www.neuropsychopharmacology.org

Letter to the Editor Physiological Evidence for Lifelong Brain Development: A Comment on Bartzokis

Irwin Feinberg*,¹

¹UCD Sleep Lab, University of California, Davis, CA, USA

Neuropsychopharmacology (2003) 28, 1215–1216, advance online publication, 9 April 2003; 10.1038/sj.npp.1300179

Sir

Bartzokis' (2002) proposal that schizophrenia is caused by errors in a lifelong process of brain development makes a valuable addition to neurodevelopmental models of schizophrenia. Bartzokis is primarily concerned with anatomical evidence (myelination) for prolonged developmental brain changes. Physiological evidence also supports his thesis that developmental brain processes persist late into life. These are dramatically demonstrated by the ontogenetic changes in NREM delta EEG and are apparent in both computermeasured 0.3–3 Hz activity and visually scored stage 4. Both measures show that the rate of delta production peaks in early childhood, declines rapidly across adolescence and then diminishes more slowly during adulthood, reaching a plateau at 50-60 years of age. Period-amplitude analysis demonstrates that the production of 0.3-3 Hz integrated amplitude declines by about 60% between ages 5 and 22 years, a change of -3.5%/year (Feinberg et al, 1990). All children show this delta decline. It must therefore be considered a normal developmental process. The delta decline continues across adulthood but at a slower rate. Nevertheless, the change is still substantial. Thus, delta at age 72 years is about 50% of the 22-year old mean, an average change of -1%/year (Feinberg *et al*, 1983).

Until recently, most other sleep researchers and I interpreted the delta decline in childhood-adolescence as due to developmental processes and assumed that the decline during adulthood was produced by aging (degenerative) brain events. However, there is no evidence indicating that different brain processes produce the delta decline in these two age periods (Feinberg, 2000). In fact, in old age, when degenerative brain changes increase markedly, delta remains at plateau levels. The decline of delta sleep across adulthood, which appears to be a continuation

of the childhood decline, therefore provides physiological evidence that supports Bartzokis' hypothesis that some kind of developmental change takes place in the human brain over most of the life span. The ontogenetic changes in delta are especially interesting because this EEG component appears to reflect a homeostatic process by which sleep reverses the effects of waking brain activity (Feinberg, 1974; Borbely, 1982), presumably acting on plastic neuronal systems (Moruzzi, 1966).

Recent investigators of neurodevelopmental models of schizophrenia have tended to overlook the relevance of sleep EEG evidence. However, it is useful to recall that it was a search for the explanation of the delta decline during adolescence that gave rise to the first modern neurodevelopmental model of schizophrenia based on synaptic pruning (Feinberg, 1982/83). The sleep EEG remains a useful tool for new research on late brain development. Computer-quantified NREM delta is a highly reliable measure (Tan *et al*, 2000) that can be studied repeatedly and noninvasively.

REFERENCES

- Bartzokis G (2002). Schizophrenia: breakdown in the wellregulated lifelong process of brain development and maturation. *Neuropsychopharmacology* **27**: 672–683.
- Borbely A (1982). A two-process model of sleep regulation. *Hum Neurobiol* 1: 195-204.
- Feinberg I (1974). Changes in sleep cycle patterns with age. J Psychiatr Res 10: 283-306.
- Feinberg I (1982/83). Schizophrenia: caused by a fault in programmed synaptic elimination during adolescence. J Psychiatr Res 17: 319–334.
- Feinberg I (2000). Slow wave sleep (SWS) and growth hormone (GH) diverge sharply during puberty: biological implications (Letter). *JAMA* **284**: 2717.
- Feinberg I, Fein G, Floyd TC, Aminoff MJ (1983). Delta (0.5–3 Hz) EEG waveforms during sleep in young and elderly normal subjects. In: Chase MH, Weitzman ED (eds). *Sleep Disorders: Basic and Clinical Research*. Spectrum Publications, Inc.: New York. pp 449–462.



^{*}Correspondence: Dr I Feinberg, UCD Sleep Lab, TB148, University of California, Davis CA 95616, USA, E-mail: ifeinberg@ucdavis.edu Received 17 October 2003; accepted 9 January 2003 Online publication: 3 February 2003 at http://www.acnp.org/citations/

Npp020303383/default.pdf

- Feinberg I, March JD, Flach K, Maloney T, Chern W-J, Travis F (1990). Maturational changes in amplitude, incidence and cyclic pattern of the 0 to 3 Hz (Delta) electroencephalogram of human sleep. *Brain Dysfunct* **3**: 183–192.
- Moruzzi G (1966). The functional significance of sleep with particular regard to brain mechanisms underlying conscious-

ness. In: Eccles JC (ed). Brain and Conscious Experience. Springer-Verlag: New York. pp 345-388.

Tan X, Campbell IG, Palagini L, Feinberg I (2000). High internight reliability of computer-measured NREM delta, sigma and beta: biological implications. *Biol Psychiatry* **48**: 1010–1019.