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CORTICOFUGAL GATING OF THE AUDITORY THALAMUS

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The corticofugal projection of the auditory system is believed to play a crucial role in tuning our attention to certain sound while filtering the unwanted noise. With the use of *in vivo* extracellular recording techniques, we revealed that the corticofugal projection exerted point-to-point modulatory effects on medial geniculate body (MGB) neurons of anesthetized guinea pigs. That both the temporal firing pattern and onset responses to sound were modified by electrical stimulation of the auditory cortex suggest that the corticofugal projection could sharpen the ascending auditory information. Further, our immunohistochemical findings that dense Fos-labeled neurons in the ventral division of the MGB were found only after both administration to the auditory cortex with bicuculline, an agent known to releasing intracortical inhibition, and presentation of acoustic stimulus, but not with the latter alone suggest that the transmission of ascending thalamocortical information, especially for attentive purpose, is critically governed by corticofugal modulation. Our *in vivo* intracellular recording data further demonstrated that the majority of neurons in the lemniscal component of the MGB showed acoustic-evoked depolarization as well as a facilitatory response to electrical stimulation of the auditory cortex. On the other hand, the majority of non-lemniscal MGB neurons showed acoustic-evoked hyperpolarization and received an inhibitory corticofugal input. These suggest that corticofugal projections amplified the matched ascending auditory information via the lemniscal MGB but switched off the non-lemniscal MGB so as to prepare the auditory cortex for sole processing of auditory information via the lemniscal route. Fading of this input from the auditory cortex might therefore relieve the inhibition on the non-lemniscal MGB, leading to a shift of attention across sensory modalities. (Supported in part by HK RGC grants)

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DEVELOPMENTALLY REGULATED EXPRESSION OF TONEBP AND UREA TRANSPORTER-A IN KIDNEY

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Osmolality in the mammalian kidney medulla is very high. Although increases in salt and urea both lead to hyperosmolality, only increased salt concentration causes hypertonicity. Hypertonicity in the medullary interstitium created by the high concentration of salt is an important local signal for the renal medulla. The hypertonicity stimulates the transcription factor tonicity responsive enhancer binding protein (TonEBP). TonEBP stimulates genes whose products drive cellular accumulation of organic osmalytes and HSP70, which protect cells from the deleterious effects of hypertonicity and urea, respectively. Genetically modified mice with deficiency in TonEBP in the kidney display severe atrophy in the renal medulla because cells fail to adapt to hypertonicity. Recent studies suggest that TonEBP is a major regulator in the urinary concentration. TonEBP directly stimulates transcription of aquaporin-2 indicating that it contributes to the water permeability of the collecting duct independent of vasopressin. In addition, TonEBP stimulates the promoter of UT-A1/3 that provide the urea permeability in the inner medullary collecting duct (IMCD). In the kidneys of TonEBP knockout mice, expression of UT-A1 and UT-A2 is reduced indicating that UT-A2 in the descending thin limb is also a target of TonEBP in addition to UT-A1. Mice deficient in either UT-A1/3 or UT-A2 display reduced urea accumulation in the renal medulla. Thus, TonEBP appears to be a key regulator in the counter current urea recycling that leads to the massive accumulation urea in the papilla. In order to explore the relationship between the hypertonicity in the renal medulla created by Na-K-2Cl cotransporter type 2 (NKCC2) and response of TonEBP and its target genes in the context of development of the urinary concentrating ability, we examined their expression in developing mouse and rat kidneys. We find that the expression of NKCC2 precedes TonEBP, which, in turn, is followed by expression of its target genes AR and UT-A during the renal development. Treatment of neonatal animals with furosemide dramatically reduced expression of TonEBP, AR, and UT-A1. The sequential expression of NKCC2, TonEBP, and its targets AR and UT-A, and reduced expression TonEBP and its targets in response to furosemide treatment support the hypothesis that local hypertonicity produced the activity of NKCC2 activates TonEBP during development, and is an important signal for the medullary accumulation of urea.