**Legend**

Blue cell is the example reported in the figure;

**P** means “proximal” (5-15 µm from the soma); **D** means “proximal” (30-40 µm from the soma)

**I** means “current”

Results of statistical test: “p” is for paired t-test; “pw” is for Wilcoxon signed rank test.

**Figure 1: (“Na”=Na+ concentration)**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | **NaP** | **NaD** | **IfastP** | **IfastD** | **IslowP** | **IslowD** |
| 13042021a | 1.94(-29.1%) | 0.90(-11.4%) | 38.8(-26.0%) | 15.2(-43.4%) | 15.7(-36.7%) | 8.7(-14.3%) |
| 13042021b | 0.78(-27.0%) | 0.67(-22.4%) | 31.0(-29.6%) | 19.3(-56.9%) | 7.6(-46.6%) | 11.8(-41.0%) |
| 13042021c | 1.02(-34.8%) | 1.11(-33.8%) | 35.1(-40.2%) | 18.4(-55.0%) | 4.9(-24.0%) | 5.6(-27.7%) |
| 21042021b | 0.71(-12.5%) | 0.64(-11.0%) | 27.8(-18.8%) | 21.3(-16.6%) | 4.3(-9.5%) | 4.2(19.8%) |
| 23042021a | 0.22(-31.3%) | 0.43(-32.6%) | 7.4(-10.3%) | 15.5(-67.6%) | 1.4(-51.7%) | 2.7(-29.5%) |
| 30042021a | 0.53(-50.0%) | 0.48(-41.7%) | 21.2(-47.6%) | 16.2(-69.7%) | 3.9(-53.4%) | 16.2(-27.7%) |
| 30042021b | 0.57(-25.1%) | 0.57(-20.1%) | 25.2(-53.7%) | 17.5(-47.5%) | 3.7(-16.5%) | 3.5(-15.5%) |
| 30042021c | 0.53(-31.7%) | 0.43(-23.6%) | 22.4(-61.0%) | 15.0(-48.1%) | 3.4(-20.7%) | 3.0(-24.6%) |
| 30042021d | 0.49(-31.5%) | 0.45(-9.3%) | 20.2(-42.2%) | 18.1(-16.6%) | 2.9(-18.0%) | 2.7(3.7%) |
|  | -30.3±9.8, p=0.0025  pw=0.0039 | -22.9±11.4, p=0.0023  pw=0.0039 | -36.6±16.7, p=0.00018215  pw=0.0039 | -46.8±19.2, p=0.00060652  pw=0.0039 | -30.7±16.6, p=0.02  pw=0.0321 | -17.5±18.6, p=0.0892  pw=0.0547 |

**Figure 2:**

|  |  |  |
| --- | --- | --- |
|  | Integral difference **P** (%) | Integral difference **D** (%) |
| 13012021b | 95.2488 90.1913 (5) | 109.2651 121.9320 (11) |
| 13012021c | 78.0685 78.3912 (1) | - 89.6363 115.0093 (28) |
| 14012021b | 27.9187 34.9610 (25) | 35.5140 40.2615 (13) |
| 15012021d | 72.3700 67.5662 (-6) | 49.3976 62.3373 (26) |
| 15012021e | 73.0187 81.2385 (11) | 56.4672 70.1412 (24) |
| 21012021a | 94.9296 88.0654 (-7) | 71.6345 95.7228 (34) |
| 21012021c | 27.4939 27.0792 (-1) | 44.9848 55.0568 (22) |
| 15032021c | 198.9358 210.4887 (7) | 133.3279 142.5181 (6) |
| 17022021a | 88.4593 94.5203 (6) | 53.2954 66.5693 (25) |
| mean±SD | 3.2±8.8  p=0.44  pw=0.4258 | 21.3±0.10.5  p=2.40·10-4  pw=0.0039 |

**Figure S3:**

|  |  |  |
| --- | --- | --- |
| ***isr*** | ΔFchange/ICa change **P** (%) | ΔFchange/ICa change **D** (%) |
| 11062020b | -18.6 -28.7 | 16.4 -1.1 |
| 12062020a | - 21.6 -33.3 | 6.4 -4.4 |
| 12062020b | -58.3 -58.6 | -15.9 -23.5 |
| 12062020c | -11.0 -17.0 | 19.3 3.6 |
| 12062020d | -18.3 -35.1 | 2.2 0 |
| 15062020a | -15.5 -38.2 | 19.9 -3.9 |
| 15062020b | -1.5 -9.8 | 40.0 9.7 |
| 15062020c | -9.5 -19.0 | -0.8 -11.1 |
| mean±SD | -19.3±17.0 -29.9±15.2 | 10.9±16.8 -3.8±10.0 |

|  |  |  |
| --- | --- | --- |
| ***AgaIVA*** | ΔFchange/ICa change **P** (%) | ΔFchange/ICa change **D** (%) |
| 17062020a | -37.5 -45.8 | 1.9 -6.9 |
| 25062020a | - 48.6 -43.9 | -25.1 -28.9 |
| 29062020c | -6.4 -8.1 | 16.5 13.5 |
| 30062020a | -27.0 -34.7 | 0 5.6 |
| 30062020c | -5.1 -12.2 | 6.2 -2.0 |
| 02072020a | -1.9 -3.2 | 13.4 5.9 |
| 02072020c | -10.3 -19.4 | 10.4 -10.3 |
| mean±SD | -19.5±18.2 -23.9±17.4 | 3.3±13.8 -3.3±13.9 |

|  |  |  |
| --- | --- | --- |
| ***conGVIA*** | ΔFchange/ICa change **P** (%) | ΔFchange/ICa change **D** (%) |
| 10092020a | 2.8 -13.1 | -1.3 -3.9 |
| 10092020b | -26.2 -20.0 | +4.9 +0.5 |
| 11092020a | -5.5 -15.5 | +2.0 +1.1 |
| 16092020a | 8.5 -4.2 | +20.9 -1.6 |
| 16092020b | -9.3 -25.7 | -1.0 -2.7 |
| 22092020a | -41.5 -33.8 | -14.9 -18.7 |
| 22092020b | -6.9 -28.8 | -4.4 -8.1 |
| mean±SD | -11.2±17.2 -20.2±10.1 | 0.9±10.8 -4.8±6.8 |

|  |  |  |
| --- | --- | --- |
| ***snx*** | ΔFchange/ICa change **P** (%) | ΔFchange/ICa change **D** (%) |
| 03072020a | -1.9 -5.8 | -0.5 1.0 |
| 15072020b | 7.4 -14.2 | 8.7 -4.3 |
| 16072020b | -14.1 -24.2 | 4.8 0.1 |
| 17072020a | -18.6 -9.4 | 0 -2.7 |
| 17072020b | 16.2 -4.0 | 4.2 -1.8 |
| 22072020b | -7.2 1.6 | 8.2 6.6 |
| 23072020a | -18.6 -9.4 | -6.6 1.7 |
| 23072020b | -1.4 8.9 | 4.2 -1.8 |
| mean±SD | -4.8±12.4 -7.1±10.0 | 2.9±5.1 -0.2±3.4 |

|  |  |  |
| --- | --- | --- |
| ***ml+nnc*** | ΔFchange/ICa change **P** (%) | ΔFchange/ICa change **D** (%) |
| 26102020a | -28.4 -26.1 | -15.4 -16.1 |
| 26102020c | -41.9 -46.7 | -18.7 -7.1 |
| 27102020c | -5.9 -5.7 | 12.1 4.5 |
| 28102020a | -23.2 -25.1 | -6.0 -1.7 |
| 28102020b | -17.6 -11.3 | 1.9 5.2 |
| 28102020d | -19.4 -27.2 | -9.3 -4.6 |
| 30102020b | -21.2 -3.0 | -17.4 1.9 |
| 02112020a | -7.0 -7.0 | -0.2 -0.4 |
| mean±SD | -20.6±11.5 -19.0±14.9 | -6.6±10.8 -2.3±7.0 |

**Figure 4 (*C-E*): Calcium imaging**

**Pharmacology (either hwtx, panel c, or VGCCs, panel d)**

|  |  |  |
| --- | --- | --- |
| ***hwtx*** | ΔF/change(%) ICa/change(%) **P** | ΔF/change(%) ICa/change(%) **D** |
| 16062021c | 0.091(-11.5) 93(-2.7) | 0.114(-28.7) 84(-20.7) |
| 16062021b | 0.053(-11.1) 45(-11.9) | 0.047(-12.2) 53(-25.9) |
| 28062021b | 0.086(-12.6) 60(-1.3) | 0.091(-18.3) 61(-16.6) |
| 28062021c | 0.088(1.7) 66(-2.3) | 0.073(-25.3) 42(-22.5) |
| 24062021a | 0.025(-18.9) 18(-16.8) | 0.017(-31.4) 15(-29.1) |
| 16072021a | 0.152(-18.0) 160(-16.6) | 0.093(-39.6) 92(-34.3) |
| 16072021b | 0.108(-1.9) 105(-1.9) | 0.053(-12.2) 79(-14.9) |
| 16072021c | 0.110(-30.0) 90(-24.3) | 0.073(-50.3) 60(-45.5) |
| mean±SD | -12.8±10.0 -9.7±8.9 | -27.3±13.3 -26.2±10.1 |

p/pw 0.0316/0.0156 0.0634/0.00780.0048/0.0039 0.0020/0.0039

|  |  |  |
| --- | --- | --- |
| ***VGCCs*** | ΔF/change(%) ICa/change(%) **P** | ΔF/change(%) ICa/change(%) **D** |
| 31052021b | 0.09(-62.3) 65(-70.2) | 0.052(-16.5) 50(-30.0) |
| 31052021d | 0.095(-71.2) 83(-78.8) | 0.066(-58.5) 65(-63.2) |
| 31052021c | 0.130(-38.6) 103(-54.5) | 0.062(-22.0) 65(-33.6) |
| 26112020b | 0.179(-62.3) 114(-72.7) | 0.092(-33.1) 77(-21.9) |
| 26112020c | 0.153(-47.0) 85(-53.8) | 0.076(-23.4) 73(-14.5) |
| 24112020a | 0.080(-62.9) 46(-60.3) | 0.044(-25.1) 26(-19.9) |
| 23112020a | 0.097(-51.9) 76(-49.1) | 0.092(-21.6) 55(-22.3) |
| 09112020a | 0.160(-52.1) 118(-58.2) | 0.086(-29.3) 53(-34.4) |
| mean±SD | -56.0±10.5 -62.2±10.5 | 28.7±13.1 -30.0±15.1 |

p/pw 4.55·10-5/0.0039 6.69·10-5/0.00397.37·10-4/0.0039 0.0024/0.0039

**Figure 5 (*C-D*): Voltage Imaging CAKC pharmacology**

|  |  |  |
| --- | --- | --- |
| ***apam*** | Integral difference **P** (%) | Integral difference **D** (%) |
| 01022021c | 29.5200 41.2312 (39.7) | 58.3229 71.9799 (23.4) |
| 04022021a | 32.9012 45.7806 (39.1) | 57.9002 81.7707 (41.2) |
| 04022021b | 68.6667 82.5163 (20.2) | 106.8984 114.1069 (6.7) |
| 05032021a | 32.1376 36.0497 (12.2) | 31.8593 36.3488 (14.1) |
| 05032021c | 41.2144 48.7155 (18.2) | 46.4916 51.4848 (10.7) |
| 05032021d | 27.4035 35.8391 (29.2) | 35.5403 45.9105 (30.1) |
| 26022021b | 2.2816 2.5779 (13) | 24.0101 30.3592 (26.4) |
| mean±SD | 24.7±11.7  p=0.0042 pw=0.0039 | 21.7±12.0  p=0.0079 pw=0.0039 |

|  |  |  |
| --- | --- | --- |
| ***ibtx*** | Integral difference **P** (%) | Integral difference **D** (%) |
| 08022021b | 104.4245 111.4853 (6.8) | 29.9523 40.4125 (34.9) |
| 11022021b | 48.2153 60.3806 (25.2) | 46.5520 55.0024 (18.2) |
| 15022021a | 55.6631 75.2461 (35.2) | 11.9535 19.1865 (60.5) |
| 18022021c | 93.1521 101.9674 (9.5) | 28.0825 33.6539 (19.8) |
| 19022021b | 44.2043 58.3933 (32.1) | 81.4071 99.3055 (22) |
| 17032021b | 41.7414 45.7524 (9.6) | 61.5327 93.0306 (51.2) |
| 18032021a | 46.5967 59.4961 (27.7) | 48.3835 69.3111 (43.3) |
| mean±SD | 20.1±11.9  p=0.0063 pw=0.0039 | 36.9±16.6  p=0.0011 pw=0.0039 |

|  |  |  |
| --- | --- | --- |
| ***-VGCCs*** | Integral difference **P** (%) | Integral difference **D** (%) |
| 17032021a | 45.3454 53.8709 (18.8) | 12.0804 15.8046 (30.8) |
| 17032021a | 56.5273 66.2246 (17.2) | 26.4181 45.4170 (71.9) |
| 19032021a | 257.127 292.784 (13.9) | 65.7631 84.7060 (28.8) |
| 19032021a | 65.8725 77.9033 (18.3) | 33.2337 51.7134 (55.6) |
| 19032021c | 60.743 70.2669 (15.7) | 12.4332 13.4865 (8.5) |
| 22032021c | 46.0533 52.5361 (14.6) | 71.8003 76.6583 (6.8) |
| 23032021c | 35.0241 43.0447 (21.8) | 35.0241 43.0447 (22.9) |
| 30042021b | 99.0412 126.0354 (27.3) | 55.1516 63.5495 (15.2) |
| 30042021c | 66.1769 89.6786 (35.5) | 25.0065 27.0426 (8.1) |
| 24032021b | 142.8405 193.9103 (35.7) | 43.1308 43.9032 (1.8) |
| 25032021b | 89.4631 106.1122 (18.6) | 20.4638 20.6902 (1.1) |
| 25032021d | 53.2756 61.6788 (15.8) | 55.2991 74.5288 (34.8) |
| 26032021a | 57.5108 62.5809 (8.8) | 67.6219 80.1329 (18.5) |
| 26032021b | 77.7549 80.9728 (4.1) | 67.2371 77.3894 (15.1) |
| mean±SD | 19.0±8.9  p=6.4·10-4  pw=0.0039 | 22.9±20.5  p=4.2·10-4  pw=0.0039 |

|  |  |  |
| --- | --- | --- |
| ***VGCC/apam*** | Integrals and difference **P** (%) | Integrals and difference **D** (%) |
| 17032021a | 53.8709 53.2477 (-1.2) | 15.8046 19.7637 (25.0) |
| 17032021a | 66.2246 55.9297 (-15.7) | 49.2791 54.7530 (11.1) |
| 19032021a | 292.784 316.283 (7.4) | 85.8999 85.5383 (0) |
| 19032021a | 77.9033 72.5434 (-6.9) | 46.6094 34.0205 (-27.1) |
| 19032021c | 70.2669 70.1810 (0.1) | 13.4865 16.7226 (24) |
| 22032021c | 53.8229 57.0807 (6.5) | 79.0570 69.0205 (-12.7) |
| 23032021c | 69.7896 66.7146 (-4.4) | 43.7367 42.2305 (-3.4) |
| mean±SD | -2.1±7.9  p=0.8592 pw=0.6875 | 2.4±19.1  p=0.5492 pw=0.8125 |

|  |  |  |
| --- | --- | --- |
| ***VGCC/ibtx*** | Integrals and difference **P** (%) | Integrals and difference **D** (%) |
| 30042021b | 126.0354 143.8653 (14.1) | 63.5495 74.6628 (17.5) |
| 30042021c | 89.6786 101.7630 (13.5) | 19.5426 24.7628 (26.7) |
| 24032021b | 196.5700 203.6576 (3.6) | 46.7991 61.4935 (31.4) |
| 25032021b | 106.1122 128.2273 (20.8) | 20.6902 29.1075 (40.7) |
| 25032021d | 76.5763 90.5168 (10.9) | 63.9128 70.8946 (18.2) |
| 26032021a | 63.5040 72.2883 (13.8) | 82.7857 86.5605 (4.6) |
| 26032021b | 78.3790 84.4521 (7.8) | 76.0309 84.7907 (11.5) |
| mean±SD | 12.1±5.4  p=0.0065 pw=0.0039 | 21.5±12.2  p=0.0039 pw=0.0039 |

**Figure 5**

|  |  |  |
| --- | --- | --- |
| ***ibtx/hwtx*** | Integrals and difference **P** (%) | Integrals and difference **D** (%) |
| 26112021b | 94.8229 101.0680 (6.6) | 105.7019 100.7836 (-4.6) |
| 16112021a | 31.6637 35.0680 (11.0) | 35.3135 37.7511 (6.9) |
| 17122021b | 52.9554 51.7771 (-2.2) | 37.0614 24.6858 (-33.3) |
| 07122021a | 52.8234 38.4622 (-25.8) | 106.9010 80.6338 (-24.6) |
| 16122021a | 68.9458 65.4422 (-5.1) | 54.1325 53.3849 (-1.4) |
| 13122021b | 139.2886 124.3491 (-10.7) | 145.9363 130.9839 (-10.2) |
| 30112021c | 95.6997 106.7557 (11.5) | 63.1898 70.7426 (11.9) |
| mean±SD | -2.3±13.8  p=0.6311 pw=0.6875 | -7.9±16.3  p=0.1596 pw=0.2188 |

**Figure S4**

|  |  |  |
| --- | --- | --- |
| ***Tram*** | Integral difference Prox (%) | Integral difference Dist (%) |
| 03032021c | 156.3862 138.0284 (-11.7) | 58.0466 54.0645 (-7.7) |
| 03032021d | 168.2103 209.4095 (24.5) | 50.5893 54.4925 (7.7) |
| 26052021a | 111.1193 119.8399 (7.9) | 47.4557 44.9131 (-5.4) |
| 26052021b | 93.0631 100.1365 (7.6) | 17.7898 23.1530 (30.1) |
| 27052021a | 122.3168 114.2871 (-6.6) | 59.2678 71.7215 (21.0) |
| 27052021b | 127.8671 121.694 (-4.8) | 43.9899 36.7164 (-16.5) |
| 29032021a | 40.6711 45.4508 (11.7) | 53.4470 74.0653 (38.5) |
| 25052021b | 8.7318 7.4015 (-15.2) | 18.2217 16.2739 (-10.7) |
| mean±SD | 2.2±0.12.7  p=0.6032 pw=0.8438 | 6.7±0.21.1  p=0.3365 pw=0.5469 |  |

**Figure S6 (“Na”=Na+ concentration)**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | **NaP** | **NaD** | **IfastP** | **IfastD** | **IslowP** | **IslowD** |
| 08042021a | 0.43(-20.0%) | 0.40(-7.1%) | 21.8(-22.4%) | 12.9(5.7%) | 1.0(-1.7%) | 1.9(-30.1%) |
| 08042021b | 0.43(-14.7%) | 0.40(0%) | 17.8(-7.1%) | 17.3(-7.1%) | 3.0(2.6%) | 3.9(7.9%) |
| 08042021c | 0.78(13.1%) | 0.65(55.7%) | 30.4(-11.6%) | 26.9(-24.6%) | 5.8(12.2%) | 4.3(85.7%) |
| 08042021d | 1.21(10.4%) | 0.38(47.6%) | 58.7(-24.5%) | 12.1(-7.6%) | 7.5(23.4%) | 2.7(95.5%) |
| 01042021a | 0.38(4.0%) | 0.46(-4.3%) | 15.9(-18.3%) | 14.4(-33.7%) | 2.1(19.3%) | 3.5(6.7%) |
| 31042021a | 0.60(2.8%) | 0.73(25.0%) | 24.2(-8.0%) | 21.3(-6.8%) | 3.9(47.8%) | 6.7(72.7%) |
| 31042021b | 0.54(-5.6%) | 0.55(22%) | 24.1(-14.4%) | 19.3(-9.8%) | 3.7(-16.5%) | 5.4(40.0%) |
| 31042021d | 0.69(-4.8%) | 0.60(-4.1%) | 21.1(-36.6%) | 15.5(2.2%) | 7.6(-29.0%) | 6.5(-26.1%) |
|  | -1.9±11.6, p=0.83  pw=1 | 16.8±24.8, p=0.92  p=0.9375 | -17.9±9.9, p=0.0128  pw=0.0078 | -10.2±13.1, p=0.0602  pw=0.0391 | 1.4±25.2, p=0.69  pw=0.9453 | 31.5±49.4, p=0.11  pw=0.1484 |

**Figure S7**

|  |  |  |
| --- | --- | --- |
|  | Integral difference Prox (%) | Integral difference Dist (%) |
| 11032021a | 91.0372 100.9220 (11) | 49.8819 60.4952 (21) |
| 24022021a | 39.2356 41.7769 (6) | 61.1317 61.7616 (1) |
| 08032021b | 73.3962 71.5128 (-2) | 20.3376 29.5328 (45) |
| 28012021e | 45.6251 59.4401 (30) | 41.5585 50.7186 (22) |
| 28012021b | 30.0288 32.0788 (7) | 54.1173 53.2998 (-2) |
| 28012021d | 43.2858 51.1265 (18) | 46.0049 48.6832 (6) |
| 29012021a | 38.7861 35.0863 (-10) | 61.6034 76.5501 (24) |
| mean±SD | 8.6±13.1  p=0.1206 pw=0.1563 | 16.7±16.5  p=0.0234 pw=0.0469 |

**Figure S8**

|  |  |  |
| --- | --- | --- |
|  | ΔF/change(%) ICa/change(%) **P** | ΔF/change(%) ICa/change(%) **D** |
| 07062021a | 0.041(-5.6) 31(1.4) | 0.027(-4.8) 14(-1.3) |
| 07062021b | 0.051(4.1) 38(-1.2) | 0.045(-15.8) 27(-10.2) |
| 07062021c | 0.081(-6.1) 94(-9.6) | 0.041(-1.9) 30(9.1) |
| 07062021d | 0.144(-10.5) 141(-13.3) | 0.119(-5.3) 105(-10.4) |
| 08062021b | 0.050(-6.5) 38(2.4) | 0.035(0) 27(-3.2) |
| 09062021a | 0.079(-20.4) 79(-17.9) | 0.050(-16.6) 57(-13.5) |
| 09062021b | 0.056(6.0) 63(6.9) | 0.045(1.0) 64(4.1) |
| mean±SD | -5.6±8.9 -4.5±9.2 | -6.2±7.2 -3.6±8.3 |

p/pw 0.1702 0.1648/0.3750 0.0563 0.2577/0.2969