Effects of propranolol on baroreceptor reflex sensitivity in the conscious spontaneously hypertensive rat (SHR)

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Several authors have suggested that propranolol increases baroreceptor reflex sensitivity (BRS) in normotensive (Pickering, Gribben, Peterson, Cunningham & Sleight, 1972) or hypertensive (Takeshita, Tanaka & Nakamura, 1978) subjects, although others (Simon, Kiowski & Julius, 1977; Krediet & Dunning, 1979) could not confirm these results in hypertensives. We have investigated the acute effects of injections of propranolol on BRS in conscious SHR as well as their progenitor normotensive Wistar Kyoto (WK) controls.

Male SHR and WK (T.N.O. Proefdierenbedrijf, Zeist) weighing 250–300 g were used. Arterial pressure was recorded directly in freely moving conscious animals from a catheter positioned in the left femoral artery exteriorized on the back between the shoulder blades. Intravenous (i.v.) injections were given via a catheter in the right jugular vein. BRS was determined by i.v. injection of phenylephrine (1–10 μg/kg) and plotting systolic peak interval against mean arterial pressure (MAP) according to Smyth, Sleight & Pickering (1969). The slope of the regression line was used as an index for reflex sensitivity if the correlation coefficient was greater than 0.60 and the P value was less than 0.05. After a 1 h period to obtain baseline values for MAP, heart rate (HR) and BRS rats were injected subcutaneously (s.c.) with control saline (0.1 ml 0.9% NaCl) or (±)-propranolol (5 mg/kg).

Propranolol induced a rapid fall in HR in both SHR and WK. Maximal bradycardia was 63 ± 9 b/min (n = 11, $P < 0.001$ when compared with control SHR, n = 7) for SHR and 46 ± 6 b/min (n = 8, $P < 0.001$ when compared with control WK, n = 6). HR had returned to control values after 3–5 hours. Propranolol had a biphasic effect on MAP, first causing a rise and then a longer-lasting fall. The rise lasted 0.5–1 h and reached a maximum of 12 ± 2 mm Hg ($P < 0.01$) in SHR and 9 ± 3 mm Hg ($P < 0.05$) in WK. After 1 h MAP gradually fell, reaching maximal hypotension of 25 ± 5 mm Hg (SHR, $P < 0.01$) and 14 ± 3 mm Hg (WK. $P < 0.01$) at 4 hours.

BRS was significantly lower in SHR when compared to WK both before and after control saline or propranolol injection (Table 1). Propranolol did not influence BRS significantly in SHR or WK when compared to saline-injected control animals. These data do not support earlier suggestions that propranolol-induced increased BRS contributes to the antihypertensive effect of this drug.

References

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Table 1 Baroreceptor reflex sensitivity (ms mm Hg^{-1}) in conscious SHR and WK before and after s.c. injection of control saline (S) or propranolol (P, 5 mg/kg)

			Time after injection (h)	
	n	*Before*	*0.5–1*	*2–2.5*
SHR S	7	0.31 ± 0.04*	0.38 ± 0.09*	0.55 ± 0.14*
SHR P	11	0.41 ± 0.04*	0.37 ± 0.05**	0.37 ± 0.05**
WK S	6	0.62 ± 0.10	0.74 ± 0.13	0.97 ± 0.13
WK P	8	0.67 ± 0.09	0.71 ± 0.10	1.00 ± 0.20

Significances in the differences between SHR and corresponding WK: *$P < 0.05$; **$P < 0.01$. There was no statistically significant difference between S and P injected SHR or WK.
All values are presented as means ± s.e. mean.