

What hundreds of biomolecules tell us about our nerve cells

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Researchers at the Luxembourg Centre for Systems Biomedicine (LCSB), of the University of Luxembourg, have, under Dr. Manuel Buttini, successfully measured metabolic profiles, or the metabolomes, of different brain regions, and their findings could help better understand neurodegenerative diseases. The metabolome represents all or at least a large part of the metabolites in a given tissue, and thus, it gives a snapshot of its physiology.

"Our results, obtained in the mouse, are promising," says Manuel Buttini: "They open up new opportunities to better understand [neurodegenerative diseases](#), such as Parkinson's, and could offer new ways to intervene therapeutically. In addition, with the help of metabolic profiles, such as those we have measured, the efficacy of novel therapeutic interventions could be tested more efficiently than with more common approaches." The researchers have just published their results in the *American Journal of Pathology* .

Neurodegenerative processes, such as those occurring in Parkinson's disease, are characterized by pathological alterations of the [brain](#) cells: these cells lose their structure and function, a process that is accompanied by changes in their metabolism. Until now, most scientists have always focused on just one or a few aspects of the disease to better describe and understand the underlying mechanisms. By analysing the whole metabolome however, LCSB researchers have realized a more global approach: they now can analyse hundreds of biomolecules, produced by [nerve cells](#) in upper, middle, and lower [brain regions](#) of the

mouse. In the process, they not only look at healthy brains, but also at brains in which neurodegeneration occurs.

"To study the metabolite signatures of the brain, we used gas-chromatography coupled to mass spectrometry. This approach is particularly suitable for the analysis of samples from complex tissues," explains Dr. Christian Jäger, one of the three main authors of the study. With metabolic studies, an area in which the LCSB is one of the worldwide leading institutions, one can assess known and still unknown biomolecules in tissue samples. After the measurements, LCSB-researchers have used a bioinformatical approach known as Machine Learning to specifically derive the metabolic profile of each brain region.

These efforts were spearheaded by Dr. Enrico Glaab, the second main author of the study. "We found that a multitude of different molecules together reflect a specific functional state of nerve cells in each brain region." By comparing their observations with microscopic analysis of pathologic processes in nerve cells, the LCSB researchers could show which particular [metabolic profile](#) is associated with the degeneration of these cells.

"It was clearly the joined efforts of experts from quite different fields, an interdisciplinary approach that is encouraged at LCSB, that made this study possible. In this case, experts in Neurobiology, Biochemistry, Molecular Biology, and Bioinformatics came together to enable the successful completion of the study," says Dr. Alessandro Michelucci, the third main author of the study.

"Our observations are important, on the one hand, for paving the way for the discovery of novel therapeutic opportunities to combat neurodegeneration," says Dr. Manuel Buttini, "and, on the other hand, for the development of new drugs to fight diseases such as Parkinson's

or Alzheimer's. Indeed, by analysing metabolite profiles rather than just microscopic cellular changes or individual biomolecules, a better understanding of the effect of novel therapeutics for brain diseases should be feasible."

More information: "The Mouse Brain Metabolome : Region-Specific Signatures and Response to Excitotoxic Neuronal Injury." *American Journal of Pathology*, Am J Pathol 2015, 185: 1-14;
[dx.doi.org/10.1016/j.ajpath.2015.02.016](https://doi.org/10.1016/j.ajpath.2015.02.016)

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