What is the chemical nature of thought? What is memory? Why, over 2,000 years since Aristotle first asked such questions, are we still searching for answers? Animal nervous systems range from the simple nerve nets found in jellies to the complexity of the human brain. While the spatial architecture of the human brain is unmatched, perhaps surprisingly, many of the important neurotransmitters and other brain chemicals are conserved across the animal kingdom. The similarities and differences in chemicals used in the nervous systems of a range of animals are highlighted. While we tend to think of serotonin as related to depression and dopamine as related to addiction, these neurotransmitters are used by almost every animal studied and impact a wide range of behaviors. Because of the conserved nature of neurochemistry, studying learning and memory in a sea snail has let to insights into human memory formation. A range of measurements are described to characterize brain chemistry, and a number of expected and unusual molecules have been discovered in a wide variety of animals.
New Tools for Single Cell Chemical Characterization of the Brain

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Abstract

In the postgenomic era, one expects the suite of chemical players in a brain region to be known and their functions uncovered. However, many cell-to-cell signaling molecules remain poorly characterized and for those that are known, their localization and dynamics are oftentimes unknown. A suite of small-scale measurement approaches are described that allow the investigation of individual neurons and small brain regions; these approaches include capillary scale separations, direct mass spectrometric-based profiling and mass spectrometry imaging. Several applications of single cell microanalysis are highlighted including the discovery of unusual metabolites to characterizing the neuropeptides in single cells. Single cell assays allow differences in the metabolome and peptidome from supposedly homogeneous populations of cells to be explored. As a further example, a unique matrix assisted laser desorption / ionization time of flight mass spectrometry approach is described that probes thousands of endocrine cells for their peptide content. Current technology efforts involve extending the depth of metabolome coverage and adapting our approaches to high throughput single cell assays. By obtaining information from tens of thousands of individual cells, rare cells are found and subtle differences in cell populations are measured. Imaging mass spectrometry and dynamic sampling of the extracellular environment also provide a functional context for the discovery of novel cell to cell signaling molecules. Our overarching goal is to uncover the complex chemical mosaic of the brain and pinpoint key cellular players in physiological and pathological processes.
Three references:

