NEUROPEPTIDE Y STIMULATION AS PRIMARY TARGET FOR PREVENTIVE MEASURES OF MALADAPTATIVE CARDIOVASCULAR REACTIONS IN OCCUPATIONAL CHRONIC STRESS EXPOSURE

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NEUROPEPTIDE Y STIMULATION AS PRIMARY TARGET FOR PREVENTIVE MEASURES OF MALADAPTATIVE CARDIOVASCULAR REACTIONS IN OCCUPATIONAL CHRONIC STRESS EXPOSURE (Abstract): Chronic stress may produce a decrease in central NPY expression and subjects exposed to it may prove hypersensitivity to a novel stressor with dysfunctions in the NPY system and cardiovascular maladaptation to stress, even hypertension. Upregulation of NPY expression may contribute to successful behavioral adaptation to stress by reducing cardiovascular tone and suppressing anxious behaviors. Adaptogens, a new class of metabolic regulators stimulate NPY expression and release. The aim of this study is to increase tolerance and adaptation to stress of hypersensitive to novel stressor, occupational chronic stress exposed subjects with cardiovascular maladaptation to mild new stressor using adaptogens as part of prevention protocol. Material and methods: 40 military personnel with known cardiostressor reactional mode and occupational chronic stress exposure were exposed to mild novel stressor: occupational medicine routine evaluation and clinically assessed for maladaptive cardiovascular response prior and before application of 30 day prevention protocol. Employees were randomly split in two groups, one receiving standard prevention protocol (lifestyle counseling) plus adaptogens in multiple dose administration, twice daily and the other receiving only standard prevention protocol. Results: We found significant statistic differences in all cardiovascular parameters in adaptogen group and only in diastolic blood pressure in control group. Conclusions: Adaptogens could be an important factor in successful prevention protocols of chronic occupational stress dysfunctions involving NPY systems. Key words: NPY, ADAPTOGENS, CHRONIC OCCUPATIONAL STRESS, CARDIOVASCULAR MALADAPTATION, NOVEL STRESSOR

Neuropeptide Y (NPY) is a central neuromodulator and peripheral sympathetic neurotransmitter with significant regulatory roles in cardiovascular, neuroendocrine, immune and metabolic adaptation to stress and its release has been linked to a variety of stress-induced changes whose actions are dependent on the activation of multiple G-protein-coupled receptors, Y1-Y5 (1). In the brain the concentrations of NPY are significantly higher than other neuropeptides, being found mainly in the limbic system, including amygdala and hypothalamus, areas known for regulation of emo-
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tional behaviours and stress response (2). Central, NPY acts as an anxiolytic and inhibits sympathetic activity with lowering blood pressure and heart rate resultants (3). Plasma NPY levels are positively related with behavioral performance under stress (4). Low plasma levels of NPY are associated with nervous autonomic system hyperactivity to stressors, hyperarousal, exaggerated alarm reactions and anxiety reactions (5). Chronic stress may produce a decrease in NPY expression in several central nervous system regions (6) and chronic stress exposed subjects may prove hypersensitivity to a novel stressor (7) with dysfunctions in the NPY system that might lead to cardiovascular maladaptation to stress and even hypertension (8). Heilig and Thorsell proposed that an upregulation of NPY expression may contribute to successful behavioral adaptation to stress through its buffering of stress promoting signals (9) and later it was demonstrated that activation of NPY systems reduces cardiovascular tone and suppresses anxious behaviours (8). Adaptogens, a new class of metabolic regulators which increase the ability of an organism to adapt to environmental factors and to avoid damage from such factors, raising the state of non-specific resistance (10) were recently proved to stimulate the expression of NPY and its release from neuroglia cells as primary upstream target (11). Panossian et al. study was done using ADAPT 232, a combination of *Eleutherococcus senticosus* root extract, *Schisandra chinensis* berry extract and *Rhodiola rosea* root extract and they demonstrated that increased tolerance and adaptation to stress obtained through this formula might be due to stimulation and release of NPY into systemic circulation as an innate defense response (12). Standard occupational prevention programs of maladaptation to chronic stress concentrate on lifestyle changes and relaxation methods promotion.

**MATERIAL AND METHODS**

Our study is open label randomized type of study done on 40 military personnel, all males, recruited during routine occupational medical evaluations between February and March 2012, in occupational medical office from Emergency Military Hospital, Iasi. Research group was randomly split in two, 20 employees being the study group (SG) and 20 employees being the control group (CG). All signed informed consent and the selection was based on inclusion and exclusion criteria. The inclusion criteria were age between 25 and 50 years, being healthy, having no significant history, BMI- 18.50-24.99 kg/m2, stress reactive type- cardistressor- arterial blood pressure ≥ 140/80 mmHg and rest heart beat >80 beats/minute. The exclusion criteria were cardiovascular disease, endocrine disease, neurologic disease, obesity, arterial blood pressure <140/80 mmHg and rest heart beat <80 beats/minute.

Military employees are prone to more maladaptive cardiovascular stress responses than general population (5) and percentage of such dysfunctions is quite significant as we found in previous studies done in our occupational medicine office. Recent studies on stress protective effect of a combination of adaptogens- ADAPT 232- through NPY expression stimulation and release from neuroglia cells (11) incited us to determine if this combination of standardized adaptogens might be useful as preventive measure in maladaptation to occupational stress. We considered the occupational medicine routine evaluation a mild novel stressor and
cardiovascular dysfunctions finded( arterial blood pressure $\geq 140/80$ mmHg and rest heart beat $>80$ beats/ minute) an exaggerated alarm reaction and anxious behavior of a chronic occupational stressed hypersensitive subject with low central levels of NPY (5). We selected apparently healthy male military employees with known cardioskstressor reactional mode, aged 25 to 50 years and as told earlier in the text, they were randomly split in 2 groups. Girst group,SG group received a standardized combination of adaptogens – Adaptonic- 

*Eleutherococcus senticosus* root extract, *Schisandra chinensis* berry extract and *Rhodiola rosea* root extract from Alevia, *Falticeni*, multiple dose administration, twice daily and lifestyle counselling and CG group received only standard protocol that is lifestyle counselling . We hypothesized that stimulation of NPY through Adaptonic will improve tolerance to novel stressors in a chronic occupational stress exposed subject. Subjects were reevaluated 30 days after, being exposed to same mild stressor but with 30 days interference and we studied alarm reaction through cardiovascular parameters.

**RESULTS AND DISCUSSION**

We used descriptive statistic studies and TTEST from Microsoft Excel 2003. There were no significant statistic differences between the two groups on age parameter (35.60±7.38 years for SG compared with 35.95±8.17 years for CG. We found significant statistic differences (p<0.05) in all cardiovascular parameters (tab.I). Thus the stimulation of NPY through the combination of adaptogens- Adaptonic- improved tolerance to novel stressor in the chronic stress exposed subjects.

**TABLE I**

<table>
<thead>
<tr>
<th>Group</th>
<th>N</th>
<th>Age(years)</th>
<th>Systolic blood pressure in t0 (mmHg)</th>
<th>Systolic blood pressure in t1 (mmHg)</th>
<th>Diastolic blood pressure in t0 (mmHg)</th>
<th>Diastolic blood pressure in t1 (mmHg)</th>
<th>Rest heart rate (beats/min) in t0</th>
<th>Rest heart rate (beats/min) in t1</th>
</tr>
</thead>
<tbody>
<tr>
<td>Study group (SG)</td>
<td>20</td>
<td>35.60±7.38</td>
<td>156.20±11.63</td>
<td>138.50±6.3</td>
<td>91.50±7.27</td>
<td>73.25±7.38</td>
<td>96.50±7.96</td>
<td>74.85±6.01</td>
</tr>
<tr>
<td>Control group (CG)</td>
<td>20</td>
<td>35.95±8.16</td>
<td>154.80±9.75</td>
<td>154±9.4</td>
<td>90.25±7.34</td>
<td>86.50±6.97</td>
<td>96.15±10.70</td>
<td>94.80±8.91</td>
</tr>
</tbody>
</table>

In group 2 we found significant statistic differences only in parameter: diastolic blood pressure (p<0.05). This finding could be due to prior experience of NPY systems to the mild stressor we used that is medical evaluation, taking in account that NPY influence vascular tonus but adaptation to the stressor is incomplete as cardiovascular parameters: systolic blood pressure and rest heart rate had no significant statistic differences ( p>0.05) (tab. I).

Testing plasma levels of NPY as routine measure of occupational medical evaluation in chronic military stress exposed subjects, with cardiovascular maladaptation to mild novel stressor might bring important, adia-
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cent information about their alarm reaction capacities and gives us the possibility to correct any dysfunction of the stress response system before the units are involved in high-stress, high-risk operations.

CONCLUSIONS
We found out that adaptogens could be an important factor in a successful preventive measures protocol of chronic stress dysfunctions involving NPY systems. Early diagnosis of these type of dysfunctions and their treatment with a combination of adaptogens might prove organizational and individual health saving. Extensive studies on larger populations and with different occupations are neede for further development of the treatment protocol.

REFERENCES