

Introduction

Signal processing in first- and second-order vestibular neurons

Kenna D. Peusner

Department of Anatomy and Regenerative Biology, The George Washington University Medical Center, 2300 I Street NW, Washington, DC, USA

Tel.: +1 202 994 3489; Fax: +1 202 994 8885; E-mail: anakdp@gwumc.edu

This symposium was held in Anaheim California, on February 8, 2010, at the 33rd annual Midwinter Meeting of the Association for Research in Otolaryngology (ARO). The meeting program and abstracts are published online (<http://aro.org/abstracts/abstracts.html>). Organized by Jay Goldberg and Kenna Peusner, the symposium was directed toward clinicians who want to bridge the gap between basic science and treating patients for vestibular disorders, vestibular neuroscientists using structural and functional approaches to understand the labyrinth and its central pathways at the system, cellular, and molecular levels, and auditory neuroscientists intrigued by the similarities and differences in signal processing in the two systems. This special issue contains those presentations on signal processing in second-order vestibular neurons and their connections. The articles underwent peer-review for this special issue. We would like to thank the Journal of Vestibular Research for the production of this special issue devoted to the symposium.

The vestibular system demonstrates a remarkable plasticity in response to changing environmental demands [9] and to recover function after pathologies affecting the peripheral vestibular receptors on one side [16]. Second-order vestibular neurons are characterized by a high degree of plasticity in their connections with first-order vestibular neurons and non-labyrinthine inputs (for review, see [20]). As demonstrated in this symposium, recent research has been directed toward defining synaptic transmission and ionic

conductances involved in signal processing from the vestibular periphery to the first brain centers located in the vestibular nuclei. The experiments utilize multiple structural and functional approaches performed on intact animals, isolated vestibular circuits in culture, or brain slice preparations.

The article by Beraneck and Straka entitled “Vestibular Signal Processing by Separate Sets of Neuronal Filters” reviews recent research on detecting static head position and head motion by the peripheral vestibular receptors and the activation of specific receptor areas by high or low frequency movements during locomotion. Vestibular nerve afferents convey the different dynamics of head motion in a wide range of frequencies to second-order vestibular neurons, which are equipped dynamically to process the signals [18]. From the firing patterns generated by second-order vestibular nuclei neurons, the authors propose that there are two different populations of vestibular nuclei neurons that process high or low frequency signals within two separate pathways [19]. Tonic-firing vestibular nuclei neurons process low frequency signals, and are well-suited for synaptic integration, whereas phasic-firing vestibular nuclei neurons process high frequency signals and are designed to detect events. This dual system may underlie the ability of the brain to distinguish between tilt and linear translation, or self-induced motion and passive body movements (for review, see [1]). Finally, differences in the dynamic properties between frog and mammalian vestibular nuclei neurons are discussed in relation to species-specific locomotor patterns.

The article by Popratiloff et al. entitled, “Expression of Glutamate Receptors and Potassium Channels in Vestibular Nuclei Neurons During Development of Signal Processing” is a review of developmental changes in AMPA receptor subunits, GluR1-GluR4 [12], and the expression of dendrotoxin (DTX)-sensitive, low threshold, potassium channels (Kv1) in a morphologically distinct class of VOR neurons, the principal cells of the chick tangential nucleus, in the late-term embryo (E16) [3] and hatchling chicken (H1-H9) [4,16]. In studies of AMPA receptor subunit immunolabeling using confocal imaging, hatchling principal cells express higher levels of GluR4 that are capable of generating fast excitatory postsynaptic events. This result is supported by recording faster kinetics of spontaneous synaptic events in hatchling compared to embryonic principal cells [15]. In addition, Kv1 expression in principal cell bodies decreases after hatching [11], consistent with recording decreased DTX-sensitive potassium conductance and greater excitability of principal cells to depolarizing stimuli after hatching. Finally, Kv1 channels relocate to different cellular compartments after hatching, which must contribute to the changing pattern of evoked spike firing recorded in principal cells and their presynaptic inputs. Altogether, these developmental changes in ionic conductances allow the principal cells to respond to presynaptic inputs more rapidly and precisely after birth.

In the article by Kolkman et al., “Intrinsic Physiology of Identified Neurons in the Prepositus Hypoglossi and Medial Vestibular Nuclei” experiments are presented to determine if the intrinsic membrane properties of NPH and MVN neurons differ according to neurotransmitter phenotype and/or axonal connections. Like a subset of MVN neurons, some NPH neurons process signals concerned with head and eye movements during VOR activity and send axons to the oculomotor nuclei (for review, see [6]). Most of the experiments described are performed on three transgenic mouse lines that express green fluorescent protein to identify three subtypes, either GABAergic neurons only, glutamatergic and glycinergic neurons, or glycinergic neurons only. Two separate sets of experiments are performed. In the first set, recordings are obtained from NPH neurons in brain slice preparations and the results compared to previously published data on MVN neurons from the same [2,5] and other laboratories [8,17]. In the second set of experiments, dextran crystals are injected into the high cervical spinal cord or caudal medulla of transgenic mice to determine the neurotransmitter phenotypes of the dextran-labeled MVN neurons and

record from them. The intrinsic membrane properties recorded from vestibulospinal neurons situated in the MVN are compared to recordings from MVN neurons that project to the oculomotor nucleus, which were published previously from the same laboratory [14]. The Authors conclude that a graded expression of ion channels likely exists among different MVN and NPH neuron classes, but differential tuning of the intrinsic membrane properties in different classes of MVN and NPH neurons allows them to perform their specific functions.

Normally, body movements and postural adjustments detected by the vestibular system produce rapid cardiovascular changes. The compensatory adjustments in blood pressure due to signaling within the vestibulo-sympathetic reflex pathway during postural adjustments enable humans to stand up without losing consciousness, known as orthostatic tolerance (for review [22]). These changes are mediated by functional integration of peripheral and central vestibular signals in blood pressure control centers located in the ventrolateral medulla oblongata. Holstein et al. in an article entitled, “Anatomical Observations of the Caudal Vestibulo-Sympathetic Pathway” reviews the neuroanatomical connections of the system and neurotransmitter phenotypes of neurons in the circuitry. Briefly, neurons in caudal portions of the vestibular nuclear complex, including the MVN and inferior vestibular nucleus, produce monosynaptic and polysynaptic inputs to caudal brainstem centers involved in regulating sympathetic outflow [23]. The caudal brainstem centers include multiple nuclear groups, with the rostral (RVLM) and caudal ventrolateral medullary regions (CVLM) the focus of this review. RVLM contains the glutamatergic bulbospinal neurons [10], which receive monosynaptic GABAergic inputs from CVLM [7] and send their axons to preganglionic sympathetic neuron in the spinal cord (e.g. [13]). Finally, the article reviews the immunolabeling data on the presence of glutamate, GABA, catecholamines, and the newly recognized modulator, imidazoleacetic acid-ribotide, in the RVLM.

References

- [1] D.E. Angelaki and K.E. Cullen, Vestibular system: the many facets of a multimodal sense, *Annu Rev Neurosci* **31** (2008), 125–150.
- [2] M.W. Bagnall, L.E. McElvain, M. Faulstich and S. du Lac, Frequency-independent synaptic transmission supports a linear vestibular behavior, *Neuron* **60** (2008), 343–352.

- [3] G. Gamkrelidze, C. Giaume and K.D. Peusner, The differential expression of low-threshold sustained potassium current contributes to the distinct firing patterns in embryonic central vestibular neurons, *J Neurosci* **15** (1998) 1449–1464.
- [4] G. Gamkrelidze, C. Giaume and K.D. Peusner, Firing properties and dendrotoxin-sensitive sustained potassium current in vestibular nuclei neurons of the hatchling chick, *Exp Brain Res* **134** (2000), 398–401.
- [5] A.H. Gittis and S. du Lac, Firing properties of GABAergic versus non-GABAergic vestibular nucleus neurons conferred by a differential balance of potassium currents, *J Neurophysiol* **97** (2007), 3986–3996.
- [6] S.M. Highstein and G.R. Holstein, The anatomy of the vestibular nuclei, *Prog Brain Res* **151** (2006), 157–203.
- [7] G.R. Holstein, G.P. Martinelli, S.C. Henderson, V.L.J. Friedrich, R.D. Rabbitt and S.M. Highstein, Gamma-aminobutyric acid is present in a spatially discrete subpopulation of hair cells in the crista ampullaris of the toadfish, *Opsanus tau*, *J Comp Neurol* **471** (2004), 1–10.
- [8] E. Idoux, M. Serafin, P. Fort, P.P. Vidal, M. Beraneck, N. Vibert, M. Muhlethaler and L.E. Moore, Oscillatory and intrinsic membrane properties of guinea pig nucleus prepositus hypoglossi neurons *in vitro*, *J Neurophysiol* **96** (2006), 175–196.
- [9] G. Mandl, G. Melvill Jones and M. Cynader, Adaptability of the vestibulo-ocular reflex to vision reversal in strobe reared cats, *Brain Res* **209** (1981), 35–45.
- [10] S.F. Morrison, Glutamate transmission in the rostral ventrolateral medullary sympathetic premotor pathway, *Cell and Mol Neurobiol* **23** (2003), 761–772.
- [11] A. Popratiloff, C. Giaume and K.D. Peusner, Developmental change in expression and subcellular localization of two Shaker-related potassium channel proteins (Kv.1 and Kv1.2) in the chick tangential vestibular nucleus, *J Comp Neurol* **461** (2003), 466–482.
- [12] A. Popratiloff, Y.-X. Wang, J. Narvid, C. Giaume, R.S. Petralia and K.D. Peusner, AMPA receptor subunit expression in chick vestibular nucleus neurons, *J Neurosci Res* **76** (2004), 662–677.
- [13] C.A. Ross, D.A. Ruggiero, T.H. Joh, D.H. Park and D.J. Reis, Rostral ventrolateral medulla: selective projections to the thoracic autonomic cell column from the region containing C1 adrenaline neurons, *J Comp Neurol* **228** (1984), 168–185.
- [14] C. Sekirnjak and S. du Lac, Physiological and anatomical properties of mouse medial vestibular nucleus neurons projecting to the oculomotor nucleus, *J Neurophysiol* **95** (2006), 3012–3023.
- [15] M. Shao, J.C. Hirsch, C. Giaume and K.D. Peusner, Spontaneous synaptic activity in chick vestibular nucleus neurons during the perinatal period, *Neuroscience* **127** (2004), 81–90.
- [16] M. Shao, A. Popratiloff, J. Yi, A. Lerner, J.C. Hirsch and K.D. Peusner, Adaptation of chicken vestibular nucleus neurons to unilateral vestibular ganglionectomy, *Neuroscience* **161** (2009), 988–1007.
- [17] M. Shino, S. Ozawa, N. Furuya and Y. Saito, Membrane properties of excitatory and inhibitory neurons in the rat prepositus hypoglossi nucleus, *Eur J Neurosci* **27** (2008), 2413–2424.
- [18] H. Straka and N. Dieringer, Basic organization principles of the VOR: lessons from frogs, *Prog Neurobiol* **73** (2004), 259–309.
- [19] H. Straka, M. Beraneck, M. Rohregger, L.E. Moore, P.P. Vidal and N. Vibert, Second-order vestibular neurons form separate populations with different membrane and discharge properties, *J Neurophysiol* **92** (2004), 845–861.
- [20] H. Straka, N. Vibert, P.P. Vidal, L.E. Moore and M.B. Dutia, Intrinsic membrane properties of vertebrate vestibular neurons: function, development and plasticity, *Prog Neurobiol* **76** (2005), 349–392.
- [21] C. Sekirnjak and S. du Lac, Physiological and anatomical properties of mouse medial vestibular nucleus neurons projecting to the oculomotor nucleus, *J Neurophysiol* **95** (2006), 3012–3023.
- [22] B.J. Yates and A.M. Bronstein, The effects of vestibular system lesions on autonomic regulation: Observations, mechanisms, and clinical implications, *J Vest Res* **15** (2005), 119–129.
- [23] B.J. Yates, L. Grélot, I.A. Kerman, C.D. Balaban, J. Jakus and A.D. Miller, Organization of vestibular inputs to nucleus tractus solitarius and adjacent structures in cat brain stem, *Am J Physiol* **267** (1994), R974–R983.