Characterisation of very fast oscillations (VFOs) in human frontal cortical slices *in vitro*

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Very fast oscillations (VFOs; 80-500Hz) are observed in the electrocorticogram of epilepsy patients, both inter-ictally and preceding seizure onset. We studied the properties of VFOs in human cortical slices *in vitro* to probe the mechanisms underlying this activity.

Human frontal cortex was obtained from patients undergoing surgery for intractable epilepsy or tumour removal, and was categorised as 'epileptic' or 'non-epileptic' according the patient's seizure history and to whether the resected region contained the presumed epileptic focus. Informed consent was obtained prior to surgery. Standard *in vitro* techniques were used to record extracellular field potentials from 450µm slices. VFOs were detected and analysed with an automated MATLAB programme.

4/74 'epileptic' slices from 2/9 patients displayed spontaneous interictal-like discharges containing VFOs. VFOs were either superimposed on an accompanying sharp wave (SW) or occurred independently. The mean frequency of SW-associated VFOs was 279.4±162.2Hz (n=788 events from 2 patients), whereas that of independent VFOs was significantly lower (265.1±100.1Hz, n=803 events from 2 patients; $p=0.034$).

11 slices from 5 additional patients displayed similar VFOs in the presence of the kainate receptor agonist kainate (100-400nM). Like spontaneous VFOs, kainate-evoked SW-associated VFOs (n=618 events from 2 patients) were significantly faster than independent VFOs (n=1558 events from 5 patients; $p<0.001$); and both were significantly higher in frequency than their spontaneous counterparts (321.1±172.1Hz and 294.4±129.5Hz respectively; $p<0.0001$).

Rarely (1/52 slices from 12 patients), spontaneous independent VFO was observed in non-epileptic tissue (293.9±107.9Hz, n=226 events). Additionally, kainate induced SW-associated (1 slice, 100nM kainate) and independent (2 slices from 2 patients, 600-700nM kainate) VFOs in a few non-epileptic slices.

Intracellular sharp electrode recording from lamina III of an epileptic slice revealed compound EPSPs in a fast-spiking interneurone occurring synchronously with SW-associated VFOs in the nearby field. High-pass filtering revealed a fast component to the compound EPSPs at the same frequency as the field VFO. This fast component was 180° out-of-phase with the field and the peak of each component lagged the negative-going peak of the field potential by a median of 2.7ms (IQ range=1.8-4.1ms).

In conclusion, VFOs (spontaneous or kainate-induced) are present in a higher proportion of epileptic (7/9) than non-epileptic (4/12) human frontal cortical preparations. SW-associated and independent VFOs had distinct frequencies, suggesting differences in their mechanism of generation. SW-associated VFOs, at least, may be accompanied by phase-locked excitatory inputs to local interneurones, but these inputs do not appear to be a causal factor in VFO generation.