



Nociception in the Hypertensive Rat

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by

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ABSTRACT

The relationship between nociceptive responses, blood pressure and locomotor activity was studied in spontaneously hypertensive (SHR) and normotensive Wistar-Kyoto (WKY) rats. No gender differences were observed and when two strains derived from the SHR were examined, the analgesic trait was linked to the hypertensive (HT) and not the hyperactive (HA) strain.

Administration of the antihypertensive drugs to SHRs showed that the pain responses could be returned to normal in the SHR by treatment with drugs which influence the renin-angiotensin-system (RAS), but not by antihypertensive drugs which work through other mechanisms.

Subcutaneous administration of angiotensin II to WKY rats increased blood pressure and nociceptive thresholds such that they were similar to untreated SHRs. This did not occur when blood pressure was raised with norepinephrine. Icv infusions of angiotensin did not influence nociception and icv angiotensin receptor blockade did not influence blood pressure.

Human hypertensives treated with beta blockers and with blood pressures identical to normotensive controls had a reduced sensitivity to pain. However, those treated with ACE inhibitors had identical pain sensitivity to normotensives which is in concert with the animal data.

Radiotelemetric blood pressure recording was investigated as an improved method in this area of research where the reduction of stress is important. Heart rates and blood pressures were lower in the telemetered animals compared to those tested via the tail-cuff method and the effect of antihypertensive drugs was altered.

In view of the role of opioids in hypertension, pain and consummatory behaviours, alcohol consumption was studied. Alcohol consumption in the WKY was lower than in the SHR and this difference was abolished by captopril treatment. This pattern was shown to alter with the age of the animal.

Overall, the studies showed that the SHR has a decreased sensitivity to nociceptive stimuli which is not directly linked to blood pressure or central angiotensin levels. Peripheral angiotensin, at an unknown site, modulates pain perception in the SHR.

Hypoalgesia in human hypertensives is influenced by ACE inhibitors in a manner similar to the rat model.

Radiotelemetry will be the method of choice for blood pressure monitoring in this area of research.

The SHR may provide a useful model for investigation of the self administration of drugs of abuse.