may be more plausible, at least for the relation between amygdala and opioid systems. One possible periventricular site of action for naloxone and β-endorphin is the locus coerulus, which is the source of the noradrenergic fibers that innervate the amygdala, and which receives a projection from the hypothalamic β-endorphin system.

Only further research will tell. Introini-Collison and McGaugh have suggested that the interaction between the influences on memory of post-training naloxone or β-endorphin and epinephrine may take place at, or be mediated by, the amygdala[12].

But, meanwhile, nobody can deprive the amygdala of its current moment of glory as the Hamlet of memory research. Hamlet in the sense of a small gathering of little places that β-noradrenergic ligands can call their home. Hamlet in the sense of a structure that tells memories to be or not to be[5]. Hamlet as a metaphor for a nut, the amygdala being almond-shaped. Hamlet as a metaphor for being bounded and at the centre of something.

IVAN IZQUIERDO

*Centro de Memoria, Departamento de Bioquimica, Instituto de Biociencias, UFRGS (centro), 90049 Porto Alegre RS, Brazil.*

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# LETTERS

*Amino acids are not uncharged (lipid-soluble) substances*

## Why we might as well forget pyroglutamate as an amino acid

Correspondents Moret and Briley write of pyroglutamate as the 'forgotten amino acid' (*TiPS*, August 1988)[1]. No wonder – although perhaps an amino acid analog, pyroglutamate really is *not* an amino acid! Confusion has not been decreased by a recent tendency to rename this compound (also long and properly known as pyrrolidone 2-carboxylic acid) as 'oxoproline'.

Were we more universally fastidious in writing the structural formulas of the amino acids as $RCH(NH_3^+)\text{-}COO^-$, instead of using the antique and misleading style derived from the time of Emil Fischer, namely $RCH(NH_2)\text{-}COOH$, and if we tried picturing pyroglutamate in an equally realistic style, we would at once discover that pyroglutamate has a chemical nature quite unlike that of the amino acids. The hypothetical zwitterion (Fig. 1a) is unlikely to exist in aqueous systems, since the nitrogen atom is part of an amido group (Fig. 1b) and not an amino group. This amido group should protonate only below a pH of less than zero. Hence pyroglutamate is *not* an amino acid and can scarcely be a zwitterion; the structural formula representing its state of charge in neutral aqueous solution should be as shown in Fig. 1c. Rather it is an anion, and by no means a dipolar ion or a zwitterion.

In some circumstances, however (for example, the inhibition of glutamate binding at striatal membranes[1], and the inhibition of amino acid transport by an occasional transport system) it can tell us something useful and valuable about certain biological recognition sites for true amino acids.

Teachers of biochemistry in whatever discipline should reconsider their use of textbooks that show amino acids incorrectly as uncharged (and hence lipid-soluble) substances. The damage must be greatest for the most biological of our students. Biorecognition of these molecules and the membrane control of their movements is unlikely to be understood by anyone who sees pyroglutamate as an amino acid.

HALVOR N. CHRISTENSEN

*Department of Biological Chemistry, The University of Michigan, Ann Arbor, MI 48109, USA.*

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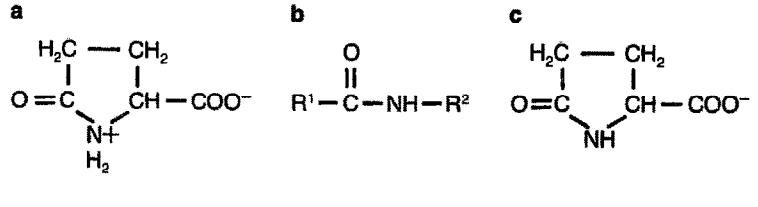


*Fig. 1. Structural formulas for amino acids and amido groups.* **a**, *Hypothetical structure of an improbable zwitterion of pyroglutamate as if it were an amino acid;* **b**, *general formula for amido groups;* **c**, *formula for pyroglutamate in neutral solution.*