News Release

Title

Coupling of functional and structural plasticities at the neuronal trigger zone

Key Points

○ Deprivation of auditory inputs switched dominant potassium channels at the axon initial segment from Kv1 to Kv7 in neurons of central auditory circuits.

○ Due to slow activation kinetics of Kv7, the switching enabled the neurons to generate action potentials more efficiently.

○ The functional plasticity of the axon initial segment would compensate for the loss of auditory inputs and maintain auditory circuits after hearing loss.

Summary

Professor Hiroshi Kuba at Cell Physiology in Nagoya University Graduate School of Medicine (Dean: Masahide Takahashi, M.D., Ph.D.) revealed a new form of neuronal plasticity at the axon initial segment (AIS).

The AIS is a neuronal compartment involved in initiation of action potentials (APs), and is the key in understanding regulation of activity in the brain. Recently, it was revealed that the AIS is the site of structural plasticity and contributes to homeostatic regulation of neuronal activity. We here extend this observation and demonstrate for the first time that the AIS plasticity is not limited to the structural changes, but also occurs as changes in ion-channel expressions at the site. We found in neurons of avian cochlear nucleus that auditory deprivation caused subtype-specific changes in voltage-gated K^+ channels in parallel with an elongation of the AIS; Kv1 decreased, while Kv7 increased, showing a complementary change in their expressions at the AIS. Importantly, Kv1 has rapid kinetics and is activated strongly with depolarization, while Kv7 has slow kinetics and behaves rather like passive conductance. Indeed, this slow kinetics of Kv7 reduced shunting conductance during AP initiation, enabling the elongated AIS to trigger APs more efficiently. Thus, these structural and biophysical reorganizations of the AIS worked cooperatively to compensate for the loss of auditory nerve activity and play a role in preservation of auditory circuits after hearing loss. Our findings not only emphasize the importance of synergistic control of structure and function of the AIS, but propose a new concept on neural plasticity and open a new possibility of activity regulation in the brain. Given that cell-specific differentiation of the AIS is widely observed in the brain, the brand-new form of AIS plasticity could be a universal mechanism for regulating excitability of neurons.

This work was published online in Nature Communications on Nov. 19, 2015.

Research Background

The axon initial segment (AIS) is a neuronal compartment involved in initiation of action potentials (APs), and is the key in understanding regulation of activity in the brain. Recently, it was revealed that the AIS is the site of structural plasticity and contributes to homeostatic regulation of neuronal activity. We here extend this observation and demonstrate for the first time that the AIS plasticity is not limited to the structural changes, but also occurs as changes in ion-channel expressions at the site. Moreover, these structural and functional changes were effectively coupled and enabled efficient control of neuronal activity.

Research Results

We made immunohistochemistry and electrophysiology in neurons of avian cochlear nucleus, and found that auditory deprivation caused subtype-specific changes in voltage-gated K^+ channels in parallel with an elongation of the AIS; Kv1 decreased, while Kv7 increased, showing a complementary change in their expressions at the AIS. Importantly, Kv1 has rapid kinetics and is activated strongly with depolarization, while Kv7 has slow kinetics and behaves rather like passive conductance. Indeed, computer simulation revealed that this slow kinetics of Kv7 reduced shunting conductance at the AIS during AP initiation, enabling the elongated AIS to trigger APs more efficiently. Thus, these structural and biophysical reorganizations of the AIS worked cooperatively to compensate for the loss of auditory nerve activity and play a role in preservation of auditory circuits after hearing loss.

Research Summary and Future Perspective

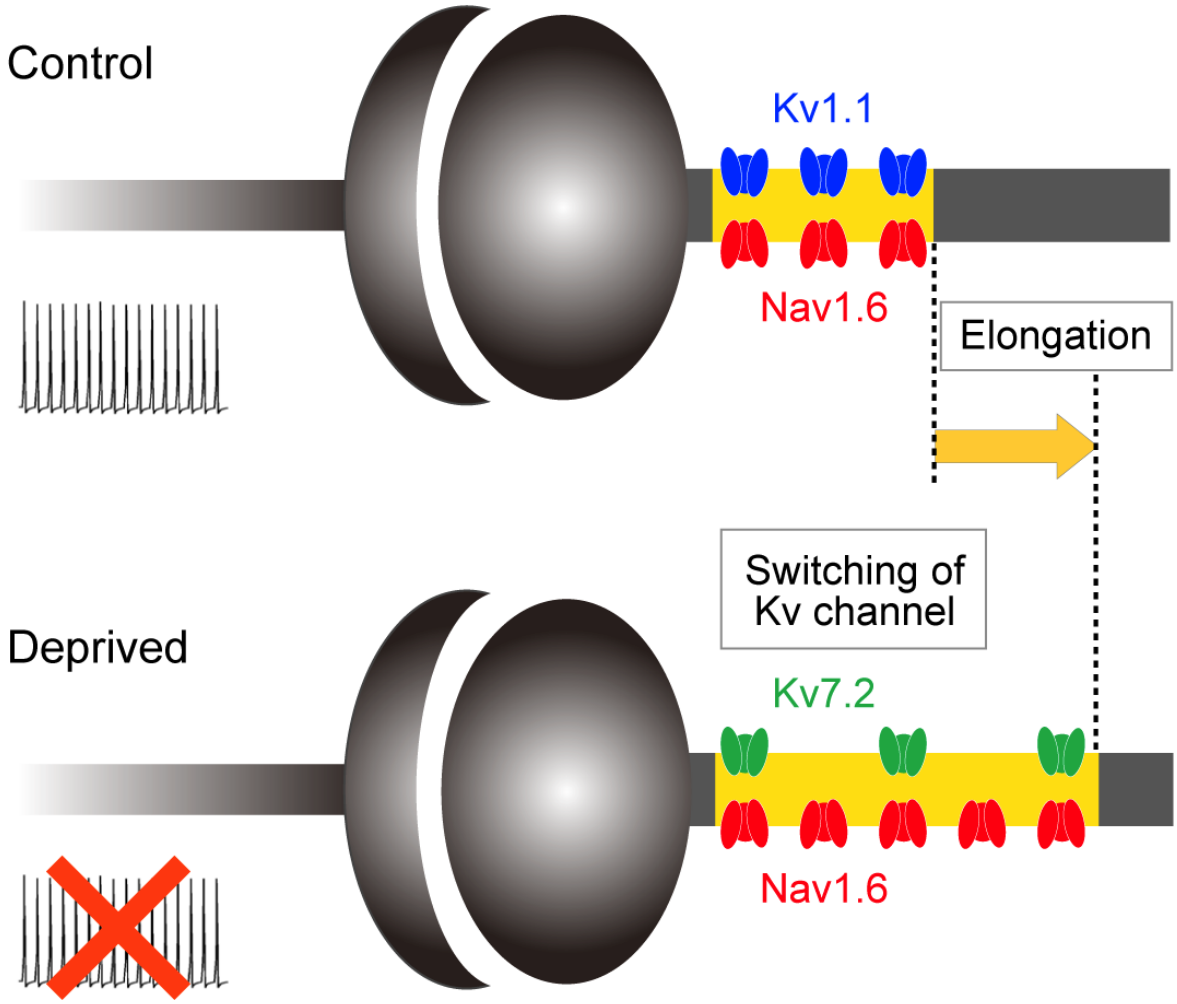
Our findings not only emphasize the importance of synergistic control of structure and function of the AIS, but propose a new concept on neural plasticity and open a new possibility of activity regulation in the brain. Given that cell-specific differentiation of the AIS is widely observed in the brain, the brand-new form of AIS plasticity could be a universal mechanism for regulating excitability of neurons.

Article

Kuba H, Yamada R, Ishiguro G, Adachi R.
Redistribution of Kv1 and Kv7 enhances neuronal excitability during structural axon initial segment plasticity.
Nature Communications 2015; DOI: 10.1038/NCOMMS9815 (November 19, 2015, online)

Japanese ver.

http://www.med.nagoya-u.ac.jp/medical/dbps_data/_material_/nu_medical/_res/topix/2015/Kv7_20151119jp.pdf


Control
Kv1.1
Nav1.6
Elongation
Switching of
Kv channel
Deprived
Kv7.2
Nav1.6