Study Protocol - Development and Validation of a System for the Prediction of Challenging Behaviors of People with Autism Spectrum Disorder Based on a Smart Shirt: a mixed-method design

Document date: 09/04/2022

INTRODUCTION

Autism spectrum disorder (ASD) refers to a heterogeneous neurodevelopmental condition whose symptoms range from mild to severe. ASD is childhood-onset and lifelong. It affects between 1 and 2% of the population[1] and is characterized by social communication deficits, repetitive and unusual sensory-motor behaviors, as well as restricted interests [2]. The literature indicates an estimation that about 55% of people diagnosed with ASD also exhibit intellectual disabilities [3], and about 25% of this population are pre-or minimally verbal [4]. The sensory processing disturbances and the communication difficulties of people with ASD can cause challenging behaviors (CBs) to emerge [5–10].

The term CB is used to describe a broad range of unusual behaviors shown by individuals with intellectual disabilities and ASD. They include aggression, destructiveness, self-injurious, and a range of other behaviors such as unacceptable social and sexual conduct, screaming, non-compliance, and eating inedible objects [11,12]. The fundamental forms of CBs are, among others, self-injurious and aggression, with the prevalence of these increasing into the teenage years [11]. Most of the studies report on high rates of CBs among individuals with ASD, with a prevalence of up to 94% of these individuals presenting at least one type of CB [13,14]. Other studies reported on the appearance of CBs among 82% of participants, with 32.5% involving aggressive behavior towards themselves or others [15,16]. CBs may significantly impair the physical and mental health and or quality of life of the persons presenting such behaviors, those who care for them, those who live nearby, and, in extreme cases, may even result in death [17–20].

Moreover, the consequences of CBs can go far beyond their immediate physical impact since individuals with CBs are significantly more likely to be excluded from community-based services and be retained in institutional settings [21]. Moreover, such individuals are likely to be excluded from services provided within these settings [15]. CBs may also be an obstacle to learning new skills, particularly in school settings [22]. These behaviors place the child and others around them at risk for physical injury while limiting involvement in educational activities [23]. CBs are considered as constant distress to the people supporting individuals with ASD, such as caregivers, family members, and friends.

On top of the adverse physical outcomes of aggressive behaviors, these behaviors present an emotional burden expressed by depression and anxiety, leading to the enhancement of support teams, thereby enhancing financial burden for the family and the educational/rehabilitation systems supporting these individuals [24]. Moreover, another extra burden of aggressive CBs is the common usage of potent antipsychotic drugs with significant side effects [25]. These behaviors might also prevent the parents from paying attention to siblings of the child with ASD and might lead to the child's removal from the home environment and placing him in an institution.

Applying therapeutic strategies in cases where the person with ASD experiences CBs is intensely warranted forasmuch as the CB becomes established as part of a child's behavioral repertoire, it is unlikely to decrease and will typically remain or worsen without intervention [26]. An effective intervention alerting the outburst of CB and positively lessening the severity of CB might enhance the involvement of the person with ASD within society, reduce the financial and emotional burden of the family and caregivers, decreasing the need for medications [27].

Several forms of intervention have been proposed for established CB in people with intellectual disabilities as well as ASD, including medications [28–31], behavioral intervention [32–41], cognitive/emotion-oriented interventions [42–47], sensory stimulation/integration interventions [48–

53], music therapy [54–58], psychosocial intervention, [59–63] communication training [64–69], physical exercises, [70–74] and others [75–80]. Despite the wide availability of intervention modes, no consensus has been reached for established and high effective CB treatment. However, most interventions aim to prevent the occurrence of CB, guiding the person to more adaptive behaviors avoiding having to manage the consequences of CB.

In line with this prevention strategy, the literature recently enriched with the proposal of using technological devices to predict the CB occurrence based on the individual with ASD's physiological parameters. The presence of atypical physiological arousal in people with ASD has been known for a long time, and the functional relation between homeostatic regulation and CB has already been hypothesized [81–83]. More recently, atypical autonomic reactivity was reported as a common feature in people with ASD, possibly occasioning CB when environmental demand exceeds the person's coping ability [84–87]. However, high variability of physiological reactivity to external stimuli was reported along with the possible existence of subtypes of people with ASD characterized by different physiological profiles (e.g., hypo-aroused, "normally" aroused, and hyper-aroused) [86,88,89]. The use of physiological-biological signals such as the electrocardiogram (ECG), heart rate (HR) and HR variability (HRV), respiratory rate (and changes in respiratory rate), as well as body movements are reiterated in several articles as markers for CB in people with autism [90–94].

Smart Wearable Shirts (SWS) are wearable medical devices (WMD) that are considered as a technological breakthrough, enabling continuous surveillance regarding human vital physiological signs without any disturbance to the activities of daily living (ADL). The SWS technology mentioned above has been used in clinical research for the last two decades. During the last few years, SWS enabled the collection of varied physiological data outside the laboratory for long durations (weeks). The constant surveillance enabled by these devices allows the identification of physiological anomalies that deviate from the typical individual's behaviors that can be received, analyzed, and treated [95]. Furthermore, garments, such as t-shirts, have been found as the second most preferred device to be used by individuals with ASD [96], with a moderate to high suitability index for this population [94]. However, few studies have used SWS with individuals with ASD so far [94,97].

The analysis of physiological data can be achieved by Machine Learning (ML) concept. It is recognized as a method to provide automated approaches and tools for data analysis [98]. It utilizes the algorithms by machines to detect aspecific patterns in the data through a training process [99]. Deep learning (DL) is a subfield of ML that attempts to learn high-level abstractions in the data by utilizing hierarchical architectures. It is perceived as an emerging approach and has been widely applied in traditional artificial intelligence domains, such as semantic parsing, transfer learning, NLP, computer vision, and many more [100]. Supervised learning is a discipline in ML and DL in which the data provides labeled targets for the algorithms. The overall aim of supervised learning is to find a function f(x) that predicts a target y [98]. Several studies aimed to classify emotional stress and CBs using ML and DL-based methods based on bio-signals and wearable devices. While some gained impressive results [101–103], none of them tried to predict CBs among participants with ASD. The current study presents the utilization of a learning algorithm to classify if a measured series of input bio-signal variations is considered as a current CB or if a CB is likely to be developed among adults with ASD.

The current protocol consists of three phases, each with a specific goal. The first aim is to assess the differences in physiological reaction measured with an SWS between adults with high-functioning ASD and typically developed peers. The second goal is to learn which physiological parameters can best predict the CB. The prediction power of a suggested parameter will be confirmed by using a learning algorithm utilized for real-time CB prediction, combined with an ad-hoc developed smartphone application that sends an alert notification when the CB is likely to occur. Finally, the present investigation aims to test the developed system with people with ASD and assess its acceptability and usefulness for users with ASD and their caregivers.

MATERIALS AND METHODS

Study design

An observational study design will be implemented in the first two phases of the current research. In phase one, participants' physiological reactions to two visual stimuli will be collected and analyzed. The physiological characteristics of CBs presented by people with ASD will be collected in phase two. A single case study with a mixed-method design will be implemented in phase three, where the system validity proof of concept will be performed.

Ethics and safety issues

The research proposal was approved by the Ariel University institutional review board (AU-HEA-ML-20201203). The study will be carried out following the Declaration of Helsinki principles. At the recruitment, written informed consent will be collected from all participants or their legal guardians. The SWS planned to use in the current protocol is a non-invasive medical device. However, if a participant does not tolerate SWS, he can withdraw from the study at any time without any repercussions.

Participants

Sample size calculation was performed to identify the number of participants needed to obtain the statistical significance. According to the performed calculation, a group of 20 subjects diagnosed with high functioning ASD whose age will range between 20 and 40 years residing at home (observation group – OG) along with an age and sex-matched control group (CG) of 20 typical developed peers will be enrolled in the first protocol phase. For the study's second phase, 10 people with ASD presenting aggressive or disruptive CBs whose age will range between 20 and 40 years and their caregivers will be recruited. Finally, one participant with ASD whose age will be between 20 and 40 years attending a special school and living at home, which exhibits aggressive or disruptive CBs, will participate in the third phase of the research.

Data collection

Smart Wearable Shirt

The Hexoskin SWS (Hexoskin Inc., Montreal, QC, Canada) is a wearable device shirt that has several sensors aimed to measure physiological signals. The shirts will be used in the current study. The wearable shirt is declared by its producer as a non-invasive SWS with textile embedded sensors that allow the collection of multiple parameters. A detailed description of sensors equipped in the Hexoskin SWS is available on the producer's website (https://www.hexoskin.com). The data that will be collected from the Hexoskin SWS will be ECG, R-R intervals, and N-N intervals. ECG is defined as a raw time-voltage signal that represents the heart's electrical activity from one instant to the next [104]. The ECG is collected by the Hexoskin SWS, with a sampling frequency of 256Hz, and 12-bit resolution. R-R interval is defined as the heart function performed by two main steps: the activation step, called depolarization and labeled as QRS complex, followed by the resting state, the repolarization. The R-R interval is defined as the time interval between two consecutive QRS complexes [104]. The Hexoskin SWS provides an in-build analysis of R-R interval performed off-line and given as a CSV file. The R-R interval analysis of an ECG segment consists of both normal and abnormal R-R interval samples. The normal R-R interval is called N-N interval and represents ideally pure sinus beats and is best for ECG analysis purposes. The abnormal R-R interval differs from sinus rhythm in their length, and they represent disturbances of both technical and physiological origins [105]. The N-N intervals analysis is performed off-line by the Hexoskin SWS and is provided as a CSV file. The Hexoskin SWS will be used in all three phases of the research.

Behavioral diary

The caregivers of participants enrolled in phase two will be asked to fill out a daily behavioral diary reporting on the arousal level of the subject. Three arousal levels will be collected: quiet, agitated, and CB. "Quiet" state refers to a period in which the subject is relaxed or doing a minimum activity peacefully (e.g., resting on the sofa; playing peacefully with puzzles; quietly doing homework). Moments in which the participant is sleeping, is excited, is carrying out an activity that involves him a lot (e.g., activities in which he laughs a lot), and is doing sports (even in calm) will not be referred to the "quiet" state. "Agitated" describes a behavioral activation state higher than "Quiet". It can correspond to situations in which a physiological reaction is observed, such as redness, sweating, increased respiratory rate, and others. It can occur in cases of euphoria (e.g., the subject is watching a show that he enjoys very much), intense activity (e.g., doing a sport activity), anger (e.g., the subject has been told that he cannot do an activity that he has requested and therefore vigorously protests) or tiredness (e.g., the subject has had a long day and is intensely protesting because he wants to go home), but cannot be defined as CB. "CB" arousal state will be defined as an extreme agitation state with an intense physiological response (redness, sweating, or increased respiratory rate) which can be accompanied by fierce anger (with or without aggressive or disruptive behaviors), strong states of anxiety, or a need to move. In general, “CB” should correspond to reactions identified as exaggerated, excessive for the situation, and inadequate to the social context. Aggression behaviors will include self- or other-directed physical or verbal aggression. For each arousal level reported, caregivers will be asked to report on the following items: the beginning and ending time and date of the state, and a brief specification note describing the type of activity that the participant is doing and the topography of the occurred behavior. The behavioral diary will be collected within the second protocol phase.

Quebec User Evaluation of Satisfaction with Assistive Technology

The Quebec User Evaluation of Satisfaction with Assistive Technology second edition (QUEST 2.0) [106] is defined as a 12-item questionnaire designed to assess users' satisfaction with a wide range of assistive technology. The items were designed based on the literature referred to the assistive technology assessment and the Matching Person and Technology model [107]. The 12 items are grouped in two areas representing the user satisfaction with the assistive technologies related to the assistive device (eight items) and provided service (four items). A score on a five-point Likert scale is given to each item from 1 ("not satisfied at all") to 5 ("very satisfied"). A space for comments is provided next to each item to identify the causes of user satisfaction or dissatisfaction. At the end of the QUEST 2.0 form, a list with the 12 investigated aspects of satisfaction is presented, and the user is asked to choose the three aspects most important to him. Strong psychometric proprieties were published for the QUEST 2.0 [108]. The QUEST 2.0 will be administered in phase three of the current protocol with the participant's caregivers.

Focus group

The focus group is defined as a qualitative data collection method often used in health research. The technique is used to produce a controlled discussion on specific issues within a group of people who share different relations with the focused topics [109,110]. Under the focus group method, the group discussion is recorded, transcribed, and analyzed. In addition, a search for themes relevant to the investigated topic and the group agreement on such themes is performed [111]. Research questions that will be raised during the focus group of the current protocol are as follows:

- Did wearing the SWS upset the participants?
- Was the system able to detect all relevant CB?
- Was the system operation speed sufficient to allow the in-time application of appropriate prevention strategies?
- Has the use of the system reduced the amount of CB?
- What improvements can be applied to the system to increase its effectiveness?

Procedure

The research procedure outlined in Figure 1. The protocol's expected starting date is June 2022.

--------------------------------------INSERT FIGURE 1 ABOUT HERE------------------------------------

Phase one – comparison between people with and without ASD physiological outcomes

For the first phase of the current protocol, the physiological parameters of the people in the OG and CG will be acquired using the Hexoskin SWS while participants watch two different five-minute videos. One video will show relaxing images and will emit relaxing music (relaxing video). The second video will present impressive human body deformities accompanied by anxious music (disturbing video). Both videos will be presented to the participant when he is in a sitting position. Before starting the relaxing video, the participant will be invited to relax and lean back onto the chair's backrest. The participant can close his eyes or keep them open at his discretion to promote relaxation. To watch the disturbing video, participants will be asked not to lean against the chair backrest and keep their eyes open for the duration of the video watching. The first video watched by each participant will be chosen randomly between the two videos. The duration of the entire session will be approximately 15 minutes.

Phase two - classify the variations of the physiological parameters in people with ASD

Each participant enrolled in phase two of the protocol will be asked to wear the Hexoskin SWS for seven consecutive days during waking hours, performing his usual daily activities. During the same seven days, the caregivers who care for the participant will be asked to report the participant's status in the behavioral diary. Each evening the data collected by the Hexoskin SWS will be uploaded in an online cloud along with the behavioral diary of the day. Once the data from all the 10 participants have been collected, an DL algorithm will be developed to learn the variations in the individual's physiological parameters that occur before a CB and predict future CB. Moreover, a smartphone application will be developed to receive the Hexoskin SWS data in real-time and send it to a remote server where it is analyzed through the developed algorithm and the classified CB events will be extracted and presented on the applications' notification screen. In other words: if the algorithm detects the possibility of an incoming CB, a notification is sent to the caregiver's smartphone to inform of the possible advent of a CB, therefore enabling the implementation of the selected intervention strategy. The system architecture is explained in Figure 2.

--------------------------------------INSERT FIGURE 2 ABOUT HERE-----------------------------------

Phase three – System proof of concept

The developed system prototype and its efficacy will be tested on one participant with ASD for seven days with healthcare professionals and teachers in a special school setting for one week. The participant will wear the Hexoskin SWS during all hours of attendance at the special school. At the end of the seven days, the QUEST 2.0 will be administered to each professional and teacher who will interact with the system, in addition, to a focus group that will be carried out with them to address the research questions mentioned above. Information obtained from the QUEST 2.0 administration will be discussed within the focus group. In the last part of the focus group, a summation of solutions to each research question will be proposed to the group, and the number of participants that agree or disagree with the proposed summation answers will be collected.

Data analyses

Phase one

Data collected by the Hexoskin SWS from participants in the OG and CG will be analyzed and compared. From ECG received data, HR will be calculated between two consecutive QRS complexes. Considering the time interval between two QRS complexes as “t”, the corresponding temporal HR will be 60/t [112]. In order to remove unwanted artifacts from HR, a percentage threshold value will be set using the sliding window method and minimum allowed peak width will be identify. The removal process will be performed for positive and negative peaks in two rounds. A window will be slid over the HR signal, and its median value will be calculated. The maximum (positive and negative) allowed peak amplitude will be determined for every window by multiplying the window’s median value for a threshold value. Threshold value for positive peaks was set at 30% (for the first removal round) and 25% (for the second removal round) of the window’s mean value. For negative peaks, threshold value was set at 50% (for the first removal round) and 30% (for the second removal round) of the window’s mean value. Then, all peaks with amplitude bigger than the allowed value will be identified from every window. If one of these peaks is narrower than the minimum allowed peak width, it will be replaced with the reference window median value. Otherwise, if an identified peak width is bigger than the allowed peak width, it value will be replaced with the maximal allowed HR (for positive peaks) or the minimal allowed HR (for negative peaks). The maximal allowed HR will be calculated with the following formula: "$209 - (0.7 \times (Participant\ age))$" [113]. The minimal allowed HR will be 60 bpm [114]. After removing abnormal peaks, the signal will be filtered with a Gaussian filter with a sigma equal to 1. After the HR signal filtering process, the obtained cleaned HR signal will be used to classify the participant stress within the following levels: “no stress”, “mild stress”, “moderate stress”, and “high stress”. Each stress level will refer to an HR signal that is positioned within a specific range of values. The “no stress” level will include the HR values below 90% of the cleaned HR signal's lowest peak. If this HR value is lower than The “high stress” level will comprise values above 90% of the cleaned HR signal’s highest peak. If this value is above the maximal allowed HR, it is substitute with 90% of the maximal allowed HR value. The range left between these two thresholds will be divided into two equal parts (lower and upper half). The HR data positioned in the lower half of this range will be classified as "mild stress" and those positioned in the upper half as "moderate stress". Each HR value will be classified and assigned with a numerical value corresponding to a stress level (“no stress” = 0, “mild stress” = 1, “moderate stress” = 2, and “high stress” = 3). After acquiring the sequences of the stress levels of all participants of Phase one, the sequences of the subjects in the OG and CG will be compared using a version of the Smith-Waterman algorithm adapted for the analysis of the obtained data.

Phase two

The data gathered by the Hexoskin SWS from participants enrolled in phase two will be analyzed as described above and a DL algorithm will be developed in order to predict the incoming participants' stress levels. To find CBs patterns among subjects, the authors intend to construct a classifier based on supervised learning to find anomalies in the subject's data that might indicate on CB that is about to occur. A long-short term memory (LSTM) algorithm will be taught to recognize data patterns corresponding to CBs occurrence using the data collected by the participants' caregivers through the behavioral diary and the information collected in Phase one.

LSTM is an extension of the recurrent neural network (RNN). In contrast to other application of ML and DL, in the process of analyzing and predicting time series information, each data point is based on previous information, which must be examined as well. RNN is the most used network for time series applications since it can form the target vector observing the current input data history, using shared wights among the hiding units of the network across each time step of the data. The authors choose the use of LSTM, and not the RNN, because RNN has one significant problem that is called the vanishing gradient, where gradient of output error is based on previous inputs vanishes when time lags between inputs and errors increases. To overcome this problem the LSTM is introduced. LSTM has a memory, which come to practice by replacing the nonlinear units of RNN in the hidden layers with memory blocks. The network propagate error throughout the entire network, and as a result, it is capable of learning long-term dependencies, and forgetting unnecessary information based on the data at hand [115].

The accuracy of the prediction model will be calculated according to common estimation methods such as the confusion matrix and the area under the curve (AUC) Values. These values range from 0.5 to 1, with 1 being perfect classification and 0.5 being no better than luck.

Phase three

The themes that will emerge from the focus group will be extracted from the discussion transcription. Axial coding strategy will be applied to calculate the extensiveness of each theme discussion. This qualitative data analysis consists of assigning a reference number to each theme and then marking any sentence related to that theme with that number. A reliability check for the code-to-sentence matches will be applied by giving the list of codes to an independent researcher experienced in qualitative analysis and asking him to identify the sentence that matches each code.[111] The level of agreement to each summation answer to the research questions will be obtained by calculating the percentage of participants that agree with the proposed statement. The authors will discuss the developed answers to the research questions in the light of the relevant emerged themes and level of agreement of the discussion group.

Dissemination

The authors plan to submit a manuscript on the identified differences in physiological arousal between people with and without ASD. A second manuscript will describe the system development procedure and results obtained from the proof of concept (phase three). These manuscripts will be submitted to peer-reviewed journals for publication. Obtained results will be presented at academic conferences and used for professional training. The developed smartphone application will be freely available for download from the main android-based application distribution sources (e.g., Google Play) at the end of the study. The authors' institutions and networks will support the result diffusion with dissemination strategies.

DISCUSSION

Many individuals with ASD present aggressive or disruptive CB. Although interventions were proposed to cope with such behaviors, they frequently occur unexpectedly. There is a need for effective strategies to support such interventions anticipating the occurrence of CB. To the authors' knowledge, this study represents the first attempt of using SWS and simultaneous multiple physiological parameters analysis to predict CBs. The system that will be developed within the current project can improve the quality of life of people with ASD presenting aggressive and disruptive CBs as well as their caregivers and health professionals, helping in carrying out the selected intervention modality to reduce CB and prevent the onset of burnout symptoms. Moreover, the proposed system will be cost-effective, easy to use even for non-expert users, and widely accessible by buying the SWS and downloading the smartphone application. Furthermore, the results that will be obtained at the end of this project can be helpful for further development of wearable devices to predict CB, a field of growing interest among health and medical researchers. Finally, the mixed-method design proposed for phase three of the protocol will involve health care professionals that cope daily with CB. Their participation will allow the integration of their clinical experience and perceived needs in the proposed system improvement and provide valuable information to be kept into consideration for future development of similar devices.

AUTHORS' CONTRIBUTIONS

MZ obtain the funds for the current research project. MZ and ML designed the protocol and selected the SWS to be used. MZ and HH identified the adequate data analysis for the algorithm development. ML and AR defined the methodology for the clinical part of the data collection (behavioral diary and focus group). AR wrote the protocol text. All the authors read the protocol draft and suggested improvement until consensus was reached.

FUNDING STATEMENT

This work was supported by the Israeli Innovation Authority.

COMPETING INTERESTS STATEMENT

The authors have no competing interest to declare.

REFERENCES

1. Baron-Cohen, S.; Scott, F.J.; Allison, C.; Williams, J.; Bolton, P.; Matthews, F.E.; Brayne, C. Prevalence of autism-spectrum conditions: UK school-based population study. *Br. J. Psychiatry* **2009**, *194*, 500–509, doi:10.1192/BJP.BP.108.059345.
2. American Psychiatric Association *Diagnostic and Statistical Manual of Mental Disorders*; 5th ed.; American Psychiatric Association: Washington (DC), 2013; ISBN 0-89042-555-8.
3. Knapp, M.; Romeo, R.; Beecham, J. Economic cost of autism in the UK. *Autism* **2009**, *13*, 317–336, doi:10.1177/1362361309104246.
4. Arnold, S.; Reed, P. Reading assessments for students with ASD: a survey of summative reading assessments used in special educational schools in the UK. *Br. J. Spec. Educ.* **2016**, *43*, 122–141, doi:10.1111/1467-8578.12127.
5. Chiang, H.M. Expressive communication of children with autism: the use of challenging behaviour. *J. Intellect. Disabil. Res.* **2008**, *52*, 966–972, doi:10.1111/J.1365-2788.2008.01042.X.
6. O'Donnell, S.; Deitz, J.; Kartin, D.; Nalty, T.; Dawson, G. Sensory processing, problem behavior, adaptive behavior, and cognition in preschool children with autism spectrum disorders. *Am. J. Occup. Ther.* **2012**, *66*, 586–594, doi:10.5014/ajot.2012.004168.
7. Baker, A.E.Z.; Lane, A.; Angley, M.T.; Young, R.L. The relationship between sensory processing patterns and behavioural responsiveness in autistic disorder: A pilot study. *J. Autism Dev. Disord.* **2008**, *38*, 867–875.
8. Murphy, G.H.; Beadle-Brown, J.; Wing, L.; Gould, J.; Shah, A.; Holmes, N. Chronicity of Challenging Behaviours in People with Severe Intellectual Disabilities and/or Autism: A Total Population Sample. *J. Autism Dev. Disord. 2005 354* **2005**, *35*, 405–418, doi:10.1007/S10803-005-5030-2.
9. Prizant, B.M.; Wetherby, A.M. Critical Issues in Enhancing Communication Abilities for Persons with Autism Spectrum Disorders. In *Handbook of autism and pervasive developmental disorders: Assessment, interventions, and policy*; Volkmar, F.R., Paul, R., Klin, A., Cohen, D., Eds.; John Wiley & Sons, Inc.: Hoboken, NJ, 2005; pp. 925–945.
10. Reese, R.M.; Richman, D.M.; Belmont, J.M.; Morse, P. Functional Characteristics of Disruptive Behavior in Developmentally Disabled Children with and without Autism. *J. Autism Dev. Disord. 2005 354* **2005**, *35*, 419–428, doi:10.1007/S10803-005-5032-0.
11. Emerson, E. *Challenging behaviour: Analysis and intervention in people with severe intellectual disabilities*; 2nd ed.; Cambridge University Press: Cambridge, UK, 2001; ISBN 0521794447.
12. Holden, B.; Gitlesen, J.P. A total population study of challenging behaviour in the county of Hedmark, Norway: Prevalence, and risk markers. *Res. Dev. Disabil.* **2006**, *27*, 456–465, doi:10.1016/J.RIDD.2005.06.001.
13. Jang, J.; Dixon, D.R.; Tarbox, J.; Granpeesheh, D. Symptom severity and challenging behavior in children with ASD. *Res. Autism Spectr. Disord.* **2011**, *5*, 1028–1032, doi:10.1016/j.rasd.2010.11.008.
14. Matson, J.L.; Wilkins, J.; Macken, J. The relationship of challenging behaviors to severity and symptoms of autism spectrum disorders. *J. Ment. Health Res. Intellect. Disabil.* **2008**, *2*, 29–44, doi:10.1080/19315860802611415.

15. Murphy, O.; Healy, O.; Leader, G. Risk factors for challenging behaviors among 157 children with autism spectrum disorder in Ireland. *Res. Autism Spectr. Disord.* **2009**, *3*, 474–482, doi:10.1016/j.rasd.2008.09.008.

16. Woodbury-Smith, M.R.; Clare, I.C.H.; Holland, A.J.; Kearns, A. High functioning autistic spectrum disorders, offending and other law-breaking: Findings from a community sample. *J. Forensic Psychiatry Psychol.* **2006**, *17*, 108–120, doi:10.1080/14789940600589464.

17. Mukaddes, N.M.; Topcu, Z. Case Report: Homicide by a 10-Year-Old Girl with Autistic Disorder. *J. Autism Dev. Disord. 2006 364* **2006**, *36*, 471–474, doi:10.1007/S10803-006-0087-0.

18. Nissen, J.M.J.F.; Haveman, M.J. Mortality and avoidable death in people with severe self-injurious behaviour: results of a Dutch study. *J. Intellect. Disabil. Res.* **1997**, *41*, 252–257, doi:10.1046/J.1365-2788.1997.04545.X.

19. Blacher, J.; McIntyre, L.L. Syndrome specificity and behavioural disorders in young adults with intellectual disability: cultural differences in family impact. *J. Intellect. Disabil. Res.* **2006**, *50*, 184–198, doi:10.1111/J.1365-2788.2005.00768.X.

20. Felce, D.; Perry, J.; Lowe, K.; Jones, E. The Impact of Autism or Severe Challenging Behaviour on Lifestyle Outcome in Community Housing. *J. Appl. Res. Intellect. Disabil.* **2011**, *24*, 95–104, doi:10.1111/J.1468-3148.2010.00571.X.

21. Hieneman, M. Positive Behavior Support for Individuals with Behavior Challenges. *Behav. Anal. Pract.* **2015**, *8*, 101–108, doi:10.1007/s40617-015-0051-6.

22. Chadwick, O.; Piroth, N.; Walker, J.; Bernard, S.; Taylor, E. Factors affecting the risk of behaviour problems in children with severe intellectual disability. *J. Intellect. Disabil. Res.* **2000**, *44*, 108–123, doi:10.1046/J.1365-2788.2000.00255.X.

23. Sigafoos, J.; Arthur-Kelly, M.; O'Reilly, M.F. *Challenging behaviour and developmental disability*; Paul, H., Ed.; Brookes Publishing Co: Baltimore, MD, 2003; ISBN 1-86156-378-7.

24. Allen, D. Positive behavioural support as a service system for people with challenging behaviour. *Psychiatry* 2009, *8*, 408–412.

25. Scheifes, A.; Walraven, S.; Stolker, J.J.; Nijman, H.L.I.; Egberts, T.C.G.; Heerdink, E.R. Adverse events and the relation with quality of life in adults with intellectual disability and challenging behaviour using psychotropic drugs. *Res. Dev. Disabil.* **2016**, *49–50*, 13–21, doi:10.1016/j.ridd.2015.11.017.

26. Berg, W.K.; Peck, S.; Wacker, D.P.; Harding, J.; McComas, J.; Richman, D.; Brown, K. The Effects of Presession Exposure To Attention on the Results of Assessments of Attention As a Reinforcer. *J. Appl. Behav. Anal.* **2000**, *33*, 463–477, doi:10.1901/jaba.2000.33-463.

27. Rose, D.; Horne, S.; Rose, J.L.; Hastings, R.P. Negative emotional reactions to challenging behaviour and staff burnout: Two replication studies. *J. Appl. Res. Intellect. Disabil.* **2004**, *17*, 219–223, doi:10.1111/j.1468-3148.2004.00194.x.

28. McPheeters, M.L.; Warren, Z.; Sathe, N.; Bruzek, J.L.; Krishnaswami, S.; Jerome, R.N.; Veenstra-VanderWeele, J. A systematic review of medical treatments for children with autism spectrum disorders. *Pediatrics* 2011, *127*, e1312–e1321.

29. Sawyer, A.; Lake, J.K.; Lunsky, Y.; Liu, S.K.; Desarkar, P. Psychopharmacological treatment of challenging behaviours in adults with autism and intellectual disabilities: A

systematic review. *Res. Autism Spectr. Disord.* **2014**, *8*, 803–813, doi:10.1016/J.RASD.2014.03.021.

30. Blankenship, K.; Erickson, C.A.; McDougle, C.J. Pharmacotherapy of Autism and related disorders. *Psychiatr. Ann.* **2010**, *40*, 203–209, doi:10.3928/00485713-20100330-06.

31. Malone, R.P.; Gratz, S.S.; Delaney, M.A.; Hyman, S.B. Advances in drug treatments for children and adolescents with autism and other pervasive developmental disorders. *CNS Drugs* **2005**, *19*, 923–934, doi:10.2165/00023210-200519110-00003/FIGURES/TAB1.

32. Scotti, J.R.; Ujcich, K.J.; Weigle, K.L.; Holland, C.M.; Kirk, K.S. Interventions with Challenging Behavior of Persons with Developmental Disabilities: A Review of Current Research Practices. *J. Assoc. Pers. with Sev. Handicap.* **1996**, *21*, 123–134, doi:https://doi.org/10.1177/154079699602100303.

33. Fettig, A.; Barton, E.E. Parent Implementation of Function-Based Intervention to Reduce Children's Challenging Behavior: A Literature Review. *Topics Early Child. Spec. Educ.* **2014**, *34*, 49–61, doi:10.1177/0271121413513037.

34. Lydon, S.; Healy, O.; O'Reilly, M.; McCoy, A. A systematic review and evaluation of response redirection as a treatment for challenging behavior in individuals with developmental disabilities. *Res. Dev. Disabil.* **2013**, *34*, 3148–3158, doi:10.1016/J.RIDD.2013.06.010.

35. Machalicek, W.; O'Reilly, M.F.; Beretvas, N.; Sigafoos, J.; Lancioni, G.E. A review of interventions to reduce challenging behavior in school settings for students with autism spectrum disorders. *Res. Autism Spectr. Disord.* **2007**, *1*, 229–246, doi:10.1016/J.RASD.2006.10.005.

36. Didden, R.; Korzilius, H.; Van Oorsouw, W.; Sturmey, P. Behavioral treatment of challenging behaviors in individuals with mild mental retardation: Meta-analysis of single-subject research. *Am. J. Ment. Retard.* **2006**, *111*, 290–298, doi:10.1352/0895-8017(2006)111[290:BTOCBI]2.0.CO;2.

37. Inoue, M. Assessments and Interventions to Address Challenging Behavior in Individuals with Intellectual Disability and Autism Spectrum Disorder in Japan: A Consolidated Review. *Yonago Acta Med.* **2019**, *62*, 169–181, doi:10.33160/YAM.2019.06.001.

38. Machalicek, W.; Raulston, T.; Knowles, C.; Ruppert, T.; Carnett, A.; Alresheed, F. Challenging behavior. In *Comorbid Conditions Among Children with Autism Spectrum Disorders.*; Matson, J.L., Ed.; Springer: Cham, 2016; pp. 137–170 ISBN 9783319191836.

39. MacNaul, H.L.; Neely, L.C. Systematic Review of Differential Reinforcement of Alternative Behavior Without Extinction for Individuals With Autism. *Behav. Modif.* **2018**, *42*, 398–421, doi:10.1177/0145445517740321.

40. Erturk, B.; Machalicek, W.; Drew, C. Self-Injurious Behavior in Children With Developmental Disabilities: A Systematic Review of Behavioral Intervention Literature. *Behav. Modif.* **2018**, *42*, 498–542, doi:10.1177/0145445517741474.

41. Weston, R.; Hodges, A.; Davis, T.N. Differential Reinforcement of Other Behaviors to Treat Challenging Behaviors Among Children With Autism: A Systematic and Quality Review. *Behav. Modif.* **2018**, *42*, 584–609, doi:10.1177/0145445517743487.

42. O'Neil, M.E.; Freeman, M.; Christensen, V.; Telerant, R.; Addleman, A.; Kansagara, D. A Systematic Evidence Review of Non-pharmacological Interventions for Behavioral

Symptoms of Dementia. *Heal. Serv. Res. Dev. Serv.* **2011**, 69.

43. Doyle, K.L.; Morgan, E.E.; Morris, S.; Smith, D.M.; Little, S.; Iudicello, J.E.; Blackstone, K.; Moore, D.J.; Grant, I.; Letendre, S.L.; et al. Real-world impact of neurocognitive deficits in acute and early HIV infection. *J. Neurovirol.* **2013**, *19*, 565–573, doi:10.1007/s13365-013-0218-2.

44. Subramaniam, P.; Woods, B. The impact of individual reminiscence therapy for people with dementia: Systematic review. *Expert Rev. Neurother.* **2012**, *12*, 545–555, doi:10.1586/ern.12.35.

45. Cotelli, M.; Manenti, R.; Zanetti, O. Reminiscence therapy in dementia: A review. *Maturitas* **2012**, *72*, 203–205, doi:10.1016/j.maturitas.2012.04.008.

46. Zetteler, J. Effectiveness of simulated presence therapy for individuals with dementia: A systematic review and meta-analysis. *Aging Ment. Heal.* **2008**, *12*, 779–785, doi:10.1080/13607860802380631.

47. Neal, M.; Barton Wright, P. Validation therapy for dementia. *Cochrane Database Syst. Rev.* **2003**, doi:10.1002/14651858.CD001394.

48. Wan Yunus, F.; Liu, K.P.Y.; Bissett, M.; Penkala, S. Sensory-Based Intervention for Children with Behavioral Problems: A Systematic Review. *J. Autism Dev. Disord.* **2015**, *45*, 3565–3579, doi:10.1007/S10803-015-2503-9/TABLES/4.

49. Case-Smith, J.; Weaver, L.L.; Fristad, M.A. A systematic review of sensory processing interventions for children with autism spectrum disorders. *Autism* **2015**, *19*, 133–148, doi:10.1177/1362361313517762.

50. Lang, R.; O'Reilly, M.; Healy, O.; Rispoli, M.; Lydon, H.; Streusand, W.; Davis, T.; Kang, S.; Sigafoos, J.; Lancioni, G.; et al. Sensory integration therapy for autism spectrum disorders: A systematic review. *Res. Autism Spectr. Disord.* **2012**, *6*, 1004–1018, doi:10.1016/j.rasd.2012.01.006.

51. Watling, R.; Hauer, S. Effectiveness of Ayres Sensory Integration® and Sensory-Based Interventions for People With Autism Spectrum Disorder: A Systematic Review. *Am. J. Occup. Ther.* **2015**, *69*, 6905180030p1-6905180030p12, doi:10.5014/ajot.2015.018051.

52. Leong, H.M.; Carter, M.; Stephenson, J. Systematic review of sensory integration therapy for individuals with disabilities: Single case design studies. *Res. Dev. Disabil.* **2015**, *47*, 334–351, doi:10.1016/J.RIDD.2015.09.022.

53. Barton, E.E.; Reichow, B.; Schnitz, A.; Smith, I.C.; Sherlock, D. A systematic review of sensory-based treatments for children with disabilities. *Res. Dev. Disabil.* **2015**, *37*, 64–80, doi:10.1016/J.RIDD.2014.11.006.

54. Gold, C.; Wigram, T.; Elefant, C. Music therapy for autistic spectrum disorder. *Cochrane Database Syst. Rev.* **2006**, doi:10.1002/14651858.CD004381.PUB2/INFORMATION/EN.

55. Simpson, K.; Keen, D. Music interventions for children with autism: Narrative review of the literature. *J. Autism Dev. Disord.* **2011**, *41*, 1507–1514, doi:10.1007/s10803-010-1172-y.

56. Fakhoury, N.; Wilhelm, N.; Sobota, K.F.; Kroustos, K.R. Impact of music therapy on dementia behaviors: A literature review. *Consult. Pharm.* **2017**, *32*, 623–628, doi:10.4140/TCP.N.2017.623.

57. Stephenson, J. Music therapy and the education of students with severe disabilities. *Educ. Train. Dev. Disabil.* **2006**, *41*, 290–299.

58. James, R.; Sigafoos, J.; Green, V.A.; Lancioni, G.E.; O'Reilly, M.F.; Lang, R.; Davis, T.; Carnett, A.; Achmadi, D.; Gevarter, C.; et al. Music Therapy for Individuals with Autism Spectrum Disorder: a Systematic Review. *Rev. J. Autism Dev. Disord.* **2015**, *2*, 39–54, doi:10.1007/s40489-014-0035-4.

59. Reichow, B.; Servili, C.; Yasamy, M.T.; Barbui, C.; Saxena, S. Non-Specialist Psychosocial Interventions for Children and Adolescents with Intellectual Disability or Lower-Functioning Autism Spectrum Disorders: A Systematic Review. *PLOS Med.* **2013**, *10*, e1001572, doi:10.1371/JOURNAL.PMED.1001572.

60. Lim, J.M. Emotion regulation and intervention in adults with autism spectrum disorder: a synthesis of the literature. *Adv. Autism* **2019**, *6*, 48–62, doi:10.1108/AIA-12-2018-0050.

61. Bishop-Fitzpatrick, L.; Minshew, N.J.; Eack, S.M. A Systematic Review of Psychosocial Interventions for Adults with Autism Spectrum Disorders. *Adolesc. Adults with Autism Spectr. Disord.* **2014**, 315–327, doi:10.1007/978-1-4939-0506-5_16.

62. Vanderkerken, L.; Heyvaert, M.; Maes, B.; Onghena, P. Psychosocial interventions for reducing vocal challenging behavior in persons with autistic disorder: A multilevel meta-analysis of single-case experiments. *Res. Dev. Disabil.* **2013**, *34*, 4515–4533, doi:10.1016/J.RIDD.2013.09.030.

63. Seida, J.K.; Ospina, M.B.; Karkhaneh, M.; Hartling, L.; Smith, V.; Clark, B. Systematic reviews of psychosocial interventions for autism: An umbrella review. *Dev. Med. Child Neurol.* **2009**, *51*, 95–104, doi:10.1111/j.1469-8749.2008.03211.x.

64. Mirenda, P. Supporting individuals with challenging behavior through functional communication training and AAC: research review. *Augment. Altern. Commun.* **1997**, *13*, 207–225, doi:10.1080/07434619712331278048.

65. Walker, V.L.; Snell, M.E. Effects of augmentative and alternative communication on challenging behavior: A meta-analysis. *Augment. Altern. Commun.* **2013**, *29*, 117–131.

66. Lequia, J.; MacHalicek, W.; Rispoli, M.J. Effects of activity schedules on challenging behavior exhibited in children with autism spectrum disorders: A systematic review. *Res. Autism Spectr. Disord.* **2012**, *6*, 480–492, doi:10.1016/j.rasd.2011.07.008.

67. Gerow, S.; Hagan-Burke, S.; Rispoli, M.; Gregori, E.; Mason, R.; Ninci, J. A Systematic Review of Parent-Implemented Functional Communication Training for Children With ASD. *Behav. Modif.* **2018**, *42*, 335–363, doi:10.1177/0145445517740872.

68. Gregori, E.; Wendt, O.; Gerow, S.; Peltier, C.; Genc-Tosun, D.; Lory, C.; Gold, Z.S. Functional Communication Training for Adults with Autism Spectrum Disorder: A Systematic Review and Quality Appraisal. *J. Behav. Educ.* **2020**, *29*, 42–63, doi:10.1007/s10864-019-09339-4.

69. Goldstein, H. Communication Intervention for Children with Autism: A Review of Treatment Efficacy. *J. Autism Dev. Disord.* **2002**, *32*, 373–396, doi:10.1023/A:1020589821992.

70. Forbes, D.; Forbes, S.C.; Blake, C.M.; Thiessen, E.J.; Forbes, S. Exercise programs for people with dementia. *Cochrane Database Syst. Rev.* **2015**, *2015*, 195–196, doi:10.1002/14651858.CD006489.pub4.

71. Eggermont, L.H.P.; Scherder, E.J.A. Physical activity and behaviour in dementia: A review of the literature and implications for psychosocial intervention in primary care. *Dementia* **2006**, *5*, 411–428, doi:10.1177/1471301206067115.

72. Ogg-Groenendaal, M.; Hermans, H.; Claessens, B. A systematic review on the effect of exercise interventions on challenging behavior for people with intellectual disabilities. *Res. Dev. Disabil.* **2014**, *35*, 1507–1517, doi:10.1016/J.RIDD.2014.04.003.

73. Sorensen, C.; Zarrett, N. Benefits of Physical Activity for Adolescents with Autism Spectrum Disorders: A Comprehensive Review. *Rev. J. Autism Dev. Disord.* **2014**, *1*, 344–353, doi:10.1007/S40489-014-0027-4/TABLES/4.

74. Bremer, E.; Crozier, M.; Lloyd, M. A systematic review of the behavioural outcomes following exercise interventions for children and youth with autism spectrum disorder. *Autism* **2016**, *20*, 899–915, doi:10.1177/1362361315616002.

75. Ferguson, J.; Craig, E.A.; Dounavi, K. Telehealth as a Model for Providing Behaviour Analytic Interventions to Individuals with Autism Spectrum Disorder: A Systematic Review. *J. Autism Dev. Disord.* **2019**, *49*, 582–616, doi:10.1007/S10803-018-3724-5/FIGURES/5.

76. Tanner, K.; Hand, B.N.; O'Toole, G.; Lane, A.E. Effectiveness of interventions to improve social participation, play, leisure, and restricted and repetitive behaviors in people with autism spectrum disorder: A systematic review. *Am. J. Occup. Ther.* **2015**, *69*, 6905180010p1-6905180010p12.

77. Walker, V.L.; Carpenter, M.E.; Lyon, K.J.; Button, L. A Meta-Analysis of Paraprofessional-Delivered Interventions to Address Challenging Behavior Among Students With Disabilities. *J. Posit. Behav. Interv.* **2021**, *23*, 68–80, doi:10.1177/1098300720911147.

78. Lindgren, S.; Wacker, D.; Suess, A.; Schieltz, K.; Pelzel, K.; Kopelman, T.; Lee, J.; Romani, P.; Waldron, D. Telehealth and Autism: Treating Challenging Behavior at Lower Cost. *Pediatrics* **2016**, *137*, S167–S175, doi:10.1542/PEDS.2015-2851O.

79. McDonnell, A.; Sturmey, P.; Oliver, C.; Cunningham, J.; Hayes, S.; Galvin, M.; Walshe, C.; Cunningham, C. The effects of staff training on staff confidence and challenging behavior in services for people with autism spectrum disorders. *Res. Autism Spectr. Disord.* **2008**, *2*, 311–319, doi:10.1016/J.RASD.2007.08.001.

80. Wahman, C.L.; Pustejovsky, J.E.; Ostrosky, M.M.; Santos, R.M. Examining the Effects of Social Stories^{TM} on Challenging Behavior and Prosocial Skills in Young Children: A Systematic Review and Meta-Analysis. *Topics Early Child. Spec. Educ.* **2022**, *41*, 267–279, doi:10.1177/0271121419855692.

81. Kinsbourne, M. Do repetitive movement patterns in children and animals serve a dearousing function? *J. Dev. Behav. Pediatr.* **1980**, *1*, 39–42, doi:10.1097/00004703-198003000-00009.

82. Ornitz, E.M.; Ritvo, E.R. Perceptual Inconstancy in Early Infantile Autism: The Syndrome of Early Infant Autism and Its Variants Including Certain Cases of Childhood Schizophrenia. *Arch. Gen. Psychiatry* **1968**, *18*, 76–98, doi:10.1001/ARCHPSYC.1968.01740010078010.

83. Hutt, C.; Hutt, S.J. Effects of environmental complexity on stereotyped behaviours of children. *Anim. Behav.* **1965**, *13*, 1–4, doi:10.1016/0003-3472(65)90064-3.

84. Klusek, J.; Roberts, J.E.; Losh, M. Cardiac autonomic regulation in autism and Fragile X syndrome: A review. *Psychol. Bull.* **2015**, *141*, 141–175, doi:10.1037/a0038237.

85. Levine, T.P.; Conradt, E.; Goodwin, M.S.; Sheinkopf, S.J.; Lester, B. Psychophysiological Arousal to Social Stress in Autism Spectrum Disorders. In *Comprehensive Guide to Autism*; Springer New York: New York, 2014; pp. 1177–1193.

86. Lydon, S.; Healy, O.; Reed, P.; Mulhern, T.; Hughes, B.M.; Goodwin, M.S. A systematic

review of physiological reactivity to stimuli in autism. *Dev. Neurorehabil.* **2016**, *19*, 335–355, doi:10.3109/17518423.2014.971975.

87. Cohen, I.L.; Yoo, J.H.; Goodwin, M.S.; Moskowitz, L. Assessing Challenging Behaviors in Autism Spectrum Disorders: Prevalence, Rating Scales, and Autonomic Indicators. In *International Handbook of Autism and Pervasive Developmental Disorders*; Matson, J., Sturmey, P., Eds.; Springer New York: New York, 2011; pp. 247–270.

88. Hirstein, W.; Iversen, P.; Ramachandran, V.S. Autonomic responses of autistic children to people and objects. *Proc. R. Soc. London. Ser. B Biol. Sci.* **2001**, *268*, 1883–1888, doi:10.1098/RSPB.2001.1724.

89. Schoen, S.A.; Miller, L.J.; Brett-Green, B.; Hepburn, S.L. Psychophysiology of children with autism spectrum disorder. *Res. Autism Spectr. Disord.* **2008**, *2*, 417–429, doi:10.1016/J.RASD.2007.09.002.

90. Ozdenizci, O.; Cumpanasoiu, C.; Mazefsky, C.; Siegel, M.; Erdogmus, D.; Ioannidis, S.; Goodwin, M.S. Time-Series Prediction of Proximal Aggression Onset in Minimally-Verbal Youth with Autism Spectrum Disorder Using Physiological Biosignals. In Proceedings of the Annual International Conference of the IEEE Engineering in Medicine and Biology Society; IEEE, 2018; Vol. 2018-July, pp. 5745–5748.

91. Goodwin, M.S.; Mazefsky, C.A.; Ioannidis, S.; Erdogmus, D.; Siegel, M. Predicting aggression to others in youth with autism using a wearable biosensor. *Autism Res.* **2019**, *12*, 1286–1296, doi:10.1002/aur.2151.

92. Goodwin, M.S.; Özdenizci, O.; Cumpanasoiu, C.; Tian, P.; Guo, Y.; Stedman, A.; Peura, C.; Mazefsky, C.; Siegel, M.; Erdoğmuş, D.; et al. Predicting Imminent Aggression Onset in Minimally-Verbal Youth with Autism Spectrum Disorder Using Preceding Physiological Signals. In Proceedings of the Proceedings of the 12th EAI International Conference on Pervasive Computing Technologies for Healthcare; ACM: New York, NY, USA, 2018; Vol. 18, pp. 201–207.

93. Nuske, H.J.; Finkel, E.; Hedley, D.; Parma, V.; Tomczuk, L.; Pellecchia, M.; Herrington, J.; Marcus, S.C.; Mandell, D.S.; Dissanayake, C. Heart rate increase predicts challenging behavior episodes in preschoolers with autism. *Stress* **2019**, *22*, 303–311, doi:10.1080/10253890.2019.1572744.

94. Taj-Eldin, M.; Ryan, C.; O'Flynn, B.; Galvin, P. A Review of Wearable Solutions for Physiological and Emotional Monitoring for Use by People with Autism Spectrum Disorder and Their Caregivers. *Sensors* **2018**, *18*, 4271, doi:10.3390/s18124271.

95. Banaee, H.; Ahmed, M.U.; Loutfi, A. Data mining for wearable sensors in health monitoring systems: A review of recent trends and challenges. *Sensors* **2013**, *13*, 17472–17500, doi:10.3390/s131217472.

96. Koo, S.H.; Gaul, K.; Rivera, S.; Pan, T.; Fong, D. Wearable technology design for autism spectrum disorders. *Arch. Des. Res.* **2018**, *31*, 37–55, doi:10.15187/adr.2018.02.31.1.37.

97. Black, M.H.; Milbourn, B.; Chen, N.T.M.; McGarry, S.; Wali, F.; Ho, A.S. V.; Lee, M.; Bölte, S.; Falkmer, T.; Girdler, S. The use of wearable technology to measure and support abilities, disabilities and functional skills in autistic youth: a scoping review. *Scand. J. Child Adolesc. Psychiatry Psychol.* **2020**, *8*, 48–69, doi:10.21307/sjcapp-2020-006.

98. Murphy, K.P. *Machine learning: a probabilistic perspective*; MIT press: Cambridge, MA, 2012; ISBN 0262304325, 9780262304320.

99. Gulshan, V.; Peng, L.; Coram, M.; Stumpe, M.C.; Wu, D.; Narayanaswamy, A.; Venugopalan, S.; Widner, K.; Madams, T.; Cuadros, J.; et al. Development and validation of a deep learning algorithm for detection of diabetic retinopathy in retinal fundus photographs. *JAMA - J. Am. Med. Assoc.* **2016**, *316*, 2402–2410, doi:10.1001/jama.2016.17216.

100. Guo, Y.; Liu, Y.; Oerlemans, A.; Lao, S.; Wu, S.; Lew, M.S. Deep learning for visual understanding: A review. *Neurocomputing* **2016**, *187*, 27–48, doi:10.1016/j.neucom.2015.09.116.

101. Munla, N.; Khalil, M.; Shahin, A.; Mourad, A. Driver stress level detection using HRV analysis. In Proceedings of the 2015 International Conference on Advances in Biomedical Engineering (ICABME); IEEE, 2015; pp. 61–64.

102. Wu, M.; Cao, H.; Nguyen, H.L.; Surmacz, K.; Hargrove, C. Modeling perceived stress via HRV and accelerometer sensor streams. In Proceedings of the Proceedings of the Annual International Conference of the IEEE Engineering in Medicine and Biology Society, EMBS; IEEE, 2015; Vol. 2015-Novem, pp. 1625–1628.

103. Coutts, L. V.; Plans, D.; Brown, A.W.; Collomosse, J. Deep learning with wearable based heart rate variability for prediction of mental and general health. *J. Biomed. Inform.* **2020**, *112*, 103610, doi:10.1016/j.jbi.2020.103610.

104. Goldberger, A.L.; Goldberger, Z.D.; Shvilkin, A. *Goldberger's Clinical Electrocardiography: A Simplified Approach*; 9th ed.; Elsevier: Philadelphia, PA, 2017; ISBN 0323508774.

105. Peltola, M.A. Role of editing of R–R intervals in the analysis of heart rate variability. *Front. Physiol.* **2012**, *3*, 148, doi:10.3389/fphys.2012.00148.

106. Demers, L.; Weiss-Lambrou, R.; Ska, B.; Demers, L. Item Analysis of the Quebec User Evaluation of Satisfaction with Assistive Technology (QUEST). *Assist. Technol.* **2000**, *12*, 96–105, doi:10.1080/10400435.2000.10132015.

107. Scherer, M.J. *Living in the State of Stuck: How Technology Impacts the Lives of Persons with Disabilities*; 4th ed.; Brookline Books: Brookline, MA, 2005; ISBN 9781571290984.

108. Demers, L.; Weiss-Lambrou, R.; Ska, B. The Quebec User Evaluation of Satisfaction with Assistive Technology (QUEST 2.0): An overview and recent progress. *Technol. Disabil.* **2002**, *14*, 101–105, doi:10.3233/TAD-2002-14304.

109. Kitzinger, J. The methodology of Focus Groups: the importance of interaction between research participants. *Sociol. Health Illn.* **1994**, *16*, 103–121, doi:10.1111/1467-9566.ep11347023.

110. Flores, J.G.; Alonso, C.G. Using Focus Groups in Educational Research: Exploring Teachers' Perspectives on Educational Change. *Eval. Rev.* **1995**, *19*, 84–101, doi:10.1177/0193841X9501900104.

111. Breen, R.L. A practical guide to focus-group research. *J. Geogr. High. Educ.* **2006**, *30*, 463–475, doi:10.1080/03098260600927575.

112. Becker, D.E. Fundamentals of electrocardiography interpretation. *Anesth. Prog.* **2006**, *53*, 53–64, doi:10.2344/0003-3006(2006)53[53:FOEI]2.0.CO;2.

113. Tanaka, H.; Monahan, K.D.; Seals, D.R. Age-predicted maximal heart rate revisited. *J. Am. Coll. Cardiol.* **2001**, *37*, 153–156, doi:10.1016/S0735-1097(00)01054-8.

114. Sidhu, S.; Marine, J.E. Evaluating and managing bradycardia. *Trends Cardiovasc. Med.*

2020, *30*, 265–272, doi:10.1016/j.tcm.2019.07.001.

115. El Boujnouni, I.; Tali, A. Heart Rate Variability Prediction based on the combination of Wavelet Decomposition and LSTM Networks. *Int. J. Sci. Eng. Res.* **2019**, *10*.

Figure 1. Protocol flow-chart. OG = Observation group; CG = Control group; SWS = Smart wearable shirt; ASD = Autism spectrum disorder; CB = Challenging behavior; QUEST 2.0 = Quebec User Evaluation of Satisfaction with Assistive Technology 2nd edition.

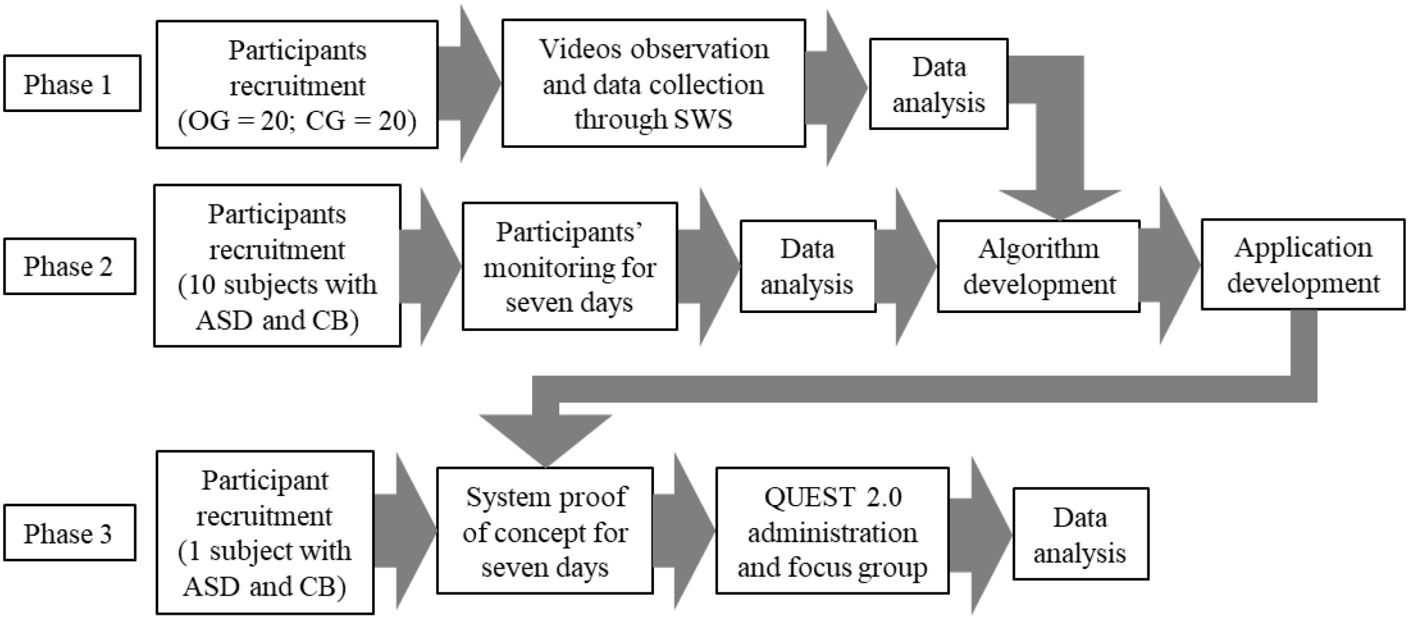

Figure 2. Brief system architecture description. Physiological signals are captured by the Hexoskin smart wearable shirt (SWS) and recorded by the provided data recorder. Recorded data are transferred in real-time to the caregiver smartphone via Bluetooth and then sent to a remote server via an internet connection where they are analyzed. If the ad-hoc developed algorithm detects the incoming occurrence of challenging behavior (CB), the remote server immediately sends a notification alert on the caregiver's smartphone.