The Single Cell Chemical Characterization of the Cells in the Brain

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In the postgenomic era, one expects the suite of chemical players in a brain region to be known and their functions uncovered. Perhaps surprisingly, many neurochemicals remain poorly characterized and for those that are known, their localization, dynamics and function are oftentimes unknown. Several approaches for assaying the chemical content within targeted brain regions and from individual brain cells are highlighted, including mass spectrometry imaging (MSI) and single cell measurements. Using these approaches, we can measure lipids, fatty acids, neurotransmitters and neuropeptides, among others. For single cell measurements, the cells of interest are scattered across a microscope slide, the exact cell positions determined via optical microscopy, and mass spectra are acquired only at the cell positions. The single cell assays allow differences in the metabolome and peptidome from supposedly homogeneous populations of cells to be explored. By obtaining information from tens of thousands of individual cells, rare cells are found and unusual neurochemicals are discovered. For select cells, follow-up capillary electrophoresis-mass spectrometry and other information rich assays can be performed. Several applications of single cell mass spectrometry are highlighted from the discovery of unusual metabolites to characterizing the both known and previously unknown neuropeptides and hormones in single cells. Our overarching goal is to uncover the complex chemical mosaic of the brain and pinpoint key cellular players involved in a range of physiological and pathological processes.

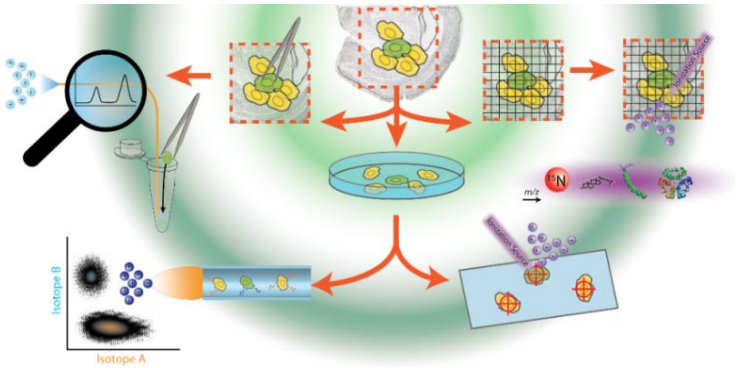

Fig 1. A variety of sampling approaches enable the mass spectrometry (MS) characterization of cells, including capillary electrophoresis MS, mass cytometry, MS imaging, and microMS.