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Chronic Stress Increases Serotonin and Noradrenaline in Rat Brain and Sensitizes Their Responses to a Further Acute Stress

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Abstract: The effects of 1 h/day restraint in plastic tubes for 24 days on the levels of serotonin (5-HT), 5-hydroxyindoleacetic acid (5-HIAA), tryptophan (TP), and noradrenaline (NA) in six regions of rat brain 20 h after the last restraint period were investigated. The levels of 5-HT, 5-HIAA, and NA but not TP increased in several regions. The effects of 1 h of immobilization on both control and chronically restrained rats were also studied. Immobilization per se did not alter brain 5-HT, 5-HIAA, and TP levels, but decreased NA in the pons plus medulla oblongata and hypothalamus. However, immobilization after chronic restraint decreased 5-HT, increased 5-HIAA, and decreased NA in most brain

regions in comparison with values for the chronically restrained rats. We suggest that chronic restraint leads to compensatory increases of brain 5-HT and NA synthesis and sensitizes both monoaminergic systems to an additional acute stress. These changes may affect coping with stress demands. **Key Words:** Serotonin—5-Hydroxyindoleacetic acid—Tryptophan—Noradrenaline—Chronic restraint. Adell A. et al. Chronic stress increases serotonin and noradrenaline in rat brain and sensitizes their responses to a further acute stress. *J. Neurochem.* **50**, 1678–1681 (1988).

Stress alters the utilization of central neurotransmitters, in particular that of noradrenaline (NA) and serotonin (5-HT), and also alters behavior. Most work has concerned NA. Acute stress generally increases its turnover and levels are decreased if the stress is sufficiently severe (Stone, 1975; Tanaka et al., 1982; Ida et al., 1984; Lehnert et al., 1984; Glavin, 1985). Less attention has been paid to 5-HT although several studies suggest that acute stress increases turnover as brain levels of 5-hydroxyindoleacetic acid (5-HIAA) increase but those of 5-HT are unaltered (Curzon et al., 1972; Morgan et al., 1975; Joseph and Kennett, 1981; Kennett and Joseph, 1981). It has been suggested that stress-induced increases of 5-HT turnover do not merely reflect its intraneuronal metabolism (Grahame-Smith, 1971), but also increased functional activity of serotonergic neurons (Joseph and Kennett, 1981, 1983; Kennett and Joseph, 1981).

Unlike acute stress, repeated stress does not deplete brain NA. This may reflect adaptation due to en-

hanced activity of the enzymes involved in NA biosynthesis (Kobayashi et al., 1976; Kvetnansky, 1980; Stone and McCarty, 1983) so that stress-dependent increased demands for the transmitter are met.

There have been relatively few studies of the effect of chronic stress on brain 5-HT metabolism (Roth et al., 1982; Hellhammer et al., 1984; Kennett et al., 1985, 1986) and little is known about possibly adaptive changes of 5-HT metabolism although tryptophan hydroxylase (tryptophan-5-monoxygenase; EC 1.14.16.4) activity is reported to be increased after repeated stress exposure in some brain nuclei and decreased in others (Culman et al., 1984).

To elucidate possible serotonergic adaptive mechanisms we have investigated the effects of a daily period of restraint for 24 days on the concentrations of 5-HT, 5-HIAA, and tryptophan (TP) in six regions of rat brain. NA was also measured. We have also studied the effects of the above procedure on 5-HT metabolism and NA changes elicited by acute immobilization stress.

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Abbreviations used: 5-HIAA, 5-hydroxyindoleacetic acid; 5-HT, 5-hydroxytryptamine (serotonin); NA, noradrenaline; TP, tryptophan.



Els 3 articles més citats, publicats als anys 1988-89 i que complien els requisits del premi Ramon Turró, van ser:

<p>Adell, A; Garcia-Marquez, C; Armario, A; Gelpi E (1988)</p> <p>Chronic stress increases serotonin and noradrenaline in rat brain and sensitizes their responses to a further acute stress</p> <p>Journal of Neurochemistry 50; 1678-1681</p> <p>Departament de Neuroquímica, CSIC, Barcelona</p>	<p>155 cites</p>
<p>Tolosa, E; Montserrat, L; Bayes, A (1988)</p> <p>Blink reflex studies in focal dystonias - enhanced excitability of brain-stem interneurons in cranial dystonia and spasmodic torticollis</p> <p>Movement Disorders 3; 61-69</p> <p>Neurology Service, Hospital Clinic i Provincial de Barcelona, Faculty of Medicine, Barcelona</p>	<p>104 cites</p>
<p>Adell, A; Trullas, R; Gelpi, E (1988)</p> <p>Time course of changes in serotonin and noradrenaline in rat brain after predictable or unpredictable shock</p> <p>Brain Research 459; 54-59</p> <p>Departament de Neuroquímica, CSIC, Barcelona</p>	<p>56 cites</p>

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