the accumulation of aberrant, neurotoxic forms of host proteins in the brain for which there is no known cure. In the landmark study reported in *Proc. Natl. Acad. Sci. U. S. A.* [(2001) 98, 9295–9299], a mouse cell line was chronically infected with a strain of mouse scrapie causing the massive accumulation of neurotoxic scrapie prion protein (PrPSc), a defective variant of a surface protein found in brain cells (PrPC). Using this model, Enari et al. showed that exposure of the cells to an antibody directed against the prion protein blocked the infection of neighboring susceptible cells and further abolished the accumulation of PrPSc in the chronically infected cells. Encouraged by the findings *in vitro*, the research team will now test the prion antibody in mice, in the hope that the approach might soon be used in the treatment of prion diseases. SS

**Vitamin D: the neglected neurosteroid?**

Recent articles in this journal have focused attention on the growing body of evidence showing that steroid hormones can alter brain function in novel ways. The autocrine and paracrine roles played by steroids synthesized in the brain (also known as neurosteroids) are yet to be fully elucidated. The physiological properties of known neurosteroids are diverse, and differ temporally (neurodevelopment versus adult brain) and regionally within the brain.

We wish to draw attention to vitamin D as a neuroactive steroid whose probable synthesis in the CNS qualifies it as a neurosteroid. A precursor of vitamin D is generated from a cholesterol derivative by the action of ultraviolet light on the skin. Its active form, calcitriol, is formed by two hydroxylation reactions. The expression of mRNA coding for the 1α-OH hydroxylase (the P450 enzyme required in the final step to produce the active form 1,25-dihydroxyvitamin D3) has been

**Editor’s choice**

**bmn.com/neuroscience**

As a busy neuroscientist, searching through the wealth of information on BioMedNet can be a bit daunting – the new gateway to neurobiology on BioMedNet is designed to help.

The new neuroscience gateway is updated weekly and features relevant articles selected by the editorial teams from *Trends in Neurosciences, Current Opinion in Neurobiology* and *Trends in Cognitive Sciences*.

The regular updates include:

- **News** – our dedicated team of reporters from BioMedNet News provides a busy researcher with all the news to keep up to date on what’s happening – right now.
- **Journal Scan** – learn about new reports and events in neuroscience every day, at a glance, without leafing through stacks of journals.
- **Conference Reporter** – daily updates on the most exciting developments revealed at the Annual Meeting for the Society for Neuroscience – providing a quick but comprehensive report of what you missed by staying home.
- **Mini Reviews and Reviews** – a selection of the best review and opinion articles from all *Trends* and *Current Opinion* journals in the field.

Why not bookmark the gateway at **bmn.com/neuroscience** for access to all the news, reviews and informed opinion on the latest scientific advances in neuroscience.

**Letters**

This month’s *In Brief* articles were written by Lianna Orlando (orlando@helix.mgh.harvard.edu) and Sonia Sequeira (sequeirs@mskcc.org)
observed in the CNS (Ref. 5). Apart from traditional roles in Ca^{2+} homeostasis, vitamin D induces the expression of many CNS genes⁴. Vitamin D is one of the most potent up-regulators of nerve growth factor ¹⁻⁹ and can also induce the low affinity neurotrophin receptor (p75NTR)¹⁰. Vitamin D receptors (VDR) are widely distributed throughout the developing and adult rat brain¹¹⁻¹³ and have been identified in the human brain¹⁴. Thus, there is great scope for Vitamin D to act on the CNS in a developmental-, cell- and tissue-specific manner, depending not only on the expression of VDR-target genes but also on interactions with other growth factor signalling pathways.

Because the crucial rate-limiting step in the production of vitamin D is the action of ultraviolet light on the skin, an individual’s behaviour (e.g. outdoor activity, dress) and place of residence (e.g. latitude) can interact with seasonal fluctuations in the intensity of ultraviolet light to determine levels of vitamin D. Hypovitaminosis D is common in the community, with a large US community-based survey finding 9% of adults to be deficient (i.e. 25-hydroxyvitamin D levels ≤ 38 nmol/L)¹⁵. Even in subtropical regions, dress and behaviour can result in hypovitaminosis D (Ref. 16).

In the absence of hypocaelia, hypovitaminosis D has no apparent immediate impact on brain function, however there is evidence to suggest vitamin D can improve mood¹⁷ (and, therefore, might be associated with seasonal affective disorders). Low vitamin D has also been proposed as a risk factor for schizophrenia (low prenatal vitamin D)¹⁸ and multiple sclerosis (low prenatal vitamin D (Ref. 19) and low vitamin D during childhood and adulthood)²⁰. Several studies have also linked vitamin D with general neuroprotection²¹,²² and changes associated with Alzheimer’s disease²³. Thus, chronic hypovitaminosis D should be examined in more detail as a candidate risk factor for neurodevelopmental and neurodegenerative disorders.

Vitamin D is also known as ‘soltriol’, because of its association with sunshine. With respect to the recent interest in neurosteroids, we feel that it is now time for vitamin D to ‘emerge from the shadows’. In view of the prevalence of hypovitaminosis D in the general public, the impact of this neurosteroid on the developing and adult brain requires clarification.

**Response - Vitamin D: the neglected neurosteroid?**

In the past decade, firm evidence has emerged that steroids, in addition to their effects on gene expression via intracellular steroid receptors, might directly modulate neuronal excitability through allosteric modulation of neurotransmitter receptors. Steroids with these particular properties have been called ‘neuroactive steroids’, whereas the term ‘neurosteroids’ has been reserved for steroids that are synthesized in the brain itself without the aid of peripheral sources²⁴. In their comment, McGrath et al. address the putative role of vitamin D as a neurosteroid. Vitamin D acts via intracellular receptors on the regulation of gene expression, similar to classical steroid hormones. Vitamin D receptors are members of the steroid receptor superfamily to which the receptors for steroid hormones and also thyroid hormone receptors or retinoid acid receptors also belong²⁵. Although Vitamin D is formed from cholesterol it is a matter of debate whether vitamin D should really be called a steroid. Rapid non-genomic effects have been described for 1α, 25-dihydroxyvitamin D₃, the steroid hormone metabolite of vitamin D₃ (Ref. 4). However, whereas a variety of ligand-gated ion channels have been shown to be steroid-sensitive²⁶, an allosteric modulation