

# Role of adenosine A2 receptors in regulation of cerebral blood flow during induced hypotension

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The mechanisms responsible for vascular autoregulation in the brain during changes in mean arterial blood pressure are ambiguous. Potentially, adenosine, a purine nucleoside and potent vasodilator, may be involved as earlier studies have documented an increase in brain adenosine concentrations with cerebral ischemia and hypotension. Consequently, we tested the hypothesis that adenosine is involved in vasodilatation during hypotension within the autoregulatory range (>50 mm Hg) by exposing adenosine 2a receptor (A2aR) knockout and wild type (WT) mice to short (2 to 5 mins) periods of hypotension. We found that autoregulation was significantly ( $P < 0.05$ ) impaired by 29% in A2a knockout mice as compared with WT animals. Furthermore, the A2R antagonist (A2a>A2b:10–85>1), ZM-241385, in a dose (1, 5, 10 mg/kg, intraperitoneally)-related manner, attenuated autoregulation in WT mice. In knockout mice treated with ZM-241385 (5 and 10 mg/kg), autoregulation was further impaired indicating that A2b receptors also participated in cerebral vasodilatation. Treatment with dipyridamole (1.0 mg/kg) that increases extracellular concentrations of adenosine improved autoregulation in the A2aR knockout mice. We would conclude that adenosine through both A2a and A2b receptors is involved in physiologic vascular regulation during hypotension even within the autoregulatory range.

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## Introduction

The brain has the capacity to modulate cerebral blood flow (CBF) during changes in blood pressure. This phenomenon is known as autoregulation (Lassen, 1959). The mechanism(s) responsible for the regulation of cerebral arteriolar tone during autoregulation is unclear, but a number of theories have been proposed (Paulson *et al.*, 1990), including the myogenic (Heistad and Kontos, 1983), neural (Hamel, 2006), and metabolic hypotheses (Heistad and Kontos, 1983). All three hypotheses entail biochemical (or transmitter) signal(s) whose action leads to a change in arterial diameter. A number of biochemical factors have been proposed to have such a role. For example, *in vivo* and *in vitro* studies

have suggested involvement of arachidonic acid metabolites (Harder *et al.*, 2000; Roman, 2002), nitric oxide (Jones *et al.*, 2003), calcitonin gene-related peptide (Hong *et al.*, 1994; Wei *et al.*, 1992), to mention a few, in vasoreactivity during alteration in mean arterial blood pressure (MABP) or intraluminal pressure.

Another potential signaling compound is the purine nucleoside adenosine, which is a potent vasodilator (Berne *et al.*, 1974; Ngai *et al.*, 2001). Brain adenosine concentrations are increased during hypoxia (Winn *et al.*, 1981; Zetterstrom *et al.*, 1982), ischemia (Winn *et al.*, 1979) and neuronal activation (Winn *et al.*, 1980a). However, there is controversy as to whether adenosine is elevated in brain during hypotension. To resolve this controversy, we performed studies to test the hypothesis that adenosine is involved in autoregulation during decreases in MABP and to determine the relative contribution of the adenosine 2a receptor (A2aR) and the 2b receptor (A2bR). We restricted our analysis to changes in MABP within the autoregulatory range and used short periods of decreases in MABP in wild type

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# Role Of Adenosine In Cerebral Metabolism And Blood Flow

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## **Role Of Adenosine In Cerebral Metabolism And Blood Flow:**

Role of Adenosine in Cerebral Metabolism And Blood Flow Vladimir Stefanovich, I. Okyayuz-Baklouti, 1988-12 It is becoming increasingly realized that adenosine plays an important role in the central metabolism and blood flow and that therapeutic possibilities may arise from the pharmacological manipulation of the adenosine system The growing interest in this field has prompted a group of international experts to contribute to this volume on adenosine The book contains thorough reviews on adenosine research and presents numerous new ideas and data on the role and function of adenosine in the mammalian brain

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*Regulation of Coronary Blood Flow* Michitoshi Inoue, Masatsugu Hori, Shoichi Imai, Robert M. Berne, 2013-11-09 Research centering on blood flow in the heart continues to hold an important position especially since a better understanding of the subject may help reduce the incidence of coronary arterial disease and heart attacks This book summarizes recent advances in the field it is the product of fruitful cooperation among international scientists who met in Japan in May 1990 to discuss the regulation of coronary blood flow

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knowledge of the expanding biological roles of these substances      *Primer on Cerebrovascular Diseases* K. Michael Welch, 1997-04-24 *Primer on Cerebrovascular Diseases* is a handy reference source for scientists students and physicians needing reliable up to date information on basic mechanisms physiology pathophysiology and medical issues related to brain vasculature The book consists of short specific chapters written by international experts on cerebral vasculature and presents the information in a comprehensive and easily accessible manner The book also contains valuable information on practical applications of basic research Presents topics in a comprehensive and accessible format Written by international authorities on cerebral vasculature Provides practical applications for researchers      *Biomedical Index to PHS-supported Research* , 1990      *Pediatric Critical Care E-Book* Jerry J. Zimmerman, 2016-11-29 Still the 1 resource for today s pediatric ICU teams *Pediatric Critical Care* 5th Edition covers the entire field from basic science to cutting edge clinical applications Drs Bradley P Fuhrman and Jerry J Zimmerman accompanied by an expert team of editors and contributors from around the world bring you today s best information on the current and future landscape of pediatric critical care so you can consistently deliver optimum care to your young patients Boasts highly readable concise chapters with hundreds of useful photos diagrams algorithms and clinical pearls Clear logical organ system approach allows you to focus on the development function and treatment of a wide range of disease entities Includes new content on the expanding use of ultrasound at the bedside and the increase in nursing responsibilities in the PICU Eighteen new chapters cover topics such as delirium metabolism endocrinology nutrition nursing and much more Features expanded and updated information on critical communication professionalism long term outcomes palliative care ultrasonography PCCM in resource limited settings ventilator induced lung injury non invasive ventilation updated CNS pathophysiology the Erythron and immunity and infection      *Neurology of the Newborn E-Book* Joseph J. Volpe, 2008-06-11 The 5th edition of this indispensable resource captures the latest insights in neonatal neurology in a totally engaging readable manner World authority Dr Joseph Volpe has completely revised his masterwork from cover to cover describing everything from the most up to the minute discoveries in genetics through the latest advances in the diagnosis and management of neurologic disorders He delivers all the clinical guidance you need to provide today s most effective care for neonates with neurological conditions Provides comprehensive coverage of neonatal neurology solely written by the field s founding expert Dr Joseph Volpe for a masterful cohesive source of answers to any question that arises in your practice Focuses on clinical evaluation and management while also examining the many scientific and technological advances that are revolutionizing neonatal neurology Organizes disease focused chapters by affected body region for ease of reference Offers comprehensive updates from cover to cover to reflect all of the latest scientific and clinical knowledge from our most current understanding of the genetic underpinnings of neurologic disease through the most recent neuroimaging advances state of the art guidelines for evaluation diagnosis and prognosis and the newest management approaches for every type of neonatal neuropathology Features a wealth of new high quality images that capture the many

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*Cumulated Index Medicus* ,1994

**Cortical NO interneurons from embryogenesis to functions** Bruno

Cauli,Yoshiyuki Kubota,Ludovic Tricoire,2014-01-23 Neuronal processing and physiology rely on a delicate interplay between glutamatergic excitatory neurons and GABAergic inhibitory interneurons in a spatially temporally and cell type specific manner Understanding these processes is complicated further by the large diversity characterizing the cerebral cortex Although recent advances have significantly improved our knowledge of its neuronal types the identity and the roles of several subpopulations of GABAergic interneurons remain elusive Presumably because of their apparent paucity their diversity the highly labile nature of nitric oxide NO as well as its pleiotropic actions the functional importance of NO producing GABAergic interneurons is particularly enigmatic This Research Topic will cover the different aspects of cortical NO interneurons from their diversity embryonic origins to their functions in the cortical circuit and physiology Oxygen

Transport to Tissue-V D. W. Lubbers,2012-12-06 On the understanding that few people ever read the preface to any book and also on the understanding that even those few people who do read the preface realize that virtually nothing of any substance is ever said I shall write at such length as will be proportional to my expected readership The meetings of the International Society on Oxygen Transport to Tissue provide a forum for discussion amongst scientists who although being from very diverse and specialized backgrounds have tissue oxygenation as a unifying theme of interest The wide variety of research material presented in this volume and the multiplicity of the experimental techniques described should serve as an adequate gauge to the range of expertise and knowledge of the society s members Such diversity should also stress the importance of the need for multidisciplinary approaches to complex biological problems In attempting a fundamental characterization of a biological process such as tissue oxygenation the application of very many separate research skills are necessary such as mathematics engineering biophysics biochemistry physiology histology and clinical medicine The success of the ISOTT has and we hope will continue to be causing a combination of individuals to direct their specialized knowledge to the many facets of a single process tissue oxygenation

*Primer on Cerebrovascular Diseases* Louis R. Caplan,Jose Biller,Megan C. Leary,Eng H. Lo,Ajith J Thomas,Midori Yenari,John H. Zhang,2017-02-10 *Primer on Cerebrovascular Diseases* Second Edition is a handy reference source for scientists students and physicians needing reliable up to date information on basic mechanisms physiology pathophysiology and medical issues related to brain vasculature The book consists of short specific chapters written by international experts on cerebral vasculature presenting the information in a comprehensive and easily accessible manner Numerous changes have occurred in the field since the publication of the first edition in 1997 particularly our understanding of the genetic aspects of cerebrovascular disease This updated edition reflects the advances made over the last two decades not only demonstrating the promise for therapy but also for a molecular understanding of cerebrovascular diseases The new edition includes new and expanded topics including carotid stenting Iatrogenic causes of stroke axonal transport and injury RNAs proteomics and more 2018 BMA Medical Book Awards Highly Commended in

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