Botulinum protease-cleaved SNARE fragments induce cytotoxicity in neuroblastoma cells

Ternary complex formation by synaptobrevin (green) and syntaxin/synaptosomal-associated protein of 25kDa (red) is necessary for vesicle fusion, membrane trafficking, and cell homeostasis. Botulinum proteases cleave the three SNAREs proteins as indicated, resulting in a loss of cell viability. Lipofection reagents were used to deliver botulinum proteases or short SNARE peptides into neuroblastoma cells, revealing cytotoxic effects of SNARE fragments.

Read the Editorial Highlight for this article on page 753 and the full article on page 781.

Insights into the physiological function of the β-amyloid precursor protein: beyond Alzheimer’s disease

This article reviews studies on the structure, expression and post-translational processing of β-amyloid precursor protein (APP), as well as studies on the effects of APP in vitro and in vivo. We conclude that the published data provide strong evidence that APP has a trophic function. APP is likely to be involved in neural stem cell development, neuronal survival, neurite outgrowth and neurorepair. However, the mechanisms by which APP exerts its actions remain to be elucidated. The available evidence suggests that APP interacts both intracellularly and extracellularly to regulate various signal transduction mechanisms.

Read the full article on page 756.
Impaired one carbon metabolism and DNA methylation in alcohol toxicity

In this review, we summarize the role of one-carbon metabolism (OCM) aberrations in chronic alcohol-induced toxicity. OCM is a major donor of methyl groups for methylation reactions, particularly DNA methylation critical for epigenetic regulation of gene expression. Alcohol interference with OCM and consequent reduced availability of methyl groups, improper DNA methylation, and aberrant gene expression can play a causative role in alcohol toxicity.

Choline-mediated modulation of hippocampal sharp wave–ripple complexes in vitro

In this study we asked whether choline, the precursor and degradation product of acetylcholine, directly affects hippocampal network activity. Using mouse hippocampal slices we found that choline efficiently suppresses spontaneously occurring sharp wave–ripple complexes (SPW–R). In addition, choline reduces synaptic transmission between hippocampal subfields. These effects are mediated by direct activation of muscarinic as well as nicotinic cholinergic pathways. Together, choline turns out to be a potent regulator of patterned activity within hippocampal networks.
**In vivo** brain macromolecule signals in healthy and glioblastoma mouse models: $^1$H magnetic resonance spectroscopy, post-processing and metabolite quantification at 14.1 T

In $^1$H magnetic resonance spectroscopy, the precise knowledge of the macromolecule signals is essential. After introducing a novel method for a flexible and robust post-processing of measured macromolecule signals, the absence of significant differences in metabolite quantification as a result of regional macromolecule variability was demonstrated in the mouse brain while several alterations of the macromolecule spectrum were observed in a mouse model of human glioma.

![Macromolecule Spectrum](image)

Read the full article on page 806.

**Inhibition of Rho-kinase protects cerebral barrier from ischaemia-evoked injury through modulations of endothelial cell oxidative stress and tight junctions**

Inhibition of Rho-kinase (ROCK) activity in a mouse model of human ischaemic stroke significantly improved functional outcome while reducing cerebral lesion and oedema volumes compared to vehicle-treated counterparts. Studies conducted with brain microvascular endothelial cells exposed to OGD ± R in the presence of Y-27632 revealed restoration of intercellular junctions and suppression of prooxidant NADPH oxidase activity as important factors in ROCK inhibition-mediated BBB protection.

![Schematic Diagram](image)

Read the full article on page 816.
Hydrogen sulfide protects blood–brain barrier integrity following cerebral ischemia

To determine H₂S effects on blood–brain barrier (BBB) disruption following stroke, we used two structurally unrelated H₂S donors ADT and NaHS. Both ADT and NaHS remarkably protected BBB integrity following experimental stroke. The slow-releasing donor ADT also reduced post-ischemic inflammation–induced expression and activity of MMP9 and NOX4 in the ischemic brain possibly by inhibiting NF-κB activation.

2,3,7,8-Tetrachlorodibenzo-p-dioxin promotes astrocyte activation and the secretion of tumor necrosis factor–α via PKC/SSeCKS–dependent mechanisms

2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) elicits neurotoxic effects. Here, we show TCDD induces pro-inflammatory responses in astrocytes. TCDD initiates an increase of [Ca²⁺], followed by the activation of PKC, which then induces the activation of Src-suppressed C-kinase substrate (SSeCKS). SSeCKS promotes NF-κB activation and the secretion of TNF-α and nitric oxide in astrocytes.
Targeted gene mutation of E2F1 evokes age-dependent synaptic disruption and behavioral deficits

E2F1 is a transcription factor regulating cell cycle progression and apoptosis. Although E2F1 dysregulation under toxic conditions can lead to neuronal death, little is known about its physiologic activity in the healthy brain. Here, we report significant age-dependent olfactory and memory deficits in mice with dysfunctional E2F1. Coincident with these behavioral changes, we also found age-matched synaptic disruption and persisting reduction in adult neurogenesis. Our study demonstrates that E2F1 contributes to physiologic brain structure and function.

A new semisynthetic derivative of sauroine induces LTP in hippocampal slices and improves learning performance in the Morris Water Maze

A semisynthetic derivative of sauroine, diacetyl sauroine (DAS), induces chemical long-term potentiation in rat hippocampal slices increasing the NMDA receptor-dependent current. 2 mg/kg prior to each session in a Morris Water Maze (MWM) improves behavior performance. In slices prepared from the tested rats the electrical stimulation-dependent long-term potentiation (LTP) was greatly enhanced. Therefore, DAS may have potency as a nootropic drug against the memory decline.
Serum miR-206 and other muscle-specific microRNAs as non-invasive biomarkers for Duchenne muscular dystrophy

There has been a long-standing need for reliable, non-invasive biomarkers for Duchenne muscular dystrophy (DMD). We found that the levels of muscle-specific microRNAs, especially miR-206, in the serum of DMD were 2- to 4-fold higher than in the controls. High levels corresponded to low muscle strength, muscle function, and quality of life (QoL). These miRNAs were able to discriminate DMD from controls by receiver operating characteristic (ROC) curves analyses. Thus, miR-206 and other muscle-specific miRNAs are useful as non-invasive biomarkers for DMD.

Inhibition of glucosylceramide synthase stimulates autophagy flux in neurons

Inhibition of GlcCer synthase enhances autophagy by inhibiting AKT-mTOR signaling, and increases the number and size of lysosomal/late endosomal structures. Furthermore, inhibition of GlcCer synthase decreased levels of mutant α-synuclein in neurons, which may represent a potential therapeutic target for Parkinson’s disease.