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Background to your research	
Plain English title	Developing new treatments to improve motivation in Parkinson's disease

A plain English description of the research

Apathy, or a loss of motivation, is a common non-motor symptom in Parkinson's disease (PD). However, despite its prevalence, we don't have a full understanding of what causes it, so treatment options are limited. In this project, we aim to test the potential of a new therapy, a drug called atomoxetine, for apathy in PD. Atomoxetine is a drug that boosts levels of noradrenaline, which is a chemical in the brain (similar to dopamine) that is reduced in PD. We believe it could have some important benefits in improving motivation in PD. Our study is designed to provide the first proof of this, by administering a one-off dose of atomoxetine to individuals with PD and testing if this improves their performance on tests of motivation. We will also ask our participants to undergo a brain scan, so we can better understand the brain changes linked to motivation problems. Importantly, our research team has conducted previous studies where over 100 individuals with PD have been given atomoxetine, without any negative side-effects, so we know that it is a safe and well-tolerated drug. The study would involve three visits to our clinic. Visit one would be a short brain scan. At the next two visits, participants would be given either atomoxetine or a placebo (a non-active tablet), and tested on computerised tests to measure motivation. We would then be able to measure how atomoxetine improved motivation in comparison to the placebo condition. All visits will be conducted in a specialised clinical research facility at the Addenbroke's hospital, Cambridge, with an experienced team of doctors and researchers.

Summarise the research aims (i.e. projected study length and any suitable links to online information)

The aim of the research is to determine if atomoxetine can improve motivation in people with PD. By linking our findings to information from brain scans, we will be able to determine the brain changes that contribute to changes in motivation that can occur in PD. The ultimate aims of our study will be i) to establish that atomoxetine is a drug that can improve motivation in people with PD; and ii) that we gain a better understanding of why certain people with PD have problems with their motivation, so that we are better able to predict who might benefit from treatment with atomoxetine. The outcome of our study would be to establish the initial proof-of-concept for treating apathy in PD with atomoxetine. So, the next step to

follow our study would be to conduct a longer trial, where we could see if atomoxetine improves motivation in everyday life. The study will run from June 2018 until January 2019.

Who is funding the research?

Parkinson's UK

The participants

What key criteria should participants meet?

Participants should have a diagnosis of Parkinson's disease made by a neurologist. The main requirements for our study are that they are safe to have atomoxetine and to have an MRI brain scan. So there are some requirements that a person needs to meet to be involved in the study. These include:

- They should not have any heart problems.
- They must have no pacemakers/metal implants; no extensive metallic dental work; no metal of any kind above the chest line; no tattoos above the chest line.
- They should not be taking a Monoamine oxidase inhibitor for their PD; these include drugs called Rasagaline and Selegiline.
- There are certain anti-depressant medications should not be taken with atomoxetine, so if you are on anti-depressant medication we would discuss with you the type you are on and confirm that it is safe to take with atomoxetine.

We appreciate that some of these criteria are complicated, so if you are keen to participate but you are not sure whether you meet the criteria, we will be very happy for you to get in touch and we can discuss your eligibility for the study with you.

What will taking part involve for the participants? (schedule of activity i.e. if home visits possible, length of visits, medication changes)

- Participants will visit us for 3 sessions.
- Session 1 will involve a brain scan and some questionnaires, altogether this session will take about 1.5 hours.
- Sessions 2 and 3 will be on separate days, at least 6 days apart. These will involve computerised tasks assessing motivation, following either a single dose of atomoxetine or placebo. No experience with computers is required to do the tasks. During some of the tasks, we will use a special camera to take a video of your eyes, this is because pupil size can be an indication of how effectively the atomoxetine medication is working.
- Regular antiparkinson medication can be taken as usual, as there are no problematic interactions with atomoxetine.
- Blood samples (about two teaspoons) will be taken to measure atomoxetine blood levels.
- Sessions 2 and 3 will last about 4 hours in total. There will be resting time after the atomoxetine/placebo is administered, when participants, and friends/family members that have accompanied them, can relax (read, watch television, chat with the research team). After 2 hours atomoxetine reaches its active levels in the brain, at this point we will take blood samples. The computerised tasks will then take approximately 2 hours, including regular breaks.

We will reimburse travel costs for participants.