Motion perception deficit: risk factor or non-specific marker for neuro-developmental disorders?

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In their comprehensive review of motion perception in autistic spectrum disorder (ASD), Milne and colleagues (2005) mention both that deficits in motion perception are found in only a subset of autistic individuals, and that such deficits have also been evidenced in other neurodevelopmental disorders than ASD. I think that this point deserves further discussion. Indeed, it bears quite directly on the issue whether a motion perception deficit reflects an underlying cause of ASD or not. If it does, how can one explain that it is not present in all autistic children, and that it is present in children with other disorders but no autistic symptom? If it does not, why is it associated with ASD (and other developmental disorders)? Explaining this paradox requires a relatively sophisticated causal model. I will describe and discuss the respective merits of two classes of models that may serve this purpose: the multiple risk factor model and the non-specific marker model.

The multiple risk factor model

Given data on the prevalence of motion perception deficits both within the autistic and other populations, it must be concluded that a motion perception deficit (or the underlying dorsal visual stream dysfunction) is neither necessary nor sufficient to cause ASD, just as it is neither necessary nor sufficient to cause dyslexia or any other disorder (White, Frith et al., submitted). This quite directly excludes any theory of autism generally invoking a motion perception deficit as *the* underlying *cause* of ASD, in the classic sense of the word *cause*. Yet it might still be a real causal factor in the aetiology of ASD and other disorders. This could be the case if these disorders were multi-factorial, with dorsal visual stream dysfunction as one of the factors involved.

For the sake of discussion and simplicity, let us restrict our analysis to ASD and dyslexia, and assume that each of these disorders can result from the conjunction of at least two distinct risk factors chosen from a specific set. Let us assume that A1, A2 and M (for motion perception deficit) are risk factors for ASD, and that D1, D2 and M are risk factors for dyslexia. As an illustration, plausible candidates for A1, A2, D1 and D2 might be mentalising deficit, weak central coherence, phonological awareness deficit, and poor verbal short-term memory, respectively. Under these assumptions, ASD can be caused by any of the following combinations: A1+A2, A1+M, A2+M, A1+A2+M; and similarly for dyslexia[1]. Such a model accounts for the following facts:

- Both ASD and dyslexia are cognitively, neurologically and genetically heterogeneous.
- M is more frequent in both the autistic and dyslexic populations than in the control population.
- M is found only in a subset of autistic children (not in those with just A1+A2, or any other combination of A*n* factors if n>2).
- M is also found in a subset of dyslexic children who have no autistic symptom (they have D1+M, D2+M, or D1+D2+M).
- M alone does not cause either ASD or dyslexia.
- Therefore, M is neither necessary, nor sufficient to cause ASD (and neither is any other risk factor).
- Still, M can be thought of as one of the factors leading to ASD.

Therefore, it seems that such a basic multi-factorial model can account for some of the intriguing results from the study of motion perception in ASD and in dyslexia (see Bishop et al., 2001, for a similar account of auditory deficits in specific language impairment).

Furthermore, frequencies of risk factors can be such as to predict the frequencies of different profiles of autistic and dyslexic individuals. For instance, assuming frequencies d1=.2, d2=.2, m=.05, a1=.05, a2=.05, then frequencies of the different profiles are as follows (Table 1):

[1] Of course, such a model is overly simplistic in that it assumes all-or-none rather than quantitative risk factors, but this has no incidence on the illustrative purpose of the present discussion

Profile	D1+D2	D1+M	D2+M	D1+D2+M	A1+A2	A1+M	A2+M	A1+A2+M
Frequency	.04	.01	.01	.002	.0025	.001	.001	0.00002

Table 1. Fictive frequencies of the different profiles of dyslexia and ASD, assuming d1=.2, d2=.2, m=.05, a1=.05, a2=.05.

Such figures predict a prevalence of dyslexia of around 6%, with about one third affected by a motion perception deficit, and a prevalence of ASD of around 0.5%, with about 45% affected by a motion perception deficit, all broadly consistent with the available estimates from the literature. Obviously, this parameter-fitting exercise is done for illustration purposes only, but is in fact totally trivial and could be performed for any desired prevalence.

Multiple risk factor models are therefore an efficient way to understand disorders such as ASD, with multiple but non-systematic symptoms. The particular model presented here allows us to understand a motion perception deficit as one of several risk factors that can lead to ASD. Nevertheless this is not the only possibility.

The non-specific marker model

I have recently proposed an alternative to the multi-factorial model, which addresses the more general question of how a sensory or motor deficit could be statistically associated with a developmental disorder, without being causally related to its main cognitive symptoms (Ramus, 2004, in press). The relationship between motion perception deficits and autism is obviously a particular case of this question. The model was initially developed to address sensorimotor deficits in dyslexia, and is based on neurobiological data and work on animal models specific to dyslexia. Nevertheless some of its features might generalise to other neuro-developmental disorders.

Briefly, the model specifies that:

- The core cognitive symptoms of dyslexia (the phonological deficit) originate from small cortical disruptions like molecular layer ectopias and microgyri (i.e., abnormalities of neural migration), located in left perisylvian areas involved in phonological processing (e.g., the left superior temporal gyrus, the inferior frontal gyrus…). This is consistent with post-mortem dissections (Galaburda, Sherman, Rosen, Aboitiz, & Geschwind, 1985), as well as structural and functional brain imaging studies of dyslexia (Démonet, Taylor, & Chaix, 2004; Eckert, 2004).
- The associated sensory symptoms of dyslexia originate from subcortical abnormalities in (possibly magnocellular) sensory pathways, particularly the thalamus. This is again consistent with post-mortem studies (Galaburda, Menard, & Rosen, 1994; Livingstone, Rosen, Drislane, & Galaburda, 1991). Possibly, motor symptoms might arise from a further spread of disruption from the thalamus to the cerebellum (Stein & Walsh, 1997).
- Perhaps counter-intuitively, thalamic abnormalities are *secondary* to cortical ones, not the other way around. This is consistent with animal models of these neurological abnormalities (Herman, Galaburda, Fitch, Carter, & Rosen, 1997; Peiffer et al., 2001).
- Furthermore, whereas abnormalities of neural migration are expected to be of largely genetic origin (Sherman, Stone, Denenberg, & Beier, 1994; Wang et al., submitted), thalamic abnormalities seem to develop under the conjunction of cortical abnormalities and more extrinsic fœtal hormonal factors (notably testosterone). This is consistent with animal models (G. D. Rosen, Herman, & Galaburda, 1999). Such a conjunction of genetic and extrinsic factors leading to sensorimotor deficits would explain why only a subset of dyslexics show sensorimotor deficits.
- In principle, such a model might apply not only to dyslexia, but to any neurodevelopmental disorder with relatively specific cognitive symptoms (which might arise from similar cortical abnormalities in different locations), and with associated sensorimotor deficits.

In practice, can this model (or a model of this kind) be extended to autism? The neurobiological literature does not particularly point to neural migration abnormalities in autism; nevertheless abnormalities of the cerebral cortex have been repeatedly reported (Abell et al., 1999; Bailey et al., 1998; McAlonan et al., 2005). It is at least conceivable that such cortical abnormalities might be the proximal cause of cognitive deficits (such as a mentalising or executive function deficit), and that, like in the animal models of ectopias and microgyri, a conjunction of these cortical abnormalities and hormonal factors might induce secondary thalamic disruption, hence sensorimotor deficits.

But is it really the case that ASD, like dyslexia, is associated with a more general sensorimotor syndrome (as opposed to just the motion perception deficit mentioned in the target article)? Yes indeed, motor difficulties have long been reported in autism (e.g., Hallett et al., 1993), and more recent investigations have found that just the same package of sensory and motor deficits can be observed in autistic as in dyslexic children (Milne et al., in press; White, Frith et al., submitted). Furthermore, there is even a suggestion that a morphological correlate of fœtal testosterone is related to motion perception in the ASD population (Milne et al., in press), reinforcing the hormonal factor hypothesis.

ASD and dyslexic populations are therefore remarkably similar, if not in terms of cognitive deficit, at least in terms of the sensorimotor syndrome arising in some of these individuals. A non-specific marker model can parsimoniously account for this fact in both populations.

Teasing apart the two models

Are there any predictions that differ between the two models, and that could be used to tease them apart? I can see at least two, concerning the severity and the heritability of sensorimotor deficits.

The multiple risk factor model predicts that the magnitude of each of the risk factors should be correlated with the severity of the disorder (at least in a more plausible version of the model where risk factors are quantitative rather than all-or-none, and have cumulative effects). Indeed, although each risk factor is neither necessary nor sufficient by itself to cause the disorder, it is nevertheless causally related to the disorder. If one focuses on the subset of autistic children who present a motion perception deficit, the severity of this deficit should be related to the severity of their disorder, all things being equal. On the other hand, in the non-specific marker model, only correlations between the severity of the disorder and the cognitive (cortical) deficits are predicted, not with the associated sensorimotor deficits.

Unfortunately few studies have provided data allowing these predictions to be tested. I am not aware of any study on ASD looking at the correlation between motion perception and a quantitative measure of autistic severity. However, in our various studies looking at sensory or motor disorders in dyslexia, we have never found a reliable correlation between motion perception (nor any other sensorimotor measure) and reading, once IQ is partialled out (Ramus, Pidgeon, & Frith, 2003; Ramus, Rosen et al., 2003; White, Milne et al., submitted) (see also Hulslander et al., 2004; S. Rosen, 2003).

Another possible prediction of the multiple risk factor model is that individual risk factors should be heritable, since ASD itself is highly heritable. However, this prediction is not clear-cut: it could indeed be that A1 and A2 are of genetic origin, while M is of environmental origin. If M explains sufficiently little phenotypic variance in twin studies, then this would be compatible with the very high heritability of ASD (90% by most estimates, Folstein & Rosen-Sheidley, 2001). But in this case this greatly minimises the causal contribution of M to the model. On the other hand, the non-specific marker model explicitly traces the motion perception deficit back to extrinsic hormonal factors (in conjunction with genetically determined cortical abnormalities). It therefore predicts little heritability for sensorimotor deficits (although a genetic contribution to the hormonal factors cannot be excluded).

Again, such detailed heritability data is missing from the ASD literature. In the dyslexia literature, a few studies have reported no significant heritability for auditory and visual deficits (Bishop et al., 1999; Olson & Datta, 2002), quite unlike the phonological deficit whose heritability may reach 70% (Gayan & Olson, 2001).

From these limited predictions and results, one may conclude that, at least in the case of dyslexia, the non-specific marker model fares slightly better. If one doesn't want to assume that similar models can explain both ASD and dyslexia, then more data on ASD is required. Certainly severity correlations should be readily available in existing data sets. Perhaps the authors of the target article will be so kind as to check the correlation between motion perception and the Autism-Spectrum Quotient (or a similar measure) in their own data sets.

Conclusion

The two classes of models described here are not necessarily mutually exclusive. The whole point of the non-specific marker model is to emphasise that the statistical association between a symptom (e.g., motion perception deficit) and a disorder (e.g., ASD) does not entail that the symptom plays a causal role in the aetiology of the disorder. There are other possibilities, and indeed the possibility that a motion perception deficit might be a non-specific marker is quite well supported by neurobiological data in the context of dyslexia research (Ramus, 2004). Yet, at the cognitive level, it is perfectly plausible that a multiple risk factor model holds, with mentalising deficit, weak central coherence and poor executive function as risk factors for ASD, and poor phonological awareness, poor verbal short-term memory and slow lexical retrieval as risk factors for dyslexia. Such a unifying model would thus include both multiple cognitive risk factors, and non-specific sensorimotor markers.

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