

CNV and Dopamine Receptor Reactivity: Correlations with the Apomorphine Test

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Following animal pharmacological studies, Marczyński (1978) postulated that slow negative shifts may be mediated and modulated by joint action of cholinergic and dopaminergic systems. We have tested this hypothesis; in the following study we have examined in humans the effects of a dopamine agonist (apomorphine) on the CNV and PINV.

Twenty normal male subjects and 28 hospitalised psychiatric in-patients (14 male, 14 female) were tested. The patients, as diagnosed using the research diagnostic criteria of Spitzer et al. (1978), included 17 depressive, 2 neurotic, 7 schizophrenic and 2 manic individuals. Mean age of the patients was 42.5 years and of the controls 24.4 years. All were within 25% of normal body weight and were not suffering from somatic diseases or endocrine disorders. All had been free of drugs for at least 2 weeks. The endocrine test and the SP recording were conducted on different days but within the same week.

The experimental paradigm consisted of a warning stimulus, S1 (1000 Hz, 50 msec duration tone), followed 1 sec later by an imperative stimulus S2 (18 c/sec flashing light) terminated by a button press. Averages of 48 artefact-free trials were recorded with eyes closed from a Cz-A1 derivation (TC = 10 sec; high frequency cut-off = 75 Hz). Measures were made of CNV amplitude (M2), CNV resolution (M5) and PINV amplitude (M2-M5) (see Fig. 1). This last measure was only included where PINV amplitude $\geq -5 \mu\text{V}$.

The neuroendocrine test was conducted during bed-rest of the subjects, after an overnight fast. Three baseline blood samples were collected at 20 min intervals prior to the subcutaneous injection of 0.5 mg apomorphine HCl. Apomorphine, which is a specific agonist of dopamine (DA) receptors, provokes a significant increase in plasma growth hormone (GH) release. The amount released closely relates to DA receptor sensitivity (provided that the endocrine glands and the pituitary are undamaged). Six further blood samples were collected at 20 min intervals and a radioimmunoassay of plasma GH response to apomorphine made. In analysing results, the maximum GH value after drug administration was used.

CNV amplitude, CNV resolution and GH peak were all significantly larger in controls than in patients (CNV = $-22.9 \mu\text{V} \pm 9$ vs. $-14.8 \mu\text{V} \pm 6$). Resolution = $20 \mu\text{V} \pm 10$ vs. $8.8 \mu\text{V} \pm 8$; GH peak = $28.5 \text{ ng/l} \pm 10$ vs. $9.6 \text{ ng/l} \pm 9$). This last result reflects a high proportion of patients who showed a 'blunted response' to apomorphine

TABLE I

SP AMPLITUDE/GH RESPONSE CORRELATION COEFFICIENTS

	Peak GH response to apomorphine (all subjects)	
	Controls (N = 20)	Patients (N = 28)
CNV amplitude (absolute value) (M2)	-0.10	0.56**
CNV resolution (M5)	-0.60**	0.46*
	Peak GH response to apomorphine (subjects with PINV (M2 - M5 \geq 5 μ V))	
	Controls (N = 7)	Patients (N = 22)
PINV amplitude	0.83*	-0.04

* $P \leq 0.05$; ** $P \leq 0.01$.

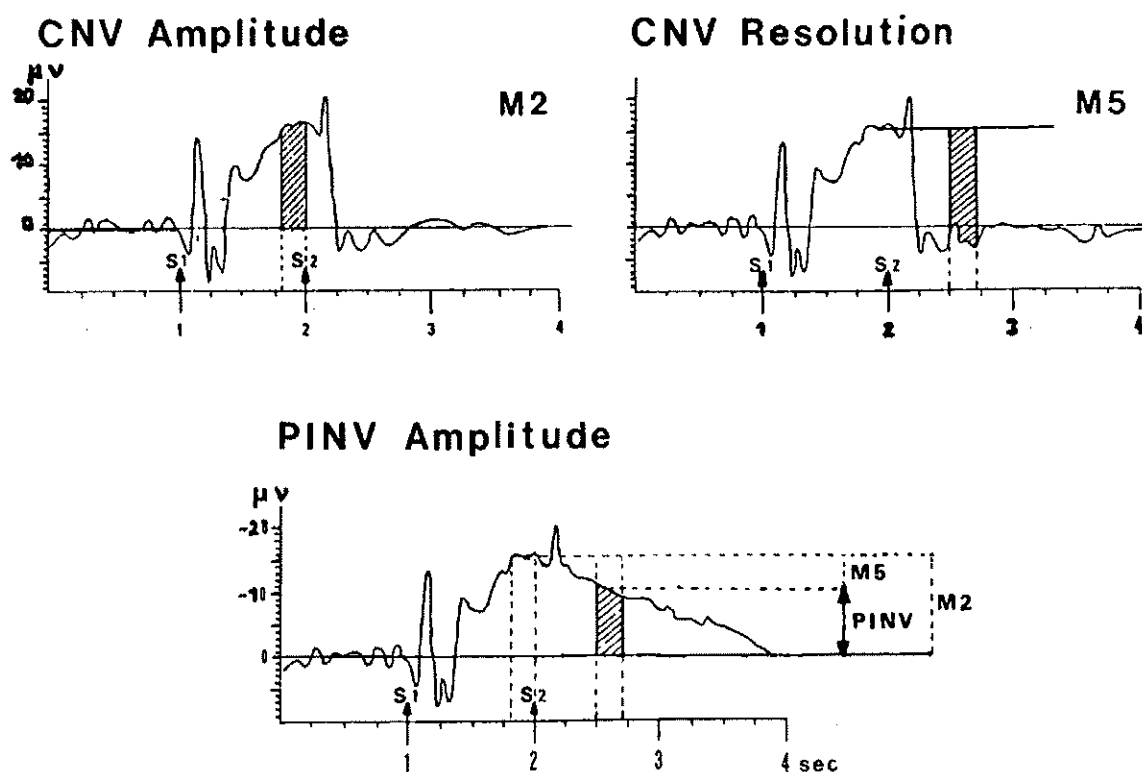


Fig. 1. Criteria used for SP measurement. Each measure (striped area) was a mean voltage over 200 msec and was made on an average of 48 trials. Measures were with respect to a baseline which was, for CNV amplitude (M2) and PINV, the mean voltage level for 1 sec preceding S1. For CNV resolution (M5) baseline was taken as the M2 level.

(14 patients out of 28 had a GH release ≤ 5 ng/l vs. none in controls). There was no difference between the groups in PINV amplitude. However, PINV was present in 22 patients out of 28, but in only 7 controls out of 20.

The correlations between SP amplitude measures and GH peak response after apomorphine injection are presented in Table I.

The results provide general support for Marczyński's model (1978) and are consistent with previous findings of our own and other groups (Thompson et al. 1978; Timsit-Berthier and Timsit 1981; Agren et al. 1983; Timsit-Berthier et al. 1983). Results by Marissiaux (1983) suggest that the absence of significant correlations with CNV amplitude (M2) in controls may be associated with the relative simplicity of our task and hence with alertness.

The negative correlation between CNV resolution and GH response in controls is consistent with Marczyński's model. However, the positive correlation in patients appears at first sight anomalous, but may be due to a high correlation ($P < 0.01$) between the M2 and M5 measures in patients only.

The positive correlation between PINV amplitude and GH response in controls is also consistent with Marczyński's model. The absence of such a correlation in patients may well reflect the fact that the PINV is, as suggested by Rockstroh et al. (1982), not a unitary phenomenon.

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