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REPLY

GBG, Hormones, Genes, and Anomalous Dominance: A Reply to Commentaries

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The present issue includes three further commentaries on our assessment of the Geschwind-Behan-Galaburda (GBG) model of cerebral lateralization (Bryden, McManus, & Bulman-Fleming, 1994). Like the commentaries accompanying our original article, these papers sometimes criticize various aspects of our evaluation and very frequently add new information about those areas in which those commentators are more fluent that we are. In writing the original paper we had hoped to stimulate debate and interest in a critical assessment of the GBG hypothesis, and we are delighted to have elicited commentaries from such a wide variety of individuals. It is evident that an assessment of GBG will require the integration of information across many disciplines, and an interchange such as is appearing here will help to stimulate such integration.

In the current commentaries, both Berenbaum and Denburg, and Gilger and Pennington offer more detailed assessments of particular areas than we could provide. Berenbaum and Denburg review the evidence for prenatal effects of testosterone and indicate several places in which testosterone effects are different from those predicted by the GBG model. So far as we are aware, the GBG model was built on the basis of speculations, rather than on empirical data, concerning the role of fetal testoster-

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one. If one examines Fig. 1 of the target article (Bryden, McManus, & Bulman-Fleming, 1994), where we diagram the GBG model as we understand it, fetal testosterone (T) is an unobserved intervening variable; the observations made by GBG and those we have examined in our assessment of the model are correlations between the numerous variables along the right-hand side of the figure. Logically, it is possible that it is some factor ("X") other than T that produces all of these effects. We agree with Berenbaum and Denburg that studies such as that of Grimshaw (1993; see also Grimshaw, Bryden, & Finegan, 1995) lead to findings incompatible with the notion that fetal T drives lateralization in the way GBG suggest, but this only serves to replace T with X and does not solve the problem of how to account for the correlations between observable variables that we have found to be robust.

Gilger and Pennington have expanded on their views regarding the genetics of developmental dyslexia (Gilger, Pennington, Green, Smith, & Smith, 1992). They argue that the data are best explained by a "subtype" approach, in which a portion of those individuals carry a gene for, say, reading disability (RD) that is also responsible for (or closely linked to a gene for) some form of immune dysfunction (ID). A fundamentally similar point, though perhaps not as elegantly expressed, was made by Kaplan and Crawford (1994), in the earlier round of commentaries. We would agree with the points made by Gilger and Pennington, although we would also point out the fact that even though there may be genetic linkages between certain immune disorders and RD, this does not constitute a verification of the GBG model, since that model explicitly also requires associations between RD, ID, and lateralization. The association between RD and ID, although extremely interesting and needing explanation, cannot alone be seen as support for the GBG model. Indeed, if the link between RD and ID is a result of a quantitative trait locus for dyslexia in the same chromosomal region as that coding for HLA subtypes (Cardon, Smith, Fulker, Kimberling, Pennington, & DeFries, 1994), then it may well be that handedness is specifically *excluded* from the three-way association. However, the GBG model has stimulated research into such issues and therefore has had a beneficial effect.

The preliminary data reported by Gilger and Pennington on antinuclear antibodies (ANA) are perhaps open to a different interpretation than the one they place upon them. They find that 20.5% of RD persons and 16.5% of non-RD relatives of RD persons show ANA, whereas only 5% of the general population show ANA. The nonsignificant difference between RD and non-RD members of a family, along with the absence of evidence of co-segregation, leads Gilger and Pennington to conclude that there is no genetic link between RD and ANA. This, however, ignores the most significant feature of the data that ANA are much more common in families with RD than in controls. Therefore, at the *family level* there is an

association between RD and ANA even though this is not due to genetic association at the *individual level*. The conclusion must be that some aspect of the common family environment is responsible for the association. One possibility is that, as Geschwind suggested, the fetus may have an anomalous endocrine environment provided by the mother. If that environment were under maternal genetic control, and if it resulted in RD and ANA in the offspring, then there would be an association between RD and ANA between families, but with no evidence of genetic co-segregation, since the characteristics are being transmitted maternally rather than through the individual's own genotype. We emphasize that such a hypothesis is pure speculation, but it does encourage us to think in terms of broader hypotheses than conventional genes acting in a traditional way—and as such is at least in the spirit of Geschwind's theorizing.

Van Strien suggests that anomalous dominance (AD) is not as central to the GBG model as would would have it. We believe that he is mistaken in this assertion, remembering that the Geschwind–Galaburda book was entitled "Cerebral Lateralization." Furthermore, we would have to disagree with some of his other points. Whereas Van Strien sees Geschwind's ideas on handedness as being "essentially the same" as those of Annett (1985), Annett's (1994) own commentary on our paper indicates her own belief that Geschwind did not properly understand her model. Probably the key problem with Van Strien's formulation is that AD no longer has any meaning, whereas GBG quite clearly feel that it is a simplifying concept which provides additional value over and above that provided by the concepts of handedness, language lateralization, etc. That is where we take issue with it: if AD is only handedness by another name, as Van Strien suggests, then it should be called handedness and not confused by a different name; if it has added value, as proposed by GBG, then that added value should also be demonstrated. Neuropsychology is not helped by the addition of yet another technical term that is poorly defined; perhaps we should think back to the earlier concept of "latent left-handedness" and remember the problems that it produced (Harris, 1988; McManus, 1983). We should also point out that AD for right hemisphere functions is not rare, as Van Strien indicates, but quite common (cf., Bryden, Hécaen, & DeAgostini, 1983).

Van Strien takes exception to our citation of a poor correlation between handedness and the right-ear advantage in dichotic listening as being grounds for rejecting handedness alone as a good predictor of language lateralization, suggesting that the alternative view that dichotic listening does not provide a good measure of language lateralization is at least as valid. Zatorre's (1989) study of dichotic performance in patients whose language lateralization had been assessed by sodium amytal, in fact, indicates a very strong relation between dichotic laterality and language lateralization. Even the Rasmussen and Milner (1977) data yield a ϕ coefficient

of only .31 for the relation between handedness and language lateralization, hardly strong support for the position that handedness is a better measure of brain lateralization than dichotic listening.

Ultimately, we feel that Van Strien misses the point. While it would be nice to carry out good MRI studies, the ultimate point is one of linking brain anatomy and physiology to *behavior*, and one therefore needs good behavioral measures. Certainly none of us would wish to deny that there is a neural substrate for functional asymmetries, as Van Strien suggests, but we remain to be convinced that the GBG model tells us anything about that substrate. It may be that the new imaging studies will provide evidence in favor of the GBG model, but that is speculation. If they are to provide such evidence, though, it is going to have to be in the context of a host of negative associations which have already been demonstrated.

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