40 Spontaneous Na+ concentration transients in individual mitochondria of intact astrocytes

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Astrocytes surrounding glutamatergic synapses remove released glutamate by a Na^+-dependent cotransporter, which causes robust increases in cytosolic Na^+ concentration (Na^+_{cyt}). We recently showed using a fluorescent probe specific for mitochondrial Na^+ (CoroNa Red), that Na^+_{cyt} increases occur also in the mitochondrial population where it is dynamically regulated. In the present study, we report that mitochondria of astrocytes can exhibit individual, spontaneous, and fully reversible increases in their Na^+ concentration. We developed an image analysis algorithm based on the wavelet transform that allowed us to quantify the frequency and intensity of fluctuations under different conditions. In a field of ~30 astrocytes, up to 1000 fluctuations per minute were typically detected under control conditions. The fluctuation duration and amplitude for a single mitochondrion averaged 12.2 ± 0.8 sec and 35.5 ± 3.2 mM, respectively. Under the same experimental conditions, mitochondrial electrical potential did not present such fluctuations. However, mitochondrial Na^+ fluctuations were abolished by mitochondrial depolarization and required the availability of metabolic substrates. The fluctuation frequency was diminished at low Na^+_{cyt}. Blockers of several pathways potentially mediating fluctuations (e.g. calcium uniporter, permeability transition pore) failed to inhibit them. However, fluctuations appear to be linked to cellular proton homeostasis, since cytosolic acidification increased fluctuation frequency, whereas inhibition of Na^+/H^+ exchanger decreased it. Finally, application of glutamate led to a small decrease in the frequency of fluctuations. This study shows that besides global Na^+ responses at the population level, individual mitochondria exhibit highly dynamic and regulation of their Na^+ content with a possible link to proton homeostasis.