

Supplementary Material

Supplementary Table S1

Molecules/cells and procedures	Articles
hypoxia-inducible factor-1 α (HIF-1 α)	Bok et al. (2017)
low-intensity pulsed ultrasound	Chen et al. (2018)
tissue-type plasminogen activator	Draxler et al. (2018)
miR-132	Zuo et al. (2019), Feng et al. (2021)
antagonist 8-cyclopentyl-1,3-dipropylxanthine	Geng et al. (2020)
agonist 2-Chloro-N6-cyclopentyladenosine	
aripiprazol	Gil et al. (2018)
PR-957	Guo et al. (2018)
stem cells	Kawai et al. (2010), Patkar et al. (2011), Huang et al. (2014), Cunningham et al. (2020), Doeppner et al. (2014), Kawai et al. (2010), Ma et al. (2015), Wang et al. (2015), Wang et al. (2020)
irisin	Li et al. (2016), Jin et al. (2021)
chloral hydrate	Liu et al. (2015)
RhPDCD5protein	Lu et al. (2016)
miR-216a	Shuang et al. (2017/2018)
progesteron	Wong et al. (2014)
adenoviruses-mediated RNA interference	Wu et al. (2017)
targeting cytosolicphospholipase A2 α	
IL-33	Yang et al. (2017)
shengmai powder (insenoside Rb1, ruscogenin and schisandrin A,	Zhang et al. (2020)
no treatment	Suenaga-Young et al. (2016), Truong et al. (2012), Feng et al. (2020), Kamat et al. (2015), Li et al. (2018), Oliveira et al. (2020), Pallast et al. (2020), Park et al. (2014), Vahid-Ansari et al. (2016), Yan et al. (2021)
Korean medicinal herbs (Polygonum multiflorum Thunb., Rehmannia glutinosa (Gaertn) Libosch., Polygala tenuifolia Willd., and Acorus gramineus Soland)	Ahn et al. (2015)
metallothionein-1	Campagne et al. (1999)
dihydrocapsaicin	Cao et al. (2017)
glycyrrhizin	Chen et al. (2017)
methylene blue	Cheng et al. 2021
lipopolysaccharide	Doll et al. (2015)
recombinant human fibroblast growth factor 21	Dongxue et al. (2020)
coicis semen	Du et al. (2021)
MLC901 (herbal extract preparation derived from Chinese medicine)	Gandin et al. (2015)
DLX6-AS1 (lncRNA mus distal-less homeobox 6 antisense 1)	Hu et al. (2020)

octadecylpropyl sulfamide	Kossatz et al. (2018)
cystamine	Li et al. (2014)
OGG1 glycosylase (7,8-Dihydro-8-oxoguanine DNA glycosylase)	Liu et al. (2011)
Hematopoietic Growth Factor	Liu et al. (2016)
korean red ginseng	Liu et al. (2018)
(R)-4-ACPBPA, (S)-4-ACPBPA	Nieuwenhuijzen et al. (2021)
pharmacological inhibitor of NLRP3 (CY-09)	Sun et al. (2020)
S100A11	Xia et al. (2018)
heat shock protein 72	Xu et al. (2011)
synthetic peptide LP17	Xu et al. (2019)

Supplementary Table S2

Neurological scale						
Study / Year	Sham	Control	Weight (g)	Age (w)	Neurological scale	Test day
Zuo 2019	6	6	20–25	-	Garcia	1
Zhang 2020	8	8	18-22	6-12	Garcia	1
Shuang 2017	3	3	-	6	Garcia	1
Lu 2016	18	18	-	-	Garcia	1
Geng 2020	-	-	20-25	-	Garcia	1
Wong 2014	3	3	25,9-41,2	15-25	Clark	1, 7
Patkar 2011	8	8	25-30	14-12	Clark	1, 2, 7
Li 2016	8	8	-	8-12	Longa	3
Wu 2017	3	3	-	12-16	Longa	1, 3, 7, 14
Kamat 2015	5	5	27-30	10-12	Longa	1
Cheng 2021	10	10	20-24	-	Garcia	1
Hu 2020	6	6	18-25	8	Clark	1
Du 2021	5	5	25-30	-	Longa	1,3,5,7,10,14

Supplementary Table S3

Foot fault						
Study / Year	Sham	Control	Weight (g)	Age (w)	Test day	Testing time (min)
Zuo 2019	6	6	20–25	-	0, 7, 14, 21,28	2
Guo 2018	10	10	18-20	6-8	1, 2, 3	2
Wong 2014	4	4	25,9-41,2	15-25w	1, 2, 7	-
Feng 2021	6	6	22-25	-	1	2
Draxler 2019	7	7	25	8-12	1	5
Cao 2017	8	11	21-32	10-16	0,3,7,14,21,28	2
Doeppner 2014	15	16	23-25	10-12	4,7,14,28,56,84	-
Xu 2011	11	20	23-32	-	0,2,8,28	-

Supplementary Table S4

Cylinder							
Study / Year	Sham	Control	Weight (g)	Age (w)	Test day	Testing time (min)	Cylinder size
Yang 2017	8-12	8-12		8-12	0, 3, 5, 7	10	9 cm diameter, 15 cm height
Patkar 2011	8	8	25-30	14-12	0, 2, 14, 28	2	10 cm diameter
Gil 2018	6	6	18-20	6	1-5, 5-9, 10-14	-	9 cm diameter, 15 cm height
Vahid-Ansari 2016	10	10	25-28	10-11	30	-	10 cm diameter, 15 cm height
Pallast 2020	7	15		8	0,3,7,14,21,28	5	10 cm diameter, 15 cm height
	10	19	22-29	10-14	0,1,3,7,14,21,28	15	
	10	10	25-30	12-16	0,1,3,5,7	5	12 cm diameter, 19 cm height
Doll 2015							
Wang 2015	6-8	6-8			0,3,5,7,9,11,13,15,20,25,28		5 cm diameter, 20 cm height
	8	8	20-25,5	8-10		5	10 cm diameter, 15 cm height
Nieuwenhuijzen 2021					0,7,14,28,42		
	10	10		8-12	0,7,14,28,42		10 cm diameter, 15 cm height
Wang 2020	14	14	22-28	8-9	0,3,7,14,21,28	5	
Liu 2018	8	12			0,1,2,3,7,14,21,28	6	8cm diameter, 25 cm height

Supplementary Table S5

Rotarod									
Study / Year	Sham	Control	Weight (g)	Age (w)	Test day	Testing time (min)	Velocities (rpm)	Trials/day	Training
Truong 2012	10	5	20,3-25,3	4	2, 4, 7, 14, 21, 28, 42, 56	2	4-40	4	No
Suenagaa-Young 2016	8	8	-	10	1, 3, 5, 7, 14, 21, 35	2	4-40	3	Yes

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Bok 2017	4	4	-	-	1,3,5,7	5	4-40	5	Yes
Liu 2015	6	6	-	-	0, 1, 3, 7, 28	2	5	5	Yes
Wu 2017	3	3		-	0, 1, 3, 7, 14	5	2-20		Yes
Kawai 2010	6	8	20-25	8-10	0, 1, 14, 28	5	0-45	3	Yes
Chen 2018	6	6	-	6	7	3	60		Yes
Yang 2017	9-12	9-12	-	8-12	0, 3, 5, 7	5	4-120	3	Yes
Huang 2014	14	14	-	-	0, 2, 4, 6, 8, 12, 16, 20, 24	-	10-25	3	-
Dongxue 2020	4	10	20-25g	-	0,1,3,7,14	-	-	-	Yes
Gandin 2015	20	20	-	9	0,1,3,5,7,9,11, 13,15	2	4-40	3	
Liu 2016	6	7	-	19-20	14, 42	5	4-40	5	Yes
Feng 2020	14	10	-	-	0, 2, 21	10	30	2	Yes
Doll 2015	10	10	25-30	12-16	11	5	4-44	4	Yes
Liu 2011	9	9	25-30	20-24	0,1,2,3,7	5	-	-	Yes
Ma 2015	9	-	20-25	-	0,1,2,3,5,7,14, 21,28	6,5	10-14	3	Yes
Xia 2019	10	10	25±2	-	7	5	4-40	-	Yes
Kawai 2010	6	8	20-25	-	0,1,14,28	5	0-45	-	Yes
Park 2014	7	12	25-32	13	0,2,4,7,14,21,2 8	4,16	4-40	3	Yes
Wang 2015	6-8	6-8	-	-	0,3,5,7,9	5	0-30	-	Yes
Chen 2017	12	12	23-25	8-10	21,28,42, 70	5	5-40	10	Yes
Doeppner 2014	15	16	23-25	10-12	4,7,14,28,56,8 4	5 1	4-40 40	-	-
Kossatz 2018	14	21	-	8-11	1,7	1	4-20	5	Yes
Oliveira 2020	8	8	25-35		0,7,28	5	15		Yes
Cunningham 2020	10	12	22,5-32,1		0,3,7,13	5	4-40	3	Yes
Campagne 1999	15	9	-	8-10	21	5	2-20	5	Yes
Xu 2011	11	20	23-32	-	0,2,7,14,21,28	5	5-10	9	Yes

Supplementary Table S6

Morris Water Maze											
Study / Year	Sham	Control	Weight (g)	Age (w)	Test day	Testing time (s)	Maze size (cm)	Platform size (cm)	Platform depth (cm)	Water temperature °C	Training/ day
Suenagaa-Young 2016	8	8	-	10	16-20	60	109	11	1	20±1	3
Truong 2012	10	4	20,3-25,3	4	55-59	45	122	8,5	2	-	4
Sun 2020	12	12	20-15	8-12	23-27	60	-	-	-	-	5
Yan 2021	9	8	20-22	6-8	1-6	60	150	-	1	22	4
Xu 2019	10	10	20-25	-	22-28	60	-	-	-	-	4
Jin 2021	5	5	20-25	-	1	60	100	12	-	23±2	4
Feng 2020	19	19	-	12-4	24-28	60	120	15	1	19±2	4
Li 2018	10	16	22-19	10-14	22-26	60	120	8	1,5	24-26	2
Xia 2019	10	10	25±2	-	1-6	60	-	-	-	-	4
Wang 2015	6-8	6-8	-	-	24-28	60	-	-	2	21-23	3
Hu 2020	-	-	18-25	8	21-26	60	120	6	1	21-23	4
Doeppner 2014	15	16	23-25	10-12	26-28 54-56 82-84	90	-	-	-	-	8
Ahn 2015	10	10	20-25	-	0,22-25	90	100	-	0,5	-	5

Supplementary Table S7

Study	D1	D5	D2	D3	D4	D5	Overall
Bok 2017	!	+	+	+	!	+	!
Chen 2018	!	+	+	+	-	+	-
Draxler 2019	!	+	!	+	-	+	-
Feng 2021	!	+	+	+	!	+	!
Geng 2020	!	+	+	+	-	+	!
Gil 2018	!	+	!	+	-	+	-
Guo 2018	+	+	+	+	+	+	+
Huang 2014	!	+	+	+	-	+	!
Kawai 2010	!	+	!	+	-	+	!
Li 2016	!	+	+	+	-	+	!
Liu 2015	+	+	+	+	+	+	+
Lu 2016	+	+	!	+	-	+	!
Patkar 2011	+	+	+	+	+	+	+
Shuang 2017	!	+	!	+	!	+	!
Suenagga-Young 2016	+	+	+	+	+	+	+
Truong 2012	+	+	+	+	+	+	+
Wong 2014	+	+	+	+	+	+	+
Wu 2017	+	+	!	+	!	+	!
Yang 2017	+	+	+	+	+	+	+
Zhang 2020	!	+	+	+	+	+	+
Zuoa 2019	+	+	+	+	+	+	+
Ahn 2015	!	+	!	+	!	+	!
Campagne 1999	!	+	+	+	+	+	!
Cao 2017	!	+	+	+	+	+	+
Chen 2017	!	+	+	+	+	+	!
Cheng 2021	+	+	+	+	+	+	+
Cunningham 2020	+	+	+	+	+	+	+
Doepfner 2014	!	+	+	+	+	+	!
Doll 2015	+	+	+	+	+	+	+
Dongxue 2020	+	+	+	+	+	+	+
Du 2021	+	+	!	+	!	+	!
Feng 2020	!	+	+	+	+	+	!
Gandin 2015	!	+	+	+	+	+	!
Hu 2020	!	+	!	+	-	+	-
Jin 2021	+	+	!	+	!	+	!
Kamat 2015	!	+	!	+	-	+	-
Kawai 2010	!	+	!	+	-	+	-

Low risk
 Some concerns
 High risk

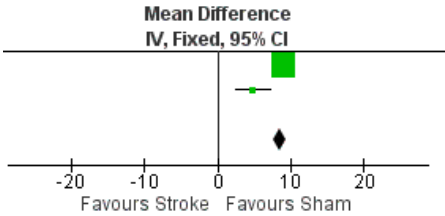
D1 Randomisation process
D5 Bias arising from period and carryover effects
D2 Deviations from the intended interventions
D3 Missing outcome data
D4 Measurement of the outcome
D5 Selection of the reported result

Kossatz 2018	!	+	+	+	+	+	!
Li 2014	+	+	+	+	+	+	+
Li 2018	!	+	+	+	+	+	!
Liu 2011	!	+	!	+	-	+	-
Liu 2016	+	+	+	+	-	+	-
Liu 2018	+	+	+	+	+	+	+
Ma 2015	!	+	+	+	+	+	!
Nieuwenhuijzen 2021	+	+	+	+	+	+	+
Oliveira 2020	+	+	!	+	-	+	-
Pallast 2020	!	+	+	+	+	+	!
Park 2014	!	+	!	+	-	+	-
Sun 2020	!	+	!	+	-	+	-
Vahid-Ansari 2016	+	+	+	+	+	+	+
Wang 2015	+	+	+	+	+	+	+
Wang 2020	+	+	+	+	+	+	+
Xia 2018	!	+	+	+	+	+	!
Xu 2011	+	+	!	+	!	+	!
Xu 2019	!	+	!	+	-	+	-
Yan 2021	!	+	!	+	-	+	-

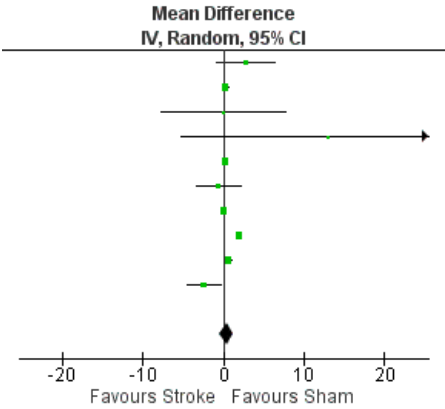
Supplementary Table S8

Tests	Time	Mean difference (95% CI)	p-value	Forest plot
Clark	24 h	9.76 (9.16, 10.36)	<0.00001	<p>Mean Difference IV, Fixed, 95% CI</p> <p>-20 -10 0 10 20 Favours Stroke Favours Sham</p>
	48 h	6.42 (4.41, 8.43)	<0.00001	<p>Mean Difference IV, Fixed, 95% CI</p> <p>-20 -10 0 10 20 Favours Stroke Favours Sham</p>

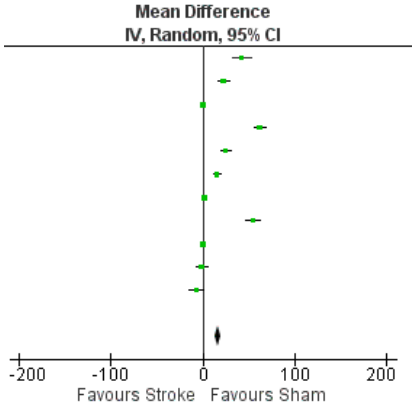
7 days 8.47 (7.57, 9.36) <0.00001



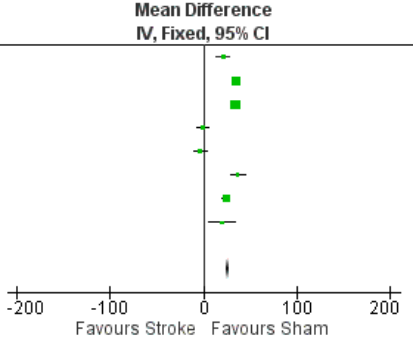
Cylinder Pre 0.41 (-0.46, 1.28) 0.35

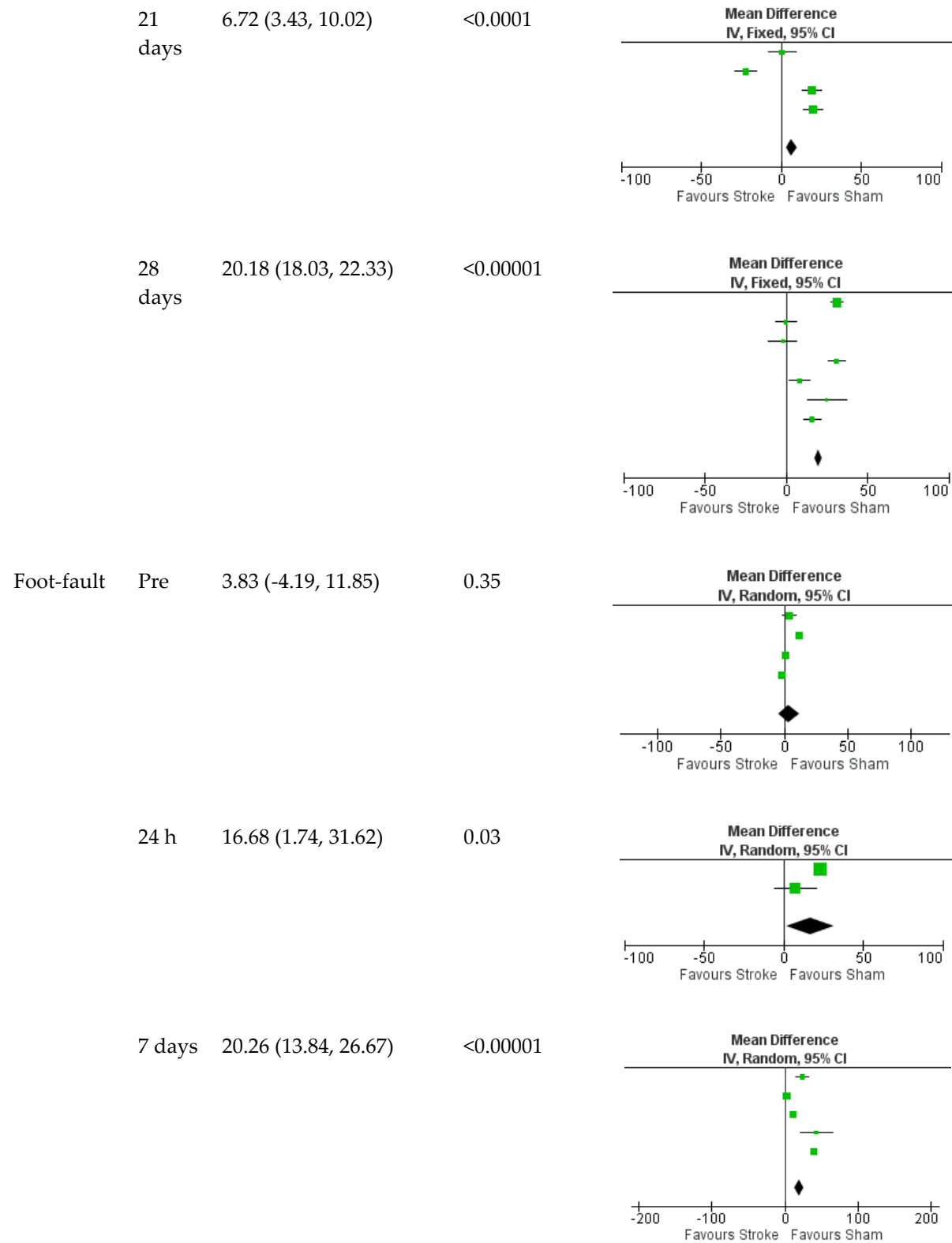


7 days 16.87 (13.78, 19.97) <0.00001

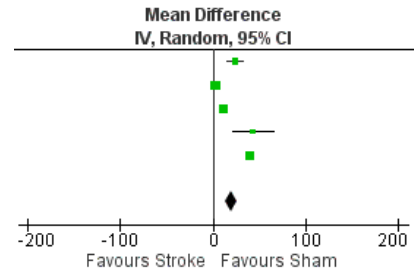


14 days 26.49 (24.75, 28.23) <0.00001

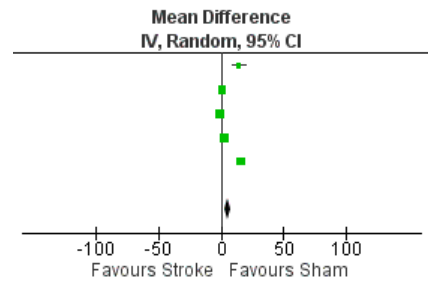




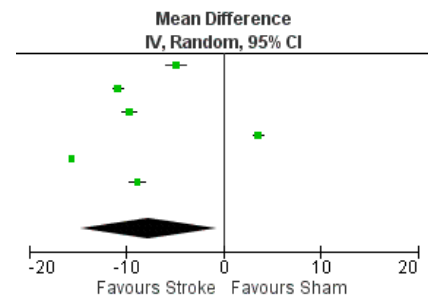
14 days 15.92 (6.85, 24.99) 0.0006



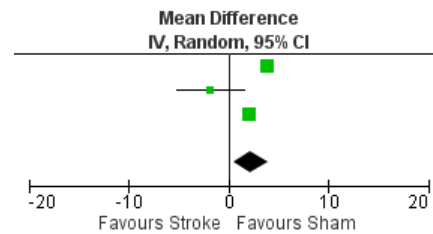
28 days 5.40 (2.88, 7.91) <0.0001



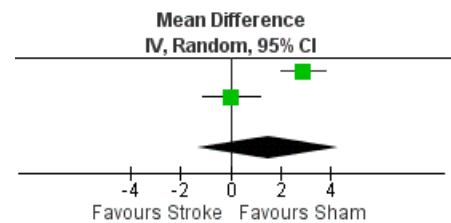
Garcia 24 h -7.71 (-14.67, -0.75) 0.03



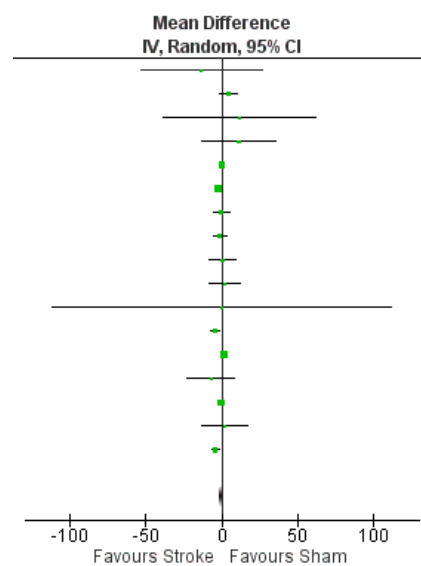
Longa 3 days 2.23 (0.52, 3.93) 0.01



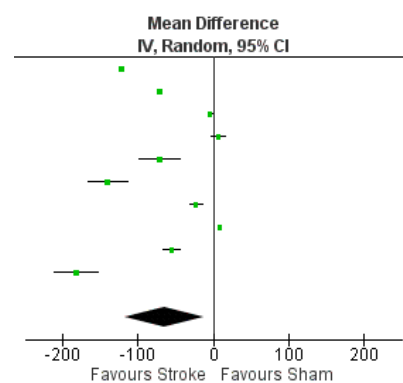
7 days 1.49 (-1.31, 4.30) 0.30



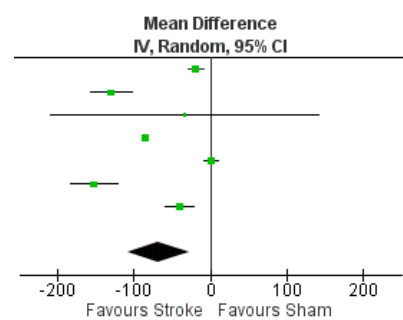
Rotarod Pre -0.68 (-1.95, 0.59) 0.30



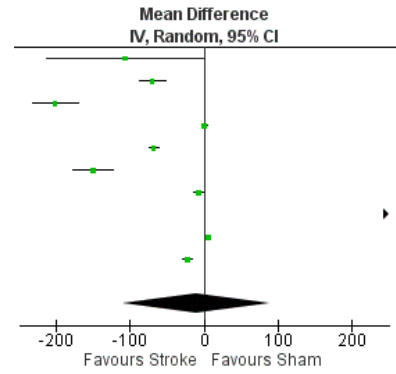
24 h -64.64 (-117.80, -11.47) 0.02



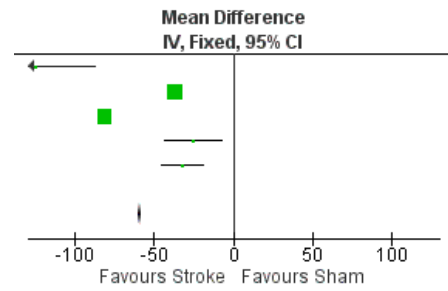
2 days -67.97 (-108.91, -27.03) 0.001



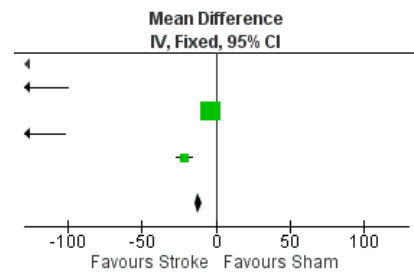
3 days -10.54 (-110.48, 89.41) 0.84



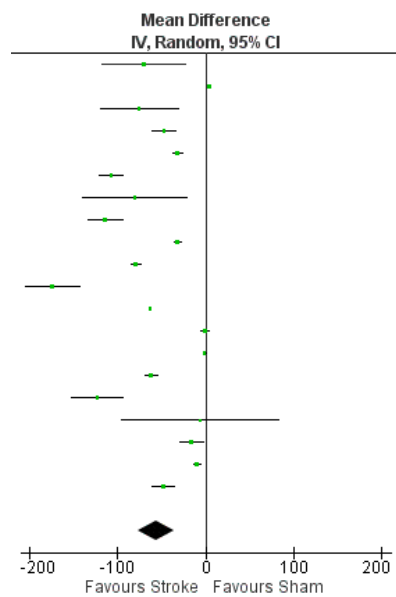
4 days -58.75 (-59.72, -57.77) <0.00001



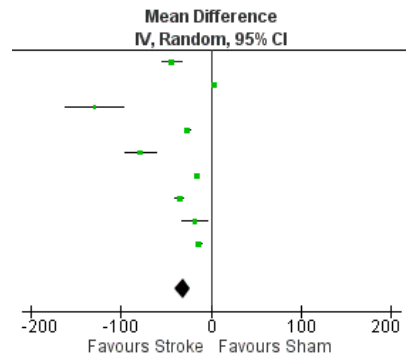
5 days -11.84 (-14.59, -9.09) <0.00001



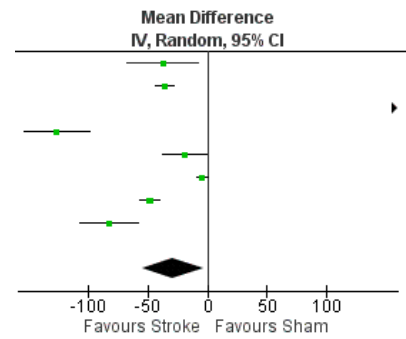
7 days -56.19 (-76.64, -35.75) <0.00001



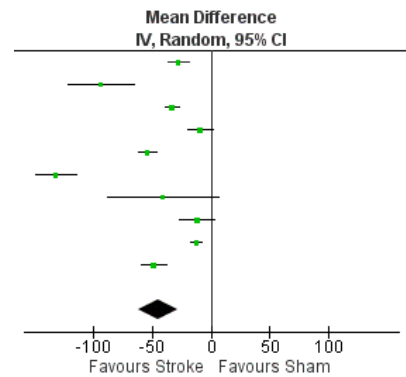
14 days -31.51 (-40.81, -22.21) <0.00001



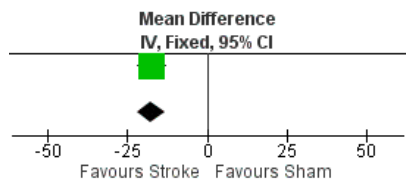
21 days -28.89 (-54.62, -3.16) 0.03



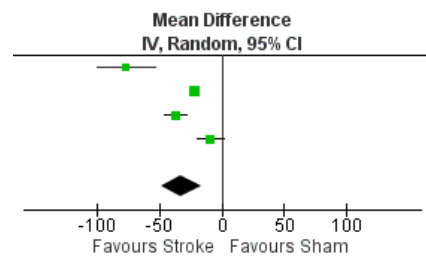
28 days -45.11 (-62.20, -28.02) <0.00001



35 days -17.57 (-21.93, -13.21) <0.001



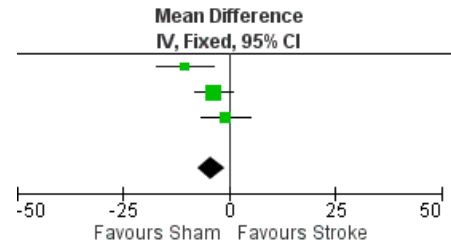
56 days -32.49 (-48.16, -16.82) <0.0001



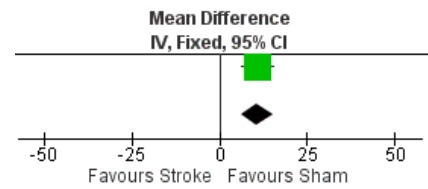
Morris
Water
Maze

Latency

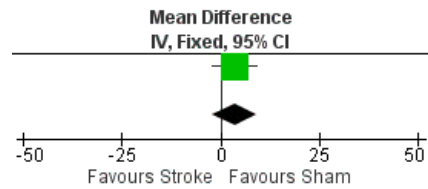
24 h -4.19 (-7.33, -1.06) 0.009



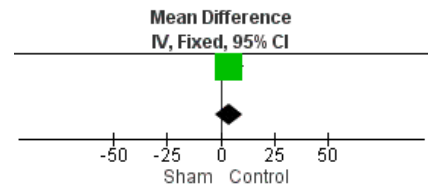
16 days 10.71 (6.09, 15.33) <0.00001



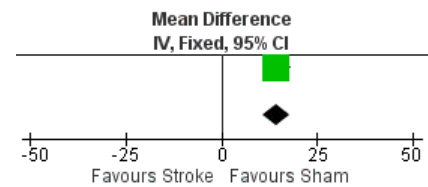
17 days 3.57 (-2.05, 9.19) 0.21



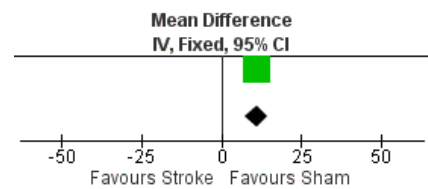
18 days 3.89 (-2.75, 10.53) 0.25



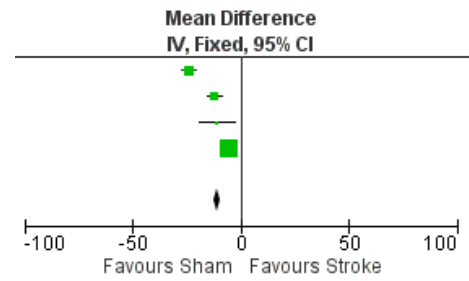
19 days 14.27 (10.69, 17.85) <0.00001



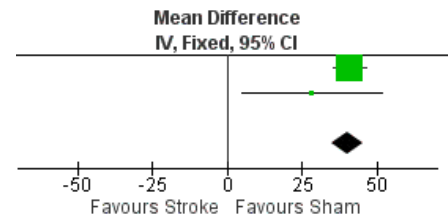
20 days 11.03 (7.51, 14.55) <0.0001



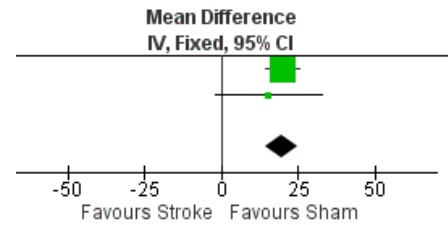
23 days -10.84 (-12.33, -9.36) <0.00001



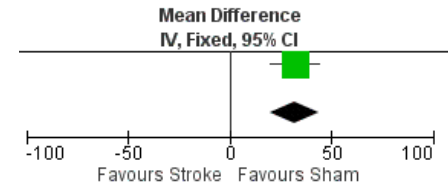
55 days 40.38 (35.16, 45.60) <0.00001



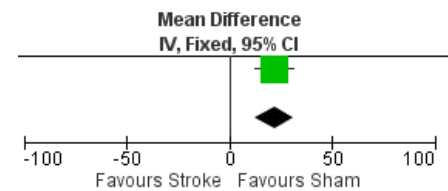
56 days 19.57 (14.21, 24.94) <0.00001



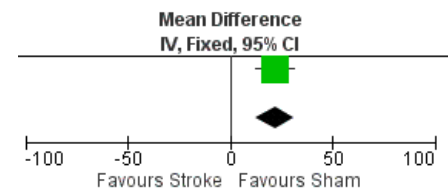
57 days 32.26 (20.20, 44.32) <0.0001



58 days 21.94 (12.53, 31.35) <0.0001



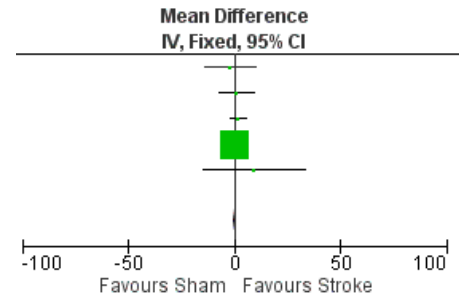
59 days 55.49 (47.26, 63.72) <0.0001



Morris
Water
Maze

Velocity

0.02 (-0.19, 0.23) 0.87



Morris
Water
Maze

Target
quadrant
time

5.88 (-2.77, 14.52) 0.18

