be made. Obviously, the need is not for many more tests of weak statistical power, but rather for a few tests, each with sufficient power to distinguish between no relationship and one of small, yet realistic, effect.

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HANDFORD REPLIES—Of course, I agree with what I take to be Eanes' main point: that many more data are needed to clarify the relationship between heterozygosity and morphological variability. Indeed, my modest contribution[1] closed with an implied request that workers (and there must be many) in possession of data sets containing the necessary information (for many taxa and based on larger samples) do the necessary sums and communicate their results. In that note[1] I also made the obvious point that lack of a significant result does not demonstrate much on its own (even though nonsignificance is also evident from the sign test[2] used by Mitton[3] in the interpretation of his results).

Regarding statistical considerations, Eanes is correct about necessary magnitudes of effects when using the F ratio. Comment has been made about the use of F ratios[1], and will not be repeated. However, I may compare my data with those of Mitton[3]. If his three localities are considered separately, his samples are comparable, both biologically and numerically, with mine[1]. In all three samples, Mitton's data yield a result which is significant by the sign test; mine do not. The sign test is, of course, independent of the magnitude of the differences in variance and of the size of the sample used in computing the variances. Given that there are some *a priori* reasons for expecting that heterozygosity may be of different biological significance among homoiotherms and poikilotherms[1], I felt my results worth communicating.

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Nigral-derived muscimol circling—ipsiversive, contraversive or controversial?

REAVILL *ET AL.*'S[1] attempted reconciliation of the dispute between Waddington[2] and Martin and Haubrich[3] raises some important issues. Briefly, the controversy centres on whether disinhibition of dopamine (DA) neurones in the substantia nigra zona compacta (SNC) contributes to the contraversive circling produced by injecting a γ-aminobutyric acid (GABA) agonist into one nigra, as this has been variously reported as being unaffected[4–6], attenuated[7–11] or even exaggerated[12] by measures which reduce nigrostriatal dopaminergic activity. We, too, firmly believe that the precise location of injection of the drug within the nigra holds the key to these disparities. Thus when muscimol (40 ng) is microinjected discretely (in 0.2 μl over 3 min) into the central region of the zonal reticulata (SNR) at all rostrocaudal levels, it evokes rapid contraversive circling which is significantly (though never completely) inhibited by pretreating the animals with haloperidol (0.1 mg per kg) or pimozide (0.25 mg per kg), intraperitoneally, or 6-hydroxydopamine (4 μg into the SNC or medial forebrain bundle). That is, it is partially DA dependent (see refs 7–11). On the other hand, injecting the agonist into ventral or lateral aspects of the SNR, irrespective of rostrocaudal coordinates, again stimulates rats to move in contralateral circles, but in this case the rate of rotation is regularly slower and is unaffected by the above treatments. In other words it is DA independent (see refs 4–6). Consequently we believe it is the disposition of muscimol in a mediolateral or dorsoventral direction within the reticulata, and not along the rostrocaudal plane of the nigra as a whole as Reavill *et al.*[1] surmized, that determines whether the resultant circling behaviour involves dopaminergic activation.

The latter could occur by muscimol suppressing the activity of inhibitory interneurones, or of nigrofugal fibres that send collaterals to the SNC. Our suggestions are in keeping with the known topography[13] and electrophysiology[14] of this area of the nigra. The assertion that Martin and Haubrich could only have achieved striatal DA release and contraversive circling with muscimol from the caudal nigra is therefore unfounded. Furthermore, our arbitray division of the SNR into two longitudinal bands from which different types of contraversive circling may be elicited should not be confused with the separate, weaker depressant action of muscimol on the compacta DA neurones directly[14]. This will give rise to ipsiversive asymmetry that is totally abolished by neuroleptics[5]. We would agree that this type of ipsiversive behaviour is most readily evoked from the rostral SNC. In fact, we have never observed ipsilaterally directed movements with muscimol from the caudal SNC. Thus a behavioural distinction can be made between GABAergic drugs acting on the SNC (rostrally) or the SNR (caudally), but this does not account for the above-mentioned discrepancies .

To dismiss as 'redundant' the significance of striatal DA release in the mechanism of nigral GABA-mediated circling could be premature, as this presupposes that all such behavioural influences are necessarily channelled back through the SNR, which has yet to be ascertained. This might be true for rotational behaviour generated artificially from the SNR by an agonist as powerful as muscimol, even in 'thalamic' rats[15], but we cannot help wondering if animals bearing chronic cerebral damage can validly be used to predict the importance of events that take place in the whole animal. The elegant experiments of Grace and Bunney[14] favour the opposite view by showing that the firing rates of compacta DA cells are reciprocally related to the activity of non-dopaminergic GABA-receptive cells in the neighbouring SNR. The focal ejections of GABA which raised DA cell firing severalfold were made into the central region of the SNR, the area most densely innervated by striatonigral GABA terminals[16]. Cells here are exquisitely sensitive to iontophoretic GABA and it is from this region that we obtained contraversive turning to muscimol which was strongly dependent on dopaminergic mechanisms. There is every reason to suppose, therefore, that these GABA–DA interactions are far from inconsequential in normal physiological conditions.

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