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FUNCTIONAL PROPERTIES AND MOLECULAR MACHINERY UNDERLYING OXYTOCIN RELEASE

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EXCELE SEVERO OCHOA

RESEARCH QUESTION AND RATIONALE

How are OXT-vesicles released in the hypothalamus?

The neuropeptide oxytocin (OXT) mediates numerous homeostatic functions as well as complex behaviors, such as social interaction, which is commonly associated with the hypothalamus as the main source of OXT. Despite its importance, the regulatory mechanisms underlying the release of oxytocin from the distal hypothalamus in the central nervous system is classical neurotransmission. However, recent evidence for the presynaptic release of OXT from the same cell clusters of hypothalamic neurons within a few hours before the second trimester, suggesting the participation of a novel synaptic vesicle (SV). Our study aims to investigate the dynamic properties of hypothalamic OXT-releasing neurons, as a first step to understanding OXT-release, in the synaptic transmission, and ultimately the regulatory machinery that controls OXT release.

WORKING HYPOTHESIS: OXT-releasing neurons from the embryonic ventral part of hypothalamus require a specific membrane machinery, distinct from the one involved in SVs.

METHODOLOGY

Assaying OXT dynamic and release

Whole-cell patch-clamp recordings were performed in cultured hypothalamic neurons. OXT release was measured using a sensitive and specific OXT-ELISA. The effect of calcium chelators (EGTA) and calcium ionophores (A23187) on OXT release was tested. The effect of SNAP-25 and SNAP-47 on OXT release was tested. The effect of SNAP-25 and SNAP-47 on OXT release was tested. The effect of SNAP-25 and SNAP-47 on OXT release was tested.

RESULTS I: OXT NEURONS EXPRESS NON-CANONICAL SNAP ISOFORMS

OXT neurons express non-canonical SNAP isoforms such as SNAP-47 and SNAP-23, which are not typically associated with synaptic transmission. SNAP-47 is highly expressed in hypothalamic OXT neurons from early development, whereas SNAP-23 is detected in axonal terminals. High levels of SNAP-47 in OXT neurons suggest a potential role in OXT exocytosis.

RESULTS II: DYNAMICS OF OXT-CONTAINING COMPARTMENTS

Fluorescence microscopy and FRAP analysis were used to study the dynamics of OXT-containing compartments. OXT release was measured during the first seconds of neuronal activation. OXT release was measured during the first seconds of neuronal activation. OXT release was measured during the first seconds of neuronal activation.

RESULTS III: OXT SECRETION IN HYPOTHALAMIC NEURONS

OXT release occurs during the first seconds of neuronal activation. OXT release was measured during the first seconds of neuronal activation. OXT release was measured during the first seconds of neuronal activation.

RESULTS IV: OXT SECRETION REQUIRES SNAP-47 EXPRESSION

OXT secretion requires SNAP-47 expression. OXT release was measured during the first seconds of neuronal activation. OXT release was measured during the first seconds of neuronal activation.

CONCLUSIONS

OXT-releasing neurons require a specific membrane machinery, distinct from the one involved in SVs. SNAP-47 is highly expressed in hypothalamic OXT neurons from early development, whereas SNAP-23 is detected in axonal terminals. High levels of SNAP-47 in OXT neurons suggest a potential role in OXT exocytosis.

