Master Biologie cellulaire,
physiologie et et pathologie

UE SAIB

La réactivité des voies aériennes

TD

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muscle lisse et asthme

Journal of Allergy

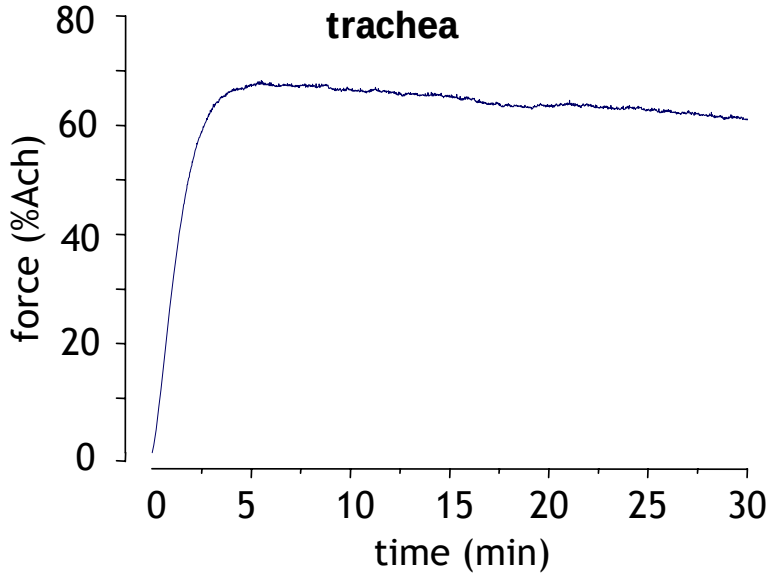
Smooth Muscle Hypercontractility in Airway Hyperresponsiveness: Innate, Acquired, or Nonexistent?

Call for Papers

Asthma symptoms are triggered/exacerbated by a range of environmental factors, such as allergens, viruses, fungi, exercise, aspirin, or pollutants. Hitherto considered a disease, asthma is henceforth viewed by many as an environmental syndrome with a heterogeneous pathogenesis. Its diagnostic signature is the reversibility of airway obstruction by drug relaxing the airway smooth muscle (ASM), confirming the importance of this tissue in asthma symptoms. Most asthmatics are also hyperresponsive to a bronchoprovocative challenge with a contractile agonist. However, the involvement of ASM in airway hyperresponsiveness (AHR), apart from its undisputed role in airway responsiveness, is still uncertain. This is mainly due to our inability to assess ASM function in vivo.

analyse de résultats expérimentaux

réponse contractile d'un anneau de trachée de rat à la stimulation par une solution extracellulaire contenant 80 mM de KCl.



analyse d'article

The contribution of inositol 1,4,5-trisphosphate and ryanodine receptors to agonist-induced Ca^{2+} signaling of airway smooth muscle cells

Yan Bai, Martin Edelmann, and Michael J. Sanderson

Am J Physiol Lung Cell Mol Physiol. 2009 August; **297**(2): L347–L361

METHODS

Lung slices.

Measurement of airway contraction and relaxation.

Airway contraction was measured by determining the change in lumen area, with respect to the initial lumen area, by pixel summing with custom-written macros.

Measurement of intracellular Ca2+ signaling.

Oregon Green 488 BAPTA-1 AM.

Fluorescence intensity was expressed in absolute units or in relative terms as a fluorescence ratio (F/F0) normalized to the initial fluorescent intensity (F0).

Flash photolysis of caged-IP3.

Flash photolysis of caged-IP3 was used to experimentally increase the [IP3]i.
Lung slices were initially loaded with Oregon Green 488 BAPTA-1 AM and subsequently incubated with 2 μM caged-IP3
A UV flash was generated focused as point source into the microscope. The intensity of flash was regulated by neutral density filters. The spot size could be adjusted with an iris diaphragm.

Preparation of Ca2+-permeabilized lung slices.

To clamp the [Ca2+]i of airway SMCs at a constant level, it is necessary to increase the permeability of the plasma membrane to Ca2+. Typically, this has been achieved by the application of detergents or toxins.
We have developed an alternative approach using caffeine and ryanodine to only increase the permeability of cell membrane to Ca2+.
Lung slices were simultaneously exposed to 20 mM caffeine and 50 μM ryanodine for 5 min. This treatment is believed to lock the RyRs in the open state and thereby brings about the depletion of the SR Ca2+ store. This, in turn, leads to a persistent Ca2+ influx via store-operated channels to elevate the [Ca2+]i. As a result, the extracellular Ca2+ concentration is used to determine the [Ca2+]i.

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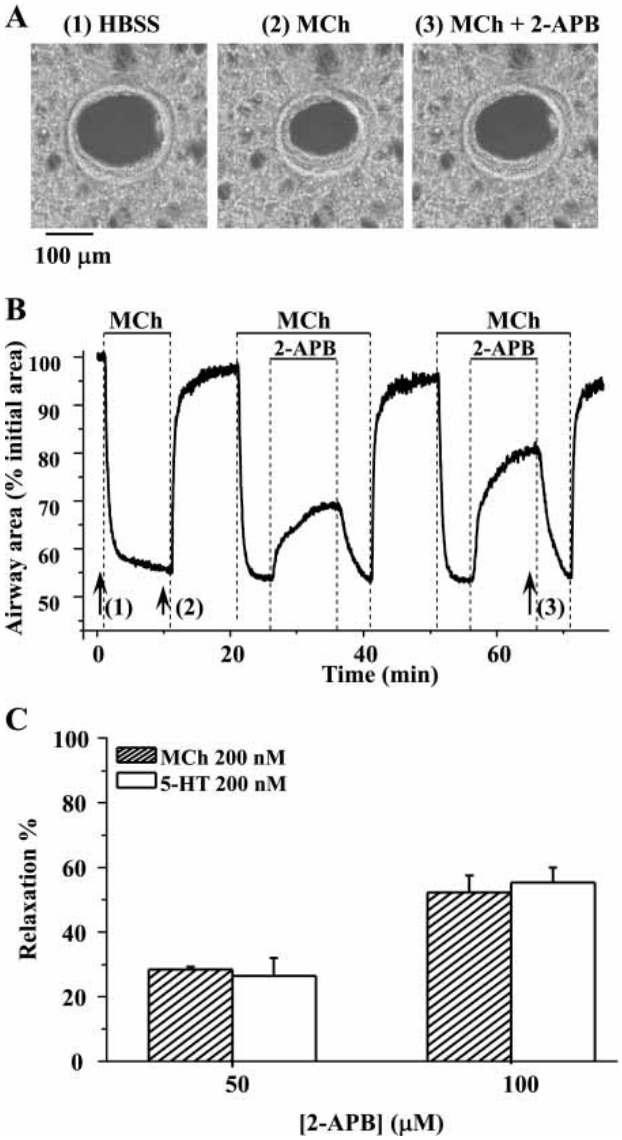

The effect of 2-aminoethoxydiphenyl borate (2-APB) on agonist-induced airway contraction.

2-APB : inhibiteur des PIP3

analyse d'article

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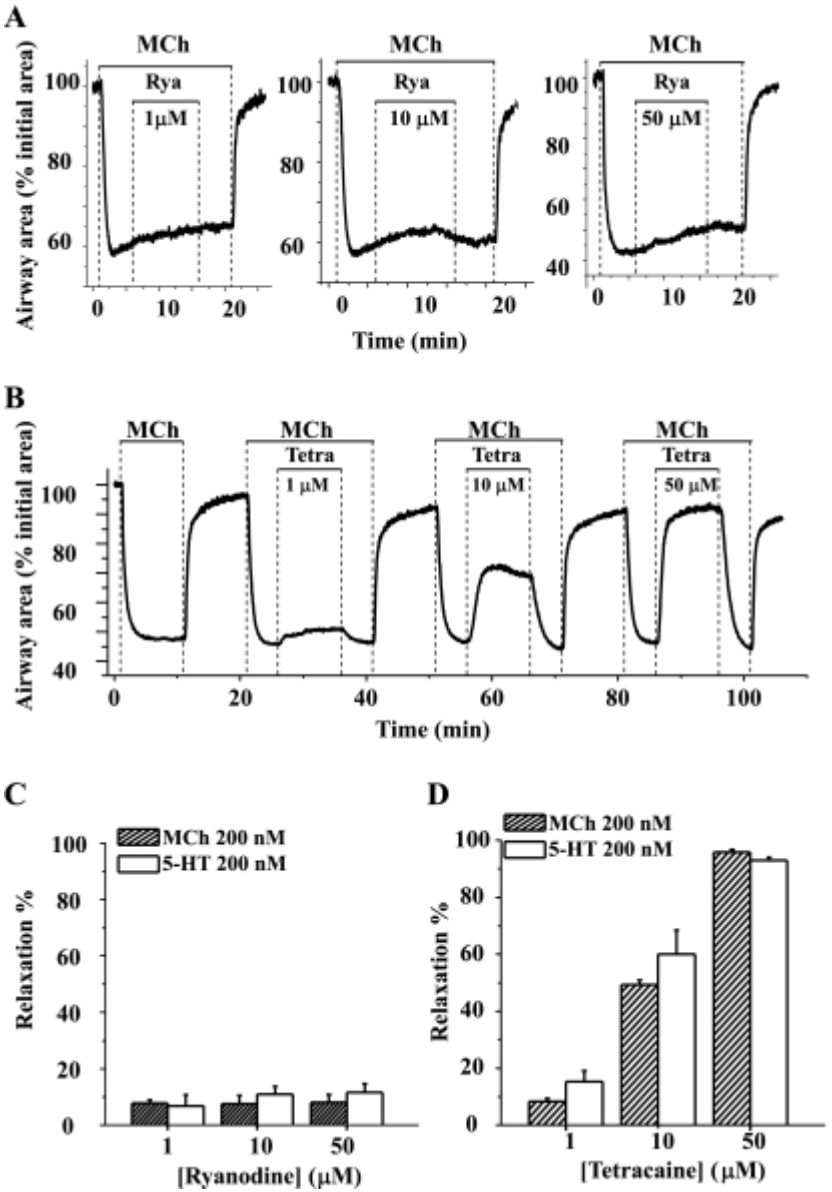

Effects of ryanodine and tetracaine on agonist-induced airway contraction.

ryanodine : inhibiteur/activateur des RyR

tétracaine: inhibiteur des RyR anesthésique local

analyse d'article

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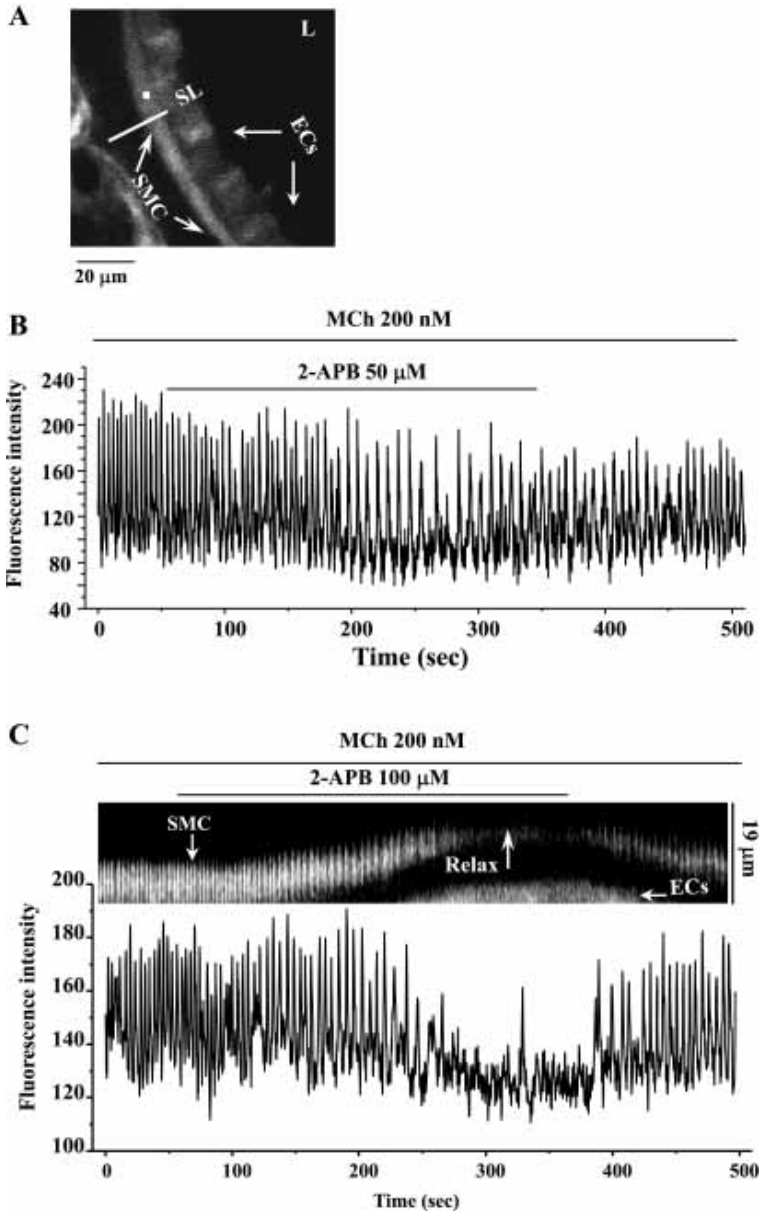

The effect of 2-APB on the Ca2+ signaling of airway smooth muscle cells (SMCs) induced by 200 nM MCh.

2-APB : inhibiteur des PIP3

analyse d'article

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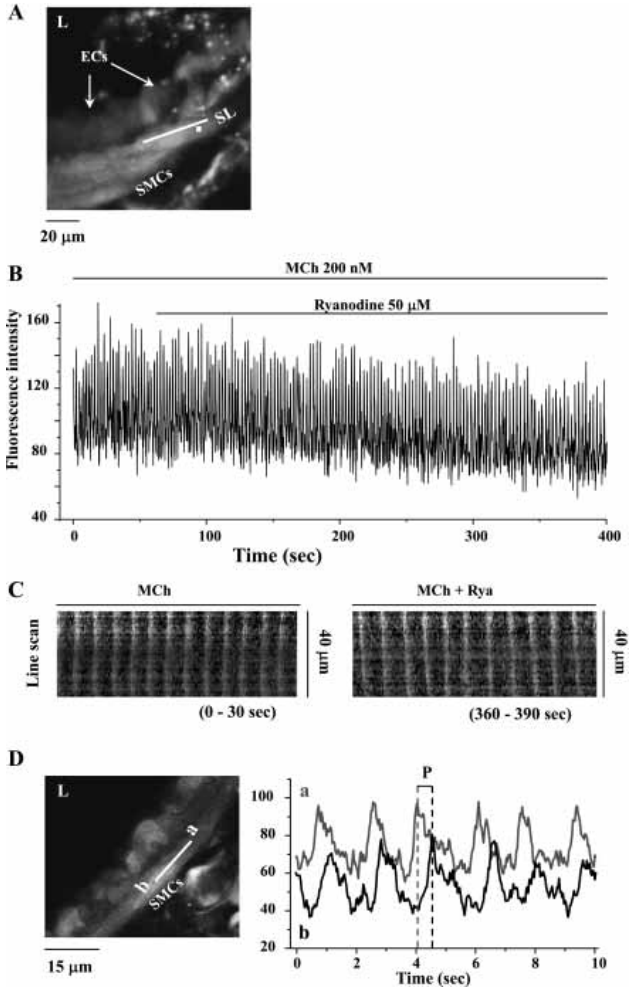

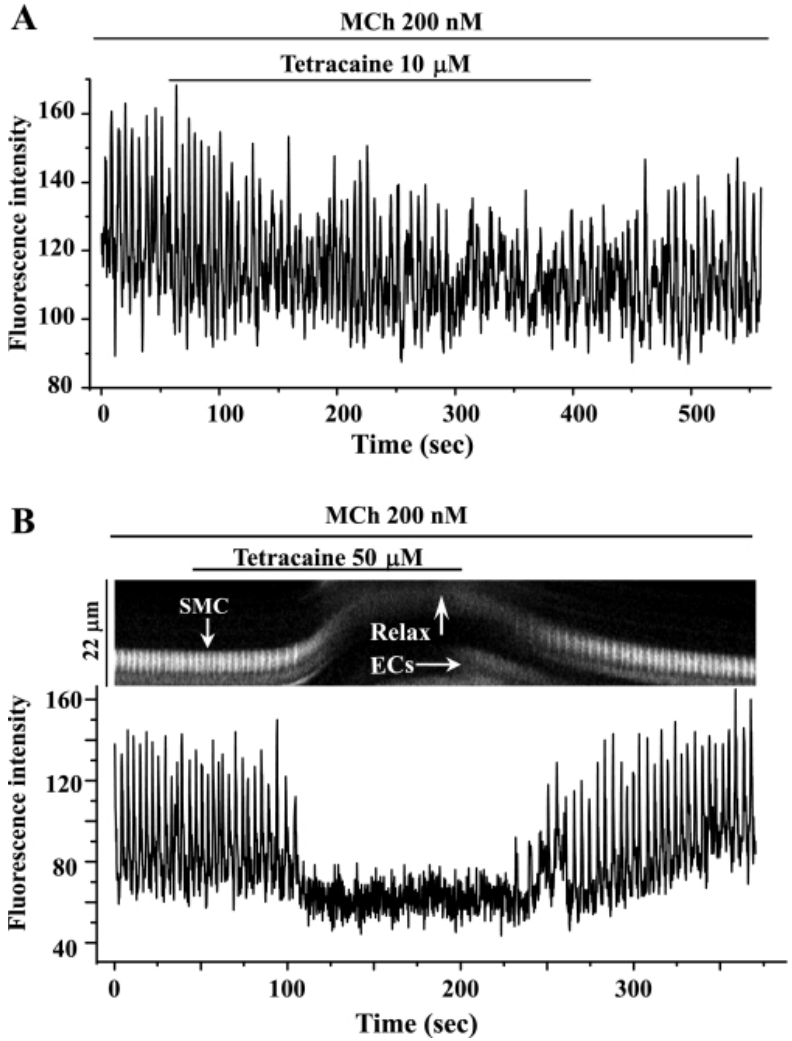

The effect of 50 μM ryanodine and tetracaine on Ca2+ signaling induced by MCh in airway SMCs.

analyse d'article

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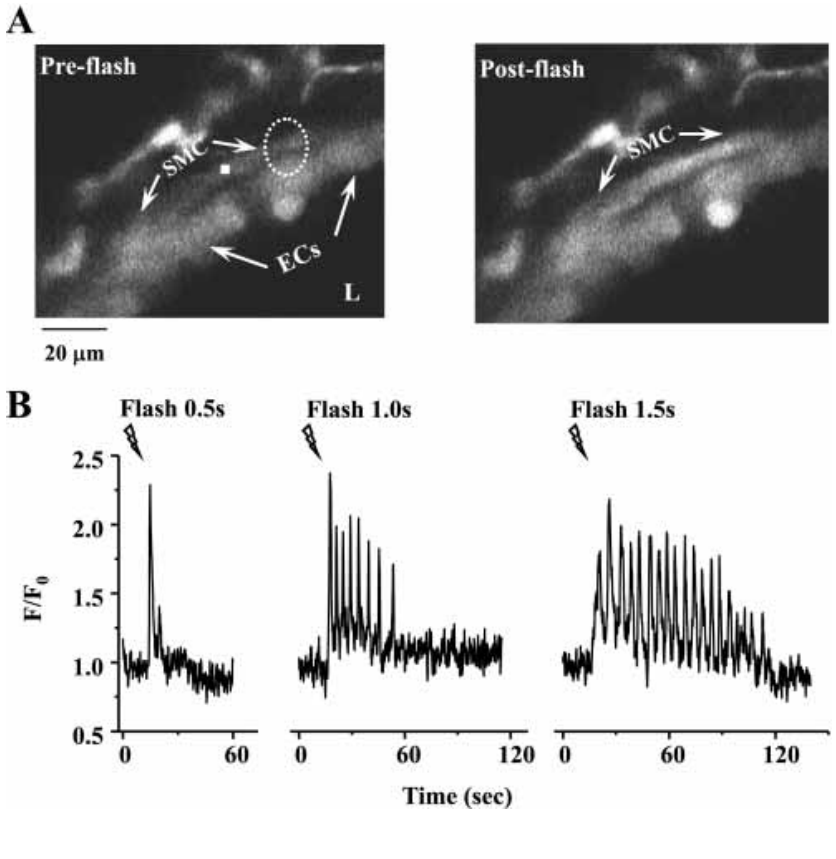

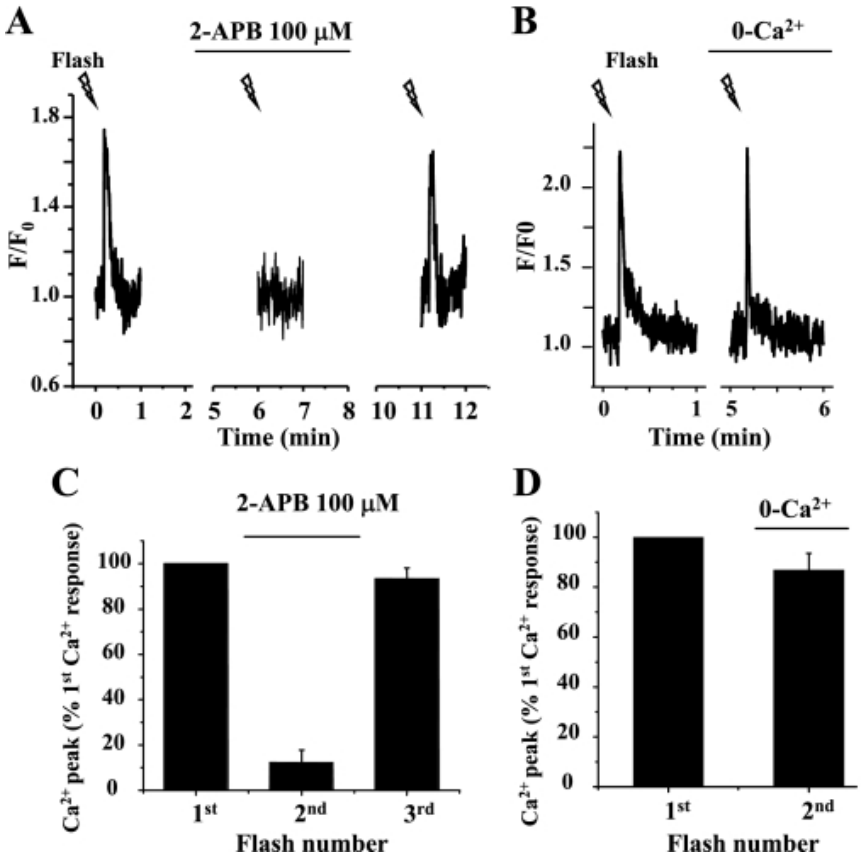

Effect of 2-APB on Ca2+ waves induced by the flash photolysis of caged-IP3.
2-APB : inhibiteur des PIP3

analyse d'article

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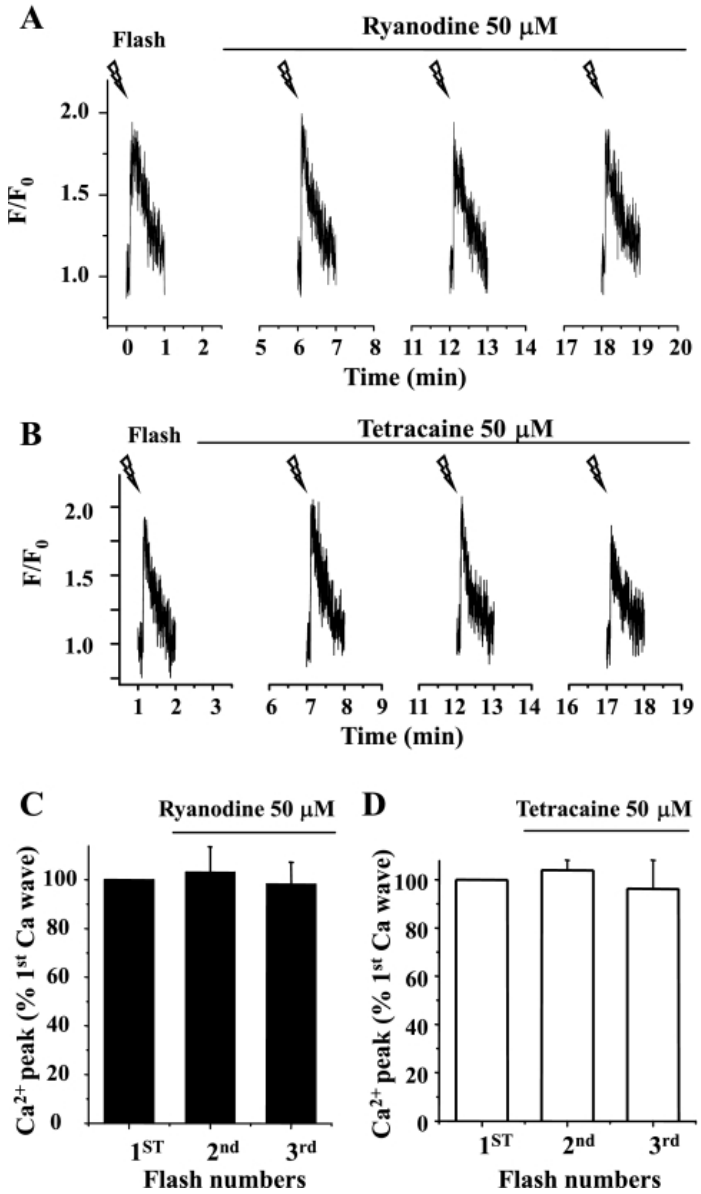

Effect of ryanodine and tetracaine on Ca2+ waves induced by flash photolysis of caged-IP3.

analyse d'article

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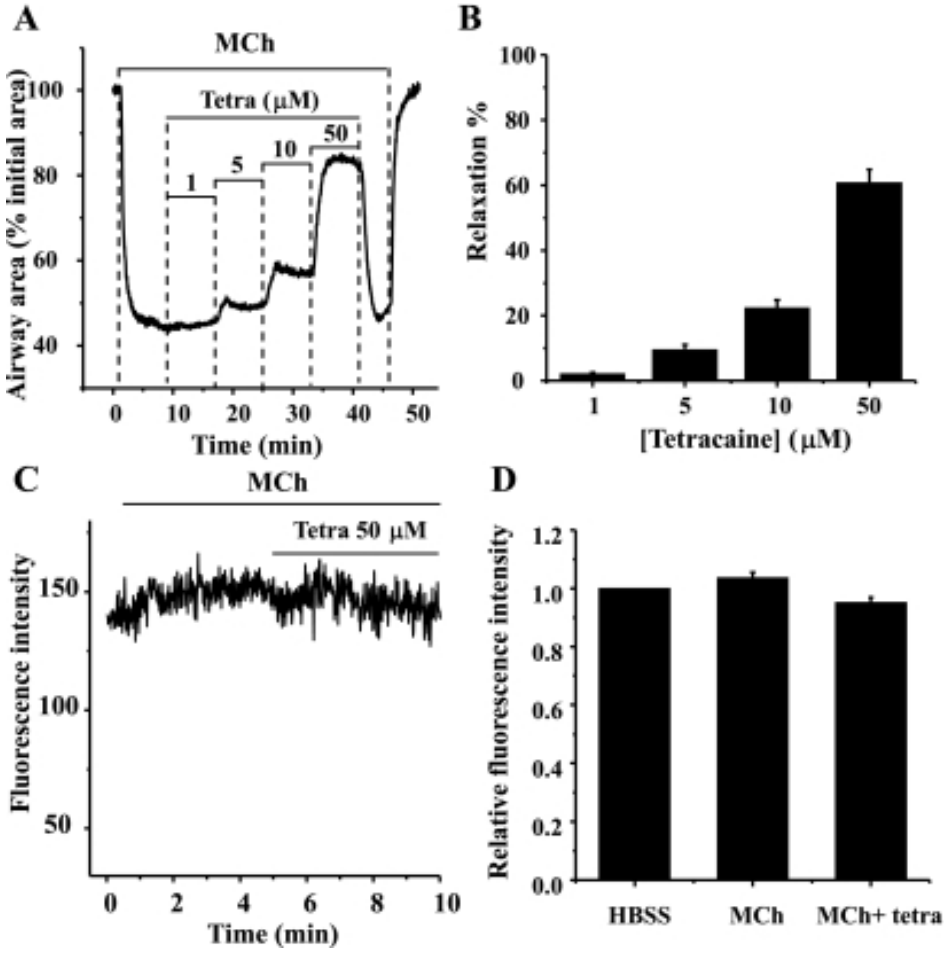

The effect of tetracaine on MCh-induced contraction and the [Ca2+]i of permeabilized airway SMCs.

Am J Physiol Lung Cell Mol Physiol. 2009 August; **297**(2): L347–L361

conclusion

These results indicate that agonist-induced Ca2+ oscillations in mouse small airway SMCs are primary mediated via IP3Rs and that tetracaine induces relaxation by both decreasing Ca2+ sensitivity and inhibiting agonist-induced Ca2+ oscillations via an IP3-dependent mechanism.