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LETTER TO THE EDITORS

Evaluation of the emotional state shortly before death – science-fiction or a new challenge?

Dear Sirs,

The last decade of the twentieth century has brought an unprecedented intensification of scientific effort in the field of brain research. Many new methodologies and processes have been observed and published. The question arises whether legal medicine can answer old questions with the newly available knowledge.

In the 1960s attempts were made to characterize different neurotransmitters in the brains of suicide victims and to correlate them to mental disorders. In certain regions lower concentrations of serotonin [11] in combination with a lowered level of a serotonin metabolite in the hindbrain [1] were described. Also, an extremely low level of serotonin in cerebrospinal fluid seemed to exclude a suicide [6]. In another example schizophrenia was diagnosed postmortem by determination of dopamine beta-hydroxylase activity which is known to be indicative of this disease [15].

Currently, there are no studies describing short emotional conditions e.g. fear, in the context of neurotransmitters and their metabolites. However such biochemical "frozen frames" of neuroexcretion could possibly help in the reconstruction of events just before death. If a victim of violent crime was aware of a life-threatening situation shortly before dying, one would expect to find biochemical "finger prints" of a stress process in the brain tissue. It has been suggested that a discrete, dedicated system for stress coordination has evolved in humans. This system consists of 2 main components: (1) the locus ceruleus-norepinephrine (LC-NE) autonomic neurons and (2) the neurons of the paraventricular nucleus (PVN) of the hypothalamus which produce corticotrophin-releasing hormone (CRH) [3]. CRH-producing neurons are also dispersed throughout the entire brain [4]. There is a feedback mechanism between these 2 components in which CRH, noradrenaline and vasopressin play an important role (Fig. 1) [3]. Within the nuclei of the stress system, regulation processes make use of the same neurotransmitters and neuromodulators. Whereas serotonin and acetylcholine are system stimulators, GABA and glucocorticoids are inhibitors [3]. Opioid peptides similar to dynorphin inhibit CRH production [12]. Also, dynorphin acts as a strong inhibitor of the LC-NE system [9]. Vasopressin, on the other hand, stimulates the CRH-mediated release of ACTH and beta-endorphin from the anterior pituitary and hypothalamus and stimulates the neurons of the locus ceruleus [2].

The 2 components of the stress coordinating system also interact with other important parts of the CNS. This in turn results in information acquisition and analysis, proper reaction to stimuli and regulation of the emotional state. The participating structures are (1) the amygdala-hippocampus complex, (2) the mesocortical and mesolimbic systems and (3) the hypothalamic arcuate nucleus.

1. The *amygdala-hippocampus complex* has a particularly important function during a stress inflicted by an external emotional stressor, e.g. fear [3]. The amygdala plays a key-role in forming such "conditioned emotions" and it also retains a memory for such states. The most recent experimental findings point to the amygdala as the coordinating centre of the stress system. A sensory stimulus from the thalamus, mediated by glutamate and NMDA receptors carries information to the lateral nucleus of the amygdala. Further interaction takes place between the efferent central nuclei of the amygdala and the nuclei of the PVN-CRH and LC-NE systems and it has been decided that this stimulus is the emotional stressor [7]. Stimulation of the amygdala through the noradrenergenic neurons of the locus ceruleus is important during acquisition and processing of the stress information [14]. Hippocampo-amygdala projections also give rise to the emotional response [7]. Moreover, it is suspected that the hippocampus can strongly inhibit the amygdala and paraventricular nucleus [5].

2) Other important interactions inside the stress system occur in the PVN, locus ceruleus and the dopaminergic *mesocortical* and *mesolimbic systems* [13]. The latter two systems are responsible for the short-term operational memory (mesocortical) and such processes as motivation, reinforcement and reward (mesolimbic with its main component, nucleus accumbens).

3) The *hypothalamic arcuate nucleus* closely connected with the paraventricular and locus ceruleus neurons, is the third significant structure involved in the regulatory functions of the stress system. CRH stimulates production of ACTH and beta-endorphin in the proopiomelanocortin-containing nerve cells of the arcuate nucleus and there ex-

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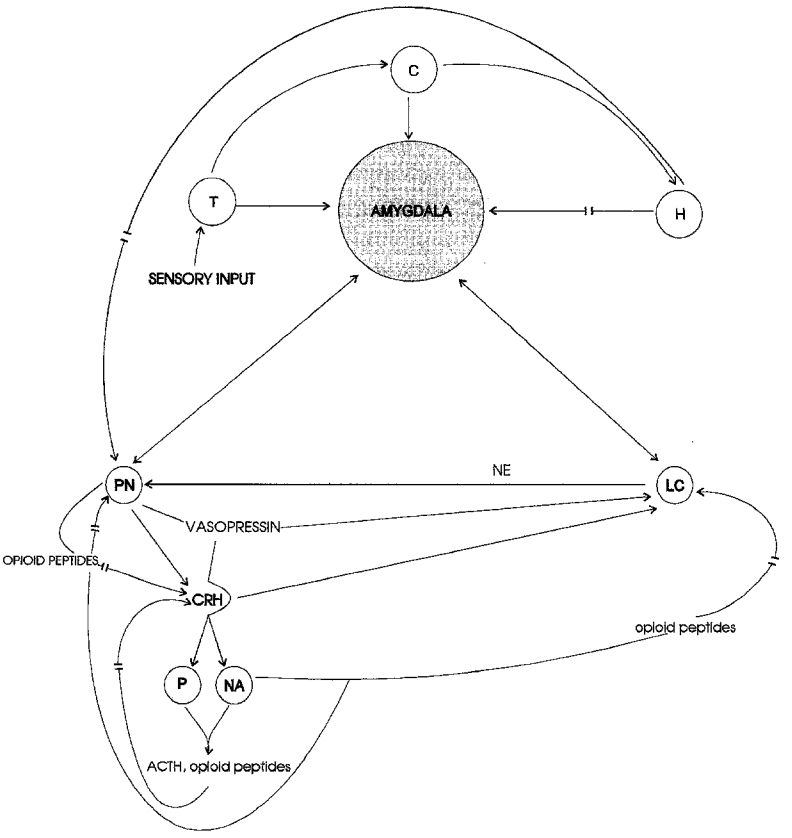

Fig. 1 A simplified representation of the central components of the stress system. CRH - corticotrophin-releasing hormone, NE - norepinephrine, ACTH - corticotrophin, T - thalamus, C - cortex, H - hippocampus, PN - paraventricular nucleus, LC - locus ceruleus, P - anterior pituitary, NA - nucleus arcuatus

ists a negative feedback mechanism between these peptides and CRH [2]. Proopiomelanocortin neurons do not only interact with PVN but also with the brainstem and other parts of the brain. They antagonize CRH neurons and the LC-NE system and consequently induce analgesia by activating the opioid receptors [10]. Through the above described process the hypothalamic arcuate nucleus could possibly influence the emotional tension.

A broad spectrum of neurotransmitters, neuromodulators and enzymes may serve as indicators of a conditioned emotion caused by a stressor. Postmortem examinations have shown that some of these markers are relatively stable [1, 6, 8, 11, 15]. Until now their concentrations have been used to make conclusions about the long-term emotional state before death [1, 6, 11, 15]. The time has come to check the hypothesis: does the brain of the deceased also contain traces of short but very intense emotions? Or is this only pure speculation?

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