Delusions, cognitive impairment and the therapeutic effect of dopamine receptor antagonists in schizophrenia - An explanation through the semblance hypothesis of memory

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An hypothesis that can explain multiple features in schizophrenia including delusions, cognitive impairment and the therapeutic effect of dopamine receptor antagonists is likely to shed some light on the disease process. The semblance hypothesis of memory[1, 2] can be extended to explain these features of schizophrenia. In contrast to the strengthening of single synapses proposed by earlier hypotheses, the basic units of the semblance hypothesis of memory consist of the functional LINKs* formed between the postsynaptic membranes of at least a pair of synapses during learning. Continued learning results in continued addition of functional LINKs, forming expanded islets of LINKed postsynapses. During the retrieval of memory in the presence of a cue stimulus, the functional LINKs formed during learning help to induce specific postsynaptic events at the synapses representing the learned item in the absence of sensory input from the learned item. This creates synaptic illusions of sensory input from the learned item, resulting in a virtual sensation of a sensory stimulus, called semblance. The postsynaptic events at the synapses representing the learned item can also induce action potentials in their neurons, provided sufficient summation of excitatory postsynaptic potentials occurs, leading to the activation of a network representing the learned item providing network semblance. It can be hypothesized that misconnections between the islets of functional LINKs could lead to schizophrenia. 1) Delusions can occur due to the semblances of sensory inputs occurring through misconnected islets of functional LINKs, leading to the virtual sensation of sensory stimuli that are unrelated to the previous associative learning. 2) The misconnected functional LINKs in schizophrenia can de-route the formation of specific semblances that are required for specific memory retrieval, causing cognitive impairment. 3) Dopamine implicated in motivation-induced learning[3] can promote the formation of functional LINKs between postsynapses. It is likely that the dopamine antagonists prevent delusions by blocking the functions of misconnected functional LINKs responsible for sensations of unassociated learned items. The semblance hypothesis and its present extension should be considered unproved until verified by further experiments.

1. Vadakkan KI (2008) Semblance hypothesis of memory. iUniverse publishers, USA.
2. www.semblancehypothesis.org
3. Wang M, Vijayraghavan S, Goldman-Rakic PS (2004) Selective D2 receptor actions on the functional circuitry of working memory. *Science* 303: 853-6

* The capital letters were used in the word LINK to denote its importance.