

PSYCHOMOTOR EXCITATION INDUCED BY OPIOIDS: IMPLICATIONS IN AFFECTIVE DISORDERS

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PSIHOMOTORNA EKSCITACIJA KOJU IZAZIVAJU OPIOIDI I NJEN ZNAČAJ ZA POREMEĆAJE AFEKTA

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SAŽETAK

Kada se morfin i beta-endorfin ubrizgaju u moždane komore neanestetiziranih mačaka izazivaju dozno-zavisno dugotrajniji nemir, kretanje, stereotipne pokrete glavom na stranu, zurenje u prazno, strah i beg udružene sa midrijazom i tremorom. Najimpresivnije karakteristike psihomotorne ekscitacije su kretanje i pokreti glavom na stranu. Periodi kretanja su se izmenjivali sa periodima mirnoće. Do smenjivanja ovih perioda je dolazilo naglo, u nepravilnim vremenskim intervalima. Glavna razlika između ekscitatornih efekata morfina i beta-endorfina je povraćanje. Naime, psihomotornoj ekscitaciji koju izaziva morfin prethodi kratkotrajno, dozno-zavisno povraćanje. Nepeptidni opioidni agonisti metodom i petidin kada se ubrizgaju intracerebroventrikularno (i.c.v.) mačkama izazivaju slične bihevioralne fenomene. S druge strane, nepeptidni opioidni agonist ketociklazocin, kao i peptidni opioidi metionin- i leucin-enkefalin primenjeni i.c.v. nisu izazvali psihomotornu ekscitaciju kod mačaka. Bez obzira na to, enkefalini su izazvali prolazno i nepostojano povraćanje. Nalorfin je prevenirao sve fenomene izazvane nepeptidnim i peptidnim opioidima. Litijumove soli ubrizgane intracerebroventrikularno su sprečile ili prekinule psihomotornu ekscitaciju izazvanu beta-endorfinom. Bihevioralni efekti beta-endorfina su se takođe mogli značajno smanjiti ili suzbiti kod mačaka prethodno tretiranih sa 6-OH-dopaminom i.c.v. Očigledno je, dakle, da u regulaciji psihomotorne ekscitacije izazvane opioidima učestvuju uglavnom opioidni μ -receptori. Inhibitorni efekat litijuma je najverovatnije vezan za centralne opioidne receptore i endogene peptide, ali drugi mehanizmi se ne mogu isključiti. Rezultati dobijeni sa 6-OH-dopaminom snažno sugeriraju da su pored opioidnih mehanizama bar kateholaminergički (najverovatnije dopaminergički) mehanizmi uključeni u pojavu bihevioralnih fenomena izazvanih opioidima. Značaj psihomotorne ekscitacije je diskutovan u odnosu na afektivne poremećaje.

Ključne reči: Psihomotorna ekscitacija, opioidi, opioidni receptori, litijum, kateholamini, afektivne psihoze.

ABSTRACT

Morphine and beta-endorphin injected into the cerebral ventricles of unanaesthetized cats produce dose-dependent and long-lasting restlessness, locomotion, stereotyped sideways movements of the head, vacant staring, apprehension and flight accompanied with mydriasis and tremor. The most impressive features of the psychomotor excitation are the locomotion and side ways movements of the head. The periods of locomotion alternated with periods of tranquility. These periods occurred in bursts at irregular time intervals. The main difference in the excitatory phenomena of morphine and beta-endorphin is the emesis. Namely, the psychomotor excitation induced by morphine was preceded by shortlasting and dose-dependent emesis. The non-peptide opioid agonists methadone and pethidine injected intracerebroventricularly (i.c.v.) in cats evoked similar behavioural phenomena. On the other hand, the non-peptide opioid agonist ketocyclazocine, as well as the peptide opioids methionine- and leucine-enkephalin administered also i.c.v. failed to cause psychomotor excitation in cats. Nevertheless enkephalins evoke transient and inconsistent emesis. Nalorphine prevents all phenomena induced by non-peptide and peptide opioids. Lithium salts injected i.c.v. prevent and reverse the psychomotor excitation evoked by beta-endorphin. The behavioural effects of beta-endorphin are also significantly reduced or abolished in cats pretreated with i.c.v. 6-OH-dopamine. It is apparent, therefore, that the psychomotor excitation induced by the non-peptide and peptide opioid agonists is mediated mainly by opioids μ -receptors. The inhibitory effect of lithium most probably is mainly associated with central opioid receptors and endogenous peptides, but other mechanisms cannot be excluded. The results obtained with 6-OH-dopamine strongly suggest that besides opioid mechanisms, at least catecholaminergic (most probably dopaminergic) mechanisms are involved in the emergence of the behavioural phenomena evoked by opioids. The significance of psychomotor excitation is discussed in relation to affective disorders.

Key words: Psychomotor excitation, Opioids, Opioid receptors, Lithium, Catecholamines, Affective psychoses.

INTRODUCTION

Considerable evidence indicates that opioids may play an important role in modulating behaviour and motor activity. Morphine and

related endogenous opioids are behavioural depressants for most laboratory species. Their stimulating effects in other species including mice and cats are often overlooked. Early investigators revealed that parenteral administration of morphine produces pecu-

