Reply to Champagne-Lavau, M. et al. “Language functions in right-hemisphere damage and schizophrenia: Similar or different pragmatic deficits?”

Mitchell, R.L.C. “Schizophrenia as a disorder of lateralisation for language that affects left and right hemisphere language functions”.

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Dear Sirs,

I would like to follow up some of the issues raised by Champagne et al. in their recent submission to Brain, particularly those relating to my own recent review article in Brain. Clarification of the theoretical and practical issues at stake is a crucial step for this fledgling area of research and the next generation of lateralisation models in schizophrenia.

To reiterate the premise of Mitchell and Crow (2005), we do not claim that schizophrenia should be considered ‘a right-hemisphere disorder’, just as we do not feel it should be considered ‘a left-hemisphere disorder’. The communication disturbances in schizophrenia include abnormalities of language function associated with both hemispheres. The effects of abnormal lateralisation on the cognitive functions of both hemispheres were recently highlighted in an investigation by Caligiuri et al. In the Brain review, we asserted that one of the key features of schizophrenia is abnormal lateralisation of language functions to the two hemispheres. This functional abnormality could be expressed in the schizophrenic brain by various means, e.g. reduced or inefficient callosal transfer of information, the right hemisphere playing a greater role in ‘left-hemisphere language functions’ than normal, and ‘right-hemisphere language functions’ being ‘crowded-out’ by the partial neurodevelopmental transmigration of left hemisphere language functions to the right hemisphere.

To avoid confusion, in the discussion below, I shall use the same terminology as that used by Champagne et al., and use the term ‘pragmatic functions’ to refer to the higher order language functions termed ‘right-hemisphere language functions’ in our review.

Champagne et al. begin by questioning an early step in the logic underlying an association between pragmatic language functions and communication disturbance in schizophrenia, namely that they feel the association between pragmatic deficits and RBD is controversial. As exemplified by these authors’ introduction, comparatively few neuroimaging studies of pragmatic language functions exist, so it may be too early as yet to boldly question current understanding of their mediation. Some of the differences emerging between the older lesion studies and the newer neuroimaging studies may be explained by the sometimes neglected foundations of these two research techniques; that lesion studies indicate brain regions necessary to perform a certain cognitive function, whereas neuroimaging studies only indicate brain regions sufficient to perform that function.

Their following argument suggests that the cognitive reasons for deficits displayed following right-hemisphere brain damage (RBD) are not yet clear and that it is naive to search for a single cognitive dysfunction to explain impaired pragmatic functions. I do not question Champagne et al.’s assertion that it is unlikely that a single functional cause can explain the pragmatic deficits displayed by RBD patients. Indeed, in their study the two patient groups displayed differing profiles of executive function impairment. However, bringing underlying cognitive processes into the discussion needs further thought on the localisation of said processes to make sense of any distinctions between RBD and schizophrenia patients.

It is claimed by the authors that their report described the first study to compare the performance of RBD patients and those with schizophrenia. This claim is not true. Previous comparisons of these two patient groups on pragmatic functions have included works by Borod et al. Chapman, and Ross et al. In Borod et al.’s papers, there was no (significant) difference between the performance accuracy of patients with schizophrenia and those with RBD on emotional prosody comprehension and expression tasks. Similarly, in the study by Ross et al., the performance of schizophrenic patients was statistically identical to that of RBD patients on emotional prosody comprehension and expression tasks of varying verbal-articulatory complexity. Like Champagne et al., Chapman compared the ability of patients with brain damage and those with schizophrenia to interpret
metaphors. Patients with schizophrenia made more literal misinterpretations than figurative, whilst brain damaged patients showed the opposite preference. However, Chapman did not distinguish between patients with damage to the left and right hemispheres.

In terms of pragmatic deficits, Champagne et al. report that patients with schizophrenia showed difficulty interpreting non-idiomatic and idiomatic metaphors, and indirect requests, whilst patients with RBD only showed difficulty interpreting non-idiomatic metaphors and direct requests. Despite these differences in the profile of pragmatic deficits, the point is perhaps, that patients with schizophrenia did not display normal pragmatic functions. In view of the known neurological differences between the pathology of RBD and schizophrenia, some differences in the profile of pragmatic deficits are to be expected. Champagne et al. do not report the precise location of damage for their RBD patients. The preponderance of evidence in schizophrenia research indicates abnormalities of lateralisation whose functional effects are localised to the lateral temporal lobe. If one assumes that not all the RBD patients tested by Champagne et al. displayed temporal lobe brain damage, then a difference in profile between the two groups is understandable. According to a popular model of the organisation of pragmatic functions in the right hemisphere\(^1\), comprehension of emotional prosody is mediated by the right hemisphere homologue of Wernicke’s area, and the expression of emotional prosody is mediated by the right hemisphere homologue of Broca’s area. Therefore an RBD patient whose lesion lay outside the right hemisphere equivalent of Wernicke’s area would be comparatively unlikely to display emotional prosody decoding deficits, despite having unilateral right hemisphere damage. In the context of Champagne et al’s study, the similarities/differences between patients with schizophrenia, and patients with RBD may be at least partially explained by between group variability in the brain regions affected in each of the two groups. In view of the functional neuroanatomic differences between anterior and posterior regions of the right hemisphere, it may also be unwise to treat RBD patients as a homogeneous group.

A further difference which it might be important to consider is that whereas disturbance of language functions and failure of lateralisation in schizophrenia is thought to arise neurodevelopmentally\(^2\), the loss of pragmatic language functions in the RBD group arises following traumatic loss. These two patient groups may share some aspects of reaction to structural brain alterations, namely diffuse functional effects and some subsequent re-organisation of function. However, acute traumatic loss following a stroke represents a very different onset of pathology relative to the neurodevelopmental onset of pathology in schizophrenia. The death of neural tissue following a stroke is not the same as functional abnormality of otherwise intact brain tissue. At only 1-4 months post-cerebrovascular accident, there is also still some potential for further reorganisation of language functions\(^3\) in the RBD patient group, which may well affect the nature and severity of impact on their ability to perform pragmatic tasks. Follow-up comparisons to patients with schizophrenia may well be required.

As stated in Mitchell and Crow (2005), the language deficits of patients with schizophrenia can still best be understood as abnormalities of lateralisation, although current explanatory models need reformulating in light of what we now know about pragmatic language functions and the anterior-posterior torque or directionality of the brain. There is no simple segregation of language to the left hemisphere, but a separation of functional components between the hemispheres. Our intention was not to suggest that schizophrenia was a right hemisphere disorder, but to simply draw attention to the group of pragmatic language functions that have long remained in the shadow of their more well known left hemisphere counterparts. In view of the psychological sequelae of language disturbance in schizophrenia, if the mechanisms underlying pragmatic language dysfunctions were the same in the two patient groups, this would have worrying implications for the psychiatric status of patients with RBD. Fortunately psychosis is a relatively infrequent consequence of RBD.

Yours Sincerely

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6. Ross ED. Manuscrupt under review.