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EDITORIAL

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Adult neurogenesis in the hippocampus

Adult neurogenesis in mammals at one point in time was simply not a topic of investigation, because it required methods not available to the neuroanatomical pioneers in the 19th century. But Cajal surely would have loved the idea, because as he said in his Croonian lectures of 1894 (held in French in a truly border-transcending spirit by a Spaniard in London [Jones, 1994]):

> A network that remains pre-established like a telegraphic grid, where neither new stations nor new lines can create themselves, is something rigid, permanent, non-modifiable, which hurts the sentiment that we all have that, the organ of thought is, within certain limits malleable and capable of perfection, especially during its period of development, by means of well-directed mental gymnastics [… au moyen d'une gymnastique mentale bien dirigée]. Santiago Ramón y Cajal, Croonian Lecture, 1894

Already at the end of the 19th century, thus, the idea of plasticity was in the air, and after methods became available to not only study synaptic plasticity, but also discover new neurons in the adult brain, adult neurogenesis has become an influential, if not fundamental idea of neurobiology. Brains are not computers, rather they have a reciprocal malleability of their structures which is essential for their healthy function.

Altman's and Das' discovery of adult hippocampal neurogenesis in rats marks a milestone in brain plasticity research, because new neurons do not just add new connections (even though new neurons also means new synapses), they place new nodes into the network (Altman & Das, 1965). Because of the central role of the hippocampus in cognition, including the “highest” functions in humans (like autobiographic memory), adult hippocampal neurogenesis has begun to influence concepts of how our brain functions in general. These sometimes bold and creative claims still generate uneasiness among a few scientist, and against multifold and broad evidence, the mere existence of adult hippocampal neurogenesis in humans has been questioned repeatedly. That debate, useful in the beginning to clarify standards and intensify exchange, has become stale and for some dogmatic, as if the openness of a question would be an argument against (rather than for) studying it. Against this small but loud negative trend, we would like to present exciting research that draws the picture of a brimming and energetic field with broad relevance.

Adult neurogenesis in mammals remains a hot topic and the articles in this special issue, both review and original articles, highlight interesting current developments in the field of adult hippocampal neurogenesis, aptly demonstrating that the new neurons today cover a lot of ground in neurobiology and cannot be ignored.

Terreros-Roncal et al. (2023) summarizes the state-of-the-art to study adult neurogenesis across species, highlighting that comparative approaches not only pave the way to translation, but also allow fundamental insight. The possibly most immediately relevant translational consequences of adult hippocampal neurogenesis might lie in its role in Alzheimer's disease, a challenging and complex topic discussed by Choi and Tanzi (2023). A study by Lee et al. (2023) brings a concrete example, characterizing the elusive role of APOE polymorphisms by addressing APOE in human neural precursor cells ex vivo. Closely related is the more general question how adult neurogenesis responds to and is involved in cognitive aging. Here, a focus on epigenetic changes has brought a new perspective on how an impairment of precursor cell function might affect the aging process Zocher and Toda (2023). New longitudinal studies as the one by Lopes et al. (2023) highlight the emerging role of adult neurogenesis in establishing individual behavioral trajectories and related levels of brain plasticity over the life course. An extensive review by Gao et al. (2023) summarizes the state-of-the-art of how physical activity stimulates adult hippocampal neurogenesis. Two reports by von Berlin et al. (2023) and Olpe and Jessberger (2023) turn to fundamental questions of development and population dynamics in adult neural precursor cells, a subject that continues to bring up surprising new findings, revealing the complexity of adult neurogenesis as a process and the intricacy of its regulation. Regulation of adult neurogenesis interacts with this complexity. Parylak et al. (2023) highlight the stage specific molecular control in its dependency on neuronal activity, presumably the most important network-intrinsic driver of neurogenesis. In turn, as reported by Groisman et al. (2023) control of key molecules determines the establishment of appropriate connectivity, including the important link to GABAergic transmission.

Together the articles collected in this special issue air the excitement that drives research in the field and the many new threads that have opened up, when new techniques became available and researchers with different expertise brought in their unique perspectives. This collection is also a call to appreciate and celebrate the richness of insights that studies of adult neurogenesis can convey.

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