Abstract

Background: There are unique signatures of gait impairments in different dementia disease subtypes, such as Alzheimer's disease (AD), dementia with Lewy bodies (DLB) and Parkinson's disease (PDD). This suggests gait analysis is a useful differential marker for dementia disease subtypes, but this has yet to be assessed using inexpensive wearable technology.

Research Question: This study aimed to assess whether a single accelerometer-based wearable could differentiate dementia disease subtypes through gait analysis.

Methods: 80 people with mild cognitive impairment or dementia due to AD, DLB or PD performed six ten-metre walks. An accelerometer-based wearable (Axivity) assessed gait. Data was processed using algorithms validated in other neurological disorders and older adults. Fourteen spatiotemporal characteristic were computed, that broadly represent pace, variability, rhythm, asymmetry and postural control features of gait. One way analysis of variance and Kruskall Wallis tests identified significant between-group differences, and post-hoc independent t-tests and Mann Whitney U's established where differences lay. Receiver Operating Characteristics and Area Under the Curve (AUC) demonstrated overall accuracy for single gait characteristics.

Results: The wearable was able to differentiate dementia disease subtypes ($p \leq .05$) and demonstrated significant differences between the groups in 7 gait characteristics with modest accuracy. For reference the instrumented walkway showed 2 between-group differences in gait characteristics.

Significance: This study found that a wearable device can be used to differentiate dementia disease subtypes, providing a foundation for future research to investigate the application of wearable technology as a clinical tool to aid diagnostic accuracy, allowing the correct treatment and care to be applied. Wearable technology may be particularly useful as its use is less restricted to context, making it easier to implement.

Keywords: wearable technology, gait, dementia, Alzheimer's disease, Lewy bodies

1. Introduction

Digital technology is increasing of interest as a tool to enhance measurement for research and clinical practice. Wearable devices (small body worn devices containing movement sensors) are useful for identifying gait impairment [1, 2] and have been validated in a range of neurological disorders [3-5] and older adults. Wearables are inexpensive, easy-to-use and have the advantage that they are not limited by context – allowing gait characteristics to be captured in both the clinic and free-living environments, providing a more holistic picture of gait function [6-10].

Different dementia disease subtypes, including Alzheimer's disease (AD) and Lewy body disease (LBD), have unique signatures of gait impairment that may be a useful marker for differential dementia diagnosis [11, 12]. This evidence was derived from an instrumented walkway which has some practical limitations in terms of implementation of evidence into clinical and research practice [13]. The equipment is costly with large space requirements and the walking task is restricted by the mat's dimensions [14]. Alternative instruments for gait analysis may be needed to translate this research for clinical use, such as wearable technology. However, the ability of wearables and their associated algorithms to differentiate dementia disease subtypes has yet to be established.

Therefore, the aim of this study was to assess whether an accelerometer-based wearable device can differentiate dementia disease subtypes based on their gait impairment. To illustrate how different approaches to gait analysis may provide different outcomes, we report gait metrics derived from an instrumented walkway for reference and descriptive purposes.

2. Methods

2.1 Participants

Participants with probable mild cognitive impairment (MCI) due to AD and LBD (including dementia with Lewy bodies (DLB) and Parkinson's disease) or probable dementia due to AD and LBD were recruited. Two old age psychiatrists (A.T. and P.D.) reviewed patients' clinical notes and study assessments in order to verify the diagnosis for the study. A third old age psychiatrist (J.P.T.) reviewed disagreements regarding diagnosis in order to reach a consensus. Standard research diagnostic criteria for dementia were applied [15-21]. All participants had mental capacity to consent to the study.

All participants had to be over 60 years old and able to walk for two minutes, as ascertained by self-report. Participants were excluded if they had drug-induced or vascular parkinsonism, any co-existing neurological conditions or movement disorders other than AD, DLB or PDD, severe mental illness (major depression, bipolar disorder, schizophrenia), evidence of stroke

affecting motor function or poor command of the English language. The NHS Local Research Ethics Committee, Newcastle and North Tyneside 1 approved this study, Reference: 16/NE/005, IRAS project ID: 192941, and all subjects provided informed written consent in accordance to the declaration of Helsinki.

2.2 Protocol

Age, height and body mass were recorded. Faller status was assessed; participants were considered fallers if they reported at least one fall within twelve months prior to assessment. Dementia medication was recorded. Premorbid IQ was assessed using the National Adult Reading Test (NART). Cognitive function was assessed using the standardised Mini Mental State Examination (sMMSE). Motor disease was assessed with the Movement Disorders Society Unified Parkinson's Disease Rating Scale – III (UPDRS-III). Co-morbidities were considered using the Cumulative Illness Rating Scale – Geriatrics (CIRS-G). The Activities Balance Confidence scale (ABC) assessed balance confidence, while the Geriatrics Depression Scale (GDS) assessed indication of depression. Impairments in Activities of Daily Living were assessed using the Bristol Activities of Daily Living Scale (BADLS).

Participants performed six 10 metre walks at their comfortable pace. They wore an accelerometer-based wearable (AX3,

Axivity, York, UK; dimensions 23.0mm x 32.5mm x 7.6mm; 11gms; 512Mb memory; 100 Hz, 10-bit resolution, ± 8g range). The wearable was fixed to the skin above the fifth lumbar vertebra (L5) with double-sided tape and Hypafix tape. At the same time they walked over a 7 m x 0.6 m (length x width) instrumented walkway centred in the 10m pathway (GaitRite, software version 4.5, CIR Systems Inc., United States of America, spatial accuracy: 1.27 cm, temporal accuracy: ~4.17 ms, 240 Hz). The data are reported for reference.

2.3 Data processing

Data from the wearable was downloaded to a computer and analysis carried out using Matlab. The algorithm and data segmentation processing is described in Godfrey [22], Del Din [3] and Mc Ardle [10]. Fourteen gait characteristics were derived from the wearable. Gait characteristics represented pace (step velocity, step length, step time variability), variability (swing time variability, stance time variability, step velocity variability, step length variability), rhythm (step time, swing time, stance time), asymmetry (step time asymmetry, swing time asymmetry, stance time asymmetry) and postural control (step length asymmetry) domains of gait and were adapted from Lord [23] model of gait, developed in older adults and validated in Parkinson's disease .

2.4 Statistical analysis

Statistical analysis was conducted using IBM SPSS 24. Normality was assessed using Shapiro-Wilks tests and inspection of histograms. One-way ANOVA and Kruskall Wallis tests identified differences in gait characteristics between AD, DLB and PDD, with post-hoc Student's t-test and Mann-Whitney U tests establishing where these differences exist between subtypes. As this analysis was exploratory, p values of $\leq .05$ were considered statistically significant; however, Bonferroni corrections are also reported for reader's interest. The utility of discrete gait characteristics to successfully discriminate between dementia disease subtypes was determined by the area under the curve (AUC) of receiver operating characteristic (ROC) curves. Accuracy values were interpreted as follows: .5=test due to chance, .5 to .7 = low accuracy, .7 to .9 = moderate accuracy, .9 to 1 = high accuracy, and 1= the perfect test.

3. Results

3.1 Demographics

80 people across the spectrum of cognitive impairment participated in the study, ranging from MCI to moderate dementia, with cognitive scores indicated a predominately mild dementia group (see Table 1). Data from six participants were excluded due to data processing problems (device did not sync

= 3, wrong trial time recorded = 2, accelerometer not turned on = 1), leaving 32 in the AD group, 28 in the DLB group and 14 in the PDD group.

There were significantly more males in the PDD ($p = .001$) and DLB ($p = .003$) group compared to the AD group, and the PDD ($p \leq .001$) and DLB ($p \leq .01$) groups also had significantly higher scores on the MDS-UPDRS-III scale, indicating greater motor disease, and higher scores on BADLS (PDD: $p = .028$; DLB: $p = .020$), indicating greater impairments in activities of daily living. The PDD group had lower balance confidence compared to AD ($p = .020$) and DLB groups ($p = .025$), and greater motor disease compared to DLB ($p = .004$). All demographic, clinical and cognitive data are reported in Table 1.

<Insert Table 1>

3.2 Differentiation of subtypes

3.2.1 Wearable

Seven of the 14 gait characteristics measured by the wearable showed significant group differences (see Table 2). People with PDD demonstrated greater stance time asymmetry compared to both DLB ($p = .014$) and AD ($p = .022$), with greater swing time asymmetry compared to DLB ($p = .007$) and AD ($p = .014$). The PDD group also had greater step ($p \leq .001$), swing

(p = .002) and stance time variability (p = .003) compared to AD. Both PDD (p = .003) and DLB (p = .012) showed greater step velocity variability compared to AD. The DLB group also demonstrated greater step length variability (p = .022) compared to AD. The ability of gait characteristics to discriminate between dementia disease groups was assessed by statistically significant AUC values, which are reported in Table 3, with moderate accuracy found for all significant gait characteristics.

For reference, two out of 14 gait characteristics measured by the instrumented walkway demonstrated significant group differences with Gaitrite (see Table 2). People with PDD had greater step time variability (p = .013; AUC = .725, CI: .558-.893) compared to AD, and both PDD (p = .006; AUC = .741, CI: .583-.899) and DLB (p = .011; AUC = .700, CI: .567-.833) demonstrated greater step length variability compared to AD.

<Insert Table 2>

<Insert Table 3>

4. Discussion

This was the first study to assess the ability of an accelerometer-based wearable to differentiate dementia disease subtypes through gait analysis. Differential markers of

dementia disease subtypes are diagnostically important as similarities in clinical and pathological features make subtypes such as AD and DLB difficult to distinguish [24, 25], and may lead to incorrect treatment and disease management [26, 27].

These findings suggest that a wearable could be clinically useful for dementia diagnosis. Providing data from an instrumented walkway for reference purposes allows the possibility for the investigator to weigh up the limitations and merits of both approaches when deciding which to use. Instrumented walkways are non-invasive and require minimal preparation and processing time. However, they are expensive, require significant space and resources which may not be clinically feasible and appear less discriminative of different dementia disease subtypes than the wearable.

With regards to wearable technology, a secure online platform has been developed using e-Science Central [3, 28], a cloud-based platform that allows the storage, analysis and sharing of data in the cloud. Analysis of data could be carried out via the e-Science platform using an executable of validated MATLAB® scripts thereby generating a closed standalone analysis package. This can be deployed across multiple sites and allows secure and robust data management with an automatic pipeline for data analysis and outcomes, and streamlining these analytical processes are currently underway

and will be available for clinical purposes in the future. Therefore, the application of wearables to healthcare settings is desirable due to its simple and flexible approach, unobtrusive nature and low-cost [7]. Within this study, the wearable technology was employed in a standardized fashion within a controlled environment; however, these devices are not constrained to laboratory settings and can measure holistic pictures of gait in free-living environments; incorporating spatiotemporal gait characteristics within the context of habitual walking activities [29]. Protocols have been developed to enable the continuous monitoring of gait in the real-world, which may be more sensitive to disease-specific differences in gait impairment [29, 30], and may enhance our knowledge of gait in AD and LBD in the future.

Additionally, emerging research demonstrates the potential for machine learning algorithms to capture disease-specific patterns from multiple gait characteristics [31]. Therefore, the identification of multiple differential gait characteristics derived from the wearable in this study may provide key targets for future machine learning approaches in order to automatically classify these unique signatures of gait. Identification of the most accurate combination of characteristics should be a key research aim with a larger cohort study.

To further enhance accuracy of classification, metrics derived directly from the accelerometer signal may be a useful avenue to pursue, such as frequency-based metrics [32]. These will enrich information provided by the wearable and can be incorporated into classification methods such as machine learning algorithms, perhaps strengthening models for differentiating dementia disease subtypes [33]. The use of wearables in the lab and free-living environments have broad applications from establishing gait as a digital biomarker to classify dementia disease subtypes to monitoring trajectories of change in older populations and identify individuals at risk of developing cognitive impairment [7]. Therefore, we suggest wearable technology is an avenue of research worth pursuing in the dementia field, as it has multiple uses within the clinical setting.

This study was novel in its approach to differentiating dementia disease subtypes using wearable technology. Although this is the largest study of its kind, the sample size is still limited, and thus future research needs to recruit a larger cohort to improve confidence in these findings and to control for potential cofounders, such as motor disease burden and balance confidence – which significantly differed between groups in this study. As step velocity variability (Expected group difference: .05 SD, $\beta \geq .90$, $\alpha \leq .05$) and step length variability (.03 SD, $\beta \geq .90$, $\alpha \leq .05$) significantly differed between AD and

DLB when assessed with wearable technology, we used these metrics for a power calculation and recommend 45-50 participants in each group for adequate power in future studies. As it was an exploratory study, we chose not to correct for multiple comparisons. Dementia disease subtypes were classified through consensus diagnosis by expert clinicians; however, certain diagnosis can only be made post-mortem, which was beyond the scope of this study. This study initially aimed to compare gait from people with vascular dementia (VaD) to that of AD and LBD; however, we only succeeded in recruiting seven participants with VaD. The sample size was considered too small for appropriate statistical analysis. There were significant obstacles when recruiting people with VaD that should be noted when considering future research into VaD and gait impairment. True VaD cases without significant mobility issues are rare, and diagnosis of VaD in general is difficult due to lack of validated criteria and heterogeneity in clinical presentation [34]. Approximately, only 10% of all VaD cases have sufficient levels of cerebrovascular burden to fully account for their cognitive impairments, suggesting that most cases are representative of mixed dementia rather than true VaD [34]. While mixed dementia is also an important cohort to consider, this study aimed to characterise well defined cases of common dementia disease subtypes, and as such, did not include this population.

Beyond dementia subtyping, wearable technology is still in its early stages and while this study demonstrates the potential and the opportunity to apply them within clinical settings, the outcomes produced by the algorithms, such as gait variability and asymmetry, show discrepancies with those from other gait analysis techniques, such as the instrumented walkway [3]. However, the wearable captures continuous data while the instrumented walkway records discrete footfalls, making comparison between instruments difficult. Regardless, further optimisation of algorithms associated with the wearable is required before they are ready to be employed clinically.

Conclusion

Wearable technology has potential to differentiate dementia disease subtypes and may provide advantages over traditional methods to quantify gait. Due to their inexpensive and flexible nature, wearable technology may have multiple clinical applications beyond differentiation of dementia disease subtypes, such as monitoring change and identifying at-risk individuals.

Declarations

4.1 Statement of ethics

This study was approved by the NHS Local Research Ethics Committee, Newcastle and North Tyneside. Reference: 16/NE/005, IRAS project ID: 192941.

4.2 Availability of data and material

The datasets generated and analysed during the current study are not publicly available to ongoing analysis and publication but are available from the corresponding author on reasonable request.

5. References

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Table 1: Demographic, clinical and cognitive information for dementia disease subtypes

				Differences between all groups	
	AD	**DLB**	**PDD**	**F/X²**	**p**
N	32	28	14		
Age	77±6	76±6	78±6	.5	.596
Gender (m/f)	15/17[D,P]	22/6[A]	13/1[A]	**11.8**	**.003**
Height	1.67±.11	1.70±.10	1.67±.08	.6	.572
BMI	26.03±4.62	27.24±4.82	25.37±3.58	.9	.394
Dementia Meds (n%)	56%	75%	64%	1.8	.389
Fall in the past year (n%)	47%	61%	71%	2.6	.262
NART	117±6	115±6	117±6	2.1	.348
sMMSE (0-30)	23±4	24±4	24±4	.3	.715
CDR (0-3)	.8±.3	.8±.3	.9±.5	6.3	.394
% of participants with MCI	38%	39%	50%	**.7**	**.719**
UPDRS (0-108)	7±6[D,P]	23±15[A,P]	46±18[A,D]	**40.5**	**≤.001**
CIRS-G	8±4	10±4	11±4	4.6	.098
GDS	4±3	5±3	6±4	2.0	.372
ABC	80±18[P]	81±17[P]	64±25[A,D]	**6.2**	**.045**
BADLS	9±7[D,P]	13±6[A]	15±9[A]	**7.4**	**.025**

BMI = Body Mass Index, NART = National Adult Reading Test, sMMSE = Standardised Mini Mental State Examination, CDR = Clinical Dementia Rating scale, MCI = Mild cognitive impairment, UPDRS-III = Unified Parkinson's disease Rating Scale III, CIRS-G = Cumulative Illness Rating Scale – Geriatrics, GDS = Geriatric Depression Scale, ABC = Activity Balance Confidence Scale, BADLS = Bristol Activities of Daily Living Scale. P value in the table represents difference between groups derived from Kruskal Wallis tests or ANOVA; annotations within table represents differences between groups from t-tests or Mann Whitney U tests, and are interpreted as follows: A = different to AD, D = different to DLB, P = different to PDD

Table 2: Gait impairments derived from the instrumented walkway and wearable across dementia disease groups

	Wearable Measures					Instrumented Walkway Measures				
	AD (n= 32)	**DLB (n=28)**	**PDD (n=14)**	**F/X^2**	**p**	**AD (n=32)**	**DLB (n=28)**	**PDD (n=14)**	**F/X^2**	**p**
Pace										
Step Velocity (m/s)	.90±.17	.92±.13	.86±.14	.7	0.498	1.02±.25	1.00±.23	.89±.25	1.5	0.235
Step Length (m)	.52±.08	.54±.065	.49±.07	2.0	0.138	.57±.12	.57±.12	.51±.12	1.5	0.231
Step Time SD (ms)	35(13-109)^{P}	50(20-172)	84(29-152)^{A*}	**11.0**	**0.004***	22 (9-48) ^{P}	24(13-80)	33(13-60) ^{A}	**6.2**	**0.046**
Variability										
Swing Time SD (ms)	37(14-115) ^{P}	46(20-127)	70(32-139) ^{A}	**9.8**	**0.008**	20 (9-45)	22(11-42)	29(11-87)	4.8	0.089
Stance Time SD (ms)	41(16-126)^{P}	50(18-171)	70(35-166) ^{A}	**8.9**	**0.012**	30(12-69)	31(16-118)	41(14-76)	2.6	0.277
Step Vel SD (m/s)	.105(.05-.22)^{D,P}	.132(.07-.28)^{A}	.151(.06-.26)^{A*}	**11.2**	**0.004***	.065(.03-.11)	.074(.05-.18)	.069(.05-.14)	2.3	0.104
Step Len SD (m)	.056(.02-.12)^{D}	.084(.03-.14)^{A}	.086(.02-.17)	**6.6**	**0.037**	.030(.01-.04) ^{D,P}	.034(.02-.06) ^{A}	.036(.02-.06) ^{A}	**10.2**	**0.006**
Rhythm										
Step Time (ms)	576±56	594±60	584±54	.8	0.452	570±56	580±67	585±70	.4	0.709
Stance Time (ms)	727±67	744±66	739±52	.6	0.568	723(615-902)	758(599-981)	778(629-1029)	1.3	0.529
Swing Time (ms)	410(345-541)	432(349-603)	433(348-613)	1.2	0.537	392±37	396±50	384±53	.4	0.703
Asymmetry										
Step Time Asy (ms)	29.2(8.2-109.0)	33.0(4.5-73.3)	41.9(20.8-133.6)	5.7	0.059	12.21(.44-34.1)	17.00(1.8-48.9)	12.7(1.8-64.7)	3.4	0.181
Swing Time Asy (ms)	30.0(10.7-159.3)	32.9(5.1-73.5)^{P}	47.0(16.9-87.3)^{D}	**8.1**	**0.018**	6.6(1.0-31.3)	13.8(3.3-37.8)	13.3(.6-44.1)	5.0	0.082
Stance Time Asy (ms)	28.7(10.7-146.8)^{P}	31.3(4.2-76.8)^{P}	48.1(20.5-91.3)^{A,D}	**6.7**	**0.034**	8.1(.3-33.1)	13.9(.1-35.6)	15.7(1.0-47.4)	3.7	0.159
Postural Control										
Step Len Asy (m)	.077(.02-.30)	.064(.02-.25)	.106(.05-.24)	3.5	0.174	.014(0-.13)	.020(0-.07)	.017(0-.05)	.1	0.959

Normally distributed data analysed using one-way ANOVA is displayed as (mean ± standard deviation) while non-parametric analysis is displayed as (median (minimum- maximum)). Statistical significance set at $p \leq .05$. P value in the table represents difference between groups derived from Kruskal Wallis tests or ANOVA; annotations within table represents differences between groups from t-tests or Mann Whitney U tests, and are interpreted as follows: A = different to AD, D = different to DLB, P = different to PDD, SD =within-person standard deviation (i.e. gait variability), asy = asymmetry, m = metre, s = second, ms = millisecond. = measures that remained significant when Bonferroni correction is applied at $p < .004$*

Table 3: Area under the curve values for gait metrics derived from the wearable across dementia disease groups

	AD (n=32) vs DLB (n=28)				AD (n=32) vs PDD (n=14)				DLB (n=32) vs PDD (n=14)			
		95% Confidence Interval				95% Confidence Interval				95% Confidence Interval		
	Area	Lower Bound	Upper Bound	p value	Area	Lower Bound	Upper Bound	p value	Area	Lower Bound	Upper Bound	p value
Pace												
Step Velocity	0.499	0.647	0.35	0.988	0.614	0.783	0.444	0.223	0.645	0.825	0.466	0.128
Step Length	0.403	0.547	0.259	0.197	0.598	0.777	0.419	0.294	0.686	0.859	0.513	0.051
Step Time SD	0.632	0.491	0.773	0.08	0.799	0.661	0.937	**0.001**	0.681	0.512	0.85	0.058
Variability												
Swing Time SD	0.597	0.451	0.743	0.197	0.786	0.645	0.927	**0.002**	0.702	0.539	0.864	**0.035**
Stance Time SD	0.623	0.48	0.765	0.103	0.77	0.625	0.915	**0.004**	0.656	0.486	0.826	0.104
Step Vel SD	0.692	0.559	0.825	**0.011**	0.775	0.626	0.923	**0.003**	0.594	0.413	0.776	0.324
Step Length SD	0.674	0.537	0.811	**0.021**	0.676	0.497	0.855	0.059	0.515	0.326	0.704	0.873
Rhythm												
Step Time	0.586	0.441	0.731	0.254	0.54	0.366	0.715	0.667	0.452	0.269	0.634	0.612
Stance Time	0.569	0.423	0.715	0.358	0.533	0.362	0.705	0.72	0.444	0.265	0.623	0.557
Swing Time	0.573	0.426	0.719	0.335	0.583	0.401	0.764	0.377	0.503	0.314	0.691	0.979
Asymmetry												
Step Time Asy	0.541	0.393	0.69	0.584	0.719	0.57	0.867	**0.019**	0.679	0.511	0.846	0.062
Swing Time Asy	0.471	0.322	0.62	0.7	0.732	0.576	0.888	**0.013**	0.755	0.599	0.912	**0.008**
Stance Time Asy	0.489	0.339	0.639	0.882	0.692	0.533	0.851	**0.04**	0.758	0.609	0.907	**0.007**
Postural Control												
Step Length Asy	0.433	0.287	0.579	0.374	0.598	0.434	0.763	0.294	0.686	0.522	0.85	0.051

SD =within-person standard deviation (i.e. gait variability), asy = asymmetry, statistical significance set at $p \leq .05$