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Editorial

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Linking autism to an imbalanced catabolism of synaptic monoamines

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An interdisciplinary study of autism led to implicate a relatively poor catabolism of one of the monoamines released in the synapse, namely *serotonin*. This deficit would result from persistent epigenetic regulations of two enzymes (i.e.: MAOA- and COMT+) across neural differentiation, for counteracting an accidental excess of MAOA in the early gestation. Epigenetic traits would outlast this temporary excess and be inherited by generations of neurons, and possibly by next human generations. In addition, the late occurrence of autistic symptoms may be consistent with the rising of the MAOB enzyme that degrades another monoamine (*dopamine*), but only significantly around two years after birth. The consequent long-term imbalance of synaptic monoamines is assumed here to impact the architecture of sleep and learning [1], inducing a range of developmental problems.

This theory is drawn on Guided Propagation Networks (GPNs), the computer simulations of which show the growth of aberrant structures when modulation parameters akin to monoamines do not satisfy inner learning constraints. Comparisons are made between a reference well-tuned network and others grown with shifted parameters, all using the same learning data. Unlike the reference network, impaired GPNs display features that have been observed in the autistic brain: **1.** More local connections (here underlying either repetitive behavior or over-activity); **2.** Missing or impaired long-distance connections (which convey emotional conditioning towards decision-making modules); **3.** Overgrowth: the overall connectivity can involve 1.5 more cells and links. Apart from these computer experiments [2], the 4:1 sex ratio observed in autism can be calculated in a family tree which combines genetic variants and epigenetic regulations. According to this calculation which involves two types of genetic masking of the relevant epigenetic traits (i.e.: X-silencing and low-COMT), there would be more 'healthy carriers' of the enzymatic regulation at issue than people with overt forms of autism.

On the medical side, an epileptic 11-year old boy with severe autism received *Sodium Valproate* daily for its ability to both stimulate MAOA and treat epilepsy. In this case study, behavioral changes have been recorded by parents and caregivers unaware of the autism target. This one-year monitoring showed improvement of sleep and then gaze, followed by a gradual decrease of stereotypy among other behavioral changes arising nine months after the treatment initiation. Hyperactivity which hindered learning across this treatment could afterwards be reduced by low dose of the *methylphenidate* psychostimulant. The proposed dual therapy thus involves a MAOA inducer and a psychostimulant, together with re-education, all monitored by relevant biomarkers [3]. If validated by future investigations, this approach is first intended to prevent early gestation from environmental factors that are likely to stimulate the production of MAOA, including small-sized fatty acids.

References

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