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# On postnatal CNS plasticity

## *Editorial*

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The uniqueness of an individual is a consequence of the type of proteins coded in his/her genome, expressed along pre-and post-natal periods, with a rather fixed sequential timing. A single gene can encode multiple proteins, which can be directly transcripted at any time point, or modified by (i) alternative splicing of the mRNA transcript, (ii) changes of the translation start or stop sites, or (iii) frame-shifting. A single protein may be involved in more than one process, and similar functions may be carried out by different proteins and/or by their products, peptides and amino acids. Furthermore, the timing of expression of proteins and single amino acids is modulated by environmental cues, providing a wide framework for plasticity.

Postnatal CNS plasticity was a topic of the Neurobiological Session of the 9$^{th}$ International Congress on Amino Acids and Proteins, hold in Vienna, Austria, during August 8–12, 2005, organised by Profs. Gert Lubec (Vienna, Austria) and Friedrich H. Leibach (Augusta, GA, USA). One of the symposia was fully dedicated to that topic, focusing on CNS plasticity following perinatal asphyxia (Klawitter et al., 2006; Hoeger et al. 2006), and on sensitivity priming of dopamine systems by sub-chronic-intermittent caffeine administration (Simola et al., 2006). The central filtering capability of sensorial information was discussed by Stevens et al. (2006), providing evidence that 5-HT$_{1A}$ signalling is involved in sensory inhibition produced by psychomimetic drugs, mimicking the abnormalities in central filtering capability of sensory stimuli shown by schizophrenic patients, supporting the idea of evaluating 5-HT$_{1A}$ receptor active compounds as antipsychotic drugs.

Simola et al. (2006) present results showing that caffeine induces long-lasting changes in dopaminergic systems, perhaps influencing the expression of glutamate-mediated neuroplasticity involved in learning and memory processes, suggesting that long-term caffeine exposure may have a potential as a therapeutic strategy for cognitive deficits.

Klawitter et al. (2006) discuss the idea of Poly(ADP-ribose) Polymerase (PARP) as a therapeutic target against the detrimental effects induced by energy failure. Indeed, the isoenzymes PARP-1 and PARP-2 are immediately activated when the integrity of the genome is menaced and/or damaged (Kihara et al., 1994; Akhter et al., 2001; Amé et al., 2004), leading to over activation if the insult is severe and/or sustained. In turn, PARP-1 over activation leads to $NAD^+$ exhaustion and energy crisis (Berger, 1985), and to a caspase-independent apoptosis (Yu et al., 2002). Hence, PARP-1 inhibition has emerged as a main target for neuroprotection following hypoxic/ischemic insults. In agreement, the paper by Klawitter et al. (2006) presents evidence that the PARP-1 inhibitor, nicotinamide, reversed the effect of perinatal asphyxia on several neuronal parameters, including neurite atrophy and neuronal loss. However, the use of nicotinamide has been challenged because of its low potency, limited cell uptake and short cell viability (Virag and Szabo, 2002). Nevertheless, the authors suggest that the low potency of nicotinamide on PARP-1 inhibition may provide an advantage when used in developing animals, because the drug will only antagonise the effect of PARP-1 over-activation, without impairing DNA repair and proliferation.

Hypothermia has been shown by several multicenter trial studies (Shankaran et al., 2005; Gunn and Thoresen, 2006) to be effective against the deleterious consequences of perinatal asphyxia, but there is still concern about a narrow therapeutic window (Engidawork et al. 2001), about a lack of a clear mechanism of action (Herrera-Marschitz et al., 1993, 1994; see Gluckman et al. 2005), and about a long-term morphological and/or functional protective profile. Thus, Hoeger et al. (2006) have discussed about the protection provided by moderate or profound hypothermia on morphological and behavioural parameters, showing that hypothermia failed to attenuate neuronal loss, but improved survival, and on parameters of motor and emotional behavioural deficits.

Thus, the four papers, with different experimental models and assessing different brain and neurocircuitry mechanisms provide further evidence that the CNS preserves great structural and functional postnatal plasticity, vulnerable, however, to distortions, to be added to those depending upon genetic predisposition, as discussed at previous neurobiology symposia hold at the series of International Congress on Amino Acids and Proteins (Kretschmer et al., 2002, 2005).

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