Hydrogen sulfide increases intracellular Ca$^{2+}$ concentration by inhibition of mitochondrial respiration in cultured rat spinal cord astrocytes.

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Hydrogen sulfide (H$_2$S), which is produced by astrocytes in the central nervous system, inhibits the mitochondrial electron transport chain (ETC). We have previously shown that H$_2$S releases Ca$^{2+}$ from the endoplasmic reticulum (ER) in spinal cord astrocytes. Here, we examined the relationship between H$_2$S-induced metabolic changes and Ca$^{2+}$ response.

Intracellular Ca$^{2+}$ concentration ([Ca$^{2+}$]$_i$) in cultured rat spinal cord astrocytes was measured using Fura 2-AM. Na$_2$S was used as a H$_2$S donor. The extracellular lactate and intracellular ATP were measured by enzymatic reaction using lactate dehydrogenase and luciferase, respectively.

Na$_2$S (150 µM) increased [Ca$^{2+}$]$_i$, which was inhibited by rotenone, an ETC inhibitor, and FCCP, an uncoupler of oxidative phosphorylation. Na$_2$S also increased extracellular lactate, and decreased intracellular ATP content when glycolysis was inhibited by iodoacetic acid. The increase in both Ca$^{2+}$ and extracellular lactate by Na$_2$S were inhibited by emetine, an inhibitor of translocon complex, which mediates Ca$^{2+}$ leak from the ER.

In conclusion, inhibition of the mitochondrial ETC by H$_2$S induces Ca$^{2+}$ release from the ER and lactate production in spinal cord astrocytes. H$_2$S may facilitate the supply of lactate from astrocytes to neurons as an energy substrate.