DOWN-REGULATING MITOCHONDRIA

By Tadafumi Kato

The role of mitochondrial function in bipolar disorder is proposed. Although global down regulation of mitochondria-related genes in the postmortem brains may reflect mitochondrial dysfunction in bipolar disorder, decreased sample pH can confound such data. It is a matter of debate whether decreased pH reflects the pathology of bipolar disorder or an artifact. Rollins et al. first reported that the pH in the postmortem brain is associated with mitochondrial DNA haplogroups. This suggests that global down-regulation of mitochondria-related genes associated with decreased sample pH may somehow relate to mitochondrial function.

Comment on: *Rollins, B., Martin, M. V., Sequeira, P. A., Moon, E. A., Morgan, L. Z., Watson, S. J., Schatzberg, A., Akil, H., Myers, R. M., Jones, E. G., Wallace, D. C., Bunney, W. E., and Vawter, M. P. (2009).Mitochondrial variants in schizophrenia, bipolar disorder, and major depressive disorder.* PLoS ONE *4, e4913.*

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ASIC1A: A NEW THERAPEUTIC TARGET IN DEPRESSION?

By Philippe Marin

Existing antidepressants, which mainly target monoaminergic systems, still have major deficiencies, including insufficient efficacy, undesirable side-effects and delayed action, underpinning the great demand for innovative treatments. Targeting acid-sensing ion channel-1a (ASIC1a) might be an efficient strategy to combat depression (Coryellet et al., 2009). The group demonstrated that genetic and pharmacological inhibition of ASIC1a produced antidepressant-like effects in multiple depression-related behaviors, which are independent of and additive to those induced by drugs that modify monoaminergic transmission. Moreover, restoring ASIC1a expression in the amygdala suppressed the antidepressant-like phenotype in ASIC1a-/- mice, underscoring the critical influence of the amygdala in mood regulation.

Comment on: *Coryell, M. W., Wunsch, A. M., Haenfler, J. M., Allen, J. E., Schnizler, M., Ziemann, A. E., Cook, M. N., Dunning, J. P., Price, M. P., Rainier, J. D., Liu, Z., Light, A. R., Langbehn, D. R., and Wemmie, J. A. (2009). Acid-sensing ion channel-1a in the amygdala, a novel therapeutic target in depression-related behavior.* J. Neurosci. *29, 5381-5388.*

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NICOTINE CAN HELP

By Marina Picciotto

Partial agonists of alpha4/beta2-containing nicotinic acetylcholine receptors (nAChRs) are novel antidepressant-like compounds. The monoamine system is the primary target for therapeutics that treat depression, but dysfunction of the cholinergic system is also postulated to contribute to human depression. Recent human studies suggest that decreasing cholinergic transmission through nAChRs can augment antidepressant response. This is consistent with studies showing that existing partial agonists are effective in mouse models of antidepressant action. This hypothesis was evaluated directly by identifying novel partial agonists of alpha4/beta2 nAChRs, which demonstrated that interfering with signaling through alpha4/beta2 nAChRs was sufficient for behavioral effects consistent with antidepressant action. This study suggests that the cholinergic system is an untapped area for understanding the etiology and treatment for major depressive illness.

Comment on: *Mineur, Y. S., Eibl, C., Young, G., Kochevar, C., Papke, R. L., Gundisch, D., and Picciotto, M. R. (2009). Cytisine-based nicotinic partial agonists as novel antidepressant compounds,* J. Pharmacol. Exp. Ther. *329, 377-386.*

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WHY DO PEOPLE SMOKE?

By J. Mark Davis

Probably because it improves mood and the salience of positive events. Gilbert et al. studied a group of smokers and found that nicotine improves positive affect and decreases negative affect, but it also seems to have differential effects on the brain's hemispheres. The group found that nicotine enhances accuracy of identification of words with a positive valence (e.g., smart or happy) that are presented to the left hemisphere, as well as words with a negative valence (e.g., dirty or cruel) presented to the right hemisphere. Furthermore, for smokers who received a nicotine patch (versus a placebo), increases in depression were associated with decreases in identification of emotionally-loaded words presented to the right hemisphere.

Comment on: *Gilbert, D. G., Carlson, J. M., Riise, H., Rabinovich, N. E., Sugai, C., and Froeliger, B. (2008). Effects of nicotine and depressive traits on affective priming of lateralized emotional word identification.* Exp. Clin. Psychopharmacol. *16, 293-300.*

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