ISRCTN12062123 https://doi.org/10.1186/ISRCTN12062123

Finding a new way to measure fatigue in clinical studies

Submission date
31/07/2023

Recruitment status
No longer recruiting

Registration date
08/08/2023

Overall study status
Completed

Last Edited
14/11/2024

Condition category
Musculoskeletal Diseases

[ ] Prospectively registered
[ ] Protocol
[ ] Statistical analysis plan
[X] Results
[ ] Individual participant data

Plain English summary of protocol

Background and study aims
Fatigue is a defining feature of frailty and ageing, as well as a key factor in the loss of work productivity and impaired health-related quality of life in rheumatic and chronic disease. Current clinical measurements rely on patients' self-assessments which are hard to quantify reproducibly. Severity fluctuates which is also difficult to capture using subjective fatigue measures. No validated objective measures of fatigue exist.
Digital devices that capture activity in the natural environment provide an indirect, objective measurement of fatigue and daily living impact. They offer readily accessible data that could reduce errors from recall bias and identify physiological response patterns. The availability of reliable objective measures will also remove a key barrier to pharmaceutical industry investment in fatigue.
This pilot study aims to explore the use of medical-grade physical activity monitors and biosensors coupled with advanced data analytics and statistical modelling to identify signatures of physical fatigue, and also to explore neuropsychological tests as objective measures of mental fatigue.

Who can participate?
Patients aged 18 years and over with primary Sjogren's Syndrome (PSS)

What does the study involve?
Participants will wear two medical-grade devices to capture continuous physical activity, sleep data and physiological measures. This will occur over two separate 7-day periods 6-8 weeks apart. Neuropsychological tests will be carried out and confounding factors will be recorded. Subjective levels of physical and mental fatigue will be recorded three times daily via a patient diary during the 7-day observation period.

What are the possible benefits and risks of participating?
There are no direct benefits to participants but the data will be used to prepare funding applications for a larger study to find out more about the disease.

Where is the study run from?
Newcastle upon Tyne Hospitals NHS Foundation Trust (UK)

When is the study starting and how long is it expected to run for?
May 2018 to August 2022

Who is funding the study?
NIHR Newcastle Biomedical Research Centre (UK)

Who is the main contact?
Prof. Wan-Fai Ng, wng@ucc.ie

Contact information

Type(s)
Scientific, Principal investigator

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Public

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Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

Integrated Research Application System (IRAS)
247550

ClinicalTrials.gov (NCT)

Nil known

Protocol serial number
IRAS 247550, CPMS 40821

Study information

Scientific Title
Develop objective assessment tools for measuring fatigue in clinical studies

Acronym
TOOLS

Study objectives
The main objective is to identify activity patterns and associated physiological responses which correlate with self-report physical fatigue severity; and to explore whether neuropsychological performance corresponds to subjective report of mental fatigue severity.

Ethics approval required
Ethics approval required

Ethics approval(s)
approved 01/02/2019, North East - Newcastle & North Tyneside 1 REC (NHSBT Newcastle Blood Donor Centre, Newcastle upon Tyne, NE2 4NQ, United Kingdom; +44 (0)2071048084; nrescommittee.northeast-newcastleadnnorthtyneside1@nhs.net), ref: 19/NE/0002

Study design
Single-centre observational pilot study

Primary study design
Observational

Study type(s)
Other

Health condition(s) or problem(s) studied
Fatigue in primary Sjogren's Syndrome

Interventions
This is an exploratory pilot study. There will be four visits in total for each participant. A written consent will be signed, the neurocognitive tests will be completed and the participant will be fitted with two medical-grade devices to capture; continuous physical activity/”sleep” data and other physiological measures such as; Electrocardiogram (ECG), heart rate (HR), respiratory rate (RR), skin temperature (ST). The participant will be asked to wear the device for 7 days and will be asked to complete a fatigue diary four times a day. The diary will ask the participant to record any specific activities and comments when they have experienced fatigue (open answers). It will also include the PSS-specific ESSPRI which is a validated questionnaire which considers PSS symptoms. The second visit will occur after the 7-day period of monitoring and the participant will return the devices.

The participant will be asked to come back to clinic 6-8 weeks later for visit 3 to complete the study assessments and have both devices fitted for another 7-day period. The final fourth visit will take place after the 7-day monitoring period and the participant will return the devices. The following study assessments will occur at each visit:

Fatigue:
Fatigue will be measured using the Profile of Fatigue (PRO-F) and the Multidimensional Fatigue Inventory (MFI). Both questionnaires have separate measures for the physical and mental components of fatigue. Additionally, we will use the Cognitive Failures Questionnaire to quantify subjective cognitive symptoms.

To objectively evaluate different domains of cognitive function, we will use validated neuropsychological tests including: immediate/working memory (Digit span, corsi blocks); executive functioning and attention (verbal fluency, Stroop, Trail Making Test, Vigilance /continuous performance test); psychomotor functions (Digit symbol tests) memory (Rey-Auditory Verbal Learning Test; AVLT). Other measures of fatigue include validated questionnaires; orthostatic hypotension, insomnia severity index, Epworth sleepiness scale, functional outcomes of sleep short questionnaire and the hospital and anxiety questionnaire will be used for screening.

Demographics:
Data will be collected on age, sex, height, and weight to assess general health. Marital status, number of children, work status and number of persons in the household will indicate the level of support available at home which could impact fatigue. Medical history will be taken to detail any co-morbidities and treatments that may have a bearing on results.

Venesection:
A blood sample (25 ml) will be collected at each visit. Blood samples will include 2 PAXgene RNA, 3x EDTA (1 for plasma extraction) and 1 serum. A urine sample will be collected at the beginning and end of each study period for metabolomics analysis.

Biosensor devices fitted:
Participants will be shown how to use the devices and fitted with the patch. VitalPatch by Vitalconnect is a disposable patch worn on the chest. It measures heart rate, respiratory rate, skin temperature, body posture, fall detection and activity (steps). It is a CE-marked Medical Device - EU Class I, FDA 510(k). ActiGraph link (Medical Device EU Class 1, FDA cleared class II) measures raw acceleration, energy expenditure, MET rates, steps taken and physical activity intensity. This device also offers continuous subject data collection.

Patient diary:
A diary will be provided to report fatigue four times daily.

Intervention Type
Other

Primary outcome(s)
Measured using biosensor data in fatigued and non-fatigued patients:
1. Physical fatigue measured using activity monitors recording; total amount of moderate to vigorous physical activity (daily/weekly), sleep (nighttime rest) efficiency, activity/inactivity bouts (number and duration), mean daily/weekly activity counts. Data collected for two 7 day periods over 8 weeks.
2. Mental fatigue measured using neuropsychological tests; immediate/working memory (Digit

span, corsi blocks); executive functioning and attention (verbal fluency, Stroop, Trail Making Test, Vigilance/continuous performance test); psychomotor functions (Digit symbol tests) memory (Rey-Auditory Verbal Learning Test; AVLT). Data collected at visit 1 and visit 3.
3. Patient reported fatigue measured using a patient diary which is completed 4 times daily during the 7 day monitoring period. The Profile of Fatigue (PRO-F), the Multidimensional Fatigue Inventory (MFI) and Cognitive Failures Questionnaire are completed at the end of each monitoring period.

Key secondary outcome(s))
There are no secondary outcome measures

Completion date
31/08/2022

Eligibility

Key inclusion criteria
1. Age ≥18 years
2. Fulfils the American European Consensus Group (AECG) classification criteria for primary Sjögren's syndrome
3. Willing and able to provide informed written consent and attend clinic for visits

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

Total final enrolment
105

Key exclusion criteria
1. Hospital Anxiety and Depression Score (HADS ≥11)
2. Fibromyalgia or chronic pain syndromes.
3. History of cerebrovascular diseases, dementia (mini mental state examination score 24), other central nervous system injuries/disorders that impair neurocognitive function
4. A history of severe skin allergies

Date of first enrolment
15/04/2019

Date of final enrolment
12/08/2022

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
The Newcastle upon Tyne Hospitals NHS Foundation Trust
Freeman Hospital
Freeman Road
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Newcastle upon Tyne
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NE7 7DN

Sponsor information

Organisation
Newcastle upon Tyne Hospitals NHS Foundation Trust

ROR
https://ror.org/05p40t847

Funder(s)

Funder type
Government

Funder Name
NIHR Newcastle Biomedical Research Centre

Alternative Name(s)
Newcastle Biomedical Research Centre, Newcastle NIHR Biomedical Research Centre

Funding Body Type
Private sector organisation

Funding Body Subtype

Research institutes and centers

Location
United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study will be available upon request from Victoria Macrae (victoria.macrae@newcastle.ac.uk).

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Abstract results	AB0799	19/06/2024	14/11/2024	No	No
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes
Study website	Study website	11/11/2025	11/11/2025	No	Yes