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Serum visfatin concentration in acutely ill and weight-recovered patients with anorexia nervosa

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Summary Visfatin is a recently described protein that is thought to regulate the process of adipocyte differentiation. Findings suggest that visfatin may be actively involved in the control of weight regulatory networks. However, to what extent and which role it plays in

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eating disorders is still poorly understood, as mixed results have been reported. The aim of the current study was to investigate serum visfatin concentrations on a cross sectional sample between acute anorexia nervosa patients ($n = 44$), weight recovered patients ($n = 13$) and healthy controls ($n = 46$) and a longitudinal sample of acute patients ($n = 57$) during weight recovery at three different time-points. Results did not show significant differences in visfatin between the three groups; however, acute patients showed a higher visfatin/BMI-SDS ratio than controls and recovered patients. Longitudinal results revealed an increase of visfatin levels during therapy. Our results suggest that high ratios of visfatin/BMI-SDS could be a state marker in acute anorexia nervosa, displaying a compensatory mechanism of the individual to maintain normal visfatin levels under malnourished conditions.

1. Introduction

Adipokines play a central role in the control of energy metabolism. They provide signals about the nutrient status of an organism, such as energy intake and expenditure as well as insulin sensitivity (Badman and Flier, 2007) and have therefore become a matter of central interest in the field of eating disorder research. Over the last years, particular attention has been paid to the role of leptin (Ehrlich et al., 2009; Föcker et al., 2011; Hebebrand et al., 2007). In contrast, our knowledge of the novel adipokine visfatin is still sparse. Visfatin appears to be a multifunctional protein, acting as hormone, cytokine, and enzyme (for a review, see Sonoli et al., 2011). It was firstly identified as a Pre-B Cell Colony-Enhancing Factor (PBEF; Samal et al., 1994), which facilitated the maturation of early B-lymphocytes. It was also found to act as an enzyme called nicotinamide phosphoribosyl transferase (NAMPT), which is involved in the nicotine adenine dinucleotide (NAD+) salvage pathway. In 2005, Fukuhara et al. demonstrated that the adipokine visfatin, which amino acid sequence was identical to NAMPT/PBEF, acted as a protein mediator secreted by fat cells. It appears that visfatin secretion increases in the course of adipocyte differentiation and its synthesis is regulated by several factors including glucocorticoids, tumor necrosis factor alpha, interleukin 6, and growth factor hormone (Jia et al., 2004).

Although the role of visfatin in energy homeostasis or weight regulation is of particular interest with respect to eating disorders and diabetes, reported results have been very heterogeneous, as highlighted in Table 1. Several studies have demonstrated elevated visfatin levels both in obese adults (Auguet et al., 2013; Jin et al., 2008; Manco et al., 2007; Pagano et al., 2006; Terra et al., 2012; Wen et al., 2012) and children (Davutoglu et al., 2009; Dogru et al., 2007; Pagano et al., 2006; Revollo et al., 2004; Sandeep et al., 2007) as well as in patients with diabetes mellitus (Chen et al., 2006; Dogru et al., 2007; Pagano et al., 2006; Revollo et al., 2004; Sandeep et al., 2007), suggesting a possible link to insulin and glucose homeostasis. Further investigations found visfatin to be closely correlated with white adipose tissue (WAT) accumulation (Curat et al., 2006; Jia et al., 2004). However, initial reports that visfatin is preferentially expressed by visceral adipose tissue (VAT; Araki et al., 2008; Barth et al., 2010; Fukuhara et al., 2005) could not be confirmed by other studies (Berndt et al., 2005; Haider et al., 2006a; Körner et al., 2007). Similarly heterogeneous results were reported from studies testing for associations between visfatin levels and BMI in healthy individuals. Some authors found positive correlations while others found no relationship at all (see Table 1). Equally mixed results were observed in obese samples (Pagano et al., 2006; Ziora et al., 2012). Important for eating disorder research are also notions of visfatin sharing associations with thyroid hormones (Caixàs et al., 2009; Ozkaya et al., 2009) as well as bone formation (Xie et al., 2007), steroid hormone synthesis and ovarian functioning (Chan et al., 2007; Reverchon et al., 2013; Tsouma et al., 2014; Zhang et al., 2014), however, results are again quite heterogeneous.

These inconsistent findings may be partly due to the fact that researchers have not applied standard laboratory procedures, i.e. studies have used either serum or plasma samples and employed different immunoassays (see Table 1). According to a recent study (Körner et al., 2007) some of these immunoassays may deliver erroneous results due to unspecific binding.

Research investigating visfatin under catabolic conditions has been rare. Reduced dietary intake (De Luis et al., 2008; Haider et al., 2006b; Manco et al., 2007; Martos-Moreno et al., 2011) as well as exercise (Choi et al., 2007) have been associated with reduced visfatin concentrations in some but not all studies (Kang et al., 2011).

Insights into the role of visfatin as an adipokine in weight disorders and its function in metabolic processes might be gained by investigating visfatin levels in anorexia nervosa (AN), a severe illness characterized by markedly reduced calorie intake and fear of weight gain leading to a significant decrease in overall adipose tissue (Treasure and Schmidt, 2005). To date, only two studies have investigated visfatin levels in AN — again with mixed results (see Table 1). Both used a cross-sectional design and applied an Enzyme Immunoassay (EIA; Phoenix Pharmaceuticals Inc., USA), which according to Körner et al. (2007) may have limited performance due to non-specific binding. Longitudinal data and data from recovered AN patients are still missing.

The aim of the current study was to investigate visfatin levels in patients with acute AN, recovered from AN as well as longitudinally, using the only immunoassay (ELISA) that has been shown to measure serum visfatin with an acceptable specificity (Körner et al., 2007), with the overarching goal of establishing the potential clinical utility of visfatin as an endocrine biomarker in AN.