Low Frequency Activity of Cortical Networks on Microelectrode Arrays is Differentially Altered by Bicuculline and Carbaryl

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Thousands of chemicals need to be characterized for their neurotoxicity potential. Neurons grown on microelectrode arrays (MEAs) are an in vitro model used to screen chemicals for functional effects on neuronal networks. Typically, after removal of low frequency components, effects on high frequency events (neuronal action potentials, or "spikes") are used to differentiate chemical effects. However, such approaches discard information and low frequency activity has yet to be examined for its utility in screening chemicals. In this pilot study, spontaneous network activity in primary cultures of rat cortex was collected in MEAs and differential effects of bicuculline (BIC 25 μM, n=4) and carbaryl (CAR 30μM, n=2) as compared to controls were examined. Activity was sampled at 25 kHz without an analog filter and subsequently separated into low (1-100 Hz) and high (>200 Hz; spikes) frequencies for separate analysis. Low frequency activity was extracted in Matlab in 1 sec segments for 300 seconds/electrode/well using a Kaiser window with no overlap. Wave amplitudes (μV), obtained at every 1Hz, were grouped by 5 frequency bands of interest: δ (1-4Hz), θ (4-8Hz), α (8-14Hz), β (14-30Hz), and γ (30-50Hz). Spectral amplitudes in a given band were averaged across pre- and post-treatment for every electrode and the difference calculated. The resulting electrode power differences were averaged across a well to obtain a well wide average power difference. BIC had significantly higher power vs. control in the δ, θ, α, β, and γ ($p<0.01$) bands. By contrast, CAR showed an increased power difference only in the θ and α bands ($p<0.05$). For high frequency activity, BIC increased spike rates to an average of 225% of control, while CAR decreased spike rates to 20% control. This study demonstrates that low frequency activity is differentially altered by chemical treatment, and thus may be a useful tool in distinguishing chemical influence on neuronal networks. (This abstract does not represent Agency Policy)

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