PS3.2.3

Individual susceptibility to stress-related psychopathology after cardiac surgery

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Background: Cardiac surgery patients are at risk for stress-related psychopathology after hospital stay. We found that post-traumatic stress disorder (PTSD) and depression occur in 10.5% and 13.1% respectively of cases, 1.5–4 years after surgery. This possibly counteracts beneficial effects of the surgical intervention and postoperative treatment. The aim of this study was to identify patient related determinants of psychopathology after cardiac surgery.

Methods: This is a multi-centre follow up study of the Dexamethasone for Cardiac Surgery (DECS) trial, in which patients received a single, intravenous dose of dexamethasone (1 mg/kg) in a randomised, double-blind, placebo-controlled way. Questionnaires were mailed to 1244 participants 1.5 to 4 years after cardiac surgery to assess PTSD, depression, childhood trauma, life events, trait anxiety, pre-existing psychopathology, and substance use. Salivettes were sent to obtain saliva and genotype hypothalamic–pituitary–adrenal-axis (HPA-axis) related haplotypes. Data was available for 996 (80.1%) participants. Backward linear regression was performed with all factors mentioned above, including age and gender.

Results: Trait anxiety, life events, childhood trauma, and mineralocorticoid (MR) haplotype 2 were retained in the model with an adjusted R2 of 0.54 ($p < 0.01$) for PTSD. With regard to depression, trait anxiety, life events, MR haplotype 2, age, and female gender contributed significantly to the model (adjusted $R^2 = 0.50$; $p < 0.01$).

Conclusions: Predisposition for psychopathology after cardiac surgery mainly depends on trait anxiety and life events, but genetic variation of the MR, gender, and age are important as well.

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Evidence for an association between mineralocorticoid receptor gene haplotypes and psychobiological measures of atypical depression

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Precision medicine promises a stratified diagnostic and therapeutic treatment. Neuropattern™ is a new diagnostic tool based on 13 conceptual endophenotypes of the stress response network. In this study, Neuropattern™ was used to detect the clinical relevance of haplotypes of the mineralocorticoid receptor gene. These haplotypes derive from well-studied, functional single nucleotide polymorphisms (rs2070951 & rs5522), previously associated with depression, optimism/pessimism, and HPA-axis activity. Here, we analyzed if Neuropattern™ can generate more specific information for clinical application. In a population of in- and outpatients, specific MR haplotypes were significantly associated with 13 out of 20 biological, psychological, and symptom measures of a conceptual endophenotype associated with atypical depression. In addition, we could validate previous findings for MR gene haplotypes, in that two copies of the GA haplotype were related to a higher number of diagnoses across ICD-10 diagnostic categories, as well as to a higher number of Patient Health Questionnaire screening diagnoses. Furthermore, two copies of the GA haplotype were associated with a lower cortisol awakening response. In sum, our exploratory study suggest that (1) MR gene haplotypes might serve as valuable biomarkers for a subgroup of atypical depression, and (2) that conceptual endophenotypes can be valuable tools to elucidate the clinical relevance of biomarkers for stress-related disorders.

Conflict of interest: ERdK (advisor) and RHdR (CEO) of Dynacorts Therapeutics BV.

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