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Short communication

Antinociception after intrathecal biphalin application in rats: a reevaluation and novel, rapid method to confirm correct catheter tip position

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Abstract:
The opioid peptide dimmer biphalin [(Tyr-D-Ala-Gly-Phe-NH-)$_2$] has high potency both *in vivo* and *in vitro*. Its antinociceptive activity depends on the route of administration: the lowest potency is after subcutaneous, and the highest after intrathecal or inracerebroventricular administration. We tested the analgesic activity of biphalin in a wide range of doses after intrathecal administration to rats. Doses as low as 0.005 nmol produced significant analgesia. Increasing the dose up to 2 nmol elevated and prolonged antinociception without any evident side effects, indicating that biphalin is an extremely potent opioid after intrathecal application with a wide therapeutic window. The highest dose tested (20 nmol) produced full analgesia and body rigidity lasting 2–3 h. After muscle tone returned to normal, antinociception lasted for several more hours. During these studies we observed a correlation between responses to biphalin and catheter placement. Postmortem verification of catheter placement revealed that in those rats in which high-dose biphalin did not produce analgesia or muscle rigidity, the catheter was positioned incorrectly or the flow of drug solution was obstructed. Therefore, a secondary conclusion is that assessment of transient rigidity after administration of a high dose of biphalin may be used as an easy method to confirm intrathecal placement of the catheter.

Key words:
biphalin, morphine, antinociception, pain, intrathecal