

Muscle and Nerve 2017 vol.55 N3, pages 417-423

## Effects of ATP and adenosine on contraction amplitude of rat soleus muscle at different temperatures

Ziganshin A., Khairullin A., Zobov V., Ziganshina L., Gabdrakhmanov A., Ziganshin B., Grishin S.  
Kazan Federal University, 420008, Kremlevskaya 18, Kazan, Russia

### Abstract

© 2016 Wiley Periodicals, Inc. Introduction: The aim of this study was to evaluate the effects of adenosine 5'-triphosphate (ATP) and adenosine on the contractility of mammalian skeletal muscle under hypothermic conditions. Methods: Contractions of isolated rat soleus muscle were induced by either electrical stimulation (ES) or carbachol at physiological temperatures (37°C) and hypothermic conditions (30–14°C) and recorded in the presence of ATP, adenosine, suramin, and 8-(p-sulfophenyl)-theophylline (8-SPT). Results: At 37°C, incubation of the muscles with ATP inhibited ES-induced contractions; the inhibitory effect of ATP disappeared at 14°C. Adenosine inhibited ES-induced contractions at all temperature levels; 8-SPT fully prevented the action of adenosine. ATP and adenosine did not significantly affect carbachol-induced contractions at 37°C, while at lower temperatures ATP potentiated them. Suramin fully prevented effects of ATP. Conclusions: ATP is involved in both pre- and postsynaptic regulation of rat soleus muscle contractility, and these processes are significantly more pronounced at low temperatures. *Muscle Nerve* 55: 417–423, 2017.

<http://dx.doi.org/10.1002/mus.25263>

### Keywords

adenosine, ATP, hypothermia, P2 receptors, skeletal muscle, suramin

### References

- [1] Ziganshin BA, Elefteriades JA. Deep hypothermic circulatory arrest. *Ann Cardiothorac Surg* 2013;2:303–315.
- [2] Ziganshin BA, Rajbanshi BG, Tranquilli M, Fang H, Rizzo JA, Elefteriades JA. Straight deep hypothermic circulatory arrest for cerebral protection during aortic arch surgery: safe and effective. *J Thorac Cardiovasc Surg* 2014;148:888–898; discussion 898–900.
- [3] Andrews PJ, Sinclair HL, Rodriguez A, Harris BA, Battison CG, Rhodes JK, et al. Hypothermia for intracranial hypertension after traumatic brain injury. *N Engl J Med* 2015;373:2403–2412.
- [4] Nielsen N, Wetterslev J, Cronberg T, Erlinge D, Gasche Y, Hassager C, et al. Targeted temperature management at 33 degrees C versus 36 degrees C after cardiac arrest. *N Engl J Med* 2013;369:2197–2206.
- [5] Moler FW, Silverstein FS, Holubkov R, Slomine BS, Christensen JR, Nadkarni VM, et al. Therapeutic hypothermia after out-of-hospital cardiac arrest in children. *N Engl J Med* 2015;372:1898–1908.
- [6] Erecinska M, Thoresen M, Silver IA. Effects of hypothermia on energy metabolism in Mammalian central nervous system. *J Cereb Blood Flow Metab* 2003;23:513–530.
- [7] Alassar A, Bazerbashi S, Moawad N, Marchbank A. What is the value of topical cooling as an adjunct to myocardial protection? *Interact Cardiovasc Thorac Surg* 2014;19:856–860.

- [8] Ziganshin AU, Rychkov AV, Ziganshina LE, Burnstock G. Temperature dependency of P2 receptor-mediated responses. *Eur J Pharmacol* 2002;456:107-114.
- [9] Ziganshin AU, Kamaliev RR, Grishin SN, Ziganshin BA, Burnstock G. Interaction of hydrocortisone with ATP and adenosine on nerve-mediated contractions of frog skeletal muscle. *Eur J Pharmacol* 2009;607:54-59.
- [10] Foldes FF, Kuze S, Vizi ES, Deery A. The influence of temperature on neuromuscular performance. *J Neural Transm* 1978;43:27-45.
- [11] Burnstock G. Purinergic signalling: its unpopular beginning, its acceptance and its exciting future. *Bioessays* 2012;34:218-225.
- [12] Sabala P, Czajkowski R, Przybylek K, Kalita K, Kaczmarek L, Baranska J. Two subtypes of G protein-coupled nucleotide receptors, P2Y(1) and P2Y(2) are involved in calcium signalling in glioma C6 cells. *Br J Pharmacol* 2001;132:393-402.
- [13] Jacobson KA, Jayasekara MP, Costanzi S. Molecular structure of P2Y receptors: mutagenesis, modeling, and chemical probes. *Wiley Interdiscip Rev Membr Transp Signal* 2012;1.
- [14] Burnstock G. Purinergic signalling: pathophysiology and therapeutic potential. *Keio J Med* 2013;62:63-73.
- [15] Orriss IR. The role of purinergic signalling in the musculoskeletal system. *Auton Neurosci* 2015;191:124-134.
- [16] Garcia N, Priego M, Obis T, Santafe MM, Tomas M, Besalduch N, et al. Adenosine A(1) and A(2)A receptor-mediated modulation of acetylcholine release in the mice neuromuscular junction. *Eur J Neurosci* 2013;38:2229-2241.
- [17] Bryan PT, Marshall JM. Adenosine receptor subtypes and vasodilatation in rat skeletal muscle during systemic hypoxia: a role for A1 receptors. *J Physiol* 1999;514(Pt 1):151-162.
- [18] Warren GL, Hulderman T, Liston A, Simeonova PP. Toll-like and adenosine receptor expression in injured skeletal muscle. *Muscle Nerve* 2011;44:85-92.
- [19] Sarafoff N, Byrne RA, Sibbing D. Clinical use of clopidogrel. *Curr Pharm Des* 2012;18:5224-5239.
- [20] Geraets D, Kienzle M. Clinical use of adenosine. *Iowa Med* 1992;82:25-28.
- [21] Forrester T. An estimate of adenosine triphosphate release into the venous effluent from exercising human forearm muscle. *J Physiol* 1972;224:611-628.
- [22] Vizi ES, Nitahara K, Sato K, Sperlagh B. Stimulation-dependent release, breakdown, and action of endogenous ATP in mouse hemidiaphragm preparation: the possible role of ATP in neuromuscular transmission. *J Auton Nerv Syst* 2000;81:278-284.
- [23] Cunha RA, Sebastiao AM. Adenosine and adenine nucleotides are independently released from both the nerve terminals and the muscle fibres upon electrical stimulation of the innervated skeletal muscle of the frog. *Pflugers Arch* 1993;424:503-510.
- [24] Magalhaes-Cardoso MT, Pereira MF, Oliveira L, Ribeiro JA, Cunha RA, Correia-de-Sa P. Ecto-AMP deaminase blunts the ATP-derived adenosine A2A receptor facilitation of acetylcholine release at rat motor nerve endings. *J Physiol* 2003;549:399-408.
- [25] Akasu T, Hirai K, Koketsu K. Increase of acetylcholine-receptor sensitivity by adenosine triphosphate: a novel action of ATP on ACh-sensitivity. *Br J Pharmacol* 1981;74:505-507.
- [26] Giniatullin RA, Sokolova EM. ATP and adenosine inhibit transmitter release at the frog neuromuscular junction through distinct presynaptic receptors. *Br J Pharmacol* 1998;124:839-844.
- [27] Sokolova E, Grishin S, Shakirzyanova A, Talantova M, Giniatullin R. Distinct receptors and different transduction mechanisms for ATP and adenosine at the frog motor nerve endings. *Eur J Neurosci* 2003;18:1254-1264.
- [28] De Lorenzo S, Veggetti M, Muchnik S, Losavio A. Presynaptic inhibition of spontaneous acetylcholine release mediated by P2Y receptors at the mouse neuromuscular junction. *Neuroscience* 2006;142:71-85.
- [29] Malomouzh AI, Nikolsky EE, Vyskocil F. Purine P2Y receptors in ATP-mediated regulation of non-quantal acetylcholine release from motor nerve endings of rat diaphragm. *Neurosci Res* 2011;71:219-225.
- [30] Tomas J, Santafe MM, Garcia N, Lanuza MA, Tomas M, Besalduch N, et al. Presynaptic membrane receptors in acetylcholine release modulation in the neuromuscular synapse. *J Neurosci Res* 2014;92:543-554.
- [31] Giniatullin A, Petrov A, Giniatullin R. The involvement of P2Y12 receptors, NADPH oxidase, and lipid rafts in the action of extracellular ATP on synaptic transmission at the frog neuromuscular junction. *Neuroscience* 2015;285:324-332.
- [32] Ziganshin AU, Kamaliev RR, Grishin SN, Ziganshina LE, Zefirov AL, Burnstock G. The influence of hypothermia on P2 receptor-mediated responses of frog skeletal muscle. *Eur J Pharmacol* 2005;509:187-193.
- [33] Grishin SN, Ziganshin AU. Modulatory role of purines in neuromuscular transmission. *Biochemistry (Moscow) Supplement Series A: Membrane and Cell Biology* 2013;7:183-191.
- [34] Salgado AI, Cunha RA, Ribeiro JA. Facilitation by P(2) receptor activation of acetylcholine release from rat motor nerve terminals: interaction with presynaptic nicotinic receptors. *Brain Res* 2000;877:245-250.
- [35] Yegutkin GG. Enzymes involved in metabolism of extracellular nucleotides and nucleosides: functional implications and measurement of activities. *Crit Rev Biochem Mol Biol* 2014;49:473-497.

- [36] Ghildyal P, Manchanda R. Effects of cooling and ARL 67156 on synaptic ecto-ATPase activity in guinea pig and mouse vas deferens. *Auton Neurosci* 2004;115:28-34.
- [37] Grishin SN, Teplov AY, Galkin AV, Devyataev AM, Zefirov AL, Mukhamedyarov MA, et al. Different effects of ATP on the contractile activity of mice diaphragmatic and skeletal muscles. *Neurochem Int* 2006;49:756-763.
- [38] Igusa Y. Adenosine 5'-triphosphate activates acetylcholine receptor channels in cultured *Xenopus* myotomal muscle cells. *J Physiol* 1988;405:169-185.
- [39] Voogd TE, Vansterkenburg EL, Wilting J, Janssen LH. Recent research on the biological activity of suramin. *Pharmacol Rev* 1993;45:177-203.
- [40] McGeary RP, Bennett AJ, Tran QB, Cosgrove KL, Ross BP. Suramin: clinical uses and structure-activity relationships. *Mini Rev Med Chem* 2008;8:1384-1394.
- [41] Hoyle CH, Knight GE, Burnstock G. Suramin antagonizes responses to P2-purinoceptor agonists and purinergic nerve stimulation in the guinea-pig urinary bladder and taenia coli. *Br J Pharmacol* 1990;99:617-621.
- [42] Lambrecht G, Braun K, Damer M, Ganso M, Hildebrandt C, Ullmann H, et al. Structure-activity relationships of suramin and pyridoxal-5'-phosphate derivatives as P2 receptor antagonists. *Curr Pharm Des* 2002;8:2371-2399.
- [43] Marti E, Canti C, Gomez de Aranda I, Miralles F, Solsona C. Action of suramin upon ecto-apyrase activity and synaptic depression of Torpedo electric organ. *Br J Pharmacol* 1996;118:1232-1236.
- [44] Savegnago L, Nogueira CW, Fachinetto R, Rocha JB. Characterization of ATP and ADP hydrolysis activity in rat gastric mucosa. *Cell Biol Int* 2005;29:559-566.
- [45] Kiffer-Moreira T, Fernandes Sampaio ME, Alviano DS, Axelband F, Cesar GV, Cosentino-Gomes D, et al. Biochemical characterization of an ecto-ATP diphosphohydrolase activity in *Candida parapsilosis* and its possible role in adenosine acquisition and pathogenesis. *FEMS Yeast Res* 2010;10:735-746.
- [46] Henning RH, Nelemans A, Scaf AH, Van Eekeren J, Agoston S, Den Hertog A. Suramin reverses non-depolarizing neuromuscular blockade in rat diaphragm. *Eur J Pharmacol* 1992;216:73-79.
- [47] Henning RH, Rowan EG, Braga MF, Nelemans A, Harvey AL. The prejunctional inhibitory effect of suramin on neuromuscular transmission in vitro. *Eur J Pharmacol* 1996;301:91-97.
- [48] Broadley KJ, Broome S, Paton DM. Hypothermia-induced supersensitivity to adenosine for responses mediated via A1-receptors but not A2-receptors. *Br J Pharmacol* 1985;84:407-415.
- [49] Nikolsky EE, Strunsky EG, Vyskocil F. Temperature dependence of carbachol-induced modulation of miniature end-plate potential frequency in rats. *Brain Res* 1991;560:354-356.
- [50] Balnave RJ, Gage PW. On facilitation of transmitter release at the toad neuromuscular junction. *J Physiol* 1974;239:657-675.