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Background: Targeted delivery of nerve growth factor (NGF) has emerged as a potential treatment for Alzheimer's Disease (AD) due to its regenerative effects on the basal forebrain cholinergic neurons. The hypothesis is currently being tested in AD patients using encapsulated cell (EC) biodelivery of NGF. Feasibility of the surgical procedure and safety has been reported (Eriksdotter et al 2012, Wahlberg et al 2012). Here, we report the results from the second cohort of patients who received a second generation of NGF EC implants. The primary endpoint was safety and tolerability. The secondary endpoints were effects on cognition and biological markers, including atrophy on MRI, and nicotine binding on PET. **Methods:** Four patients with mild to moderate AD were recruited to an open-label, phase 1b study for a six month treatment period. Each patient received four NGF EC biodelivery devices targeting the cholinergic basal forebrain stereotactically. Using the Sleeping beauty transposon gene transfer technology resulted in an increased release of NGF up to 10 ng NGF/device/24h. The patients were monitored with regard to safety, tolerability, clinical signs of disease progression and implant function. **Results:** All four patients were implanted successfully with double implants bilaterally without complications. None of the reported adverse events were assessed as being NGF related. All patients completed the study, including implant removal at 6 months. A majority (13/16) of the implants released NGF upon removal with 50% of the implants releasing NGF at the same rate, or higher, than at implantation. **Conclusions:** This study demonstrates the safety and tolerability of sustained release of EC biodelivery of NGF without signs of toxicity as well as the surgical feasibility of implantation and removal of multiple NGF EC biodelivery devices in AD patients.

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BENEFITS OF HEALING GARDENS IN AD: IS EVIDENCE DIFFICULT TO PROVE? —THE NANCY PERSPECTIVE

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Background: The French Alzheimer Plan (FAP) 2008-2012 recommends the creation of therapeutic gardens as integral part of care-taking institutions for individuals with AD. One of the main difficulties remains to establish a practical methodology for evaluation the various benefits observed by the medical and nursing staff in their daily practice. It is a real challenge to conduct multicenter studies on therapeutic gardens because of the unique features of each garden; gardens of very different characteristics cannot be compared in a meaningful way. **Methods:** Ten gardens in the Lorraine Regions will be put in place by the same team and designed and equipped following the criteria which are based upon the experience gained in the pilot project which is the garden «art, mémoire et vie» of the Nancy University Hospital. The methodology concerning the preparation of such a project with the nursing team has been described elsewhere and will be applied consistently in this larger setting. In stage I a detailed analysis and validation of the plan will be carried out to ensure a good topographic legibility of the environment for the patients and in stage II the creation of art work will be added which fits both purpose and environment. The totality of the garden is to be integrated in a therapeutic project shared by all medical and nursing team **Results:** Ultimately the objective is the creation of a network of partner projects dedicated to research on psychosocial activities practiced in such therapeutic gardens. This project has been submitted in the frame of call for offers of the "Pacte Lorraine 2014-2016". **Conclusions:** This project will allow research on benefits of therapeutic gardens in a comparative and multicenter study because all gardens will be designed and equipped by the same team and based upon the same principles. This opens up new options for research aiming at continuous improvement of such gardens and the therapeutic concepts that are practiced using these gardens.

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THE EFFECTS OF AGE, COGNITION, AND FATIGUE ON A PROLONGED DRIVE

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Background: Age related changes in cognitive abilities can impact an individual's ability to function safely and independently. Of particular concern are changes in driving ability. Studies have demonstrated more driving errors and accidents in the older population, however, minimal research has been conducted to understand how cognitive changes might underlie these findings. Driving while fatigued increases a person's risk of accidents, but it is unknown if older adults are more vulnerable to errors while driving when fatigued. This study aimed to examine driving performance using a driving simulator in older adults with and without cognitive impairment and healthy young adults. **Methods:** Thirty-two healthy young (18-30 years old), 24 young-old (55-65 years old), 15 old-old (over 65 years old), and 17 older adults with MCI (over 55 years old) all who are currently driving with a valid driver's license participated. A 60-minute computerized driving scenario designed to elicit fatigue was presented on a 45" flat screen monitor using STISIM software. Lane position, speed, variability, and driving errors were measured and compared across each 10-minute segment of the drive. **Results:** Results showed that the young and the young-old groups were similar in performance with minimal decrements across the 60-minute time span, although the young adults tended to show more errors as they became fatigued. Although the old-old group initially had difficulty during the first 10 minute in variability in lane position, this rapidly improved, and they looked like the young and young-old groups for the remainder of the time. In contrast, the MCI group had difficulty with the task at the outset of the study which worsened with fatigue. **Conclusions:** The current results demonstrate interactions between fatigue, cognitive functioning, and age in terms of experience. While the older adults with MCI demonstrated poor driving performance even without fatigue, the experience of healthy older adults appears to moderate the effect of fatigue on their driving performance. In addition, the young adults were more vulnerable to the effects of fatigue, consistent with the previous research (Fittness, Reyner, & Horne, 2012).

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BRAZILIAN PROPOLIS IMPROVES COGNITIVE FUNCTIONS AND REGULATES SERUM CYTOKINE BALANCES IN PATIENTS WITH MILD COGNITIVE IMPAIRMENT AT HIGH ALTITUDE

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Background: Recently, much attention has been paid to the association of hypoxia with cognitive impairments, because brain is highly vulnerable to hypoxic stress due to its high oxygen requirement. People living in Qinghai-Tibet Plateau experience chronic hypoxia daily at high altitude, and we have found that elderly individuals in the Qinghai-Tibetan Plateau are excursions with mild cognitive impairment (MCI), which is frequently seen as a prodromal stage of Alzheimer's disease (AD) (Zhu et al., 2002). Current medical researches on the cognitive functions pay a special attention in nature materials because their traditional usages. Propolis is a resinous substance produced by honeybees as a defense against intruders which has been used as therapeutic properties since ancient times, and we have recently found that propolis prevents the hypoxia-induced neuroinflammation in animals (Wu et al., 2013, Wu & Zhu et al., 2013). [Objective] In the present study, we focus to investigate whether Brazilian propolis can improve the cognitive functions in the patients with MCI at high altitude. **Methods:** 70 patients with MCI living in Qinghai province at 2,600m above sea levels were divided into two groups randomly (Propolis group=35, Placebo group=35) A double blind test was utilized. After received Brazilian Propolis (226.8mg) daily or Placebo (without Propolis) for 24 weeks, mini Mental State Examination (MMSE), Alzheimer's disease Assessment