Adrenergic Stimulation-mediated Transepithelial Current from Human Endolymphatic Sac Epithelium

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INTRODUCTION

Endolymphatic sac has been thought to be an organ that is involved in the regulation of inner ear fluid volume and endolymphatic ion homeostasis. It is thought that the deterioration of ion transport in the endolymphatic sac can cause inner ear disorders such as Meniere's disease, enlarged vestibular aqueduct syndrome. Single epithelial cell layer of endolymphatic sac faces lumen of endolymphatic sac through which ion transport occurs between endolymph and interstitial space. So far, various ion channels such were identified in the luminal epithelial cells of endolymphatic sac using animal models, however, there is no studies using human tissue. In addition, no study has identified net physiologic transepithelial current in the endolymphatic sac epithelium. This study was performed to investigate characteristic of net physiologic current and identify specific ion dependent current from human endolymphatic sac (ES) epithelium. And we performed to investigate the modulation of transepithelial current from human endolymphatic sac (ES) epithelium by adrenergic stimulation.

METHODS

1. Harvesting endolymphatic sac

▪ Endolymphatic sac was harvested during translabyrinthine acoustic tumor removal. This study was approved by institutional review board of Severance Hospital.

2. Measuring transepithelial current

▪ Scanning vibrating electrode system (*Applicable Electronics, USA*)
▪ Tissue was folded luminal side facing outside for measuring current (Fig. 1)

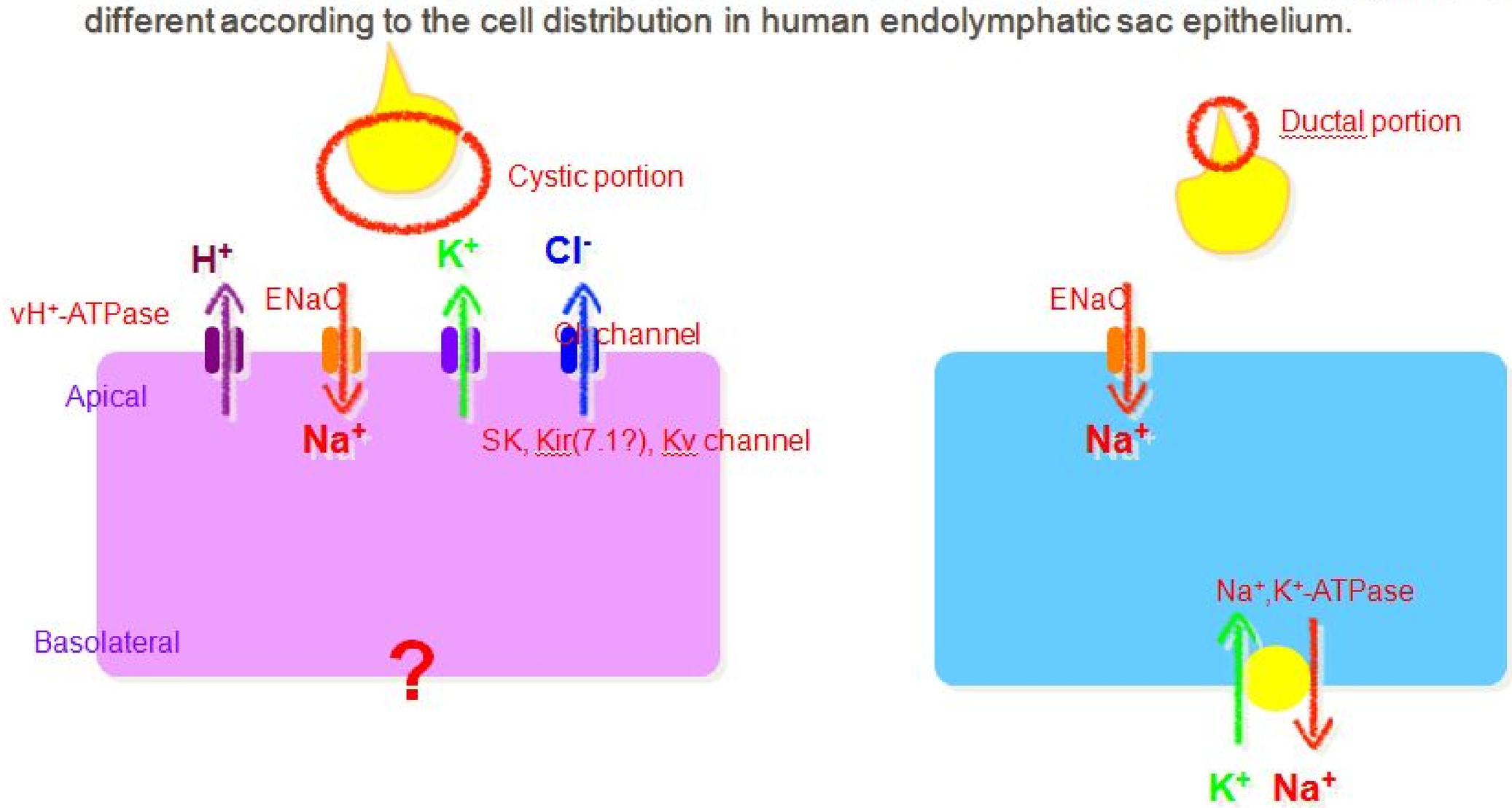
Figure 1. Example and principle of measuring transepithelial current using SVET

▪ The current was measured in the cystic portion and ductal portion of endolymphatic sac.
▪ Adrenergic stimulators [isoproterenol (10M) andepinephrine (100M)] for adrenergic stimulation were used for evaluation of each response.
▪ Specific ion channel blockers for Na^+ channels, K^+ channels, Cl^- channels were applied for identification of ion channels dependent on adrenergic stimulation.

RESULTS

1. Channel distribution in human endolymphatic sac

- Channel distribution is likely to be different in different cell types and net physiologic current is different according to the cell distribution in human endolymphatic sac epithelium.



2. Adrenergic stimulation in normal human ES

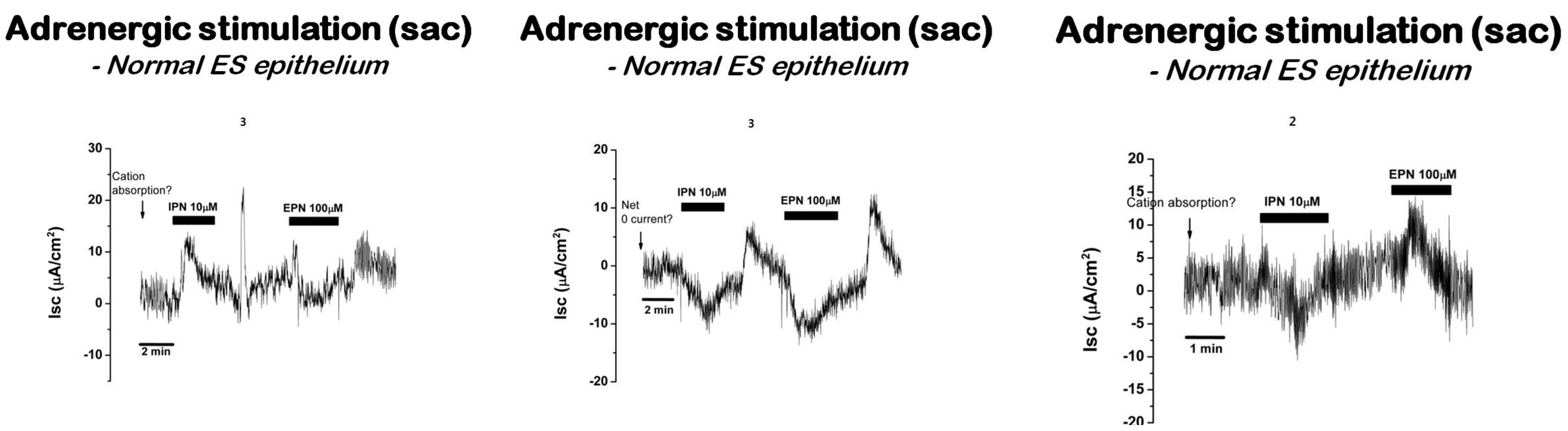


Figure 2. Changes of transepithelial current by adrenergic stimulation in human ES epithelium were various.

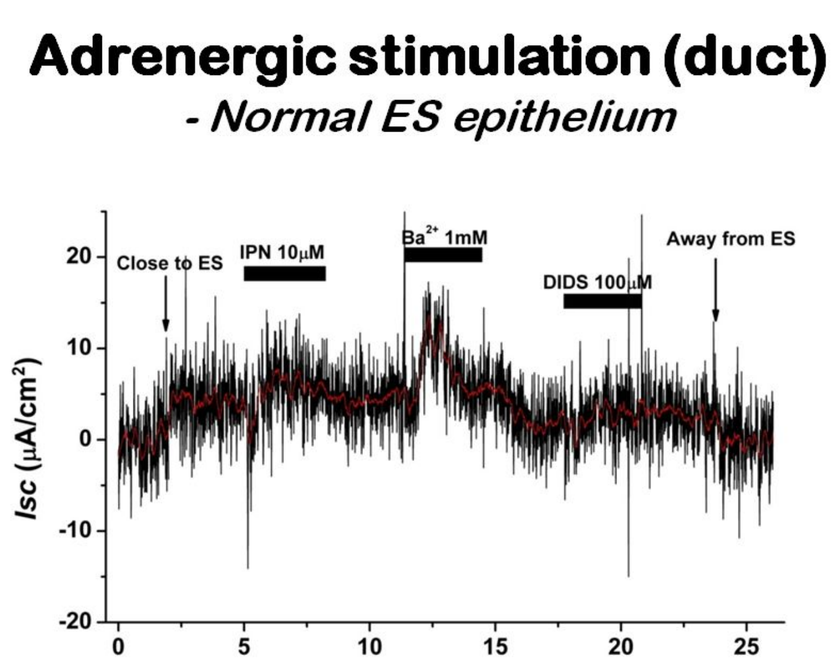


Figure 3. Transepithelial current was modulated by adrenergic stimulation in normal ES. Changes of transepithelial current by adrenergic stimulation were variable according to the area of ES

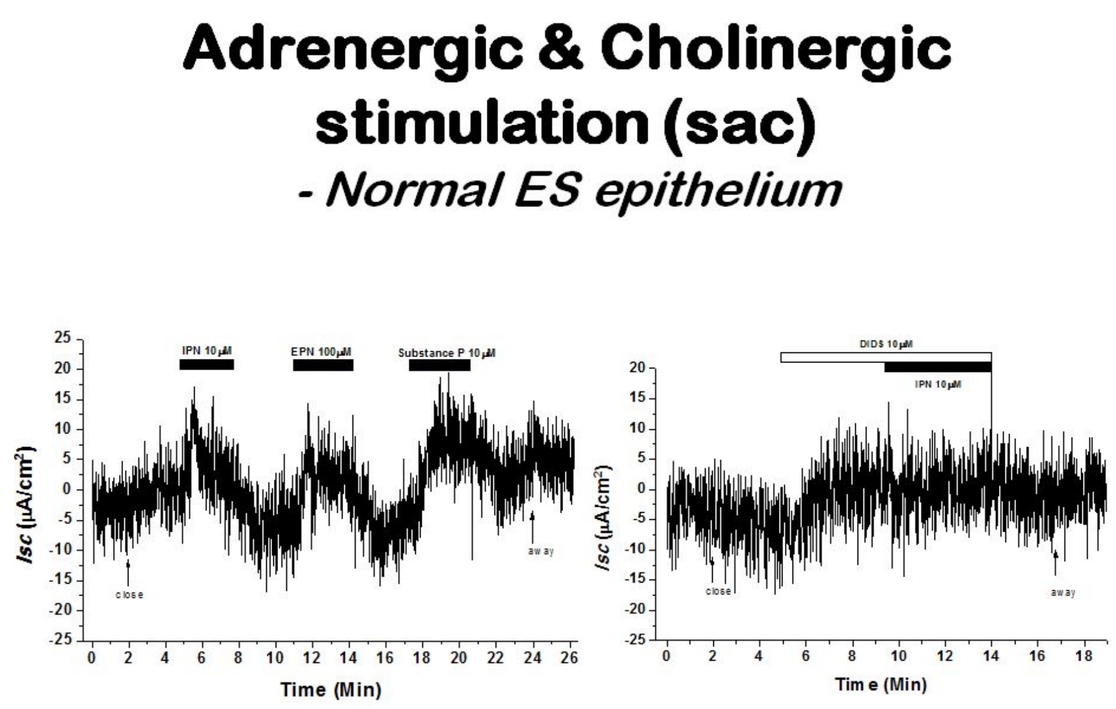


Figure 4. Transepithelial current was modulated by adrenergic & cholinergic stimulation in normal ES.

RESULTS

3. Identification of ion channels on adrenergic stimulation in normal human ES

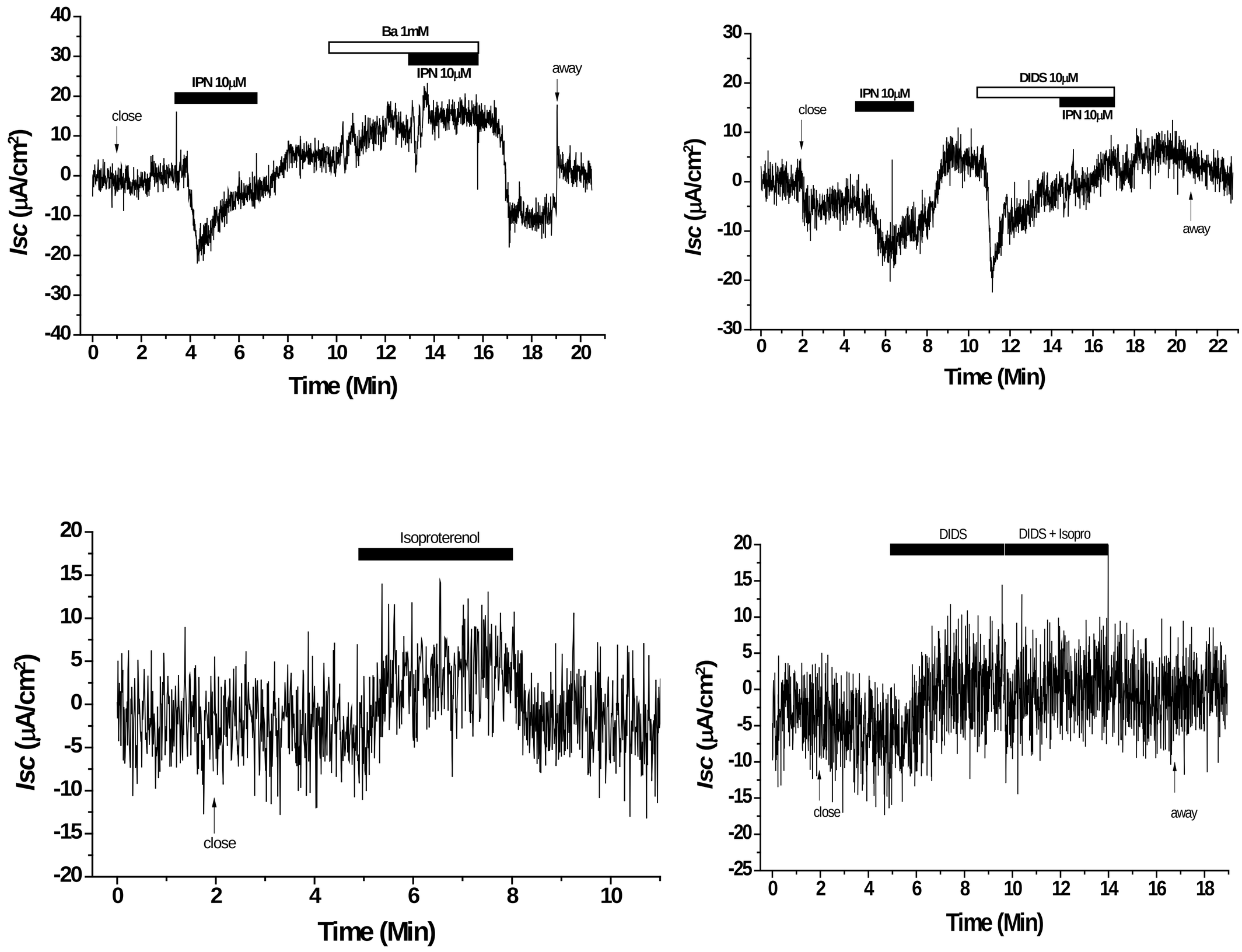


Figure 5. The isoproterenol-dependent cation absorption current, cation secretion current, and anion secretion current was blocked by Ba^{2+} (1mM), and DIDS (10M) in normal huma n ESs

4. Adrenergic stimulation in human ES of Meniere's disease patients

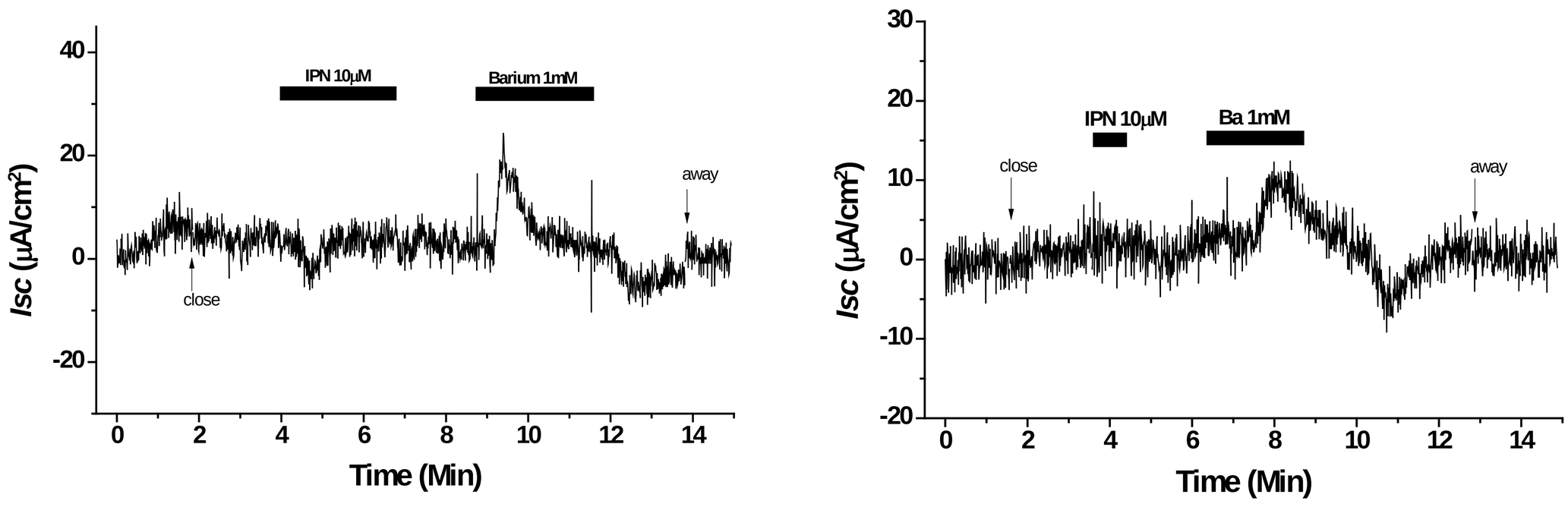


Figure 6. There was no effect of adrenergic stimulation(isoproterenol and epinep hrine) in ESs of Meniere's disease patients.

Summary & Conclusion

- Channel distribution is likely to be different in different cell types and net physiologic current is different according to the cell distribution in human endolymphatic sac epithelium.

- Ion transport in the endolymphatic sac epithelium is influenced by adrenergic stimulation.

- Transepithelial current in the ES of Meniere's disease patients was not likely to be changed by adrenergic stimulation.

- These results reflect that excessive stress-mediated adrenergic stimulati on in the inner ear can influence on the ion channel functions of inner ear epithelium, which can aggravate the symptoms of Meniere's disease by disturbing inner ear homeostasis.

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