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| **Supplementary File 1A. Baseline cardiorespiratory values in male and female rats prior to receiving 20 µg/kg fentanyl** | Figure 1: Dose Response | | Figure 3: Pretreatment | | Figure 4: Reversal | |
| Males | Females | Males | Females | Males | Females |
| Oxygen Saturation Baseline (%) | 94 ± 0.5 | 95 ± 0.4 | 96 ± 0.4 | 96 ± 0.4 | 95 ± 0.6 | 95 ± 0.3 |
| Heart Rate Baseline (beats per minute) | 445 ± 16 | 426 ± 13 | 462 ± 12 | 439 ± 17 | 436 ± 10 | 416 ± 13 |
| Respiratory Rate Baseline (breaths per minute) | 109 ± 6 | 95 ± 3 | 108 ± 5 | 114 ± 3 | 103 ± 4 | 102 ± 4 |
| **Supplementary File 1B. Baseline cardiorespiratory values in male and female rats prior to receiving 50 µg/kg fentanyl** | Figure 1: Dose Response | | Figure 3 – Figure  Supplement 1 | | Figure 4 – Figure  Supplement 1 | |
| Males | Females | Males | Females | Males | Females |
| Oxygen Saturation Baseline (%) | 94 ± 1 | 95 ± 1 | 94 ± 1 | 96 ± 1 | 94 ± 1 | 95.2 ± 1.1 |
| Heart Rate Baseline (beats per minute) | 408 ± 10 | 485 ± 13\* | 450 ± 21 | 434 ± 14 | 421 ± 17 | 451 ± 33 |
| Respiratory Rate Baseline (breaths per minute) | 95 ± 2 | 110 ± 4 | 101 ± 5 | 98 ± 4 | 100 ± 1 | 105 ± 8 |

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| **Supplementary File 1C. Nadir and recovery values in male and female rats that received 20 µg/kg fentanyl** | Figure 1: Dose Response | | Figure 3: Pretreatment | | Figure 4: Reversal | |
| Males | Females | Males | Females | Males | Females |
| Oxygen Saturation Nadir (%) | 50 ± 4 | 50 ± 4 | 42 ± 6 | 38 ± 1 | 53 ± 6 | 45 ± 2 |
| Heart Rate Nadir (beats per minute) | 182 ± 26 | 144 ± 10 | 253 ± 32 | 177 ± 55 | 226 ± 45 | 146 ± 20 |
| Respiratory Rate Nadir (breaths per minute) | 59 ± 3 | 49 ± 4 | 67 ± 4 | 45 ± 12 | 66 ± 5 | 60 ± 4 |
| Oxygen Saturation Recovery (minutes) | 11 ± 1 | 10 ± 1 | 12 ± 2 | 14 ± 2 | 14 ± 3 | 11 ± 1 |
| Heart Rate Recovery (minutes) | 15 ± 13 | 16 ± 1 | 15 ± 3 | 13 ± 5 | 15 ± 3 | 18 ± 1 |
| Respiratory Rate Recovery (minutes) | 12 ± 2 | 14 ± 1 | 10 ± 1 | 17 ± 4 | 11 ± 1 | 15 ± 3 |

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| **Supplementary File 1D. Nadir and recovery values in male and female rats that received 50 µg/kg fentanyl** | Figure 1: Dose Response | | Figure 3 – Figure Supplement 1 | | | Figure 4 – Figure  Supplement 1 | |
| Males | Females | Males | | Females | Males | Females |
| Oxygen Saturation Nadir (%) | 30 ± 3 | 37 ± 2 | | 41 ± 4 | 35 ± 6 | 40 ± 5 | 38 ± 4 |
| Heart Rate Nadir (beats per minute) | 181 ± 16 | 145 ± 20 | | 159 ± 17 | 179 ± 37 | 135 ± 17 | 188 ± 33 |
| Respiratory Rate Nadir (breaths per minute) | 48 ± 6 | 41 ± 5 | | 56 ± 10 | 55 ± 9 | 50 ± 8 | 61 ± 6 |
| Oxygen Saturation Recovery (minutes) | 31± 6 | 28 ± 7 | | 30 ± 5 | 22 ± 6 | 29 ± 5 | 28 ± 6 |
| Heart Rate Recovery (minutes) | 23 ± 5 | 48 ± 1 | | 43 ± 9 | 33 ± 5 | 35 ± 7 | 41 ± 1 |
| Respiratory Rate Recovery (minutes) | 16 ± 3 | 43 ± 1† # | | 26 ± 7 | 18 ± 4 | 13 ± 4 | 38 ± 3 |