

## The role of interleukin-1 in neuroinflammation and Alzheimer disease: an evolving perspective

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**Abstract:** Elevation of the proinflammatory cytokine Interleukin-1 (IL-1) is an integral part of the local tissue reaction to central nervous system (CNS) insult. The discovery of increased IL-1 levels in patients following acute injury and in chronic neurodegenerative disease laid the foundation for two decades of research that has provided important details regarding IL-1's biology and function in the CNS. IL-1 elevation is now recognized as a critical component of the brain's patterned response to insults, termed neuroinflammation, and of leukocyte recruitment to the CNS. These processes are believed to underlie IL-1's function in the setting of acute brain injury, where it has been ascribed potential roles in repair as well as in exacerbation of damage. Explorations of IL-1's role in chronic neurodegenerative disease have mainly focused on Alzheimer disease (AD), where indirect evidence has implicated it in disease pathogenesis. However, recent observations in animal models challenge earlier assumptions that IL-1 elevation and resulting neuroinflammatory processes play a purely detrimental role in AD, and prompt a need for new characterizations of IL-1 function. Potentially adaptive functions of IL-1 elevation in AD warrant further mechanistic studies, and provide evidence that enhancement of these effects may help to alleviate the pathologic burden of disease.

### Detection of delirium by nurses among long-term care residents with dementia

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**Background:** Delirium is a prevalent problem in long-term care (LTC) facilities where advanced age and cognitive impairment represent two important risk factors for this condition. Delirium is associated with numerous negative outcomes including increased morbidity and mortality. Despite its clinical importance, delirium often goes unrecognized by nurses. Although rates of nurse-detected delirium have been studied among hospitalized older patients, this issue has been largely neglected among demented older residents in LTC settings. The goals of this study were to determine detection rates of delirium and delirium symptoms by nurses among elderly residents with dementia and to identify factors associated with undetected cases of

delirium.

**Methods:** In this prospective study (N = 156), nurse ratings of delirium were compared to researcher ratings of delirium. This procedure was repeated for 6 delirium symptoms. Sensitivity, specificity, positive and negative predictive values were computed. Logistic regressions were conducted to identify factors associated with delirium that is undetected by nurses.

**Results:** Despite a high prevalence of delirium in this cohort (71.5%), nurses were able to detect the delirium in only a minority of cases (13%). Of the 134 residents not identified by nurses as having delirium, only 29.9% of them were correctly classified. Detection rates for the 6 delirium symptoms varied between 39.1% and 58.1%, indicating an overall under-recognition of symptoms of delirium. Only the age of the residents (= 85 yrs) was associated with undetected delirium (OR: 4.1; 90% CI: [1.5–11.0]).

**Conclusion:** Detection of delirium is a major issue for nurses that clearly needs to be addressed. Strategies to improve recognition of delirium could result in a reduction of adverse outcomes for this very vulnerable population.

### The influence of obesity on falls and quality of life

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**Objective:** To determine (1) whether obese older adults had higher prevalence of falls and ambulatory stumbling, impaired balance and lower health-related quality of life (HRQL) than their normal weight counterparts, and (2) whether the falls and balance measures were associated with HRQL in obese adults.

**Methods:** Subjects who had a body mass index (BMI) greater than 30 kg/m<sup>2</sup> were classified into an obese group (n = 128) while those with BMI between 18.5 and 24.9 kg/m<sup>2</sup> were included into a normal weight group (n = 88). Functional tests were performed to assess balance, and questionnaires were administered to assess history of falls, ambulatory stumbling, and HRQL.

**Results:** The obese group reported a higher prevalence of falls (27% vs. 15%), and ambulatory stumbling (32% vs. 14%) than the normal weight group. Furthermore, the obese group had lower HRQL, (p = 0.05) for physical function (63 ± 27 vs. 75 ± 26; mean ± SD), role-physical (59 ± 40 vs. 74 ± 37), vitality (58 ± 23 vs. 66 ± 20), bodily pain (62 ± 25 vs. 74 ± 21) and general health (64 ± 19 vs. 70 ± 18). In the obese

group, a history of falls was related ( $p = 0.05$ ) to lower scores in 4 domains of HRQL, and ambulatory stumbling was related ( $p = 0.01$ ) to 7 domains.

**Conclusion:** In middle-aged and older adults, obesity was associated with a higher prevalence of falls and stumbling during ambulation, as well as lower values in multiple domains of HRQL. Furthermore, a history of falls and ambulatory stumbling were related to lower measures of HRQL in obese adults.

### **A natural mineral supplement provides relief from knee osteoarthritis symptoms: a randomized controlled pilot trial**

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**Background:** This small, pilot study evaluated the impact of treatment with a natural multi-mineral supplement from seaweed (Aquamin) on walking distance, pain and joint mobility in subjects with moderate to severe osteoarthritis of the knee.

**Methods:** Subjects ( $n = 70$ ) with moderate to severe osteoarthritis of the knee were randomized to four double-blinded treatments for 12 weeks: (a) Glucosamine sulfate (1500 mg/d); (b) Aquamin (2400 mg/d); (c) Combined treatment composed of Glucosamine sulfate (1500 mg/d) plus Aquamin (2400 mg/d) and (d) Placebo. Primary outcome measures were WOMAC scores and 6 Minute Walking Distances (6 MWD). Laboratory based blood tests were used as safety measures.

**Results:** Fifty subjects completed the study and analysis of the data showed significant differences between the groups for changes in WOMAC pain scores over time ( $p = 0.009$  ANCOVA); however, these data must be reviewed with caution since significant differences were found between the groups at baseline for WOMAC pain and stiffness scores ( $p = 0.0039$  and  $p = 0.013$ , respectively, ANOVA). Only the Aquamin and Glucosamine groups demonstrated significant improvements in symptoms over the course of the study. The combination group (like the placebo group) did not show any significant improvements in OA symptoms in this trial. Within group analysis demonstrated significant improvements over time on treatment for the WOMAC pain, activity, composite and stiffness (Aquamin only) scores as well as the 6 minute walking distances for subjects in the Aquamin and Glucosamine treatment groups. The Aquamin and Glucosamine groups walked 101 feet (+7%) and 56 feet (+3.5%) extra respectively. All treatments were well tolerated and the adverse events profiles were not

significantly different between the groups.

**Conclusion:** This small preliminary study suggested that a multi mineral supplement (Aquamin) may reduce the pain and stiffness of osteoarthritis of the knee over 12 weeks of treatment and warrants further study.

**Trial registration:** ClinicalTrials.gov number: NCT00452101.

### **Physicians' experiences with end-of-life decision-making: Survey in 6 European countries and Australia**

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**Background:** In this study we investigated (a) to what extent physicians have experience with performing a range of end-of-life decisions (ELDs), (b) if they have no experience with performing an ELD, would they be willing to do so under certain conditions and (c) which background characteristics are associated with having experience with/or being willing to make such ELDs.

**Methods:** An anonymous questionnaire was sent to 16,486 physicians from specialties in which death is common: Australia, Belgium, Denmark, Italy, the Netherlands, Sweden and Switzerland.

**Results:** The response rate differed between countries (39–68%). The experience of foregoing life-sustaining treatment ranged between 37% and 86%; intensifying the alleviation of pain or other symptoms while taking into account possible hastening of death between 57% and 95%, and experience with deep sedation until death between 12% and 46%. Receiving a request for hastening death differed between 34% and 71%, and intentionally hastening death on the explicit request of a patient between 1% and 56%.

**Conclusion:** There are differences between countries in experiences with ELDs, in willingness to perform ELDs and in receiving requests for euthanasia or physician-assisted suicide. Foregoing treatment and intensifying alleviation of pain and symptoms are practiced and accepted by most physicians in all countries. Physicians with training in palliative care are more inclined to perform ELDs, as are those who attend to higher numbers of terminal patients. Thus, this seems not to be only a matter of opportunity, but also a matter of attitude.