Stress Response and Antihypertensive Treatment†

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Summary

Results from many studies suggest that the central nervous system may play an important role in enhancing and maintaining sympathetic, metabolic and haemodynamic effects in patients with hypertension. Likewise, emotional and mental stresses may provoke phasic and sustained adrenergic responses in normotensive and untreated hypertensive patients. Because the various antihypertensive medications have different mechanisms of action, and elicit different neurovegetative responses, it is useful to distinguish between the effects of different treatments on sympathetic activity.

To identify the effect of stress on sympathetic reactivity, we evaluated the extracardiovascular and haemodynamic responses to various stressor agents using noninvasive techniques. This psychophysiological approach allowed us to standardise stress, to identify individual cardioneurovegetative responses both before and during treatment, and to establish the effects of various treatments on the cardioneurovegetative response.

The extracardiovascular psychophysiological response of patients with a family history of hypertension and of normotensive patients who later became hypertensive was characterised by an inability to recover after mental challenge. Therefore, prolonged sympathetic activity resulting from mental stimulation may contribute to the development of hypertension.

Antihypertensive medications affected sympathetic reactivity differently. For example, nifedipine worsened sympathetic reactivity, while verapamil was able to correct abnormal neuroadrenergic responses. Furthermore, verapamil was successfully combined with enalapril in patients whose hypertension was resistant to monotherapy with the angiotensin converting enzyme (ACE) inhibitor.

Therefore, the functional and structural consequences of sympathetic stimulation resulting from daily activation and pharmacological blood pressure adjustments are important in hypertensive patients, because they may have abnormal sympathetic reactivity to various stimuli.

Sympathetic activity results from the interaction between genetic, behavioural and socio-cultural factors. In fact, the results of many studies show that the sympathetic branch of the autonomic nervous system can play a key role in the onset and the maintenance of primary arterial hypertension.

Elevated noradrenaline (norepinephrine) and adrenaline (epinephrine) levels have been found in hypertensive patients, and increased noradrenergic tone (Goldstein 1983) and enhanced cardioneurovegetative reactivity (Falkner et al. 1981) are characteristically found in younger patients. Furthermore, recording from sympathetic fibres directed

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to muscle has proved that central noradrenergic outflow (Anderson et al. 1989) is increased during physical (Mark et al. 1985) and psychological stimulation (Anderson et al. 1987).

Studies in which ambulatory monitoring was used to measure blood pressure have found that arterial pressure rises to a greater extent during the day in hypertensive patients than in normotensive subjects (Mancia 1990). Furthermore, the increase in diurnal blood pressure is due to psychological influences rather than physical exertion (Pickering et al. 1982; Polonia et al. 1992), and is closely related to target organ damage (Devereux et al. 1983; Pessina et al. 1985). In addition, it has been found that patients who experience job strain (little control over the high psychological demands during working hours) have significantly increased arterial blood pressure (Schnall et al. 1990). It was also observed that the systolic blood pressure of these patients remained elevated throughout the day, even when patients were not working (van Egeren 1992).

Most hypertensive patients receive treatment to control their blood pressure. In addition to reducing blood pressure, this treatment can also elicit a sympathetic counter-regulatory response (Julius 1990). The autonomic effects of the medication and the functional reaction of the patient (Sullivan 1981) compound the individual neurovegetative arousal. Therefore, both the sympathetic stress response and the well-being of the patient could be influenced by the choice of antihypertensive agent.

Therefore, the purpose of this paper is to review some of the studies we have performed, evaluating the impact of various antihypertensive agents upon the extracardiovascular and haemodynamic stress response.

1. Study Methodology

After a psychological challenge, the sympathetic response is based on ‘cognitive evaluation’ of previous exposure to the stimulus (Lazarus et al. 1980). After the subject has considered previous experiences with the stimulus and evaluated the environmental conditions, emotional activation of the sympathetic nervous system may occur. Therefore, to study the sympathetic response of an individual to mental stress, and to verify the sequence of events occurring after exposure to stress, the effect of many different stressor agents was investigated.

In common with other investigators, we have found that psychological tasks can elicit a greater response in hypertensive patients than physical challenges (Pirrelli et al. 1989). Therefore, we used several mental challenges (Mental Arithmetic, Stroop Color Word Interference, Mild Electric Stimulations, White Noise), and assessed the effect of each challenge on blood pressure. Each mental challenge was carried out for 5 minutes and was preceded and followed by recovery periods lasting 10 minutes.

To obtain a stress response profile, every 30 seconds throughout the experimental period we monitored several haemodynamic (systolic and diastolic blood pressure and heart rate) and extracardiovascular (muscular contraction, skin conductance and peripheral temperature) variables. Muscular contraction may be related to the attention paid to the stimulus (Raskin et al. 1973), and skin conductance was found to change with emotional (Scarpa-Scerbo et al. 1992) and cholinergic arousal of the sympathetic nervous system. Because peripheral temperature tends to decrease during a psychophysiological challenge, we used this as an indicator of peripheral vascular contraction and adrenergic stress response (Bloom & Trautt 1977).

In response to physiological stress, all of these variables (except for temperature) increased during exposure to a stimulus and returned towards baseline during the recovery period; temperature, however, responds inversely. Psychophysiological findings (Waters et al. 1987) and functional studies validate the reliability and usefulness of assessing these variables. In particular, an absence of response suggests that the stimulus was not effective or that changes in blood pressure did not accompany the emotional response. However, to date, few studies have investigated the effect of various tasks on the emotional response.