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Serum insulin-like growth factor 1 and late-life depression: A population-based study

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Summary
Objective: Serum insulin-like growth factor 1 (IGF-1) concentration decreases, while the prevalence of depressive symptoms increases with advancing age. Although basic research indicates a link between low IGF-1 concentration and depression, this has scarcely been investigated in humans. This study investigates whether lower IGF-1 concentrations are associated with prevalent and incident late-life depression over a 3-year period.
Methods: The study included 1188 participants, aged ≥65 years, from the Longitudinal Aging Study Amsterdam (LASA), an ongoing, population-based cohort study. Depression was assessed at baseline and after three years using the Center for Epidemiological Studies-Depression Scale (CES-D) and the Diagnostic Interview Schedule (DIS), and categorized into minor depression and major depression (MDD). Serum IGF-1 concentration was determined at baseline. Associations were adjusted for relevant confounders.
Results: Serum IGF-1 concentrations were within the normal range (mean 13.9 nmol/l, standard deviation 5.3 nmol/l). At baseline, in men, as compared to high concentrations, mid concentrations decreased the probability of prevalent minor depression (odds ratio [OR] = 0.35, 95% confidence interval [CI] = 0.15—0.82). In women, as compared to high concentrations, low concentrations tended to increase the probability of prevalent MDD (OR = 2.66, 95% CI = 0.89—7.89).
At three-year follow-up, in men, no significant prospective associations were detected. In women, as compared to high concentrations, mid concentrations decreased the probability of incident minor depression (OR = 0.43, 95% CI = 0.19—0.95).

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Conclusions: Several associations, which differed across the genders, were observed between IGF-1 and depression. Cross-sectional findings were not supported by longitudinal findings, which suggest that IGF-1 may not play an important predictive role in the development of depression in older persons over time. However, a more acute role of IGF-1 in current depression, as indicated by the cross-sectional results, may be possible. Further studies are needed to elucidate the complex relation between IGF-1 and late-life depression.

1. Introduction

Depression is a common and burdensome disorder in older individuals (Beekman et al., 1999; Copeland et al., 2004). While the prevalence of major depression (MDD) is relatively low (1.8%), the prevalence of all clinically relevant depressive syndromes, some of which do not fully fulfill criteria for MDD, is high (13.5%) in community dwelling elderly (Beekman et al., 1999). Both may have detrimental consequences for the wellbeing and functioning of older persons, and are associated with increased mortality (Alexopoulos, 2005; Cuijpers et al., 2013; Scafato et al., 2012).

To date, the exact etiology and pathophysiology of depression are still unclear, but are presumed to be multifactorial (Alexopoulos, 2005). It is hypothesized that biological factors, such as insulin-like growth factor 1 (IGF-1) may play a role (Duman, 2004).

In healthy adults, the secretion of growth hormone (GH) and IGF-1 decreases with advancing age, a process also known as the 'somatopause' (Bartke, 2008; Corpas et al., 1993). Decreased functioning of the GH-IGF-1 axis is also found in adult patients with growth hormone deficiency (GHD). Adult GHD is, amongst others, associated with decreased cognitive functioning, impaired quality of life (QoL) and psychiatric symptoms (de Boer et al., 1995; Giusti et al., 1998; Mahajan et al., 2004). GH supplementation has been shown to improve these symptoms (Kokshoorn et al., 2011; Mahajan et al., 2004). Since features of normal aging resemble those of GHD, it has been suggested that the 'somatopause' contributes to age-associated changes and disorders (Bartke, 2008; Corpas et al., 1993; Mahajan et al., 2004; Mitschelen et al., 2011). For instance, lower IGF-1 concentrations are related to impaired cognitive functioning, which frequently coincides with late-life depression, in healthy elderly (Arwert et al., 2005). In addition, IGF-1 receptors have been localized within many brain structures that are associated with mood such as the hippocampus and the amygdala (Adem et al., 1989). Also, there is evidence that IGF-1 has direct effects on the central nervous system (CNS) through blood-brain barrier passage and local autocrine and paracrine mechanisms (Schneider et al., 2003). Moreover, basic research has shown that the expression of neurotrophic and growth factors, such as IGF-1, is decreased by chronic stress and depression in brain regions associated with depression, and increased by antidepressant treatment (Duman, 2004; Mitschelen et al., 2011). Recently, an animal study demonstrated that adult-onset long-term IGF-1 deficiency is able to induce depressive behavior in normally developed mice (Mitschelen et al., 2011). Nevertheless, only few studies with limited sample sizes and no or short follow-up time have addressed the relation between IGF-1 and depression in humans (Deuschle et al., 1997; Franz et al., 1999; Lesch et al., 1988a, 1988b; Rupprecht et al., 1989; Schilling et al., 2011; Weber-Hamann et al., 2009). So far, only one epidemiological study has been reported, in which lower IGF-1 concentrations were associated with any depressive disorder in women, while higher IGF-1 concentrations were associated with any depressive disorder in men (Sievers et al., 2014). However, in this study only a screening self-report questionnaire was used for the assessment of any depressive disorder, which complicates interpretation of the results. Moreover, the relation between IGF-1 and depression has not yet been specifically studied in older individuals.

Therefore, we aimed to investigate the association between IGF-1 and depression cross-sectionally as well as prospectively in a large, representative cohort of community dwelling elderly, using both a depression symptoms rating scale and a diagnostic psychiatric evaluation. We hypothesized that persons with lower IGF-1 concentrations would be more likely to have current minor depression or MDD and would be more likely to develop minor depression or MDD in the future than persons with higher IGF-1 concentrations.

2. Materials and methods

2.1. Study design and sample

The data for this study were collected within the framework of the Longitudinal Aging Study Amsterdam (LASA). LASA is an ongoing, prospective, multidisciplinary Dutch cohort study on predictors and consequences of changes in physical, cognitive, emotional and social functioning in community dwelling elderly. The data collection and sampling procedures have previously been described in detail elsewhere (Deeg et al., 2002). Briefly, a nationally representative random sample of older men and women aged 55—85 years, stratified by age, sex, urbanization and expected 5-year mortality rate, was drawn from the population registers of 11 municipalities in three geographical regions in the Netherlands. At LASA baseline (1992/1993) 3107 subjects, 99% Caucasian, were enrolled. Examinations were performed in the participants' homes at baseline and every three years thereafter by trained and intensively supervised interviewers. Informed consent was obtained from all participants. The study was approved by the Medical Ethics Committee of the VU University Medical Center (VUmc).

For the present study, respondents who participated in the second LASA data collection cycle (1995/1996) and who were aged 65 year or older as of January 1st 1996 ($n = 1509$) were selected, because in these participants blood samples for IGF-1 measurements were collected ($n = 1319$).