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Metabolomic profiles in individuals with negative affectivity and social inhibition: A population-based study of Type D personality

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Population study;
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Summary
Background: Individuals with negative affectivity who are inhibited in social situations are characterized as distressed, or Type D, and have an increased risk of cardiovascular disease (CVD). The underlying biomechanisms that link this psychological affect to a pathological state are not well understood. This study applied a metabolomic approach to explore biochemical pathways that may contribute to the Type D personality.
Methods: Type D personality was determined by the Type D Scale-14. Small molecule biochemicals were measured using two complementary mass-spectrometry based metabolomics platforms. Metabolic profiles of Type D and non-Type D participants within a population-based study in Southern Germany were compared in cross-sectional regression analyses. The PHQ-9 and GAD-7 instruments were also used to assess symptoms of depression and anxiety, respectively, within this metabolomic study.
Results: 668 metabolites were identified in the serum of 1502 participants (age 32—77); 386 of these individuals were classified as Type D. While demographic and biomedical characteristics were equally distributed between the groups, a higher level of depression and anxiety was observed in Type D individuals. Significantly lower levels of the tryptophan metabolite kynurenine were associated with Type D (p-value corrected for multiple testing = 0.042), while no significant associations could be found for depression and anxiety. A Gaussian graphical model analysis enabled the identification of four potentially interesting metabolite networks that are enriched in metabolites (androsterone sulfate, tyrosine, indoxyl sulfate or caffeine) that associate nominally with Type D personality.
Conclusions: This study identified novel biochemical pathways associated with Type D personality and demonstrates that the application of metabolomic approaches in population studies can reveal mechanisms that may contribute to psychological health and disease.

1. Introduction

The Type D personality describes a "general propensity to psychological distress" (Denollet and Conraads, 2011) and has proven to have substantial significance in cardiovascular disease prediction (Denollet et al., 1996; Kupper and Denollet, 2007). While the global symptoms of social inhibition (SI) and negative affectivity (NA) define the Type D individual (Denollet, 2005), poorer mental (depression, anxiety, and increased exhaustion) (Versteeg et al., 2012) and physical health (Mols and Denollet, 2010) are associated with this personality pattern. Prevalence rates between 13.5 and 35% have been reported (Grande et al., 2012). A recent meta-analysis of prospective studies demonstrated a significant association between Type D and mortality, however this prognostic effect appears to be relevant in patients with coronary artery disease (CAD) but not congestive heart failure (CHF) (Grande et al., 2012), as indicated by large cohort studies of patients with heart failure and various cardiovascular diagnoses (Pelle et al., 2010; Coyne et al., 2011; Grande et al., 2011). Despite the mounting evidence for a risk association with Type D, underlying biologic mechanisms that link this personality type to a pathological state are still being identified. While general stress reactivity (increased heart rate, blood pressure, and cardiac output) is known to be associated with Type D (Einvik et al., 2011), metabolic syndrome was also shown to be more prevalent among healthy people with Type D personality (Mommersteeg et al., 2010). Interestingly, the SI subscale of the Type D construct was shown to be more strongly associated with night time systolic blood pressure than the NA component (Nyklicek et al., 2011). Oxidative stress (Kupper et al., 2009) as well as increases in the inflammatory cytokine TNFα (Denollet et al., 2008, 2009b) were both observed in Type D individuals; although more robust associations were shown between sTNF receptors than with TNFα (Mommersteeg et al., 2012). Additionally, Type D individuals suffering from acute coronary disease are known to have dysregulated cortisol production (Whitehead et al., 2007; Molloy et al., 2008).

The elucidation of biochemical mechanisms in mental health disorders is a new challenge within metabolomic studies, in which numerous metabolites are simultaneously analyzed. A metabolite profile captures a momentary glimpse into cellular metabolic pathways that are predominant in an individual, and therefore provide a functional readout of the physiological state of the human body (Gieger et al., 2008). Metabolic profiles result from the interactions of individual genetic predispositions, environmental, and behavioral factors. Thus, perturbations in metabolic pathways may drive biochemical pathways that are also associated with mental health diseases such as major depressive (Paige et al., 2007) and bipolar disorder (Quinones and Kaddurah-Daouk, 2009). Comprehensive metabolic studies revealed associations between changes in metabolic profiles and schizophrenia (Orešič et al., 2011b, 2012; Xuan et al., 2011) as well as Alzheimer's disease (Orešič et al., 2011a). We therefore employed a metabolomic approach to identify a biochemical signature of the Type D personality in a population-based study.

2. Material and methods

2.1. Study participants and cross-sectional study design

Data are based on the KORA (Cooperative Health Research in the Region of Augsburg) F4 study (2006—2008), a follow-up