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Understanding motivation problems in clinical disorders

Submission date
02/09/2024

Recruitment status
No longer recruiting

Registration date
03/09/2024

Overall study status
Completed

Last Edited
08/10/2024

Condition category
Nervous System Diseases

[_] Prospectively registered
[X] Protocol
[_] Statistical analysis plan
[_] Results
[_] Individual participant data
[_] Record updated in last year

Plain English summary of protocol

Background and study aims
The aim of the study is to gain a better understanding of goal-directed decision-making and how it goes wrong in Parkinson's disease and early psychosis - although very different disorders, both are associated with motivation problems and underpinned by dysregulation of dopamine signalling.
Motivation is a broad term that encompasses many different processes, pathways and neural substrates. It is clear that no one’s experience of ‘apathy’ is the same, and this may relate to subtle differences in the pathways in the brain affected. For instance, people might lose their interest in learning things, connecting with family members or doing hobbies. This could be, for instance, because these activities take on less value in the currency of the brain, because of difficulty converting a decision into an action, because of greater attendance to the effortful 'costs' of an action, or due to difficulties of planning or ability to maintain drive and attention towards a goal. These distinct processes could all lead to a similar observation of less goal-directed behaviour.
The idea of this project is to try and scrutinise processes like those described above using a novel, decision-making experiment, and, importantly, to see if it correlates with how people describe their motivation symptoms. A related aim is to see how physical effort and having more options to choose from affects decision-making, and (in patients with Parkinson's disease) how dopamine can influence choices. The researchers will also use modern computational modelling techniques to better understand aspects of the decision-making process (a tool increasingly being used to understand these complex processes). They also hope to conduct a qualitative study on a subset of participants to better understand the behavioural data.

Who can participate?
Patients aged 18-80 years with Parkinson's disease or aged 18-40 years with early psychosis

What does the study involve?
Participants with Parkinson's disease will be invited to participate in two sessions, once having taken, the other having delayed, their usual dopaminergic medication. Each study session takes around 2 - 2.5 hours. Participants will complete a computer-based decision-making task (about 1 hour and 15 minutes), clinical assessments and questionnaires (about 40 minutes). For a segment of the decision-making task, participants' decisions will determine the amount of

physical effort that participants will need to exert via a grip force device. A subset of participants will participate in a clinical interview at a later date to enable qualitative exploration of motivation problems for use in mixed methods research.

What are the possible benefits and risks of participating?
It is hoped that this research will make progress in distinguishing the different processes in individuals experiencing motivation problems, which could in turn lead to better and more accurate identification of these symptoms in the clinic and even targeted treatments. There is no immediate benefit for participants aside from contributing to research. The main risks relate to the use of the grip force device, which may include discomfort or musculoskeletal complications (participants with known wrist injuries or carpal tunnel syndrome will be excluded from participation).

Where is the study run from?
University of Birmingham (UK)

When is the study starting and how long is it expected to run for?
January 2024 to October 2025

Who is funding the study?
Wellcome Trust (UK)

Who is the main contact?
Dr Jamie Talbot, jxt289@student.bham.ac.uk

Contact information

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Principal investigator

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Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

Integrated Research Application System (IRAS)
336513

Protocol serial number
ERN_1761-Oct2023, CPMS 63297

Study information

Scientific Title
Dynamics of motivated decision-making in striatal disorders

Study objectives

The main hypotheses are that self-reported apathy scores, or boosting dopamine in Parkinson's disease, will relate to one or more metrics of decision-making. The main outcome variables for analysis will be reaction times, choice accuracy, or model parameters fitted using sequential sampling models

The key hypotheses are:
1. Apathy (and/or its behavioural dimension) will be associated with greater caution in decisions involving physical effort
2. Apathy or its component dimensions will be associated with slower information processing (slower drift rates) or greater caution (higher thresholds) in decisions involving more options
3. Boosting dopamine will reduce caution (lower thresholds) in choices leading to physical effort due to reduced aversion to effort, or reduced drift rates, non-decision time or thresholds in tasks choices leading to rewards.
4. Boosting dopamine may lead to lower subjective ratings of choice difficulty/cognitive effort.

Ethics approval required
Ethics approval required

Ethics approval(s)
approved 22/07/2024, London - South East Research Ethics Committee (Health Research Authority, 2 Redman Place, Stratford, E20 1JQ, United Kingdom; +44 (0)20 7104 8222; londonsoutheast.rec@hra.nhs.uk), ref: 24/LO/0512

Study design
Basic science study

Primary study design
Observational

Study type(s)
Other

Health condition(s) or problem(s) studied
Parkinson's disease and early psychosis

Interventions
Participants will complete a computer-based decision-making task, as well as questionnaires probing mood, motivation and cognition. Participants with Parkinson's disease will perform two sessions, once having delayed their usual dopaminergic medication and once within 4 hours of taking their medication. Patients with psychosis will perform one session. A subset of participants will be invited to participate in a qualitative interview at a later date.

Intervention Type
Behavioural

Primary outcome(s)
1. Reaction time (relating to stimulus presentation to choice interval) measured on each trial; total trials = 320 per experimental session.
2. Choice (relating to which of available options was chosen, corresponding to a level of effort or reward) - measured on each trial; total trials = 320 per experimental session.
3. Self-rated apathy measured using The Dimensional Apathy Scale - total score and dimensional

subscores (auto-activation, affective and executive dimensions). Administered once during the first experimental session.
4. (Qualitative study only): Lived experience of apathy symptoms gleaned from clinical interviews in a subset of participants after completing the behavioural task. Leading questions are based on the Lille Apathy Rating Scale (LARS).

Key secondary outcome(s))
1. Global cognition measured using the Montreal Cognitive Assessment (MOCA) during the first experimental session
2. Mood measured using Patient Health Questionnaire-8 (PHQ-8) during the first experimental session
3. Anhedonia measured using the Snaith-Hamilton Pleasure Scale (SHAPS) during the first experimental session
4. Apathy measured using the Apathy Motivation Index (AMI) during the first experimental session
5. Volume of spontaneous thought, measured using Adapted Glasgow Content of Thoughts Inventory (GCTI) during the first experimental session
6. Fatigue measured using the Fatigue Severity Scale (FSS) during the first experimental session
7. Working memory measured using the digit span test during the first experimental session
8. (Patients with Parkinson's disease): Parkinson's symptom severity measured using the Unified Parkinson's Disease Rating Scale (UPDRS) during the first experimental session. UPDRS part III (motor exam) will also be performed during the second session
9. (Patients with psychosis): Negative symptom burden measured using Brief Negative Symptom Scale (BNSS) during the first session
10. Subjective ratings of choice difficulty (sliding scale between 0-10) recorded during the behavioural task (84 ratings per session)
11. Physical force production (area under curve, maximum force, yank force) recorded during the behavioural task (recorded on every trial of effort subtask; total 160 trials per experimental session)

Completion date
25/10/2025

Eligibility

Key inclusion criteria
Inclusion criteria for those with early psychosis:
1. Aged 18-40 years (inclusive) at the time of eligibility assessment
2. Able to understand written and spoken English
3. Meets one or more criteria for Ultra High Risk for psychosis groups as assessed by the Comprehensive Assessment of At Risk Mental States (CAARMS) or the Structured Interview for Psychosis –Risk Syndromes (SIPS), the Social and Occupational Functioning Assessment Scale (SOFAS) and the Functional Intraoral Glasgow Scale (FIGS)
4. Meets criteria for early/first episode psychosis (meet International Classification of Diseases [ICD-10] criteria for a diagnosis of schizophrenia and related psychoses (ICD-10 code F20, F22, F25, F28, F29) and within 3 years of first diagnosis of psychotic disorder at the time of eligibility assessment

Inclusion criteria for those with Parkinson's disease:
1. Age 18-80 years (inclusive)
2. Formal diagnosis of idiopathic Parkinson's disease

3. Able to understand written and spoken English
4. Hoehn and Yahr Parkinson's grade 1 – 4

Participant type(s)
Patient, Service user

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Upper age limit
80 years

Sex
Male

Key exclusion criteria
1. Lack of capacity/inability to consent
2. Significant neurological or psychiatric comorbidity other than psychosis/at-risk mental state (e.g. significant mood disorder, nervous system disorders such as stroke, traumatic brain injury)
3. Current or lifetime diagnosis of antisocial personality disorder, autism or other neurodevelopmental disorder
4. Significant risk to self or other people, as determined by their clinical team
5. Detained under the Mental Health Act
6. History of alcohol or substance use disorder (abuse/dependence) within 6 months prior to eligibility assessment (nicotine and caffeine dependence are not exclusionary)
7. Significant upper limb motor impairment (i.e. that would impair squeezing a handheld force-meter or clicking a mouse/button)
8. Significant wrist injuries, carpal tunnel syndrome, or musculoskeletal problems that would cause discomfort in squeezing tasks
9. Bed-bound or unable to attend University for in-person study

Date of first enrolment
20/08/2024

Date of final enrolment
25/10/2025

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
University of Birmingham
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Sponsor information

Organisation
University of Birmingham

ROR
https://ror.org/03angcq70

Funder(s)

Funder type
Charity

Funder Name
Wellcome Trust

Alternative Name(s)
Wellcome, WT

Funding Body Type
Private sector organisation

Funding Body Subtype
Trusts, charities, foundations (both public and private)

Location
United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan

The datasets generated during the current study will be stored in a publicly available repository or will be available upon request from Jamie Talbot (jtalbot.esq@gmail.com).

IPD sharing plan summary

Stored in publicly available repository, Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Participant information sheet	version 1.1	04/01/2024	03/09/2024	No	Yes
Participant information sheet	People with Parkinson's disease version 1.2	17/07/2024	03/09/2024	No	Yes
Participant information sheet	People with psychosis version 1.1	04/01/2024	03/09/2024	No	Yes
Protocol file	version 1.1	04/01/2024	03/09/2024	No	No