Editorial: In praise of cognitive neuropsychiatry

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Having recently “retired” from my position as a Principal Research Fellow in the Wellcome Centre for Imaging Neuroscience at UCL, I welcomed the editors’ offer to look back over many years devoted to cognitive neuropsychiatry.

IS SCHIZOPHRENIA A BRAIN DISORDER?

I wonder if the readers of this journal remember that time, not so long ago, when functional psychoses such as schizophrenia had nothing to do with the brain? This belief was not limited to antipsychiatrists such as Szasz. When my colleague, psychiatrist Eve Johnstone, published her classic paper in 1976 in the *Lancet* demonstrating enlarged ventricles in association with chronic schizophrenia (Johnstone, Frith, Crow, Husband, & Kreel, 1976), the UK’s leading neurologist wrote a letter to the journal suggesting that this enlargement was due to chronic treatment with neuroleptic drugs (Marsden, 1976). This position that the brain had nothing to do with schizophrenia had to be abandoned, not only because of the many replications demonstrating structural changes (see Steen, Mull, McClure, Hamer, & Lieberman, 2006, for a recent review), but also because of robust demonstrations of a role for dopamine in the production of positive symptoms such as hallucinations and delusions (Johnstone, Crow, Frith, Carney, & Price, 1978; Seeman & Lee, 1975). Such observations led to exciting questions about how abnormalities in the physical activity of a brain can lead to abnormalities in subjective experience. This problem was put in stark form when a
politician who visited the Medical Research Council (MRC) research unit at
Northwick Park, UK at about this time, asked the unit’s director Tim Crow
the key question, “Is there something wrong with their brains, or are they
just mental?” My feeling was that answers, such as “hallucinations are
caused by overactive dopamine receptors”, were not adequate. How was it
possible to bridge the gap between the mental and the physical?

THE JOY OF BOXES AND ARROWS
The answer is “cognitive neuroscience”, which, unfortunately, did not then
exist. In those days it was called cognitive neuropsychology. Cognition is an
ambiguous term, which acquired new meanings in the twentieth century and
is often used as synonymous with information processing. The importance
of cognition is that it provides a language that can be used to talk both about
psychological processes in the mind and physiological processes in the brain.
Using this language, damage to the brain can be linked to psychological
problems, such as failures of short-term memory (Shallice & Warrington,
marker of a cognitive neuropsychology paper became the box and arrow
diagram. At one level the boxes represent encapsulated psychological
processes or memory buffers which interact with one another (the arrows)
to generate behaviour or experience. At another level the boxes are discrete
brain regions, which have specific connections (the arrows) to other brain
regions. If a particular box or connection is removed as a result of brain
damage, then we can predict what behaviours will remain intact on the basis
of the rest of the diagram (Frith, 2004). Cognitive neuropsychology is
concerned with effects of overt brain damage, but exactly the same approach
can be applied to abnormalities for which no overt damage has yet been
detected.

In those pre brain-scanning days, neuropsychologists were often asked to
estimate where the brain damage might be on the basis of performance on a
battery of tests. The same approach can and, very occasionally, was applied
to psychiatric disorders such as schizophrenia (e.g., Kolb & Whishaw, 1983).
Can the pattern of impairment indicate where the hidden brain damage
might be? This should be called neuropsychiatry (leaving out cognitive)
because there is no attempt to delineate the information processing
mechanisms involved and therefore no box and arrow diagrams. The other
problem is that this approach, derived from lesion studies, is focused on
impairments, while the striking features of disorders such as schizophrenia
are hallucinations, delusions, and so on that are abnormal through their
presence rather than their absence. A major concern of cognitive neuropsy-
chiatry is to explain such positive features in terms of established cognitive
processes. Furthermore, this approach is aimed at explaining specific symptoms, rather than diagnostic categories such as schizophrenia (see, for example, the special issue of *Cognitive Neuropsychiatry*; Spence & David, 2004).

From my own contributions, my favourite is the idea that a “self-monitoring” defect might explain symptoms like delusions of control (Frith, 1987). This preference is based on the elegance of the box and arrow diagram (see Figure 1), although there has also been some experimental support (e.g., Blakemore, Smith, Steel, Johnstone, & Frith, 2000; Shergill, Samson, Bays, Frith, & Wolpert, 2005).

The joy of box and arrow diagrams like this one, as recognised more than 100 years ago by Lichtheim (1885), is that you can explain a whole range of different disorders by damaging particular boxes and arrows (see for example, Frith, Blakemore, & Wolpert, 2000). In contrast to self-monitoring theory, the idea that theory of mind might be impaired in schizophrenia (for a review see Harrington, Siegert, & McClure, 2005) hardly deserves to be considered an example of cognitive neuropsychiatry since there is no associated box and arrow diagram.

**Figure 1.** How passivity experiences might be explained. Actions occur, but, through a failure of monitoring, seem to happen independently of the subject’s willed intentions.
But then, just as this journal was about to be founded, functional brain imaging burst onto the scene. This was the cognitive neuropsychologist’s dream come true. It was no longer necessary to wait for a patient with the right kind of lesion. You could now put a normal volunteer in a scanner and see the boxes lighting up. You could write a brain region on each of the boxes in your favourite box and arrow diagram (Petersen, Fox, Posner, Mintun, & Raichle, 1988). You could publish your papers in *Nature* and *Science* (Petersen et al., 1988; Posner, Petersen, Fox, & Raichle, 1988). We all rushed into brain scanning. A few brave people questioned its value, but it was noted that such criticism was typically associated with lack of access to a scanner.

However, after a decade of studies it has become clear that brain imaging cannot replace the study of patients with lesions. Just because activity is observed in a particular location does not mean that this region has a vital role in the cognitive process engaged. Rather, observation of this activity provides a hypothesis to be tested in patients with the appropriate lesion. The situation is even more complicated for psychiatric disorders since we know that, in most cases, there are no specific lesions associated with such disorders. Thus, having observed some interesting pattern of brain activity associated with some particular symptom it is not at all clear how to generate a hypothesis, let alone test it. Bigger magnets and cleverer analysis software are not going to help us to escape from this impasse. Once again, the lead must be taken by cognitive neuropsychiatry.

**THE TRIUMPH OF BAYES**

The essential requirement is to provide a computational basis for our box and arrow diagrams. For example, the diagram for selection of action shown in Figure 1 must be replaced by a computational account of motor control such as the system of inverse and forward modelling proposed by Daniel Wolpert and colleagues (Miall & Wolpert, 1996). There are also exciting developments in learning and decision theory providing computational models for the role of dopamine in these processes (e.g., Pessiglione, Seymour, Flandin, Dolan, & Frith, 2006). However, for me, the most interesting new development in cognitive neuroscience concerns the application of Bayesian inference to perception (Yuille & Kersten, 2006), a computational account of analysis by synthesis. I find this account of perception exciting (see Frith, 2007) because, in terms of this mechanism, perception is a form of belief.
The main function of the brain is to constantly acquire knowledge about the world on the basis of evidence coming through the senses. The Bayesian account of perception proposes that there is a continuous cycle of prediction and updating on the basis of prediction errors. Our perception is a model of the world, in other words, a belief about what the world is probably like. This probability estimate is a measure of the strength of the belief. In terms of such a mechanism, perception works like this: On the basis of our belief about the world we can predict the signals that should strike our senses; on the basis of the errors in our prediction we can update our belief about the world and make it more probable. Thus, perception depends upon a combination of the evidence from our senses and our prior beliefs. Bayes' theorem indicates the optimum form for this combination. This approach provides a computational account of belief formation and supplies a common framework for developing accounts of hallucinations and delusions. In both these classes of symptoms, evidence is not being used optimally for generating beliefs about the world. In the case of schizophrenia, this problem seems to apply particularly to the world of minds, rather than physical entities (Hohwy, 2007). The basic principles are now in place for developing a computational model of theory of mind (e.g., Kilner, Friston, & Frith, 2007; Wolpert, Doya, & Kawato, 2003). Such models will have a major impact in the search for neural underpinnings and the delineation of cognitive disorders.

WHY WE NEED COGNITIVE NEUROPSYCHIATRY MORE THAN EVER

But, rather than entering a brave new world for cognitive neuropsychiatry, I fear we may be coming round full circle. On the one hand, a Bayesian revolution already happened in the early days of the application of cognitive theory to psychiatric symptoms such as hallucinations (Bentall & Slade, 1985) and delusions (Hemsley & Garety, 1986), but this work was not followed through or linked to brain function. On the other hand, molecular genetics has appeared as the major player in the search for causes of psychiatric disorders. Today the politician's question might be, “Is something wrong with their genes, or are they just mental?” And the answer, “Hallucinations are caused by a polymorphism in the CCK-AR gene” (Sanjuan et al., 2004) would still be unsatisfactory. We need to keep our nerve if we want to bridge the gap between the physical and the mental in the study of psychiatric disorders. And, to keep our nerve, we need, more than ever, the support of the readers, editors, and publishers of Cognitive Neuropsychiatry.
REFERENCES


