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Reappraisal of anoxic spreading depolarization as a terminal event during oxygen–glucose deprivation in brain slices in vitro

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Abstract

© 2020, The Author(s). Anoxic spreading depolarization (aSD) has been hypothesized as a terminal event during oxygen–glucose deprivation (OGD) in submerged cortical slices in vitro. However, mechanical artifacts caused by aSD-triggered edema may introduce error in the assessment of neuronal viability. Here, using continuous patch-clamp recordings from submerged rat cortical slices, we first confirmed that vast majority of L4 neurons permanently lost their membrane potential during OGD-induced aSD. In some recordings, spontaneous transition from whole-cell to out-side out configuration occurred during or after aSD, and only a small fraction of neurons survived aSD with reperfusion started shortly after aSD. Secondly, to minimize artifacts caused by OGD-induced edema, cells were short-term patched following OGD episodes of various duration. Nearly half of L4 cells maintained membrane potential and showed the ability to spike-fire if reperfusion started less than 10 min after aSD. The probability of finding live neurons progressively decreased at longer reperfusion delays at a rate of about 2% per minute. We also found that neurons in L2/3 show nearly threefold higher resistance to OGD than neurons in L4. Our results suggest that in the OGD ischemia model, aSD is not a terminal event, and that the “commitment point” of irreversible damage occurs at variable delays, in the range of tens of minutes, after OGD-induced aSD in submerged cortical slices.

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