

Search strategy for the protocol: A protocol for systematic review and meta-analysis of data from preclinical studies employing the forced swimming test.

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1. Systematic review in specialized literature:

Medline and Embase were the database selected. The search in Medline were performed using the platform Pubmed (Advanced search in <http://www.ncbi.nlm.nih.gov/pubmed>) and in Embase with OVID in the University of Edinburgh (<http://ovidsp.tx.ovid.com.ezproxy.is.ed.ac.uk/sp-3.14.0b/ovidweb.cgi?&S=NEFMFPPOJLDDABAJNCLKCCOBCFOCAA00&New+Database=Single|22>). The selection of Keywords was based in on the different denominations of Forced Swimming Test (FST) found in the literature (See 8, Table 1 and 2, Review#1). We decided arbitrarily, based on our previous experience (Lino de Oliveira et al., 2005; Mezadri et al., 2011; Costa et al., 2013; Possamai et al., 2015), to include in the review only the data from studies using the MeSH terms related to rats and mice (Hooijmans et al. 2010) that are the most common laboratory species submitted to FST. The list of antidepressants included in the research was by McCann, 2013. The relevant period of Publication date started in 1977, when the first paper was published (Porsolt et al., 1977). The strategy for the review in Embase was similar to that performed in the Pubmed except that Keywords for selection of studies on rats and mice were based in De Vries et al., 2011.

2. Inclusion criteria:

The following inclusion criteria were applied to the outcome of systematic review:

- 2.1. Publication date: since 1977, the year the first paper was published, to present.
- 2.2. Language: any language.
- 2.3. Animal species: rats and mice, regardless of age and sex.
- 2.4. Type of publication: all types of publications containing studies describing the effect of all classes of clinically tested antidepressant drugs in FST, compared to control animals treated or not with vehicle, were include, regardless of randomization. The antidepressants included in this review were listed in the protocol by Mccann, 2013.
- 2.5. Studies with any route, dose and treatment schedule for drug administration were eligible.

3. Exclusion criteria:

3.1. Publications in duplicate.

3.2. Publications using FST in rats or mice, only as a stressor, without showing the data of the behavioural measures.

3.3. Experiments reporting data of co-treatments. The publications containing these experiments were kept if they also report experiments with single treatments.

4. Systematic review in specialized literature:

4.1. Systematic review in Medline:

For the search in the Medline the Pubmed (Advanced search in <http://www.ncbi.nlm.nih.gov/pubmed>) was used. The selection of Keywords (Table 1, Review#1) was based in the different denominations of Forced Swimming Test found in the literature. For Reviews #2 and #3, MeSH terms were selected according to Hooijmans et al. 2010 and Mccann, et al., 2013, respectively. Review#1, #2 and #3 produced 7891, 2970975 and 233677, respectively. The more relevant combination of the terms (Table 1, Review#7) produced 3083 hits. Applying a period of publication to Review#7 from 1977/01/01 to 2015/12/31 did not change the outcome. The types of publications retrieved in Review#7 is in Table 2. We found 79 reviews, 04 systematic reviews related to the subject and zero meta-analysis.

Table 1: Outcome of systematic reviews in Medline performed in 2015/02/18 with publications from 1977 to present.

Review #	MeSH terms	Hits
1	(forced swimming test OR forced swimming tests OR forced swimming test, fst OR fst OR forced swim OR Porsolt test OR Porsolt tests)	7891
2	("rodentia"[MeSH Terms] OR mice[Tiab] OR mus[Tiab] OR mouse[Tiab] OR murine[Tiab] OR woodmouse[tiab] OR rats[Tiab] OR rat[Tiab] OR murinae[Tiab] OR muridae[Tiab] OR cottonrat[tiab] OR cottonrats[tiab] OR rodentia[Tiab] OR rodent[Tiab] OR rodents[Tiab])	2970975

3	<p> ((SSRI) OR (SSRIs) OR (selective serotonin reuptake inhibitor) OR (selective serotonin reuptake inhibitors) OR (selective serotonin re- uptake inhibitor) OR (selective serotonin re-uptake inhibitors) OR (selective serotonin-reuptake inhibitors) OR (selective serotonin- reuptake inhibitor) OR (fluoxetine) OR (citalopram) OR (Escitalopram) OR (fluvoxamine) OR (paroxetine) OR (sertraline) OR (dapoxetine) OR (SNRI) OR (SNRIs) OR (serotonin and noradrenaline reuptake inhibitors) OR (serotonin and noradrenaline reuptake inhibitor) OR (serotonin and noradrenaline re-uptake inhibitors) OR (serotonin and noradrenaline re- uptake inhibitor) OR (serotonin-noradrenaline reuptake inhibitors) OR (serotonin and norepinephrine reuptake inhibitors) OR (serotonin and norepinephrine reuptake inhibitor) OR (serotonin and norepinephrine re-uptake inhibitors) OR (serotonin and norepinephrine re-uptake inhibitor) OR (serotonin-norepinephrine reuptake inhibitors) OR (Duloxetine) OR (Levomilnacipran) OR (Sibutramine) OR (Bicifadine) OR (Venlafaxine) OR (Desvenlafaxine) OR (Milnacipran) OR (Tramadol) OR (TCA) OR (TCAs) OR (tricyclic antidepressant) OR (tricyclic antidepressants) OR (tricyclic anti-depressant) OR (tricyclic anti- depressants) OR (Amitriptyline) OR (Butriptyline) OR (Clomipramine) OR (Desipramine) OR (Dosulepin) OR (Doxepin) OR (Imipramine) OR (Iprindole) OR (Lofepamine) OR (Melitracen) OR (Nortriptyline) OR (Opipramol) OR (Protriptyline) OR (Trimipramine) OR (SARI) OR (SARIs) OR (serotonin antagonist and reuptake inhibitor) OR (serotonin antagonist and reuptake inhibitors) OR (serotonin antagonist and re- uptake inhibitor) OR (serotonin antagonist and reuptake inhibitors) OR (Etoperidone) OR (Loriprazole) OR (Mepiprazole) OR (Lubazodone) OR (Nefazodone) OR (Trazodone) OR (NRI) OR (NRIs) OR (noradrenaline reuptake inhibitor) OR (noradrenaline reuptake inhibitors) OR (noradrenaline re-uptake inhibitor) OR (noradrenaline re-uptake inhibitors) OR (norepinephrine reuptake inhibitor) OR (norepinephrine reuptake inhibitors) OR (norepinephrine re-uptake inhibitor) OR (norepinephrine re-uptake inhibitors) OR (Atomoxetine) OR </p>	233677
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	<p>(Reboxetine) OR (Viloxazine) OR (NDRI) OR (NDRIs) OR (norepinephrine dopamine reuptake inhibitor) OR (norepinephrine dopamine reuptake inhibitors) OR (norepinephrine dopamine re-uptake inhibitor) OR (norepinephrine dopamine re-uptake inhibitors) OR (norepinephrine-dopamine reuptake inhibitor) OR (norepinephrine-dopamine reuptake inhibitors) OR (norepinephrine-dopamine re-uptake inhibitor) OR (norepinephrine-dopamine re-uptake inhibitors) OR (norepinephrine and dopamine reuptake inhibitor) OR (norepinephrine and dopamine reuptake inhibitors) OR (norepinephrine and dopamine re-uptake inhibitor) OR (norepinephrine and dopamine re-uptake inhibitors) OR (noradrenaline dopamine reuptake inhibitor) OR (noradrenaline dopamine reuptake inhibitors) OR (noradrenaline dopamine re-uptake inhibitor) OR (noradrenaline dopamine re-uptake inhibitors) OR (noradrenaline-dopamine reuptake inhibitor) OR (noradrenaline-dopamine reuptake inhibitors) OR (noradrenaline-dopamine re-uptake inhibitor) OR (noradrenaline-dopamine reuptake inhibitors) OR (noradrenaline and dopamine reuptake inhibitor) OR (noradrenaline and dopamine reuptake inhibitors) OR (noradrenaline and dopamine re-uptake inhibitor) OR (noradrenaline and dopamine re-uptake inhibitors) OR (Bupropion) OR (Dexmethylphenidate) OR (Methylphenidate) OR (NDRA) OR (NDRAs) OR (norepinephrine dopamine releasing agent) OR (norepinephrine dopamine releasing agents) OR (norepinephrine-dopamine releasing agent) OR (norepinephrine-dopamine releasing agents) OR (norepinephrine and dopamine releasing agent) OR (norepinephrine and dopamine releasing agents) OR (noradrenaline dopamine releasing agent) OR (noradrenaline dopamine releasing agents) OR (noradrenaline-dopamine releasing agent) OR (noradrenaline-dopamine releasing agents) OR (noradrenaline and dopamine releasing agent) OR (noradrenaline and dopamine releasing agents) OR (Amphetamine) OR (Dextroamphetamine) OR (Dextromethamphetamine) OR (Lisdexamfetamine) OR (TeCA) OR (TeCAs) OR (tetracyclic antidepressant) OR (tetracyclic antidepressants)</p>	
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	OR (tetracyclic antidepressant) OR (tetracyclic anti-depressants) OR (Amoxapine) OR (Maprotiline) OR (Mianserin) OR (Mirtazapine) OR (MAOI) OR (MAOIs) OR (monoamine oxidase inhibitor) OR (monoamine oxidase inhibitors) OR (Isocarboxazid) OR (Moclobemide) OR (Phenelzine) OR (Pirlindole) OR (Selegiline) OR (Tranlycypromine) OR (antidepressant) OR (antidepressants) OR (antidepressant) OR (anti-depressants)))	
4	#1 AND #2	5385
5	#1 AND #3	3115
6	#2 AND #3	66835
7	#1 AND #2 AND #3	3083

Observation: Lorpiprazole term was not found in PubMed.

Table 2: Types of articles retrieved in Review#7 using the Pubmed.

Number of hits retrieved	Type of publications
3082	Journal articles
1527	Research Support, Non-U.S. Gov't
443	Comparative Study
418	Research Support, U.S. Government
141	English Abstract
79	Review
10	Evaluation Studies
10	Validation Studies

05	Clinical Trials
04	Systematic Reviews
04	Randomized Controlled Trial
02	Electronic Supplementary Materials
02	Video- Audio Media
01	Books and documents
01	Case Reports
01	Comment
01	Randomized Controlled Trial
00	Addresses, Autobiography, Bibliography, Biography, Classical Article, Clinical Conference, Clinical Trial, Phase I, Clinical Trial, Phase II, Clinical Trial, Phase III, Clinical Trial, Phase IV, Congresses, Consensus Development Conference, Consensus Development Conference, NIH, Controlled Clinical Trial, Corrected and Republished Article, Dataset, Dictionary, Directory, Duplicate, Meta-analysis, Publication, Editorial, Festschrift, Government Publications, Guideline, Historical Article, Interactive Tutorial, Interview, Introductory Journal Article, Lectures, Legal Cases, Legislation, Letter, Meta-Analysis, Multicenter Study, News, Newspaper Article, Observational Study, Overall, Patient Education Handout, Periodical Index, Personal Narratives, Portraits, Practice Guideline, Pragmatic Clinical Trial, Published Erratum, Research Support, American Recovery and Reinvestment Act, Research Support, N.I.H., Extramural, Research Support, N.I.H., Intramural, Research Support, U.S. Gov't Non-P.H.S., Research Support, U.S. Gov't, P.H.S., Retracted Publication, Retraction of Publication, Scientific Integrity Review, Technical Report, Twin Study, Webcasts.

4.2. Systematic review in Embase:

The strategy for the in Embase was similar to that performed in the Medline (see item 8.2.1) except that OVID was used to access the database, the selection of Keywords for Review#2 (Table 3) was based in De Vries et al., 2011 and only one combination of keywords was performed to obtain relevant literature (Review#4). Review#1, #2 and #3 produced 10625, 2809884 and 288332, respectively. Review#4 (Table 3) produced 4116 hits from 1977 to the present date.

Table 3: Outcome of systematic reviews in Embase performed in 2015/02/18 with publications from 1977 to present.

Review #	MeSH terms	Hits
1	forced swimming test OR forced swimming tests OR forced swimming test, fst OR fst OR forced swim OR Porsolt test OR Porsolt tests	10625
2	exp rodent OR rodentia OR rodent OR rodents OR murinae OR mouse OR mice OR mus OR musculus OR murine OR woodmouse OR apodemus OR rat OR rats OR rattus OR norvegicus	2809884
3	(SSRI) OR (SSRIs) OR (selective serotonin reuptake inhibitor) OR (selective serotonin reuptake inhibitors) OR (selective serotonin re-uptake inhibitor) OR (selective serotonin re-uptake inhibitors) OR (selective serotonin-reuptake inhibitors) OR (selective serotonin-reuptake inhibitor) OR (fluoxetine) OR (citalopram) OR (Escitalopram) OR (fluvoxamine) OR (paroxetine) OR (sertraline) OR (dapoxetine) OR (SNRI) OR (SNRIs) OR (serotonin and noradrenaline reuptake inhibitors) OR (serotonin and noradrenaline reuptake inhibitor) OR (serotonin and noradrenaline re-uptake inhibitors) OR (serotonin and noradrenaline re-uptake inhibitor) OR (serotonin-noradrenaline reuptake inhibitors) OR (serotonin and norepinephrine reuptake inhibitors) OR (serotonin and norepinephrine re-uptake inhibitors) OR (serotonin and norepinephrine re-uptake inhibitor) OR (serotonin- norepinephrine reuptake inhibitors) OR	288332

	<p> (Duloxetine) OR (Levomilnacipran) OR (Sibutramine) OR (Bicifadine) OR (Venlafaxine) OR (Desvenlafaxine) OR (Milnacipran) OR (Tramadol) OR (TCA) OR (TCAs) OR (tricyclic antidepressant) OR (tricyclic antidepressants) OR (tricyclic anti-depressant) OR (tricyclic anti- depressants) OR (Amitriptyline) OR (Butriptyline) OR (Clomipramine) OR (Desipramine) OR (Dosulepin) OR (Doxepin) OR (Imipramine) OR (Iprindole) OR (Lofepramine) OR (Melitracen) OR (Nortriptyline) OR (Opipramol) OR (Protriptyline) OR (Trimipramine) OR (SARI) OR (SARIs) OR (serotonin antagonist and reuptake inhibitor) OR (serotonin antagonist and reuptake inhibitors) OR (serotonin antagonist and re- uptake inhibitor) OR (serotonin antagonist and re-uptake inhibitors) OR (Etoperidone) OR (Loripirazole) OR (Mepiprazole) OR (Lubazodone) OR (Nefazodone) OR (Trazodone) OR (NRI) OR (NRIs) OR (noradrenaline reuptake inhibitor) OR (noradrenaline reuptake inhibitors) OR (noradrenaline re-uptake inhibitor) OR (noradrenaline re-uptake inhibitors) OR (norepinephrine reuptake inhibitor) OR (norepinephrine reuptake inhibitors) OR (norepinephrine re-uptake inhibitor) OR (norepinephrine re-uptake inhibitors) OR (Atomoxetine) OR (Reboxetine) OR (Viloxazine) OR (NDRI) OR (NDRIs) OR (norepinephrine dopamine reuptake inhibitor) OR (norepinephrine dopamine reuptake inhibitors) OR (norepinephrine dopamine re-uptake inhibitor) OR (norepinephrine dopamine re-uptake inhibitors) OR (norepinephrine- dopamine reuptake inhibitor) OR (norepinephrine-dopamine reuptake inhibitors) OR (norepinephrine-dopamine reuptake inhibitor) OR (norepinephrine-dopamine re-uptake inhibitors) OR (norepinephrine and dopamine reuptake inhibitor) OR (norepinephrine and dopamine reuptake inhibitors) OR (norepinephrine and dopamine re-uptake inhibitor) OR (norepinephrine and dopamine re-uptake inhibitors) OR (noradrenaline dopamine reuptake inhibitor) OR (noradrenaline dopamine reuptake inhibitors) OR (noradrenaline dopamine re-uptake inhibitor) OR (noradrenaline dopamine re-uptake inhibitors) OR (noradrenaline-dopamine reuptake inhibitor) OR (noradrenaline- </p>	
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	dopamine reuptake inhibitors) OR (noradrenaline-dopamine re-uptake inhibitor) OR (noradrenaline-dopamine reuptake inhibitors) OR (noradrenaline and dopamine reuptake inhibitor) OR (noradrenaline and dopamine reuptake inhibitors) OR (noradrenaline and dopamine re-uptake inhibitor) OR (noradrenaline and dopamine re-uptake inhibitors) OR (Bupropion) OR (Dexmethylphenidate) OR (Methylphenidate) OR (NDRA) OR (NDRAs) OR (norepinephrine dopamine releasing agent) OR (norepinephrine dopamine releasing agents) OR (norepinephrine-dopamine releasing agent) OR (norepinephrine-dopamine releasing agents) OR (norepinephrine and dopamine releasing agent) OR (norepinephrine and dopamine releasing agents) OR (noradrenaline dopamine releasing agent) OR (noradrenaline dopamine releasing agents) OR (noradrenaline-dopamine releasing agent) OR (noradrenaline-dopamine releasing agents) OR (noradrenaline and dopamine releasing agent) OR (noradrenaline and dopamine releasing agents) OR (Amphetamine) OR (Dextroamphetamine) OR (Dextromethamphetamine) OR (Lisdexamfetamine) OR (TeCA) OR (TeCAs) OR (tetracyclic antidepressant) OR (tetracyclic antidepressants) OR (tetracyclic antidepressant) OR (tetracyclic anti-depressants) OR (Amoxapine) OR (Maprotiline) OR (Mianserin) OR (Mirtazapine) OR (MAOI) OR (MAOIs) OR (monoamine oxidase inhibitor) OR (monoamine oxidase inhibitors) OR (Isocarboxazid) OR (Moclobemide) OR (Phenelzine) OR (Pirlindole) OR (Selegiline) OR (Tranylcypromine) OR (antidepressant) OR (antidepressants) OR (anti-depressant) OR (anti-depressants)	
4	#1 AND #2 AND #3	4116

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