

Immunotherapy Applied to Neuropsychiatric Disorders: A New Perspective

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Manipulation of the immune system has led to amazing and paradigm –shifting changes in therapeutics and population hazard control measures. It was one of the most important medical discoveries of all time, allowing epidemics control, a great fall in infant, adult and elderly morbidity/mortality and new target development therapies for several hematological and metabolic diseases [1,2].

Several target treatments have already been development in neurobiological models, particularly for neuroinflammatory diseases, such immunosuppressant-resistant myasthenia gravis (rituximab) and multiple sclerosis (alemtuzumab). These diseases are, in principle, caused by abnormal immunological function, and these novel treatments act by impeding specific inflammatory action against motor plaque receptors (miastenia gravis) or myelin degradation (multiple sclerosis) [3,4].

There is new evidence to suggest that active and passive immunotherapy may be beneficial not only for infections, but for several neuropsychiatric disorders, including Alzheimer's disease, methamphetamine dependence and nicotine dependence. Though acting by different mechanisms, results are indicative of improvement in general symptoms, preventing relapse of disease, and perhaps even prevention of onset symptoms of said diseases [5-7].

Alzheimer's disease is one of the main diseases where immunotherapy was studied as an alternative in clinical trials. Molecular targets include β -amyloid plaques which are amassed in brain matter in this clinical setting, and neurofibrillary intracellular tangles composed of tau protein, which are also toxic to neurons [8]. Phase I trials have shown modest results in active immunization with β -amyloid-like proteins, with lowered plaque burden and improved cognitive symptoms in transgenic mice [9-11]. Comparable results were obtained when passive immunization against epitopes in β -amyloid plaques was used, and both passive (anti tau antibodies) and active (tau epitopes paired with adenovirus proteins) immunization against tau intracytoplasmatic proteins was performed in mice [12-17]. Unfortunately, these alternative treatments have documented side effects such as Th1 response leading to exacerbated glial activation (in β -amyloid vaccines and anti- β -amyloid antibodies phase I trials), neuron damage and motor side effects in animal models (in tau protein trials) in animal models [13,17]. However, improved cognitive function was observed in subjects receiving this therapy, especially in those considerate moderately affected by Alzheimer's disease [11-17].

A novel application to active and passive immunotherapy is in the treatment of addictive disorders, such as nicotine, cocaine and methamphetamine.

Cocaine dependence is the most researched drug addiction in this modality of treatment. Clinical experiences are varied from vaccines involving hap ten formulas, anti-idiotypic cocaine antibodies or passive immunization. The results in animal models were positive, with the feasibility for application in human models. Passive immunization in cocaine-dependent rats also showed the possibility of use of catalytic antibodies, with the potential to promote hydrolysis before cocaine molecules reach their intended targets [18-21].

Nicotine hap tens have also been used as molecular targets for

nicotine dependent subjects, mainly in active immunization scenarios, with reduction of total nicotine concentration in brain tissue and cerebrospinal fluid, preventing initiation of drug dependence in the pleasure centers of the brain (mesolimbic and mesocortical pathways) in non-addicted models of study [20-24]. The use of hap tens and specific antibodies against other central nervous system stimulants – PCP and methamphetamine – has been shown in successful scenarios, lowering drug preference in animal models of non-addiction [25-27].

In conclusion, immunotherapy is a novel area in the treatment of neuropsychiatric disorders, not only because it may hold the key to treating irreversible and degenerative conditions such as Alzheimer's disease, or by provoking hydrolysis of specific addictive molecules such as cocaine, but because it may prevent onset of symptoms of addiction and drug craving. In this way, dependence and addictive behavior could become preventable to the general population when and if exposed to a specific addictive drug, much in the same way a vaccinated population is immune to a specific infectious target.

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