Upregulation of a protein in the brains of patients with neurodegenerative diseases due to its altered membrane binding

The proteins of the Neuronal Calcium Sensor (NCS) family act as calcium dependent molecular switches in order to maintain the communication between the brain cells. Most of NCS proteins are involved in neurodegenerative diseases resulting from calcium deregulation. Neuronal Calcium Sensor-1 (NCS1) is a protein which belongs to this family and is upregulated in the prefrontal cortex of patients with schizophrenia, bipolar disorders, Parkinson's and Alzheimer's diseases.

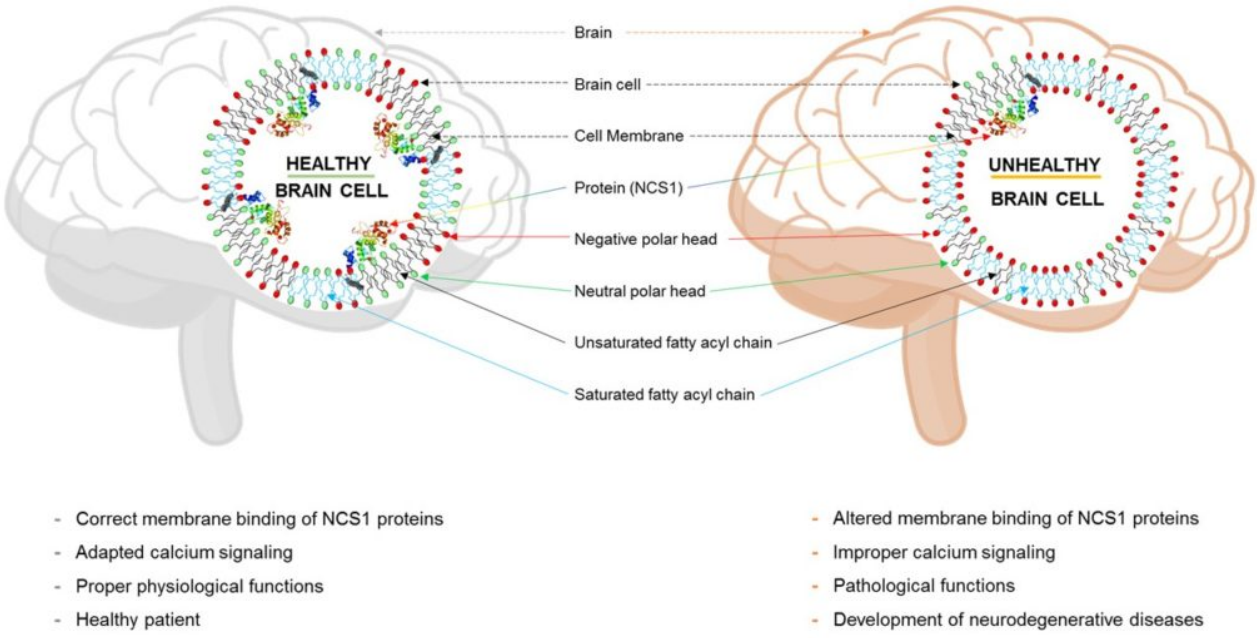

Fig. 1.

NCS1 interacts with different substrates to ensure its multiple cell functions. NCS1 also interacts with cell membranes in a dynamic way, according to the calcium concentration. Cell membranes are mainly made of phospholipids which are composed of a polar head and two fatty acyl chains. The polar head either has a negative *(red circle in the figure)* or a neutral charge *(green circle in the figure)*. The length and the unsaturation of the fatty acyl chains may also differ. The unsaturation of the fatty acyl chains is due to the presence of a double bond between two adjacent carbon atoms *(unsaturated and saturated fatty acyl chains are respectively in black and blue in the figure)*. All these differences in the phospholipid composition influence the membrane binding of

proteins. The Langmuir monolayer model is a biophysical method allowing to mimic a cell membrane and to determine the synergy between proteins and the different phospholipids composing the membranes. According to our results, NCS1 preferentially interacts with phospholipids composed of a neutral polar head and unsaturated fatty acyl chains *(green circle with black fatty acyl chains in the figure)*. On the figure, this interaction is illustrated by the NCS1 protein *(multicolored structure)* binding specific domains of the membrane that are mostly composed of those phospholipids.

However, the cell membrane composition in the brain of patients with schizophrenia, Parkinson's and Alzheimer's diseases drastically changes. Indeed, a decrease of unsaturated fatty acyl chains concentration is observed in the cell membranes of their brains *(less black fatty acyl chains on the right part of the figure)*. Moreover, the number of neutral polar heads decreases to the benefit of the negative ones *(less green circles on the right part of the figure)*. These changes have a huge impact on the membrane binding and the functions of NCS1. In point of fact, fewer specific domains composed by phospholipids with neutral polar head and unsaturated fatty acyl chains are available, fewer NCS1 proteins properly bind the membranes and ensure their functions. Hence, the upregulation of NCS1 observed in the brain of patients affected by neurodegenerative diseases could be induced in order to balance the deficiency of membrane-bound NCS1.

Samuel Lemire *and* ***Élodie Boisselier***
CUO-Recherche, Hôpital du Saint-Sacrement,
Centre de recherche du CHU de Québec and Département d'ophtalmologie,
Faculté de médecine, Université Laval, Québec, Québec, Canada

Publication

Membrane binding of Neuronal Calcium Sensor-1 (NCS1).
Lemire S, Jeromin A, Boisselier É.
Colloids Surf B Biointerfaces. 2016 Mar 1