The antidepressant impact of minocycline in rodents: A systematic review and meta-analysis

Daniel J. Reis\(^1\,*\,*\), Emily J. Casteen\(^1\,*\), and Stephen S. Ilardi\(^1\)

\(^{1}\)University of Kansas, Department of Psychology, Lawrence, KS, 66045, USA

* daniel.reis@ku.edu

\(^{\ast}\)These authors contributed equally to this work
PubMed Search Algorithm

| Step | Search Term |
|------|-------------|
| 1    | Rat* or mouse* or mice* or murine or rodent |
| 2    | Minocycline* or Minocin* |
| 3    | 1 and 2 |
| 4    | Depression or Depressed or dep* or depressive-like or depression-like |
| 5    | Antidepressant or Antidepressant-like |
| 6    | Antibiotic |
| 7    | mental health* |
| 8    | Psycholo* and stress |
| 9    | 4 or 5 or 6 or 7 or 8 |
| 10   | 3 and 9 |

Variable Dictionary for Supplementary Data

| Variable | Description |
|----------|-------------|
| study    | Study number |
| author   | Author name |
| year     | Year of publication |
| tx_dur   | Duration of minocycline treatment in days |
| tx_dose  | Minocycline treatment dose in billions of milligrams per kilogram |
| tx_n     | Sample size of treatment group |
| c_n      | Sample size of control group |
| hedges   | Standardized mean difference between treatment and control group (Hedge’s g) – Negative value = greater depression reduction in treatment group |
| se       | Standard error of standardized mean difference |
| paradigm | Behavioral paradigm |
| measure  | Specific paradigm measure to assess for depressive-like behavior |
| rodent   | Rodent species employed – mouse or rat |
| disease  | Animal model of disease (0 = no, 1 = yes) |
| dis_pre  | Minocycline treatment prior to disease induction (0 = no, 1 = yes; note – 0 for both dis_pre and dis_tre = healthy animal) |
| dis_tre  | Minocycline treatment following disease induction (0 = no, 1 = yes; note – 0 for both dis_pre and dis_tre = healthy animal) |
| Studies                          | SMD (95% CI) | Weight (%) |
|--------------------------------|-------------|------------|
| Amorim, D. 2017                |             |            |
| Forced Swim Test               |             |            |
| Burke, N. 2014 Group 1         | -1.03 (-2.09, 0.03) | 1.1 |
| Open Field Test                |             |            |
| Burke, N. 2014 Group 2         | -0.51 (-1.91, -1.11) | 1.1 |
| Open Field Test                | -0.67 (-1.96, 0.32) | 2.6 |
| Chijiwa, T. 2015 Group 1       | -1.32 (-2.26, -0.36) | 2.7 |
| Forced Swim Test               | 0.06 (-1.13, 1.25) | 2.4 |
| Chijiwa, T. 2015 Group 2       | -2.39 (-4.02, -0.76) | 1.8 |
| Deak, T. 2015                  | 0.20 (0.57, 0.87) | 2.9 |
| Henry, C. 2008 Group 1         | -0.74 (-1.48, 0.00) | 2.9 |
| Henry, C. 2008 Group 2         | -1.72 (-2.58, -0.86) | 2.8 |
| Mahmoud, M. 2015 Group 1       | 1.16 (-2.49, 0.17) | 1.0 |
| Forced Swim Test               | -1.90 (-3.32, -0.28) | 1.0 |
| Majidi, J. 2016 Group 1        | -0.34 (-1.27, 0.59) | 0.9 |
| Sucreose Preference Test       | -0.57 (-1.30, 0.56) | 0.9 |
| Forced Swim Test               | -0.90 (-1.98, 0.08) | 0.9 |
| Majidi, J. 2016 Group 2        | -1.04 (-2.04, -0.04) | 0.8 |
| Sucreose Preference Test       | -1.04 (-2.04, -0.04) | 0.8 |
| Forced Swim Test               | -1.58 (-2.97, -0.49) | 0.8 |
| McKim, D. 2016                 | -0.29 (-1.43, 0.85) | 2.4 |
| Social Interaction             |             |            |
| Molina-Hernandez, M. 2008a     | -1.00 (-1.90, -0.19) | 2.7 |
| Forced Swim Test               | -0.97 (-1.93, -0.01) | 2.7 |
| Nagpal, K. 2013                | -1.38 (-2.49, -0.27) | 1.2 |
| Tail Suspension Test           | -0.44 (-1.43, 0.55) | 1.2 |
| Rinwa, P. 2013 Group 1         | -1.31 (-2.07, -0.55) | 1.4 |
| Open Field Test                | -1.56 (-2.16, -0.96) | 1.4 |
| Rinwa, P. 2013 Group 2         | -1.85 (-2.94, -0.86) | 1.3 |
| Open Field Test                | -2.35 (-3.43, -1.27) | 1.3 |
| Rinwa, P. 2013 Group 3         | -1.47 (-2.39, -0.55) | 1.3 |
| Open Field Test                | -2.58 (-3.71, -1.45) | 1.3 |
| Saravi, S. 2016a               | -0.57 (-1.53, 0.36) | 0.9 |
| Tail Suspension Test           | -1.55 (-2.59, -0.51) | 0.9 |
| Saravi, S. 2016b               | -4.42 (-6.07, -2.77) | 1.8 |
| Forced Swim Test               |             |            |
| Singh B. 2017                  | -2.25 (-3.83, -0.67) | 1.9 |
| Forced Swim Test               | -5.96 (-9.13, -2.85) | 0.5 |
| Singh T. 2016 Group 1           | -2.04 (-4.77, 0.71) | 0.5 |
| Forced Swim Test               | -2.10 (-3.23, -0.97) | 1.2 |
| Tail Suspension Test           | -2.08 (-3.21, -0.96) | 1.2 |
| Tong, L. 2017 Group 1           | -0.19 (-0.99, 0.61) | 0.9 |
| Tail Suspension Test           | 0.46 (-0.35, 1.27) | 0.9 |
| Forced Swim Test               | -0.72 (-1.55, 0.11) | 0.9 |
| Tong, L. 2017 Group 2           | -1.92 (-2.92, -0.92) | 0.9 |
| Tail Suspension Test           | -1.14 (-2.01, -0.27) | 0.9 |
| Forced Swim Test               | -1.98 (-2.99, -0.97) | 0.9 |
| Tong, L. 2017 Group 3           | -0.15 (0.05, 0.65) | 0.9 |
| Tail Suspension Test           | -0.38 (-1.19, 0.43) | 0.9 |
| Forced Swim Test               | -0.30 (-0.51, 1.11) | 0.9 |
| Tong, L. 2017 Group 4           | -1.22 (-2.11, -0.33) | 0.9 |
| Tail Suspension Test           | -0.61 (-1.76, 0.50) | 0.9 |
| Forced Swim Test               | -1.59 (-3.00, -0.98) | 0.9 |
| Weng, W.-J. 2017 Group 1       | 0.76 (0.07, 1.59) | 0.9 |
| Tail Suspension Test           | -0.28 (-1.09, 0.53) | 0.9 |
| Forced Swim Test               | 0.44 (0.37, 1.25) | 0.9 |
| Tong, L. 2017 Group 6           | -1.42 (-2.33, -0.51) | 0.8 |
| Tail Suspension Test           | -2.21 (-3.14, -1.28) | 0.8 |
| Forced Swim Test               | -2.29 (-3.36, -1.22) | 0.8 |
| Weng, W.-T. 2017 Group 2       | -1.47 (-2.91, -0.33) | 1.2 |
| Forced Swim Test               | -0.41 (-1.40, 0.58) | 1.2 |
| Weng, W.-T. 2017 Group 3       | -1.80 (-2.94, -0.66) | 1.2 |
| Forced Swim Test               | -1.48 (-2.55, -0.41) | 1.2 |
| Wang, M.-L. 2016 Group 1       | 0.63 (0.19, 1.45) | 2.8 |
| Forced Swim Test               | -0.84 (-1.59, -0.09) | 2.9 |
| Xu, N. 2017 Group 1             | -0.36 (-1.20, 0.42) | 1.4 |
| Forced Swim Test               | 0.61 (0.21, 1.43) | 1.4 |
| Xu, N. 2017 Group 2             | -1.19 (-2.07, -0.31) | 1.4 |
| Forced Swim Test               | -1.10 (-1.97, -0.23) | 1.4 |
| Zheng, L.-S. 2015 Group 1      | 0.05 (-0.83, 0.93) | 1.4 |
| Tail Suspension Test           | 0.09 (-0.79, 0.07) | 1.4 |
| Forced Swim Test               | -1.16 (-2.12, -0.20) | 1.3 |
| Zheng, L.-S. 2015 Group 2      | -1.16 (-2.15, -0.21) | 1.3 |
| Tail Suspension Test           | -0.98 (-2.21, 0.25) | 2.3 |
| Forced Swim Test               | -1.07 (-1.41, -0.74) | 2.3 |

Summary (V² = 75.66%):