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Age-dependent, subunit specific action of hydrogen sulfide on GluN1/2A and GluN1/2B NMDA receptors

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Abstract

© 2017 Yakovlev, Kurmasheva, Ishchenko, Giniatullin and Sitdikova. Hydrogen sulfide (H 2 S) is an endogenously produced neuroactive gas implicated in many key processes in the peripheral and central nervous system. Whereas the neuroprotective role of H 2 S has been shown in adult brain, the action of this messenger in newborns remains unclear. One of the known targets of H 2 S in the nervous system is the N-methyl-D-aspartate (NMDA) glutamate receptor which can be composed of different subunits with distinct functional properties. In the present study, using patch clamp technique, we compared the effects of the H 2 S donor sodium hydrosulfide (NaHS, 100 μM) on hippocampal NMDA receptor mediated currents in rats of the first and third postnatal weeks. This was supplemented by testing effects of NaHS on recombinant GluN1/2A and GluN1/2B NMDA receptors expressed in HEK293T cells. The main finding is that NaHS action on NMDA currents is age-dependent. Currents were reduced in newborns but increased in older juvenile rats. Consistent with an age-dependent switch in NMDA receptor composition, in HEK239T cells expressing GluN1/2A receptors, NaHS increased NMDA activated currents associated with acceleration of desensitization and decrease of the deactivation rate. In contrast, in GluN1/2B NMDA receptors, which are prevalent in newborns, NaHS decreased currents and reduced receptor deactivation without effect on the desensitization rate. Adenylate cyclase inhibitor MDL-12330A (10 μM) did not prevent the age-dependent effects of NaHS on NMDA evoked currents in pyramidal neurons of hippocampus. The reducing agent dithiothreitol (DTT, 2 mM) applied on HEK293T cells prevented facilitation induced by NaHS on GluN1/2A NMDA receptors, however in GluN1/2B NMDA receptors the inhibitory effect of NaHS was still observed. Our data indicate age-dependent effect of H 2 S on NMDA receptor mediated currents determined by glutamate receptor subunit composition. While the inhibitory action of H 2 Son GluN1/2B receptors could limit the excessive activation in early age, the enhanced functionality of GluN1/2A receptor in the presence of this gasotransmitter can enlarge synaptic efficacy and promote synaptic plasticity in adults.

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Keywords

Adenylate cyclase, GluN1/2A, GluN1/2B, Hippocampal slices, Hydrogen sulfide, NMDA receptors, Redox modulation

References

[1] Abe K., Kimura H. (1996). The possible role of hydrogen sulfide as an endogenous neuromodulator. J. Neurosci. 16, 1066–1071.

[2] Aizenman E., Lipton S. A., Loring R. H. (1989). Selective modulation of NMDA responses by reduction and oxidation. Neuron 2, 1257–1263. DOI: 10.1016/0896-6273(89)90310-3

[3] Ben Ari Y., Khalilov I., Kahle K. T., Cherubini E. (2012). The GABA excitatory/inhibitory shift in brain maturation and neurological disorders. Neuroscientist18, 467–486. DOI: 10.1177/1073858412438697

[4] Bodhinathan K., Kumar A., Foster T. C. (2010). Intracellular redox state alters NMDA receptor response during aging through Ca/calmodulin-dependent protein kinase II. J. Neurosci. 30, 1914–1924. DOI: 10.1523/JNEUROSCI.5485-09.2010

[5] Bolton A. D., Phillips M. A., Constantine-Paton M. (2013). Homocysteine reduces NMDAR desensitization and differentially modulates peak amplitude of NMDAR currents, depending on GluN2 subunit composition. J. Neurophysiol. 110, 1567–1582. DOI: 10.1152/jn.00809.2012

[6] Borschel W. F., Myers J. M., Kasperek E. M., Smith T. P., Graziane N. M., Nowak L. M., et al. (2012). Gating reaction mechanism of neuronal NMDA receptors. J. Neurophysiol. 108, 3105–3115. DOI: 10.1152/jn.00551.2012

[7] Brimecombe J. C., Boeckman F. A., Aizenman E. (1997). Functional consequences of NR2 subunit composition in single recombinant N-methyl-D-aspartate receptors. Proc. Natl. Acad. Sci. U S A 94, 11019–11024. DOI: 10.1073/pnas.94.20.11019

[8] Brimecombe J. C., Potthoff W. K., Aizenman E. (1999). A critical role of the N-methyl-D-aspartate (NMDA) receptor subunit (NR) 2A in the expression of redox sensitivity of NR1/NR2A recombinant NMDA receptors. J. Pharmacol. Exp. Ther. 291, 785–792.

[9] Bruintjes J. J., Henning R. H., Douwenga W., van der Zee E. A. (2014). Hippocampal cystathionine beta synthase in young and aged mice. Neurosci. Lett. 563, 135–139. DOI: 10.1016/j.neulet.2014.01.049

[10] Chang L. R., Liu J. P., Zhang N., Wang Y. J., Gao X. L., Wu Y. (2009). Different expression of NR2b and PSD-95 in rat hippocampal subregions during postnatal development. Microsc. Res. Tech. 72, 517–524. DOI: 10.1002/jemt.20708

[11] Chen L., Zhang J., Ding Y., Li H., Nie L., Yan X., et al. (2013). KATP channels of parafacial respiratory group (pFRG) neurons are involved in HS-mediated central inhibition of respiratory rhythm in medullary slices of neonatal rats. Brain Res. 1527, 141–148. DOI: 10.1016/j.brainres.2013.07.009

[12] Eghbal M. A., Pennefather P. S., O'Brien P. J. (2004). HS cytotoxicity mechanism involves reactive oxygen species formation and mitochondrial depolarisation. Toxicology 203, 69–76. DOI: 10.1016/j.tox.2004.05.020

[13] Enokido Y., Suzuki E., Iwasawa K., Namekata K., Okazawa H., Kimura H. (2005). Cystathionine beta-synthase, a key enzyme for homocysteine metabolism, is preferentially expressed in the radial glia/astrocyte lineage of developing mouse CNS. FASEB J. 19, 1854–1856. DOI: 10.1096/fj.05-3724fje

[14] Eto K., Asada T., Arima K., Makifuchi T., Kimura H. (2002). Brain hydrogen sulfide is severely decreased in Alzheimer's disease. Biochem. Biophys. Res. Commun. 293, 1485–1488. DOI: 10.1016/s0006-291x(02)00422-9

[15] Fabbretti E., Sokolova E., Masten L., D'Arco M., Fabbro A., Nistri A., et al. (2004). Identification of negative residues in the P2X ATP receptor ectodomain as structural determinants for desensitization and the Ca+-sensing modulatory sites. J. Biol. Chem.279, 53109–53115. DOI: 10.1074/jbc.M409772200

[16] Gerasimova E., Lebedeva J., Yakovlev A., Zefirov A., Giniatullin R. A., Sitdikova G. (2015). Mechanisms of hydrogen sulfide (HS) action on synaptic transmission at the mouse neuromuscular junction. Neuroscience 303, 577–585. DOI: 10.1016/j.neuroscience.2015.07.036

[17] Gerasimova E., Yakovleva O., Burkhanova G., Ziyatdinova G., Khaertdinov N., Sitdikova G. (2017). Effects of maternal hyperhomocysteinemia on the early physical development and neurobehavioral maturation of rat offspring. Bionanoscience 7, 155–158. DOI: 10.1007/s12668-016-0326-6

[18] Giuliani D., Ottani A., Zaffe D., Galantucci M., Strinati F., Lodi R., et al. (2013). Hydrogen sulfide slows down progression of experimental Alzheimer's disease by targeting multiple pathophysiological mechanisms. Neurobiol. Learn. Mem. 104, 82–91. DOI: 10.1016/j.nlm.2013.05.006

[19] Greiner R., Pálinkás Z., Bäsell K., Becher D., Antelmann H., Nagy P., et al. (2013). Polysulfides link HS to protein thiol oxidation. Antioxid. Redox Signal. 19, 1749–1765. DOI: 10.1089/ars.2012.5041

[20] Guidi M., Kumar A., Foster T. C. (2015). Impaired attention and synaptic senescence of the prefrontal cortex involves redox regulation of NMDA receptors. J. Neurosci. 35, 3966–3977. DOI: 10.1523/JNEUROSCI.3523-14.2015

[21] Han Y., Qin J., Chang X., Yang Z., Tang X., Du J. (2005). Hydrogen sulfide may improve the hippocampal damage induced by recurrent febrile seizures in rats. Biochem. Biophys. Res. Commun. 327, 431–436. DOI: 10.1016/j.bbrc.2004.12.028

[22] Hardingham G. E., Bading H. (2010). Synaptic versus extrasynaptic NMDA receptor signalling: implications for neurodegenerative disorders. Nat. Rev. Neurosci. 11, 682–696. DOI: 10.1038/nrn2911

[23] Harris A. Z., Pettit D. L. (2008). Recruiting extrasynaptic NMDA receptors augments synaptic signaling. J. Neurophysiol. 99, 524–533. DOI: 10.1152/jn.01169.2007

[24] He J., Guo R., Qiu P., Su X., Yan G., Feng J. (2017). Exogenous hydrogen sulfide eliminates spatial memory retrieval impairment and hippocampal CA1 LTD enhancement caused by acute stress via promoting glutamate uptake. Neuroscience 350, 110–123. DOI: 10.1016/j.neuroscience.2017.03.018

[25] Hu L. F., Lu M., Tiong C. X., Dawe G. S., Hu G., Bian J. S. (2010). Neuroprotective effects of hydrogen sulfide on Parkinson's disease rat models. Aging Cell 9, 135–146. DOI: 10.1111/j.1474-9726.2009.00543.x

[26] Kamat P. K., Kalani A., Givvimani S., Sathnur P. B., Tyagi S. C., Tyagi N. (2013). Hydrogen sulfide attenuates neurodegeneration and neurovascular dysfunction induced by intracerebral administered homocysteine in mice. Neuroscience 252, 302–319. DOI: 10.1016/j.neuroscience.2013.07.051

[27] Kamat P. K., Kalani A., Tyagi N. (2015). Role of hydrogen sulfide in brain synaptic remodeling. Methods Enzymol. 555, 207–229. DOI: 10.1016/bs.mie.2014.11.025

[28] Kida K., Yamada M., Tokuda K., Marutani E., Kakinohana M., Kaneki M., et al. (2011). Inhaled hydrogen sulfide prevents neurodegeneration and movement disorder in a mouse model of Parkinson's disease. Antioxid. Redox Signal. 15, 343–352. DOI: 10.1089/ars.2010.3671

[29] Kimura H. (2000). Hydrogen sulfide induces cyclic AMP and modulates the NMDA receptor. Biochem. Biophys. Res. Commun. 267, 129–133. DOI: 10.1006/bbrc.1999.1915

[30] Kimura H. (2010). Hydrogen sulfide: from brain to gut. Antioxid. Redox Signal. 12, 1111–1123. DOI: 10.1089/ars.2009.2919

[31] Kimura H. (2014). Hydrogen sulfide and polysulfides as biological mediators. Molecules 19, 16146–16157. DOI: 10.3390/molecules191016146

[32] Kimura H. (2016). Hydrogen polysulfide (HS) signaling along with hydrogen sulfide (HS) and nitric oxide (NO). J. Neural Transm. 123, 1235–1245. DOI: 10.1007/s00702-016-1600-z

[33] Kimura Y., Kimura H. (2004). Hydrogen sulfide protects neurons from oxidative stress. FASEB J. 18, 1165–1167. DOI: 10.1096/fj.04-1815fje

[34] Köhr G., Eckardt S., Lüddens H., Monyer H., Seeburg P. H., Kohr G., et al. (1994). NMDA receptor channels: subunit-specific potentiation by reducing agents. Neuron 12, 1031–1040. DOI: 10.1016/0896-6273(94)90311-5

[35] Kuksis M., Ferguson A. V. (2015). Actions of a hydrogen sulfide donor (NaHS) on transient sodium, persistent sodium, and voltage-gated calcium currents in neurons of the subfornical organ. J. Neurophysiol. 114, 1641–1651. DOI: 10.1152/jn.00252.2015

[36] Kuksis M., Smith P. M., Ferguson A. V. (2014). Hydrogen sulfide regulates cardiovascular function by influencing the excitability of subfornical organ neurons. PLoS One 9:e105772. DOI: 10.1371/journal.pone.0105772

[37] Kumar A., Foster T. C. (2013). Linking redox regulation of NMDAR synaptic function to cognitive decline during aging. J. Neurosci. 33, 15710–15715. DOI: 10.1523/JNEUROSCI.2176-13.2013

[38] Lau C. G., Takeuchi K., Rodenas-Ruano A., Takayasu Y., Murphy J., Bennett M. V., et al. (2009). Regulation of NMDA receptor Ca signalling and synaptic plasticity. Biochem. Soc. Trans. 37, 1369–1374. DOI: 10.1042/BST0371369

[39] Lee M., Tazzari V., Giustarini D., Rossi R., Sparatore A., Del Soldato P., et al. (2010). Effects of hydrogen sulfide-releasing L-DOPA derivatives on glial activation: potential for treating Parkinson disease. J. Biol. Chem. 285, 17318–17328. DOI: 10.1074/jbc.M110.115261

[40] Li J. H., Wang Y. H., Wolfe B. B., Krueger K. E., Corsi L., Stocca G., et al. (1998). Developmental changes in localization of NMDA receptor subunits in primary cultures of cortical neurons. Eur. J. Neurosci. 10, 1704–1715. DOI: 10.1046/j.1460-9568.1998.00169.x

[41] Li Z., Wang Y., Xie Y., Yang Z., Zhang T. (2011). Protective effects of exogenous hydrogen sulfide on neurons of hippocampus in a rat model of brain ischemia. Neurochem. Res. 36, 1840–1849. DOI: 10.1007/s11064-01--0502-6

[42] Lipton S. A., Stamler J. S. (1994). Actions of redox-related congeners of nitric-oxide at the nmda receptor. Neuropharmacology 33, 1229–1233. DOI: 10.1016/0028-3908(94)90021-3

[43] Liu Y. Y., Bian J. S. (2010). Hydrogen sulfide protects amyloid-beta induced cell toxicity in microglia. J. Alzheimers Dis. 22, 1189–1200. DOI: 10.3233/JAD-2010-101002

[44] Liu X.-B., Murray K. D., Jones E. G. (2004). Switching of NMDA receptor 2A and 2B subunits at thalamic and cortical synapses during early postnatal development. J. Neurosci. 24, 8885–8895. DOI: 10.1523/JNEUROSCI.2476-04.2004

[45] Malik R., Ferguson A. V. (2016). Hydrogen sulfide depolarizes neurons in the nucleus of the solitary tract of the rat. Brain Res. 1633, 1–9. DOI: 10.1016/j.brainres.2015.12.029

[46] Marutani E., Kosugi S., Tokuda K., Khatri A., Nguyen R., Atochin D. N., et al. (2012). A novel hydrogen sulfide-releasing N-methyl-D-aspartate receptor antagonist prevents ischemic neuronal death. J. Biol. Chem. 287, 32124–32135. DOI: 10.1074/jbc.M112.374124

[47] Nagpure B. V., Bian J. S. (2014). Hydrogen sulfide inhibits A2A adenosine receptor agonist induced β-amyloid production in SHSY5Y neuroblastoma cells via a cAMP dependent pathway. PLoS One 9:e88508. DOI: 10.1371/journal.pone.0088508

[48] Njie-Mbye Y. F., Kulkarni M., Opere C. A., Ohia S. E. (2012). Mechanism of action of hydrogen sulfide on cyclic AMP formation in rat retinal pigment epithelial cells. Exp. Eye Res. 98, 16–22. DOI: 10.1016/j.exer.2012.03.001

[49] Paoletti P. (2011). Molecular basis of NMDA receptor functional diversity. Eur. J. Neurosci. 33, 1351–1365. DOI: 10.1111/j.1460-9568.2011.07628.x

[50] Perniss A., Preiss K., Nier M., Althaus M. (2017). Hydrogen sulfide stimulates CFTR in Xenopus oocytes by activation of the cAMP/PKA signalling axis. Sci. Rep. 7:3517. DOI: 10.1038/s41598-017-03742-5

[51] Renga B. (2011). Hydrogen sulfide generation in mammals: the molecular biology of cystathionine-β-synthase (CBS) and cystathionine-γ-lyase (CSE). Inflamm. Allergy Drug Targets 10, 85–91. DOI: 10.2174/187152811794776286

[52] Rosenquist T. H., Finnell R. H. (2001). Genes, folate and homocysteine in embryonic development. Proc. Nutr. Soc. 60, 53–61. DOI: 10.1079/PNS200076

[53] Rossi D. J., Brady J. D., Mohr C. (2007). Astrocyte metabolism and signaling during brain ischemia. Nat. Neurosci. 10, 1377–1386. DOI: 10.1038/nn2004

[54] Shibuya N., Koike S., Tanaka M., Ishigami-Yuasa M., Kimura Y., Ogasawara Y., et al. (2013). A novel pathway for the production of hydrogen sulfide from D-cysteine in mammalian cells. Nat. Commun. 4:1366. DOI: 10.1038/ncomms2371

[55] Shibuya N., Tanaka M., Yoshida M., Ogasawara Y., Togawa T., Ishii K., et al. (2009). 3-Mercaptopyruvate sulfurtransferase produces hydrogen sulfide and bound sulfane sulfur in the brain. Antioxid. Redox Signal. 11, 703–714. DOI: 10.1089/ars.2008.2253

[56] Sibarov D. A., Abushik P., Giniatullin R. A., Antonov S. M. (2016). GluN2A subunit-containing NMDA receptors are the preferential neuronal targets of homocysteine. Front. Cell. Neurosci. 10:246. DOI: 10.3389/fncel.2016.00246

[57] Sitdikova G. F., Fuchs R., Kainz V., Weiger T. M., Hermann A. (2014). Phosphorylation of BK channels modulates the sensitivity to hydrogen sulfide (HS). Front. Physiol.5:431. DOI: 10.3389/fphys.2014.00431

[58] Sitdikova G. F., Weiger T. M., Hermann A. (2010). Hydrogen sulfide increases calcium-activated potassium (BK) channel activity of rat pituitary tumor cells. Pflugers Arch.459, 389–397. DOI: 10.1007/s00424-009-0737-0

[59] Skeberdis V. A., Chevaleyre V., Lau C. G., Goldberg J. H., Pettit D. L., Suadicani S. O., et al. (2006). Protein kinase A regulates calcium permeability of NMDA receptors. Nat. Neurosci. 9, 501–510. DOI: 10.1038/nn1664

[60] Sullivan J. M., Traynelis S. F., Chen H. S. V., Escobar W., Heinemann S. F., Lipton A. (1994). Identification of two cysteine residues that are required for redox modulation of the NMDA subtype of glutamate receptor. Neuron 13, 929–936. DOI: 10.1016/0896-6273(94)90258-5

[61] Talukder I., Kazi R., Wollmuth L. P. (2011). GluN1-specific redox effects on the kinetic mechanism of NMDA receptor activation. Biophys. J. 101, 2389–2398. DOI: 10.1016/j.bpj.2011.10.015

[62] Tang L. H., Aizenman E. (1993). The modulation of N-methyl-D-aspartate receptors by redox and alkylating reagents in rat cortical neurones in vitro. J. Physiol. 465, 303–323. DOI: 10.1113/jphysiol.1993.sp019678

[63] van Zundert B., Yoshii A., Constantine-Paton M. (2004). Receptor compartmentalization and trafficking at glutamate synapses: a developmental proposal. Trends Neurosci. 27, 428–437. DOI: 10.1016/j.tins.2004.05.010

[64] Wang R. (2012). Physiological implications of hydrogen sulfide: a whiff exploration that blossomed. Physiol. Rev. 92, 791–896. DOI: 10.1152/physrev.00017.2011

[65] Whitfield N. L., Kreimier E. L., Verdial F. C., Skovgaard N., Olson K. R. (2008). Reappraisal of HS/sulfide concentration in vertebrate blood and its potential significance in ischemic preconditioning and vascular signaling. Am. J. Physiol. Regul. Integr. Comp. Physiol. 294, R1930–R1937. DOI: 10.1152/ajpregu.00025.2008

[66] Yakovlev A. V., Kurmasheva E. D., Giniatullin R., Khalilov I., Sitdikova G. F. (2017). Hydrogen sulfide inhibits giant depolarizing potentials and abolishes epileptiform activity of neonatal rat hippocampal slices. Neuroscience 340, 153–165. DOI: 10.1016/j.neuroscience.2016.10.051

[67] Yang Y. J., Wu P. F., Long L. H., Yu D. F., Wu W. N., Hu Z. L., et al. (2010). Reversal of aging-associated hippocampal synaptic plasticity deficits by reductants via regulation of thiol redox and NMDA receptor function. Aging Cell 9, 709–721. DOI: 10.1111/j.1474-9726.2010.00595.x

[68] Yang H. Y., Wu Z. Y., Wood M., Whiteman M., Bian J. S. (2014). Hydrogen sulfide attenuates opioid dependence by suppression of adenylate cyclase/cAMP pathway. Antioxid. Redox Signal. 20, 31–41. DOI: 10.1089/ars.2012.5119

[69] Yong Q. C., Pan T. T., Hu L. F., Bian J. S. (2008). Negative regulation of β-adrenergic function by hydrogen sulphide in the rat hearts. J. Mol. Cell Cardiol. 44, 701–710. DOI: 10.1016/j.yjmcc.2008.01.007

[70] Zhou M., Baudry M. (2006). Developmental changes in NMDA neurotoxicity reflect developmental changes in subunit composition of NMDA receptors. J. Neurosci. 26, 2956–2963. DOI: 10.1523/jneurosci.4299-05.2006

[71] Zhou X., Chen Z., Yun W., Ren J., Li C., Wang H. (2015). Extrasynaptic NMDA receptor in excitotoxicity: function revisited. Neuroscientist 21, 337–344. DOI: 10.1177/1073858414548724