Neuroscience Letters 449 (2009) 220–223

Contents lists available at ScienceDirect

Neuroscience Letters

journal homepage: www.elsevier.com/locate/neulet

Muscarinic acetylcholine receptors and voltage-gated calcium channels contribute to bidirectional synaptic plasticity at CA1-subiculum synapses

Oded Lipa Shor[a,b], Pawel Fidzinski[a,b,*,1], Joachim Behr[a,b,1]

[a] Department of Psychiatry and Psychotherapy, Charité Universitätsmedizin Berlin, Chariteplatz 1, 10117 Berlin, Germany
[b] Johannes Mueller Institute of Physiology, Charité Universitätsmedizin Berlin, Tucholskystr. 2, 10117 Berlin, Germany

ARTICLE INFO

Article history:
Received 20 August 2008
Received in revised form 5 November 2008
Accepted 6 November 2008

Keywords:
Hippocampus
Neuromodulation
Long-term potentiation
Long-term depression
Learning and memory

ABSTRACT

Hippocampal output is mediated via the subiculum, which is the principal target of CA1 pyramidal cells, and which sends projections to a variety of cortical and subcortical regions. Pyramidal cells in the subiculum display two different firing modes and are classified as being burst-spiking or regular-spiking. In a previous study, we found that low-frequency stimulation induces an NMDA receptor-dependent long-term depression (LTD) in burst-spiking cells and a metabotropic glutamate receptor-dependent long-term potentiation (LTP) in regular-spiking cells [P. Fidzinski, O. Shor, J. Behr, Target-cell-specific bidirectional synaptic plasticity at hippocampal output synapses, Eur. J. Neurosci., 27 (2008) 1111–1118]. Here, we present evidence that this bidirectional plasticity relies upon the co-activation of muscarinic acetylcholine receptors, as scopolamine blocks synaptic plasticity in both cell types. In addition, we demonstrate that the L-type calcium channel inhibitor nifedipine converts LTD to LTP in burst-spiking cells and LTP to LTD in regular-spiking cells, indicating that the polarity of synaptic plasticity is modulated by voltage-gated calcium channels. Bidirectional synaptic plasticity in subicular cells therefore appears to be governed by a complex signaling system, involving cell-specific recruitment of ligand and voltage-gated ion channels as well as metabotropic receptors. This complex regulation might be necessary for fine-tuning of synaptic efficacy at hippocampal output synapses.

Hippocampal output is mediated via the subiculum, which is the principal target of CA1 pyramidal cells [1], and which sends projections to a variety of cortical and subcortical regions [38]. The critical role of the subiculum in the encoding and retrieval of memory traces has been demonstrated in both rats [11] and humans [13]. These findings, coupled with the anatomical connections, support the view that the subiculum is a prominent player in hippocampal–cortical information processing.

The ability of synapses to undergo activity-dependent changes is regarded as crucial for memory formation [28]. Long-term potentiation (LTP) and long-term depression (LTD) of synaptic efficacy have been the subject of investigation in various brain structures [27], including the subiculum [10,24,19,25]. In response to afferent stimulation or depolarizing current injections, pyramidal cells in the subiculum and the CA1 display two different firing modes. These modes are classified as burst-spiking (BS) and regular-spiking (RS), respectively [22,29,40–42,14]. In CA1, the majority of pyramidal cells displays RS behaviour, whereas in the subiculum both firing modes are found, with an increasing percentage of BS cells towards the distal subiculum [40,20]. We found that low-frequency stimulation (LFS) induces an NMDA receptor (NMDAR)-dependent LTD in subicular BS cells and a metabotropic glutamate receptor (mGluR)-dependent late-onset LTP in subicular RS cells [12]. Both forms of synaptic plasticity require postsynaptic calcium signaling. In the present study, we present evidence that this bidirectional plasticity relies upon the co-activation of muscarinic acetylcholine receptors (mAChR), as scopolamine blocks synaptic plasticity in both cell types. Moreover, nifedipine modulates the direction of synaptic plasticity in each cell type, indicating the involvement of voltage-gated calcium channels (VGCC) in the induction process.

Wistar rats (4–6 weeks) of both sexes were decapitated under deep ether anaesthesia and the brains were quickly removed. 400 μm thick horizontal slices from the ventral-to-middle part containing the hippocampus and the entorhinal cortex were prepared using a vibratome (Campden Instruments, Loughborough, UK). The preparation was performed in ice-cold, saccharose-based artificial cerebrospinal fluid (ACSF) (in mM): NaCl 87, Na_2PO_4 1.25, $NaHCO_3$ 26, KCl 2.5, $CaCl_2$ 0.5, $MgCl_2$ 7, saccharose 75, and glucose 25 at a pH of 7.4. After preparation, slices were kept under submerged condi-

* Corresponding author at: Max-Delbrück-Centrum/Leibniz Institut für molekulare Pharmakologie, Robert-Rössle-Str. 10, 13215 Berlin, Germany.
Tel.: +49 30 9406 2966; fax: +49 30 9406 2960.
E-mail address: pawel.fidzinski@mdc-berlin.de (P. Fidzinski).
[1] These authors contributed equally to this work.

0304-3940/$ – see front matter © 2008 Elsevier Ireland Ltd. All rights reserved.
doi:10.1016/j.neulet.2008.11.012

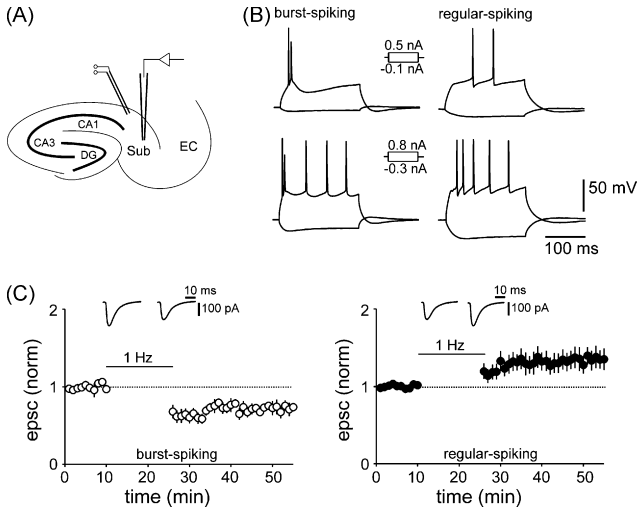

Fig. 1. (A) Schematic illustration of the stimulation and recording sites in a horizontal hippocampal brain slice. Hippocampal areas: CA3, CA1; Sub: subiculum; EC: entorhinal cortex; DG: dentate gyrus. (B) Voltage responses of subicular BS and RS neurons to depolarizing and hyperpolarizing current pulses. BS cell display single burst discharges whereas RS cells discharge with single spikes. Upon stronger depolarization, BS cells display burst discharges followed by single spikes. (C) LFS at 1 Hz induces LTD in BS cells but LTP in RS cells. Averaged time courses of evoked EPSC amplitudes before and after induction with LFS are shown. Superimposed traces are averages from 10 single responses each and were recorded during baseline (left) and 25 min after induction (right).

tions at 35 °C for ~30 min and then transferred to a physiological ACSF solution at room temperature for further storage. The composition of physiological ACSF was as follows (in mM): NaCl 129, Na_2PO_4 1.25, $NaHCO_3$ 26, KCl 3, $CaCl_2$ 1.6, $MgSO_4$ 1.8, and glucose 10 at a pH of 7.4.

Whole-cell recordings in the pyramidal cell layer of the subiculum were performed in voltage-clamp mode at a holding potential of −70 mV (unless otherwise stated) at near physiological temperatures (32–34 °C). Patch-clamp electrodes (4–6 MΩ) were filled with (in mM): K-gluconate 135, KCl 20, HEPES 10, phosphocreatine 7, Mg-ATP 2, Na-GTP 0.3 EGTA 0.2 and adjusted with KOH to a pH of 7.2. All experiments were performed in the presence of bicuculline or SR-95531 (gabazine) to block $GABA_A$ receptor-mediated responses. Previous studies demonstrated the existence of recurrent connections within the subicular network [16,23] that frequently cause polysynaptic responses upon repetitive stimulation. Therefore, the concentrations of $MgSO_4$ and $CaCl_2$ were elevated to 4 mM each to reduce the probability of polysynaptic responses [31,36,6].

For characterization of intrinsic discharge and membrane properties, hyper- and depolarizing-steps were applied in current-clamp mode (200 ms, 0.1 nA). Excitatory postsynaptic currents (EPSCs) were evoked by alvear stimulation (Fig. 1A). The stimulus intensity was set after adjusting the EPSC amplitudes to 40–60% of the maximum response and ranged between 1.5 and 4 V. For induction of synaptic plasticity, paired-pulse low-frequency stimulation at 1 Hz (15 min, 50 ms inter-stimulus interval) was applied in current-clamp mode. Normalized EPSCs were averaged for the last 5 min of baseline recordings. LTP and LTD were calculated as percentage values of the normalized baseline EPSC amplitude between 20 and 25 min after induction. Statistical analysis was performed by applying Student's *t*-test (SPPS, SPSS Inc., USA). Statistical significance was set to $p < 0.05$. Signals were low-pass filtered at 3 kHz, sampled at 10 kHz by an ITC-16 interface (Instrutech Corp., Great Neck, NY, USA) and processed by TIDA software (HEKA GmbH, Lambrecht, Germany). Analysis of the paired-pulse was applied to discriminate between presynaptic and postsynaptic modifications in synaptic transmission [46]. The paired-pulse ratio (PPR) was defined as the response ratio (2nd EPSP amplitude/1st EPSP amplitude) to a pair of stimuli given at an inter-stimulus interval of 50 ms.

The following drugs were used: nifedipine, 20 μM; scopolamine, 30 mM; bicuculline, 5 μM; SR 95531 hydrobromide (gabazine), 1 μM. Drugs were purchased from Sigma–Aldrich, Germany and Tocris, UK. All drugs were applied throughout the entire experiment and for at least 10 min prior to recording of baseline EPSCs.

Upon injection of depolarizing current steps (200 ms, 0.1–0.8 nA) subicular BS cells responded with a burst of two to four spikes at ~170 Hz followed by single spikes without frequency adaptation whereas RS cells displayed trains of single spikes with frequency adaptation (Fig. 1B). Out of 64 investigated cells, 42% were classified as BS and 58% as RS. No significant difference was found between the resting membrane potentials of the BS and RS cells (BS: -58.6 ± 0.8 mV, $n = 27$; RS: -58.4 ± 1.0 mV, $n = 37$, $p = 0.73$), whereas the input resistance was lower in BS cells than in RS cells (BS: 79.6 ± 3.7 MΩ, $n = 27$; RS: 107.6 ± 6.3 MΩ, $n = 37$, $p < 0.01$). Upon synaptic stimulation, BS cells displayed slightly higher paired-pulse facilitation than RS cells (BS: 1.76 ± 0.1, $n = 8$; RS: 1.34 ± 0.6, $n = 14$, $p < 0.01$).

As reported in our recent study [12], LFS induced LTD in BS cells ($72.2 \pm 4.9\%$ of baseline, $n = 8$, $p < 0.01$) but a late-onset LTP in RS cells ($133.3 \pm 12.4\%$ of baseline, $n = 14$, $p < 0.05$; Fig. 1C). As we observed no obvious difference between slices from male and female animals, data were pooled. Li et al. demonstrated that subicular LTD induced by a pairing protocol depends on the activation of mAChR [25]. We therefore tested the effect of the muscarinic receptor antagonist scopolamine on LFS-induced bidirectional synaptic plasticity. Application of scopolamine had no effect upon baseline transmission and did not change the PPR in either cell type (BS: 1.60 ± 0.1, $n = 10$, $p = 0.3$ vs. control; RS: 1.44 ± 0.1, $n = 11$, $p = 0.9$ vs. control, data not shown). Scopolamine blocked LTD in BS cells and LTP in RS cells (BS: $96.9 \pm 4.7\%$ of baseline, $n = 10$, $p = 0.67$; RS: $95.2 \pm 4.0\%$ of baseline, $n = 11$, $p = 0.14$; Fig. 2A) indicating that the co-activation of mAChR is necessary for both forms of synaptic plasticity.

Although glutamate receptors are the predominant source for calcium signals involved in the induction of synaptic plasticity, additional sources such as VGCC may play a modulatory function in this process [7]. In BS cells, application of the L-type calcium channel blocker nifedipine prevented the induction of LTD and unmasked a late-onset LTP ($129.4 \pm 11.3\%$ of baseline, $n = 10$, $p < 0.05$; Fig. 2B). A reverse effect was observed in RS cells, where nifedipine blocked the induction of LTP and unmasked LTD ($86.5 \pm 4.0\%$ of baseline, $n = 9$, $p < 0.05$; Fig. 2B). As with scopolamine, nifedipine had no effect on the paired-pulse ratio (BS: 1.73 ± 0.1, $n = 10$, $p = 0.3$ vs. control; RS: 1.31 ± 0.1, $n = 9$, $p = 0.8$ vs. control, data not shown). These results suggest that VGCC modulate intracellular calcium signals in subicular BS and RS cells, and determine the polarity of synaptic plasticity in a cell-specific manner.

In the present study, we show that LFS-induced LTD in BS cells and LTP in RS cells require the co-activation of mAChR. In addition, we demonstrate that the polarity of synaptic plasticity is modulated by VGCC, as the L-type calcium channel inhibitor nifedipine converts LTD to LTP in BS cells and LTP to LTD in RS cells.

The involvement of muscarinergic neurotransmission in memory consolidation and cognition processes is widely recognized [18]. The hippocampal formation, including the subiculum, receives its major cholinergic projections from the medial septal nucleus and the vertical limb nucleus of the diagonal band, respectively [30,26]. Out of five mAChR subtypes known to date, M_1, M_2 and M_4 are predominant in the central nervous system. The M_1 recep-

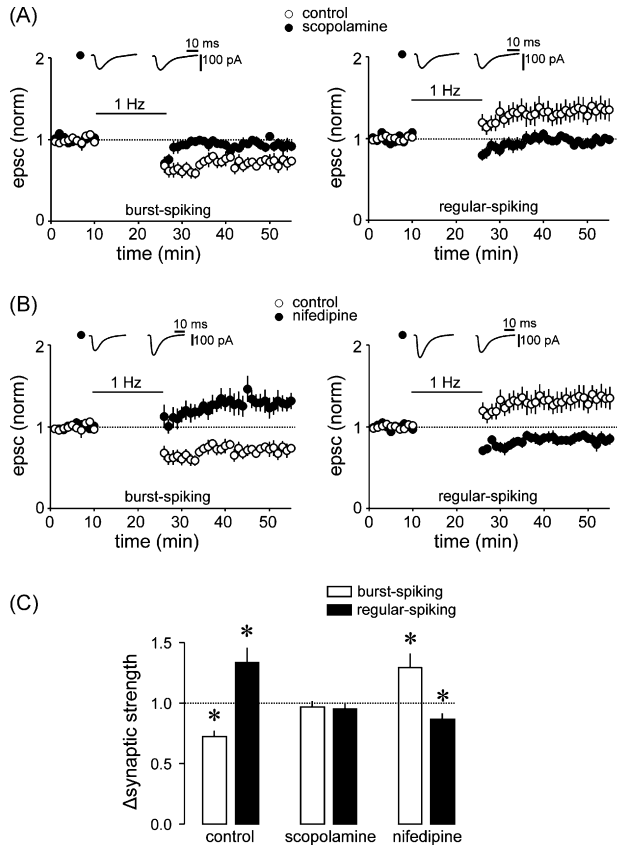

Fig. 2. Involvement of muscarinergic neurotransmission and voltage-gated calcium channels in subicular bidirectional plasticity. (A) Application of scopolamine blocked LTD in BS cells and LTP in RS cells. (B) Application of nifedipine reversed the polarity of synaptic plasticity from LTD to LTP in BS cells and from LTP to LTD in RS cells. Superimposed traces show EPSCs recorded in the presence of the respective drug. (C) Summary of changes in synaptic strength for each cell type.

tor, which is the predominant muscarinic receptor subtype in the hippocampus [44], activates the phospholipase C pathway leading to the production of inositoltrisphosphate and diacylglycerol, whereas M_2 and M_4 receptors are negatively coupled to cyclic adenosine monophopsphate (cAMP) production [8]. Functionally, mAChR exert a diversity of modulatory effects on neuronal cells. Apart from increasing intrinsic neuronal excitability [3], mAChR interact with ionotropic and metabotropic glutamate receptors, modulate cytoplasmic calcium signals by release from intracellular calcium stores, and modulate NMDAR-dependent LTP as well as mGluR-dependent LTD [44,17,5,34,2,15,4]. There is thus a variety of possible pathways by which muscarinic neurotransmission can be involved in cell-specific synaptic plasticity in the subiculum. Our previous study demonstrated that LFS results in NMDAR-dependent LTD in BS cells and mGluR-dependent LTP in RS cells. As both forms of synaptic plasticity rely upon postsynaptic calcium, it is feasible that muscarinic activation modulates postsynaptic calcium signals either by direct interaction with mGluR/NMDAR, or by affecting calcium release from intracellular stores. Cholinergic co-activation might be necessary for shaping the spatial and temporal pattern of calcium signals required for synaptic plasticity at CA1-subiculum synapses.

The involvement of VGCC in synaptic plasticity and spatial memory has been demonstrated by several groups [32,33,21,7]. However, depending on the investigated structure and the pattern of activation, VGCC have been shown to produce contrasting effects on synaptic plasticity. Some groups reported that co-activation of VGCC and the resulting increase in calcium transients was necessary for the induction of NMDAR-dependent LTD in the CA1 and the entorhinal cortex [45,9]. Others showed that spatial segregation of calcium signals by inhibition of VGCC enhanced LFS-induced LTD and blocked LTP in the CA1 [39,43]. Here, NMDAR-dependent LTD in BS cells and mGluR-dependent LTP in RS require co-activation of VGCC. This observation suggests that, in the subiculum, VGCC contribute to distinct, cell-specific forms of synaptic plasticity by interaction with NMDAR in BS cells and with mGluR in RS cells.

The present results indicate that LFS-induced LTD in BS cells and LTP in RS cells are governed by a complex signaling system, involving the recruitment of ligand and voltage-gated ion channels as well as metabotropic receptors. Given that the amplitude of calcium transients depends on the sequential activation of several ligand- and voltage-gated ion channels [7], and that the temporal sequence of calcium source activation predicts the polarity of synaptic plasticity [37,35], such a complex system might be necessary for the fine-tuning of synaptic efficacy at hippocampal output synapses.

Acknowledgements

This work was supported by the German Research foundation (DFG) Grants to J. Behr (SFB-TR3-TP B4, GRK 1123). We thank Kate Gilling for proof reading and O. Maassen for excellent technical assistance.

References

[1] D.G. Amaral, M.P. Witter, The hippocampal formation, in: G. Paxinos (Ed.), The Rat Nervous System, Academic Press, New York, 1995, pp. 443–494.
[2] Z.I. Bashir, On long-term depression induced by activation of G-protein coupled receptors, Neurosci. Res. 45 (2003) 363–367.
[3] L.S. Benardo, D.A. Prince, Ionic mechanisms of cholinergic excitation in mammalian hippocampal pyramidal cells, Brain Res. 249 (1982) 333–344.
[4] J.L. Berkeley, J. Gomeza, J. Wess, S.E. Hamilton, N.M. Nathanson, A.I. Levey, M1 muscarinic acetylcholine receptors activate extracellular signal-regulated kinase in CA1 pyramidal neurons in mouse hippocampal slices, Mol. Cell. Neurosci. 18 (2001) 512–524.
[5] M.J. Berridge, Neuronal calcium signaling, Neuron 21 (1998) 13–26.
[6] M.S. Berry, V.W. Pentreath, Criteria for distinguishing between monosynaptic and polysynaptic transmission, Brain Res. 105 (1976) 1–20.
[7] B.L. Bloodgood, B.L. Sabatini, Regulation of synaptic signalling by postsynaptic, non-glutamate receptor ion channels, J. Physiol. 586 (2008) 1475–1480.
[8] M.P. Caulfield, Muscarinic receptors—characterization, coupling and function, Pharmacol. Ther. 58 (1993) 319–379.
[9] B.R. Christie, L.K. Schexnayder, D. Johnston, Contribution of voltage-gated Ca^{2+} channels to homosynaptic long-term depression in the CA1 region in vitro, J. Neurophysiol. 77 (1997) 1651–1655.
[10] S. Commins, J. Gigg, M. Anderson, S.M. O'Mara, The projection from hippocampal area CA1 to the subiculum sustains long-term potentiation, Neuroreport 9 (1998) 847–850.
[11] S.A. Deadwyler, R.E. Hampson, Differential but complementary mnemonic functions of the hippocampus and subiculum, Neuron 42 (2004) 465–476.
[12] P. Fidzinski, O. Shor, J. Behr, Target-cell-specific bidirectional synaptic plasticity at hippocampal output synapses, Eur. J. Neurosci. 27 (2008) 1111–1118.
[13] J.D. Gabrieli, J.B. Brewer, J.E. Desmond, G.H. Glover, Separate neural bases of two fundamental memory processes in the human medial temporal lobe, Science 276 (1997) 264–266.
[14] J.R. Greene, A.J. Mason, Neuronal diversity in the subiculum: correlations with the effects of somatostatin on intrinsic properties and on GABA-mediated IPSPs in vitro, J. Neurophysiol. 76 (1996) 1657–1666.
[15] A.A. Grishin, P. Benquet, U. Gerber, Muscarinic receptor stimulation reduces NMDA responses in CA3 hippocampal pyramidal cells via Ca2+-dependent activation of tyrosine phosphatase, Neuropharmacology 49 (2005) 328–337.
[16] E. Harris, M. Stewart, Intrinsic connectivity of the rat subiculum. II. Properties of synchronous spontaneous activity and a demonstration of multiple generator regions, J. Comp. Neurol. 435 (2001) 506–518.
[17] M.E. Hasselmo, Neuromodulation: acetylcholine and memory consolidation, Trends Cogn. Sci. 3 (1999) 351–359.
[18] M.E. Hasselmo, The role of acetylcholine in learning and memory, Curr. Opin. Neurobiol. 16 (2006) 710–715.
[19] Y.Y. Huang, E.R. Kandel, Theta frequency stimulation up-regulates the synaptic strength of the pathway from CA1 to subiculum region of hippocampus, Proc. Natl. Acad. Sci. U.S.A. 102 (2005) 232–237.

[20] T. Jarsky, R. Mady, B. Kennedy, N. Spruston, Distribution of bursting neurons in the CA1 region and the subiculum of the rat hippocampus, J. Comp. Neurol. 506 (2008) 535–547.
[21] D. Jeon, I. Song, W. Guido, K. Kim, E. Kim, U. Oh, H.S. Shin, Ablation of Ca2+ channel beta3 subunit leads to enhanced N-methyl-D-aspartate receptor-dependent long term potentiation and improved long term memory, J. Biol. Chem. 283 (2008) 12093–12101.
[22] H.Y. Jung, N.P. Staff, N. Spruston, Action potential bursting in subicular pyramidal neurons is driven by a calcium tail current, J. Neurosci. 21 (2001) 3312–3321.
[23] A. Knopp, A. Kivi, C. Wozny, U. Heinemann, J. Behr, Cellular and network properties of the subiculum in the pilocarpine model of temporal lobe epilepsy, J. Comp. Neurol. 483 (2005) 476–488.
[24] M. Kokaia, Long-term potentiation of single subicular neurons in mice, Hippocampus 10 (2000) 684–692.
[25] H. Li, J. Zhang, W. Xiong, T. Xu, J. Cao, L. Xu, Long-term depression in rat CA1-subicular synapses depends on the G-protein coupled mACh receptors, Neurosci. Res. 52 (2005) 287–294.
[26] F.H. Lopes da Silva, M.P. Witter, P.H. Boeijinga, A.H.M. Lohman, Anatomic organization and physiology of the limbic cortex, Physiol. Rev. 70 (1990) 453–511.
[27] R.C. Malenka, M.F. Bear, LTP and LTD: an embarrassment of riches, Neuron 44 (2004) 5–21.
[28] S.J. Martin, P.D. Grimwood, R.G. Morris, Synaptic plasticity and memory: an evaluation of the hypothesis, Annu. Rev. Neurosci. 23 (2000) 649–711.
[29] d.l.P. Menendez, F. Suarez, M.A. Pozo, Electrophysiological and morphological diversity of neurons from the rat subicular complex in vitro, Hippocampus 13 (2003) 728–744.
[30] M.-M. Mesulam, E.J. Mufson, B.H. Wainer, A.I. Levey, Central cholinergic pathways in the rat: an overview based on an alternative nomenclature (Ch1–Ch6), Neuroscience 10 (1983) 1185–1201.
[31] R. Miles, R.K.S. Wong, Inhibitory control of local excitatory circuits in the guinea-pig hippocampus, J. Physiol. (Lond.) 388 (1987) 611–629.
[32] S. Moosmang, N. Haider, N. Klugbauer, H. Adelsberger, N. Langwieser, J. Muller, M. Stiess, E. Marais, V. Schulla, L. Lacinova, S. Goebbels, K.A. Nave, D.R. Storm, F. Hofmann, T. Kleppisch, Role of hippocampal Cav1.2 Ca2+ channels in NMDA receptor-independent synaptic plasticity and spatial memory, J. Neurosci. 25 (2005) 9883–9892.
[33] S.L. Morgan, T.J. Teyler, VDCCs and NMDARs underlie two forms of LTP in CA1 hippocampus in vivo, J. Neurophysiol. 82 (1999) 736–740.
[34] M.S. Nash, J.M. Willets, B. Billups, R.A. John Challiss, S.R. Nahorski, Synaptic activity augments muscarinic acetylcholine receptor-stimulated inositol 1,4,5-trisphosphate production to facilitate Ca2+ release in hippocampal neurons, J. Biol. Chem. 279 (2004) 49036–49044.
[35] T. Nevian, B. Sakmann, Spine Ca2+ signaling in spike-timing-dependent plasticity, J. Neurosci. 26 (2006) 11001–11013.
[36] J.G. Nicholls, D. Purves, Monosynaptic chemical and electrical connexions between sensory and motor cells in the central nervous system of the leech, J. Physiol. 209 (1970) 647–667.
[37] M. Nishiyama, K. Hong, K. Mikoshiba, M.M. Poo, K. Kato, Calcium stores regulate the polarity and input specificity of synaptic modification, Nature 408 (2000) 584–588.
[38] S.M. O'Mara, S. Commins, M. Anderson, J. Gigg, The subiculum: a review of form, physiology and function, Prog. Neurobiol. 64 (2001) 129–155.
[39] C.R. Raymond, S.J. Redman, Spatial segregation of neuronal calcium signals encodes different forms of LTP in rat hippocampus, J. Physiol. 570 (2006) 97–111.
[40] N.P. Staff, H.Y. Jung, T. Thiagarajan, M. Yao, N. Spruston, Resting and active properties of pyramidal neurons in subiculum and CA1 of rat hippocampus, J. Neurophysiol. 84 (2000) 2398–2408.
[41] M. Stewart, R.K. Wong, Intrinsic properties and evoked responses of guinea pig subicular neurons in vitro, J. Neurophysiol. 70 (1993) 232–245.
[42] J.S. Taube, Electrophysiological properties of neurons in the rat subiculum in vitro, Exp. Brain Res. 96 (1993) 304–318.
[43] R. Udagawa, M. Nakano, N. Kato, Blocking L-type calcium channels enhances long-term depression induced by low-frequency stimulation at hippocampal CA1 synapses, Brain Res. 1124 (2006) 28–36.
[44] L.A. Volpicelli, A.I. Levey, Muscarinic acetylcholine receptor subtypes in cerebral cortex and hippocampus, Prog. Brain Res. 145 (2004) 59–66.
[45] Y.D. Zhou, C.D. Acker, T.I. Netoff, K. Sen, J.A. White, Increasing Ca2+ transients by broadening postsynaptic action potentials enhances timing-dependent synaptic depression, Proc. Natl. Acad. Sci. U.S.A. 102 (2005) 19121–19125.
[46] R.S. Zucker, W.G. Regehr, Short-term synaptic plasticity, Annu. Rev. Physiol. 64 (2002) 355–405.