

Appendices

Appendix A. Search Strategies using MEDLINE, MEDLINE In Process and EMBASE

Database(s): **Ovid MEDLINE®**

Search Performed between 1946 and November Week 1 2017

Search Strategy:

#	Searches	Results
1	Riluzole/ or riluzole.mp.	1447
2	exp Brain Injuries/	63700
3	exp Nervous System Diseases/	2731558
4	exp Nerve Degeneration/	26048
5	exp Spinal Diseases/	119292
6	neurotrauma*.mp.	1410
7	neurodegenerat*.mp.	84752
8	((neuro* or brain* or nerve*) adj4 (trauma* or demyelinat*)).mp.	80431
9	((neuro* or brain* or nerve*) adj4 injur*).mp.	130711
10	concussion*.mp.	8712
11	demyelinate*.mp.	32248
12	2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11	2883102
13	1 and 12	976

Database(s): **Ovid MEDLINE® Epub Ahead of Print and In-Process & Other Non-Indexed**

Citations

Search performed on November 13, 2017

Search Strategy:

#	Searches	Results
1	Riluzole/ or riluzole.mp.	154
2	exp Brain Injuries/	7
3	exp Nervous System Diseases/	651
4	exp Nerve Degeneration/	2
5	exp Spinal Diseases/	25
6	neurotrauma*.mp.	298
7	neurodegenerat*.mp.	13832
8	((neuro* or brain* or nerve*) adj4 (trauma* or lemyelinat*)).mp.	8648
9	((neuro* or brain* or nerve*) adj4 injur*).mp.	14730
10	concussion*.mp.	1396
11	lemyelinate*.mp.	2622
12	(chronic adj4 encephalopath*).mp.	214
13	(heredodegenerat* adj4 (nerv* or neuro*)).mp.	1
14	lewy body.mp.	383
15	Multiple System Atroph*.mp.	384
16	lemyelina??.tw,hw.	10939
17	(prion adj4 (disease* or infect*)).mp.	557

18	neuropath*.mp.	12693
19	myoton*.mp.	454
20	(spin?? Adj4 atroph*).mp.	547
21	neurofibromatos*.mp.	1284
22	motor neuron disease*.mp.	514
23	Amyotrophic Lateral Sclero*.mp.	2363
24	multiple 2emyel*.mp.	7768
25	leukoencephal*.mp.	741
26	encephalomyel*.mp.	1485
27	neuromyelit*.mp.	564
28	or/2-27	62326
29	1 and 28	90

Database(s): **Embase**

Search performed between 1974 and 2017 November 13

Search Strategy:

#	Searches	Results
1	riluzole/ or riluzole.mp.	4085
2	neurotrauma*.mp.	2957
3	neurodegenerat*.mp.	122803
4	((neuro* or brain* or nerve*) adj4 (trauma* or 2emyelinat*)).mp.	149490

5	((neuro* or brain* or nerve*) adj4 injur*).mp.	228215
6	concussion*.mp.	11568
7	3emyelinate*.mp.	52046
8	exp neurologic disease/	3057346
9	exp spine disease/	199100
10	2 or 3 or 4 or 5 or 6 or 7 or 8 or 9	3257636
11	1 and 10	3103

Appendix B. Reasons for Exclusion following Full-Text Investigation

Author (Year)	Reason for Exclusion
Albo et al (2004)	Did not evaluate outcomes of interest
Bergerot et al (2004)	Ventral root avulsion injury
Brocard et al (2016)	Did not evaluate outcomes of interest
Chew et al (2014)	Spinal root avulsion injury
Coderre et al (2007)	Chronic constriction injury of sciatic nerve
Ghayour et al (2017)	Sciatic nerve crush injury
Hassanzadeh et al (2010)	Did not evaluate outcomes of interest
Hobo et al (2011)	Peripheral nerve injury
Kai et al (2006)	Chronic constriction injury of sciatic nerve
Lin et al (2017)	Spinal seizure-like activity
Mazzone et al (2011)	Did not evaluate outcomes of interest
McAdoo et al (2005)	Did not evaluate outcomes of interest
Medico et al (2004)	Post-traumatic peripheral neuropathy
Mu et al (2000)	Did not evaluate outcomes of interest
Nicholson et al (2014)	Painful nerve root compression
Nogradi et al (2007)	Spinal root avulsion injury
Pinter et al (2010)	Ventral root avulsion injury
Samano et al (2012)	Did not evaluate outcomes of interest
Schmidt et al (2008)	Not on spinal cord pathology
Shortland et al (2006)	Spinal root avulsion injury
Springer et al (1997)	Did not evaluate outcomes of interest

Stutzmann et al (1996)	No evaluation of statistical significance
Xie et al (2011)	Dorsal root ganglion injury
Xie et al (2012)	Dorsal root ganglion injury
Zmyslowski et al (2017)	Sciatic nerve crush injury

Appendix C. Evaluation of Risk of Bias using the SYRCLE’s tool: Ates et al (2007) to Lips et al (2000)

Type of Bias and Associated Questions	Ates (2007)	Hama (2011)	Hosier (2015)	Karadima s (2015)	Kitzma n (2009)	Lang-Lazdunski (2000)	Lang-Lazdunski (1999)	Lang-Lazdunski (2000)	Lips (2000)
Was the allocation sequence adequately generated and applied?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Were the groups similar at baseline or was there adjustment for confounders in the analysis?	Yes	Yes	NA	NA	NA	NA	NA	NA	Yes
Was the allocation adequately concealed?	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes
Were the animals randomly housed during the experiment?	NA	NA	Yes	NA	Yes	Yes	NA	NA	NA
Were the caregivers and/or investigators blinded from which intervention each animal received	NA	NA	Yes	NA	Yes	NA	NA	NA	NA

during the experiment?									
Were animals selected at random for outcome assessment?	Yes	Yes	Yes	Yes	NA	Yes	Yes	Yes	Yes
Was the outcome assessor blinded?	NA	NA	Yes	Yes	NA	Yes	Yes	Yes	Yes
Were incomplete outcome data adequately addressed?	Yes	NA	NA	NA	NA	Yes	NA	NA	Yes
Are reports of the study free of selective outcome reporting?	NA	NA	NA	Yes	NA	NA	NA	NA	NA
Was the study apparently free of other problems that could results in high risk of bias?	No – replace d rats that died with new rats	No – smaller control group	Yes	Yes	Yes	No – replaced rats that died with new rats	Yes	Yes	No – replace d rabbits that died with new rabbits

Appendix C. Evaluation of Risk of Bias using the SYRCLE's tool: Moon et al (2014) to Wu et al (2014)

Type of Bias and Associated Questions	Moon (2014)	Mu (2000)	Satkunendrarajah (2016)	Schwartz and Fehlings (2001)	Vasconcelos (2016)	Wu (2013)	Wu (2014)
Was the allocation sequence adequately generated and applied?	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Were the groups similar at baseline or was there adjustment for confounders in the analysis?	Yes	NA	NA	NA	NA	Yes	NA
Was the allocation adequately concealed?	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Were the animals randomly housed during the experiment?	NA	NA	NA	NA	Yes	Yes	Yes
Were the caregivers and/or investigators blinded from which intervention each animal received during the experiment?	NA	NA	Yes	Yes	Yes	NA	Yes

Were animals selected at random for outcome assessment?	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Was the outcome assessor blinded?	Yes	Yes	Yes	NA	Yes	Yes	NA
Were incomplete outcome data adequately addressed?	NA	NA	NA	NA	NA	NA	NA
Are reports of the study free of selective outcome reporting?	NA	NA	NA	NA	NA	NA	NA
Was the study apparently free of other problems that could results in high risk of bias?	Yes	Yes	Yes	Yes	Yes	Yes	Yes