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Understanding synaptic changes underlying neuronal communication by vital imaging of tetrapartite synapses

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Chemical synapses are the main sites of neuronal communication in mammalian brains that are perceived as tetrapartite entities composed of not only pre- and postsynaptic compartments but also of the closely associated astroglial processes and the surrounding extracellular matrix (ECM). Both astrocytic processes and ECM appear to be dynamic partners that are tightly regulated by neuronal activity and can feedback and regulate various signaling processes pre- and postsynaptically. Considering various evidences, it can be conceived that a functional synapse would have well-organized above-mentioned four components (‘’Synaptic Quadriga’’ or “Tetrapatrite Synapse”) in order to have proper functioning (Dityatev et al., Results Probl Cell Differ. 2006; Trends Neurosci. 2010; Dityatev and Rusakov, Curr Opin Neurobiol, 2011). The structural and functional organization/reorganization of these components is the key to understand the adaptations of neuronal communication to various physiological and pathological conditions such as synaptopathies. So, it is highly desirable and of high relevance to study the sequence and logic of changes in these components during structural synaptic plasticity in vitro and in vivo. To this end, we have developed four AAV based viral vectors that can fluorescently label all these components. Our data show that these vectors can faithfully label all the four compartments of the tetrapartite synapse. Hence, for the first time, we have tools to study all components simultaneously in vitro as well as in vivo. We have acquired high-resolution time-lapse images of tetrapartite synapses after various stimulations that affect neuronal activity and expression of ECM and in response to toxic elements such as excitotoxic concentrations of glutamate and Aß oligomers and peptides. Comparative analysis of the structural changes under different conditions might reveal key mechanisms that govern the organization and functionality of the tetrapartite synapse.