Development of neuronal network

Activity-driven mechanisms

Gene expression

Signaling molecules

Activity-driven mechanisms
Central question

- How is synaptic activity translated into structural and functional changes?
Neurotrophins (peptides and receptors)

- Neuronal survival
- Growth and differentiation
- Synaptogenesis
- Synaptic plasticity

(Chao, Nat Rev Neurosci 2003)
BDNF-GFP: synthesis and storage
BDNF-GFP is targeted to dendritic secretory granules
BDNF-GFP: release

anti-GFP

TrkB receptor

BDNF-GFP

GABA

Cl⁻

[Ca²⁺]

Na⁺

Pyramidal Cell

Surface staining

Surface staining
BDNF production and processing
Physiological/pathological effects of released proBDNF vs BDNF

- proBDNF
- Plasmin
- p75NTR
- TrkB
- Cell survival
- Neuritic outgrowth
- Glutamatergic plasticity
+
Mechanism of tPA-modulated induction of LTP
The target-derived factor model
The target-derived factor model

BDNF

TrkB
Dendritic backpropagation of APs in cultured neurons
Pre- and post-synaptic action of BDNF at glutamatergic synapses

1. Reduced fatigue
2. Increased mepsc frequency
3. New boutons
4. NMDA enhanced function
5. Ca++ elevation
6. AMPA receptor insertion
7. Spine growth
8. Increased epsc amplitude
9. Glutamate release
Pre- and post-synaptic action of BDNF at GABAergic synapses
+ de chlore et des effets excitateurs du GABA

Extracellulaire milieu

Intracellulaire milieu

Développement
NKCC1 accumule le Cl⁻ dans les neurones
Une séquence maturative

Jeune

Cl⁻ → NKCC1 → Cl⁻

GABA_A R → KCC2

Adulte

Cl⁻ → NKCC1 → Cl⁻

GABA_A R → KCC2
Activity-dependent regulation of KCC2 determines the nature and efficacy of GABAergic neurotransmission
Direct gating of Na\(^+\) channels by TrkB

- **a** Patch-clamped hippocampal neuron
- **b** Current clamp
- **c** Voltage clamp
- **d** Graph showing calculated $E_{Na^+}$: $+58$ mV
Role of BDNF-mediated fast excitation in synaptic plasticity