Acute response to cholinergic challenge predicts long-term response to galantamine treatment in patients with Alzheimer's Disease

Anne Catrien Baakman[1], Carmen Gavan[2], Lotte Van Doeselaar[3], Marieke de Kam[3], Karen Broekhuizen[3], Ovidiu Bajenaru[2], Laura Camps[3], Eleonora Swart[4], Kees Kalisvaart[5], Nikki Schoonenboom[6], Evelien Lemstra[7], Philip Scheltens[7], Adam Cohen[3], Joop Van Gerven[8], and Geert Jan Groeneveld[3]

[1]Amsterdam UMC Locatie VUmc
[2]Spitalului Universitar de Urgenta
[3]Centre for Human Drug Research
[4]Amsterdam University Medical Centres
[5]Kennemer Gasthuis
[6]Spaarne Gasthuis
[7]Amsterdam UMC VUMC Site
[8]Central Committee on Research Involving Human Subjects (CCMO

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Abstract

Cholinesterase inhibitors have been shown to improve cognitive functioning in patients with Alzheimer's Disease (AD), but are associated with side effects and only 20-40% of the patients clinically improve. In this study, we aimed to investigate the acute pharmacodynamic (PD) effects of a single dose of galantamine on CNS functioning in mild to moderate AD patients and its potential to predict long-term treatment response. This study consisted of a challenge phase, in which a single dose of 16 mg galantamine was administered to 50 mild to moderate AD patients in a double-blind, placebo-controlled cross-over fashion. Acute PD effects were monitored with use of a CNS test battery. In the subsequent treatment phase of the study, patients were treated with open-label galantamine according to regular care. After 6 months of galantamine treatment, patients were categorized as either responder or as non-responder based on their MMSE, NPI and DAD scores. An analysis of covariance was performed to study the difference in acute PD effects between responders and non-responders. Acute decreases of absolute frontal alpha (-20.4; 95%CI=-31.6,-7.47; p=.0046), beta (-15.7; 95% CI=-28.3,-0.93; p=.0390) and theta (-25.9; 95%CI=-38.4,-10.9; p=.0024) EEG parameters and of relative frontal theta power (-3.27%; 95%CI=-5.96,-0.58; p=.0187) on EEG after a single dose administration of galantamine significantly distinguished long-term treatment responders (n=11) from non-responders (n=32) after 6 months. This study demonstrates that patients who demonstrate a reduction in EEG power in the alpha and theta frequency after a single administration of galantamine 16 mg will most likely respond to treatment.

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