

# Close association between polymorphisms of the nitric oxide synthetase 3 gene and neurological disorders other than stroke

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## To the editor

I read with great interest the article by Du et al in a recent issue of your journal.<sup>1</sup> The article makes highly interesting reading. Interestingly, the past few years have seen the discovery of a number of close associations between polymorphisms of the nitric oxide synthetase 3 (NOS3) gene and neurological diseases other than stroke.

For instance, increased expression of NOS3 results in altered mitochondrial function in neurons. As a consequence, the intracellular levels of reactive oxygen species are accentuated, as are the levels of p53 and Bax, resulting in the dementia and neurodegeneration seen in individuals with Alzheimer's disease.<sup>2</sup> The G894T polymorphism acts as a risk factor for sporadic frontotemporal lobar degeneration. In fact, in a recent study, Venturelli et al have reported an incidence rate of 40% for the G894T polymorphism in individuals afflicted with frontotemporal lobar degeneration.<sup>3</sup> Similarly, the risk of post-stroke dementia is increased in stroke patients with the rs1799983 polymorphism of the NOS3 gene. For instance, the hazard ratio is 3.14 in stroke patients with the TT genotype in comparison with those having the GG genotype.<sup>4</sup>

Similarly, individuals with Pick's disease and Lewy body disease demonstrate altered NOS3 expression and accelerated proliferation of NOS3-positive neurons.<sup>5</sup> An increased incidence of Parkinson's disease is also associated with the rs12829185 and rs3782218 polymorphisms of the NOS1 gene and the rs944725 polymorphism of the NOS2A gene.<sup>6</sup> Further, Sohn et al have recently demonstrated increased proliferation of NOS3-expressing glial cells in amyotrophic lateral sclerosis, as well as in progressive supranuclear palsy.<sup>5</sup>

The above examples illustrate a clear association between NOS3 and many neurological diseases, ranging from Alzheimer's disease to Pick's disease. Modulation of NOS3 function may alter and beneficially attenuate the progression of these diseases. Hopefully, the coming years will see the development of these NOS3 modulators.

## Disclosure

The author reports no conflicts of interest in this work.

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