

# Aggression following traumatic brain injury: Testing the effectiveness of risperidone

<b>Submission date</b> 15/12/2016	<b>Recruitment status</b> No longer recruiting	<input checked="" type="checkbox"/> Prospectively registered <input checked="" type="checkbox"/> Protocol
<b>Registration date</b> 19/12/2016	<b>Overall study status</b> Completed	<input type="checkbox"/> Statistical analysis plan <input checked="" type="checkbox"/> Results
<b>Last Edited</b> 15/09/2020	<b>Condition category</b> Injury, Occupational Diseases, Poisoning	<input type="checkbox"/> Individual participant data

## Plain English Summary

### Background and study aims

Traumatic brain injury (TBI) is an injury to the brain caused by a head injury (trauma to the head). Depending on the part of the brain that is injured, it can cause changes in behaviour, physical abilities or even personality. Many people who suffer a TBI experience long lasting emotional problems such as irritability and anger, which can lead to aggressive behaviour. This can be extremely distressing for people with TBI and their family. Both drug and non-drug treatments are used to manage aggression in people after a head injury. Although doctors use many drugs for this purpose, their use is often based on evidence of successful treatment of aggression in other conditions, such as autism or epilepsy. One drug that has shown promise in people with autism is an antipsychotic called risperidone. Risperidone is also used regularly to treat aggressive behaviour in people who have had a head injury. However, there is currently insufficient information to know how effective risperidone is for improving irritability and aggression after head injury. The aim of this study is to find out whether it is feasible to conduct a larger scale trial to determine if risperidone is a worthwhile treatment for people experiencing irritability and aggression following a head injury (TBI) when the possible benefits and possible side effects are weighed up.

### Who can participate?

Adults with TBI who have been referred to a clinician for the management of aggression

### What does the study involve?

Participants are randomly allocated to one of two groups. Those in the first group are treated with a placebo (dummy drug) for 12 weeks and those in the second group are treated with risperidone for 12 weeks. The starting dose of trial treatment will be 1 capsule per day, which is 1mg of risperidone, which may be increased up to a maximum of 4 capsules per day. Participants in both groups are followed up weekly for 12 weeks to assess aggression levels as well as a check of general health and wellbeing.

### What are the possible benefits and risks of participating?

There are no direct benefits involved with participating. To reduce the risk of side effects for

those allocated to risperidone, all participants start on a low dose and increase the dose slowly. Therefore, major side effects are unlikely although this cannot be guaranteed. The most common side effects of risperidone are drowsiness and weight gain.

Where is the study run from?

1. St George's Hospital (UK)
2. Hammersmith Hospital (UK)
3. Neuropsychiatry (West Kent and Medway) (UK)
4. Wolfson Rehabilitation Service (UK)

When is the study starting and how long is it expected to run for?  
November 2015 to October 2018

Who is funding the study?  
National Institute for Health Research (UK)

Who is the main contact?  
Dr Verity Leeson  
after@imperial.ac.uk

**Study website**  
<http://www.aftertrial.org/>

## Contact information

**Type(s)**  
Scientific

**Contact name**  
Dr Verity Leeson

**Contact details**  
Trial Coordinating Office  
Centre for Mental Health  
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## Additional identifiers

**EudraCT/CTIS number**  
2015-000641-23

**IRAS number**

**ClinicalTrials.gov number**

**Secondary identifying numbers**

19575

## **Study information**

**Scientific Title**

Aggression Following TBI: Effectiveness of Risperidone

**Acronym**

AFTER

**Study hypothesis**

The aim of this study is to assess the feasibility of conducting a substantive full scale definitive randomised controlled trial investigating the efficacy of risperidone versus placebo in the treatment of aggression in adults with Traumatic Brain Injury (TBI).

**Ethics approval required**

Old ethics approval format

**Ethics approval(s)**

London - Westminster Research Ethics Committee, 21/09/2015, ref: 15/LO/1181

**Study design**

Randomised; Interventional; Design type: Treatment, Drug

**Primary study design**

Interventional

**Secondary study design**

Randomised controlled trial

**Study setting(s)**

Hospital

**Study type(s)**

Treatment

**Participant information sheet**

Not available in web format, please use the contact details to request a patient information sheet

**Condition**

Specialty: Mental Health, Primary sub-specialty: Physical

**Interventions**

Eligible participants will be randomised to receive either risperidone or placebo at a ratio of 1:1, stratified by site. A flexible dosing regimen of risperidone will be used. Dosing will start with 1 mg once daily and be titrated in 1mg increments, not more than once every 7 days, to a

maximum of 4mg a day (2mg bd). The dose may also be reduced to a lower dose (minimum 1 mg once daily) at any time. The decision about whether to amend the dose will be based on the participant's response to the trial medication in terms of level of aggression, and whether any unacceptable side effects that may be due to the trial medication are reported. A lower dose may be maintained before the maximum dose is reached where substantial improvement occurs, or where side effects are reported. Equivalent numbers of placebo capsules will also be administered to the appropriate participants. Participants are followed up weekly for a total of 12 weeks.

### **Intervention Type**

Other

### **Phase**

Phase IV

### **Primary outcome measure**

Self-reported aggression is measured using the Modified Overt Aggression Scale (MOAS) at baseline and weekly for 12 weeks.

### **Secondary outcome measures**

1. Irritability is assessed using the Irritability Questionnaire (IRQ) at baseline and 12 weeks
2. Social functioning is measured using the Extended Glasgow Outcome Scale (GOS-E) at baseline and 12 weeks
3. Health-related Quality of life (QoL) is measured using the EQ-5D-5L and SF-12 questionnaires at baseline and 12 weeks
4. Adverse events profile is assessed using the UKU scale at baseline and 12 weeks
5. Carer Wellbeing is assessed using the wellbeing section of the 'carer wellbeing and support questionnaire (CWS) at baseline and 12 weeks
6. Health economics are assessed using the Client Service Receipt Inventory (CSRI) at baseline and 12 weeks

### **Overall study start date**

27/11/2015

### **Overall study end date**

22/10/2018

## **Eligibility**

### **Participant inclusion criteria**

1. Aged between 18 and 65 years
2. A confirmed clinical diagnosis of TBI which occurred at least six months prior to recruitment, evidenced as a rating of moderate/severe or mild (probable) based on Mayo Clinic criteria
3. Referred to the clinician for the management of aggression and for whom the clinician is considering a pharmacological intervention for this problem after investigating and addressing physical, psychological and social triggers
4. Competent and willing to provide written, informed consent
5. The patient or their carer is able to understand how to manage prescribed medication

### **Participant type(s)**

Patient

**Age group**

Adult

**Lower age limit**

18 Years

**Sex**

Both

**Target number of participants**

Planned Sample Size: 50; UK Sample Size: 50

**Total final enrolment**

14

**Participant exclusion criteria**

1. Suffering from Post-Traumatic Amnesia (PTA), which constitutes a sub-acute confusional state
2. Co-morbid severe mental illness such as schizophrenia and other psychoses, bipolar disorder, major depressive disorder, personality disorder, and dementia, and where the clinicians are treating primarily a psychiatric disorder rather than aggressive behaviour
3. Already prescribed an antipsychotic drug or any other drug that may interact with risperidone at the time of randomisation. A wash-out period of at least two weeks is required prior to randomisation.
4. Any other contraindication for using risperidone including a previous history of severe adverse events
5. Has no fixed abode or any other reason for which compliance with trial medication and monitoring could pose a major problem
6. Is pregnant or trying to conceive, breastfeeding, or a woman of childbearing potential not using a highly effective birth control
7. Lactose intolerance
8. Known cardiovascular disease (e.g., heart failure, myocardial infarction, conduction abnormalities including family history of QT prolongation, dehydration, hypovolaemia, bradycardia, or electrolyte disturbances (hypokalaemia, hypomagnesaemia), or cerebrovascular disease
9. A clinically significant low white blood cell count or a drug-induced leukopenia/neutropenia
10. A history of seizures

**Recruitment start date**

09/01/2017

**Recruitment end date**

16/01/2018

**Locations**

**Countries of recruitment**

England

United Kingdom

**Study participating centre**

**St George's Hospital**

Blackshaw Road

London

United Kingdom

SW17 0QT

**Study participating centre**

**Hammersmith Hospital**

Du Cane Road

White City

London

United Kingdom

W12 0HS

**Study participating centre**

**Neuropsychiatry (West Kent and Medway)**

Darent House

Hospital Road

Sevenoaks

United Kingdom

TN13 3PG

**Study participating centre**

**Wolfson Rehabilitation Service**

Queen Mary's Hospital

Roehampton Lane

London

United Kingdom

SW15 5PN

## **Sponsor information**

**Organisation**

Central and North West London NHS Foundation Trust

**Sponsor details**

1st Floor, Bloomsbury Building  
St Pancras Hospital  
4, St Pancras Way  
London  
England  
United Kingdom  
NW1 0PE

**Sponsor type**

Hospital/treatment centre

**ROR**

<https://ror.org/05drfg619>

## **Funder(s)**

**Funder type**

Government

**Funder Name**

National Institute for Health Research

**Alternative Name(s)**

National Institute for Health Research, NIHR Research, NIHRresearch, NIHR - National Institute for Health Research, NIHR (The National Institute for Health and Care Research), NIHR

**Funding Body Type**

Government organisation

**Funding Body Subtype**

National government

**Location**

United Kingdom

## **Results and Publications**

**Publication and dissemination plan**

One conference will be organised at the end of the project to disseminate findings. This event will be free of charge to attend and open to a wide range of delegates. A summary report will be produced and sent to a wide range of stakeholders. Papers will be prepared for publication in high impact peer-reviewed journals. Findings of the study will also be presented in local, national and international meetings and conferences. The results of the trial will be posted by the sponsor on EudraCT and made available to the public via the EU Clinical Trials Register. Care will be paid to disseminating to care staff and family carers via appropriate organisations.

## Intention to publish date

22/10/2019

## Individual participant data (IPD) sharing plan

The current data sharing plans for the current study are unknown and will be made available at a later date.

## IPD sharing plan summary

Data sharing statement to be made available at a later date

## Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
<a href="#">Protocol article</a>	protocol	21/06/2018		Yes	No
<a href="#">Basic results</a>			17/06/2020	No	No
<a href="#">Results article</a>	results	10/09/2020	15/09/2020	Yes	No
<a href="#">HRA research summary</a>			28/06/2023	No	No