes the settings in which this usage could be embedded.

1 Introduction

Society 5.0 [1] aims to create a human-centered society of the future through better use of technology. Neurodiversity is an increasingly important topic in today's society where the vision of Society 5.0 can be achieved. A definition of neurodiversity is the viewpoint that brain differences are normal rather than deficits. This concept can help reduce stigma around learning and thinking differences. Neurodiversity describes these natural variations in the human brain, which affect sociability, learning, attention and mood. Neurodiverse groups include ADHD, autism, dyspraxia, dyslexia, dyscalculia, dysgraphia, and Tourette syndrome. People who are 'neurotypical' are those whose brain works in the way that society expects[1]. Neurodiverse people often suffer from stigmatization and lack of inclusion, e.g., children with Autism cannot follow normal school careers. Neurodiverse individuals have also contributed to society and it is important that they also continue to do so. Diagnostic advancements lead to an increased awareness and recognition of neurodiversity by parents, teachers and healthcare professionals. As a movement, neurodiversity "emphasizes natural variation and the unique skills, experiences, and traits of neurodivergent individuals" rather than "focusing on pathology and impairment" [2].

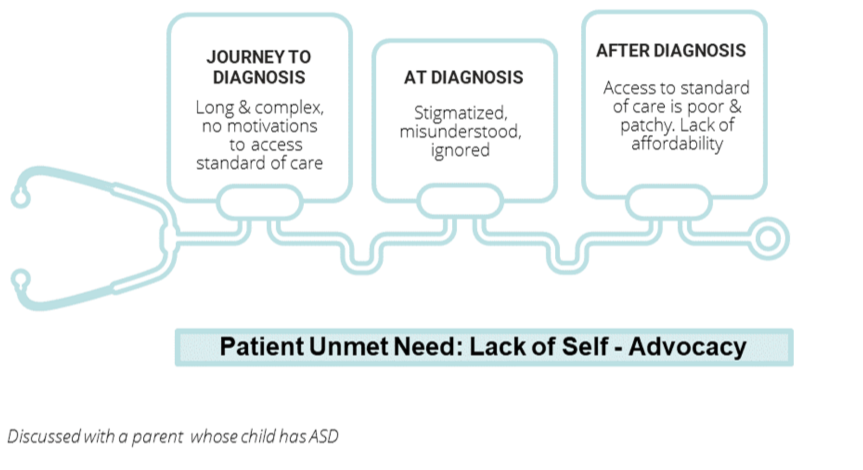

Figure 1: Autism Disease Burden: parent and child (patient) journey

Human suffering along the journey to diagnosis and after diagnosis is illustrated in Figure 1. These are exacerbated through the lack of awareness of neurodiversity and how to address these in a human centered manner.

Can technology help to build bridges and act as an enabler to better accommodate neurodiversity? We aim to investigate whether

1. The interaction with technical devices could enable improved social interaction and communication
2. Digital biomarkers could support the development of new tools to improve daily living by more comprehensive monitoring and self-advocacy

In this paper we discuss the feasibility of how technology with digital biomarkers could help to develop self-advocacy in the case of autism spectrum disorder (ASD).

[1] https://ioni24.wildapricot.org/about-us

2 Autism Spectrum Disorder (ASD)

Autism Spectrum Disorder (ASD) is a group of neurodevelopmental disorders that causes persistent deficits in children's social communication skills and behavior [3].

In the Diagnostic and Statistical Manual of Mental Disorders 5 (DSM-5), social communication skills are described as (i) deficits in social-emotional reciprocity, (ii) deficits in nonverbal communicative behavior, and (iii) deficits in developing, maintaining, and understanding relationships. Recently, the WHO's International Classification of Function (ICF) for Autism has been well received by people affected by ASD and those treating them since it attempts to embrace the biomedical and neurodiverse paradigms. More importantly, the ICF emphasizes the strengths and abilities of autistic individuals [4].

ASDs are complex life-long conditions that begin in early childhood and last throughout a person's life [5]. The incidence of diagnosed ASD preschoolers is increasing [6], especially through increased awareness from parents, teachers and healthcare professionals and referrals to specialist centers by pediatricians.

Early signs of ASD can be noticed by parents/caregivers or pediatricians before a child reaches one year of age. Nevertheless, symptoms become more consistently visible at the age of 2 to 3 years. Some children show only mild functional impairment related to their ASD until they start school, after which their deficits may be pronounced when amongst their peers [7].

Social communication and interaction deficits can include for example making little or inconsistent eye contact, appearing not to look or listen to people who are talking, not responding or being slow to respond to verbal bids for attention, having difficulties with the back and forth of conversation, having difficulties to adjust behavior to different social situations or to share in imaginative play or in making friends.

Restrictive/repetitive behaviors may include for example repeating certain behaviors or having unusual behaviors, such as repeating words or phrases (a behavior called echolalia), having a lasting intense interest in specific topics, such as numbers, details, or facts, showing overly focused interests, such as with moving objects or with parts of objects, becoming upset by slight changes in a routine and having difficulty with transitions, as well as being more sensitive or less sensitive than other people to sensory input, such as light, sound, clothing, or temperature.

One major source of disruption and stress for parents is caring for a child who experiences difficulty regulating their emotions [8].Children with ASD frequently have emotional regulation difficulties associated with internalizing symptoms, such as anxiety and depression, and externalizing behaviors, such as aggression and hyperactivity. Not surprisingly, such problem behaviors have been found to predict stress in parents of children with ASD, suggesting a possible role of emotion dysregulation in parent quality of life and family functioning [8].

Evidence shows that early intervention may have a positive impact on cognitive, social skill and language development [9, 10, 11, 12, 13]. However, results demonstrate high heterogeneity in responses to treatment with some children progressing more rapidly than others [14, 15]. Children with ASD and their families often have to endure long and distressful journeys until ASD gets diagnosed, and until access to therapy is granted. There is a scarcity in therapists and early intervention sites creating a bottle-neck for families to access early intervention. The challenges of implementing large-scale, community-based early intervention have been acknowledged by WHO[2]. Also, the Swiss government recognized early intervention as one of three key priorities to improve the care situation of people with ASD in Switzerland [16].

[2]WHO EXECUTIVE BOARD EB133/4 133rd session 8 April 2013 Provisional agenda item 6.1

Early intensive intervention, only offered by specialist centers, is resource-intensive and causes a high economic burden for families and the healthcare system. Cost for early intensive therapy per child are estimated at 50'000 to 100'000 SFr [17]. Newer publications estimate the total cost per child for a 2-year intensive treatment up to 200'000 SFr [18].

Health Policy Makers and governments are increasingly faced with the urgent challenge for more effective resource planning and allocation towards early and intensive intervention approaches while it is not yet possible to identify which children benefits from which program [19].

Overall, there is a need to improve and broaden access to personalized and early interventions. Potential options to achieve this are for example:

1. Differentiated medical decision making and implementation of personalized medicine: identify profiles of children that are likely to respond to early treatment and/or monitor and evaluate their progress

2. Therapeutic aids or monitoring tools tailored to individual needs of children with ASD that for example parents/caregivers could use in their home settings complementary to therapist sessions

Advancement in digital health and in digital biomarker research, as described in the next section, can offer a solution path to address above mentioned unmet needs and could facilitate transition phases from parent dependent care to self-advocacy during the development from childhood to an adult independent person (Figure 2)

3 Potential Role of Digital Biomarkers in Autism

The use of endophenotypes for psychiatric disorders is one of the proposed methods for connecting behavioural symptoms, disease diagnosis with genetic risk variant detection. It is being increasingly used in developmental disabilities, particularly looking at highly heritable polygenetic conditions such as ADHD, autism, and many psychiatric disorders [20]. Endophenotypes are heritable, objective biological markers that can be measured directly [21]. These may be categorized as neurophysiological, endocrinological, neuroanatomical, or cognitive. Since these are directly measured and quantifiable, endophenotypes may be more insightful to traditional methods of diagnoses and/or measure of disease progression and follow ups [21].

Sensory phenotypes are an example of endophenotypes for psychiatric disorders [21]. Patients with Autism show heightened sensorimotor function which prompts atypical sensory reactivity and sensory over-responsivity. This is characterized by an extremely negative response to sensory stimuli. ASD's sensory over-responsivity correlates to abnormal changes in the connectivity between the thalamus and the cortex [21].

Digital phenotyping is a method for measuring phenotypes using digital technology, such as smartphones and wearable devices, allowing continuous collection of clinical data [22]. Collection of data can be passive e.g., GPS, accelerometer, gyroscopes or active e.g., surveys and audio samples.

Eye tracking is being researched as a tool to measure social orienting in Autism, with mixed results and currently, considered as inconclusive [23]. The majority of the eye tracking studies have reported less attention to faces, defined as fixation time in Autistic young children in comparison to their typically developing (TD) peers. In contrast, some studies did not observe differences in attention to faces between these two groups. Possible confounds for this difference in results may include presentation of the face stimulus, social context and stimuli such as the

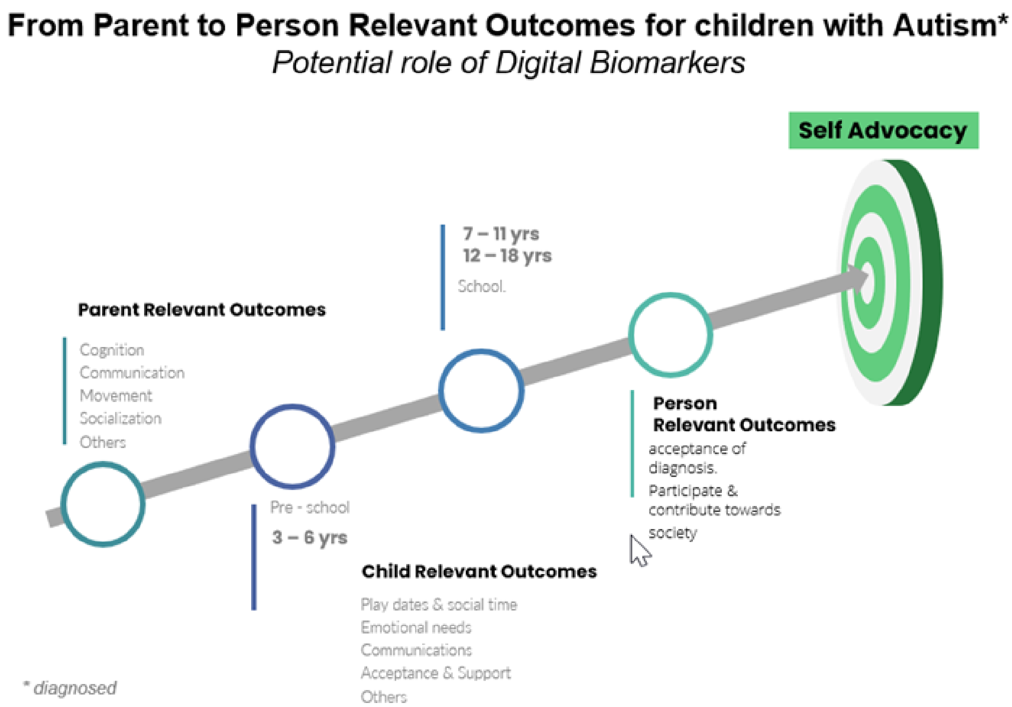

Figure 2: The potential role of Digital Biomarkers in Autism

number of people involved, and the complexity of the communication i.e., with or without social interactions, child directed speech, and eye contact [23]. Hence, Autistic young children showed diminished attention to faces when the stimulus is more socially engaging and/or social intricacy escalates.

This level of social orienting at baseline appears to be a promising predictor of early development trajectories and outcomes of young children with Autism [14, 15]. Social motivation theory postulates that reduced social attention towards complex social engagement negatively impacts social learning experiences [23]. This then impacts the development of social skills in early development such as Joint Attention, Turn Taking and Imitation.

Another critical aspect relates to the definition of positive compared with no or minimal outcomes in Autism research [19]. Current outcomes measures might not be sensitive enough to record gains in children making very slow or small gains. However, these small progressions might be meaningful to their parents, teachers, therapists, health care professionals and most importantly, to the child. Parent, Child and Person relevant outcomes are illustrated below. The use of technologies such as eye tracking is currently being investigated to address this need in Autism research [23] and potential practical applications [24, 25].

Current unmet needs and these promising results on digital biomarkers in ASD provide a use case for exploring and implementing a personalized medicine approach among autistic preschoolers: identifying which children might benefit from which educational approaches soon after their diagnosis and/or monitoring their progress.

4 A Feasibility Study

In order to address this use case, we conduct a feasibility study that uses a publicly available dataset from the DREAM study.

4.1 The DREAMS Dataset

The Development of Robot-Enhanced therapy for children with AutisM Spectrum (DREAM, [26]) dataset was developed from a randomized-controlled trial comparing robot-enhanced therapy with standard human therapy based on applied behavior analysis (ABA), a structured intervention following behavioral learning principles. The study was conducted between March 2017 and August 2018.

The clinical trial included 61 children between 3 and 6 years of age, all diagnosed with ASD. 30 of the children interacted with a humanoid robot (RET-group), and the remaining 31 children received standard human treatment (SHT-group) (see Figure 3).

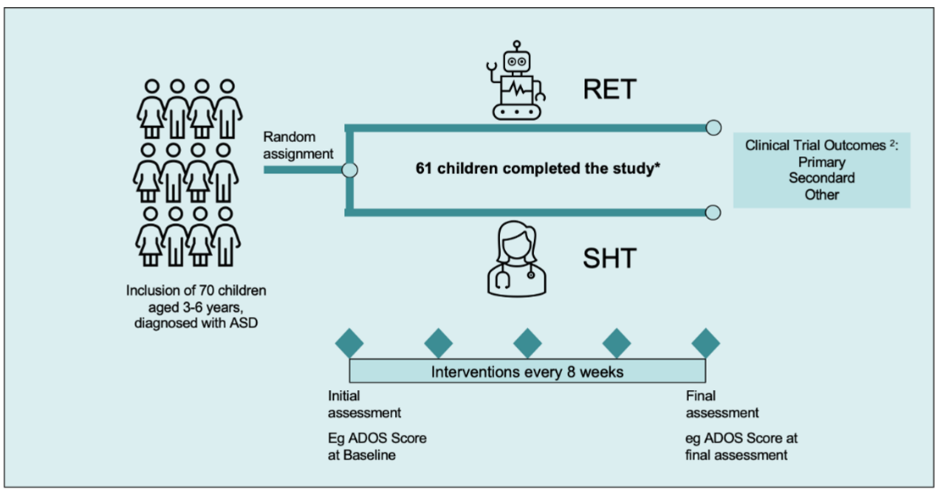

Figure 3: Clinical Trial Design of the DREAM Study

Following a clinical study protocol the participants underwent an initial assessment followed by 8 bi-weekly interventions, and a final assessment. Each intervention targeted three social skills: imitation, joint-attention, and turn-taking. Each intervention was divided into three to six parts ("sessions"), following a task script. For comparability reasons, the therapy environment was designed for the two configurations (RET and SHT) as similar as possible. Slight variations were undertaken for different tasks, e.g., some tasks used a touch screen placed between the child and the interaction partner, the so-called Sandtray.

Twelve unique intervention scripts were used, specifying different exercises and three difficulty levels. As the child reached maximum performance on one level, she/he moved to the next level. All therapies were recorded using a sensorized intervention table able to record and interpret the child's behavior during the intervention (analyzing, for example, eye gaze, body movement, facial expression).

A total of 3121 therapy sessions were recorded including 306 hours of therapy. To our knowledge, this is the largest publicly available dataset from a clinical study of ASD.

The public data set includes, besides Child ID, gender, age in months and date and time of recording: 3D skeleton data, comprising joint positions for upper body, head position and orientation and 3D eye gaze vectors, both measured at 25 Hz. Furthermore, the data comprises the therapy condition (RET or SHT) and task (Joint attention, Imitation, or Turn-taking), as well as initial Autism Diagnostic Observation Schedule (ADOS) scores.

4.2 Objectives

The objective of our feasibility study is to use the DREAM dataset to build predictive models which are capable of a) monitoring the performance of ASD pre-schoolers and b) predicting those who would benefit most from such interventions.

This shall be done by predicting the children's performance on given tasks on the basis of the digital biomarkers described above. With the existing DREAM dataset, we can train machine learning models since e.g. the progression of study participants to higher levels of task difficulty is known as a ground truth. Later, our models can be fed with biomarkers and predict children's performance – such that children can receive a feedback without the presence of e.g. therapists.

4.3 Proposed Approach

4.3.1 Task definition and data preparation

Before we describe the classifier algorithms that we propose to apply for predicting task performance, let us first define the prediction task a bit more precisely: based on the study protocol described in Section 4.1, we construct data objects to be classified by merging all sessions belonging to a given intervention and targeting the same task. We include data from the initial assessment and from interventions 1 to 7. For instance, it may turn out that child 3 had two sessions with the task of joint attention in intervention 1 – these two sessions are then merged and treated as one data object. Each of these data objects is then assigned a class (ground truth) as follows:

- if the data originated from an initial assessment, we observe the difficulty level that was used in intervention 1 for the same task. If the child had to start at level 1, we set $class = 0$, if the child started on either level 2 or 3, we set $class = 1$
- for data originating from any other intervention i, we observe the difficulty level used in intervention $i + 1$ – stagnation, i.e. staying on the same level means $class = 0$, moving to the next level results in $class = 1$

Working only with initial assessment sessions results in 132 data objects, whereas adding the intervention sessions yields 948. While more data usually leads to better results, we have already observed in some preliminary experiments that including the intervention sessions has the drawback that there are only three difficulty levels, i.e. moving to the next level occurs rarely and, consequently, most sessions have $class = 0$.

4.3.2 Feature Engineering and Prediction Algorithms

The approach that we propose relies on a comparison of two basic types of algorithm:

- Application of white-box models, i.e., human-interpretable ML models such as decision trees or rule learners as used in e.g., [27, 28]. Such an approach requires the definition of "meaningful" features, e.g., as proposed in [28] – durations of fixations and saccades (quick eye movements). These features are aggregations of raw measurements over entire therapy sessions. For our purposes, fixating something for longer periods can generally be a valuable feature, but fixation of so-called "Areas of Interest" (AoI, see [28]) might be even more relevant, considering e.g., the face of the robot or therapist, as well as the sandtray, as relevant AoIs (see Section 3). Since the exact positions of AoI are not known, we suggest to work with a grid, collecting the number of gazes and/or fixations falling into each grid cell – with the hope that the machine learning algorithms can detect which gaze targets (grid cells) lead to success. We further hypothesize that the degree of motion that a child exhibits during a session – as e.g. measured by the standard deviation of x, y and z coordinates of the limbs – can be an indicator of attention (where an excessive amount of motion or null values of coordinates indicates a lack of focus). The human interpretability of these models is their biggest advantage allowing therapists and parents deeper insights into a child's success in performing tasks. A big drawback is the difficulty to represent the temporal evolution of a child's behaviour, e.g. whether motion got stronger or fixations got rarer in certain parts of a session. Human experts need to define the most reasonable way of aggregating the temporal data – with a high likelihood of losing relevant information.

- Application of **black-box models**, i.e. models such as convolutional neural networks (CNNs) as in [29, 30], which often perform better than their white-box counterparts, but do not offer directly human-interpretable models. A large advantage of CNNs (or generally deep learning approaches) is their ability to work with the raw data, e.g. head gaze vectors recorded at 25Hz – and thus including the temporal evolution of gaze patterns – and to determine relevant patterns, without the need for experts to define "meaningful" aggregated features as explained above (which might not be features that are actually most helpful). Instead, CNNs provide a kind of automated feature learning and extraction mechanism [31] for tasks like image or text classification that have a large number of "raw" inputs such as pixels or individual words. Explanations of CNN predictions can be generated using e.g. SHAP [32] – we will need to investigate whether these explanations are sufficient for the information needs of parents and therapists.

End results from this research are expected to better describe the heterogeneity in outcomes and performance trajectories to early educational intervention. We expect that ML has the potential to discover new patterns on these difficult research questions, i.e. to contribute to medical insight. Both approaches will employ Good Machine Learning Practices GMLP[3]

However, both approaches are limited by the fact that the DREAM dataset does not contain information about the activities of the robot or therapist. In particular, we do not know at which points in time the child is prompted for an action. Such information would be very valuable for judging the degree to which the child's attention (e.g. fixation of an AoI) is required at a given time. In fact, children may successfully complete tasks even though they hardly fixate the therapist/robot or sandtray – provided that the scarce fixations that occur happen at the right moment. Future endeavours (including our own) may benefit greatly from constructing datasets purposefully to reflect a scenario as described in the next section – including e.g. the timestamps of prompts for action.

[3]https://www.fda.gov/medical-devices/software-medical-device-samd/artificial-intelligence-and-machine-learning-software-medical-device

5 Future Work: Tool Design

The models to be developed are to be provided in the framework of a tool for children diagnosed with ASD for use in therapeutic or home settings, with optional support from therapists or special needs teachers, caregivers, or parents. As a result, this design proposal should address the goals that the infrastructure should be as adequate, portable, affordable, scalable, and practical as possible. As illustrated by the DREAM dataset [26], it is possible to collect sensor data in the context of structured therapy sessions using robots and humans.

While the sensor data from the DREAM dataset is extensive, the experimental set-up is very resource-intensive, most likely not feasible for use in the daily life of children diagnosed with ASD. With this line of reasoning, there are initiatives to develop applications for robot assisted therapy for children with ASD to be used in the child's own home environment, guided by a parent or caregiver [33]. These systems are typically based on affordable devices such as tablets or mobile phones and as a result much closer to practical use, but also much more limited in terms of sensor capabilities.

For this reason, we propose a lightweight/technical approach with the use of mobile devices. Concretely, an approach with the possible use of consumer tablets is pursued here. An app to be developed will run on these tablets, on which children already diagnosed can complete individual therapy exercises or tasks, and the success of the therapy will be displayed for different stakeholders, see Figure 4. In addition, the app should be able to run therapy or exercise sessions on the one hand and record or create the exercise session by the therapists and special needs teachers on the other hand.

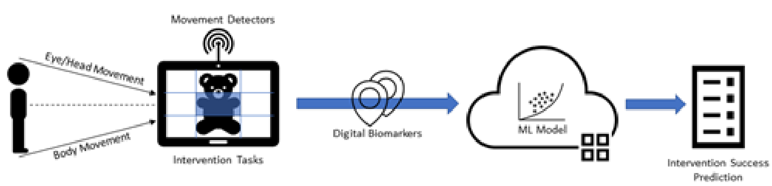

Figure 4: The suggested approach using mobile devices

An efficient technical feasibility is given – extensive web technology-based software libraries for eye movement detection—mostly from the field of web design analysis—are available. In addition, various augmented (AR) and virtual reality (VR) applications on mobile devices show that head and/or body movements can also be adequately captured, mostly without initial training. However, it might be necessary to fix the tablet on a holding device so that the detection accuracy could be increased. AR and/or VR in particular could offer a more advanced therapy perspective, similar to the robot-based therapy from the "DREAM" setting [26]. It would indeed be conceivable —- and still to be investigated and verified -— that the therapy success could also be increased by the additional use of avatars in addition to human visages.

The technical requirements are manageable compared to the requirements of the therapy setting. With the app and the underlying system, it should be possible for the children to use the app with the support and/or guidance of parents and other caregivers, as well as for therapists and special needs teachers to use the system themselves to design the practice sessions. These practice sessions and the whole therapy setting need to be the subject of further research and a comprehensive design process. It would be conceivable that a variety of short exercises in the course of therapy are offered as AR/VR or with videos or livestreams (with two devices). Furthermore, it should be possible for special educators or support persons to accompany the session with pre- or post-questions, e.g., via a dialogue system.

Equipped with this analysis strategy, we aim to develop a marketable and reimbursable digital medical device, meeting Medical Device Regulation MDR and Germany's DIGA and similar requirements. We have spoken to the Swiss Autism Patient Organisation, clinicians, therapists and individual patients verifying that there is an unmet need for such a device, using DBM, to improve patient advocacy and help their parents and teachers. Our ongoing feasibility study will deliver an early prototype of a digital tool to identify preschoolers, already diagnosed for ASD, with the highest likelihood to respond to therapy and monitor their treatment success. The prototype will be further tested with patient organisations, clinicians, and therapists. Once the feasibility is verified, we will also conduct more research and will be able to attract investors for further sustainable economic growth. In 2021, the FDA approved an AI based medical device to be used by health care providers to aid in the diagnosis of ASD [34]. This can potentially help facilitate earlier intervention and then more efficient use of specialist resources . This device also used a video input of the child from the carer‘s smartphone but without DBM, along with other inputs. Potential impact of the applications of AI: (a) in shortening the journey to diagnosis in primary care settings and (b) reducing patient and caregiver burden after diagnosis using DBM from video inputs are encouraging approaches as how technology can be a potential agent of change towards neurodiversity.

6 Conclusions

Motivated by the urgent need to improve and broaden access to personalized and early interventions for children diagnosed and affected by ASD, in this paper, we presented the settings for a feasibility study that aims to find out the extent to which technologies that are based on digital biomarkers can support neurodiverse children. Specifically, the already existing DREAM dataset was taken as a ground truth to build predictive models capable of a) monitoring the performance of children diagnosed with ASD and b) predicting those who would benefit most from early interventions.

Based on the intermediate findings, we envision an approach that, by incorporating predictive models, will support ASD pre-schoolers to train certain social skills. The approach will combine sensors for tracking digital biomarkers, to be fed to the machine learning models for triggering the feedback to children, based on the identified success pattern. Therefore, it makes advancements in the resolution of an important problem that afflicts Society 5.0.

Acknowledgements

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