# Inhibition of the kynurenine pathway in a rat model of cardiac arrest and cardiopulmonary resuscitation.

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Argomento: Trauma e arresto cardiaco

Tryptophan (TRP) catabolism by the kynurenine pathway (KP) is activated following resuscitation from cardiac arrest (CA). However, the relation between KP activation and outcome remains controversial. To explore this issue, we studied the effects of the inhibition of the KP in a rat model of CA and cardiopulmonary resuscitation (CPR) by using the inhibitor of 1 indoleamine 2,3-dioxygenase-1 (IDO_i), which catalyzes the first and limiting step of KP from TRP to kynurenine (KYN).

**Methods**

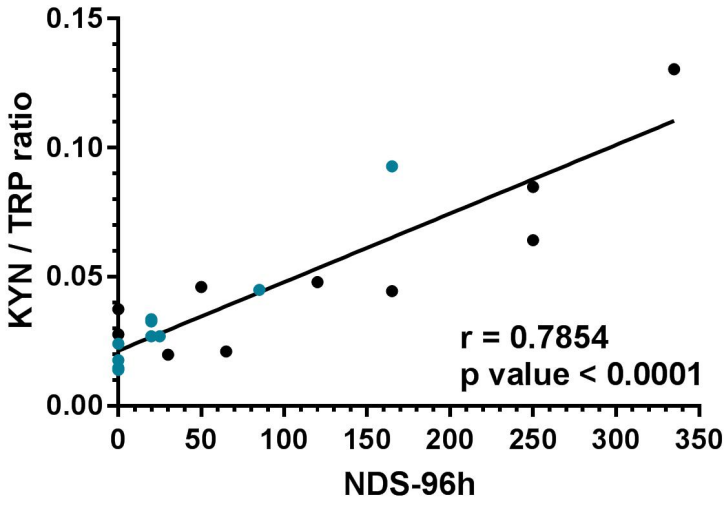
Twenty-six rats were assigned to receive pretreatment with IDO_i or vehicle by *gavage*. Ventricular fibrillation was induced and untreated for 8 minutes. CPR then was performed for 8 minutes. ECG and arterial and right atrial pressures were monitored up to 4 hours after CPR. After resuscitation, 96-hours survival with neurologic recovery was evaluated. The ratio of KYN to TRP in plasma as indicator of KP activation was measured by liquid chromatography and mass spectrometry.

**Results**

More than 80% of the animals were successfully resuscitated and more than 60% survived up to 96 hours in both groups. Animals that received IDO_i had higher coronary perfusion and mean arterial pressure and heart rate compared to animals treated with vehicle ($p < 0.0001$) 10 minutes after resuscitation. Faster neurologic recovery was observed in animals pretreated with IDO_i than in animals treated with vehicle ($p < 0.01$ at 24 h after resuscitation). Ninety- six hours after resuscitation a marked activation of KP assessed as ratio of KYN to TRP in plasma **resulted in more severe neurological impairment ($r=0.8$, $p< 0.0001$).**

**Conclusions**

These findings demonstrated that the inhibition of KP improves hemodynamic and neurologic dysfunction in a rat model of CA and CPR.




Linear regression of Neurological Deficit Score (NDS) at 96 h after resuscitation and plasma kynurenine (KYN) and tryptophan (TRP) ratio.