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Synaptophysin

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* Synaptophysin Is a Reliable Marker for Axonal Damage

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synaptophysin#:~:text=Synaptophysin%20is%20an%20integral%20membrane,normal%20and%20neoplastic%20neuroendocrine%20cells.

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Chapters and Articles

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Identification,

morphology and secretory products of the pulmonary endocrine system

John R. Gosney BSc, MB, ChB, MD, MRCPath, in Pulmonary Endocrine Pathology, 1992

Synaptophysin

Like the neurofilament proteins, synaptophysin is better characterized as a marker of

neoplasms of the DES than of its cells (Chapter 7), although it has been recently employed with considerable success as a marker of PECs (Lee *et al.*, 1987). It is a component of the membrane of neuronal synaptic vesicles and can be demonstrated even when they are empty (Wiedenmann and Franke, 1985), but its precise location in cells of the DES is unknown (Navone *et al.*, 1986).

Immunohistology of Endocrine Tumors

Ronald A. DeLellis, Sandra J. Shin, in Diagnostic Immunohistochemistry (Second Edition), 2006

Synaptophysin and other synaptic vesicle proteins

Synaptophysin is a calcium–binding glycoprotein (38 000 kD), which is the most abundant integral membrane

protein constituent of synaptic vesicles of neurons. It is also present in a wide spectrum of neuroendocrine cells and in many of their corresponding tumors.

Typically, synaptophysin reactivit y is present in a punctate pattern in synaptic regions of neurons and is present diffusely throughout the cytoplasm of neuroendocrine cells.

Ultrastructurally, synaptophysin is present in microvesicles, whereas chromogranin is present in secretory

granules. These differences indicate that chromogranins and synaptophysin are complementary generic neuroendocrine markers. Synaptophysin immunoreactivity, however, is not specific to neuroendocrine cells since it is also present in adrenal cortical cells.

Synaptic vesicle protein 2 (SV2) is present in the central and peripheral nervous system and in a wide variety of neuroendocrine cell types.

Comparative studies of the distribution of SV2, synaptophysin, and chromogranin A in neuroendocrine tumors have shown excellent agreement with the exception of hindgut carcinoids which showed weak synaptophysin immunoreactivity, no staining for chromogranin A but strong staining for SV2.38

Vesicular monoamine transporters (VMATs) mediate the transport of amines into vesicles of neurons

and endocrine
cells. VMAT1 and VMAT2 are differentially expressed by gastrointestinal endocrine tumors with patterns specific for each tumor type.39 For example, serotonin–producing endocrine tumors expressed VMAT1 predominantly while histamineproducing endocrine tumors (gastric carcinoids) expressed VMAT2 almost exclusively. Peptide hormone–producing gastrointestinal tumors (rectal carcinoids) and pancreatic endocrine

tumors, on the other hand, contained few VMAT1- or -2-positive cells.39

Synaptotagmins (p65) which form a large calcium–binding family are implicated in neurotransmitter release, although synaptotagmin I is the only isoform demonstrated to have a role in vesicle fusion. In the pancreatic islets, synaptotagmins have been co–localized with insulin, but the roles of this family of proteins have not been fully explored as

markers of neuroendocrine tumors.40,41

The vesicle–associated membrane proteins (VAMPs or synaptobrevin) occur in three isoforms and are proteins that are anchored to the cytoplasmic portion of synaptic membrane vesicles and secretory granules. VAMP2 and 3 are present in pancreatic beta cells, but the roles of this family of proteins have not been widely studied as markers of neuroendocrine tumors.42

In contrast to synaptophysin and other synaptic vesicle proteins, SNAP–25 (synaptosomal protein of 25KD) and syntaxin are present in the plasma membrane.

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Estrogen Effects on Hippocampal Synapses

Teresa A. Milner, ... Elizabeth M. Waters, in The Synapse, 2014

2.1.1.1 Presynaptic Proteins

Synaptophysin is a presynaptic protein associated with small synaptic vesicles, whereas syntaxin is associated with the presynaptic membrane; both proteins are implicated in vesicular docking (Calakos and Scheller, 1994; Calakos et al., 1994). As seen in Figure 2, both synaptophysin-ir (Figure 2(A)) and syntaxin-ir are most intense in lamina lacking

principal cell bodies in the hippocampus. Estrogens regulate the levels of synaptophysin and syntaxin in the hippocampal CA1 regions in both the female rats (Brake et al., 2001) and mice (Li et al., 2004; Spencer et al., 2008); however, the direction of the change in synaptophysin levels differs depending on the species and paradigm as seen in Figures 3 and 4.

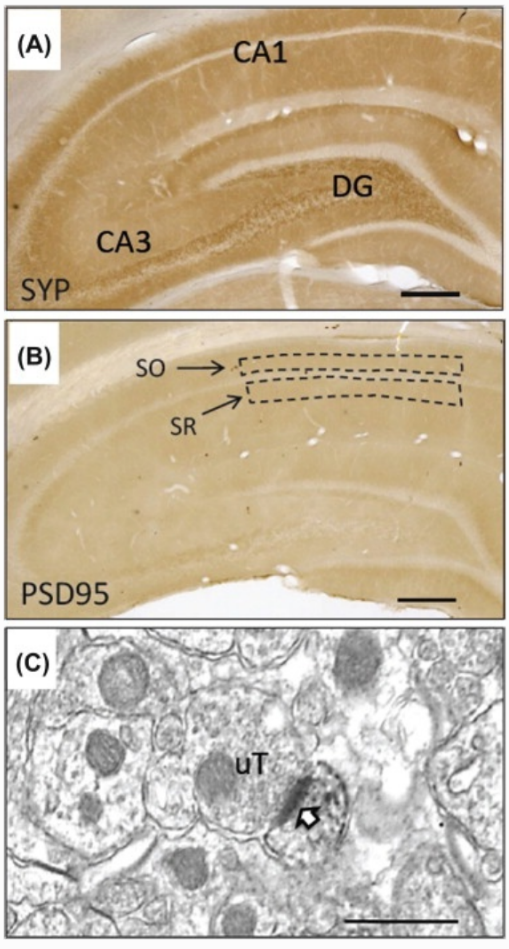

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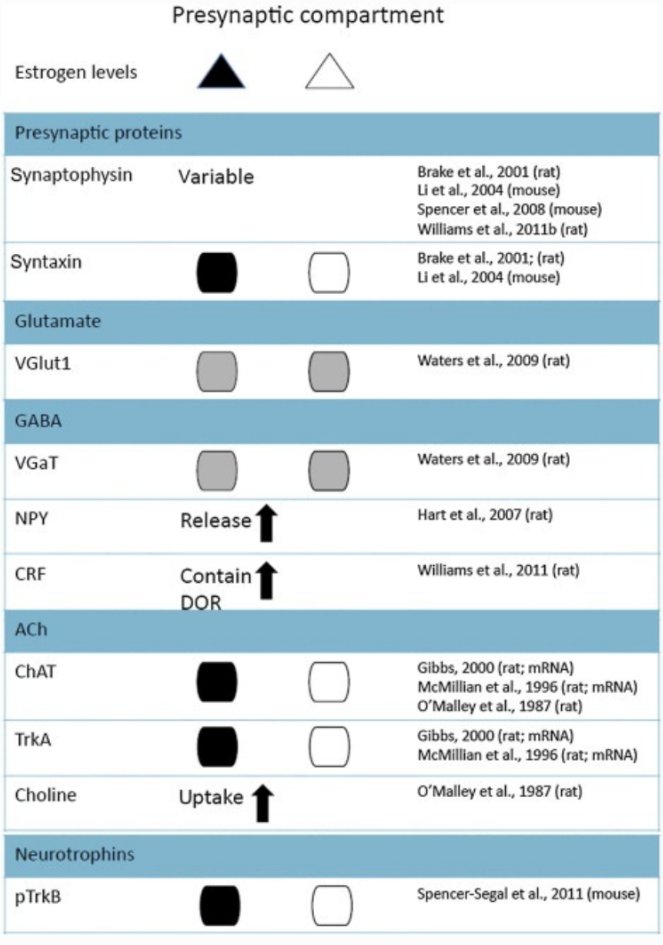
Figure 2. Localization of representative pre- and postsynaptic proteins in the rat hippocampus. (A) Light photomicrograph showing

synaptophysin (SYP)-ir in the CA1 region as well as the dentate gyrus (DG) and CA3. (B) Light photomicrograph showing PSD-95-ir in the stratum orients (SO) and stratum radiatum (SR) of CA1. Dotted lines represent regions examined by densitometry in the CA1. (C) Electron photomicrograph showing an unlabeled terminal (uT) that forms an asymmetric synapse (arrow) on a PSD-95-containing dendritic spine in SR of CA1. Scale bars = 300 μm (A, B); 500 nm (C). All

photomicrographs were taken from young females.

A and B from Williams and Milner, 2011.



Presynaptic compartment			
Estrogen levels	▲	△	
Presynaptic proteins			
Synaptophysin	Variable		Brake et al., 2001 (rat) Li et al., 2004 (mouse) Spencer et al., 2008 (mouse) Williams et al., 2011b (rat)
Syntaxin	■	□	Brake et al., 2001; (rat) Li et al., 2004 (mouse)
Glutamate			
VGlut1	■	■	Waters et al., 2009 (rat)
GABA			
VGaT	■	■	Waters et al., 2009 (rat)
NPY	Release ↑		Hart et al., 2007 (rat)
CRF	Contain ↑ DOR		Williams et al., 2011 (rat)
ACh			
ChAT	■	□	Gibbs, 2000 (rat; mRNA) McMillian et al., 1996 (rat; mRNA) O'Malley et al., 1987 (rat)
TrkA	■	□	Gibbs, 2000 (rat; mRNA) McMillian et al., 1996 (rat; mRNA)
Choline	Uptake ↑		O'Malley et al., 1987 (rat)
Neurotrophins			
pTrkB	■	□	Spencer-Segal et al., 2011 (mouse)

Figure 3. Summary of estrogen effects on proteins in the presynaptic compartment.

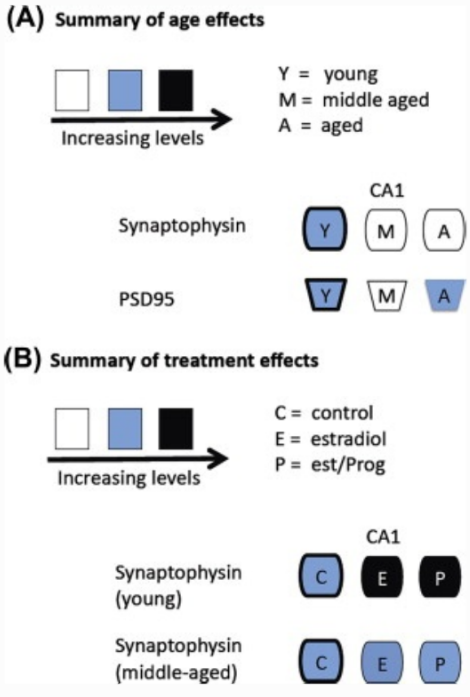


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Figure 4. Summary of age and treatment effects on pre- and

postsynaptic protein levels in the dorsal hippocampal formation. (A) With age, females showed regionally specific changes in levels of presynaptic protein synaptophysin and postsynaptic protein PSD-95. Significant changes with age, if evident, were found in comparison to the young (Y) group noted by the thick black outline. (B) Significant changes with hormone treatment (E i proestrus (high estrogen phase) (Spencer et al., 2008). In contrast, consistent elevations in

syntaxin levels in the CA1 region have been reported in OVXed rats after 2 days of EB injections (Brake et al., 2001) and in OVXed mice after 5 days of EB injections (1 μg/0.1 ml, s.c.) (Li et al., 2004).

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Special Issue on Neurosteroids

Lars Fester, ... Gabriele M. Rune, in The Journal of Steroid

Biochemistry and Molecular Biology, 2012

1.4 Expression of synaptic proteins

Spinophilin is a postsynaptic protein, which is enriched in spines,
whereas synaptophysin is a constituent of the transmitter vesicle membrane and therefore a presynaptic protein. When visualized

by immunohistochemistry both synaptic
proteins, spinophilin and synapto physin, showed a distinctive punctate staining in the dendritic layers of rat hippocampus. Image analysis of confocal laser scanning micrographs of immunohistochemical stainings revealed no differences in the immunoreactivity for spinophilin and synaptophysin between male and female
animals [7] (Fig. 3c).

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Neuroendocrine Tumours

Günter Klöppel, in Best Practice & Research Clinical Endocrinology & Metabolism, 2007

Small vesicle-associated markers

Synaptophysin is an integral membrane glycoprotein (molecular weight

38,000) that occurs in presynaptic vesicles of neurons and small clear vesicles of normal and neoplastic neuroendocrine cells. It is expressed independently of the other neuroendocrine markers, notably secretory granule products. Other markers related to synaptophysin are SV2 and synaptobrevin.