

# Affective temperaments – a link between affective and cardiovascular disorders

Doctoral theses

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## **Introduction**

Patients suffering from multiple chronic conditions are the main challenge for the 21<sup>st</sup> Century healthcare systems. Certain chronic conditions like cardiovascular disorders and depression often form clusters worsening the quality of life as well as the life expectancy of an individual. Huge research experience has been accumulated on the effort to improve cardiovascular outcomes through the treatment of depression. However, results failed to prove the desired effects. A possible explanation of such a failure is that depression is a heterogeneous illness, the symptom formation of which changes between individuals and even in the same individual during his/her life. To explore certain symptom clusters which may underlie individual vulnerability to cardiovascular disorders, affective temperaments might give a clue. Affective temperaments, which are responsible for the emotional domain of personality, are genetically determined trait-like characteristics. Everybody has his/her own individual temperament profile, but temperaments especially in their marked forms may

determine the onset, symptom formation and prognosis of major affective disorders. Although the association between affective temperaments and major affective disorders are widely researched both in familial-genetic and in clinical research, their possible association with cardiovascular disorders have not been explored yet.

### **Aims**

The aim of our research was to explore the association between affective temperaments and cardiovascular disorders as well as suicide, the most serious complication of major affective disorders. According to this aim, we examined the association of affective temperaments with hypertension and with acute cardiac complications in hypertensive patients. Moreover, we examined the role of affective temperaments in smoking initiation and cessation and explored temperamental differences according to gender. We also examined the association of affective temperaments with suicide attempts in personal medical history and completed suicide in first and second degree relatives.

Research questions:

1. Is there any difference in the affective temperament profile of hypertensive and non-hypertensive outpatients, who do not suffer from ICD-10 diagnosed depression?
2. Is there any affective temperament predicting hypertension and if yes, is the effect independent from other, known risk factors (like age, diabetes or increased weight)?
3. Is there an association between affective temperaments, depression and depressive symptoms measured by the Beck Depression Inventory (BDI) and the acute cardiac complications (acute myocardial infarction [AMI] and acute coronary syndrome [ACS]) in hypertension?
4. Are there any affective temperaments associated with smoking status (never/former/current), which is the most important preventable risk factor of cardiovascular disorders?
5. Is there any gender difference in affective temperaments related to smoking initiation or cessation?

6. How can affective temperaments contribute to the exploration of the association between depression and smoking?
7. Is there any association between affective temperaments and suicide attempts in personal medical history and completed suicide in first and second degree relatives?

## **Methods**

### **Sample and measures**

*Personality and cardiovascular risk: Association between hypertension and affective temperaments — a cross-sectional observational study in primary care settings*

179 primary hypertensive, and 72 non-hypertensive control patients (receiving chronic care in general practice) filled in the background questionnaire about socio-demographic characteristics and health-related information as well as the Temperament Evaluation of Memphis, Pisa, Paris & San Diego Autoquestionnaire (TEMPS-A).

*Affective temperaments contribute to cardiac complications in hypertension independently of depression*

The sample consisted of 93 males out of 228 primary hypertensive patients, regularly controlled by their general practitioners. 16 out of 228 underwent hospitalisation due to acute cardiac complication (CC+); AMI in eight cases and ACS in eight cases. Hypertensive patients without CC (CC-) comprised the control group (n=212). Information on cardiovascular and psychiatric history as well as latest (within 3 months) cholesterol levels were collected from medical documentation. Information on lifestyle-related risk factors and cardiovascular family history was collected from patients. Depression symptoms were measured by BDI and affective temperaments by TEMPS-A.

*The association of affective temperaments with smoking initiation and maintenance in adult primary care patients*

Data of 459 regularly controlled primary care patients were analysed. Information on tobacco use (number of cigarettes per day, length of abstinence in

years) and socio-demographic characteristics (age, gender, education) was collected from patients. We explored predictor variables of smoking initiation and maintenance. Analysing smoking initiation, the whole sample was divided into two subgroups, those who have never smoked (n=252) and those who have ever tried cigarette (current and former smokers, n=207). To measure smoking maintenance, a subsample of the whole sample (former smokers n=212 and current smokers n=207) was used. We used affective temperaments, ICD-10 diagnosed depression, age, education, depressive symptoms and anxiety symptoms as predictor variables. We used TEMPS-A, BDI and the Hamilton Anxiety Rating Scale (HAM-A) as outcome measures.

*Affective temperament, history of suicide attempt and family history of suicide in general practice patients*

We collected data from 509 consecutively investigated primary care patients. Information on psychiatric medical history was collected from their general practitioners while data on suicide attempts and completed suicide in first and second degree relatives, as

well as family history of psychiatric disorders, outpatient and hospital care were provided by the patients. 495 patients out of 509 provided data on completed suicide in family history, while 457 provided data on suicide attempts in his/her medical history. There were altogether 443 patients who answered both questions. Affective temperaments were measured by TEMPS-A.

### **Statistical analyses**

Chi-square or Fisher's exact test was applied for the assessment of group differences in categorical variables. Gender-tests were used for the comparison of continuous variables between groups and Mann-Whitney U test was used to analyse non-parametric continuous variables. During multivariate analyses we applied one-way ANOVA. In cases of violation of the homogeneity of variance we used the Brown-Forsythe F-ratio. In cases where the subsets were not homogeneous the Games-Howell post-hoc test was used. In all other situations the Hochberg GT2 post-hoc test was applied due to unequal sample sizes. To establish the relationship of affective temperaments with hypertension we used binary logistic



regression. To control for the family-wise error rate, we applied multiple comparison tests developed for generalized linear models to dominant affective temperaments simultaneously. To establish the association of affective temperaments with acute cardiac complications and smoking behaviour we used a step forward likelihood ratio binary logistic regression. Statistical analysis was carried out using SPSS version 20.0 and R version 15.1.

## **Results**

*Personality and cardiovascular risk: Association between hypertension and affective temperaments — a cross-sectional observational study in primary care settings*

Hypertensive patients were significantly older than non-hypertensive controls (62 vs. 51 years,  $p < 0.0001$ ) as well as bigger proportion of them were overweight or obese (75% vs. 44%,  $p < 0.0001$ ). 58 patients out of 179 had dominant affective temperament. The prevalence of dominant cyclothymic temperament was significantly higher in the hypertensive group ( $p = 0.041$ ). Results of the multivariable logistic regression analysis showed that

higher BMI ( $>25 \text{ kg/m}^2$ ) (OR=6.2; 95% CI=3.06-13.30,  $p<0.0001$ ), older age ( $> 60$  years) (OR=4.7; 95% CI=2.34-9.95,  $p<0.0001$ ), diabetes mellitus (OR=7.0; 95% CI=2.53-25.22,  $p=0.0006$ ) and dominant cyclothymic temperament (OR=11.9; 95% CI=1.27-111.17,  $p=0.024$ ) predicted hypertension independent of each other.

*Affective temperaments contribute to cardiac complications in hypertension independently of depression*

The mean duration of hypertension was  $14 \pm 7$  years in the whole sample. The 16 cases with acute cardiac complications differed only in cholesterol levels, which were lower in CC+ patients in comparison with CC-hypertensive patients. Otherwise neither demographic (age, gender) nor cardiovascular risk factors (blood pressure, duration of hypertension, BMI, smoking, multiple cardiovascular disorders in family history) showed higher differences than could be due to the chance between the two groups. Analysing negative attitude, performance difficulty and somatic element subscales of the BDI, performance difficulty (5.7 vs. 3.6;  $t=-2.39$ ;  $p=0.018$ ) and somatic element scores (1.9 vs. 1.0;  $t=-2.52$ ;

p=0.012), but not the negative attitude subscale revealed significantly higher scores in the CC+ group. Cyclothymic temperament scored significantly higher in the CC+ group and according to the results of the step-forward LR binary logistic regression, cyclothymic temperament was independent predictor of acute cardiac complications [ $\beta=0.152$ ; SE=0.054; Wald  $\chi^2(1)=0.79$ ; p=0.005] increasing its risk with 16% (OR=1.16; 95% CI=1.047-1.295).

*The association of affective temperaments with smoking initiation and maintenance in adult primary care patients*

Never smokers constituted 55% of the total sample, and former smokers were represented in a slightly larger proportion (24.4%) than current smokers (20.6%). Current smokers were younger ( $54\pm 14$  years) than never ( $59\pm 15$  years) or former smokers ( $62\pm 13$  years) ( $F(2, 419)=7.7$ ; p=0.001), and were less educated ( $\chi^2(4)=21.615$ ; p<0.0001). The average number of cigarettes smoked per day (CPD) was 15 ( $\pm 8$ ). Among lifetime smokers, 112 (54%) quit successfully with a mean of 16 years ( $\pm 12$  years) prior to data collection. Smoking initiation was

higher among males than females ( $\chi^2 (1)=7.99$ ;  $p=0.005$ ) and males were more successful in cessation as well ( $\chi^2 (1)=6.94$ ;  $p=0.008$ ). ICD-10 diagnosed depression, BDI and HAM-A point scores did not reveal significant differences between the two groups. Depressive ( $F(2,424)=6.23$ ;  $p=0.002$ ), cyclothymic ( $F(2, 424)= 7.06$ ;  $p=0.001$ ) and irritable temperament ( $F(2,424)=10.23$ ;  $p<0.0001$ ) scores revealed significant differences among the three smoking subgroups. Multivariable analysis showed that higher point scores on the irritable temperament subscale predicted smoking initiation in females independently of other predictors, increasing the odds of smoking initiation by 26%, while higher scores on the anxious subscale resulted in reversed results. Exploring the role of affective temperaments in smoking maintenance we found that higher scores on the depressive temperament scale in males predicted smoking maintenance, increasing the odds of persistent smoking by 30.5%.

*Affective temperament, history of suicide attempt and family history of suicide in general practice patients*

73 patients (14%) out of the whole sample suffered from ICD-10 diagnosed depression while 56 (11%) suffered from ICD-10 diagnosed anxiety disorders. We found a significantly bigger proportion of dominant depressive temperament in females, while dominant irritable temperament was significantly more prevalent among males. Those patients who suffered from depressive or anxiety disorders reached significantly higher scores on all of the affective temperamental subscales which contain depressive component. Dominant depressive ( $p < 0.0001$ ), cyclothymic ( $p < 0.0001$ ) and anxious temperament ( $p = 0.0001$ ) was present in a significantly bigger proportion in depressive or anxious patients. 9.1% ( $n = 45$ ) of the responders' first and second degree relatives completed suicide, while 4.8% ( $n = 22$ ) of the responders attempted suicide in the past. Those with a positive family history of completed suicide were themselves more likely to attempt suicide in their lifetime ( $6/38 = 15.8\%$ ) comparing to those with negative family history ( $16/405 = 4.0\%$ ,  $\chi^2(1) = 11.235$ ,  $p = 0.001$ ). Patients with previous suicide attempt reached higher scores on the depressive and cyclothymic subscales, while those with

positive family history of completed suicide scored higher on the cyclothymic and anxious subscales.

## **Conclusions**

Our new results regarding the association between affective temperaments, cardiovascular disorders and suicide can be summarized as follow:

1. Cyclothymic temperament is independent predictor of hypertension in patients who do not suffer from major affective disorders.
2. Cyclothymic temperament shows association with acute cardiac complications in hypertensive patients and this association is independent from previous ICD-10 diagnosed depression and current depressive symptoms.
3. Suicide attempts and completed suicide among first and second degree relatives are more common among cyclothymic patients. Moreover, those attempting suicide scored higher on the depressive temperament as well, while completed suicide in

the family history was associated with higher anxious temperament scores.

4. Depressive, cyclothymic and irritable temperaments showed association with smoking status. Irritable temperament increases the odds of smoking initiation in females while depressive temperament increases the odds of maintenance in males.

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