Title: HD-DRUM, a tablet-based drumming training application intervention for people with Huntington's disease: application development using an integrated knowledge translation framework approach.

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Conflicts of interest: JCG received financial renumeration for the recording of the audio and timing content of the HD-DRUM application.

Author contributions: CMB: conception, methodology, analysis, interpretation and writing of paper manuscript, funding; MB, AER, CD, PP: conception, methodology, review and editing of paper manuscript, JCG: creation and design of musical and timing content of intervention, review and editing of paper manuscript, VI: analysis, review and editing of paper manuscript.

ABSTRACT

Background: Huntington's Disease (HD) is a neurodegenerative disease that leads to the progressive loss of cognitive-executive and motor functions, largely due to basal ganglia (BG) atrophy. Currently, there are no therapeutic interventions tailored to address executive and motor dysfunction in people with HD. Music-based interventions may aid executive abilities by compensating for impaired BG-reliant timing and rhythm generation with external rhythmic beats. Here, we applied an integrated knowledge translation (IKT) framework to co-design a tablet-based rhythmic drumming training application (HD-DRUM) to stimulate executive and motor abilities in people with HD.

Objectives: The primary aim was to develop the HD-DRUM application for at-home-use, so that it addressed accessibility needs of people with HD and allowed the quantification of performance improvements and adherence for controlled clinical evaluation.

Methods: The IKT framework was applied to iteratively refine the design of HD-DRUM. This process involved three phases of knowledge-user engagement and co-design: a) an online survey with people with HD (n = 29) to inform about their accessibility needs, b) usability testing of tablet-based touchscreens as hardware solutions and c) usability testing of the design and build of HD-DRUM with regards to meeting the identified accessibility needs by people affected by HD and their clinicians (n = 12).

Results: The survey identified accessibility problems due to cognitive and motor control impairments such as difficulties finding and navigating through information and using computer keyboards and mice to interact with applications. Tablet-based touch-screens were identified as a feasible and accessible solution for the delivery of the application. Key elements to ensure that the application design and build met the needs of people with HD were identified and implemented. These included facilitation of intuitive navigation through the application with large and visually distinctive buttons, the use of audio and visual cues as training guides, as well as gamification, positive feedback, and drumming to background music as means to increase motivation and engagement.

The co-design development process resulted in the proof-of-concept HD-DRUM application that is described here according to the template for intervention description and replication (TIDieR) checklist. HD-DRUM can be used at home, allows the quantification of performance improvements and adherence for clinical evaluation, the matching of training difficulty to users' performance levels using gamification, and future scaling-up for reaching a wide range of interested users.

Conclusions: Applying an IKT-based co-design framework involving knowledge user engagement allowed the iterative refinement of the design and build of the tablet-based HD-DRUM application intervention with the aim to stimulate BG-reliant cognitive and motor functions. Mapping the intervention against the TIDieR framework for describing complex interventions, allowed the detailed description of the HD-DRUM intervention and identification of areas that required refinement prior to finalising the intervention protocol.

Trial registration: ISRCTN 11906973

INTRODUCTION

Background and Rationale

Huntington's disease (HD) is an inherited progressive neurodegenerative disease where cell loss in basal ganglia (BG) networks of the brain manifests as cognitive decline, loss of motor control, and mood disturbances. Striatal atrophy [1] and white matter degeneration [2] are observed many years prior to the onset of movement symptoms. These early brain changes are accompanied with impairments in psychomotor speed and executive functions [3, 4] including problems in decision-making, multi-tasking, and motor sequence learning, all of which may hamper a person's everyday functional abilities such as working capacity [5].

Currently, there are no disease-modifying treatments for HD and only very few studies into HD-specific cognition-oriented interventions have been conducted [6]. However, accumulating evidence suggests that neurologic music therapy (NMT) in the form of rhythmic auditory stimulation and therapeutic instrumental music performance training [7] may be beneficial in the rehabilitation of acquired brain injuries [8-11] and of neurodegenerative disease, including HD [12] and Parkinson's disease (PD), which is another movement disorder that affects the basal ganglia [13-15]. Recent reviews and meta-analyses concluded that music-based interventions may be beneficial for gait, timing of upper extremity functions, and quality of life after stroke [8], may improve gait and mobility in Parkinson's disease [13] and motor and cognitive functions in HD [12]. NMT interventions such as RAS are thought to work by compensating for the loss of BG-generated timing and rhythm signals with external rhythmic cueing [16]. Other potentially related mechanisms include accelerated learning due to increased temporal skills through rhythmic movement practices and through motivational aspects of musical rhythm [17]. However, the clinical effects of NMT interventions and the mechanistic underpinnings in the brain of people with HD remain unknown because evidence from high-quality randomised controlled trials is still scarce.

Previously, in two pilot studies we explored a rhythmic movement training (bongo drumming) as a therapeutic tool for people with HD [18, 19]. We chose drumming because it is an activity that requires the learning, planning, and execution of movement sequences, which are all abilities that depend on basal ganglia functions and become more difficult as the disease progresses. Thus, we hypothesised that drumming would not only improve motor abilities and response speed, but also cognitive functions involved in the planning and execution of movements and multi-tasking.

In our pilot research [18, 19], people with HD followed audio instructions teaching them to drum along on a pair of bongo drums. Each 10-15 min training session introduced a novel drumming pattern, starting with simple, slow patterns and gradually increasing in complexity and speed. We found that 2 months of drumming training at home was acceptable for people at premanifest and early stages of the disease and was associated with significant improvements in cognition and white matter microstructure. Anecdotally, some patients and their spouses reported benefits in hand coordination and general alertness. However, the training delivery on bongo drums also had some disadvantages. Firstly, it did not allow the quantification of training-induced performance improvements nor the recording of adherence, i.e., the duration and frequency of training engagement. Secondly, as drumming responses were not tracked, the level of training difficulty could not be matched to an individuals' performance level to avoid over- and underchallenge. Thirdly, delivering the training on CDs and bongo drums makes an increased scale of use more challenging compared with the wide accessibility of digital applications on tablets and smartphones.

An electronic health application of the drumming training that can be delivered on smartphones or tablets has the potential to address these issues. However, there is very little known about the use of digital technologies and any potential barriers in people with HD with the exception of research into wearable or portable sensors to monitor motor and cognitive alterations in HD [20, 21]. A recent review of the literature concluded that digital technologies hold promises for therapeutic research and symptom management of HD but that devices need to be standardized and protocols harmonized to optimize their clinical use in HD [20].

Electronic health applications (eHealth) are increasingly employed as cost-effective and widely accessible tools to support health care delivery, monitoring, and education [22, 23]. With the recent explosion of the eHealth market, ensuring that eHealth applications are appropriately designed and meet the needs of the end-users before employing them as health interventions has become increasingly important. Similarly, it has been recognised that published descriptions of eHealth interventions often lack sufficient detail to replicate or evaluate their effects.

Recently, the UK Medical Research Council (MRC) and National Institute for Health Research (NIHR) have updated their framework for the development and evaluation of complex interventions including eHealth [24]. The new framework recommends engagement of stakeholders, addressing uncertainties, refinement of intervention and theory, taking into account the context of intervention delivery, and economic considerations as core elements to guide research into complex interventions [25]. These recommendations reflect a growing support within health research for co-design; that is the engagement of knowledge users in the development and evaluation of interventions [26]. Knowledge users refer to any stakeholders involved in influencing, administering, and/or using the health care system, including those with lived experience. One framework developed to facilitate co-design is the integrated knowledge translation (IKT) approach which refers to an interactive process of knowledge exchange between different stakeholders to produce interventions that are useful to health care system knowledge users [27]. Within the context of eHealth, the US Institute of Medicine has identified usability (the extent to which an end-user can use the product to achieve specified goals) as a key component of good practice for the development of electronic applications [28]. Therefore, the usability of an eHealth application needs to be tested by knowledge users as part of the developmental process to ensure that end-users' needs are met. Thus, engagement of knowledge users in co-design and iterative usability testing for design refinement have emerged as important components of an IKT approach for the development of eHealth interventions [29].

We adopted the IKT framework for developing a tablet-based rhythmic movement (drumming) training application intervention for people with Huntington's disease. This paper first reports the IKT-based intervention development process and then provides a detailed description of the intervention using the TIDieR checklist [30]. This paper focuses on the documentation of data that were acquired during the iterative co-design development process including data from background research into the use of digital technology in people with HD and from usability testing of hardware and software options. The developed proof-of-concept HD-DRUM app described here is suitable for clinical evaluation.

Objectives

The primary aim of this research was to develop HD-DRUM, a tablet-based drumming training application intervention for people with HD.

METHODS

We developed a proof-of-concept tablet-based drumming training application, HD-DRUM, ready for clinical evaluation. The purpose of the HD-DRUM intervention is to provide a digital training platform that provides solutions to the challenges encountered with the use of the bongo drumming training that we investigated previously. Specifically, it allows (i) quantification of performance improvements, (ii) quantification of training engagement, (iii) matching of the training difficulty to performance levels, and (iv) scaling-up reach for a wider audience via delivery on tablets and/or smartphones.

Following the IKT framework, and in collaboration with the user-centred design and innovation agency Kinneir Dufort (KD)[31] and knowledge users, we applied a dynamic and iterative model of development that included knowledge-user engagement at different stages of the planning and development of HD-DRUM (Figure 1).

Ethical consideration

This project has received favourable ethical opinion from the Wales Research Ethics Committee 2 and from Health and Care Research Wales (REC reference: 22/WA/0147) as well as from the School of Psychology Research Ethics Committee at Cardiff University (EC.21.12.14.6493). The project is sponsored by Cardiff University (SPON1895-22). Participants provide informed consent. Privacy and confidentiality of participants are protected in accordance with the Data Protection Act 2018. All study data are coded and de-identified.

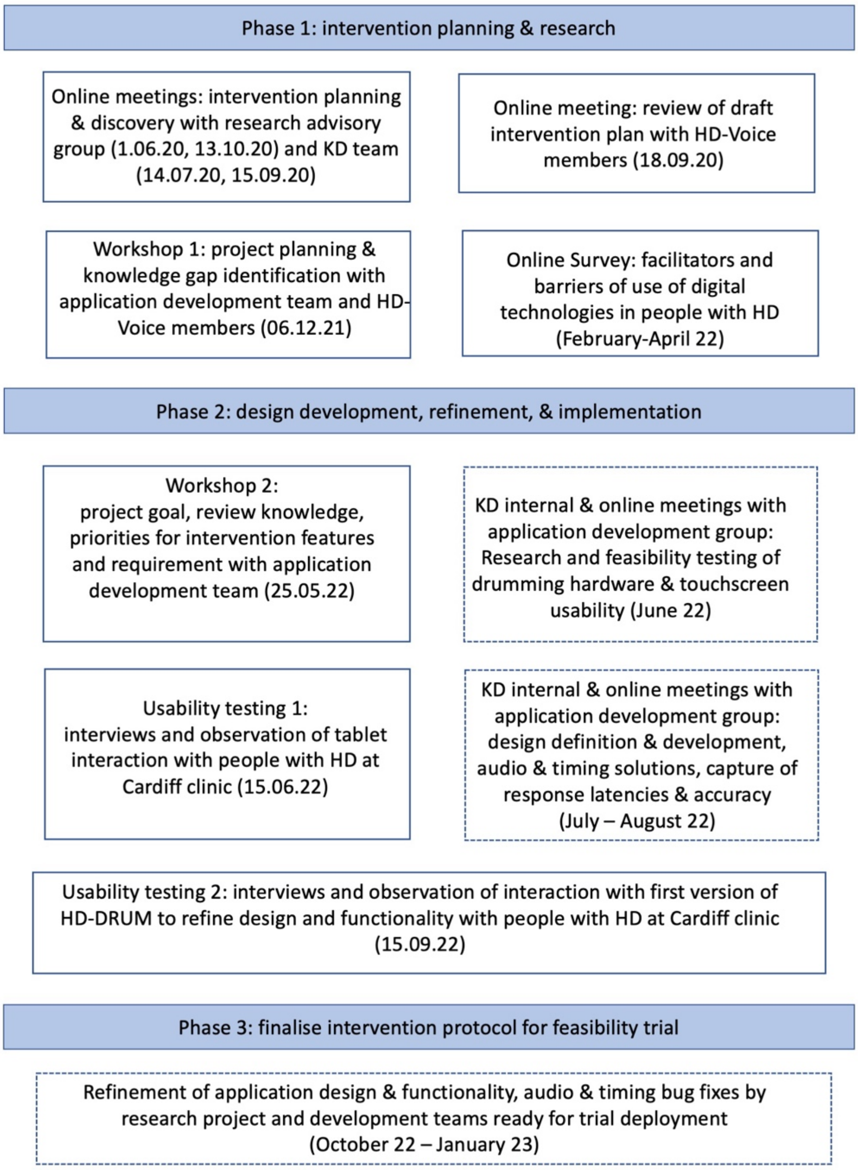

Figure 1. Overview of the integrated knowledge translation approach of the intervention development process. Abbreviations: HD = Huntington's Disease, KD = Kinneir Dufort.

Participants and Recruitment

For this study the following four groups were formed:

Application (app) development group
comprised of the lead researcher (CMB), the KD design and engineering team, and musician JCG. This was the core team that designed and built the HD-DRUM application in collaboration with the knowledge users and the research advisory group.

Research advisory and management group
comprised of an interdisciplinary team of researchers, experts, and clinicians working in the fields related to the project and research area. This group consisted of five researchers (CMB, AR, CD, MB, PP) with expertise in psychology, neuroscience, intervention development and evaluation, clinical trial methodology and statistics, and neurology. This group was

established prior to starting the IKT development process to help plan the intervention development, approach, research questions and outcome measures, and to monitor the progress of the project in line with milestones, on a monthly basis.

Knowledge user group
comprised of people affected by HD, including people with HD, their carers, and family members and clinical staff working in the HD field. Five people affected by HD were members of HD-Voice, the patient and public involvement group of the UK Huntington's Disease Association (HDA), a third sector support organisation. Twenty-nine individuals with HD were recruited *via* an advert in the HDA newsletter and participated in an online survey about facilitators and barriers of the use of digital technologies. Demographic information of age, gender, education, and disease stage for these participants was collected as part of the online survey. In addition, knowledge users were recruited for usability assessments from the Cardiff University HD clinic. Seven people participated in a usability assessment of tablet interactions in people with HD. These were four people with early to moderate manifest HD, two carers, and one clinician. Another four people with HD at various stages of disease progression (premanifest to manifest) and one member of the clinical staff took part in usability testing of the first version of the HD-DRUM app.

Research project team
comprised of three core research members responsible for running the feasibility trial into *HD-DRUM.* This group consists of the lead researcher (CMB), the postdoctoral research associate (VI) and PhD students and was established during the finalisation phase of the app development. Members of this group piloted and tested the app prior to trial deployment.

Intervention development

Phase 1: Intervention planning, research, and feasibility

Members of the research advisory group met virtually online and communicated via email to review an updated project plan based on the findings of the previous pilot studies[18, 19]. They discussed the research questions, the research approach, and outcome measures of the updated project in preparation for a funding application. In parallel, CMB engaged with the KD team to develop a road map for the design of the new intervention app that incorporated knowledge user engagement and iterative usability testing throughout the development process. The project plan was reviewed in an online meeting between the lead researcher and members of HD-Voice, who provided feedback on the feasibility of the planned intervention and research protocol in people with HD. To minimise participant burden and increase retention rates, it was suggested to shorten the originally proposed training duration of 6 months to 2 months and to limit assessments to before and after the intervention and at corresponding time points for the control group in the feasibility trial
. It was also suggested to develop a stand-alone application version for offline use to include those individuals without an internet connection in the research. This feedback was incorporated into the research protocol.

Once funding was secured for the project, the app development team met in a hybrid workshop with members of HD-Voice to review the project plan and to identify uncertainties and knowledge gaps that needed clarification prior to designing an app solution. Specifically, the need to gain an understanding of how people with HD use digital technologies, what barriers they encounter, and what design and functionality requirements needed to be met when designing and building the app was identified. Given the lack of evidence in the literature, we conducted an online survey into facilitators and barriers of use of digital technologies in people with HD.

Online survey into the use of digital technologies in people with HD

The survey consisted of 21 items and was delivered and analysed on Qualtrics (version 2022) [32]. Items included (i) the frequency of use of different digital devices (mobile phones/smartphones, tablet, computer/laptop) and the internet, (ii) the preferred digital device, (iii) the type of digital activities carried out (emails, social networking, buying goods/services, listening to music, downloading information, games, images, video calls), and (iv) how confident participants felt in conducting these activities as rated on a 5-points scale ranging from "not at all" to "very confident". Further, participants were asked to provide information as to whether they required any assistive technologies or accessibility settings and whether they had encountered any problems when using digital devices.

Phase 2: Design development, refinement, and implementation

At the start of this phase, the development team and a member of the research advisory group met to align all team members on the project goal, review and build knowledge including a discussion of the results of the on-line survey. In addition, prioritisation of various app components was discussed. The KD team then researched different options for hardware and software configurations suitable for a drumming application including drumming on a tablet touchscreen and drumming on connected or standard bongos. Direct drumming on touchscreens had the advantage of reducing costs, complexity, and technical risks (from additional circuitry and choice of audio transducers) but required usability testing with people with HD.

To assess the feasibility of tablet interactions in people with HD, we engaged with service users of the Cardiff based HD clinic. The freely available bongo drumming application *Congas & Bongos*[33] was installed on two different tablets of varying screen sizes: a 10inch Samsung Galaxy and a 12.9inch iPad Pro. For comparability purposes the "four and five finger swipe multi-tasking gesture" on the iPad Pro was deactivated prior to the test. Participants were approached in the clinic waiting room and encouraged to interact with the bongo drumming application on both tablets. The tablets were placed on a table in front of the participants. Participants were asked which screen size they preferred. The research team made notes of any feedback and suggestions from participants and any observations on how people interacted with the application.

The application development group then started the design process, which involved close collaboration between the KD team, JC who recorded the audio and timing content, and CMB who monitored alignment with project goals and specified requirements. Core elements of the development process concerned the application design, the implementation of its audio and timing features as well as response latency and accuracy capture. During the design definition and development phase, different design solutions were iteratively tested and refined internally by KD to ensure accessibility, functionality, usability, and delight. Different solutions for audio and timing specifications and latency capture were investigated and evaluated with regards to functionality, technical risk, and cost effectiveness.

The first version of the HD-DRUM application was then tested for its usability with people with HD in the Cardiff HD clinic. Usability testing took place in the waiting area of the

Cardiff HD clinic to refine the application design to the needs of people with HD by observing how participants interacted with the application and by gaining feedback and suggestions about what worked well and what needed to be improved. The tablet was placed in front of participants on a table sufficiently close to them so that they could reach the tablet comfortably and participants were encouraged to interact with the application. Researchers observed these interactions involving opening and navigating through the application and engaging with the first training sessions, made notes, and collated feedback.

Phase 3: Finalisation of the intervention protocol for feasibility trial

Design and functionality refinements based on the usability findings were implemented. The application was iteratively tested and corrected for any remaining bugs including audio and timing errors by the project research and development teams. The end result was the HD-DRUM application intervention outlined and described in Table 1.

RESULTS

Digital technologies survey

Participant demographics

Fifteen female and 14 male individuals over the age of 25 years (67% between 35 and 65 years) completed the survey anonymously (Figure 2). Half of those individuals were university-educated at undergraduate (21%) or postgraduate (31%) level including 7% with a doctoral degree. Of the remaining participants, 21% had A-level/BTECH, 14% GSCE, and 14% other educational/vocational qualifications. Most participants reported being at the premanifest (28%) or early disease stages (58%) while 14% reported middle or later stages.

Use of digital technologies, facilitators, and barriers

Figure 2 displays the main results of the online survey. Most participants (86%) reported using the internet on a daily basis (83% multiple times), and 7% used it once a week or once a month (Figure 2A).

The most popular devices were smartphones (55%) and tablets (31%) (Figure 2B) with most participants using them every day (86% for smartphones, 34% for tablets). PCs and laptops were used by 51% at least once a day, but only 10% preferred them over other devices.

Participants who used digital devices and the internet, engaged in a range of activities including sending/receiving emails, social networking, purchasing goods and service, reading the news, downloading games, images, films, news articles, playing music and participating in video calls (Figure 2B). Overall, the majority felt fairly or very confident in carrying out these activities ranging from 62% for downloading news and social networking to 81% for listening to online music (Figure 2C).

However, some participants reported that they never used a device (52% for tablet, 21% for PC/laptop, 10% for smartphone) and did not feel confident in carrying out the above activities (ranging from 4% for listening to online music to 10% for participating in video calls and social networking). In addition, 7% responded that they never used the internet. However, given that they responded to an internet based online questionnaire, perhaps they received assistance from carers, family members or friends in taking part in the survey.

While most individuals reported that they did not require any assistive technology or accessibility settings (82%), two participants mentioned that they used password reminders, and one participant that their spouse helped them with online banking. Some participants did not know what assistive technology was available.

Problems participants experienced when using digital technologies fell broadly into those related to cognitive, primarily attention and executive, deficits and those due to motor impairments (Supplementary Table). For instance, participants reported difficulties in understanding instructions, having to enlarge pages and taking a long time to find or not being able to find information or applications on their phone. Motor problems included difficulties with dexterity and grip when operating digital devices including problems with typing on a small keyboard, using a computer mouse, taking a long time to type, and accidentally clicking on incorrect information. These difficulties seemed to become apparent with advancing age and the development of clinical symptoms as all participants who reported barriers were at manifest disease stages.

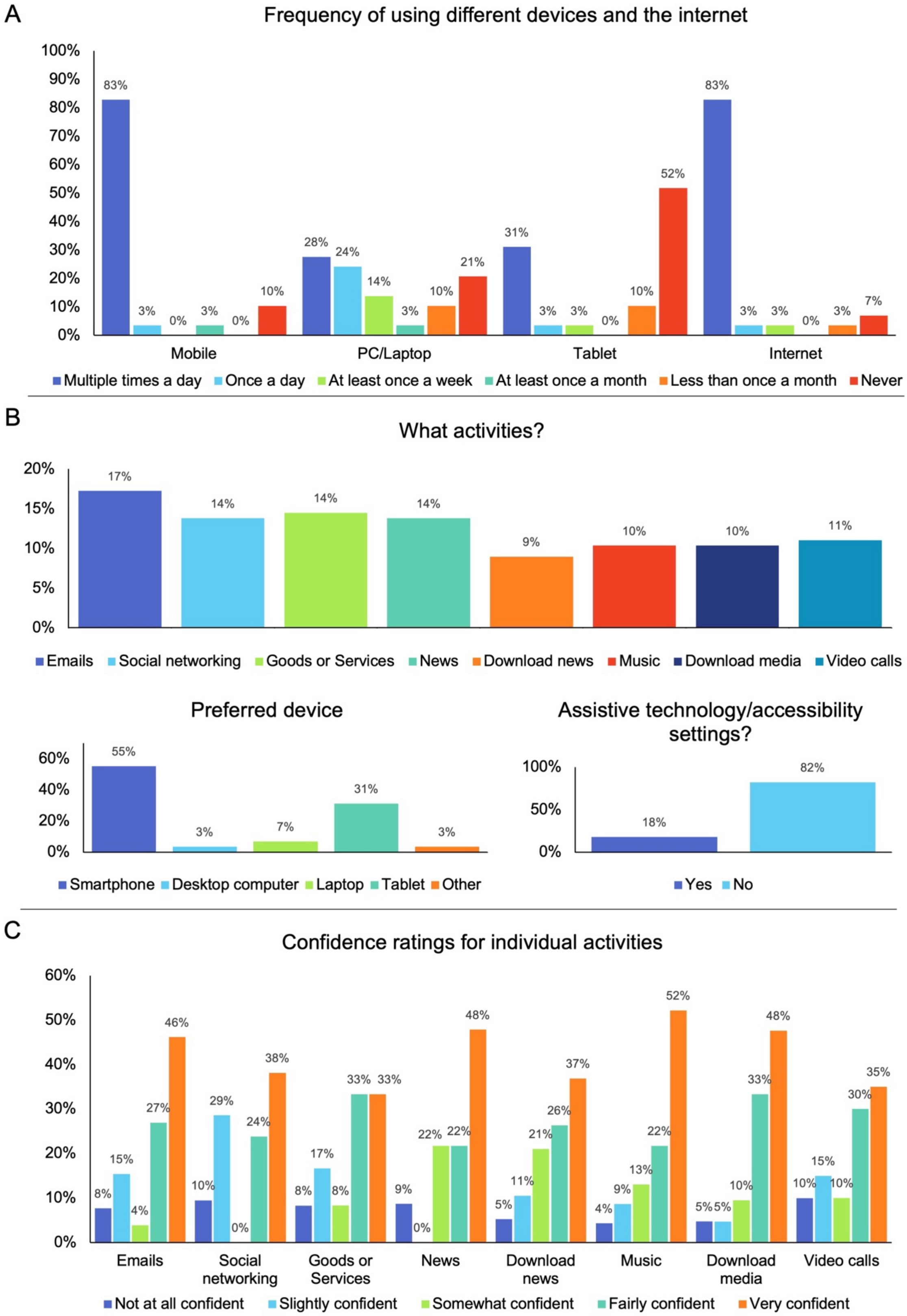

Figure 2 displays the main findings of the online digital technology survey from n = 29 individuals with Huntington's disease. A) Use of different devices, B) preferred device, what activities used for and requirement for accessibility settings, C) Confidence ratings for individual activities.

Summary and conclusion of survey results

In summary, the responses to our survey suggested that most participants were engaging with digital technologies and using smartphones, tablets, and PC/laptops for numerous online activities. However, the responses to our questions about problems with using applications identified some accessibility issues related to cognitive and motor problems, notably difficulties in understanding instructions and finding information, as well as difficulties with dexterity and grip that affected typing on a keyboard and using a mouse. These accessibility issues would need to be addressed in the application design for people with manifest HD.

Usability testing of tablet interactions in people with HD

We tested our assumption that interactions with tablet touch-screens of two different sizes were feasible for people with HD with people with HD at the Cardiff clinic.

Screen size and position

We found that both the large and small tablets performed well in terms of participants being able to tap on the virtual bongo drums. Participants did not indicate a preference for one or the other screen size. However, when asked some participants preferred the larger device due to a difference in screen and sound quality. Multiple participants said they own a tablet but not all were engaging with it. One participant who took part in the original bongo drumming pilot study said that they preferred the tablet to the physical bongos. More important than screen size was the placing of the tablets close enough for people to reach. Multiple participants moved the tablets closer to them because reaching too far out led to more mis-presses.

Interaction with the application

Participants used their index finger or index, middle, and ring fingers together to tap on the tablet. One participant with manifest HD alternated between one and multiple fingers due to limited ability to control the movement. For some people with manifest HD initiating the first tap appeared to require a lot of effort and concentration. However, once started the following interactions appeared easier. Some impulsive and perseverative responses were observed, i.e., the same tapping interaction was repeated with minimal control of speed or force. The audio feedback upon tapping on the virtual bongos was positively received. The application used showed drums in two different sizes, but it was agreed that this was not particularly necessary for our project. Multiple participants appeared joyful whilst playing and their body language demonstrated comfort when immersed in the drumming interaction.

Motivation and engagement

Multiple participants mentioned the need to gamify the application to maintain engagement. Some participants played computer games and stated that the application would have to be more engaging than games such as Solitaire. Multiple participants also mentioned the need to have music alongside the drumming to keep the training interesting and engaging. The use of headphones that could be plugged into the application was received well as it helped with more focus and would prevent family members from listening in or being bothered by the noise. A family member mentioned the potential mental health benefits of engaging in the drum playing. Multiple participants thought it would be helpful to be reminded to drum on the application as a method of engagement. Fifteen-minute sessions were generally accepted as a feasible length, but participants were hesitant to suggest this was a comfortable length of time. A participant discussed with their carer(s) that it would be fun to be able to play together, perhaps alongside other instruments.

Outcome of tablet usability testing

Successful drumming on the screen of both tablet sizes suggested that a tablet-based version of the application using virtual bongos would be feasible for use by people with HD. The smaller Samsung Galaxy 10inch was chosen as a more cost-effective and therefore accessible hardware solution than the iPad Pro. It was evident that provision of clear instructions regarding the tablet position on the table and the hand gesture used for tapping on the virtual drums (playing with the tips of index, middle, and ring fingers) to facilitate interaction with the application was important. User testing indicated the addition of reinforced screen protection and bumper cases for improved durability was necessary to mitigate difficulties with controlling the force and speed of tapping. Further, an element of gamification and positive feedback should be included in the application design as well as the playing to background music to keep the training engaging.

Usability testing of the HD-DRUM application

Usability testing of the first version of the HD-DRUM application was undertaken to gain feedback for refining the interface to ensure accessibility, functionality, usability, and delight.

Interaction with the application

A Samsung Galaxy 10inch tablet with the app installed was placed on a table in front of participants at a comfortable distance for them to tap on the tablet surface. Participants were asked to start the app from the tablet home screen by tapping on the HD-DRUM icon and to navigate through the app by scrolling through the training sessions and starting, pausing, and exiting them.

Participants were then encouraged to engage with the first training session. Each training session involved listening to audio instructions by musician Jimi (JCG) and tapping/drumming along to his instructions on two virtual drums on the tablet screen (Figure 3). When tapped the left drum, a blue triangle, produced a high-pitch bongo sound and the right drum, a red circle, a low pitch bongo sound. Participants were first instructed to distinguish these sounds and associate them with the left and right drum. They were then asked to synchronize their drumming movements as accurately as possible with the audio beats played by Jimi. To illustrate this, Jimi demonstrated audio examples of "accurate" (synchronised) and "not so accurate" (desynchronised) playing along. To help with the learning of the beats, Jimi provides additional left and right verbal cues as illustrated in the following transcribed example of the instruction for the first training session:

"Let's get started. With the left hand we are going to tap in all beats 1, 2, 3, and 4. Nice and slow. So only with your left hand, tap along with me on your left bongo, the triangle. Come on, let's start. *Audio left high-pitch bongo drumming starts and Jimi counts the beats*: 1, 2, 3, 4; 1, 2, 3, 4; 1, 2, 3, 4; 1, 2, 3, 4; left, left, left, left; left, left, left, left, 1, 2, 3, 4; 1, 2, 3, 4;1, 2, 3, 4; 1, 2, 3, 4 …. (for about 1 min).

Very good, now we are going to do the same thing, but I will not be calling out the numbers or say left or right. You just tap along with me on your left bongo. Ready? Let's go for it! *Audio left high-pitch bongo drumming starts and plays for about 1 min.*

Ok, now we will do the same thing but on the right hand. So first I will help you calling out the numbers and then you do it on your own. So now you will tap with your right hand only on your right circle bongo. Let's go for it. *Audio right low-pitch bongo drumming starts and Jimi instructs:* right, right, right, right; and right, right, right, right; and 1, 2, 3, 4; 1, 2, 3, 4; 1, 2, 3, 4; 1, 2, 3, 4; right, right, right, right ….. (for about 1 min).

Very good. Now without the voice just with the sound of the bongo with your right hand.

Audio right low-pitch bongo drumming starts and plays for about 1 min

Ok, now we are going to drum with both our hands. Left and right and left and right. To help you with the timing you will hear the sound of a high-hat such as this one (demonstrates high-hat sound) in between each beat. Let's go. *Audio left high-pitch, high-hat, right low-pitch bongo drumming starts:* Left, right, left, right, left, right (1 min).

Now we are doing this again for a bit longer without so much of my talking. Let's go for it! *Audio left high-pitch, high-hat, right low-pitch bongo drumming starts and plays for 1 min."*

Each training session consisted of a learning phase, such as the example given above, and a performance phase during which participants' performance accuracy was measured. Accurate responses were defined as responses on the target bongo drum within a prespecified time window around the target beat. Guided by the literature on finger tapping and simple and choice reaction time latencies in people with HD [34, 35], the first training sessions involved slow and regular target beats with a timing window of 1,000 milliseconds. Over the course of the 22 training sessions the duration of these timing windows was gradually reduced as the tempo of the target beats increased (see Table 1).

All participants were able to use the application and navigate through it. One participant with manifest HD required one-to-one instruction initially but then appeared to progress afterwards. Participants enjoyed the voice over by musician (JCG). Specifically, they found his instructions engaging and clear, and enjoyed the intonation of his voice, as an English speaker with a native Spanish accent, as illustrated by the following quote:

"I actually liked the voice. Easy to follow. Very clear…. I don't take auditory info very well, and for me it was ok to understand."

Participants also enjoyed the look and feel of the interface which was called "fresh, clean and clear'. Overall, participants appeared happy and joyful while interacting with the application.

All participants understood the task of drumming along to the audio instructions. Participants also seemed to understand the different expectations between training and performance parts of the intervention and were able to complete the performance sessions. A visual halo cue alongside auditory feedback seemed to help further identify the beat on which to drum; specifically expressed by some participants and simply observed in others. The addition of background music provided a good challenge for some participants, one of them noting that it made them concentrate more. The training session length of about 10-15 min was considered acceptable. Longer training sessions would not be acceptable.

Participants commented that they enjoyed the element of gamification by having to reach a certain success level to unlock the next training session and the positive feedback at the end of the session that congratulated them for having completed the session.

Refinements to the application content and instructions

Participants reported that the introduction session explaining how to use the application was too long and detailed with some confusion about whether they were supposed to drum along during the introduction or not. Therefore, the introduction session was shortened and made more focused and concise.

Some people with manifest HD found the first training rhythm of 65 beats per minute too fast as an introduction. They tended to tap on all 4 beats instead of the single beat as instructed. This seemed to have arisen due to a confusion and difficulty in distinguishing between the spoken metronome and target beat. In response, we included a slower session of less than 1 beat per second with regular tapping on all 4 beats without the metronome as the introductory session.

Participants predominantly used single fingers over flat hands and needed explicit instructions to tap on the virtual drums with a flat hand using all fingers together to mimic bongo drumming. To compensate for this, the instruction manual for the application includes detailed instructions on how to tap correctly. Participants will also receive face-to-face instructions and demonstration by the research team at the start as part of the intervention delivery.

Refinements to the application design

Home/session screen: When participants interacted with the session icons on the screen (Figure 3B), they expected that tapping on a full size, centred icon would start the session and that tapping on a minimized icon would scroll and centre that session instead of using the arrow and play buttons at the bottom of the screen. These functionalities were therefore added to the application design. The introduction session was not recognised as different content to the training session and was therefore made visually distinctive with an intro label. The session icon artwork was grouped in threes with regards to colour and shape to reflect the background track being the same for three sessions in a row.

Pause screen: The pause screen caused confusion and there was a risk of participants accidentally pressing “exit” or “restart” instead of “resume” and lose their progress as a result. Consequently, the design was changed to a more prominent (in size and location) resume button to reflect the fact that resume was the main action, and restart and exit were secondary action choices. Further, a confirmation step after pressing “restart” or “exit” was added to avoid users making these choices by mistake.

Drum and end of session screens: Static icons were replaced with dynamic ones to reflect the session that was playing and to allow the user to finish the session by either tapping the icon of the session just played, if this was to be repeated, or by tapping the icon of the newly unlocked session.

Summary

Overall participants were positive about the application design and the training content. They were able to navigate through the application and follow the audio instructions. They appreciated the visual halo cues and auditory feedback when tapping the virtual drum as well as playing along to background music and the gamification element of the application. However, some refinements to the design and functionality of the screen displays, the length and content of the introduction and the first training session, in addition to more detailed instructions with regards to the tapping responses were required to maximise accessibility, functionality, usability, and enjoyment of the app design.

Table 1. Description of the HD-DRUM application (version 1.0) intervention according to the TIDieR framework

Template for Intervention Description and Replication (TIDieR) item no	**Description**
1. Name/Description of intervention	
	HD-DRUM, a tablet-based drumming training application intervention aimed at stimulating cognitive and motor abilities in people with Huntington's disease (HD).
2. Why: Rationale, theory, goal(s)	
	Rational: Huntington's disease (HD) causes neurodegeneration in the basal ganglia leading to a progressive loss of cognitive and motor control. Drumming involves the learning of rhythmic motor sequences and our pilot research suggested benefits of bongo drumming on executive functions and on white matter microstructure in the corpus callosum and in pathways between the right supplementary motor area and putamen in people with HD [18, 19]. The holistic evaluation of the potential therapeutic benefits of drumming in HD requires a digital training solution that allows (i) the quantification of performance improvements and training engagement, (ii) the matching of the training difficulty to performance levels to avoid over- or underchallenge and (iii) scaling-up to reach a wider audience via delivery on tablets and/or smartphones. The HD-DRUM application has been designed to address these points and to meet the accessibility needs of people with HD.
3. & 4. What: Materials & Procedures	
	The HD-DRUM application has been programmed in native Android Java and runs on the Android operating system (version 21 or higher). The chosen hardware is a Samsung Galaxy Tab A8 with a 10.5inch screen (Figure 3A). A demonstration of the app is provided here [insert multi-media link here]. Participants are provided with the application on a tablet in a protective case and with a 17-page instruction manual. Participants start the application by tapping on the HD-DRUM icon on the tablet home screen. HD-DRUM consists of 23 audio recordings, one introduction and 22

	training sessions each 10-15 min long. Each training session introduces rhythmic patterns that are based on paradiddles (patterns where a single tap is followed by a double tap, for example, right tap, left tap, right tap, right tap, left tap, right tap, left tap, left tap) and different rhythmic styles including Hip-Hop, Funk, Samba, and Reggaeton (a form of dance music that originated in Puerto Rico and fuses Latin rhythms, dancehall and hip-hop/rap). Patterns are practised with and without a metronome and/or background music. The shape and colour of each session's identity is unique and reflect the session's rhythm and background track (Figure 3B). The first three sessions introduce slow and regular rhythms and are available to all users right from the beginning. Through the program the patterns then gradually increase in tempo and complexity with more target beats to hit, longer beat sequences, and more complex rhythms. After starting the application, the introduction and the first three sessions and any unlocked sessions are displayed on the HD-DRUM home screen and participants can scroll through them (Figure 3B). A session is active and can be started when its circle icon is displayed enlarged in the centre of the screen. A session can be started by either tapping on the session icon or by pressing the start button. When a drum session is opened, two virtual drums, a blue triangle and red circle appear in transparent colours on the screen and need to be tapped to start the audio instructions (Figure 3C). Alternatively, the start button can be pressed. Participants can pause the session at any time. When the session has been paused there are three options: resume, restart, or exit the session (Figure 3D). A bar on the top of the screen shows the participants how far they have progressed through the session. In each training session, participants are instructed to tap or drum along to the audio instructions on the two virtual drums (the blue triangle and the red circle) on the tablet screen. They are told to tap with the tips of all fingers simultaneously. The virtual drums mimic physical Bongo drums by producing visual (shrinking) and audio feedback (a high pitch bongo sound for the left triangle and a low pitch sound for the right circle) when tapped. In sessions 1-7 the rhythmic patterns are first practised with each hand separately and then with both hands together; after session 8 all patterns involve both hands and are practised starting with one hand and then in reverse order with the other. Each session consists of training and performance parts. During the training, participants learn and practice to tap

	along to a new rhythmic pattern. During performance parts, participants are asked to tap or drum along as accurately, i.e., as synchronised as possible with the recorded bongo sounds, while their response accuracy and latencies are recorded. To facilitate accurate performance while responses are recorded, drumming is guided by a visual halo cue that appears around the target drum when a hit is expected during performance parts only (Figure 3C). The interaction with each training session produces an output file in comma-separated format that is stored on the tablet and uploaded to a project-specific space on Google Firebase (https://firebase.google.com) when the tablet is connected to the internet. The output files contain a record of the latencies and accuracies of all tap responses and their mean statistics to quantify performance improvements and a time stamp including duration of training engagement to quantify adherence. Table 2 provides an overview of the data recorded and their intended objectives. HD-DRUM data collection complies with GDPR and data privacy regulations. No personal or identifiable user information are transmitted or stored on the tablet or on Google firebase. HD-DRUM output files are coded with a sixteen-digit-letter-string tablet ID. Firebase services encrypt data at rest and during transit using HTTPS. Each session audio file is accompanied by a Musical Instrument Digital Interface (MIDI) file that contains information about the timing of the audio drumming sounds. Accuracy levels are determined by comparing the time stamps of the sounds in the MIDI file with the recordings of participants' responses to the audio instructions. An accurate response in HD-DRUM is defined as a correct left or right-hand tap within a predefined, symmetrical time window around the expected hit stored in the MIDI file. Based on previous findings of simple and choice reaction times in HD [34] and our own usability testing in the Cardiff clinic, the largest time window for the slowest rhythmic pattern (less than 1 beat per second) in session 1 was set to 1,000 milliseconds, i.e., 500 milliseconds before and after the expected hit. Time windows were then gradually reduced with increasing tempo to 100 milliseconds (50 msec before and after expected hit) for rhythmic patterns with tempos over 100 beats per minutes (maximum 117 beats per minute).
5: Who provided	
	The Cardiff University research team provides participants with the application for home training.
6: How delivered	

	Participants engage with the training on an individual basis at home. If possible, family members and/or carers will be engaged to facilitate the training by providing a supportive environment.
7: Where delivered/required infrastructure	
	The stand-alone tablet-based training is delivered in participants' home. Participants are instructed to place the tablet flat on a table in front of them at a comfortable reaching distance. Internet connection is not required for training delivery.
8: When & how much	
	Participants are instructed to practice for ~10-15 min per day, 5 times per week, for 8 weeks.
9: Tailoring	
	The application includes an element of gamification such that from session 3 onwards, participants must reach an accuracy level of 70% or higher to unlock the next more difficult session. If their performance accuracy falls below this threshold, they are encouraged to repeat the session or practise one of the previous sessions. At the end of each session, participants receive positive feedback for either having completed the session (for accuracy levels below 70%), or for having unlocked the next session (for accuracy levels larger or equal 70%) (Figure 3E).
10: Modifications	
	The current version of HD-DRUM is a proof-of-concept prototype. The feasibility evaluation will inform future modifications to the application.
11: How well: Planned	
	Adherence with the training is remotely monitored by the research team via the output files that are generated during application engagement and uploaded onto Google Firebase when the tablet is connected to the internet. The research team monitors adherence and progression remotely and stays in weekly contact with participants via email, text, and/or phone calls.
12: How well: Actual	
	The feasibility assessments are on-going.

Table 2: Mapping of the data measured in HD-DRUM and their intended objectives.

Objectives	HD-DRUM variables measured
Quantification of performance improvements	
Low level tap events*	
	Left tap response latencies (milliseconds)
	Left tap response accuracies
	Right tap response latencies (milliseconds)
	Right tap response accuracies
Summary statistics	
	Mean tap response latency (milliseconds)
	Mean tap response accuracy
	Mean left tap response latency (milliseconds)
	Mean right tap response latency (milliseconds)
	Minimum (best) left tap response latency (milliseconds)
	Minimum (best) right tap response latency (milliseconds)
	Mean left tap response accuracy
	Mean right tap response accuracy
Quantification of adherence	
	Date and time of training engagement
	Duration of training engagement
Meta-data to quantify training session difficulty	
	Total number of target beats
	Duration of allowed time window (milliseconds) for hits
	Success accuracy threshold (%)

*Accurate responses are defined as correct left or right-hand taps within a predefined time window around the timestamp of the expected hit from the MIDI file. Accurate responses are recorded as “1” and incorrect responses, missed hits, or additional taps within a time window are recorded as “0” in the output file.

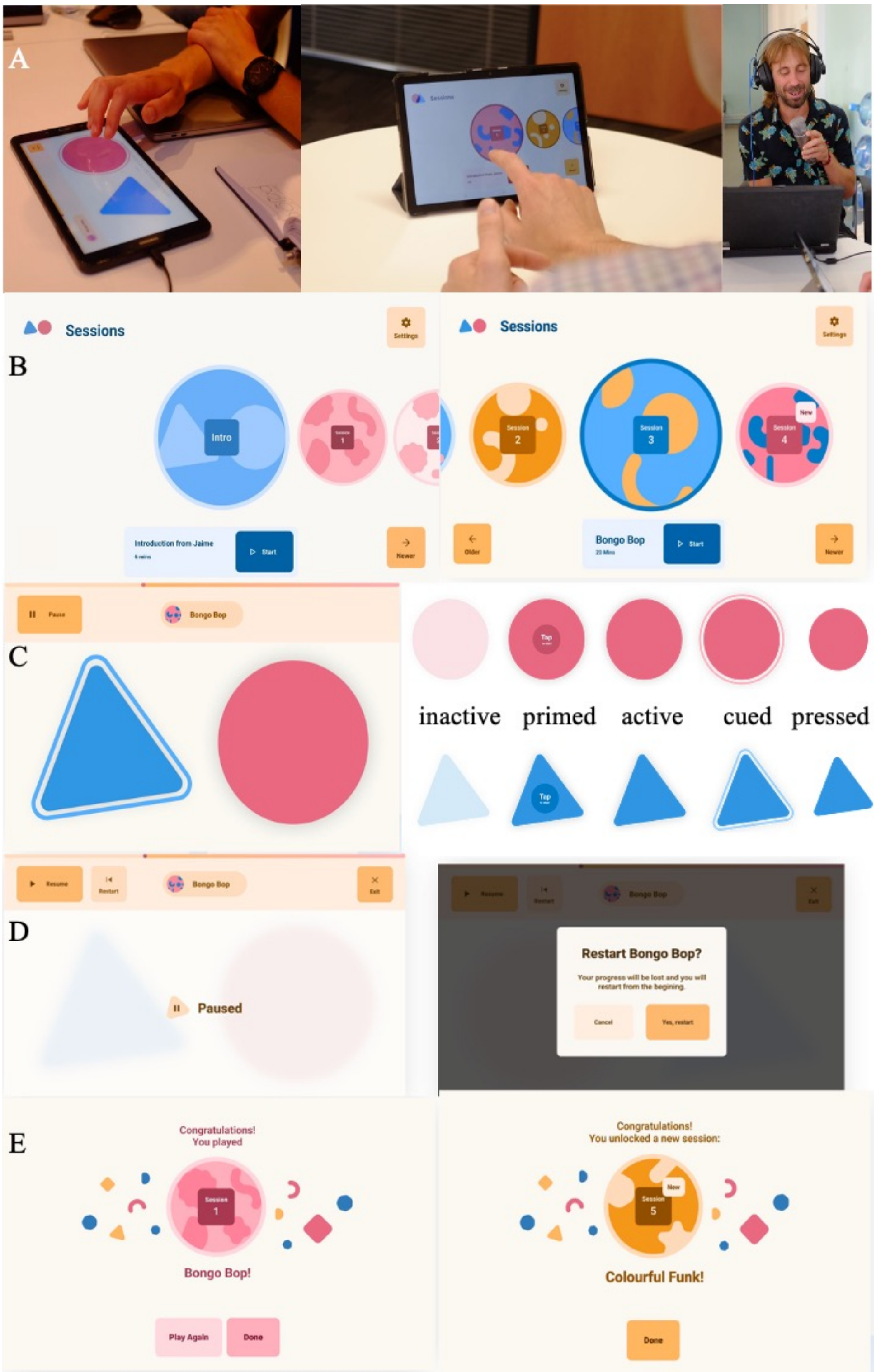

Figure 3 gives an overview of the HD-DRUM application design. A) The HD-DRUM application comprises 22 audio training session that were recorded by musician JC and runs on a Samsung Galaxy 8 tablet. B) The home screen displays the introduction and all unlocked training sessions. Users can scroll through and start sessions. C) The drum screen displays two virtual drums, a blue triangle and a red circle that respond with high and low pitch bongo sounds when tapped. A visual halo cues the expected hit during performance sessions. D) Training can be paused at any time. A confirmation screen appears when participants select restart or exit the session prior to completing it. E) At the end of each session user receive positive feedback congratulating them on having completed the session or for having unlocked the next session.

DISCUSSION

HD leads to a progressive decline in the control of executive and motor functions, largely due to atrophy in BG networks, with detrimental effects on a person's ability to function in everyday life [5]. Currently, there are no therapeutic interventions tailored to address executive and motor dysfunction in people with HD. Music-based therapies have been reported to benefit cognitive and motor functions in people with PD [13-15] and HD [12, 18, 19, 36]. It has been proposed that strong rhythmic beats may compensate for impaired BG-reliant timing and rhythm generation by providing external cues for the planning and execution of movements [16]. Music may also facilitate learning through rhythmic practices and the motivational aspects of musical rhythm [17]. However, the clinical effects of music-based interventions in people with HD and their neural mechanisms remain unknown due to a lack of evidence from high-quality clinical trials.

The objective of this research was the development of HD-DRUM, a tablet-based drumming training application intervention that uses rhythmic beats to stimulate BG-mediated cognitive and motor functions. HD-DRUM was developed to enable the objective evaluation of performance improvements and adherence in clinical trials and to address accessibility needs of people with HD in an engaging way.

For this purpose, we adopted an IKT-based co-design approach that involved knowledge user engagement in focus groups and iterative usability testing. The IKT process enabled an inter-disciplinary research team to engage with a design company, a musician, and knowledge users in a semi-formalised way to formulate, co-design, and refine the intervention application. By involving people with HD in the application development process, we were able to identify and address accessibility barriers and refine the design to maximise accessibility, functionality, usability, and enjoyment of the interactions with the interface. Co-design highlighted the importance of designing the application in a user-friendly and intuitive way with a focus on key functionalities to avoid cognitive overlad.

We started the research process by identifying knowledge gaps in the literature with regards to digital technology use and barriers in people with HD. Thus, we conducted an online survey to identify the accessibility needs that would need to be addressed in the design of the HD-DRUM application. Subsequent iterative usability testing informed about feasible and accessible hardware and software design solutions for people with HD.

The survey identified a number of accessibility issues associated with attention/executive and motor control impairments in HD, such as difficulties with finding information, navigating through applications as well as lacking the dexterity and fine motor control to type on keyboards and use computer mice to interact with applications. These difficulties were reported by individuals with manifest HD, hence appeared to become more apparent with disease progression and associated loss of executive functions and motor control in HD. Executive dysfunction may manifest as problems with focusing attention, distractor suppression, task-switching, planning, and problem-solving [4, 37, 38] that are known to interfere with everyday activities [39]. The reported problems also conform with the loss of fine motor abilities and the control of upper limb and hand movement in HD [40]. To the best of our knowledge, our survey provides the first report of how these clinical symptoms may affect the use of digital technologies in people with HD.

Based on these findings, we decided to implement the HD-DRUM application on tablets with touch-screens that do not require typing on a keyboard or using a mouse. Behavioural observations of participants' interactions with the touch-screens and the applications and their feedback from the usability testing were instrumental in the implementation of key features of the application. Usability testing confirmed that a touch-screen on a 10inch tablet was a feasible and accessible solution for people with HD from pre-manifest to manifest disease stages. The tablet solution allowed the implementation of virtual drums on the touch-screen to capture participants' responses (Figure 3). This solution addressed difficulties due to motor symptoms by facilitating easy navigation through the application by tapping on large and visually distinctive buttons (Figure 3). Accessibility issues due to attention problems and cognitive overload were addressed by keeping the design clean and simple, focusing only on key functionalities (scrolling through sessions, starting, pausing, resuming, exiting), and by having clear and concise audio instructions that were supported by a combination of audio and visual feedback (bongo sounds, shrinking drums), verbal instructions (left, right and counting), and visual halo cues training aids (Figure 3). Multi-modal learning cues were implemented based on evidence that cueing may help achieve better movement performance by compensating for attentional deficits [41, 42].

Further, elements of gamification by rewarding participants for reaching a learning target with unlocking the next training session and positive feedback at the end of each session were implemented to maintain motivation and engagement [43] . To keep the training varied and interesting, different rhythmic styles were chosen as training material and practised with and without background tracks or metronome beats (Table 2). Participants enjoyed these aspects of the training and thought that they would help with training adherence. These features that aim to maintain motivation and engagement may be of particular importance for people with HD who are affected by mood disturbances, apathy, and a lack of motivation.

The co-design development process resulted in the proof-of-concept HD-DRUM application that is described here according to TIDieR (Table 2) to provide details of the intervention's rational, key elements, design, and functionality for future replication. To the best of our knowledge HD-DRUM is the first tablet-based rhythmic training application developed with and for people with HD.

HD-DRUM addresses the methodological shortcomings of our previous pilot research into the feasibility of a bongo drumming intervention in people with HD [18, 19].

The implementation of the bongo drumming intervention as a digital tablet-based application allows the quantification of performance improvements by recording the latencies and accuracies of participants' tapping responses on the virtual drums. Further, adherence to the training is quantified by recording the frequency and duration of participants' engagement with the application. This allows the objective assessment of the feasibility of using HD-DRUM at home.

Based on knowledge user's feedback, participants' performance levels were matched to the training difficulty by means of gamification, such that a success criterion of 70% accuracy [44] needed to be reached before the next training session can be unlocked. Matching users practise to a level appropriate to their abilities is expected to increase acceptability of the intervention by avoiding frustration and boredom due to over- and underchallenge.

Further, the tablet-based application format of the training that can be used for home practice, has the potential for widening accessibility and increased scale of use and hence will allow the scaling up of sample sizes in future randomised controlled trials.

These features of the HD-DRUM application allow for the objective assessment of the feasibility and the clinical effects of the training in a controlled clinical trial. This will enable researchers to address the lack of evidence from high-quality randomised controlled trials into the clinical effects and efficacy of this type of neurologic music therapy.

HD-DRUM is currently deployed in a randomised controlled trial to assess the feasibility of 2 months of at home HD-DRUM intervention compared to usual-activity control in people with HD. Adopting the IKT framework enabled us to design the HD-DRUM application in a way that maximises the possibility of success of the trial by taking the needs of people with HD into account during the development process.

It is important to note some limitations of the here adopted co-design development process approach. Only a small group of people with HD, albeit at different disease stages, took part in the usability testing. Their feedback may not be representative and may not address the accessibility needs of all people with HD. Similarly, conducting an on-line survey about the use of digital devices and accessibility barriers will have been biased towards those individuals who were able to use the internet in the first place. The percentage of the population of people with HD that we did not reach with this type of survey is not known to us. A more inclusive way of reaching a representative sample of people with HD may be by asking participants to fill in the survey at their clinic visit or posting it to their homes.

With regards to the developed proof-of-concept HD-DRUM application, tapping on virtual drums may not provide the full sensory experience of drumming on real bongo drums, and may perhaps be less effective than playing on a real instrument. Similarly, individual training at home may be less effective as engaging in a drumming circle because it lacks the benefits of social contact and the experience of producing music together. On the other hand, the application delivery may make the training more accessible to individuals wo are not mobile and cannot attend a social music gathering. The challenge lies in balancing the need for an intervention that allows evaluation of performance improvements under controlled conditions with capturing the multiple mechanisms that may underlie the benefits of music-based interventions.

The findings of the feasibility study may help to address some of these questions and may shape future modifications and refinements of HD-DRUM. In the future, HD-DRUM may be able to provide a remotely accessible training tool to help maintain or improve movement and cognition in people with HD without the risk of harmful side-effects. It may also be feasible in the future to combine novel disease-modifying therapies for HD with behavioural interventions such as HD-DRUM to maximise therapeutic outcomes. Even a small delay in the onset of symptoms would have direct and significant benefits for the quality of life of people with HD and their families.

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DATA AVAILABILITY

The data sets generated during and/or analyzed during this study are not publicly available to protect participants' privacy and confidentiality due to the small number of participants and the rarity of Huntington's disease but are available from the corresponding author on reasonable request.

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