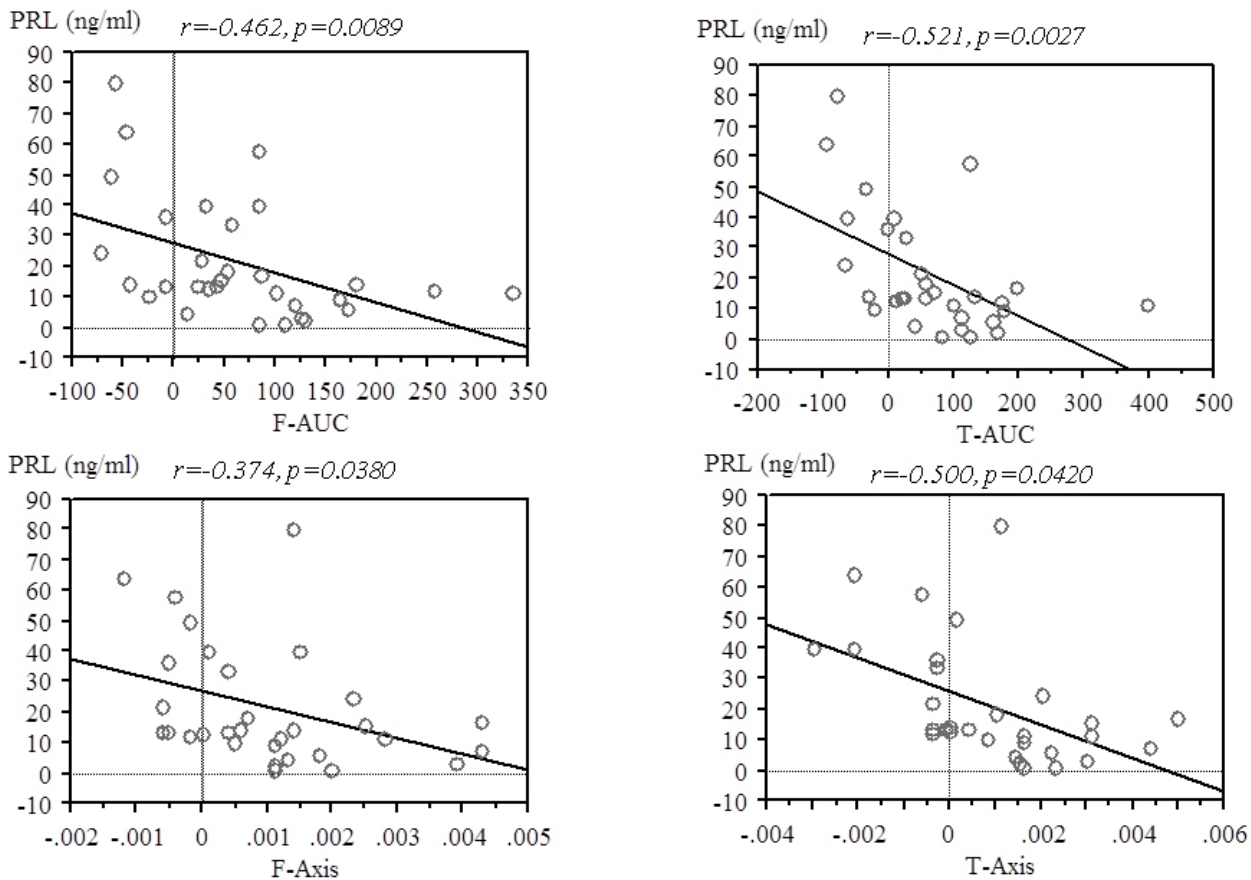


Prolactin regulates neurovascular coupling in male psychotic patients

Recent studies indicated that increased prolactin levels have negative effects on cognitive function in non-psychiatric populations and impair processing speed in patients with psychosis. According to the basic research, prolactin induces regional vasoconstriction via the inhibition of a vasodilatory beta-2-adrenergic receptor-mediated effect related to the nitrous oxide intracellular pathway. Thus, increased prolactin levels may have a risk of decreased regional cerebral blood flow against neuronal activities.



Abbreviations: PRL=prolactin, F=frontal, T=temporal, AUC=integral value, Axis=initial value

Fig. 1. Correlations between prolactin levels and NIRS integral values or initial values at frontal and temporal region of cerebral cortex in male subjects.

To investigate the relationship between prolactin levels and prefrontal hemodynamic responses, we

performed near-infrared spectroscopy (NIRS) by 22-channel topography system for 86 psychiatric patients treated with or without antipsychotics that cause prolactin elevation by its dopamine D2 receptor blockade effect. And we measured serum prolactin levels within a week from NIRS examination. Changes of the concentration of oxygenated hemoglobin in prefrontal cortices were evaluated during a verbal fluency test, and three NIRS indices (integral value: size of area during the activation, centroid value: centroid time of area throughout, and initial value: axis assessed by an initial change) were analyzed against prolactin levels and antipsychotic chlorpromazine equivalent doses by gender and by cortex region. Interestingly, serum prolactin levels were significantly negatively correlated with integral values and initial values in male subjects (Fig. 1), whereas no such correlations were found in female subjects and between the chlorpromazine equivalent doses and NIRS indices. These results indicated that a higher level in prolactin caused a decline in prefrontal hemodynamic responses in male subjects, independent of the dopamine D2 blockade.

The brain consumes high energy and requires adequate blood flow. The magnitude and spatial location of blood flow changes are tightly linked to changes in neuronal activity through a complex sequence of coordinated events involving neurons, astrocytes, and vascular cells, which is called neurovascular unit (NVU). The NVU is a physiological unit with specific structural and functional components. The recent concept of NVU consists of neurons, capillary endothelial cells, vascular tree with arterial smooth muscle cells, perivascular nerves from larger vessels, and astrocytes. Neuronal activity and blood flow are closely coupled by numerous mediators such as nitric oxide, ion channels, and astrocyte signalings. The mechanism how astrocytes regulate vascular smooth muscle contractility remains unclear, although they play a pivotal role on the formation, function, and elimination of synapses. In response to enhanced neuronal activity, astrocytes may signal to blood vessels directly through gap junctions or indirectly releasing soluble factors, resulting in enhanced delivery of oxygen and glucose to the active brain region. According to our study, hyperprolactinemia decreased NIRS integral values and initial values during tasks in male subjects, which indicated prolactin reduces regional blood flow in men. Prolactin receptors are expressed on astrocytes, which controls various clinically-relevant functions. Signaling to vascular smooth muscle via prolactin receptors on astrocytes influences the vascular tonus. Prolactin may be involved in glial responses and modulate frontotemporal blood flow during tasks because activation of prolactin receptor initiates multiple second-messenger cascades, which influence vascular tonus (Fig. 2).

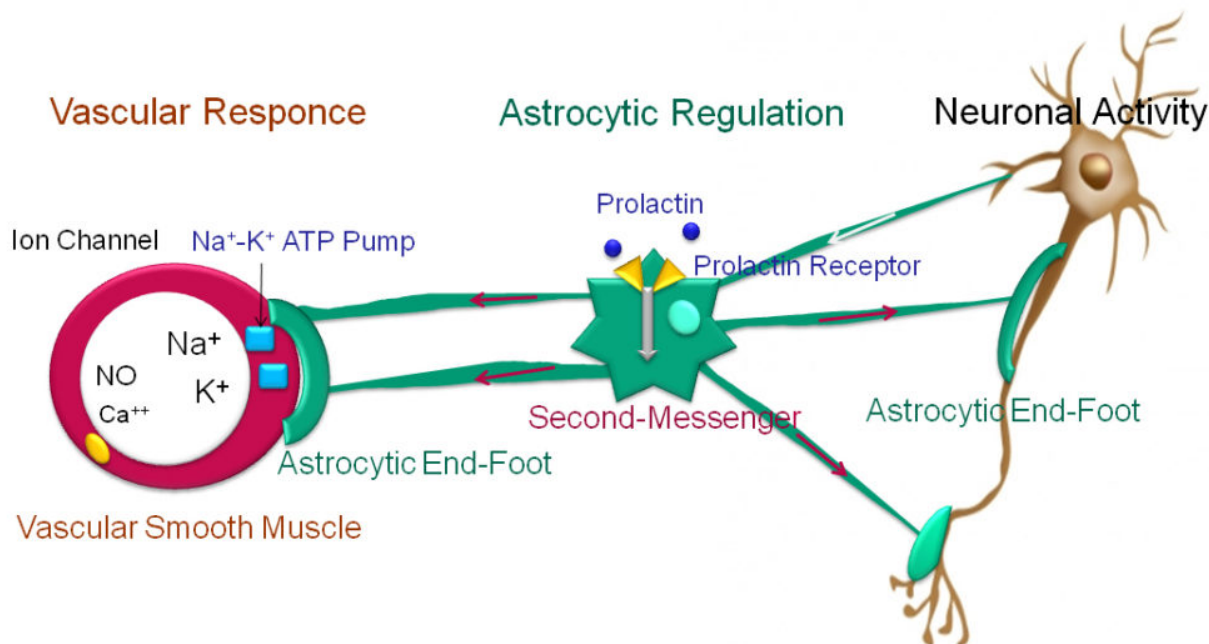


Fig. 2. The effect of prolactin on vascular response in neurovascular coupling.

Neurovascular coupling is orchestrated by astrocytes. In our study, sex differences seemed to exist in blood flow regulation by prolactin, which corresponds to the recent clinical report that the association between high prolactin levels and impaired cognitive processes in psychosis is restricted to men. Prolactin controls a vast number of physiological functions in the nervous system, and its hemodynamic effects may influence neurovascular coupling. Further studies are needed to elucidate the effect of prolactin on neurovascular coupling and the mechanism of sex differences in prolactin signaling to vascular smooth muscle.

Takahiko Nagamine¹, Masaru Nakamura²

¹Sunlight Brain Research Center, Yamaguchi, Japan

²Kosekai-Kusatsu Hospital, Hiroshima, Japan

Publication

[Serum prolactin levels are associated with prefrontal hemodynamic responses using near-infrared spectroscopy in male psychotic patients treated with antipsychotics.](#)

Nakamura M, Nagamine T

Psychiatry Clin Neurosci. 2018 Feb 6