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Possible role of the glial syncytium in Alzheimer's disease

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In a mouse model of Alzheimer's disease, time-lapse imaging revealed that calcium transients in astrocytes were more frequent, synchronously coordinated across long distances and uncoupled from neuronal activity (Kuchibhotla et al, 2009). The authors state that the increased astrocyte activity cannot be explained by a simple coupling mechanism with neuronal activity.

First, neuronal calcium homeostasis is most severely impaired near senile plaques, whereas here resting calcium was globally elevated in astrocytes.
Second, neurons exhibit a pronounced hyperactivity near plaques, whereas here astrocytes were more active both near and far from plaques.
Third, abolishing neuronal activity had no measurable effect on astrocytic calcium oscillations. So senile plaque deposition induces local synapto- and neurotoxocity, but the same plaque deposits might catalize astrocytic intra- and intercellular signaling events.

Kuchibhotla et al (2009) interpret this exciting experimental result by stating that although neurotoxicity is observed near senile plaques (amyloid-ß deposits), there exists a more general astrocyte-based network response to focal pathology. Thus, it appears that astrocytes may represent functionally adaptive cells that play distinct roles in health versus disease. At least in the mouse model of Alzheimer's disease, the astrocytic syncytium amplified the effects of focal amyloid deposition across a larger cortical network landscape, perhaps contributing to the global alterations in cortical function and possibly the memory disorders seen in Alzheimer's disease.

Moreover, the experiments discussed here also allow a contrary interpretation. First of all, if one supposes that gap junction plaques in astrocytic syncytia embody memory structures (Robertson, 2002), then the glial based memory may not be affected in Alzheimer's disease. Therefore, the severe impairment of memory in Alzheimer's disease may be caused by the destruction of the neuronal network. In addition, assuming that the astrocytic syncytium also embodies memory-based intentional programs (Mitterauer, 2007) not significantly affected in Alzheimer's disease, then these poor patients might be aware of their existential situation but unable to express it. Such suffering is comparable to a guitar player with a melody in mind unable to play it, since the strings of his guitar are broken.

These considerations may sound rather gliophilosophical, but are in part testable. The Nedergaard group found that although astrocytic gap junction plaques are reduced in brains of old mice compared to young adult mice, functional coupling remains high (Cotrina et al, 2001). Supposing that this is also the case in human brains, it should be possible to identify reduced but functional gap junction plaques in human brains with Alzheimer's disease as well. Together, glia may hyperreact to neuronal impairments in Alzheimer's disease, since they lose their neuronal partner for realizing their per se intact memory-based intentional programs.

References cited:
Cotrina M.S. et al (2001) Expression and function of astrocytic gap junctions in aging. Brain Research 901: 55-61.
Kuchibhotla K.V. et al (2009) Synchronous hyperactivity and intercellular calcium waves in astrocytes in Alzheimer mice. Science 323: 1211-15.
Mitterauer B. (2007) Where and how could intentional programs be generated in the brain? A hypothetical model based on glial-neuronal interactions. BioSystems 88: 101-112.
Robertson J. (2002) The astrocentric hypothesis: proposed role of astrocytes in consciousness and memory formation. Journal of Physiology (Paris) 96: 251-255.