Reduced Ca Currents in Frog Nerve Terminals at High Pressure[a]

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Exposure to high pressure (HP) causes suppression of synaptic transmission in individual synapses.[1] This suppression is due to a decrease in presynaptic transmitter release.[2] Indirect evidence suggests that HP primarily affects Ca^{2+} influx (I_{Ca}) in nerve terminals.[3] We examined the effect of HP on such I_{Ca}, using a "loose" patch-clamp technique, in an isolated cutaneous pectoris nerve-muscle preparation of the frog (*Rana pipiens*).[4] When the electrode (3–5 M ohms) was inserted under the perineurial sheath proximal to the nerve terminals, the local circuit currents flowing between the terminals and the parent axons could be recorded.[4] The preparation was placed in a pressure chamber and was perfused constantly with oxygenated physiological solution of the following composition (mM): NaCl,116; KCl,2; $CaCl_2$,1.8; Tris buffer,5; pH 7.4, at 18°C. Tubocurarine (5 mg/L) was added to block muscle contraction. Compression up to 6.9 MPa was accomplished with helium. The normal response was composed of a fast large inward current of sodium (I_{Na}) at the nodes, followed by a small inward current that reflects the outward potassium current (I_K) at the repolarizing terminals[4] (FIG. 1A). Blocking I_K by tetraethylammonium (TEA, 10 mM) disclosed a Ca-dependent outward current that was comprised of fast (I_{Ca_F}) and slow (I_{Ca_S}) components (FIG. 1B). Both phases, which reflect inward I_{Ca} at the terminals, were blocked by 10 μM Cd^{2+} and 1–5 μM omega-conotoxin, and only I_{Ca_S} was diminished by nifedipine and nitrendipine (15–25 μM). HP suppressed the maximal I_{Ca} by 87 ± 10% (mean ± SD, n = 13) and concomitantly reduced the action potential I_{Na} by 29 ± 11% in a pressure-dependent manner (FIG. 1C–E). I_{Ca_S} was more resistant to HP effect and could be partially restored by increased $[Ca^{2+}]_0$ (FIG. 1F–H). The data indicate that HP decreases the maximal I_{Ca} through L-type, voltage-gated Ca^{2+} channels[5] in vertebrate nerve terminals, and more so, in the N-type. It is not clear, however, whether this is a direct effect of HP on Ca^{2+} channels, because HP also reduced to some extent the amplitude of action potential invading the motor nerve terminals.

[a]This work was supported by NMRDC Work Unit M0099.01c-1010 and ONR Grant N00014-91-J-1908 to Y. Grossman. Y. Grossman is a National Research Council-NMRI Research Associate.

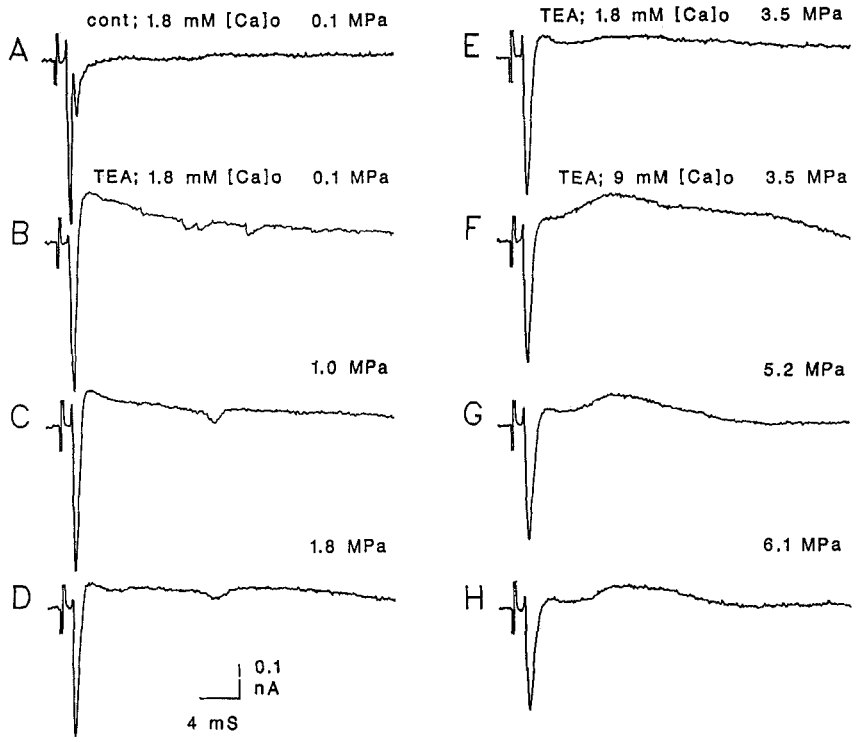

FIGURE 1. *Nerve terminal currents and high pressure.* All current records are from the same site. Holding potential was zero with respect to ground. A, control at normal pressure (0.1 MPa); B, TEA blocks all potassium currents and discloses a large calcium current; C–E, pressure-dependent reduction of calcium current; F, increased $[Ca^{2+}]_0$ may oppose pressure effect on the current amplitude; G-H, with increased pressure, the calcium current is further suppressed. Note that the node-sodium current (fast inward current) is also decreased in a pressure-dependent manner.

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