history and philosophy of the science. The suggestion that evolutionary psychology and psychiatry has been created over the past 20 years is surprising.

I would suggest that its origins are far more venerable and lie in the work of Ernst Haeckel (1834–1919), sometime Professor of Zoology at the University of Jena, who dominated the discussion of evolutionary theory in German-speaking Europe in the 19th century and who, indeed, published his theory of human evolution in 1868 (see Haeckel, 1879), 3 years prior to Darwin's *The Descent of Man* (1871). He is now perhaps best remembered for his 'biogenetic law' (i.e. that ontology recapitulates phylogeny). For human beings this means that the stages of human development replicate, in sequence, the stages of the development of the human race. In addition to biological recapitulation, Haeckel considered that the mind had also evolved and that one of the tasks of psychology was to trace this evolution.

The task was initially taken up by Freud (1950) and by Jung (1953), who started to compile historical evidence for his hypothesis of the collective unconscious in 1909. Indeed, throughout the *Collected Works* it is clear that Jung considered that ontogenesis in psychology corresponded to phylogenesis and that infantile thinking, as well as dreams, were "a re-echo of the prehistoric and the ancient".

Abed, R. T. (2000) Psychiatry and Darwinism. *British Journal of Psychiatry*, **177**, 1–3.

Darwin, C. R. (1871) *The Descent of Man, and Selection in Relation to Sex*. London: John Murray.

Freud, S. (1950) Totem and Taboo: Resemblances between the Psychic Lives of Savages and Neurotics. Reprinted (1953–1974) in the *Standard Edition of the Complete Psychological Works of Sigmund Freud* (trans. and ed. J. Strachey), vol. 13: London: Hogarth Press.

Haeckel, E. H. P. A. (1879) *The Evolution of Man: A Popular Exposition of the Principal Points of Human Ontogeny and Phylogeny* (trans. from the German edition of 1868). London: Beccles.

Jung, C. G. (1953) *The Collected Works*. London: Routledge & Kegan Paul.

C. A. Sims Suffolk Forensic Services, Forensic Psychology Services, St Clements Hospital, 564 Foxhall Road, Ipswich IP3 8LT, UK

Chromosome 22q11 deletion and brain tissue composition

We thank Eliez & Blasey (2001) for their kind comments about our paper (van Amelsvoort *et al*, 2001). However, we disagree that our paper implied that Eliez *et al* (2000) reported relatively smaller frontal lobe volumes and would like to draw their attention to the following. Normal brain maturation is accompanied by a reduction in cortical grey matter volume and an increase in white matter volume. Myelination typically progresses from posterior to anterior brain regions and occurs relatively late in frontal regions (where it continues into adulthood). Also, the maturational process from adolescence into adulthood is associated with a net volume reduction in frontal regions (Giedd *et al*, 1999; Sowell *et al*, 1999), and not a volume increase as Eliez & Blasey (2001) suggest. Consequently, we interpreted the relatively larger frontal lobe volumes found by Eliez *et al* (2000) in children and adolescents with velocardio-facial syndrome (VCFS) as compared with controls as possibly being caused by a relative delay in onset of 'maturational' grey matter reduction in VCFS. Our finding of a regional increase in volume of frontal grey matter and decrease in frontal white matter, in the absence of a difference in total frontal lobe (grey and white matter) volume, supports this interpretation and suggests that subtle differences in tissue composition occur which may reflect a delay in maturational processes (van Amelsvoort *et al*, 2001). Moreover, white matter abnormalities have been reported in VCFS and abnormal myelination could partially explain the abnormal, or delayed, maturational process. Future studies using longitudinal designs across this age span, and newer techniques such as diffusion tensor imaging, should be able to address this issue.

van Amelsvoort, T., Daly, E., Robertson, D., *et al* (2001) Structural brain abnormalities associated with deletion at chromosome 22q11. Quantitative neuroimaging study of adults with velo-cardio-facial syndrome. *British Journal of Psychiatry*, **178**, 412–419.

Eliez, S. & Blasey, C. M. (2001) Chromosome 22q11 deletion and brain structure (letter). *British Journal of Psychiatry*, **179**, 270.

—, Schmitt, J. E., White, C. D., *et al* (2000) Children and adolescents with velocardiofacial syndrome: a volumetric MRI study. *American Journal of Psychiatry*, **157**, 409–415.

Giedd, J. N., Blumenthal, J., Jeffries, N. O., *et al* (1999) Brain development during childhood and adolescence: a longitudinal MRI study. *Nature Neuroscience*, **2**, 861–863.

Sowell, E. R., Thompson, P. M., Holmes, C. J., *et al* (1999) *In vivo* evidence for post-adolescent brain maturation in frontal and striatal regions. *Nature Neuroscience*, **2**, 859–861.

T. van Amelsvoort, K. C. Murphy, D. G. M. Murphy Department of Psychological Medicine, Institute of Psychiatry, De Crespigny Park, London SE5 8AF, UK

Long-term potentiation and changes seen in depression

Reid & Stewart (2001) review evidence for a neurobiological basis of depression and it is suggested that brain plasticity plays a major role. These plasticity changes involve neuronal atrophy, neurogenesis, dendrite involution and formation, and long-term potentiation (LTP). Electroconvulsive therapy (ECT) and antidepressants enhance LTP and, as Reid & Stewart imply, the benefits (and adverse effects) of such treatments may be due to an enhancement or saturation of LTP. We question whether abnormal LTP *per se* is a critical neurobiological path to the changes seen in depression. We support the view that alterations in structural plasticity, as opposed to LTP, are more critical. Antidepressants, ECT, depression and stress can all modulate neuronal structure and LTP has been shown to be abnormal in models of depression and stress, but it does not follow that abnormal LTP is a prerequisite for these states, even though LTP is accepted to be important in, for example, associative learning.

In studies where LTP has been shown to alter neuronal structure, the increase in synaptic efficacy (assayed electrophysiologically) occurs within seconds to minutes but the earliest detected structural changes take at least 20 minutes (Yuste & Bonhoeffer, 2001). This time frame also does not correlate with the time required for the effects of antidepressant treatment (including ECT) – structural changes correlate better. Furthermore, although LTP is associated with morphological changes, these do not necessarily contribute to the potentiation (Yuste & Bonhoeffer, 2001). This casts doubt on the notion that the alterations in LTP are critical to the pathophysiological mechanism. We support the notion that the primary pathology is due to maladaptive neuronal structural change (Vaidya & Duman, 2001). The most likely reason why LTP can be affected by stress and depression,

https://doi.org/10.1192/bjp.179.6.559-a Published online by Cambridge University Press

or by treatments for depression, is because such stimuli activate neuronal molecular signalling pathways. These pathways overlap with each other and with the signalling pathways that lead to dendritic structural changes.

Reid, I. C. & Stewart, C. A. (2001) How antidepressants work. New perspectives on the pathophysiology of depressive disorder. *British Journal of Psychiatry*, **178**, 299–303.

Vaidya, V. A. & Duman, R. S. (2001) Depression: emerging insights from neurobiology. *British Medical Bulletin*, **57**, 61–79.

Yuste, R. & Bonhoeffer, T. (2001) Morphological changes in dendritic spines associated with long-term synaptic plasticity. *Annual Review of Neuroscience*, **24**, 1071–1089.

S. H. Zaman Mental Health Unit, Gloucester House, Southmead Hospital, Bristol BS10 5NB, UK

R. Zaman Bedfordshire and Luton Community NHS Trust, Mental Health Service, Bedford, UK

Authors' reply: It was kind of Drs S. H. & R. Zaman to take an interest in our paper. In their thoughtful response they draw attention to the time course of LTP induction (seconds to minutes), and point out that this does not correlate with the time required for the effects (presumably, clinical response) of antidepressant treatments. The key issue is not the speed with which LTP induction itself occurs, which is unchanged by stress or antidepressant treatments (Stewart & Reid, 1993). It is rather the time course of changes induced in the regulation of LTP by antidepressant treatments (the so-called 'metaplasticity' referred to in our paper) that is important. This develops gradually, requiring at least six spaced ECT treatments for maximum effect (Stewart *et al*, 1994) or 14 days of fluoxetine treatment (Stewart & Reid, 2000). Interestingly, the effects of ECT on the degree to which LTP can be induced are detectable even 40 days after the end of a course (Stewart & Reid, 2000). These periods each correlate very nicely with antidepressant response, with the last described also mirroring the time course of relapse after successful ECT treatment in humans without antidepressant prophylaxis. Changes in excitatory post-synaptic potentials are seen, however, immediately after a single electroconvulsive application in experimental studies (Stewart *et al*, 1994), but they are smaller and more transient than those seen after a series of applications. This also accords with clinical observation: severely ill patients receiving ECT often show clear but transient responses after the first treatment in a course.

Of course, these are electrophysiological observations, and they may be mediated by ultrastructural neuronal changes. In this sense, we agree with the subtle point being made by Zaman & Zaman. Our aims are to draw together rather than disaggregate structural and functional phenomena. That is why we used the term connectivity in the review to refer to both functional and ultrastructural (e.g. dendritic) changes underlying the plasticity of neuronal connections, which we wished to distinguish from more gross effects such as cell death or proliferation. The fact that "molecular signalling pathways" to "dendritic structural changes" and to LTP overlap is precisely why we classed them together as candidate contributors to the neurobiology of depressive disorder. They may be dissociable, as Zaman & Zaman point out, but this is not in itself evidence for or against the role of the regulation of LTP in affective disorder.

In any event the functional (electrophysiological plasticity) and structural changes (microanatomical plasticity) described in our review are each associated in reciprocal fashion with stress and antidepressant treatments, respectively – neither structural nor functional changes have been shown to have a causal role in depressive disorder. It does not allow that either phenomenon is a prerequisite for depressive states.

Stewart, C. & Reid, I. (1993) Electroconvulsive stimulation and synaptic plasticity in the rat. *Brain Research*, **620**, 139–141.

—— & —— (2000) Repeated ECS and fluoxetine administration have equivalent effects on hippocampal synaptic plasticity. *Psychopharmacology*, **148**, 217–223.

——, Jeffrey, K. & Reid, I. C. (1994) LTP-like synaptic efficacy changes following electroconvulsive stimulation. *Neuroreport*, **5**, 1041–1044.

I. Reid, C. Stewart Department of Psychiatry, University of Dundee, Ninewells Hospital, Dundee DD1 9SY, UK

Leptin and antipsychotic drugs

There is growing interest in the role of leptin in excessive body weight gain during antipsychotic drug treatment. Herrán *et al*'s (2001) paper is an important contribution to the field. Among other interesting findings they demonstrated that the functioning of the leptin system is preserved during antipsychotic drug administration. However, it is not "the first study analysing the effects of chronic antipsychotic medication on serum leptin levels", since other authors have published relevant data for humans and rats (Baptista *et al*, 2000; Lacruz *et al*, 2000; Melkerson *et al*, 2000).

An important finding by Herrán *et al* was that olanzapine- and risperidone-treated patients displayed the highest and lowest leptin levels, respectively, "even after controlling for BMI". This may support the contention that olanzapine is promoting a deleterious metabolic profile. That finding also prompts speculation that other mechanisms besides body weight gain could be involved in leptin elevation during antipsychotic treatment.

We have proposed elsewhere that insulin may be one of these additional mechanisms. Insulin is a powerful stimulus for leptin synthesis and secretion. Female rats with sulpiride-induced obesity unexpectedly displayed normal serum leptin (and insulin) levels (Lacruz *et al*, 2000). In addition, serum leptin and insulin levels correlated positively in healthy people and antipsychotic-treated patients (Baptista *et al*, 2000, 2001). As olanzapine strongly stimulates appetite, it may promote insulin (and leptin) secretion, with relative independence from body weight gain. Surprisingly, Herrán *et al* reported that treatment with clozapine (another agent with strong appetite-stimulating properties) was associated with leptin levels similar to those found in haloperidol- and phenothiazine-treated patients (in spite of a higher body weight gain). If it were possible for Herrán *et al* to furnish the information, readers would benefit from knowing (a) the insulin levels in these patients; (b) a comparison of leptin levels between clozapine-, olanzapine- and risperidone-treated patients and their specific matched controls; and (c) the gender distribution in these treatment groups. If olanzapine- and risperidone-treated subjects display higher and lower leptin levels, respectively, than their controls, and if the gender distribution is similar in the three treatment groups, an additional important contribution will have been brought to the field of psychopharmacology.

Baptista, T., Lacruz, A., Silvera, R., *et al* (2000) Body weight gain after administration of antipsychotic drugs: correlation with leptin, insulin and reproductive hormones. *Pharmacopsychiatry*, **33**, 81–88.

——, ——, Angeles, F., *et al* (2001) Endocrine and metabolic profile in the obesity associated with typical antipsychotic drug-administration. *Pharmacopsychiatry*, in press.

https://doi.org/10.1192/bjp.179.6.559-a Published online by Cambridge University Press