

## Relationships between various temperament dimensions, levels of selected cytokines and Posttraumatic Stress Disorder (PTSD) in males, incurred as a result of mechanical injuries of lower extremities

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### Summary

**Aim.** This analysis addresses the relationships between various temperament dimensions, levels of selected cytokines and PTSD in males, incurred as a result of mechanical injuries of lower extremities.

**Methods.** PTSD was assessed with a PTSD Factorial Version Inventory. Temperamental traits were evaluated by means of Formal Characteristics of Behaviour – Temperament Inventory (FCB-TI). Cytokine levels were determined using ELISA kits. The study population was selected from among a larger population of 80 persons. 15 persons with signs of inflammation were excluded. PTSD group included 33 persons, 32 subjects were included in the control group.

**Results.** Positive statistical correlation with PTSD was observed for: perseverance and emotional reactivity. On the other hand, negative relationship was shown between PTSD and: briskness, endurance and activity. No statistically significant correlations were revealed between the levels of selected cytokines (sIL-2, IL-6, IL-10, TNF-alpha & IFN-gamma) and temperamental traits. Moreover, this study investigates the relationships between temperamental traits, PTSD and various personality dimensions.

**Conclusions.** 1. Patients with temperamental traits such as high perseverance and emotional reactivity had a greater risk of PTSD. 2. Patients with temperamental traits such as high briskness, endurance and activity had lower risk of PTSD. 3. The level of cytokines (sIL-2, IL-6, IL-10, TNF-alpha, IFN-gamma) was not dependent on the temperamental traits.

**Key words:** PTSD, cytokines, temperament

## Introduction

Theoretical basis for investigating relationships between temperamental traits and Posttraumatic Stress Disorder is the activation construct [1]. Increased activation level is one of the most characteristic aspects of Posttraumatic Stress Disorder (PTSD). The concept of activation is recalled by the authors of a Regulative Theory of Temperament (RTT) [2, 3], who define activation as one of the most essential biological constructs, which is fundamental for briskness, endurance (equivalent of the power of stimulation process) and activity. The following traits are considered potential predictors of PTSD: anxiety, introversion, neuroticism [4–7]. Strelau enumerates, in particular, the following temperamental traits related to individual stress resistance characteristics: introversion, extraversion, neuroticism, anxiety (as a temperamental trait), experience-seeking, and reactivity [8, 9]. Analysis of relationships between temperamental traits as defined in the Regulative Theory of Temperament, such as experience-seeking, impulsiveness and anxiety [3] showed high positive correlations between experience-seeking and activity – both traits exhibit common behavioural characteristics and physiological mechanisms. Positive correlations were observed between anxiety and emotional reactivity as well as perseverance, and between impulsiveness and activity, whereas negative correlations were shown for emotional reactivity. Highly reactive persons show high sensitivity to stimuli and low efficiency. Emotional reactivity was found to be positively correlated with neuroticism and anxiety [10–12]. What follows, highly reactive persons may be considered less resistant to stress. Activity was found to positively correlate with extraversion and sociability [10, 12] as well as experience-seeking, impulsiveness and general activity level [12]. Highly active persons will be therefore more resistant to stress.

Comparative analysis of temperamental traits and Three Superfactors (Psychoticism–Extraversion–Neuroticism – PEN) measured with EPQ-R showed high positive relationships between extraversion and activity, as well as positive relations between neuroticism and emotional reactivity, perseverance and endurance. Psychoticism was found to have a moderate correlation with sensory sensitivity. Highly psychotic persons show deficit in sensory sensitivity [2, 3, 12]. Relationships were found between temperamental traits assessed with Formal Characteristics of Behaviour – Temperament Inventory (FCB-TI) and Big Five Personality Factors measured with NEO-FFI. Extraversion showed high positive correlations with activity; neuroticism correlated with emotional reactivity, perseverance and endurance. Emotional reactivity correlated with openness to experience; briskness correlated with conscientiousness.

Analysis of relationships between temperamental traits under RTT and personality dimensions such as experience-seeking, impulsiveness, and anxiety showed the following results: anxiety (as a trait) correlated positively with emotional reactivity and perseverance; impulsiveness correlated positively with activity and briskness, and negatively with emotional reactivity [3].

Lauterbach and Vrana [13] studied relationships between neuroticism and PTSD symptoms intensity. Depression, aggressive hostility, shyness and anxiety were found to be of prognostic value for PTSD. Moreover, various relationships between the

symptoms of neuroticism and PTSD intensity were examined. The study results reveal that “oversensitivity”, an aspect of neuroticism, can be prognostic of chronic PTSD. The study results show that increase in neuroticism level can indicate increased intensity of PTSD symptoms. Neuroticism can be a strong negative predictor for well-being [14]. In other studies [15] a positive correlation was found between neuroticism, introversion and PTSD. PTSD and extraversion were shown to be negatively correlated [13, 16].

According to Selye [17], “both, stimuli deprivation and excessive exposure to stimuli are accompanied by increased stress, at times leading to the state of distress”. Other researchers also considered the intensity of demands as a stressor [18, 19]. There is a certain burden level, above which the predestine factors are irrelevant in PTSD occurrence [20].

Preliminary researches show that dysregulated cytokine system is observed for example in bipolar affective disorder [21] and depression [22, 23]. In PTSD increase of interleukin 6 (IL-6) level was observed in cerebrospinal fluid but not in serum [24]. In contrast, interferon gamma (IFN- $\gamma$ ) and interleukin 4 (IL-4) levels were significantly lower in patients with PTSD, compared to control group [25]. Interleukin-1 beta (IL-1 $\beta$ ) level is higher in patients with PTSD [26].

### Aim

This study addresses relationships between various temperament dimensions, levels of selected cytokines and Posttraumatic Stress Disorder (PTSD) in males, incurred as a result of mechanical injuries of lower extremities. The following cytokines were taken into consideration: sIL-2, IL-6, TNF- $\alpha$ , IFN- $\gamma$ , and IL-10.

The following dimensions of temperamental traits were subject to analysis: briskness, perseverance, sensory sensitivity, activity, emotional reactivity, and endurance.

### Material and Method

#### Course of the study and research tools

The study included male subjects who sustained injuries of lower extremities and were hospitalised at the Upper Silesian Rehabilitation Centre “Repty” in Tarnowskie Góry. The study was performed during their stay at this centre. Assessment of somatic condition of each patient was based on hospital records. No additional tests were performed, apart from taking a single 10 cm<sup>3</sup> blood sample (into 4 test tubes) at 7:30 a.m. from each patient to do the following tests: complete blood count, blood film, CRP and ESR. The remaining blood specimens were centrifuged; blood serum was put to 5 Eppendorf test tubes, 1 ml each. The tubes were immediately frozen down to -40°C. The total biological material was used up in determining the levels of selected cytokines with ELISA kits.

Mental assessment was completed using:

1. PTSD Factorial Version Inventory [1, 27];
2. Formal Characteristics of Behaviour – Temperament Inventory (FCB-TI) [2, 3].

Cytokine concentrations were determined at the Department of General Biology of Medical University of Silesia in Zabrze, using ELISA (Enzyme-Linked Immunosorbent Assay) kit. The following variables were also investigated: education, age, trauma intensity, time lapse from the traumatic event, and blood biochemical parameters – Erythrocyte Sedimentation Rate (ESR), C-Reactive Protein (CRP), and white blood cells count. The study included 65 subjects who sustained mechanical injury of lower extremities. Subjects were divided into two groups: control group and study group. The study population was selected from among a larger population of 80 persons. The study group was diagnosed for PTSD with PTSD Inventory. Study group included persons who met PTSD criteria. Persons who failed to meet PTSD criteria were qualified as controls. 15 persons were excluded due to elevated white blood cells count and CRP level.

### Study group

#### *Inclusion criteria*

1. Males who sustained injuries of lower extremities 3 months before they were admitted to the Upper Silesian Rehabilitation Centre “Repty”. Within this period, they received no medications, and the injury-related wounds were completely healed. Apart from the lower extremity injuries, they suffered from no other disease. No inflammation symptoms were diagnosed.
2. Study group included only those patients whose erythrocyte sedimentation rate (ESR) was between 1 and 10 mm, CRP level between 1 and 5 mg/l (norm up to 5), white blood cells count (WBC) between 4,000 and 10,000 x 10<sup>9</sup>/l.
3. Informed consent to participate in the study was obtained from all participants.
4. Occurrence of symptoms of PTSD.

#### *Exclusion criteria*

1. Patients whose health condition could deteriorate as a result of the study; patients whose condition could falsify study results or the nature of the study.
2. Patients with a history of or currently undergoing psychiatric treatment.
3. Surgery, apart from surgery of the injured extremities.
4. Patients whose ESR was higher than 10 mm; CRP level higher than 6, WBC higher than 10,000 x 10<sup>9</sup>/l, which may be an expression of inflammatory process and falsify the results.

### Control group (non-PTSD)

Control group included 32 persons who sustained mechanical injuries of extremities, with no PTSD symptoms. No inflammation symptoms were diagnosed.

### Statistical analysis

Statistica software for Windows and Excel sheets were used for statistical analysis. Correlations between variables were verified using Student's t-test, Pearson's regression and correlations analysis, Mann-Whitney U test, box plots for groups and Spearman's rank correlation.

Study group and control group were investigated for compliance of age, education, and type of injury. No significant differences were identified between the groups. Mean age of the study group was 37.7 years, and 34.9 years for the control group.

PTSD group members (33 subjects) sustained the following injuries: traumatic amputation of extremities (5 persons), open fracture (3 persons), extremity fracture (21 persons), extensive soft tissue injury (1 person), ligament injury (3 persons). Non-PTSD group members (32 subjects) sustained the following injuries: traumatic amputation of extremities (5 persons), open fracture (4 persons), extremity fracture (16 persons), extensive soft tissue injury (2 person), ligament injury (5 persons). Statistical analysis was based on Pearson's Chi-square test. Significance level was  $p = 0.80215$ .

In terms of education, study group included 2 persons with primary education (control: 0); 17 persons with vocational education (control: 11); 10 persons with secondary education (control: 15); and 4 persons with university education (control: 6). Statistical analysis was based on Pearson's Chi-square test. Significance level was  $p = 0.80215$ . No statistically significant relationship between study group and control group was observed.

In terms of time lapse since the sustained injury, Student's t-test was used to compare both groups. Mean value for study group was 9.66 month from the injury, and 8.03 for control group. 8.03. Value  $t = -1.467$ ;  $p = 0.147$ . Next, the analysis investigated statistically significant differences between groups in terms of the study variables by means of Mann-Whitney U test.

Statistical differences between groups in terms of temperamental variables were found to be significant for the following temperamental traits: briskness, perseverance, emotional reactivity, endurance, and activity (Table 1).

**Table 1. Relationships between groups in terms of temperamental variables (control group vs. study group)**

| Variables            | p level | N significant control group | N significant study group |
|----------------------|---------|-----------------------------|---------------------------|
| Briskness            | 0.0033  | 29                          | 32                        |
| Perseverance         | 0.0030  | 29                          | 32                        |
| Sensory sensitivity  | 0.3042  | 29                          | 32                        |
| Emotional reactivity | 0.0085  | 29                          | 32                        |
| Activity             | 0.0286  | 29                          | 32                        |

It is also confirmed in graphical interpretation (box plot) presented below.

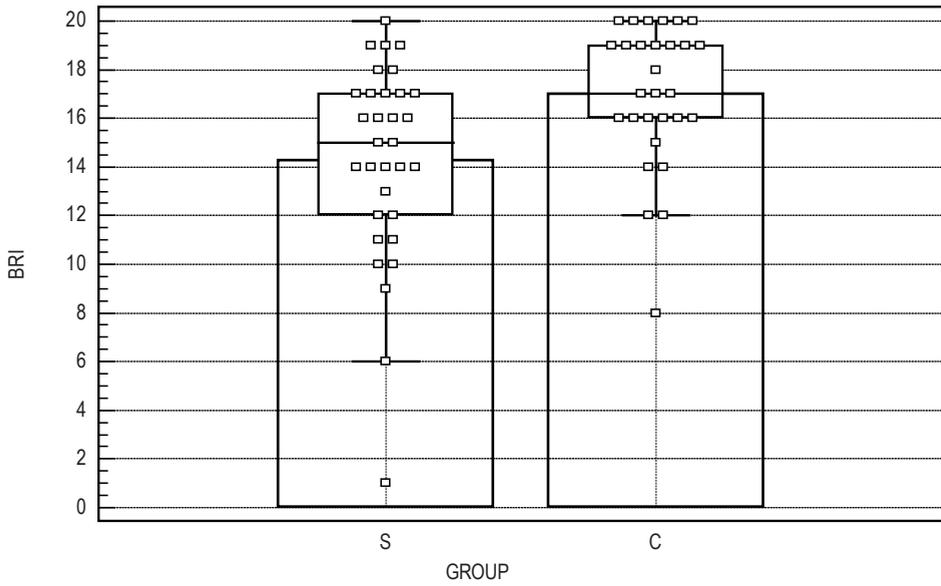


Figure 1. **Box plot for groups – variable: briskness (BRI)**  
S – study group, C – control group

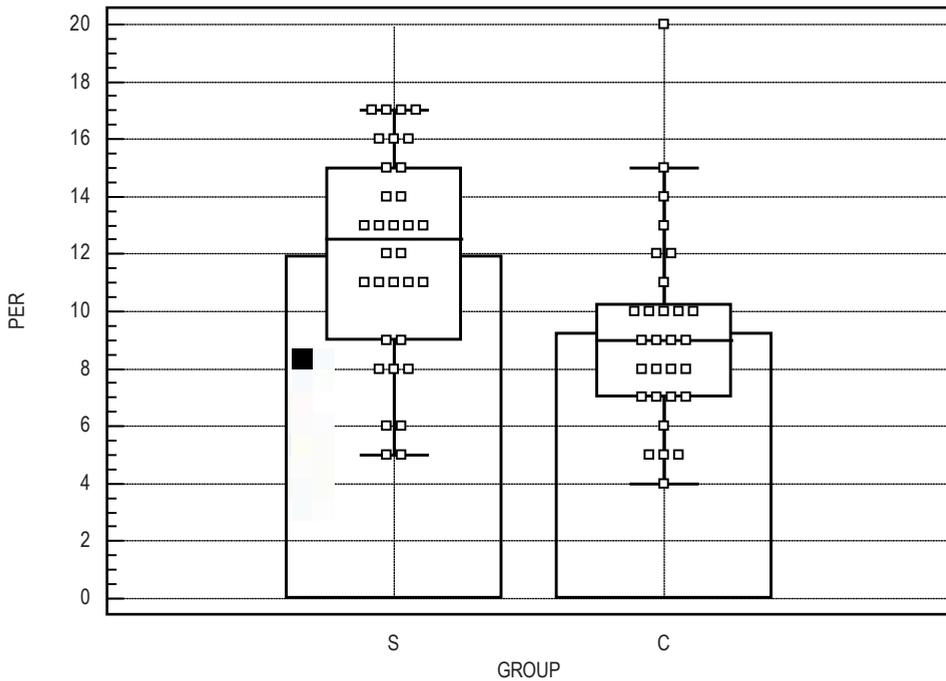


Figure 2. **Box plot for groups – variable: perseverance (PER)**

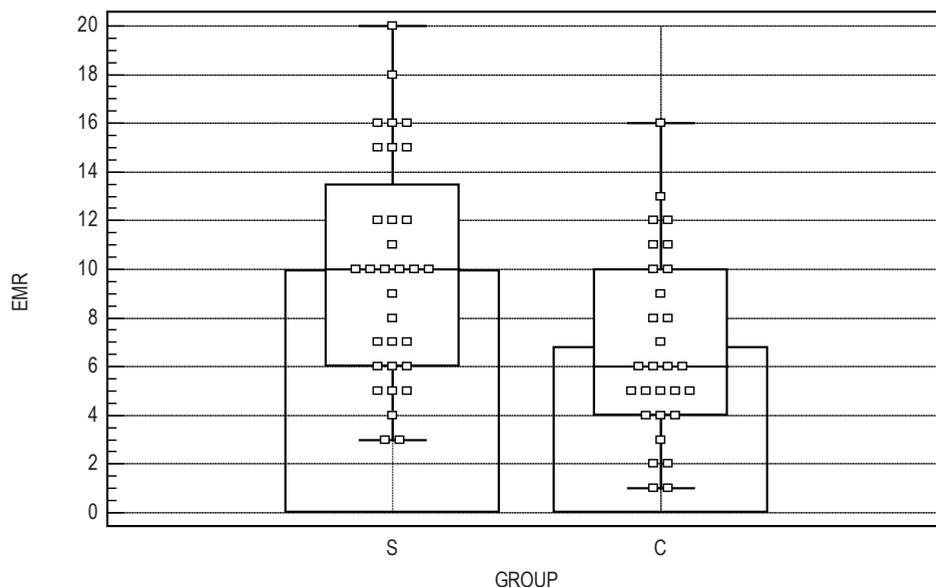


Figure 3. **Box plot for groups – variable: emotional reactivity (EMR)**

#### Correlations between PTSD and temperamental traits

The statistical analysis looks at the relationships between temperamental traits and PTSD by means of Spearman's rank correlation and Pearson's correlations. Results of statistical analysis are presented in Table 2 and 3.

Table 2. **Analysis of Spearman's rank correlation between temperamental trait and PTSD (linear model – all; N = 61)**

| Variables                     | R Spearman | P      |
|-------------------------------|------------|--------|
| Briskness vs. PTSD            | - 0.4744   | 0.0001 |
| Perseverance vs. PTSD         | 0.5048     | 0.0000 |
| Sensory sensitivity vs. PTSD  | - 0.1643   | 0.2057 |
| Emotional reactivity vs. PTSD | 0.5266     | 0.0000 |
| Endurance vs. PTSD            | - 0.4360   | 0.0004 |
| Activity vs. PTSD             | - 0.4243   | 0.0007 |

Table 3. **Pearson's regression and correlation analysis (linear model – all; N = 61)**

| Variables             | $r(X,Y)$ | P      |
|-----------------------|----------|--------|
| Briskness vs. PTSD    | - 0.3973 | 0.0015 |
| Perseverance vs. PTSD | 0.4555   | 0.0002 |

*table continued on the next page*

|                               |         |        |
|-------------------------------|---------|--------|
| Sensory sensitivity vs. PTSD  | 0.1337  | 0.3042 |
| Emotional reactivity vs. PTSD | 0.5262  | 0.0000 |
| Endurance vs. PTSD            | -0.3647 | 0.0039 |
| Activity vs. PTSD             | -0.4547 | 0.0002 |

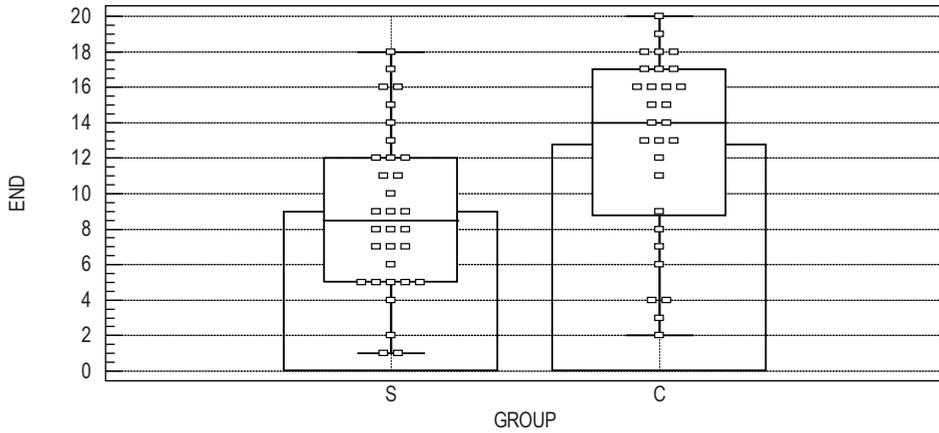


Figure 4. Box plot for groups – variable: endurance (END)

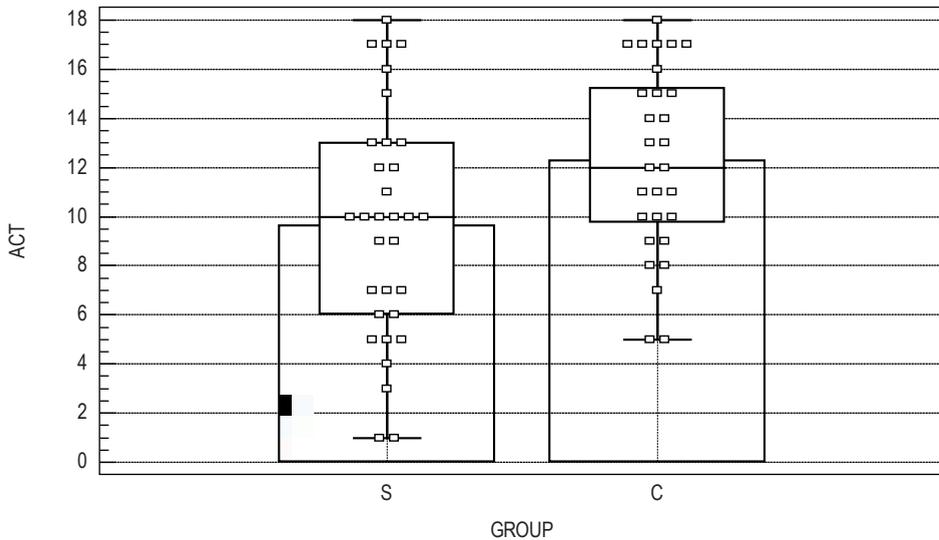


Figure 5. Box plot for groups – variable: activity (ACT)

The statistical data, except for sensory sensitivity, indicate statistically significant correlations between PTSD and temperamental traits. Negative correlations were found between PTSD and briskness, endurance and activity; positive correlations were observed between perseverance and emotional reactivity.

#### Relationships between temperamental traits and levels of selected cytokines

Statistical analysis by means of Spearman's rank correlation and Pearson's correlations. No statistically significant correlations were revealed between the levels of selected cytokines (sIL-2, TNF- $\alpha$ , IL-6, IL-10, IFN -  $\gamma$ ) and temperamental traits.

### Discussion

This study addresses the relationships between temperamental traits (briskness, perseverance, sensory sensitivity, emotional reactivity, endurance, and activity), PTSD and levels of selected cytokines. Statistical analysis revealed statistically significant correlations between temperamental traits and PTSD, except for sensory sensitivity. Negative correlation was shown between PTSD and endurance and briskness; positive correlation was found between PTSD and emotional reactivity and perseverance. No statistically significant correlations were observed between temperamental traits and the levels of selected cytokines, such as: sIL-2, IL-10, IL-6,, TNF- $\alpha$ , IFN- $\gamma$ .

According to Strelau, studies on the significance of temperament [3] suggest that the function of temperament depends on whether specific conditions allow for effective regulation of stimulation. If an individual is able to effectively regulate stimulation, he/she can select situation and forms of action in accordance with individual temperamental characteristics. It means that people adapt external conditions to stimulation and select forms of action that reflect individual temperamental capabilities. Whenever an individual is forced to adapt to external conditions that are conflicting with the individual temperamental traits, there is no possibility for effective regulation of stimulation, which induces the so-called temperamental risk factor [22]. Ineffective regulation of stimulation is associated with low resistance to stress. Stimulating conditions which are conflicting with the temperamental traits lead to reduced efficiency of actions and negative emotions.

Long-term maladjustment is associated with the risk of development of pathological forms of behaviour. Such situation may result from chronic stress. Temperamental traits have their own specific physiological and biochemical mechanisms (or at least markers) [9]. A specific combination of temperamental traits constitutes a temperamental risk factor for PTSD.

The table below (Table 4) presents relationships (correlations) between temperamental traits and PTSD, as well as the relationships between various personality dimensions and the associated correlations between temperamental traits in the study group.

Table 4. **Relationships (correlations) between temperamental traits, personality dimensions and PTSD**

| Temperamental traits   | PTSD  | Personality dimensions | Correlations with temperament |
|--|---|------------------------|-------------------------------|
| Activity<br>Emotional Reactivity<br>Perseverance<br>Endurance<br>Briskness | R = -0.4243*<br>R = 0.5266***<br>R = 0.548 ***<br>R = 0.548*<br>R = -0.4744** | extraversion           | +                             |
|  |   | impulsiveness          | +                             |
|  |   | experience-seeking     | +                             |
|  |   | neuroticism            | +                             |
|  |   | anxiety (trait)        | +                             |
|  |   | impulsiveness          | -                             |
|  |   | neuroticism            | -                             |
|  |   | anxiety (trait)        | -                             |
|  |   | neuroticism            | -                             |
|  |   | impulsiveness          | +                             |
| conscientiousness  | +   |                        |                               |

Note. “+” means positive correlations; “-” means negative correlations. R – Spearman’s rank correlation factor.

\*  $p < 0.001$ ; \*\*  $p < 0.0001$ ; \*\*\*  $p < 0.0000$

### Conclusions

1. Patients with temperamental traits such as perseverance and emotional reactivity had a greater risk of PTSD.
2. Patients with temperamental traits such as briskness, endurance and activity had lower risk of PTSD.
3. The level of cytokines (sIL-2, IL-6, IL-10, TNF- $\alpha$ , IFN- $\gamma$ ) is not dependent on the temperamental traits.

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