Platelet α_2 -adrenoceptor binding does not predict brain α_2 -adrenoceptor function

The recent review on platelet α_2 -adrenoceptors by Hamilton & Reid (1986) concluded that these receptors may not be comparable with those in brain. Although platelet receptor binding has been widely used as a possible index of central receptor status the validity of the model has not been tested. In the course of studies of central α_2 -adrenoceptor function as revealed by the use of a clonidine challenge test we have been able to measure simultaneously platelet α_2 -adrenoceptor binding using [3 H]-yohimbine as a ligand. In neither controls nor panic disorder patients did central indices of α_2 -adrenoceptor function correlate with platelet binding affinity or capacity.

Platelet binding studies were carried out using [3 H]-yohimbine (NEN) over a concentration range 0.1 to 5 nM. Nonspecific binding was determined by displacement with 5 μ M phentolamine (for full details see Boon *et al.*, 1983). Clonidine challenge testing was performed at 10.00 h ($t = 0$ min) after an overnight fast. Subjects were semi-recumbent throughout and had blood pressure and pulse rate measured by an automatic sphygmomanometer (Dinamap) every 15 min from $t = -60$ to 120 min. A 21 g butterfly was inserted into an antecubital vein at $t = -60$ min and kept open with heparin/saline. Blood samples for plasma growth hormone concentrations were taken every 15 min. Clonidine responses were

taken as peak response-baseline where baseline was determined as the mean of the three values from -30 to 0 min. Correlations between platelet parameters, basal values and clonidine responses are shown in Table 1.

It can be seen that in neither group nor in the total population did either $B_{\max}$ or K_d values for platelet α_2 -adrenoceptors correlate with either basal levels or clonidine response. These findings call into question the validity of using platelet α_2 -adrenoceptor binding values as estimates of central α_2 -adrenoceptor-function or responsiveness. However, it is possible that tests of platelet α_2 -adrenoceptor function (e.g., clonidine-induced platelet shape change) may correlate better with central responses. Furthermore, it is still possible that pharmacological interventions may affect peripheral and central receptors in a parallel fashion so peripheral receptor binding studies may still have some value in psychopharmacological research.

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Table 1

	Platelet [³ H]-Yohimbine <i>B</i> _{max}	<i>K</i> _d (nM)	Systolic BP (mm Hg)		Diastolic BP		Heart rate (beats min ⁻¹)		Growth hormone peak (miu l ⁻¹)
			Basal	Peak fall	Basal	Peak fall	Basal	Peak fall	
Patients (<i>n</i> = 8) Mean	49	3.1	123	26	78	20	68	10	13 (5)
s.e. mean	4.7	0.36	6.8	1.6	3.1	1.6	1.7	1.5	3.6
Correlations	<i>B</i> _{max}	0.15	0.00	0.17	0.33	-0.17	0.28	-0.25	0.43
	<i>K</i> _d	—	0.40	0.46	0.52	-0.15	-0.20	-0.12	0.80
Controls (<i>n</i> = 9) Mean	53	4.9	123	22	74	17	63	8	20 (8)
s.e. mean	3.8	0.56	6.3	4.3	6.3	7.5	2.6	1.2	4.6
Correlations	<i>B</i> _{max}	-0.16	0.43	-0.07	-0.14	-0.21	0.12	-0.30	-0.09
	<i>K</i> _d	—	0.15	-0.32	-0.14	-0.27	0.01	0.37	-0.44
All (<i>n</i> = 17) Mean	51	4.0	123	24	76	18	65	9	17 (13)
s.e. mean	2.9	0.40	3.3	1.2	1.8	1.5	1.7	0.9	2.9
Correlations	<i>B</i> _{max}	0.08	0.10	-0.05	-0.04	-0.22	0.08	-0.31	-0.14
	<i>K</i> _d	—	0.19	-0.29	-0.06	-0.34	-0.26	0.02	-0.04

*B*_{max} values are fmol/10⁹ platelets. Peak growth hormone levels were only calculated for subjects with basal levels of < 5 miu l⁻¹ (*n*). None of the correlations reach significance of *P* < 0.1.

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