

## Acquired Resistance in Unipolar Depression

P. Gorwood<sup>1</sup>

<sup>1</sup>CMME, Hopital Sainte-Anne INSERM U894 & Paris Descartes University, PARIS, France

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It has been proposed that depressive episodes could be "neurotoxic", decreasing memory skills and/or regularly increasing neurocognitive retardation with the repetition of episodes. We describe two protocols which could reinforce the likelihood of this neurotoxic hypothesis, and a study showing that it is indeed possible to reduce the time before getting treatment response.

On the first protocol a large sample of depressed outpatients was tested for narrative delayed memory (Weschleer paragraph), before and after antidepressant treatment (Gorwood et al., 2008). Delayed memory skills after treatment response was strongly correlated to the length and the number of past depressive episodes. The second protocol assessed neurocognitive retardation during a depressive episode and after clinical remission is obtained. Once again we observed that neurocognitive retardation (TMT-A and -B) in remitted patients was highly correlated to the number of past depressive episodes (Gorwood et al., 2014). We then tested if treatment resistance could be detected a bit earlier than the 4 to 6 weeks observation usually considered as required. Indeed, we found that a two weeks observation is enough to decide if we should continue or change the present treatment. We furthermore saw that assessing emotions rather than depressive symptoms might be even more predictive of the chances of treatment success.

These studies reinforce the concept of neurotoxicity of depressive disorder, which means that an important part of treatment resistance is acquired during the process of the disorder, and therefore stress the importance of treating early and completely each depressive episode, not only for an acute relief, but also to improve the long term prognosis of mood disorders.