**Supplementary Data**

**Table S1. Effects of lactic acid on various performance parameters for 5CTV.** Parameters are described in Methods section under 5CTV description. All values represent mean (S.D.). Lactic acid was administered in a volume of 1 ml/kg immediately prior to the beginning of 5CTV sessions.

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  |  |  | Lactic Acid (v/v, i.p.) | | |
|  | Baseline | Saline | 0.9% | 1.8% | 5.4% |
|  |  |  |  |  |  |
| Correct | 58.0 (3.3) | 58.4 (3.6) | 56.0 (2.0) | 37.4 (18.8) | 2.5 (5.6) |
| Incorrect | 16.6 (9.2) | 16.4 (11.9) | 12.1 (8.1) | 3.5 (6.7) | 0.1 (0.4) |
| Omission | 25.4 (10.9) | 25.2 (14.9) | 31.9 (9.4) | 42.3 (10.7) | 45.1 (0.8) |
| Total trials completed | 100.0 (0.0) | 100.0 (0.0) | 100.0 (0.0) | 83.2 (22.7) | 47.8 (6.2) |
| % Correct | 58.0 (3.3) | 58.4 (3.6) | 56.0 (2.0) | 41.6 (14.3) | 4.2 (8.8) |
| % Incorrect | 16.6 (9.2) | 16.4 (11.9) | 12.1 (8.1) | 3.7 (6.7) | 0.3 (0.8) |
| % Omission | 25.4 (10.9) | 25.2 (14.9) | 31.9 (9.4) | 54.8 (18.4) | 95.5 (8.7) |
| Premature | 11.1 (8.3) | 10.4 (11.3) | 4.4 (3.2) | 2.3 (3.1) | 0.0 (0.0) |
| Perseverative | 3.5 (3.6) | 1.8 (2.1) | 2.9 (3.2) | 1.9 (2.2) | 0.0 (0.0) |
| Time-out | 13.8 (11.3) | 11.3 (10.9) | 6.3 (3.8) | 3.6 (7.9) | 0.0 (0.0) |

**Table S2. Effects of ketoprofen in combination with lactic acid on various performance parameters for 5CTV.** Parameters are described in Methods section under 5CTV description. All values represent mean (S.D.). Saline or ketoprofen was administered s.c. 30 min prior to lactic acid (1.8%, i.p.) which was administered in a volume of 1 ml/kg immediately prior to the beginning of 5CTV sessions.

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  |  |  | Ketoprofen (mg/kg) | | |
|  | Baseline | Saline/1.8%  Lactic acid | 0.03 | 0.10 | 0.30 |
|  |  |  |  |  |  |
| Correct | 58.2 (2.8) | 22.6 (16.5) | 34.1 (17.4) | 46.3 (16.0) | 55.7 (5.4) |
| Incorrect | 15.3 (9.2) | 2.6 (4.8) | 2.8 (3.8) | 7.7 (6.5) | 10.4 (7.5) |
| Omission | 26.5 (9.4) | 42.7 (5.6) | 39.2 (11.9) | 36.6 (8.5) | 33.3 (10.9) |
| Total trials completed | 100.0 (0.0) | 67.9 (16.9) | 76.1 (25.8) | 90.6 (17.1) | 94.4 (2.3) |
| % Correct | 58.2 (2.8) | 29.6 (16.6) | 42.5 (12.0) | 49.2 (12.0) | 55.9 (4.7) |
| % Incorrect | 15.3 (9.2) | 3.0 (4.9) | 3.7 (3.9) | 8.0 (6.5) | 10.4 (7.5) |
| % Omission | 26.5 (9.4) | 67.4 (20.2) | 53.8 (13.9) | 42.7 (16.8) | 33.6 (11.4) |
| Premature | 8.3 (6.7) | 1.8 (3.5) | 1.2 (1.5) | 3.6 (4.2) | 4.1 (3.4) |
| Perseverative | 3.4 (3.5) | 1.5 (1.2) | 1.5 (1.7) | 2.7 (1.9) | 2.7 (2.6) |
| Time-out | 10.3 (9.1) | 3.1 (6.4) | 1.6 (1.2) | 4.9 (4.6) | 3.5 (4.0) |

**Table S3. Effects of morphine in combination with lactic acid on various performance parameters for 5CTV.** Parameters are described in Methods section under 5CTV description. All values represent mean (S.D.). Saline or morphine was administered s.c. 30 min prior to lactic acid (1.8%, i.p.) which was administered in a volume of 1 ml/kg immediately prior to the beginning of 5CTV sessions.

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  |  |  | Morphine (mg/kg) | | |
|  | Baseline | Saline/1.8%  Lactic acid | 0.3 | 1.0 | 3.0 |
|  |  |  |  |  |  |
| Correct | 56.8 (1.9) | 16.6 (13.6) | 23.6 (15.0) | 34.8 (24.3) | 55.8 (3.0) |
| Incorrect | 13.5 (7.4) | 1.0 (1.4) | 0.9 (1.0) | 5.5 (9.8) | 8.0 (9.5) |
| Omission | 29.6 (8.6) | 43.6 (5.2) | 45.0 (7.1) | 39.9 (11.8) | 36.3 (10.8) |
| Total trials completed | 100.0 (0.0) | 61.2 (15.8) | 69.5 (17.6) | 80.1 (22.9) | 100.0 (0.0) |
| % Correct | 56.8 (1.9) | 23.8 (15.5) | 31.9 (14.1) | 38.1 (21.1) | 55.8 (3.0) |
| % Incorrect | 13.5 (7.4) | 1.4 (2.0) | 1.2 (1.4) | 5.6 (9.8) | 8.0 (9.5) |
| % Omission | 29.6 (8.6) | 74.8 (16.6) | 66.9 (14.0) | 56.2 (27.6) | 36.3 (10.8) |
| Premature | 6.7 (5.2) | 0.7 (1.3) | 0.0 (0.0) | 5.6 (8.9) | 9.3 (13.7) |
| Perseverative | 3.3 (2.9) | 1.1 (1.4) | 1.4 (2.1) | 1.3 (1.4) | 3.4 (1.6) |
| Time-out | 8.8 (8.4) | 1.3 (1.9) | 1.3 (1.6) | 4.9 (8.6) | 4.3 (3.2) |

**Table S4. Effects of scopolamine on various performance parameters for 5CTV and effects of ketoprofen or morphine in combination with scopolamine.** Parameters are described in Methods section under 5CTV description. All values represent mean (S.D.). Saline , scopolamine, or scopolamine (0.1 mg/kg, s.c.) with either ketoprofen (0.3 mg/kg, s.c.) or morphine (3.0 mg/kg, s.c.) was administered s.c. 30 min prior to the beginning of 5CTV sessions.

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  |  |  | Scopolamine (mg/kg) | | | | | 0.1 Scopolamine | | |
|  | Baseline | Saline | 0.03 | | 0.1 | | 0.3 | 0.3 Ketoprofen | | 3.0  Morphine |
|  |  |  |  | |  | |  | |  |  |
| Correct | 57.1 (1.9) | 58.0 (2.3) | 50.3 (7.2) | 41.2 (12.8) | | 29.4 (16.9) | | 32.7 (10.0) | | 43.7 (12.5) |
| Incorrect | 15.8 (9.3) | 13.0 (6.7) | 4.5 (6.4) | 2.0 (1.5) | | 1.7 (2.1) | | 2.3 (1.5) | | 4.0 (3.9) |
| Omission | 27.1 (10.5) | 29.0 (7.8) | 42.3 (7.8) | 42.0 (4.6) | | 41.3 (5.3) | | 38.1 (6.5) | | 39.0 (4.4) |
| Total trials completed | 100.0 (0.0) | 100.0 (0.0) | 97.1 (8.5) | 85.2 (16.5) | | 72.4 (20.1) | | 73.0 (15.4) | | 86.7 (16.5) |
| % Correct | 57.1 (1.9) | 58.0 (2.3) | 51.5 (4.0) | 47.2 (7.2) | | 36.9 (16.5) | | 44.0 (5.8) | | 49.3 (7.4) |
| % Incorrect | 15.8 (9.3) | 13.0 (6.7) | 4.5 (6.4) | 2.4 (1.6) | | 2.2 (2.8) | | 3.0 (2.1) | | 4.2 (3.9) |
| % Omission | 27.1 (10.5) | 29.0 (7.8) | 44.0 (9.3) | 50.4 (6.8) | | 61.0 (17.8) | | 53.0 (6.7) | | 46.4 (9.9) |
| Premature | 14.3 (12.7) | 12.3 (7.8) | 2.2 (4.7) | 0.8 (1.1) | | 0.7 (1.5) | | 0.8 (1.1) | | 19.4 (27.5) |
| Perseverative | 3.1 (2.6) | 2.7 (1.3) | 5.0 (3.3) | 3.8 (3.4) | | 2.3 (2.2) | | 3.3 (2.8) | | 2.9 (3.2) |
| Time-out | 15.2 (15.0) | 14.0 (11.3) | 3.5 (4.9) | 1.9 (1.4) | | 1.7 (2.3) | | 1.4 (1.4) | | 12.5 (16.3) |