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# *Abstract*

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| **Grant Number:** | 5R01DC004199-02 |
| **PI Name:** | KANDLER, KARL |
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| **PI Title:** | |
| **Project Title:** | DEVELOPMENT OF NEURONAL CIRCUITS IN THE AUDITORY SYSTEM |

**Abstract:** DESCRIPTION (Adapted From The Applicant's Abstract): The long-term objective of this research is to understand the cellular mechanisms by which neuronal activity exerts its effects on the formation, reorganization, and stabilization of precisely organized neuronal connections. The aim of the proposed project is to elucidate these mechanisms in the development of tonotopically organized, converging excitatory and inhibitory connections in the auditory brainstem of mammals. Focus will be on the lateral superior olivary nucleus (LSO), a binaural nucleus involved in sound localization, in which tonotopically organized ipsilateral and contralateral glycinergic inputs converge on single cells. Previous studies have shown that glycine and GABA, the inhibitory neurotransmitter in the adult system, are depolarizing in the developing LSO when inhibitory connections are being refined. The applicant will test the hypothesis that the depolarizing action of these inhibitory neurotransmitters represents a novel cellular mechanism for activity-dependent refinement of developing inhibitory synapses. They will use an in vitro brainstem slice preparations from pre- and postnatal rats to determine 1) whether the depolarizing neurotransmitters glycine and GABA increase intracellular calcium concentration in developing LSO neurons, 2) whether depolarizing inhiitory synapses act like excitatory synapses, 3) whether refinement of inhibitory connections in the LSO involves the elimination of functional synapses, and 4) whether depolarizing inhibitory connections in the LSO can express activity-dependent changes in synaptic strength such as LTP and LTD. To achieve these specific aims whole-cell and perforated patch clamp recordings will be combined with single cell tracing, calcium imaging and fast, localized photolytic cleavage of neurotransmitters (photostimulation). The experiments will be important for understanding how neuronal activity participates in the formation and reorganization of auditory circuits involved in sound localization. The proposed research may provide new insights into human communication disorders such as speech perception, specific language impairment and dyslexia that result from impaired auditory processing and that likely have developmental components. Understanding the basic cellular mechanisms that rule the development and plasticity of inhibitory circuits is fundamental for understanding the cause of numerous pathological brain states, including epilepsy, that result from an abnormal organization of

inhibitory circuits.

**Thesaurus Terms:**
auditory pathway, developmental neurobiology, neuroanatomy, neurophysiology, olivary body
calcium flux, gamma aminobutyrate, glycine, neurotransmitter metabolism, sound perception, synapse
laboratory rat, voltage /patch clamp

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| **IRG:** | ZRG1 |