### Review title and timescale

1. **Review title**
   
   Give the working title of the review. This must be in English. Ideally it should state succinctly the interventions or exposures being reviewed and the associated health or social problem being addressed in the review.

   **Systematic Review and Meta Analysis of the Efficacy of Olfactory Ensheathing Glia transplants on locomotor recovery in animal models of traumatic spinal cord injury**

2. **Original language title**
   
   For reviews in languages other than English, this field should be used to enter the title in the language of the review. This will be displayed together with the English language title.

3. **Anticipated or actual start date**
   
   Give the date when the systematic review commenced, or is expected to commence.

   **19/09/2013**

4. **Anticipated completion date**
   
   Give the date by which the review is expected to be completed.

   **30/10/2015**

5. **Stage of review at time of this submission**
   
   Indicate the stage of progress of the review by ticking the relevant boxes. Reviews that have progressed beyond the point of completing data extraction at the time of initial registration are not eligible for inclusion in PROSPERO. This field should be updated when any amendments are made to a published record.

   The review has not yet started **×**

<table>
<thead>
<tr>
<th>Review stage</th>
<th>Started</th>
<th>Completed</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preliminary searches</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Piloting of the study selection process</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Formal screening of search results against eligibility criteria</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Data extraction</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Risk of bias (quality) assessment</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Data analysis</td>
<td>Yes</td>
<td>Yes</td>
</tr>
</tbody>
</table>

Provide any other relevant information about the stage of the review here.

### Review team details

6. **Named contact**
   
   The named contact acts as the guarantor for the accuracy of the information presented in the register record.

   **Ralf Watzlawick**

7. **Named contact email**
   
   Enter the electronic mail address of the named contact.

   ralf.watzlawick@charite.de

8. **Named contact address**
   
   Enter the full postal address for the named contact.

9. **Named contact phone number**
   
   Enter the telephone number for the named contact, including international dialing code.

10. **Organisational affiliation of the review**
    
    Full title of the organisational affiliations for this review, and website address if available. This field may be completed as ‘None’ if the review is not affiliated to any organisation.

    **Department of Neurology and Experimental Neurology, Charité Campus Mitte, Clinical and Experimental Spinal Cord Injury Research Laboratory (Neuroparaplegiology), Charité – Universitätsmedizin Berlin, Germany**
Review team members and their organisational affiliations

Give the title, first name and last name of all members of the team working directly on the review. Give the organisational affiliations of each member of the review team.

<table>
<thead>
<tr>
<th>Title</th>
<th>First name</th>
<th>Last name</th>
<th>Affiliation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mr</td>
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<td>Brommer</td>
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<td>Macleod</td>
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<tr>
<td>Professor</td>
<td>David W.</td>
<td>Howells</td>
<td>Stroke Division, Florey Institute of Neuroscience and Mental Health, Melbourne, Victoria, Australia</td>
</tr>
<tr>
<td>Professor</td>
<td>Jan M.</td>
<td>Schwab</td>
<td>Department of Neurology and Experimental Neurology, Charité Campus Mitte, Clinical and Experimental Spinal Cord Injury Research Laboratory (Neuroparaplegiology), Charité – Universitätsmedizin Berlin, Germany. Center for Stroke Research Berlin, Charite`–Universita/tsmedizin, Berlin, Germany</td>
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12 Funding sources/sponsors
Give details of the individuals, organizations, groups or other legal entities who take responsibility for initiating, managing, sponsoring and/or financing the review. Any unique identification numbers assigned to the review by the individuals or bodies listed should be included.

not specified

13 Conflicts of interest
List any conditions that could lead to actual or perceived undue influence on judgements concerning the main topic investigated in the review.

Are there any actual or potential conflicts of interest?
None known

14 Collaborators
Give the name, affiliation and role of any individuals or organisations who are working on the review but who are not listed as review team members.

| Title | First name | Last name | Organisation details |

Review methods

15 Review question(s)
State the question(s) to be addressed / review objectives. Please complete a separate box for each question.

The aim of this study is to systematically review the literature describing the effect of OEC transplantation into the injured spinal cord and its influence on locomotor recovery in animal models of traumatic SCI.

It also aims to perform a meta-analysis using the DerSimonian and Laird random effects model.

Furthermore we will provide an assessment for the presence and impact of possible publication bias.

16 Searches
Give details of the sources to be searched, and any restrictions (e.g. language or publication period). The full search strategy is not required, but may be supplied as a link or attachment.

Electronical search of Pubmed, ISI Web of Science and Embase. There will be no restrictions regarding language or publication period. The search results will be limited to animals.

17 URL to search strategy
If you have one, give the link to your search strategy here. Alternatively you can e-mail this to PROSPERO and we will store and link to it.

http://www.crd.york.ac.uk/PROSPEROFILES/26494_STRATEGY_20150828.pdf

I give permission for this file to be made publicly available
Yes

18 Condition or domain being studied
Give a short description of the disease, condition or healthcare domain being studied. This could include health and wellbeing outcomes.

Every year about 130,000 people are involved in trauma leading to Spinal Cord Injury (SCI) and it is estimated that 2.5 million people suffer from SCI worldwide. Until today there is a major lack of therapies to treat this condition and therefore SCI has been subject to a lot of research in the recent years. Insufficient re-growth of axonal fibres through the primary lesion leads to limited axonal regeneration. Furthermore, consecutive secondary damage and enriched molecular barriers hamper the improvement of functional outcome.
19 Participants/population
Give summary criteria for the participants or populations being studied by the review. The preferred format includes
details of both inclusion and exclusion criteria.
This review will examine animals with traumatic SCI only. There is no restriction to the kind of animal. Different types
of injury will be included, e.g. hemisection, transection, contusion, compression and photochemical injury.

20 Intervention(s), exposure(s)
Give full and clear descriptions of the nature of the interventions or the exposures to be reviewed
We will examine the effects of OEG transplantation into the injured spinal cord of in vivo animals. OEGs may be
transplanted in cultured form, uncultured or in form of blocks of olfactory mucosa. Studies examining combined
treatments, such as OEGs and stem cells, or OEGs and Metylprednisolone will be excluded.

21 Comparator(s)/control
Where relevant, give details of the alternatives against which the main subject/topic of the review will be compared
(e.g. another intervention or a non-exposed control group).
The treatment group will be compared to a control group which received the same injury but no treatment (or only
medium as a volume substitute). If no control group is included the study will be excluded.

22 Types of study to be included initially
Give details of the study designs to be included in the review. If there are no restrictions on the types of study design
eligible for inclusion, this should be stated.
We will include animal studies to assess the efficacy of OEG transplantation into the injured spinal cord.

23 Context
Give summary details of the setting and other relevant characteristics which help define the inclusion or exclusion
criteria.

24 Primary outcome(s)
Give the most important outcomes.
Functional locomotor outcome. Several different scales and tests are used to measure functional outcome, such as
the Basso, Beattie, Bresnahan (BBB) or Basso Mouse Scale for Locomotion (BMS) score. All manner of functional
outcome will be included.
Give information on timing and effect measures, as appropriate.

25 Secondary outcomes
List any additional outcomes that will be addressed. If there are no secondary outcomes enter None.
None
Give information on timing and effect measures, as appropriate.

26 Data extraction, (selection and coding)
Give the procedure for selecting studies for the review and extracting data, including the number of researchers
involved and how discrepancies will be resolved. List the data to be extracted.
Titles and abstracts will be obtained using the search strategy. Titles and abstracts will be screened by two
independent researchers to identify papers potentially meeting the inclusion criteria. Fulltexts of these papers will be
obtained and again independently screened. Papers meeting the inclusion criteria will be included. Should there be
different opinions between the two investigators a discussion with other members of the review team will settle the
issue. Data extraction: General Data: - Author, year of publication, corresponding author, title - Animal info (species,
gender, age), no. of total animals - Model of SCI (hemisection, contusion, transection) Characteristics of the
intervention: - Information about used therapeutic intervention (dose range, time point of delivery) - Surgical
information of injury model (route of delivery, time point of application) Outcome measurement: - Type of outcome
measure: behavioural outcome (mean, variance) - Number per group - Method of assessment (timing, method of
quantification)

27 Risk of bias (quality) assessment
State whether and how risk of bias will be assessed, how the quality of individual studies will be assessed, and
whether and how this will influence the planned synthesis.
The methodological quality of each study will be assessed using a modified 9-point item quality checklist (modified
from the 10 point CAMARADES quality score) (i) reporting of a sample size calculation (ii) control of animals’
temperature (iii) use of anaesthetics other than ketamine (because of its marked intrinsic neuroprotective activity (iv)
randomised treatment allocation (v) treatment allocation concealment (vi) blinded assessment of outcome (vii)
publication in a peerreviewed journal; (viii) statement of compliance with regulatory requirements (ix) and statement of
potential conflicts of interest We will assess for possible publication bias using funnel plot, Egger regression and trim
and fill. The number of missing studies will be identified using metatrim in STATA.

28 Strategy for data synthesis
Give the planned general approach to be used, for example whether the data to be used will be aggregate or at the
level of individual participants, and whether a quantitative or narrative (descriptive) synthesis is planned. Where
appropriate a brief outline of analytic approach should be given.
We will calculate normalised effect sizes for each experiment. Where a single control group served multiple treatment
groups, the size of the control group will be adjusted to account for this. We will pool these effect sizes to derive an
overall weighted mean difference effect using DerSimonian and Laird random effects meta-analysis. To investigate
the impact of study design characteristics on outcome we will use random effects meta-regression. Data will be
stratified according to: different drugs, level of SCI lesion, anaesthetic used, different animals, type of SCI, sex, used
method of induction of injury, blinded assessment of outcome and study quality.

29 Analysis of subgroups or subsets
Give any planned exploration of subgroups or subsets within the review. ‘None planned’ is a valid response if no
subgroup analyses are planned.
We are expecting a large number of studies to make use of the BBB scale, as this is the most commonly used tool to
assess for functional outcome. Should this expectation come true, we may conduct a subgroup analysis for BBB only

Review general information

30 Type of review
Select the type of review from the drop down list.
Intervention

31 Language
Select the language(s) in which the review is being written and will be made available, from the drop down list. Use
the control key to select more than one language.
English

Will a summary/abstract be made available in English?
Yes

32 Country
Select the country in which the review is being carried out from the drop down list. For multi-national collaborations
select all the countries involved. Use the control key to select more than one country.
Germany

33 Other registration details
Give the name of any organisation where the systematic review title or protocol is registered together with any unique
identification number assigned. If extracted data will be stored and made available through a repository such as the
Systematic Review Data Repository (SRDR), details and a link should be included here.

34 Reference and/or URL for published protocol
Give the citation for the published protocol, if there is one.
Give the link to the published protocol, if there is one. This may be to an external site or to a protocol deposited with
CRD in pdf format.

I give permission for this file to be made publicly available
Yes

35 Dissemination plans
Give brief details of plans for communicating essential messages from the review to the appropriate audiences.
Publication in peer-reviewed journal
Do you intend to publish the review on completion? Yes

36 Keywords
Give words or phrases that best describe the review. (One word per box, create a new box for each term)
- Spinal cord injury
- Olfactory ensheathing glia
- Systematic review and meta-analysis
- Publication bias

37 Details of any existing review of the same topic by the same authors
Give details of earlier versions of the systematic review if an update of an existing review is being registered, including full bibliographic reference if possible.

38 Current review status
Review status should be updated when the review is completed and when it is published.
Ongoing

39 Any additional information
Provide any further information the review team consider relevant to the registration of the review.

40 Details of final report/publication(s)
This field should be left empty until details of the completed review are available.
Give the full citation for the final report or publication of the systematic review.
Give the URL where available.