A neurological model of dyslexia and other domain-specific developmental disorders with an associated sensorimotor syndrome

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Abstract

Given mounting evidence that auditory, visual and/or motor dysfunction do not cause developmental dyslexia, but are often associated with it, the present paper proposes a new neurological model of dyslexia which explains how a specific phonological deficit might arise, and sometimes occur together with a more general sensorimotor syndrome. Based on a comprehensive review of the neurology of dyslexia, the model specifies that: 1) Genetically determined focal cortical anomalies in specific left perisylvian language areas are the underlying cause of the phonological deficit; 2) This phonological deficit is the primary cause of reading impairment; 3) Under certain hormonal conditions during gestation, these cortical anomalies induce secondary disruption in sensory pathways, notably in the thalamus. 4) When this happens, the individual affected displays one or several components of a sensorimotor syndrome, which may in some cases aggravate the reading impairment.

Introduction

Certain developmental disorders, including dyslexia, specific language impairment (SLI), and autism, are the subject of considerable controversy regarding their neurological and cognitive origins. Certain theoreticians consider them to be domain-specific disorders, arising from congenital dysfunctions circumscribed to certain cognitive components, e.g., phonology, syntax, or mentalising, respectively[1-4]. Others think that these disorders are much more general, and that the seemingly specific components affected are in fact part of a more extended syndrome, usually encompassing the sensory and motor domains[5-8]. Some of these researchers even hold that domain-specific developmental disorders are, in principle, unlikely to exist at all[9].

In the case of developmental dyslexia, the predominant theory is that it is due to a specific phonological deficit[1]. Nevertheless, this view has been challenged by increasing evidence of sensory and motor disorders in dyslexics, leading to competing theories implicating auditory/temporal processing deficits[10,11], visual/magnocellular dysfunction[5,12,13] or motor/cerebellar dysfunction[14,15]. In the face of this highly diverse and inconsistent data set, only one theory so far has attempted to account for all the empirical evidence: the general magnocellular theory, in which a generalised dysfunction of magno-cells affects all sensory pathways and further spreads to the posterior parietal cortex and the cerebellum, thereby encompassing all the known cognitive, sensory, and motor manifestations of dyslexia[5,16].

However, as I have argued elsewhere[17,18], the magnocellular theory only partly succeeds in explaining the whole data set. In particular, it fails to explain why the prevalence of sensorimotor dysfunction is so much lower than that of the phonological deficit in the dyslexic population. Even within the subset of dyslexics affected by sensory and/or motor disorders, the causal relationship with the reading impairment is far from clear[18,19]. On the basis of a comprehensive review of the literature, I have previously advocated that dyslexia is, in most individuals, explained by a specific phonological deficit; furthermore, a more general sensorimotor syndrome occurs more often in the dyslexic than in the general population, but does not by itself play a causal role in the aetiology of the reading impairment[18]. According to this view, a complete theory of dyslexia must explain both how a specific phonological deficit might arise, and why a sensorimotor syndrome should be significantly associated with it.

In this paper, I propose a neurological model that serves this purpose. Specifically, it explains how a phonological deficit may arise from genetically determined brain anomalies, in isolation in certain individuals, or accompanied by sensorimotor impairments in others. This model is compatible with all the known genetic, neurological, and cognitive data available on dyslexia. It easily generalises to SLI and possibly to other domain-specific developmental disorders. It further suggests explanations for a few puzzling issues like co-morbidity between and heterogeneity within disorders, and makes a number of specific predictions yet to be tested.

Insights from anatomical studies and animal models

Post-mortem examination and brain imaging studies have documented many differences between dyslexic and control brains, in the left peri-sylvian cortex[20-24], the underlying white matter[25], the thalamus[13,26], the corpus callosum[27,28], the cerebellum[29,30], etc. (see [31] for a comprehensive review). In most cases, the functional significance of these brain differences has not been elucidated. It is not even clear which of those differences are specifically relevant to dyslexia, considering the well-known comorbidity between dyslexia and many other disorders[32-34]. Nevertheless, the functional significance of two types of brain anomalies has been studied in greater detail.

Anomalies of cell migration called molecular layer ectopias and focal microgyri have been observed in the peri-sylvian cortex of dyslexic brains[20,35,36], predominantly in the left hemisphere, and with a much greater prevalence than in control brains[37]. Ectopias consist of 50-100 neurons and glia that have escaped into the molecular layer of the cortex through a breach in the external glial limiting membrane, accompanied by mild disorganization of the subjacent cortical layers. Microgyria are more severe disturbances where the organisation of all layers of the cortex is severely affected. Cytoarchitectonic anomalies have also been observed in dyslexics' thalamus: in the lateral geniculate nucleus, the magnocellular layers were more disorganised, with overall smaller cell bodies[13]. Similarly, there was a disproportionate number of small neurons in dyslexics' left medial geniculate nucleus (MGN)[26].

It is quite natural to hypothesise that anomalies in the magnocellular layers of the lateral geniculate are the cause of visual deficits, and that anomalies in the medial geniculate are the cause of auditory deficits. There is at least evidence for the latter causal link in rats[38]. Similarly, it is easy to see cortical anomalies in left peri-sylvian areas as the underlying cause of phonological, and perhaps more general language difficulties.

In this anatomical evidence, one can therefore see direct neurological support for auditory and magnocellular theories of dyslexia; this is indeed how the data is usually interpreted (e.g., [16]). The implicit causal (bottom-up) scenario is that anomalies in the thalamus engender ectopias and microgyria in certain cortical areas to which the thalamus is connected. At the cognitive level, this would translate into the auditory deficit causing a phonological deficit, and into the basic visual deficit causing visual attention/planning problems, as prescribed by the magnocellular theory. However, this implicit scenario is never spelled out, and for good reason: it is known to be incorrect[39]. Indeed, Galaburda and colleagues have shown that the causal direction is the opposite (top-down), i.e., that the cortical anomalies engender the thalamic anomalies.

The evidence comes from a whole series of studies on animal models. Indeed, it is possible to surgically induce ectopias and microgyria by poking a hole in the external glial limiting membrane of the developing cortex of rats during late neocortical neuronal migration. There are also strains of mutant mice that spontaneously develop similar malformations. Investigation of these animal models have led to a number of important findings.

First of all, newborn rats with surgically induced microgyria in the frontal, parietal or occipital cortex, subsequently develop anomalies in the MGN: they have more small and fewer large neurons in the MGN than rats receiving sham lesions, an anomaly similar to that found in dyslexics' MGN[38,40]. This suggests that the direction of causation is indeed top-down, from the cortex to sensory relays in the thalamus. Furthermore, rats with such an abnormal MGN were found to perform less well in an auditory discrimination task[38,40-42], which confirms that the observed disruption in the MGN has an impact on auditory capacities.

Another interesting aspect uncovered in these studies is that only male rats were initially found to have impaired auditory function following early inducement of microgyria[42]. Indeed, females rats showed normal auditory performance and did not show a similar anatomical disruption of the MGN in response to the microgyria, even though their cortical lesions were as extended[38]. Similarly, only male ectopic mice subsequently show auditory deficits[43]. It was subsequently found that this sex difference had a hormonal basis; indeed, female rats that were androgenised by injection of testosterone during gestation showed disrupted MGN and impaired auditory function like males[44].

Finally, the cortical anomalies themselves seem to have an impact on cognitive function: ectopic mice and rats with spontaneous or induced ectopias and microgyria exhibit a variety of learning deficits[45-48], including problems with working memory[49-51]. Furthermore, the location of the cortical disruption influences the specific type of learning deficit exhibited by the animal[52,53], but not the likelihood of further thalamic disruption and sensory impairment.

To summarise, these results suggest that (1) cortical anomalies (microgyria, ectopias) induce anomalies in sensory relays in the thalamus, but (2) only under certain fœtal hormonal conditions. If one further assumes that cortical anomalies at that stage are directly related to dyslexics' future phonological deficit, then these findings suggest that (1) the neural basis for a phonological deficit exists *prior* to the neural basis for any auditory impairment, and that (2) it may exist *in the absence* of any auditory impairment (when the disruption does not propagate to the thalamus, like in female rats[38]). These conclusions clearly do not rest easily with the magnocellular theory, nor with any type

of sensorimotor theory of dyslexia; however, they fit very well with the view that I have advocated, that of a specific phonological deficit, that may, or may not, come with additional sensorimotor disorders. This reinterpretation of the anatomical and animal data naturally leads to a new neurodevelopmental model of dyslexia.

A neurological model of dyslexia

Focal anomalies and the phonological deficit

The main claim of this model is that congenital anomalies in specific left peri-sylvian areas are the direct cause of a phonological deficit, which itself is the direct cause of reading impairment.

A simple version of this model attributes the main responsibility to cortical ectopias and microgyria. Galaburda et al.[20] found most ectopias in the left peri-sylvian cortex. This is indeed where the main brain areas involved in phonology seem to be located: mainly the supramarginal and angular gyri, the posterior superior temporal gyrus, the insula, and the inferior frontal gyrus, although there is debate as to which areas are involved specifically in phonological representations, and which are more concerned with reading or speaking [31,54-61]. Note that this does not exclude that areas which become more specifically dedicated to reading (like the left fusiform gyrus[62]) might also be the target of cortical anomalies, although there is currently no such evidence.

More generally, the multiplicity of areas involved in phonology and reading, together with the multiple differences found between dyslexic and control brains, makes it plausible that several different patterns of cortical disruption will lead to a reading impairment; this diversity may actually reflect the various manifestations of the phonological deficit in dyslexia: in verbal short-term memory, fluency of phonological retrieval, phonological awareness.

The previous section has emphasised ectopias and focal microgyria, but other brain anomalies might be related and equally significant. Ectopias and microgyria may indeed be just one manifestation of a wider disruption. For instance, the planum temporale has been argued to be excessively symmetric in dyslexics[20,63], and this is thought to be closely linked with the presence of ectopias and microgyria[64,65]. Furthermore, the increased callosal connections are also interpretable as a consequence of the excessive symmetry of the planum temporale and/or other cortical areas, as this symmetry is typically manifested by an enlargement of the usually smaller side[20]. Finally, ectopias and microgyria may also be related to the disruption of underlying white matter tracts[25]. Many of the brain anomalies documented in dyslexia may therefore be associated with ectopias and microgyria, and be part of the same disruption. Exactly which part of this disruption plays a significant functional role remains to be established. Quite plausibly, cortical ectopias and microgyria in specific left peri-sylvian areas might affect phonological representations; so might a disrupted planum temporale, as this area is thought to underlie speech representations[66-68]; and disrupted white matter might affect interfaces between phonological and orthographic representations, or between different levels of phonological representation[25,54].

Given the current uncertainty on structure/function relationships, the more general version of the present model is not committed to one particular type of brain anomaly, nor to a particular functional interpretation of each anomaly. However, it specifically hypothesises (1) that the disruption is related to ectopias and microgyria, and therefore that it appears very early in development (before the sixth month of gestation in humans); (2) that the functionally significant part of the disruption is *focal*, specific to certain cortical areas or cortico-cortical connections; (3) that these focal anomalies specifically affect the development of phonological and/or orthographic representations/processing; (4) that they are a sufficient cause of reading impairment, without the help of broader sensorimotor dysfunction (see Fig. 1). In essence, this pattern of neurological dysfunction, analogous to that observed in the female rat, gives rise to "pure phonological dyslexia".

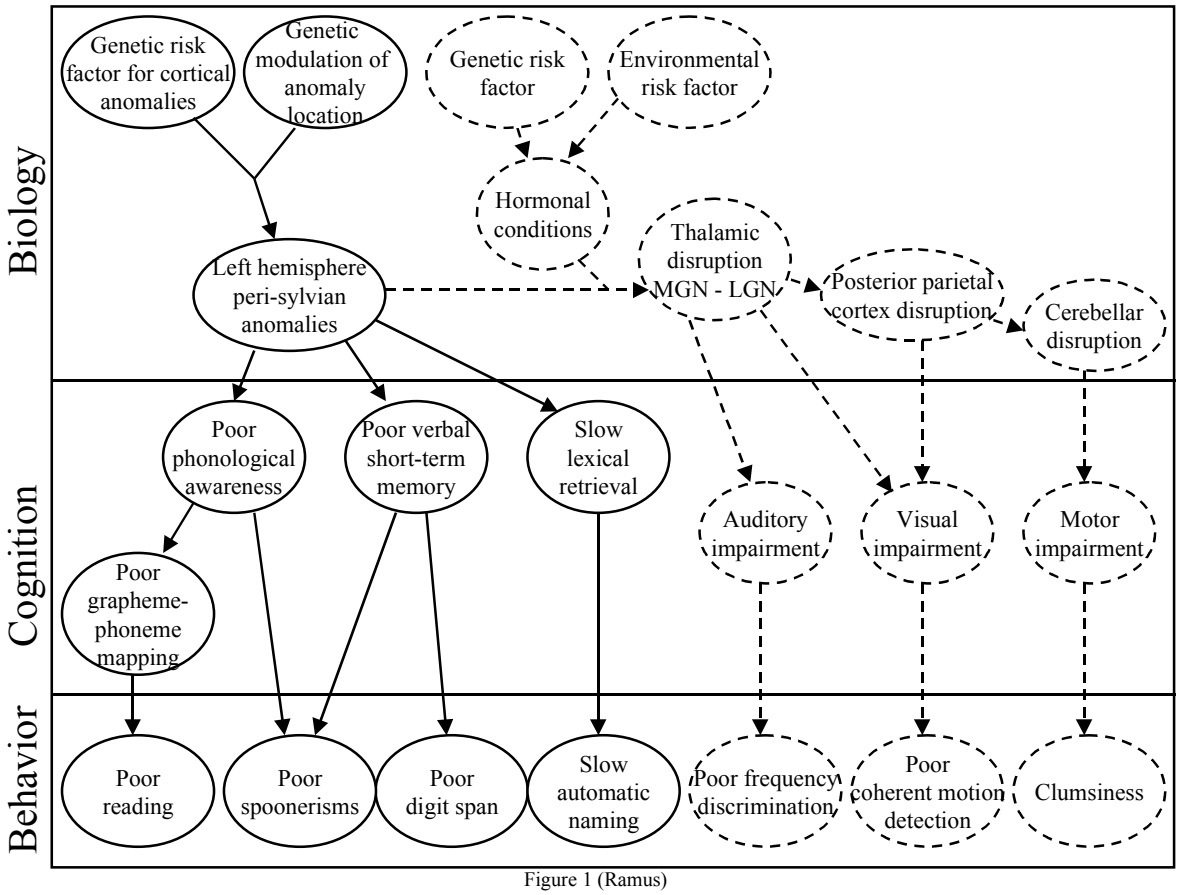

Figure 1 (Ramus)

Figure 1. A candidate causal model of the aetiology of developmental dyslexia. Bubbles represent traits at the biological, cognitive and behavioural levels of description. Arrows represent causal relationships between traits. Solid lines are used for core traits of developmental dyslexia, dashed lines for optional, associated traits. Only a subset of all possible behavioural manifestations are represented. Cases of co-morbidity with other developmental disorders (e.g., SLI) are not represented. LGN: lateral geniculate nucleus. MGN: medial geniculate nucleus.

Sex hormones and the sensorimotor syndrome

The second claim of the model is that, when the focal anomalies already discussed are present, *and* under certain hormonal conditions at an early stage of brain development, additional disruptions arise in sensory pathways, notably the thalamus, and perhaps subsequently in other areas like the posterior parietal cortex and the cerebellum[5]. These disruptions are responsible for a syndrome consisting of a constellation of sensory, motor and perhaps attentional difficulties.

The research just reviewed suggests that the "hormonal conditions" may reduce to an elevated concentration of testosterone in the fetal environment[44]. More generally, it has been proposed that testosterone plays an important role in brain development, notably by slowing the growth of the left hemisphere, and that it is involved in a number of brain and cognitive anomalies[69]. There is also indirect evidence that a high concentration of fetal testosterone is associated with autism[70], another disorder with a high incidence of the sensorimotor syndrome[71-73]. Fetal testosterone is therefore a likely candidate as a mediator for the sensorimotor syndrome. Nevertheless, the situation may be more complex. Indeed, other gonadal steroids like progesterone and estrogen have been shown to influence brain development, usually in positive ways[74,75]. It may be that testosterone acts by attenuating the protective effects of these other hormones[42], which suggests that sex differences in the neurophysiological response to cortical damage may result from a complex interaction of several hormones. Finally, it could also be these “hormonal conditions“ are a matter of hormone receptors in the brain rather than hormone concentration per se[76]. This will all be matter for future research.

The hypothesis is therefore that, under certain hormonal conditions to be precisely defined, focal cortical anomalies may induce further disruption in the thalamus, and more particularly in the medial geniculate nucleus (as demonstrated in male rats[44]), as well as in the lateral geniculate nucleus (as suggested by dyslexics' brains[13]). This would be the direct cause of subtle auditory and visual deficits. Although it has been suggested that sensory

dysfunction might be specifically or predominantly magnocellular[5,13,26], as pointed out earlier the empirical evidence seems inconclusive. The model is therefore neutral to this issue. The sensory disorders in question might well be magnocellular, parvocellular, a combination of the two, or perhaps this dichotomy serves no meaningful purpose in the characterisation of the deficit: this is a matter for future research. The main claim is that these sensory disorders arise optionally, under certain conditions in certain individuals only, and on top of the phonological deficit.

Similarly, Stein & Walsh [5] proposed that the thalamic magnocellular disruption further propagates to the posterior parietal cortex and to the cerebellum. Again, this might well be true, but the model is neutral to this issue. If this is true (and even if the thalamic abnormalities are not specifically magnocellular), this might explain further visuo-attentional[77] and motor[78] problems also evidenced in some dyslexics (see Fig. 1).

Obviously, when present, the sensorimotor syndrome may in principle aggravate the situation of the dyslexic child. In particular, a severe auditory deficit might aggravate the phonological deficit[17]. Visual or visuo-attentional deficits might also aggravate the reading impairments[5]. However, it should be noted that in both cases the proposed causal links are still speculative and await further evidence.

Extension of the model to other developmental disorders

Dyslexia and SLI have two features in common: first, relatively specific cognitive deficits; and second, the additional presence of a sensorimotor syndrome in part of the population. The model presented here seems perfectly suited to explain all disorders that share these two features.

Indeed, nothing in this model restricts the possible loci of focal anomalies to areas subserving phonology and reading. I hypothesise that, in humans like in mice[52], what makes each developmental disorder unique is the location of the focal anomalies. In this view, what makes, say, a dyslexic child qualitatively different from an SLI child, has little to do with differences in low-level perception or the like, but depends on whether the cortical are as affected implement, say, processing of speech sounds, or of syntactic structure or lexical items. The model proposed for dyslexia therefore generalises quite naturally to SLI, and perhaps to autism, dyspraxia and ADHD, or at least certain subsets of the latter disorders, insofar as the focal anomalies under discussion can arise in the relevant brain areas. On the other hand, other disorders like Williams, Down or fragile-X syndromes clearly do not fit into this class of specific developmental disorders[79,80].

In the rat model, thalamic disruption arises under high fetal testosterone conditions, whether microgyria are located in the parietal, frontal or occipital lobe[38]. Similarly, in male ectopic mice, auditory deficits are found regardless of ectopia location[81]. According to the present model, this further explains why a similar sensorimotor syndrome seems to appear across a whole range of developmental disorders, and typically only in a subset of individuals within each disorder, whether dyslexia, SLI, dyspraxia, ADHD, or autism[18,32,72,73,82-84]. I specifically hypothesise that the sensorimotor syndrome arises in any individual who presents with both the focal brain anomalies and the hormonal conditions discussed in the preceding section, regardless of the specific type of cognitive deficit.

Heterogeneity and co-morbidity

In the brains examined by Galaburda and colleagues[20], several dozens of ectopias spread over large cortical areas were found in each subject. This may seem at odds with the presumed specificity of the cognitive deficit. But this depends on the precise functional consequences of such cortical anomalies: it may well be that only a critical concentration of ectopias in one area produces any significant cognitive disruption. Nevertheless, it is perfectly likely that several distinct cognitive systems are disrupted within a dyslexic individual: indeed, there is more than one component to the phonological and reading systems, and nothing prevents a dyslexic from presenting other cognitive deficits unrelated to reading. Together with clinicians' strategy of sorting cases into a few basic diagnostic categories, this seems consistent both with the well-known heterogeneity within disorder and co-morbidity between disorders.

Within disorder: It seems to be the case that none of the usual diagnostic categories reflect homogeneous cognitive profiles. For instance, dyslexics' phonological deficit typically has three main manifestations: poor phonological awareness, poor verbal short-term memory, and slow automatic naming, which are significantly associated but may be partly independent[85]. This is consistent with the view that this triad of impairments reflects distinct disruptions of, say, the left posterior superior temporal gyrus, the left inferior frontal gyrus, and the angular/supra-marginal gyri respectively. Similarly, SLI is typically characterised by any combination of poor grammar, vocabulary, and/or speech articulation, which can be seen as reflecting distinct impairments of the syntactic, lexical, or articulatory systems. One may further speculate that the same logic might hold for mentalising and central coherence in autism, and for inhibition and action monitoring in ADHD. Finally, assuming that the number of focal anomalies may vary between individuals, the model is consistent with the existence both of individuals with a multi-faceted disorder, and

of others with a purer subtype, like pure phonological dyslexia[85] or Grammatical-SLI[86].

Between disorders: Of course, multiple focal anomalies may span several cognitive domains as well as sub-systems of the same domain. For instance, both phonological and syntactic systems may be affected, in which case the resulting disorder can be interpreted as a co-morbid case of dyslexia and SLI. This helps explain why between one third and one half of children with a developmental disorder also qualify for the diagnosis of another one[32-34,82].

Predictions of the model

Brain anomalies in other developmental disorders

Further research should reveal much more on the brain anomalies underlying dyslexia and other developmental disorders. While the present model is specified sufficiently loosely to accommodate a variety of outcomes, it also makes specific predictions: that a whole class of domain-specific disorders are characterised by focal brain anomalies, the differences between disorders reducing to differences in the localisation of the anomalies. As far as SLI is concerned, the sample studied by Galaburda et al. [20] actually included individuals whose profile was more that of co-morbid dyslexia and SLI than of pure dyslexia, which is consistent with the observed distribution of cortical anomalies across language areas. On the other hand, the current literature on the neurology of autism is only partly supportive: focal anomalies (but not ectopias/microgyria) have been found in the limbic cortex and the amygdala, although not very consistently[87,88]. It may be that only a subtype of the autism spectrum will meet these predictions.

Furthermore, the model predicts that thalamic abnormalities will be found in a sub-population only of each disorder, in parallel with the sensorimotor syndrome, but unrelated to the specific nature of the cognitive deficits.

Post-mortem dissection, high-resolution MRI and diffusion-tensor imaging studies will all be important tools to test these predictions. But they will be useful only insofar as the anatomical measures are matched with comprehensive cognitive testing, in order to test precisely the postulated structure-function correspondences within each individual.

Sex-ratio

It is commonly accepted that males are more affected by dyslexia than females (e.g., [89]), although this has been challenged[90]. Within the magnocellular theory, the finding that thalamic disruption was mediated by fetal testosterone in the mouse model has been interpreted as a possible explanation for the uneven sex ratio in dyslexia (e.g., [38]).

In the present model, the cause of reading impairment has been shifted away from the thalamus to the cortical anomalies. In this view, the sex-ratio of dyslexia has little to do with foetal hormones, but is tightly related to possible sex differences in cortical anomalies. It turns out that the female dyslexic brains that were dissected showed fewer ectopias than male ones, and were characterised instead by a large number of small myelinated glial scars[36]. This may imply that females are less likely to have a phonological deficit, and that the deficit will be less severe on average in females, or alternatively that females require more severe neuropathology in order to exhibit behavioural problems, thereby explaining the uneven sex-ratio. But the exact functional significance of these differences in cortical anomalies is unknown, so it is at present impossible to predict the theoretical sex ratio of the phonological deficit.

However, because of the hormonal mediation leading to the thalamic disruption, the model does predict an increased prevalence of the sensorimotor syndrome in males. More precisely, irrespective of the actual male/female ratio in dyslexia, it predicts that this ratio will be increased in the subpopulation with a sensorimotor syndrome, as compared to the subpopulation without it. And it predicts just the same for the sensorimotor syndrome in other developmental disorders. Such predictions could be easily tested by carrying out post-hoc analyses on already existing data sets including reliable individual data on sensory and/or motor measures.

Markers of fœtal hormonal conditions

Another prediction of the model is that if one could measure the relevant hormonal conditions in human foetuses, and relate these measures to later outcome measures of sensorimotor functions, there would be significant correlations to be found (more than with measures of each specific cognitive deficit). Unfortunately, only major longitudinal studies including all the relevant measures will be able to test this prediction.

In the meantime, one may want to look for markers of foetal hormonal conditions that would still be measurable in

the child or even in the adult. One such marker has been proposed: the ratio between the length of the second digit and that of the fourth digit (2D:4D ratio) would be inversely correlated to foetal testosterone levels[91], and has been shown to be significantly lower in autism than in the general population[70]. Furthermore, a recent study replicated this result and found that within a group of autistic-spectrum disorder children, the 2D:4D ratio was correlated with their performance in coherent motion detection and in manual dexterity[73]. Obviously, such results are to be taken with caution considering the very indirect relationship between the two measures. Their interpretation may be further complicated by the fact that, as was evoked earlier, the determining hormonal conditions might not be simply a matter of testosterone concentration.

Genetics

Because developmental disorders like dyslexia, SLI and autism have a strong genetic basis, the model predicts that ectopias and other relevant focal anomalies must arise under genetic control. This is indeed confirmed by studies of autoimmune mice that spontaneously develop ectopias[92,93]. Furthermore, since dyslexic parents do not seem to usually beget autistic offspring (although such cross-heritability of different disorders might happen more often than chance), the model also predicts that the precise location of cortical anomalies is under genetic control. This is consistent with the fact that different strains of mutant mice have ectopias in different locations[45], but the exact mechanisms influencing their location are not known yet.

On the other hand, fœtal hormonal conditions may be partly genetically determined, but are also more likely to be influenced by external factors. The model therefore predicts a lower heritability of the sensorimotor syndrome than of specific cognitive deficits. The possibility that some cases of sensorimotor dysfunction are due to genetically-determined cortical anomalies in visual, auditory or motor cortex, or in the cerebellum, may attenuate this prediction. Nevertheless, it is currently consistent with the finding that the phonological deficit is highly heritable (both in dyslexia and SLI), while auditory and visual deficits are not, or to a much lower extent[94-96].

It is also notable that all the specific cognitive disorders under consideration here have a complex genetic aetiology involving several regions on different chromosomes (e.g, [97]), unlike Williams, Fragile-X, Down syndromes, etc., which all have a simple genetic aetiology with wide-ranging cognitive consequences. One way to understand this, in the light of the present model, is to speculate than in dyslexia and other specific disorders, certain genes are risk factors for the occurrence of focal anomalies like ectopias, while other genes control the precise location of such anomalies, for instance by generating molecular gradients interacting with ectopia risk factors. Yet other genes might be risk factors for the hormonal conditions leading to the sensorimotor syndrome. These hypotheses broadly predict that the genes implicated in all these specific cognitive disorders will be partly shared (those acting as risk factors), and partly specific to each disorder (those determining specific brain locations). The more detailed predictions are potentially testable using current mouse models.

Clinical implications

Current diagnostic categories are undermined by the heterogeneity within and the overlap between categories, as well as by the occasional focus on associated deficits as part of certain diagnostic procedures (e.g., clumsiness in dyslexia[98]). They do not do justice to the variety of cognitive impairments that may arise, and their different possible combinations. Although dyslexia, SLI, autism etc. may remain convenient umbrella terms based on the most salient trait, a possibly more useful approach to learning disabilities would be in the form of a check-list enumerating all attested cognitive, sensory, and motor deficits, each child being characterised by his own combination of marks (and severity ratings) in the list. This would, in essence, replace ever imperfect labels with a comprehensive, individual neuro-cognitive profile.

Attempts at remediation might also gain from such an approach. The present model suggests that there is little point proposing auditory, visual or motor training schemes as general treatments for dyslexia and SLI, since many of these children do not have sensory or motor impairments. The comprehensive diagnostic approach could nevertheless draw attention to sensorimotor impairments when present, which might justify treatment in their own right insofar as they are themselves a cause of trouble. Certain visual disorders such as visual stress or poor binocular control do indeed seem to be a cause of reading impairment or discomfort in a minority of dyslexics (and non-dyslexics), and may therefore justify a specific treatment[99,100]. The subtle auditory deficits often associated with dyslexia and SLI, on the other hand, are not responsible for linguistic deficits[19] and are not known to cause any other adverse effect, so auditory training[101,102] does not seem particularly recommended (real hearing impairments are of course a different matter). Finally, motor impairments, insofar as they constitute a handicap for the child, certainly deserve attention. Amelioration of the handicap, and indeed any improvement of the general condition of the child, is likely to have knock-on effects on self-esteem, self-confidence, motivation, etc., which could eventually lead to improved reading. This may indeed be the most likely explanation for positive effects observed in certain motor training studies[103,104].

Non-specific effects are therefore not to be neglected, but they should be recognised for what they are, rather than sold as magic cures.

General discussion

It may be observed that the present model much resembles the traditional neuropsychological model for acquired brain lesions, in that it postulates focal disruptions causing specific cognitive deficits, assuming a rather tight fit between brain area and function, even if the function is not yet developed at the time of the disruption. Some might argue that this makes the model highly implausible[9,105]; I would like to argue otherwise. The tight fit between brain area and function seems to be a basic fact about brain organisation and development. Even for those functions that clearly have no evolutionary basis (e.g., orthographic processing), there seems to be one area of the brain that is more appropriate than others (e.g., orthographic representations reliably settle in a very specific sub-region of the left fusiform gyrus[62]), presumably because not all areas of the brain have the optimal representational, computational and connectional properties required for each particular function. And these representational, computational and connectional properties of brain areas are largely genetically determined.

Certainly, when the optimal area for a particular function is disrupted, there can be a significant amount of compensation through brain plasticity, and more so in developmental than in acquired disorders. Indeed, it is well-known that the right hemisphere can take over some linguistic functions from a dysfunctional or removed left hemisphere[106,107]. Functional brain imaging suggests that this does happen in dyslexics too, as they show less activation than controls in their disordered left temporo-parietal junction and inferior frontal gyrus, but more in the right counterpart areas[108,109]. But for all the hype about brain plasticity and reorganisation, dyslexics, left-hemispherectomised children as well as ectopic mice remain significantly impaired, demonstrating that no other brain area does the job as well as the optimal one. What is known about brain development and plasticity is therefore entirely compatible with the idea that the congenital disruption of a limited brain area will lead to long-lasting disruption of the cognitive function that it would subserve under normal development.

Skeptics may further argue that it is unlikely that the effects of an early focal brain anomaly would remain circumscribed to that particular area and cognitive function, again because of plasticity[6,9]. But this again overlooks the fact that brain plasticity is far from total. Of course, development occurs and produces knock-on effects: in dyslexia, for instance, the phonological deficit alters the development of the orthographic system, and may also impact on the acquisition of vocabulary. Yet, there is no reason to expect that it should have consequences on *all* areas of the brain (after all, dyslexics are not overall mentally retarded). Indeed, this is not observed in the case of congenital focal brain lesions which can also lead to relatively specific cognitive deficits in humans[110-112], just like in ectopic mice with focal cortical anomalies[49,51,52,113,114]. The female rat model further demonstrates that disruption in one cortical area does not necessarily produce changes just one synapse away[38]. The hypothesis of a specific cognitive deficit remaining specific throughout development therefore seems perfectly plausible and compatible with current knowledge in developmental neuroscience.

Given the data reviewed in the present paper, a sensory explanation of dyslexia, in order to be viable, has to make the following assumptions: 1) that a sensory dysfunction is present in all dyslexics at birth, but recovers in most of them to the point that it is detectable only in a minority by school-age; 2) that in dyslexics who remain auditorily impaired, some factor also alters the relationship between the severity of the auditory deficit and that of the phonological deficit (as there is no such relationship at school-age[19]); 3) that the ectopias and concomitant brain anomalies observed in dyslexics' language areas *do not* cause any phonological deficit (since these anomalies exist before the sensory disruption); 4) that the phonological deficit itself is not reflected by any additional physical disruption in those areas affected by the aforementioned anomalies, or, if it is, such disruption has so far gone unnoticed. Although such a conjunction of unlikely facts may appear implausible, it is of course possible that all these assumptions will turn out to be true. Further research should indeed aim to test these assumptions and more generally evaluate the respective predictions of the two competing frameworks, the sensorimotor one, and the domain-specific one.

The model outlined here opens up new avenues of research aiming to uncover the precise links between specific genes, brain anomalies and cognitive deficits. But in order to meet that challenge, research on developmental disorders will have to complete a methodological revolution that has only recently begun: the production and analysis of reliable individual data at all levels of description. Indeed, the present model suggests that a number of genetic, neurological and cognitive traits are consistently associated with dyslexia and other disorders, without actually *explaining* them. This implies that the usual studies focusing on group differences and correlations between measures are doomed to confuse core and associated deficits, cause and correlation. The future belongs to longitudinal studies that will be able to trace causal pathways throughout development, across genetic, neurological and cognitive measures, and within each individual subject.

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