IAIN AND COGNITION 26, 312–326 (1994)

REPLY

GBG, BMB, R & L, X & Y . . . Reply to Commentaries

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Our commentators make a variety of interesting and useful points concerning our assessment of the Geschwind–Behan–Galaburda (GBG) model of cerebral lateralization, and we are pleased to have drawn out much interest. The major points in these commentaries seem to fall into three categories which are not mutually exclusive: a discussion of the nature of the GBG theory and which parts of it are viable, concerns with measurement and statistical issues, and complaints that we have reviewed certain areas inadequately, most particularly those pertaining to dyslexia and the effects of testosterone. Let us consider these points in turn.

BABIES AND BATHWATER

Given the broad explanatory scope and theoretical range of the GBG grand unification theory" (Hampson & Moffat; also see Segalowitz, Berge, Lawson, & Brown) it is hardly surprising that the commentaries show a wide range of views on quite *what* the GBG theory is and quite *how* one can assess such a theory.

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0278-2626/94 $6.00

Our commentators differ widely in their overall perceptions of the GBG model; "An imaginative theory based on a combination of astute empirical sleuthing and creativity that has revealed some surprising relationships . . ." (Halpern) and "the breadth of biologic cross-referencing, abundance of extrapolation, and speculative (not to mention criticizable data) from which the GBG model was enthusiastically born" (Weinstein, Lobocki, & Pieper) can be contrasted with "arguably the most massive (and untidy) theory in the history of neuropsychology" (Previc), and "tenuous links between handedness, sex differences, and developmental language disorders . . . used as solid foundations for a complex net of speculative interpretation" (Annett).

A theory of what? Commentators differ widely on what the GBG theory is a theory *of*. Although we (and, it must be said, many of the commentators) saw the theory as focused on handedness and lateralization, Halpern sees the theory as "essentially a theory of sex-related differences," and Kaplan and Crawford argue that the relationship between immune disorders and language disorders is the central area of interest of the theory, criticizing those who see "anomalous dominance as the absolute core of the GBG model." Here we can only say in reply that Geschwind and his colleagues themselves seemed to see lateralization as the core of the theory: the 1987 book is entitled *Cerebral Lateralization*, as also are the three 1985 papers, the 1982 paper has handedness in its title, and in the 1987 book, 12 of the 19 chapter titles include the term asymmetry or lateralization or dominance. In answer to Kaplan and Crawford's question of "Who cares?" about handedness and lateralization, we feel sure that Geschwind did, as indeed he had done many years earlier in his important 1968 paper with Levitsky on cerebral lateralization.

Testing the GBG model. The testing of scientific models is not easy. Certainly we would not subscribe to the crude Popperian view that a single empirical failure is sufficient to damn a theory. Theories can survive without data, or even in the face of conflicting data, if they are good theories (Weinberg, 1993). Philosophers of science such as Lakatos have shown how embryonic scientific theories often require commitment and support, particularly at their more vulnerable margins, where they may not be fully explored and explicated, if they are to grow into mature, robust theories. That requirement is particularly strong if the theories are revolutionary, in Kuhn's sense, and therefore require a substantial rethinking of many current assumptions. We believe, probably along with Hellige and Previc and others, that the GBG theory *is* revolutionary; for the first time, a broad conceptual framework was provided which was truly biological and developmental and tied together many previously unrelated phenomena. It is therefore essential that the conceptual baby is not thrown out with the empirical bath water (Hellige). Nevertheless, if theories are to be scientific and testable then there must be some point

at which they make specific predictions that are empirically testable, and on which the theory depends. To us, one such point in the GBG model is the association between handedness and immune disorders. Kaplan and Crawford criticize us for our emphasis upon effects that are *surprising*, suggesting that such an approach is not logical. We argue the contrary; prior to GBG there was not, to our knowledge, a single paper in the scientific literature that asked whether left-handedness was associated with immune disorders. Geschwind and Behan (1982) changed that immediately and decisively. We believe that everyone (probably including Geschwind and Behan) found the association surprising, and that was precisely why it attracted immediate attention everywhere; the observation was novel, it was testable, and it was inexplicable using existing theories. Not surprisingly, therefore, it was the focus of many studies. Although it could be argued that even if the GBG theory were true, testing for associations between handedness and immune disorders would be a long shot and therefore not a powerful test of the theory (Halpern), it must be remembered that it was Geschwind and his colleagues themselves who first provided such empirical evidence *for* the theory; a failure to replicate must therefore throw doubt on the central tenet of the theory and, as Segalowitz et al. point out, raise questions as to the precise origins of Geschwind and Behan's own data. Finally, a clear distinction must be made between predictions from the GBG theory and from the data upon which the GBG theory was itself predicated; it may be, as Halpern suggests, that, "As predicted by the GBG model, males have a higher rate of left-handedness, superior visuo-spatial skills, much higher incidence of dyslexia and stuttering, and sex-differentiated pattern of immune disorders," but these phenomena were well known long before the GBG theory was formulated and were among the phenomena that Geschwind and his colleagues wanted to explain with their theory. But in no sense does that mean they are predictions *from* the theory.

So what is left? Several commentators rightly stress that just because some of the specific central tenets of the GBG theory have been removed it does not mean that the theory is now dead. These commentators emphasize that GBG's principal conceptual innovation, of accepting the possibility that individual neuropsychological differences result from differences in the biological, hormonal, and developmental environment in which brains arise, is still valid and legitimate (Forget & Cohen; Hampson & Moffat; Hellige; Hugdahl; Kaplan & Crawford) and requires a broader conception than a simple emphasis upon testosterone (Previc; Schachter). We accept this entirely and believe that GBG have helpfully broadened the ways in which neuropsychologists approach their problems and have extended the range of conditions that are considered together. That is useful and good. But it still seems to us that *some* of the details of the specific model proposed by GBG (particularly of testoster-

one influencing anomalous dominance and immune disorders) need not *necessarily* be part of that broader conception. At the same time, there are some suggestive and interesting data concerning handedness and allergies, (e.g. Weinstein et al.) and immune disorders and dyslexia (e.g. Kaplan & Crawford). It may very well be that a clear picture has not emerged because we have not used physiologically reasonable distinctions among immune disorders (St.-Marseille & Braun), and it may be critical to develop a more meaningful typology of dyslexia (Friedmann & Grodzinsky).

MEASUREMENT ISSUES

In order to carry out our analyses, it was necessary to accept particular definitions of variables such as handedness, immune disorder, and dyslexia. Many of our commentators have criticized our choice of measures.

Thus, Annett; Coren; Halpern; Porac; and Schachter all comment on the way in which handedness was determined for the purposes of our meta-analysis. The various studies relating handedness to immune disorder use a wide variety of different instruments for assessing handedness. In order to bring together the data from these studies, we needed to find a common ground, and we chose that which divided the sample into left-handers and right-handers. With relatively few exceptions, such a dividing point is constant across methods of measurement (Coren, 1993; Tapley & Bryden, 1983) and, as we indicated, carries less conceptual baggage. The criterion also corresponds most closely to the everyday usage of "right-handed" and "left-handed" and is also the criterion that is most frequently used in the scientific literature. Although we might agree that some standard method of measuring handedness with more categories might be desirable, the fact remains that different researchers have used different measures. Alternative criteria are simply not practical. Dividing people into "consistent right-handers" and "nonright-handers" (Annett; Coren; Halpern) becomes impractical because the likelihood of finding some sign of inconsistency increases with the number of questions asked (Bishop, 1990a), and therefore one cannot make comparisons across studies that employed questionnaires differing in structure. Likewise, a cutoff such as an Edinburgh Handedness Inventory score of +70 (Schachter) cannot be matched to a comparable score on any other test. More critically, any method that dichotomizes the handedness distribution at a point other than the left/right separation hopelessly confounds degree and direction effects. In the mouse, degree and direction are genetically separable effects (Collins, 1985), and Witelson (1992) has recently suggested that the size of the corpus callosum in humans may be related to the degree of hand preference rather than to the direction.

We illustrate some of these phenomena in Table 1, where we have

TABLE 1
Effects of Various Relations between Handedness and Disease

(a) Linear effect

	Strong L	Weak L	Weak R	Strong R	Total
With disease	10	8	48	40	106
Without dis.	40	42	352	460	894
Total	50	50	400	500	1000
% with dis.	20	16	12	8	

Odds of having disease in left-handers $= \frac{18}{82} = .220$

Odds of having disease in right-handers $= \frac{88}{812} = .108$

Odds ratio: $\frac{.220}{.108} = 2.03$

Natural log of the odds ratio (LOR): .706; $z = \frac{\text{LOR}}{\text{std. error of LOR}}$

$$z = \frac{.706}{\sqrt{\frac{1}{18} + \frac{1}{82} + \frac{1}{88} + \frac{1}{812}}} = 2.49$$

(b) Threshold effect in RH

	Strong L	Weak L	Weak R	Strong R	Total
/ith disease	10	10	80	40	140
/ithout dis.	40	40	320	460	860
otal	50	50	400	500	1000
) with dis.	20	20	20	8	

dds of having disease in left-handers $= \frac{20}{80} = .250$

)dds of having disease in right-handers $= \frac{120}{780} = .154$

dds ratio: $\frac{.250}{.154} = 1.63$;

OR: 0.486; $z = \frac{.486}{.268} = 1.81$

(c) Threshold effect in LH

	Strong L	Weak L	Weak R	Strong R	Total
/ith disease	10	4	32	40	86
/ithout dis.	40	46	368	460	914
Total	50	50	400	500	1000
% with dis.	20	8	8	8	

Odds of having disease in left-handers $= \frac{14}{86} = .163$

TABLE 1—*Continued*

(c) Threshold effect in LH—*continued*

Odds of having disease in right-handers $= \frac{72}{828} = .087$

Odds ratio: $\frac{.163}{.087} = 1.87$;

OR: 0.628; $z = \frac{.628}{.313} = 2.00$

(d) Degree effect

	Strong L	Weak L	Weak R	Strong R	Total
With disease	4	10	80	40	134
Without dis.	46	40	320	460	866
Total	50	50	400	900	1000
% with dis.	8	20	20	8	

Odds of having disease in left-handers $= \frac{14}{86} = .163$

Odds of having disease in right-handers $= \frac{120}{780} = .154$

Odds ratio: $\frac{.163}{.154} = 1.06$

LOR: .058; $z = \frac{.058}{.304} = .19$

computed odds ratios for four distributions, one in which the incidence of a disorder increases monotonically as one moves away from strong right-handedness (Table 1a), a "threshold" model in which the disease incidence is 2.5 times higher in all nonconsistent right-handers than it is in strong right-handers (Table 1b); a second threshold model in which it is strong left-handers who are different from other groups (Table 1c); and a degree model, in which the incidence in weakly-handed individuals is 2.5 times that in strongly-handed ones (Table 1d). The standard error of the natural logarithm of the odds ratio is given by the square root of the sum of the reciprocals of the four frequencies entered, thus a standard z score can be evaluated for significance (see Table 1a for the complete calculations). In each of the first three cases, when the dichotomization is at the zero point (where we have placed it in our meta-analysis), the z score is significant (albeit one-tailed for the second case). In contrast, a degree effect does not lead to a z score that even remotely approaches significance. We should also note that these calculations, based on hypothetical samples of 1000 individuals, reinforce the point of Segalowitz et al. concerning sample size.

Halpern also implies that our analysis allows low-power studies to cancel the effects of studies with larger samples, and is concerned that very different results would be expected from samples drawn from allergy clinics, left-handers' shops, and undergraduate courses. Some of her statements appear to be based on a misunderstanding of the properties of the logistic regression we carried out. Essentially, logistic regression (which can be regarded as a subset of loglinear modeling in which one variable, in this case handedness, can be treated as the dependent variable) treats the data on a case by case basis, so that every *individual subject* in the analysis is weighted equally; thus, a small study cannot "cancel" a large one. Furthermore, it operates on odds ratios, so that different sampling techniques resulting in very different marginal proportions have no effect upon the measure of association, the odds ratio. Suppose, as an example, that the likelihood of disease is about 2.4 times higher in left-handers than it is in right-handers in the general population, and that the incidence of left-handedness is 10% and that of the disease is 5%. Then, in a sample of 1000 randomly selected individuals, the distribution will be that of Table 2a; if we select equal numbers of individuals with and without the disease, then Table 2b obtains; if we select equal numbers of left- and right-handers, then Table 2c obtains. Although the *entries* change, the odds ratio does not (the small differences are a result of requiring the table entries to be integers, as Table 2d shows). Because, as mentioned above, the standard error of the log odds ratio is given by the square root of the sum of the reciprocals of the four frequencies entered, the only difference between the various sampling procedures lies in the standard error of the odds ratio. As Halpern correctly points out, this will be most affected by small entries (which have the largest reciprocals). It is worth noting that this makes the population sample the weakest way of assessing the relation of handedness and disease, because three of the four cell frequencies will tend to be small.

Many of the issues discussed above were elegantly dealt with in the commentary by Segalowitz et al., who stressed the enormity of the implicit population sample size that would be needed in order to replicate the original Geschwind and Behan (1982) findings. Our Table 2 (in the present article) shows that it is much more parsimonious to select subjects for handedness or to compare patient and control samples than it is to run a full study on an unselected population. Furthermore, the comments that Segalowitz et al. make concerning differences between London and Glasgow are also germane to virtually all studies involving patient and control samples. It is very difficult to ensure that the two groups are matched on relevant demographic variables. In contrast, selecting left-handers and then sampling right-handers from the same population (as is often done in studies with undergraduate students) creates fewer problems when it comes to testing the immune/AD association.

Some appreciation of the utility of our method of analysis using odds ratios and examining the case by study interaction for each of the diseases (heterogeneity) can be obtained from an examination of our original Table 5 (in the target article). Here, "thyroid disorders" shows an odds ratio of 1.533 and yet fails to reach significance. Because there is not significant heterogeneity, the four studies involved obtained similar effect sizes but the effect failed to reach significance because of the small sample sizes involved. On the other hand, "eczema" has an odds ratio of .875 (likelihood of disease 1.143 times higher in right-handers than in left-handers, a value larger than that for allergies, which was significant) which fails to reach significance because of heterogeneity among studies, suggesting that there may be some major problems in the determination of those who have or do not have the disorder.

To the extent that there is a linear relation between disease incidence and handedness treated as a continuous variable, then dichotomizing the handedness distribution will not conceal any robust effect. A few calculations on the data Coren presents concerning the incidence of allergies reveal that allergies are reported in 64% of those we would classify as left-handed, 77% of those who are inconsistently right-handed, and only 6% of those who are right-handed on all of Coren's questions. Such a curvilinear relation suggests that it is poor lateralization, not nonright-handedness, that is important.

Others (Coren; Halpern; Kaplan & Crawford; Weinstein et al.) comment on the problems of measuring immune disorder and particularly of the dangers of relying on self-report of medical problems; indeed, a recent population study of allergies suggests that about 70–80% of individuals who claim to have allergies do not demonstrate them on formal testing (Young, Stoneham, Petruckevitch, Barton, & Rona, 1994). Although there are certainly problems here, the commentary authors perhaps miss one of the major points about meta-analysis. Just as we test more than one subject in our experiments to control for the noise introduced by individual differences, meta-analysis combines data across many studies to control for the noise introduced by differences among studies. Even with some weak definitions of handedness, immune disorders, allergies, and the like, the meta-analysis points us in the directions worth pursuing. Except in very unusual circumstances the increased power resulting from the much larger total sample size of a meta-analysis more than compensates for the increased variance among studies resulting from methodological differences.

STATISTICAL ISSUES

Voyer performs a useful service by reanalyzing the data of our original Table 1 using a different and more conventional method of meta-analysis

TABLE 2
Hypothetical Association between Handedness and Disease

(a) Population sample

	With disease	Without disease	Total
Left-handers	10	90	100
Right-handers	40	860	900
Total	50	950	1000

Odds of having disease in left-handers $= \frac{10}{90} = .111$

Odds of having disease in right-handers $= \frac{40}{860} = .047$

Odds ratio: $\frac{.111}{.047} = 2.36; \phi = .0765$

(b) Disease sample

	With disease	Without disease	Total
Left-handers	100	47	147
Right-handers	400	453	853
Total	500	500	1000

Odds of having disease in left-handers $= \frac{100}{47} = 2.128$

Odds of having disease in right-handers $= \frac{400}{453} = .883$

Odds ratio: $\frac{2.128}{.883} = 2.41; \phi = .1497$

(c) Handedness sample

	With disease	Without disease	Total
Left-handers	50	450	500
Right-handers	22	478	500
Total	72	928	1000

Odds of having disease in left-handers $= \frac{50}{450} = .111$

Odds of having disease in right-handers $= \frac{22}{478} = .046$

Odds ratio: $\frac{.111}{.046} = 2.41; \phi = .1083$

(d) General terminology

	With disease	Without disease	Total
Left-handers	A	B	A + B
Right-handers	C	D	C + D
Total	A + C	B + D	N

TABLE 2—*Continued*

Note. Odds ratio: $\frac{A \times D}{B \times C}$.

Thus, increasing the number of those with the disease by a factor of k does not affect the odds ratio:

$$\frac{(k \times A) \times D}{B \times (k \times C)} = \frac{A \times D}{B \times C}.$$

On the other hand, $\phi = \frac{AD - BC}{\sqrt{(A + B)(C + D)(A + C)(B + D)}}$.

Increasing the proportion of those with the disease by a factor k results in a value of

$$\phi' = \frac{kAD - kBC}{\sqrt{(kA + B)(kC + D)(kA + kC)(B + D)}};$$

since ϕ' is not equal to ϕ, then unlike the case of the odds ratio, the value of ϕ depends on the marginal proportions and therefore on the study design.

han the one we carried out. A few words of explanation concerning he somewhat different findings may be helpful to readers. Meta-analysis ypically has to combine data from many studies in which the effects are eported in different ways (e.g. correlations, t tests, χ^2 tests, etc.) and ıse different types of measures (e.g. reaction times, error rates, etc.) and t is necessary to reduce these disparate values to a common metric of effect size. In the present case there are no such problems because *all* studies can be reduced to a 2 × 2 contingency table; therefore, the *raw* data from all studies can be combined into a single 2 × 2 × k table in which k is the number of independent studies or populations. Such an approach has an important advantage over Voyer's use of Hedge's w statistic, which is effectively a transformation of the χ^2 statistic into a ϕ statistic (and which is merely a Pearsonian correlation with the rows and columns scored as 1 and 2). It is well known that measures of association in contingency tables where marginal proportions are not equal cannot achieve measures of perfect correlation (because the off-diagonal cells cannot both be zero if the marginal proportions are not equal). The result is that Hedge's w is a less good descriptor of association in a 2 × 2 table than is the odds ratio which we use (which can vary from zero to infinity without regard to the marginal proportions—see Tables 1a, 1b, and 1c) because much of its variability is artifactually dependent on marginal proportions rather than being a pure measure of association. The result is that our study has more power than a conventional measure, thereby accounting for our finding that the main effect of handedness just achieves significance, in contrast to the nonsignificant result of Voyer. We believe that our form of analysis is the most powerful way of examining these data and thereby testing the GBG hypothesis in a fashion that maximizes the likelihood of finding the effects proposed by Geschwind et al.

ON DYSLEXIA

Kaplan and Crawford and to a lesser extent Hugdahl, Obrzut, and Freidmann and Grodzinsky are all concerned with our analysis of the "triadic" association among immune disorder, developmental dyslexia, and anomalous dominance (Bishop, 1990b). Our interpretation of the GBG model (original Fig. 1) would suggest that there should be a closer link between handedness and reading disorders, because they are both putatively driven by testosterone's effect on cortical development, than between either of these variables and immune dysfunction, which is consequent on the effect of testosterone on the thymus. Yet, Kaplan and Crawford present data indicating an association between immune disorders and both reading disorders and ADHD, while minimizing the relation with handedness. Hugdahl, on the other hand, finds evidence for a relation between handedness and developmental dyslexia, but less support for a relation with immune disorder. If Kaplan and Crawford are correct in linking immune disorders to dyslexia (and the comments of various reading specialists we know make this quite believeable), we would argue that the mechanism is more likely through some genetic linkage rather than through the detailed pathway proposed by GBG (as suggested by Kaplan and Crawford). Finally, it should be pointed out that the postulated "triadic" relation is not a pure (cross-over) three-way interaction, but will necessarily also include the two-way associations for which most workers have looked.

Obrzut provides some additional data concerning his study with Atkinson (Obrzut & Atkinson, 1993). This nicely illustrates some of our problems in selecting studies, given that they started with a sample of 170 learning-disabled children without ADHD, but wound up with data from only 33 of them (19%) and from only 17% of their original control sample. Although such a selection ratio presents no problem so long as it is unbiased (as we have shown earlier in commenting on different methodologies), it becomes of concern if there is any bias in the selection such that the LD children with immune disorders are more (or less) likely to be included.

Obrzut, and Friedmann and Grodzinsky are both concerned with the various definitions of developmental dyslexia. We readily admit that our review of developmental dyslexia was not as thorough as it could have been. This is in part because of the complexity of the issues and in part because of the excellent book on the subject recently published by Bishop (1990b). Friedmann and Grodzinsky suggest that a linguistic approach to dyslexia is necessary and propose that there are phonological, attentional, and visuospatial dyslexias; a similar distinction has been made by Boder (1973), among others. Friedmann and Grodzinsky are perfectly correct in pointing out that the studies we have reviewed involve diverse

definitions of dyslexia, and it is very reasonable to believe that different dyslexic subtypes might show different relations to handedness or to immune disorder.

ON SEX DIFFERENCES

The reports of several of our commentators (Forget & Cohen; Halpern; Hampson & Moffat; Small & Hoffman; Voyer) focus on sex differences and/or testosterone (T) as related to the GBG model. Certainly, GBG were stimulated by sex differences in their thinking in a variety of areas. However, GBG's focus on T was purely inferential: T could be replaced by some other factor "X" and leave unchanged the observables along the right-hand column in our Fig. 1.

Nevertheless, some of these commentators raise interesting points about the role of T in brain development and behaviour. Forget and Cohen, for example, emphasize its excitatory/facilitatory effects on CNS development (as opposed to its inhibitory role as elaborated by GBG) as well as drawing our attention to studies implicating the importance of the activational effects of sex hormones in adulthood and to their role in the establishment of plasticity in neural tissue. Likewise, Hampson and Moffat provide an excellent review of the post-natal effects of testosterone, again emphasizing that sex hormones have been shown to have activational effects in adulthood as well as early organizational effects as set forth in GBG (Goy & McEwen, 1980). They point out that many (but not all) studies support the idea of a non-monotonic relationship between testosterone and some cognitive abilities thought to be mediated by the right hemisphere, a situation that indeed "at least suggests a more complicated picture than the one envisioned by the GBG theory." Another important issue raised by Hampson and Moffat is the state of knowledge (or, more appropriately, lack of knowledge) about the time periods of maximal CNS sensitivity to androgens, specifically the critical period or periods for those cortical and/or subcortical areas important in the development of functional lateralization.

Small and Hoffman raise the issue of T's role in producing structural differences in the brains of males and females as distinct from its putative agency in the development of functional lateralization. Their point is that until it can be shown that there exist replicable sex differences in hemispheric specialization, the claim that T is important in the development of lateralization is weak. Pertinent to this argument, Voyer provides some preliminary results from an extremely interesting meta-analysis suggesting that the putative sex differences in dichotic, dichhaptic, and tachistoscopic studies of lateralization may not be robust. We would agree that sex differences in lateralization are, at best, small and would argue that differences in fetal T are therefore unlikely to be their sole source.

This observation reinforces the need for a more thorough understanding of the development of functional lateralization.

AREAS WE MISSED

In a detailed commentary, St-Marseille and Braun review the evidence for associations between HLA haplotypes and immune disorders. Their position appears to be that left-handedness cannot be linked to immune disorder through either fetal testosterone effects on the thymus or through the HLA system.

As already mentioned, both Hampson and Moffat and Forget and Cohen raise issues pertaining to the effects of testosterone (T), quite correctly pointing out that T has major effects on behavior long after birth. We purposely left out the literature concerning post-natal T effects, choosing instead to concentrate on fetal T because this is such a critical part of the GBG theory (see our Fig. 1). We have no doubt that T has many effects at puberty and in adulthood, but it is not clear just what predictions emanate from the GBG model.

Although Kaplan and Crawford accuse us of not properly covering the literature on immune disorder and dyslexia, we actually cited 7 of the 10 papers discussed by Kaplan and Crawford that were extant at the time of our review.

Elliott, Weeks, and Chua have provided an expansion of our review of Down syndrome and laterality, presenting evidence that there is abnormal dichotic performance in these individuals that is difficult to reconcile with the GBG model. Most of these subjects exhibit a left-ear (right hemisphere) advantage for the perception of verbal material presented dichotically, but appear to have speech production lateralized to the left hemisphere. This unusual condition is not typical of other mentally handicapped subjects and seems not to be associated with a corresponding reversal of the normal population right-hand advantage, though the current estimates of nonright-handedness in Down syndrome are "anywhere from 15 to 25%" (Elliott et al.), somewhat higher than the highest estimates for the general population.

THE ORIGINS OF LATERALITY

We finish this response by stepping back and looking at the broader biological and evolutionary context in which the GBG theory is embedded. Some of the commentators (e.g., Dellatolas; Halpern; Weinstein et al.) appear to view the GBG model as one in which anomalous dominance is pathological, resulting from some untoward event in prenatal development altering an otherwise normal state. Others (e.g., Annett; Elliott et

al.; Hellige; Previc; Small & Hoffman) consider it a model of the normal state of affairs and therefore focus on the evolutionary or genetic factors that give rise to lateralization of function. Although our own view is that the GBG model is more closely allied to genetic models such as those of Annett (1985) and McManus (1985) than to pathological models such as that of Coren (1992), there are certainly aspects of both extremes in it.

Lateralization of function may have arisen very early in evolution, as Hellige would argue by calling our attention to the development of the chicken, it may be a characteristic of primates (see Corballis, 1990; Ward et al., 1993), or it might possibly be a unique characteristic of humans (Annett, 1985). It may depend on computational simplicity (Small & Hoffman), on the development of sequential gesture (Kimura, 1993), on walking on two legs (Previc), or on any one of a number of other factors. It is not enough, however, to develop a scenario that accounts for the lateralization of language to the left hemisphere and for the overwhelming prevalence of right-handedness. It is also critical to account for the variance in the distributions of handedness and language lateralization, and relatively few models provide a basis for this variability. The GBG model was an attempt to do so, and our commentators are correct in asserting that it stimulated a great deal of interesting research. Annett and Previc have also presented reasonable models that are testable, and we have offered our own view of the evolution of laterality (McManus & Bryden, 1993).

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