



Introduction to the special issue of the journal of bioenergetics and biomembranes: neural plasticity in developing and adult olfactory pathways

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Pablo Picasso once quipped “youth has no age.” And, like the abstract artist himself, who lived young into his 90s, our olfactory system seems to have evolved a fountain of youth. Both the primary receptor population and interneuron population in the first odor processing center within the brain, the olfactory bulb, incorporate newborn neurons throughout life. This constant renewal—for example, the bulbs receive something on the order of 1000 newborn neurons daily—seems to underwrite an unprecedented level of plasticity. The fulsome and growing interest in olfactory plasticity, during development and throughout life, offers the promise of insights into basic questions such as how neural networks are formed and maintained, and clinical solutions such as treatments or even cures for neural injury and disease.

In this special issue of JOBB we have invited contributions that reflect the breadth of interest in this area both in terms of animal models and modes of analysis. In the first contribution, Savya and Cheetum combined the use of the tetracycline transactivator system, which allows time-window specific expression of immature and mature reporter genes, with pulse-labelling of terminally-dividing cells to analyze olfactory sensory neuron (OSNs) maturation and survival in the mouse. Surprisingly, they found that the vast majority of OSNs born in early adulthood do not survive, that maturity of OSNs does not promote survival and that neurogenesis in the olfactory epithelium mysteriously continues even in the face of these bleak chances for newborn cells to become integrated into the olfactory network. Moving to the olfactory bulb, Fardone and colleagues, build on their previous discovery that diet-induced obesity (DIO) causes declines in olfactory structures and their

functions. Here they show, using M72-IRES-tau-GFP mice and c-Fos labelling of juxtglomerular interneurons, an asymmetrical decrease in responsiveness in the ‘mirror image’ glomerular map of DIO mice compared to mice on normal diets, suggesting a fascinating but complex relationship between diet and olfactory neural function.

Of course, plasticity and learning are inextricably linked. In the next contribution, Ross and Fletcher review the effects of aversive learning-induced plasticity across olfactory pathways seeking conserved and disparate mechanisms in the developing and adult system that could inform future studies. Ultimately, genes and learning have their effects on neural circuits through structural modeling of neurons and their components. Slankster and colleagues review recent evidence across the olfactory systems of several taxa that intrinsic neuronal diversity is far more prevalent and profound a basis of olfactory neural circuit function than previously appreciated. Unfortunately, for all of us hoping for simplicity at the cellular level (at least), no two neurons, even in the same class, may be alike!

Trophic and activity-dependent interactions between afferent and target neurons are paramount in the formation, maintenance and plasticity of neural pathways, not least in the olfactory system. Exploiting the advantages of zebrafish as a model system, Pozzuto and colleagues show, using retrograde tract-tracing in *ex vivo* brain cultures, that deafferentation through OSN ablation causes major restructuring of the dendritic trees of mitral cells, the primary output neurons of the olfactory bulb. Thus, the zebrafish mitral cell system offers us an excellent model for further study of the cellular and molecular basis of afferent-target interactions.

Yes, but what about humans? Translational relevance is the touchstone of virtually every granting agency (not to mention every medical school dean)! In the contribution by Huart and colleagues the issue of plasticity in the human olfactory bulb is reviewed with a special emphasis on magnetic resonance

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imaging (MRI) studies. While, on the one hand, there exists controversy about the extent to which adult humans ‘enjoy’ the same influx of new-born neurons into the olfactory bulbs that rodents have, on the other hand, it is becoming clear that enrichment, deprivation and disease all have predictable effects on the size of olfactory bulbs. And, in this instance, size matters as these results accord with olfactory abilities measured behaviorally.

Finally, the concept of ‘critical periods,’ first articulated by Konrad Lorenz in his studies of imprinting, are reviewed with respect to the olfactory system by my colleague Len White and I. Our conclusion is that these sensitive windows for sensory experience may not exist

in the olfactory system owing to the neotenic vestige of life-long neurogenesis, though our rationale diverges from the standard explanation for this absence. It is my hope that this multifarious collection of reviews and original contributions will give the reader a taste, nay sniff, of the varied models and methods that are advancing our understanding of the development and adult maintenance of the one sensory system—olfaction—that seems to remain forever young.

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