ACTH 1-17 AND SHORT-TERM MEMORY, ANXIETY, HEART RATE, BLOOD PRESSURE

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In addition to their role in peripheral endocrine activity, several peptides have been shown to induce behavioral changes through a direct action on the central nervous system. Among the peptides studied in this context, particular interest has been aroused by the effect of ACTH and its analogues on various functions such as attention, memory and learning. These effects seem not to be related to the ACTH corticostimulant action on the adrenal gland.

The central action of ACTH on learning processes has been more specifically confirmed by the injection of synthetic ACTH analogues and ACTH derived peptides lacking in corticotrophic activity. Several experimental studies have shown that ACTH-related peptides (ACTH 1-10, ACTH 4-10, ACTH 4-9, ACTH 4-7) are able to improve learning and memory retention. The central-behavioral effects of ACTH and ACTH-related peptides seem to be mainly related to the 1-10 aminoacidic sequence while the 4-10 sequence seems to be the shortest sequence influencing central and memory processes. These effects are apparently related to a momentary increase in motivation toward environmental stimuli, or to a momentary increase in selective attention, and they seem to be also related to an increased arousal in mesolimbic structures as suggested by EEG studies in animals and man. Other studies on cardiovascular reactivity in rats and humans, together with observations of the increasing human reflex motor activity tend to confirm the hypothesis of a facilitated transmission in the mesolimbic pathways. It has also been hypothesized that these effects are related with the action of these peptides in the turnover of central serotonin.

Key-words: ACTH 1-17; Anxiety; Blood pressure; Cortisol; Heart rate; Memory; Stress.

Further evidence of the central effects of ACTH related peptides is derived from experimental studies based on their acute (i.v.) administration to healthy human volunteers, with assessment of brain electrical activity and of concurrent psychometric modifications. ACTH 4-10 has been reported to improve scores on test of visual retention and to increase central arousal as evaluated by EEG spectral analysis. Similar results were reported after administration both of ACTH 1-10 and 4-10. Among other ACTH related peptides, the synthetic analogue derived from ACTH 4-9 (ORG 2766) appears to have more powerful effects on behavior than the original molecule, because it is less degradable by enzymatic activity. Administration of this peptide in humans resulted in increased attention during mental tests, associated with EEG signs of increased arousal and vigilance.

ACTH-related peptides have also been used in clinical context. Present data on their clinical effects mainly concern ACTH 4-10 on patients with organic brain damage, geriatric patients, young mentally retarded, and the synthetic analogue ORG 2766, resulting in improvement of mood, attention and memory recall.

**Aim of the study**

Short chain ACTH peptides exert central and behavioral effects in absence of corticostimulant action. Nevertheless, what effect other molecules structurally more similar to the natural ACTH whole molecule may have on central processes is open to question.

The aim of the present study was to investigate the potential central effects of a recently synthesized peptide, ACTH 1-17 (Synchrodyn®), containing both the 1-10 central active sequence and the 10-17 peripheral corticostimulant sequence.

**MATERIALS AND METHODS**

**Experimental design**

The study provided for i.v. administration of ACTH 1-17 and placebo to healthy volunteer subjects in a double blind crossover design. Each subject participated in two different experimental sessions (placebo and ACTH 1-17) conducted 1 week apart. Subject order was randomized so that one half of the group received the peptide in the first of the two sessions and the placebo in the second or viceversa.

**Subjects**

Ten volunteer subjects, 5 males and 5 females, aged 24-30 years (mean age 26, SD 2.0) participated in the study. Subjects with a past or present history of relevant somatic or psychiatric pathology were excluded. For female subjects, experimental sessions were placed between the 10th and 20th day after the last menstruation. All subjects were informed of the aim and procedure of the study and gave written consent.

**Data collection**

Each session included serial plasma cortisol evaluation, psychophysiological and psychometric assessments.