Wearable Devices and Mobile Health – an Opportunity for Innovative Remote Patient Monitoring in Niemann-Pick Type C

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INTRODUCTION AND OBJECTIVES

Introduction

Niemann-Pick C (NP-C) is a rare inherited neurodegenerative autosomal recessive disorder primarily diagnosed in children. Disease symptoms include frequent falls, ataxia and behavioural problems. There is a lack of validated, age-related, disease-specific end points available to screen gait and ataxia long-term in NP-C. Doctors often assess NP-C impact using the Pineda Disability Scale (PDSS)[1]. Other methods employed to assess ataxia/ gait/ ambulation can include GAITRite assessment and 6-Minute Walk Test (6MWT).

PDSS, although effective in clinical assessment, the scale fails to enable patient or parental input. All of the assessments currently used are subjective in nature and only provide a very basic snapshot insight of the patients' health and wellbeing, hence none of them have become mainstream NP-C specific assessment tools.

Objective

Wearable technologies allow daily continuous activity monitoring, and smartphone apps can facilitate Patient Reported Outcome (PRO) recordings and events in real-time. We report preliminary data and experience of an approach using this technology to understand NP-C disease activity. Our objectives are to summarise data collected from wearable devices and use specific summary measures to compare wearable data to the currently employed assessments methods in evaluating disease progression.

METHODS

Data collection

NP-C patients were recruited from 2 UK specialist centres[2]. Doctors assessed each patient with PDSS, 6MWT and GAITRite.

Parents completed PROs about their child's disability; answering questions regarding Disease Impact severity, Family Impact and Wider Impact developed by the International Niemann Pick Disease Association and pushed at regular intervals to them via a mobile app. PROs were identified in collaboration with patient group.

Participants were also given a wearable device (a 3D accelerometer) which calculates step data in 30-minute epochs and transfers it via Bluetooth to a paired smartphone app downloaded to patient's personal (or carer's) phone. No restriction was made on the wear time of the device.

Data summaries

Adherence. Zero steps recorded over a full 24-hour daily cycle was interpreted to mean that a patient did not wear the device for that day and therefore was considered to be "none adherent". Days where data was not recorded at all was also considered as "none adherent". Wearable data summaries are based on the adherent days only.

Peaks. We defined peaks of activity as a local maximum value. To identify local maximum points we used the function `findpeaks` from the `pracma` package in R. Since this function might classify relatively low values which nevertheless satisfy the criterion of having locally increasing and decreasing sequences of values around them, we looked at the peaks exceeding a determined quantile of the distribution of peak values for steps. We found that the third quartile of the overall distribution, including zero counts, provided a robust definition of peak threshold. The number of peaks was then standardised by dividing it by the number of valid days in which the device was worn.

RESULTS (1)

- We collected data from 4 paediatric NP-C subjects at various stages of the disease according to PDSS, PRO and 6MWT assessments. Patient specific baseline characteristics are displayed in **Table 1**.
- The data cut-off differ for different patients, ranging from 16 days to 95 days. High adherence has been achieved in all scenarios. On average, patients adhered on 70% of the days when asked to wear the device continuously (**Table 2**).
- Patient 4 and Patient 3 seemed to be the most and least active, with an average of 11234 and 7060 daily steps, respectively **(Table 3)**.
- Patient 4 and Patient 1 seemed to have the most and the least intense activity with the average daily peak count of 4 and 2, respectively **(Table 3)**.
- The 24-hour cycles for average steps per epochs for each patient are displayed in **Figure 1**. Although each one is slightly different, there are general similarities according to the time that activity for each patient starts in the day (e.g. patients wakes up) and ends. There is also a peak of activity seen around lunchtime, with a large dip just after that and with a general reduction in activity then until bedtime.
- Rather different activity patterns between the patients were noticed when comparing weekday vs. weekend (**Figure 3**). Patient 1 generally is more active in a weekday only up to the lunch time, and after that activity seemed to be very similar during the whole week. Patient 2 seemed to be more active over the weekend. Patient 3 has very similar activity patterns during the week day and weekend while Patient 4 is more variable with an extremely high activity noticed during the weekend.
- **Table 4** shows that daily steps and daily peaks were perfectly correlated; but that neither daily steps nor daily peaks correlated with the 6MWT, PDSS nor PRO. PDSS and PRO was negatively correlated with the 6MWT, suggesting that the more severe disease score the less patient was able to walk during the 6MWT. Note that PDSS and the PRO correlated positively even though Doctor and Parent assessment of disease differed in all but one patient.

DISCUSSION AND CONCLUSIONS

Through this study it has been demonstrated that it's possible to achieve remote, continuous, long time series monitoring of patients' PA.

In selecting the technical capabilities of the device used there was a tradeoff between battery life and the 30 minutes epoch resolution. However, even this resolution was good enough to detect individual patient's patterns and changes in PA.

Further work is required to understand why the wearable device data did not correlate with the currently used clinical data. This may be achieved in conducting a larger scale study with a higher number of patients.

Data analysis demonstrated that each individual patient has physical activity patterns that are personalized to them, in terms of times of day and also day of the week. It is crucial to be able to capture and define such personalisation in order to identify subtle changes in disease improvement or progression.

REFERENCES

[1] Itturiaga C, Pineda M, Fernández-Valero EM, et al. Niemann-Pick C disease in Spain: Clinical spectrum and development of a disability scale. J Neurol Sci 2006;249:106.

[2] Patients were recruited at Great Ormond Street Children's Hospital and Manchester's Children Hospital in the UK between February and July 2016.

RESULTS (2)

Patient ID	P1	P2	P3	P4
Characteristics				
Age (years)	11	13	7	9
Gender	F	M	M	M
Disease Scores				
PDSS (Doctor Score)	12	4	13	10
PRO (Parent/Carer Score)	5	2	13	11
6MWT (meters)	530	772	296	370

Table 1. Summary of Baseline Characteristics by Patient

Patient ID	P1	P2	P3	P4
Number of days considered	95	50	78	16
Wearable adherent days	70%	66%	68%	75%

Table 2. Summary of Wearable Device Adherence by Patient

Patient ID	P1	P2	P3	P4
Average number of steps	9607	9393	7060	11234
75% percentile of all peaks	717	1161	956	1312
Average number of peaks	4.25	2.67	3.06	1.75

Table 3. Summary of Average Number of Daily Steps and Daily Peaks by Patient

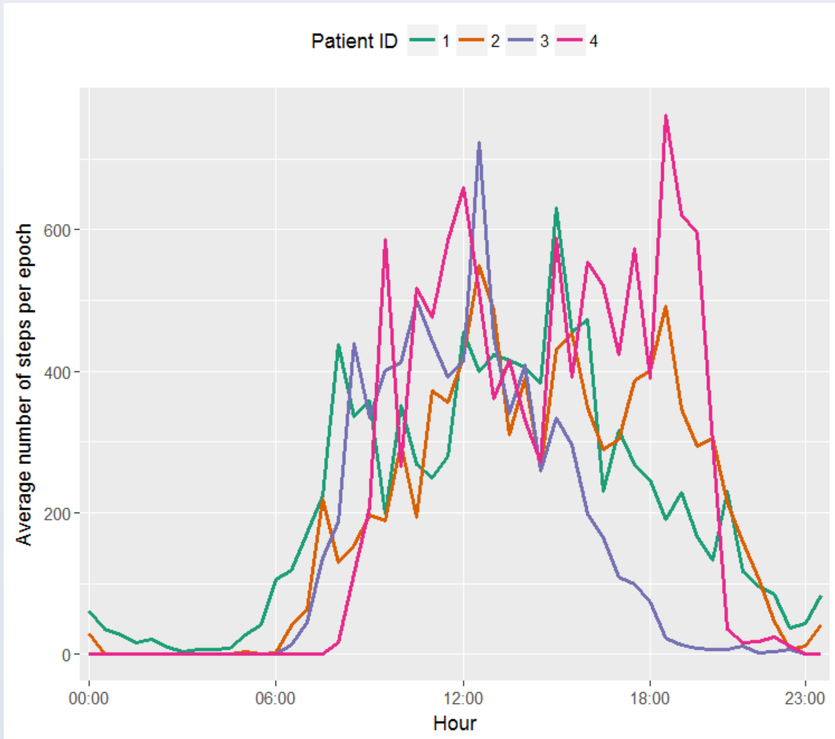

Figure 1. Figure of Average Number of Steps per Epoch by Patient

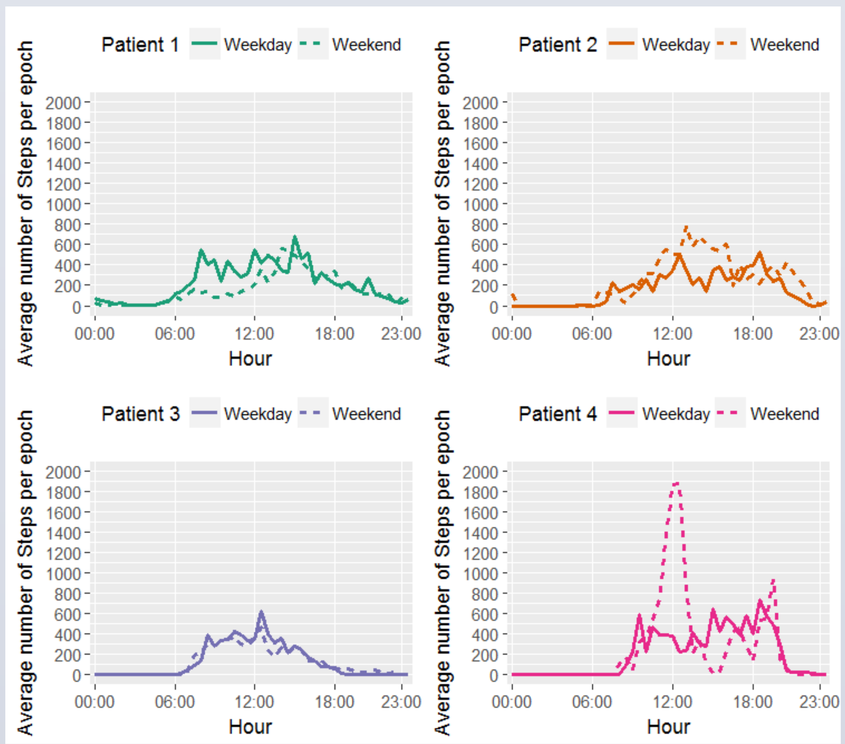

Figure 2. Figure of Average Number of Steps per Epoch by Week Period (Week Day vs. Weekend) for Each Patient

	Average of daily steps	PDSS	PRO	6MWT	Average of daily peaks
Average of daily steps	1.00	-0.72	-0.56	0.56	**-0.95**
PDSS		1.00	**0.90**	**-0.90**	0.46
PRO			1.00	**-1.00**	0.31
6MWT				1.00	-0.30
Average of daily peaks					1.00

Table 4. Spearman's Correlation Coefficient for Various Types of Assessments

Note: that for Spearman's correlation coefficient, an absolute value > 0.83 is required for significance at 10% for n =4

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