

S33-03 - INVOLVEMENT OF CYTOSKELETAL MICROTUBULES IN THE ACTION OF ANTIDEPRESSANT DRUGS

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Growing evidence suggests that alterations in cytoskeletal microtubules dynamics may be involved in the effects of antidepressant drugs on brain structural neuronal plasticity phenomena such as remodelling of axons and dendrites. The speaker will review the most recent data in the field obtained in either naïve animals or in animal models of stress/depression. These results were gathered using a multidisciplinary approach, ranging from behavioural tests to neurochemistry and molecular analyses of specific markers of microtubule dynamics and synaptic remodelling. Several classes of antidepressant drugs have been shown to differentially modulate the expression of microtubular proteins and synaptic markers in specific rat brain regions depending from the dose and length of administration. Importantly, such antidepressant-induced effects on microtubular and synaptic proteins showed a very different pattern of changes in environmental (social isolation from weaning) or genetic (Flinders Sensitive Line) rat models of depression, which were not always accompanied by recover of the “depressive-like” behavioural phenotypes. Therefore, antidepressant drugs can modulate brain cytoskeletal and synaptic remodelling, but the pattern of these phenomena seems related to a complex gene-environment interaction. These data may be considered of translational human relevance when put in the context of partial- or non responders to antidepressant therapy. Finally, MAPREG developed new molecules specifically targeting neuronal microtubules and promoting structural neuronal plasticity, which may represent novel tools for the therapy of depressive disorders. Novel data on the antidepressant efficacy of one of these promising molecules in rat models of depression will be presented.