The combined cardiac effect of the anabolic steroid, nandrolone and cocaine in the rat.

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Recent pharmacologically research shows a significant increase in the use of anabolic-steroids (AS) amongst teenagers and young adults and especially amongst sedentary, young males administering AS for cosmetic reasons. AS are often used in conjunction with psychostimulants. Survey findings suggest significant co-abuse of AS and cocaine. Unfortunately, despite documented evidence that both drugs alone can induce significant cardiovascular effects only very limited basic science research has been conducted into the potential for cardiotoxicity with this drug combination.

Nandrolone has been shown to be the AS of choice amongst many recreational users. Previous work has found heart rate (HR) increased significantly following cocaine HCI (45mg/kg, i.p.) administration in albino Wistar rats (AW) chronically treated with nandrolone compared to the cocaine effect in vehicle treated controls (Phillis et al., 2000). Subsequent studies in this thesis established that this HR effect could not be attributed to an acute effect of the last nandrolone dose prior to cocaine administration. Dose-response relationships to cocaine (0.15-45mg/kg, i.p.) for cardiovascular variables using radionuclide were conducted in freely moving, conscious AW and Sprague-Dawley (SD) rats. These studies indicated that the cardiovascular response to cocaine was not strain dependent. This allowed direct comparisons to be made to literature values for cocaine effects in both strains.

In view of the rather moderate effects of nandrolone observed, the effect of AS pre-treatment on the response to cardiac ischaemia was assessed in order to simulate pre-existing cardiac disease. Nandrolone was administered i.v. at doses reflective of the plasma concentrations possibly achieved by chronic AS users (10-160μg/kg/min). SD rats were subsequently subjected to 15 minutes occlusion of the left anterior descending (LAD) coronary artery and 10 minutes reperfusion. A significant decrease in survival time during ischaemia was noted at the highest nandrolone dose (p<0.001) and significant decreases in the fraction of rats surviving ischaemia (40 & 160μg/kg/min, both p<0.05) compared to control. A significant increase in the Lumbeth arrhythmia score was seen at the 3 highest nandrolone doses (all, p<0.05). A significant increase in the duration of VF during ischaemia was noted for the highest nandrolone dose (160μg/kg/min) compared to the lowest dose (10μg/kg/min). This pro-arrhythmic nandrolone effect could not be attributed to increases in myocardial noradrenaline (NA) by the blockade of extraneuronal uptake, since nandrolone was shown to have too low an inhibiting potency on extraneuronal noradrenaline uptake in isolated perfused rat hearts. The severity of arrhythmia in rats receiving i.v. nandrolone was not increased by cocaine HCI administration (0.5mg/kg/min, i.v) but rather was found to protect against the fatal VF induced by nandrolone alone (40μg/kg/min). In contrast to the acute effect of nandrolone, chronic nandrolone treatment of SD rats for 3, 6 or 9 weeks had no effect on the response to cardiac ischaemia or reperfusion. The basis of the difference between the effects of chronic and acute effects of nandrolone on ischaemia-induced dysrhythmia was not identified. It may relate to the much lower plasma nandrolone concentration achieved with
chronic nandrolone treatment. Alternatively, chronic treatment may result in down-
regulation of the mechanism underlying enhanced arrhythmia after acute dosing.

This is the first study to show a significant and dose dependent increase in the
Lambeth arrhythmia score during cardiac ischaemia in rats administered i.v.
nandrolone. The mechanism of this effect remains unknown. Potential mechanisms
include a CNS effect of nandrolone, an uncoupling of the protective effect of adenosine
during early ischaemia by nandrolone or an increase in pro-arrhythmic endothelin-1
(ET-1). This study suggests that nandrolone abuse in patients with a pre-existing
cardiac condition may precipitate life threatening cardiac arrhythmia.