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COMMENTARY

Salience and psychosis: moving from theory to practise

A commentary on: 'Do patients with schizophrenia exhibit aberrant salience?' by Roiser *et al*. (2008)

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All models are wrong, but some are useful (Box, 1979)

Psychosis remains one of the most distressing, yet intriguing, human conditions. The profession of psychiatry grew up in asylums trying to grapple with psychosis over a century ago. How best to understand and treat psychosis is still an ongoing academic challenge. At one level psychosis is a behavioural phenomenon. At another it is tied to the brain, its chemistry and circuits. Thus, any complete explanation of psychosis will have to try and link explanations at these two levels of analysis: a neurobiological/neurochemical level and the psychological/behavioural level. A few years ago one of us proposed that the concept of 'motivational salience' may be one such linking variable (Kapur, 2003). The link between dopamine and the limbic system and the concept of salience is strong. But, this link is built mainly on animal studies using a variety of rather simple conditioning paradigms using rewarding and aversive stimuli. To make these concepts applicable to schizophrenia, an anthropomorphized notion of salience was proposed. Salience was defined as a process whereby objects and representations, through the process of association, come to be attention-grabbing and capture thought and behaviour. While this has served as a useful general heuristic – how does one test such a broad notion? Over the past few years several innovative groups has developed interesting and novel ways to do this and Roiser *et al*. provide one such interesting approach in this issue (Roiser *et al*. 2008).

Roiser and colleagues used a probabilistic monetary task where adaptive and aberrant salience were operationalized as outcome measures, both having explicit and implicit components. They used medicated patients with schizophrenia and healthy matched controls and showed that the patients exhibited reduced adaptive salience. These were the hypothesized results because these were medicated patients and it was hypothesized that their treatment would have corrected their aberrant salience, but, dampened their adaptive salience. Interestingly however, Roiser *et al*. (2008) also found that within these treated patients, those with more positive symptoms showed increased aberrant salience compared to patients with less symptom load but also that this finding was mainly driven by the presence of delusions. Although these findings warrant further studies in unmedicated patients, using a probabilistic monetary task and making some sophisticated operationalizations the authors showed results that are predicted by the aberrant motivational salience model on the psychological level.

While Roiser *et al*. focused on a behavioural manifestation of salience, several recent studies have focused on the neurobiological level. The ventral striatum plays a central role in reward processing and it has been suggested that activations of the ventral striatum normally mediate motivational salience of environmental stimuli. A functional magnetic resonance imaging (fMRI) study by Juckel and collaborators (Juckel *et al*. 2006*b*) using a monetary incentive task showed that, compared to controls, unmedicated patients with schizophrenia displayed a reduced activation in the ventral striatum for cues predicting reward relative to a cue predicting no gain. This reduced activation was normalized when patients were treated with atypical medication but not with typical antipsychotics as evidenced by both a cross-sectional (Juckel *et al*. 2006*a*) and a longitudinal cross-over study (Schlagenhauf *et al*. 2008). The results suggest

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that the properties of the newer antipsychotics, such as lower striatal D_2 blockade, modulation by serotonin and other systems, or their faster dissociation from the receptor, are beneficial for motivational salience which is in line with the normalized aberrant salience results of medicated patients. Interestingly, in the study of Roiser *et al*. 88% of the patients took second-generation drugs (Roiser *et al*. 2008).

Using a different approach with fMRI, Murray *et al*. (2008) undertook a study of first-episode psychosis patients, and found a disruption in reward prediction error among the patients. Abnormal activations in dopaminergic regions, such as ventral tegmental area/substantia nigra and the striatum were observed and the patients also had difficulties in discriminating between motivationally salient and neutral stimuli. Using an aversive conditioning paradigm with a loud noise as unconditioned stimulus in medicated patients, we found a similar abnormality in discriminating between motivational salient and neutral stimuli using both self-report data and autonomic measures (Jensen *et al*. 2008). This was accompanied with deviant activation patterns in the ventral striatum suggesting that patients activated this region more towards neutral stimuli than healthy controls while they showed more similar activations to stimuli that the controls found motivationally salient, i.e. the conditioned stimulus. Both these studies (Jensen *et al*. 2008; Murray *et al*. 2008) thus showed evidence of abnormal assignment of motivational salience and abnormal activation patterns in the hypothesized regions in patients with psychosis.

The behavioural and imaging data reported above are consistent with the idea that patients aberrantly assign motivational salience to neutral stimuli (Kapur, 2003), and this process may be one of the aberrations that predisposes them to psychosis. However, the different studies have used a slightly different interpretation and operationalization of 'salience'. This is not surprising by itself, because concepts like 'reward' itself are operationalized in several different ways, and the concept of salience is loosely defined making such interpretations justified. The paper by Roiser *et al*. (2008), and several other recent ones are encouraging, but, the real challenge, as the title of this commentary suggests, is whether these ways of looking at psychosis will help us understand psychosis at a deeper level or deal with it more effectively. For that, more studies are needed: to replicate these initial results, to extend these studies to drug-naive patients, to examine the effect of medications in longitudinal studies and to look at the predictive value of these findings.

Declaration of Interest

None.

References

Box GEP (1979). Robustness in the strategy of scientific model building. In *Robustness in Statistics* (ed. R. L. Launer and G. N. Wilkinson). Academic Press: New York.

Jensen J, Willeit M, Zipursky RB, Savina I, Smith AJ, Menon M, Crawley AP, Kapur S (2008). The formation of abnormal associations in schizophrenia: neural and behavioral evidence. *Neuropsychopharmacology* **33**, 473–479.

Juckel G, Schlagenhauf F, Koslowski M, Filonov D, Wustenberg T, Villringer A, Knutson B, Kienast T, Gallinat J, Wrase J, Heinz A (2006*a*). Dysfunction of ventral striatal reward prediction in schizophrenic patients treated with typical, not atypical, neuroleptics. *Psychopharmacology* (*Berlin*) **187**, 222–228.

Juckel G, Schlagenhauf F, Koslowski M, Wustenberg T, Villringer A, Knutson B, Wrase J, Heinz A (2006*b*). Dysfunction of ventral striatal reward prediction in schizophrenia. *Neuroimage* **29**, 409–416.

Kapur S (2003). Psychosis as a state of aberrant salience: a framework linking biology, phenomenology, and pharmacology in schizophrenia. *American Journal of Psychiatry* **160**, 13–23.

Murray GK, Corlett PR, Clark L, Pessiglione M, Blackwell AD, Honey G, Jones PB, Bullmore ET, Robbins TW, Fletcher PC (2008). Substantia nigra/ventral tegmental reward prediction error disruption in psychosis. *Molecular Psychiatry* **13**, 239, 267–276.

Roiser JP, Stephan KE, den Ouden HEM, Barnes TRE, Friston KJ, Joyce EM (2008). Do patients with schizophrenia exhibit aberrant salience? *Psychological Medicine*. Published online: 30 June 2008. doi:10.1017/S0033291708003863.

Schlagenhauf F, Juckel G, Koslowski M, Kahnt T, Knutson B, Dembler T, Kienast T, Gallinat J, Wrase J, Heinz A (2008). Reward system activation in schizophrenic patients switched from typical neuroleptics to olanzapine. *Psychopharmacology* (*Berlin*) **196**, 673–684.