The Feasibility and Acceptability of using a Novel Wrist Worn Cueing Device to Self-Manage Drooling Problems in People with Parkinson's Disease: a Pilot Study

Journal:	*RATE Journal*
Manuscript ID	RATE-18-0022.R2
Manuscript Type:	Original Manuscript
Date Submitted by the Author:	16-Apr-2019
Complete List of Authors:	McNaney, Roisin; university of Bristol, SCEEM Miller, Prof Nick; Newcastle University, Institute of Health and Society Vines, John; Northumbria University, School of Design Olivier, Patrick; University of Newcastle, School of Computing Science Ladha, Karim; Newcastle University, School of Computing Science Jackson, Daniel; University of Newcastle, School of Computing Science Walker, Richard; University of Newcastle, Institute of Health and Society
Keywords:	Assistive Technology, Human Factors, Rehabilitation Devices, Self Care, Therapeutic Value
Abstract:	Introduction: Daytime drooling is experienced by around 50% of Parkinson's patients, who fail to swallow saliva in sufficient volume or regularity, despite normal production. This research explored the feasibility and acceptability of using a cueing device, to improve drooling. Methods: During a 4-week intervention, 28 participants were asked to use a cueing device for one hour per day. During this time, the device vibrated once-per-minute, reminding the participant to swallow their saliva. A daily diary was used to collect self-report around swallowing severity, frequency and duration. This was filled out by participants for 1 week before, 4 weeks during, and for 1 week immediately after intervention. Diaries were also collected for 1 week during a follow up, carried out 4 weeks after intervention finished. Results: Participants self-reported benefits in drooling severity ($p=0.031$), frequency ($p=<0.001$), and duration ($p=0.001$) after using the device. Improvements were maintained at follow up. Twenty-two participants explicitly reported a positive benefit to their drooling during exit interview. All felt the intervention and device were acceptable and usable. Conclusions: Using a cueing device for 1 month had perceived benefit to drooling severity, frequency and duration in patients with Parkinson's. Participants accepted the device and treatment protocol.

The Feasibility and Acceptability of using a Novel Wrist Worn Cueing Device to Self-Manage Drooling Problems in People with Parkinson's Disease: A Pilot Study

Introduction

Sialorrhoea, also ~~termed~~ termed drooling or ptyalism, is reported as a ~~significant~~ common symptom of Parkinson's. In some studies, drooling is reported to be an issue in up to 70% of participants, especially if one takes into account nocturnal drooling and increasing severity of Parkinson's [1-4]. Saliva is vital for good oral health. Impaired production of, or loss of saliva through drooling exposes individuals to a range of negative effects, from mild annoyance at perceived lack or excess of saliva in the mouth, to major health and psycho-social issues. Saliva helps regulate oral pH and microbiotic homeostasis [5]. The antimicrobial, anti-viral and anti-fungal properties of saliva aid oral cleansing, protect against infection and support tissue repair. Saliva serves as a buffer against noxious substances. It lubricates the oral cavity, thereby supporting formation and transport of the food bolus to the pharynx for swallowing. It acts as a first stage in digestion and stimulates interaction with chemosensory receptors to aid taste and smell perception. It supports smooth movement of the tongue and lips for speech. If saliva is lost through drooling the person with Parkinson's (pwPD) is at risk of lowered resistance to infection, poor oral health, and added problems with swallowing and speech. Dry mouth – a common consequence of saliva loss – is associated with risks of ulceration, tooth decay, gingivitis, candidiasis, halitosis and perioral dermatological issues [6, 7]. In many societies the effects of drooling (e.g. odor, stained clothes, constant wiping) are socially frowned upon. In this

way drooling may influence psycho-social health for the pwPD and produce an added burden for the carer (e.g. washing clothes; restricted social life) [8-10].

In Parkinson's ~~, with over half of all individuals reporting diurnal (daytime) drooling [1]—a figure which rises even further when nocturnal drooling is taken into account [2].~~ d~~D~~rooling is associated not with excess production of saliva, but principally with muscle rigidity and bradykinesia of the facial, tongue and lip muscles [11-13]. PwPD who experience drooling fail to swallow saliva in sufficient volume or regularity, despite a normal amount of saliva production [11, 12]. This leads to pooling of saliva in the mouth and risk of anterior loss. In addition to the impaired swallow mechanism in Parkinson's, the dysautonomia associated with the condition, as well as changes in sensory perception of food that affect salivation (smell, taste, vision) may complicate the picture [5, 7]. Cognitive factors may also play a role. ~~in the oral and pharyngeal structures [1] leading to pooling of saliva in the mouth. People experiencing drooling issues fail to swallow saliva in sufficient volume or regularity, despite a normal amount of saliva production. Nóbrega et al. [1], using modified barium swallow with videofluoroscopy and a drooling score, showed changes in the oral stage of swallowing in 100% of people experiencing drooling problems (n=16), and in the pharyngeal stage in 94% of patients. They also found a correlation between drooling severity and swallowing problems (dysphagia). People with the worst dysphagia had the worst drooling. In Edwards et al [3], self-reported drooling was a problem in 70% of people with Parkinson's, in both the later stages and early stages of the disease. In addition, a 2017 study by~~ Reynolds, Miller and Walker [14], found an association between swallowing frequency and drooling severity, in particular during states of distraction.

Most current pharmaceutical treatments for drooling in Parkinson's aim to decrease saliva production. However, there are potential complications associated with their use.

Firstly, as mentioned previously, lack of saliva can cause oral health problems (e.g. gingivitis, tooth destruction, tongue crusting) [155]. Secondly, ~~the use of~~ drug treatments such as s~~S~~ublingual a~~A~~tropine can lead to serious cognitive side effects, such as memory impairment and/or hallucinations [166]. Botulinum toxin injection into the salivary glands can be painful and must be repeated every three to six months. In addition, ~~i~~this carries some risk of masseter and pharyngeal muscle weakness that can both impact on chewing and swallowing. Meningaud et al. [155] extensively reviewed the modalities of treatment for drooling problems and maintained that it is important to propose, where feasible, non-invasive treatment options, such as behavioral cueing methods, before drug or surgical therapy is considered. Recent major guidelines underline the importance of this strategy [17].~~therapy is considered.~~

Cueing has been employed to successfully improve aspects of impaired activities in Parkinson's, ~~for aspects of Parkinson's~~ such as gait~~, has been used successfully in the past~~ [18-21~~7 10~~]. Cueing generally relies on the implementation of a system of temporal cues, where participants are provided with time-controlled auditory or haptic prompts to ~~change their~~instigate or modify a behavior.

The concept of temporal cueing as a treatment for drooling has been built on previous work, which has shown success ~~in the domain~~ of cueing, ~~-~~for example in gait training for Parkinson's [18]. The belief is that ~~It is built upon observations that~~ the training of a metronomic cue brings about the execution of a new motor plan, which facilitates walking and suppresses the impaired motor plan currently inhibiting the intended movement [19-21]. There is a level of automaticity in the complex movements of both walking and swallowing of saliva that link these two symptoms together and allow for cross

comparison of motor theory. Both are triggered, patterned responses involving automated neural processes that generally do not require conscious thinking for carrying out the activity. However, in the case of Parkinson's, these automatic movements can become impeded when difficulties with motor initiation arise. In terms of neurophysiology, cueing is believed to suppress pathological basal ganglia activity through activation of corticostriatal pathways [19]. That is to say, the cue causes the initiation of an alternative pathway in the brain, also linked to motor activity, which brings about the initiation of movement that has been halted.

The feasibility of cue provision to improve drooling has been minimally studied. Marks et al [2211], used a (now) commercially available device, in the form of a brooch, which emitted an auditory cue (a short 'beep') at regular intervals to remind the wearer to swallow. They found this yielded positive results for participants (n=6). Although the device was found to be effective for the control of drooling problems, their small sample size did not provide sufficient information around the effectiveness of the intervention on a wider population of people with Parkinson's, nor did the authors discuss the acceptability of the technology they trialed with their participants. A further study by Marron et al. [2312] showed that wearers of the same drooling brooch reported several aspects that reduced its acceptability. For example, hearing impaired participants could not use the device, yet the auditory cue was also a source for concern for others due toin the environment, since the beep attracteding attention when worn, drawing into question its social acceptability. The product used also incorporated a switch to turn the device on and off. S, which some users required assistance to operate this due to their impaired fine motor skills. degeneration resulting from Parkinson's.

In response to these drawbacks, we developed a simple-to-use wrist-worn digital cueing device, the PDCue (figure 1). This was iteratively designed with pwPD ~~People with Parkinson's~~ and their caregivers ~~in our previous work~~ [24~~13~~]. This early study established usability and motor and social acceptability of the device we employed~~;~~ that it was usable even by individuals with marked fine motor and sensory difficulties; and that a vibratory cue was preferable to an auditory cue [24~~13~~]. The device delivers a silent vibratory cue, once per minute when switched on, to remind the person to swallow. The once per minute setting was decided upon in accordance with previous research which established daytime non-stimulated swallowing frequency in healthy adults of around one swallow per minute [25]. This was also ~~The once per minute setting was decided upon in accordance with previous research around swallowing frequency in healthy adults (1.32 swallows per minute) [14] and was~~ the preferred interval selected by Marron et al [[23~~12~~] in their study. There is, as yet, no literature relating to the swallowing rate of ~~people with Parkinson's~~pwPD.

The purpose of ~~this~~ the pilot study presented herein ~~this paper~~ was to explore the feasibility and acceptability of using this novel cueing device to help ~~people with Parkinson's~~pwPD to self-manage their drooling, and to establish whether there was evidence of an effect on drooling severity and frequency when wearing the PDCue. We also wanted to explore some practicalities relating to recruitment and retention of participants into the study, and how appropriate our outcomes measures were, in order to inform the trial design of any larger scale studies which might arise.

Figure 1 about here

Methods

Experimental Design

This study employed quantitative methods to examine for possible effects of the cueing device on perceived drooling severity and frequency. It used qualitative methods (semi-structured exit interview) to establish opinions of participants on the acceptability and feasibility of the intervention program, and experiences of using the PDCue.~~a repeated measures design and looked at both between and within group differences. It first looked at a 2 (immediate vs delayed intervention groups) x 2 (measure times: first and second assessment point) design; then a 1 (all participants together once all had received intervention) x 3 (measure times: pre, post and 1 month after intervention) design (see fig 2 below). The study was approved by the Newcastle and North Tyneside National Research Ethics Service Committee (reference: 11/NE/0257). Informed written consent was obtained from all participants in the study. All study data were collected by employees of Northumbria Healthcare NHS Foundation Trust, who were responsible for the organization of the project.~~

Participants and Recruitment

The study was approved by the Newcastle and North Tyneside National Research Ethics Service Committee (reference: 11/NE/0257). Informed written consent was obtained from all participants in the study. All study data were collected by employees of Northumbria Healthcare NHS Foundation Trust, who were responsible for the organization of the project.

Participants were primarily recruited via the regular Parkinson's clinics at Northumbria Healthcare NHS Foundation Trust, but participants from Participant Identification Centers in

Sunderland, Gateshead and Newcastle were also included. Potential participants were identified by clinical staff and then contacted by a researcher via telephone with further information. Written information sheets were then sent to those who expressed sustained interest and, following a 1-week period, participants were visited in their homes to obtain informed consent.

Inclusion criteria were (1) anyone with a diagnosis of Idiopathic Parkinson's (stages I-III in Hoehn and Yahr scale [26~~15~~]), in accordance with the UK Parkinson's Brain Bank criteria [27~~16~~], (2) an acknowledged daytime drooling problem, either observed by a clinical professional within a Parkinson's disease clinic or through patient self-report, and (3) an ability to understand and respond to the instructions given in the study. Exclusion criteria were (1) currently receiving pharmaceutical treatment for drooling, (2) insufficient dexterity with which to use the device.

A full case history was taken from each participant regarding their Parkinson's, drooling, and history of swallowing difficulties. The Mini Mental State Exam [28] and Montreal Cognitive Assessment Test were conducted for screening purposes of cognitive impairment [29~~17~~]. The Unified Parkinson's Disease Rating Scales II and III [30~~18~~] were conducted to gain an indication of overall disease state. All assessments were performed by the same researcher in the participant's own home.

Participants were randomly allocated to either an immediate intervention group (n=17) or a delayed intervention group (n=11). This was to provide preliminary data for comparison of treatment vs no-treatment. The delayed group did not commence intervention until after they had completed a four-week period of no intervention. The randomization protocol was pre-determined using an online random number generator (https://www.randomizer.org/). The numbers were arranged into consecutive order

creating a sequence for randomizing individuals (e.g. 1- immediate, 2-immediate, 3-delayed). If a participant left the study, their group assignment (immediate or delayed) was added to the end of this list to be filled by later recruits. We aimed for a 1:1 ratio, with a target recruitment of 30 participants (15 in each group). We fulfilled the capacity of the intervention group, but time restrictions meant that we were unable to complete a delayed start for the final two participants we had recruited. As such, we entered them into the intervention group leaving final numbers of 17 immediate and 11 delayed participants. This is a limitation of the study and is discussed further in the limitations section.

Measurements

The ~~Parkinson's Disease Questionnaire (PDQ-39) subtests for wellbeing, stigma and communication [19]; the~~ 'saliva' subset of questions from the Radboud Oral Motor Inventory for Parkinson's Disease (ROMP-Saliva) [31~~20~~],~~;~~ and the Unified Parkinson's Disease Rating Scale (UPDRS) 2.2. subtest for saliva [30~~18~~] were conducted with each participant at: one week before commencing use of the cueing intervention (assessment point 1), one week immediately after finishing the intervention (assessment point 2), and four weeks later at a follow up appointment (assessment point 3). For participants in the delayed start group, an additional ~~baseline~~ assessment was collected 4 weeks prior to the immediately pre-treatment assessment (assessment point 0). Figure 2 illustrates the time line.

Figure 2 about here

ROMP-S is a validated tool [31] for use with pwPD. It is derived from the unvalidated Drooling Frequency and Severity Scale (DFSS) [32] originally drawn up for children with cerebral palsy but employed in several other populations. It was slightly modified for ROMP-S, in particular by adding the option to score that one is troubled by (perceived) accumulation of saliva without actually drooling. The nine items, rated on 5-point ordinal scales that describe gradations of drooling activity, cover day and night-time frequency and severity of drooling, effects on speech and eating and drinking, how frequently one has to wipe away saliva, limitations on daily activity and social participation, and overall impact.

UPDRS item 2.2. is a 5 point descriptive ordinal scale ranging from 0-4; no drooling (0), excess saliva but no loss (1), nighttime but not awake drooling (2), awake drooling but wiping not necessary (3), severe drooling with constant wiping/wet clothes (4). ~~was collected 4 weeks prior to assessment point 1 (assessment point 0) and was immediately followed by a 4-week period of no intervention.~~

At each assessment point, participants completed a 7-day drooling severity, frequency and duration diary ~~[21]~~. Participants monitored their drooling over the course of one self-selected hour per day when~~that~~ they would typically drool (e.g. after meal times, in the morning). Following Hauser et al (2004) [33] participants completed 100 mm visual analogue scales (VASs). They placed a cross on a 100mm line ~~Participants placed a cross on a 100mm line~~ (with 0mm being 'no problem' and 100mm being 'as bad as can be') to indicate the number of separate incidents they felt that drooling occurred (frequency), how long in minutes they felt drooling occurred (duration), and how severe they felt drooling was (severity). This method reflects standardized methods of monitoring using paper diaries employed in other medical research (e.g. [34, 35~~22, 24~~]). ~~This same diary was then used to~~

~~collect daily self-report from participants during the 4-week intervention period. A visualization of this assessment schedule can be viewed in figure 2.~~

~~Figure 2 about here~~

Finally, an exit interview was carried out with each individual to gather qualitative feedback on the participants' experiences. A semi-structured approach was taken to probe; a) experiences of drooling before taking part in the study; b) experiences of drooling after taking part in the study; and c) perceptions around the acceptability, worthwhileness and effectiveness of the PDCue as a way to self-manage their drooling.

Intervention

All participants were visited at home and received a verbal and practical tutorial on how to use the cueing device. They were asked to use the device for one hour a day, for a total of four weeks, at a time when drooling was an issue for them. Participants were asked to not use the device during the hour that they were self-reporting their drooling on the daily diary.

Data Processing and Analysis

Quantitative d~~D~~ata were analyzed using the IBM SPSS statistical software suite (v.22, IBM Corp, Armonk, NY). For data collected at the ordinal, interval or ratio level, normality of distribution was checked by inspection of histograms and using the Shapiro-Wilk and Kolmogorov-Smirnov tests [36~~23~~]. ~~None of the variables examined were considered normally distributed.~~ Data were summarized using statistics appropriate to the level of the data (e.g. median, inter-quartile range, frequency). In inferential analysis, the Wilcoxon signed ranks test or Mann-Whitney U test was applied to ordinal, interval or ratio data and the Chi-squared test to categorical data. For analysis across all 28 participants of change in scores from pre- to post-treatment (assessment points 1 and 2), and from pre-treatment to follow-up (assessment points 1 and 3) for the same variable, the Bonferroni correction was applied, setting significance at 2.5%. For all other inferential tests significance was set at 5%. Two-tailed tests were used throughout. A repeated measures design looked at both between (delayed intervention versus immediate intervention) and within group ~~differences~~differences, (all participants combined to compare baseline pre-treatment, termination of treatment and follow-up outcomes).

Qualitative data collected during the exit interviews were audio recorded and transcribed verbatim. Transcriptions were then subjected to an inductive thematic analysis using methods drawn from Braun and Clarke (2006) [37]. Data was summarized with short, one or two word codes, at the sentence-to-paragraph level. Codes were then compared to one-another and grouped, which led to the construction of broader themes that captured the core topics and concerns emerging from the data.~~.~~

Results

Fifty-eight participants were identified for potential inclusion. Twenty of these chose not to join (due to reasons such as not feeling drooling was severe enough; not having time to commit to research). Thirty-eight consented to participate. During the trial ten participants left the study. Five stated reasons of ill health, four felt the study was too much for them to manage at the time, and one gave no reason. The data analyzed came from the twenty-eight remaining participants (ten female). Compliance levels for filling out diaries varied. Out of a possible 6,699 diary entries 5,069 (76%) were provided. The demographic and case history information can be viewed in Table 1. No significant biases were observed between the two groups with regard to any of the variables investigated.

Table 1 about here

Intervention vs no intervention

Results for the first and second assessments with the no-intervention group, and assessments for the immediate intervention group before and at end of intervention, appear in table 2. There were no statistically significant differences between the immediate and delayed intervention groups at the initial baseline assessment. There were no significant changes in ROMP-S, UPDRS 2.2 or Diary reports (VAS measurements) for the no-intervention group during the 4 weeks of no treatment. There were also no statistically significant changes to ROMP-S and UPDRS 2.2 in the intervention group when comparing pre- versus termination of treatment. Patient perceived changes on the VASs did show significant improvement in the intervention group for overall severity, but for frequency of

drooling improvement was borderline (p=0.06) and perceived amount of time (duration) of drooling did not alter significantly.

~~Table 2 presents data for the delayed start (at assessment points 0 and 1) and immediate start (at assessment points 1 and 2); representing a period of no intervention for the delayed start group and intervention for the immediate start group. The difference between the two groups in change from baseline score are compared across the outcomes investigated. Only the change in drooling severity from the diaries was significantly different between the two groups; this increased (i.e. got better) for the intervention group but stayed the same for the no intervention group.~~

Table 2 about here

Comparison of pre- and post-treatment scores across all participants

Given that there appeared to be no placebo effect in the delayed intervention group during the no intervention phase (i.e. no significant improvement in any scores), once both groups had completed intervention their scores were combined to provide a larger group (n=28) for comparison of pre- versus post treatment versus follow-up assessment

Between treatment termination and four week follow-up assessment four participants left the study (two moved on to Botox treatment immediately after the intervention ended, one experienced significant health decline and one moved abroad). This left 24 participants available for longer-term follow-up assessment comparisons. Outcomes are summarized in table 3.

~~We compared measures before vs after intervention vs at follow-up for all 28 participants (assessment points 1, 2 and 3 respectively). Twenty-four participants were available for~~

~~follow-up assessment one month following completion of the intervention. Of the other four, two moved on to Botox treatment immediately after the intervention ended, one experienced significant health decline and one moved abroad. Outcomes are summarized in table 3. There were significant improvements as measured by the Unified Parkinson's Disease Rating Scale item for drooling and saliva from pre-treatment to follow-up, and from the self-reported diary for drooling severity (from pre-treatment to follow-up), frequency (pre-treatment to post treatment, and pre-treatment to follow-up) and duration (pre-treatment to post treatment, and pre-treatment to follow-up).~~

Table 3 about here

ROMP-S ratings saw no significant change comparing scores at pre- versus at termination of treatment. UPDRS 2.2. ratings showed a trend towards significance but were still statistically non-significant. VAS patient perceptions of change in overall severity, duration and frequency of drooling all evidenced significant improvements.

To examine whether scores returned to baseline status once intervention finished, baseline scores were compared with four weeks post treatment assessments. ROMP-S demonstrated a move towards significance (but was still not statistically significant), whilst UPDRS 2.2. now showed a significantly better status. The VAS ratings all showed strongly significant improvements, including after adjustments for multiple testing. The findings suggest maintenance or even improvement of status during the follow-up phase.

Exit interviews

Twenty-seven participants were available for exit interview. One participant had a significant health decline and was thus unavailable. Interviews lasted ~~a~~mean~~n~~ ~~average of~~ 17:03 minutes (shortest 6:29-longest 36:37). Following procedures outlined in the methodology section, ~~There were a total of~~ 26 thematic codes applied to the data. A total of 312 extracts of transcript were assigned these codes (ranging from 1 to 22 extracts per code). A total of 4~~5~~ higher level themes were then constructed from this qualitative data analysis, which ~~will be~~are summarised below.

The first theme to arise was the impact of drooling on the lives of the participants. By far, the most discussed impact of drooling issues pre-treatment was embarrassment (13/27), with several participants discussing emotional distress *"It really dominated my life…it was most distressing, psychologically distressing…it clearly ruled my thinking…in that I was always clasping this grubby handkerchief just in case"* (P14), and social withdraw, *"At least once a day it would happen. I was out with company and it made me feel very embarrassed. I tend to withdraw, avoid going out really. Eat on my own. I am pretty strict about manners, and I thought it looked horrible"* (P12). Several participants (4/27) also discussed physical discomfort that they experienced—constant wetness, changing of handkerchiefs, painful sores around the mouth.

The second theme related to challenges around previous experiences of drooling treatment. Several participants (3/27) had previous experience of Botox, however, for a lot of participants (8/27), Botox was not an option they would have considered. These participants discuss a lack of willingness to take additional medication; *"when I saw the consultant they said I could go and have Botox, an injection. I didn't want to take any more drugs"* (P22). Botox was associated with words such as *"toxic"* (P25) and *"poison"* (P26) and there was a clear preference for avoiding it, and other additional medication, if possible; *"I*

think if you can have something that avoids taking drugs I think that's great" (P4). These participants, unsurprisingly, preferred the PDCue as a behavioural treatment option; *"I'd rather have the watch"* (CP7).

Theme three related the effect of the PDCue on drooling. Of the 27 interviewed participants, there was a reported positive effect for 22, indicating that the majority of participants successfully engaged with the intervention and found it to be a worthwhile option for supporting the self-management of drooling. ~~Theme four then related to~~Participants also discussed emotional benefits which arose as a result of the PDCue intervention, including improvements to self-esteem, confidence and feelings of control.

The final theme related to reports of generali~~z~~zation and habituation. There were several cases of participants reporting a generalization effect, wherein they felt an increase in swallowing frequency was being carried over to times when they were not wearing the PDCue (9/27). P4 said *"Even when I wasn't wearing the* [PDCue] *every now and again I think, "Oh yes, you haven't swallowed. I need to swallow""*. P3 also noted *"even when I wasn't wearing it I was much more conscious of it".* Although unexpected, P26 also discussed an improvement to his night time drooling *"I've hardly been drooling at all. No, I haven't. Even during the night I haven't been".*

There were a small number of participants (3/27) however who reported becoming habituated to the cues, e.g. P10 *"there were occasions when I had the watch on, I seemed to have got so used to it that I didn't get any indication"*. However, these participants reported a positive effect from the intervention, despite this habituation.

Discussion

This pilot study aimed to explore the feasibility, usability and acceptability of wearing a wrist-worn vibratory cueing device to improve drooling in people with Parkinson's, and to

establish whether there was evidence of an effect of the device on drooling severity, frequency and impact. ~~A total of 28~~Twenty-eight people completed a month-long intervention with the device, using it for an hour a day. ~~These participants~~ Altogether they showed significant improvement on severity (p=0.031), frequency (p=<0.001), and duration (p=0.001) of drooling when comparing results from the self-reported ~~diary~~ VASs collected pre and post intervention. These improvements were also seen to remain at follow up assessment 4 weeks post-treatment compared to their pre-intervention baseline. A significant improvement was also seen in the UPDRS 2.2 saliva subtest (p=0.010) when comparing the pre-intervention and follow up assessment time points. Based on this we conclude there is some evidence to indicate that the device can be successful in improving saliva control, not only when wearing the PDCue but also when not using it or after intervention has been withdrawn.

Comments from the interviews confirm that people are disturbed by their drooling and that lesser drooling brings benefits for psychosocial well-being. Participants were satisfied with manipulating the device and found it acceptable to wear. They perceived the gains seen made wearing the device worthwhile. This is further reflected in comments participants made in the exit interviews concerning the perceived positive effects of the intervention device. Responses showed that 22/27 participants explicitly reported that they had noticed benefits to their drooling, with several stating that it was a preferable treatment option to other pharmaceutical interventions. In a larger trial it is unlikely that this interview-based approach could be undertaken at scale. The development of a questionnaire, drawing on the themes outlined from the qualitative data could be an approach to capturing data of this kind.

The lack of positive change in the delayed treatment group during their no-intervention phase suggests that change was not accounted for by a placebo effect from

being recruited to the study, being assessed, completing the diary exercise, nor from receiving information about drooling and drooling interventions in general. There was no improvement despite written (in the study information pack) and oral discussion that more frequent swallowing may benefit saliva loss. Whilst the present data suggest placebo effect does not play a significant role here, in a definitive trial a more active comparator condition should be introduced.

Our results showed a measurable change in score in the UPDRS item for drooling, between baseline and 4 week follow-up, lending additional weight to the improved VAS responses that participants provided. However, we did not observe any significant differences in the ROMP-S overall score. This may indicate that the types or level of changes experienced over the intervention period were not sufficient for this tool to capture. It could be that employing an overall score across multiple dimensions rather than analyzing each item separately masked significant gains in some areas. For instance, there may have been no change in night time drooling score, or even, after a short period, no shift in overall impact. Nevertheless, frequency of having to wipe the mouth or perceived excessive saliva in the mouth may have altered, but these improvements failed to make a significant difference in overall score against the non-altered variables. A similar factor may be at work in the lesser (compared to VASs) sensitivity to change of the UPDRS saliva item, since this scale combines several features which might actually vary independently (e.g. day vs night drooling; perceived excess saliva in mouth; frequency vs severity) in one scale ~~which might actually vary independently~~. Significant improvement in one sub-dimension may be missed if the other dimensions do not alter. ~~This would mask changes in one of the sub-dimensions.~~ Further analyses of individual items prior to a definitive trial may aid in separating out which aspects of drooling are more or less susceptible to influence through cueing.

~~When comparing diary scores at baseline between groups (immediate vs delayed) we observed no significant differences, except on self-reported severity (p=0.010), which reduced (i.e. got better) in the intervention group but stayed the same in the no intervention group. This result in itself deserves attention; in the delayed group, the other perceived measures collected from the diary (duration and frequency) increased (i.e. got worse), which may indicate that the process of completing the diary increased awareness of drooling. However, we had considered that this, paired with knowledge that increased swallowing frequency could reduce drooling (provided in the information sheet and during the informed consent procedure) might actually lead to an improvement in drooling in the delayed group. However, this was not the case, again furthering evidence that our results were not due to placebo effect.~~

A~~nother~~ factor to consider for a larger trial is data completeness for the diaries. We had a 76% completion rate across the study. Although this is not dissimilar to other studies [e.g. 33], a larger trial ~~A larger RCT~~ would need to consider the time requirements of participants and the burden of the study to self-report~~, although this is not dissimilar to other studies [21].~~ . We make the suggestion that completing the diary throughout the entirety of the study is not required. O~~, o~~nly completing the diary for one week pre and post-intervention (and again at follow up) would be enough in a follow up trial, as these were the results that we eventually focused on in our analysis.

Self-reported diaries are heavily used in clinical research as a way to monitor the progress of treatment and log patients' activities over time, without the requirement for a researcher to be present, despite longstanding reported issues with compliance (e.g. [34, 35]). Recent research into tools to support self-report in Parkinson's research has provided clear recommendations for improving practice, with Vega et al. finding 99% compliance with their

paper-based tool measuring self-reported symptoms over several months with a small number of participants [38]. However, another solutions would be to introduce~~Considering~~ usage logs, collected automatically by the device, which would also provide an indication of participant compliance without the need for the diary.

~~Self-reported diaries are heavily used in clinical research as a way to monitor the progress of treatment and log patients' activities over time, without the requirement for a researcher to be present, despite longstanding reported issues with compliance (e.g. [24]). Recent research into tools to support self-report in Parkinson's research has provided clear recommendations for improving practice, with Vega et al. finding 99% compliance with their paper-based tool measuring self-reported symptoms over several months with a small number of participants [25].~~

~~Our results showed a measurable change in score in the Unified Parkinson's Disease Rating Scale subtest for drooling, which adds additional weight to the diary responses that participants provided. However, we did not observe any significant changes in the Parkinson's Disease Questionnaire-39 (PDQ-39) subtests for wellbeing, stigma and communication; nor did we observe any significant differences in the Radboud Oral Motor Inventory for Parkinson's disease saliva subtest. PDQ-39 is not designed to detect changes in drooling impact. The lack of significant changes may also indicate that the types or level of changes experienced over the intervention period were not sufficient for these tools to capture. Further work, prior to a larger RCT, is required to ensure that the impact of the PDCue intervention in a larger cohort of participants could be appropriately measured. The qualitative work that we completed as part of this pilot trial showed that, during exit interviews, 22 participants explicitly reported that they had noticed benefits to their drooling, with several stating that it was a preferable treatment option to other~~

pharmaceutical interventions. All participants felt the intervention and device were acceptable and usable. However, in a larger trial it is unlikely that this qualitative approach could be undertaken at scale. The development of a questionnaire, drawing on the themes outlined from the qualitative data could be an approach to capturing data of this kind. In addition, the interviews highlighted that a small number of participants noted habituation to the device. Whilst we did not set up the study to answer the question about habituation definitively, future research should look at whether this is a factor in whether the device is effective or not for an individual. In the present study, in as far it was highly effective for some, then we can assume that habituation is not an all-pervasive problem. However, in future we suggest longer follow-up times to look at possible wearing off effects.

The concept of temporal cueing as a treatment for drooling has been built on previous work which has shown success in the domain of cueing for gait training for Parkinson's [7]; built upon observations that the training of a metronomic cue brings about the execution of a new motor plan, which facilitates walking and suppresses the impaired motor plan currently inhibiting the intended movement [8-10]. There is a level of automaticity in the complex movements of both walking and swallowing of saliva that link these two symptoms together and allow for cross comparison of motor theory. Both are triggered, patterned responses involving automated neural processes that generally do not require conscious thinking for carrying out the activity. However, in the case of Parkinson's, these automatic movements can become impeded when difficulties with motor initiation arise. In terms of neurophysiology, cueing is believed to suppress pathological basal ganglia activity through activation of corticostriatal pathways [8]. That is to say, the cue causes the initiation of an alternative pathway in the brain, also linked to motor activity, which brings about the initiation of movement that has been halted.

The body of literature exploring cueing for drooling as a symptom is minimal, with only small-scale preliminary work by Marks et al [2211] and Marron et al [2312] being the only examples exploring this space. As such, our work builds upon this nascent body of literature to provide additional evidence that cueing for drooling might be an effective way to manage the symptom, with the qualitative aspects of our study additionally demonstrating reports around increased feelings of control, confidence and self-esteem post intervention. In addition, we build on our previous work [2413] to report that acceptance and usability of our tool has been confirmed with a larger and more varied group of participants over a longer period of time. Our cueing approach warrants further exploration in a larger scale trial.

Study Limitations

There are several provisos in interpreting the current data. Firstly, one assumes that participants were wearing the devices as requested, for a designated hour each day. However, we did not collect precise usage logs. In future work there would be benefit in utilizing a more objective approach, e.g. through digital usage logs collected directly through the device (i.e. using an accelerometer to provide data on when the device is switched on and being used). Secondly, we asked participants to self-select an hour within which to self-monitor their drooling, at times when drooling was a problem. Whilst participants may have selected a self-perceived period of more susceptibility to drooling, it remains unclear how severe their chosen hour might have been. Further laboratory-based work, employing objective measures of physiological drooling (e.g. objective swallow frequency measurement, or saturated gauze weight measurement) would add insight into whether or not orally retained saliva objectively decreased through use of the device. This would also

remove, at least in laboratory conditions, the use of self-report diaries that may be open to recall bias. For field--testing, employing devices capable of measuring swallowing events in naturalistic situations (e.g. using an in-ear microphone) would be beneficial.

Finally, although 30 participants was the sample size intended for this first stage feasibility trial, we did not have matched numbers between the delayed and immediate groups. The intentions was to have 15 participants in each, but time constraints meant that we were unable to fully recruit to our delayed group (with 4 participants remaining). We made a decision to include a final 2 participants in the study as immediate intervention participants. Future studies implementing two treatment strands should not have this problem in future work, however future researchers should also consider randomisation approaches that allow for equal participant numbers throughout the recruitment process (e.g. even vs odd participant numbers to each strand). In addition, whilst the results of our pilot work delivered some positive outcomes, sufficient to suggest the cueing device may be effective, a more definitive answer awaits a trial involving larger numbers in a more highly powered study and with an active intervention comparator.

Conclusions

This study has indicated that our cueing device was acceptable and usable, and that the intervention could be a feasible first step for clinicians, before moving on to pharmaceutical options, which have been shown to have potential complications. Whilst the next step of this research will require a larger multi-center trial to elucidate whether these results are replicable and clearer in a larger population, and to look at the characteristics of responders vs non-responders to the treatment, the information presented within this paper has

provided important, preliminary data around the effect that the cueing intervention could have and issues to address in the development of outcome measures.

Clinical messages

- Providing a regular vibratory cue, through the PDCue device was shown to be an effective treatment for reducing perceived drooling in the great majority of participants.
- Participants accepted PDCue and remained motivated to self-manage their drooling with the device.
- Further studies are needed to confirm the beneficial effects that we observed and for the refinement of outcome measures.

Declarations

Conflicts of interest: The Authors declare that there is no conflict of interest

Funding: This research was funded by the National Institute of Health Research, Research for Patient Benefit program (RfPB PB-PG-0110-21326), and the EPSRC Digital Economy theme Social Inclusion through the Digital Economy Research Hub (EP/G066019/1)

Guarantor: RM

Contributorship: RM, PO, RW and NM were all involved in the conception of the research project and in researching the existing literature. RM, RW and NM were involved in protocol development, with support from PO, KL and DJ. Ethical approval and patient recruitment was conducted by RM and RW. Data capture and analysis was conducted by RM, KL, JV and DJ. RM wrote the first draft of the manuscript. All authors reviewed and edited the manuscript and approved the final version of the manuscript

Acknowledgments: We would like to acknowledge the time and effort of the staff members who helped to identify participants for the study. We would also like to thank Keith Gray for his help with the statistical analysis of the data.

References

1. Kalf JG, de Swart BJM, Borm GF, Bloem BR, Munneke M. Prevalence and definition of drooling in Parkinson's disease: a systematic review. *JNeurol*. 2009;256(9):1391-6.
2. Perez-Lloret S, Nègre-Pagès L, Ojero-Senard A, Damier P, Destée A, Tison F, et al. Oro-buccal symptoms (dysphagia, dysarthria, and sialorrhea) in patients with PD. *Eur JNeurology*. 2012;19(1):28-37.
3. Nienstedt JC, Buhmann C, Bihler M, Niessen A, Plaetke R, Gerloff C, et al. Drooling is no early sign of dysphagia in PD. *Neurogastroenterol Motil*. 2018;30(4).
4. Fereshtehnejad SM, Skogar O, Lokk J. Evolution of orofacial symptoms and disease progression in idiopathic PD: longitudinal data from the Jonkoping Parkinson registry. *Parkinsons Disease*. 2017.
5. Pedersen AML, Sørensen CE, Proctor GB, Carpenter GH. Salivary functions in mastication, taste and textural perception, swallowing and initial digestion. *Oral Dis*. 2018;24(8):1399-416.
6. Barbe AG, Ludwar L, Scharfenberg I, Hellmich M, Dano R, Barbe MT, et al. Circadian rhythms and influencing factors of xerostomia among Parkinson's disease patients. *Oral Dis*. 2019;25(1):282-9.
7. Saleh J, Figueiredo MAZ, Cherubini K, Salum FG. Salivary hypofunction: An update on aetiology, diagnosis and therapeutics. *Archives Oral Biology*. 2015;60(2):242-55.

8. Kalf J, Smit A, Bloem B, Zwarts M, Munneke M. Impact of drooling in PD. *JNeurol*. 2007;254(9):1227-32.

9. Leibner J, Ramjit A, Sedig L, Dai YF, Wu SS, Jacobson C, et al. The impact of and the factors associated with drooling in Parkinson's disease. *Parks Rel Dis*. 2010;16(7):475-7.

10. Rajiah K, Maharajan MK, Yeen SJ, Lew S. Quality of life and caregivers' burden of PD. *Neuroepidemiol*. 2017;48(3-4):131-7.

11. Nobrega AC, Rodrigues B, Torres AC, Scarpel RD, Neves CA, Melo A. Is drooling secondary to a swallowing disorder in patients with PD? Parks Rel Dis. 2008;14(3):243-5.

12. Proulx M, de Courval FP, Wiseman MA, Panisset M. Salivary production in PD. *Mov Disord*. 2005;20(2):204-7.

13. Kalf JG, Munneke M, van den Engel-Hoek L, de Swart BJ, Borm GF, Bloem BR, et al. Pathophysiology of diurnal drooling in PD. *Mov Disord*. 2011;26(9):1670-6.

14. Reynolds H, Miller N, Walker R. Drooling in Parkinson's Disease: Evidence of a Role for Divided Attention. *Dysphagia*. 2018;33(6):809-17.

15. Meningaud JP, Pitak-Arnnop P, Chikhani L, Bertrand JC. Drooling of saliva: A review of the etiology and management options. Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology, and Endodontics. 2006. p. 48–57.

16. Hyson HC, Johnson AM, Jog MS. Sublingual atropine for sialorrhea secondary to parkinsonism: A pilot study. Mov Disord. 2002;17(6):1318–20.

17. NICE. Parkinson’s disease in adults: *NICE guideline NG71*. London, GB; 2017

18. Nieuwboer, A., Kwakkel, G., Rochester, L., et al. (2007). Cueing training in the home improves gait-related mobility in Parkinson’s disease: the RESCUE trial. Journal of

Neurology, Neurosurgery, and Psychiatry, 78(2), 134–40. http://doi.org/10.1136/jnnp.200X.097923\

19. Sarma S V, Cheng ML, Eden U, Williams Z, Brown EN, Eskandar E. The effects of cues on neurons in the basal ganglia in Parkinson's disease. Front Integr Neurosci [Internet]. 2012 Jan [cited 2015 Aug 29];6:40. Available from: http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=3405280&tool=pmcentrez&rendertype=abstract
20. Georgiou N, Iansek R, Bradshaw JL, Phillips JG, Mattingley JB, Bradshaw JA. An evaluation of the role of internal cues in the pathogenesis of parkinsonian hypokinesia. Brain [Internet]. 1993 Dec [cited 2015 Aug 29];116 (Pt 6:1575–87. Available from: http://www.ncbi.nlm.nih.gov/pubmed/8293289
21. Bötzel K, Schulze S. Self-initiated versus externally triggered movements. I. An investigation using measurement of regional cerebral blood flow with PET and movement-related potentials in normal and Parkinson's disease subjects. Brain [Internet]. 1996 Jun [cited 2015 Aug 29];119:1045–8. Available from: http://www.ncbi.nlm.nih.gov/pubmed/8673482
22. Marks L, Turner K, O'Sullivan J, Deighton B, Lees A. Drooling in Parkinson's disease: a novel speech and language therapy intervention. International journal of language & communication disorders / Royal College of Speech & Language Therapists. 2001.
23. Marron A, Robinson L, Walker R. Use of a metronome brooch reminder to improve drooling problems in patients with Parkinsonism. Presented at the 9th national conference - Multidisciplinary care in Parkinson's Disease and Parkinsonism from science to practice - Royal College of Physicians,. London; 2004.

24. McNaney R, Lindsay S, Ladha K, Ladha C, Schofield G, Ploetz T, Hammerla N, Jackson D, Walker R, Miller N, Olivier P. Cueing for drooling in Parkinson's disease. InProceedings of the SIGCHI conference on Human Factors in Computing Systems 2011 May 7 (pp. 619-622). ACM.

25. Afkari, S. (2007). Measuring frequency of spontaneous swallowing. Australasian Physical & Engineering Sciences in Medicine / Supported by the Australasian College of Physical Scientists in Medicine and the Australasian Association of Physical Sciences in Medicine, 30(4), 313–7. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/18274071

26. Hoehn MM, Yahr MD. Parkinsonism : onset, progression, and mortality Parkinsonism: onset, progression, and mortality. Neurology [Internet]. 1967;17427. Available from: http://www.neurology.org/content/17/5/427.citation

27. Daniel SE, Lees AJ. Parkinson's Disease Society Brain Bank, London: overview and research. J Neural Transm Suppl [Internet]. 1993 Jan [cited 2015 Aug 29];39:165–72. Available from: http://www.ncbi.nlm.nih.gov/pubmed/8360656

28. Folstein, M.F., Robins, L.N. and Helzer, J.E., 1983. The mini-mental state examination. *Archives of general psychiatry*, *40*(7), pp.812-812.

29. Nasreddine, Z.S., Phillips, N.A., Bédirian, V., Charbonneau, S., Whitehead, V., Collin, I., Cummings, J.L. and Chertkow, H., 2005. The Montreal Cognitive Assessment, MoCA: a brief screening tool for mild cognitive impairment. *Journal of the American Geriatrics Society*, *53*(4), pp.695-699.

30. Goetz CG, Tilley BC, Shaftman SR, Stebbins GT, Fahn S, Martinez-Martin P, Poewe W, Sampaio C, Stern MB, Dodel R, Dubois B. Movement Disorder Society-sponsored revision of the Unified Parkinson's Disease Rating Scale (MDS-UPDRS): Scale

presentation and clinimetric testing results. Movement disorders. 2008 Nov 15;23(15):2129-70.

31. Kalf J, Borm G, De Swart B, Bloem B, Zwarts M, Munneke M. Reproducibility and validity of patient-rated assessment of speech, swallowing, and saliva control in parkinson's disease. Arch Phys Med Rehabil. 2011;

32. Thomas-Stonell N, Greenberg J. Three treatment approaches and clinical factors in the reduction of drooling. *Dysphagia*. 1988;3(2):73-8.

33. Hauser RA, Deckers F, Lehert P. PD home diary: Further validation and implications for clinical trials. *Mov Disord*. 2004;19(12):1409-13.

34. Montgomery GK, Reynolds NC. Compliance, reliability, and validity of self-monitoring for physical disturbances of Parkinson's disease. The Parkinson's Symptom Diary. J Nerv Ment Dis. 1990;178(10):636–41.

35. Stone, A. A., Shiffman, S., Schwartz, J. E., Broderick, J. E., & Hufford, M. R. (2003). Patient compliance with paper and electronic diaries. Controlled Clinical Trials. http://doi.org/10.1016/S0197-2456(02)00320-3

36. Shapiro SS, Francia RS. An approximate analysis of variance test for normality. Journal of the American Statistical Association. 1972 Mar 1;67(337):215-6.

37. Braun, Virginia, and Victoria Clarke. 2006. Using thematic analysis in psychology." *Qualitative research in psychology* 3, no. 2 (2006): 77-101. DOI: http://doi.org/abs/10.1191/1478088706qp063oa

38. Vega, J., Couth, S., Poliakoff, E., et al. (2018). Back to Analogue: Self-Reporting for Parkinson's Disease. In Proceedings of the 2018 CHI Conference on Human Factors in Computing Systems (CHI '18). ACM, New York, NY, USA, Paper 74, 13 pages. DOI: https://doi.org/10.1145/3173574.3173648

1. Nóbrega AC, Rodrigues B, Torres AC, Scarpel RD, Neves CA, Melo A. Is drooling secondary to a swallowing disorder in patients with Parkinson's disease? Park Relat Disord. 2008;14(3):243–5.

2. Kalf J, De Swart B, Borm G, Bloem B, Munneke M. Prevalence and definition of drooling in Parkinson's disease: A systematic review. Journal of Neurology. 2009. p. 1391–6.

3. Edwards, L. L., Pfeiffer, R. F., Quigley, E. M., Hofman, R., & Balluff, M. (1991). Gastrointestinal symptoms in Parkinson's disease. Movement Disorders : Official Journal of the Movement Disorder Society, 6(2), 151–156. http://doi.org/10.1002/mds.870060211

4. Reynolds, H., Miller, N., Walker, R. The impact of divided attention in dual task conditions on drooling in Parkinson's Disease (PD): a pilot study [abstract]. *Movement Disorders.* 2017; 32 (suppl 2). http://www.mdsabstracts.org/abstract/the-impact-of-divided-attention-in-dual-task-conditions-on-drooling-in-parkinsons-disease-pd-a-pilot-study/. Accessed February 15, 2019.

5. Meningaud JP, Pitak-Arnnop P, Chikhani L, Bertrand JC. Drooling of saliva: A review of the etiology and management options. Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology, and Endodontics. 2006. p. 48–57.

6. Hyson HC, Johnson AM, Jog MS. Sublingual atropine for sialorrhea secondary to parkinsonism: A pilot study. Mov Disord. 2002;17(6):1318–20.

7. Nieuwboer, A., Kwakkel, G., Rochester, L., et al. (2007). Cueing training in the home improves gait-related mobility in Parkinson's disease: the RESCUE trial. Journal of Neurology, Neurosurgery, and Psychiatry, 78(2), 134–40. http://doi.org/10.1136/jnnp.200X.097923

8. Sarma S V, Cheng ML, Eden U, Williams Z, Brown EN, Eskandar E. The effects of cues on neurons in the basal ganglia in Parkinson's disease. Front Integr Neurosci [Internet]. 2012 Jan [cited 2015 Aug 29];6:40. Available from: http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=3405280&tool=pmcentrez&rendertype=abstract

9. Georgiou N, Iansek R, Bradshaw JL, Phillips JG, Mattingley JB, Bradshaw JA. An evaluation of the role of internal cues in the pathogenesis of parkinsonian hypokinesia. Brain [Internet]. 1993 Dec [cited 2015 Aug 29];116 (Pt 6:1575–87. Available from: http://www.ncbi.nlm.nih.gov/pubmed/8293289

10. Bötzel K, Schulze S. Self-initiated versus externally triggered movements. I. An investigation using measurement of regional cerebral blood flow with PET and movement-related potentials in normal and Parkinson's disease subjects. Brain [Internet]. 1996 Jun [cited 2015 Aug 29];119:1045–8. Available from: http://www.ncbi.nlm.nih.gov/pubmed/8673482

11. Marks L, Turner K, O'Sullivan J, Deighton B, Lees A. Drooling in Parkinson's disease: a novel speech and language therapy intervention. International journal of language & communication disorders / Royal College of Speech & Language Therapists. 2001.

12. Marron A, Robinson L, Walker R. Use of a metronome brooch reminder to improve drooling problems in patients with Parkinsonism. Presented at the 9th national conference - Multidisciplinary care in Parkinson's Disease and Parkinsonism from science to practice - Royal College of Physicians,. London; 2004.

13. McNaney R, Lindsay S, Ladha K, Ladha C, Schofield G, Ploetz T, Hammerla N, Jackson D, Walker R, Miller N, Olivier P. Cueing for drooling in Parkinson's disease. InProceedings of the SIGCHI conference on Human Factors in Computing

Systems 2011 May 7 (pp. 619-622). ACM.

14. Afkari, S. (2007). Measuring frequency of spontaneous swallowing. Australasian Physical & Engineering Sciences in Medicine / Supported by the Australasian College of Physical Scientists in Medicine and the Australasian Association of Physical Sciences in Medicine, 30(4), 313–7. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/18274071

15. Hoehn MM, Yahr MD. Parkinsonism : onset, progression, and mortality Parkinsonism: onset, progression, and mortality. Neurology [Internet]. 1967;17427. Available from: http://www.neurology.org/content/17/5/427.citation

16. Daniel SE, Lees AJ. Parkinson's Disease Society Brain Bank, London: overview and research. J Neural Transm Suppl [Internet]. 1993 Jan [cited 2015 Aug 29];39:165–72. Available from: http://www.ncbi.nlm.nih.gov/pubmed/8360656

17. Hoops S, Nazem S, Siderowf AD, Duda JE, Xie SX, Stern MB, et al. Validity of the MoCA and MMSE in the detection of MCI and dementia in Parkinson disease. Neurology. 2009;

18. Goetz CG, Tilley BC, Shaftman SR, Stebbins GT, Fahn S, Martinez-Martin P, Poewe W, Sampaio C, Stern MB, Dodel R, Dubois B. Movement Disorder Society-sponsored revision of the Unified Parkinson's Disease Rating Scale (MDS-UPDRS): Scale presentation and clinimetric testing results. Movement disorders. 2008 Nov 15;23(15):2129-70.

19. Peto V, Jenkinson C, Fitzpatrick R, Greenhall R. The development and validation of a short measure of functioning and well being for individuals with Parkinson' s disease. Qual Life Res. 1995;

20. Kalf J, Borm G, De Swart B, Bloem B, Zwarts M, Munneke M. Reproducibility and validity of patient-rated assessment of speech, swallowing, and

saliva control in parkinson's disease. Arch Phys Med Rehabil. 2011;

21. Hauser, R.A., Deckers, F. and Lehert, P., 2004. Parkinson's disease home diary: further validation and implications for clinical trials. *Movement Disorders*, *19*(12), pp.1409-1413.

22. Montgomery GK, Reynolds NC. Compliance, reliability, and validity of self-monitoring for physical disturbances of Parkinson's disease. The Parkinson's Symptom Diary. J Nerv Ment Dis. 1990;178(10):636–41.

23. Shapiro SS, Francia RS. An approximate analysis of variance test for normality. Journal of the American Statistical Association. 1972 Mar 1;67(337):215-6.

24. Stone, A. A., Shiffman, S., Schwartz, J. E., Broderick, J. E., & Hufford, M. R. (2003). Patient compliance with paper and electronic diaries. Controlled Clinical Trials. http://doi.org/10.1016/S0197-2456(02)00320-3

25. Vega, J., Couth, S., Poliakoff, E., et al. (2018). Back to Analogue: Self-Reporting for Parkinson's Disease. In Proceedings of the 2018 CHI Conference on Human Factors in Computing Systems (CHI '18). ACM, New York, NY, USA, Paper 74, 13 pages. DOI: https://doi.org/10.1145/3173574.3173648

26.

27.

28.

29.

30.

31.

32.

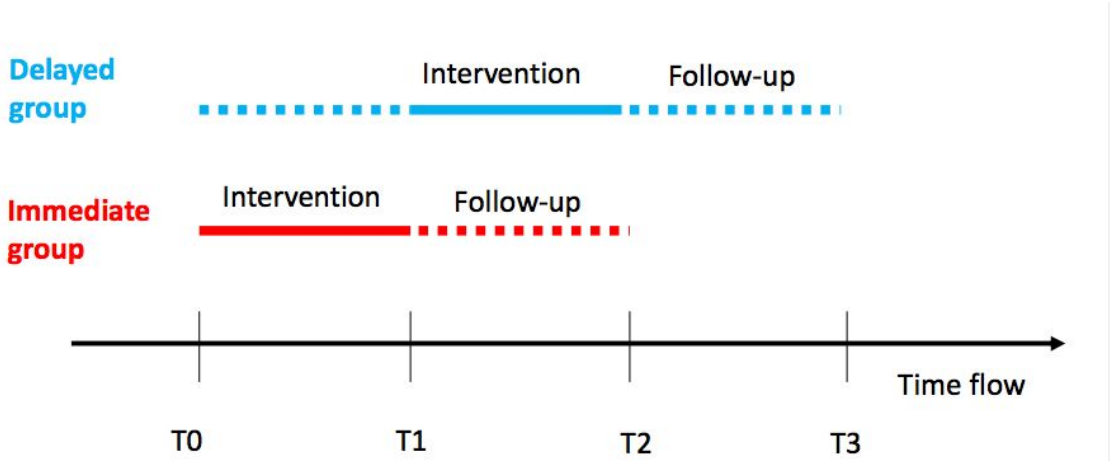
33.

~~34.~~

~~35.~~

~~36.~~

Figure 1: the cueing device



	Delayed Intervention (n=11)	Immediate Intervention (n=17)	Significance
Demographics			
Median age in years (IQR)	75 (65 to 79)	72 (65.5 to 78.5)	$U = 89.0$, $z = 0.212$, $p = 0.832$
Median years since PD diagnosis (IQR)	5 (3 to 8)	7 (2.5 to 10)	$U = 78.0$, $z = 0.732$, $p = 0.464$
N of females (%)	3 (27%)	7 (41%)	$X^2(1) = 0.562$, $p = 0.689$
N of participants living alone (%)	1 (9%)	5 (29%)	$X^2(1) = 1.638$, $p = 0.355$
Overall -Parkinson's severity (SD) - Median UPDRS II and III score combined (IQR) - Hoehn & Yahr stage	 44 (39 to 70) II: 6 (55%) III: 3 (27%) IV: 2 (18%)	 53 (35 to 81) II: 7 (41%) III: 8 (47%) IV: 2 (12%)	 $U = 76.5$, $z = 0.800$, p = 0.424 $X^2(2) = 1.115$, $p = 0.573$
Initial perception of drooling severity, self-reported by the participant N (%)	Mild= 4 (36%) Moderate= 5 (46%) Severe= 2 (18%)	Mild= 9 (53%) Moderate= 5 (29%) Severe= 3 (18%)	$X^2(2) = 0.878$, $p = 0.778$
Median months since drooling first noticed (IQR)	24 (12 to 36)	12 (9.5 to 24)	$U = 75.0$, $z = 0.888$, $p = 0.375$
N of participants with previous drooling treatment (%)	3 (27%)	5 (29%)	$X^2(1) = 0.015$, $p = 1.000$
N of participants with reported swallowing problems (%)	7 (64%)	7 (41%)	$X^2(1) = 1.348$, $p = 0.246$

Assessment	Delayed group (n=11)		Intervention group (n=17)		Significance of between group difference ~~between the two groups of change from baseline~~
	Assessment point 1 (T0)~~0~~ Median (IQR)	Assessment point 2 (T1)~~1~~ Median (IQR)	Assessment point 1 (T0) Median (IQR)	Assessment point 2 (T1) Median (IQR)	Mann-Whitney U test
~~PDQ-39~~			-	-	
~~Wellbeing~~	~~5 (4 to 13)~~	~~5 (4 to 8)~~	~~7 (3.5 to 12)~~	~~8 (3 to 10.5)~~	~~U = 77.0, z=0.784, p=0.433~~
~~Stigma~~	~~7 (1 to 9)~~	~~4 (1 to 6)~~	~~3 (1 to 7)~~	~~3 (0 to 6.5)~~	~~U = 66.0, z=1.311, p=0.190~~
~~Communication~~	~~4 (2 to 5)~~	~~4 (2 to 9)~~	~~4 (2.5 to 6.5)~~	~~6 (2 to 7)~~	~~U = 92.5, z=0.050, p=0.960~~
ROMP- Saliva	20 (17 to 25)	19 (17 to 30)	22 (16 to 23)	22 (17 to 25.5)	*U* = 83.0, *z*=0.497, *p*=0.619
UPDRS 2.2 (Saliva and drooling subtest)	3 (1 to 3)	3 (1 to 3)	3 (3 to 4)	3 (2 to 4)	*U* = 69.0, *z*=1.212, *p*=0.225
Drooling Diary					
Severity	1 (0 to 4)	1 (1 to 5)	3 (1.5 to 5)	1 (0 to 2.5)	*U* = 39.5, *z*=2.575, *p*=0.010
Duration (No. minutes drooling occurred in one hour)	1 (0 to 5)	2 (0.5 to 10)	5 (1 to 11)	1 (0 to 4.5)	*U* = 63.0, *z*=1.440, *p*=0.150
Frequency (No. instances in one hour)	1 (0 to 4)	3(1 to 4)	3 (1 to 4.5)	1 (0 to 3)	*U* = 54.0, *z*=1.876, *p*=0.061

Assessment	Entire group (n=28)			Significance of difference	
	Assessment point 1 (T0) Median (IQR)	Assessment point 2 (T1) Median (IQR)	Assessment point 3 (T3) Median (IQR)	Assessment points 1 (T0) to 2 (T1)	Assessment points 1 (T0) to 3 (T2)
~~PDQ-39~~	-	-			
~~Wellbeing~~	~~4 (6 to 10)~~	~~6 (3.25 to 10)~~	~~7 (4.25 to 9.75)~~	~~Z = 1.032, p = 0.302~~	~~Z = 0.316, p = 0.752~~
~~Stigma~~	~~3 (1 to 6.75)~~	~~3.5 (0 to 7)~~	~~2 (0 to 6)~~	~~Z = 0.835, p = 0.404~~	~~Z = 0.949, p = 0.343~~
~~Communication~~	~~4 (2.25 to 7)~~	~~4.5 (2 to 6)~~	~~3 (1.25 to 5.75)~~	~~Z = 0.523, p = 0.601~~	~~Z = 1.150, p = 0.250~~
ROMP- Saliva	20.5 (16 to 23.75)	20 (16.25 to 24.75)	17 (15 to 23.5)	$Z = 0.275$, $p = 0.783$	$Z = 1.800$, $p = 0.072$
UPDRS 2.2 (Saliva and drooling subtest)	3 (3 to 4)	3 (2 to 4)	2 (1 to 3)	$Z = 1.801$, $p = 0.072$	$Z = 2.569$, $p = 0.010$
Drooling Diary					
Severity	3.14 (2.42)	1.18 (1.57)	1.14 (1.51)	$Z = 2.151$, $p = 0.031$	$Z = 2.809$, $p = 0.005$
Duration (No. minutes drooling occurred in one hour)	7.45 (10.64)	4.75 (11.55)	1.86 (2.73)	$Z = 3.362$, $p = 0.001$	$Z = 2.631$, $p = 0.009$
Frequency (No. instances in one hour)	4.18 (5.68)	1.80 (2.32)	1.16 (1.47)	$Z = 3.982$, $p < 0.001$	$Z = 3.606$, $p < 0.001$