Output of [^{14}C]Adenine Derivatives on Electrical Excitation of Tissues from the Brain: Calcium Ion-Sensitivity and an Accompanying Re-uptake Process

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The output, from neocortical and piriform-cortical samples, is associated with formation of cyclic AMP (adenosine 3':5'-cyclic phosphate) in the tissues (Kakiuchi *et al.*, 1969; Sattin & Rall, 1970; Pull & McIlwain, 1972). With superfused neocortical tissues previously incubated with [^{14}C]- or [8- ^{14}C]-adenine the preponderant ^{14}C -labelled compounds found chromatographically in superfusates were adenosine, inosine and hypoxanthine (McIlwain & Pull, 1972; see Shimizu *et al.*, 1970). Adenine nucleotides were minor ^{14}C -labelled components of the superfusates. Change from a normal glucose-bicarbonate-buffered saline with 0.75mM- Ca^{2+} to one without Ca^{2+} resulted in increased output of ^{14}C -labelled compounds, again mainly adenosine, inosine and hypoxanthine. This greater output could still, within 20min, be augmented by electrical excitation. However, if tissues in Ca^{2+} -free media were momentarily exposed to 5mM-EDTA and this was then removed by continuing the superfusion with Ca^{2+} -free media, little or no change

was caused by electrical excitation in the output of ^{14}C -labelled compounds.

Output of ^{14}C -labelled compounds from tissues preincubated with [^{14}C]adenine, on excitation, was found to be approximately doubled by the additional presence of either 1mM-2'-deoxyadenosine or 50 μM -papaverine. In interpretation of these findings, examination was made of whether the compounds at these concentrations inhibited the uptake of [^{14}C]adenosine added as such to the tissue. Inhibition of uptake, by about 50%, was found to be caused by both the deoxyadenosine and papaverine.

A sequence familiar from other neurohumoral studies has thus been recognized in relation to adenosine derivatives of cerebral tissues: release on electrical excitation, by a Ca^{2+} -dependent mechanism; action of adenosine after release, in augmenting cyclic AMP; and removal of adenosine by at least two processes, namely conversion into inosine and hypoxanthine and by uptake to the tissue.

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