**Supplementary File 6.** Definition of model parameters and changes induced by isoproterenol (ISO) and carbachol (CCh) administration.

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| --- | --- | --- |
| ***Ion channels*** | | |
| **Maximal conductances** | | **ISO- or CCh-dependent effects** |
| Gst | Sustained inward Na+ current (Ist) | ISO: 15% increase in maximal conductance  (Kharche et al. 2011) |
| GNa1.1 | TTX-sensitive Na+ current (INa1.1) |  |
| GNa1.5 | TTX-resistant Na+ current (INa1.5) | ISO: 15% increase in maximal conductance  (Kharche et al. 2011) |
| GCaT | T-type Ca2+ current (ICaT) | ISO: 75% increase in maximal conductance  (Larson et al. 2013) |
| GCaL | L-type Ca2+ current (ICaL) | ISO: 2-fold increase in maximal conductance  (Larson et al. 2013) |
| Gf | Hyperpolarization-activated (funny) current (If) | ISO: gain of function via altered steady-state activation and gating properties  (Peters et al. 2021) |
| GK1 | Time-independent K+ current (IK1) | ISO: 15% decrease in maximal conductance (Kharche et al. 2011) |
| GKr | Rapid delayed rectifying K+ current (IKr) | ISO: 10% increase in maximal conductance and 5-mV shift of steady-state activation to  more negative potentials (Kharche et al. 2011) |
| GKs | Slow delayed rectifying K+ current (IKs) | ISO: 15% increase in maximal conductance  (Kharche et al. 2011) |
| Gto | Transient component of the 4-AP-sensitive K+ current (Ito) | ISO: 15% increase in maximal conductance  (Kharche et al. 2011) |
| Gsus | Sustained component of the 4-AP-sensitive K+ current (Isus) |  |
| GNaB | Background Na+ current (INaB) |  |
| GCaB | Background Ca2+ current (ICaB) |  |
| GK,ACh | Acetylcholine-dependent K+ current (IK,ACh) | CCh: ion current activation as in Arbel-Ganon et al. (2020) |
| ***Ion transporters*** | | |
| **Maximal transport rates** | | **ISO- or CCh-dependent effects** |
| vNKA | Na+/K+ ATPase (NKA) |  |
| vNCX | Na+/Ca2+ exchanger (NCX) |  |
| vRyR | Ca2+ release via ryanodine receptor (RyR) | ISO: enhanced Ca2+ release via 2-fold increase in KoCa (non-SR-dependent transition rate constant) (Kharche et al. 2011) |
| vSERCA | Sarcoplasmic reticulum (SR) Ca2+ pump (SERCA) | ISO: enhanced Ca2+ uptake via 50% decrease in Kmf to reduce Ca2+-affinity (Kharche et al. 2011) |