The Neural Substrates of Affect Impairment in Schizophrenia

The field of emotion research has made great strides recently, and the methods are now sufficiently developed that they can begin to shed light on a core feature of schizophrenia—the deficit in affective function—that Bleuler considered to be a cardinal feature of the disorder. A key goal is to eventually identify how the neural circuitry of emotion goes awry in schizophrenia. Four papers in this issue certainly advance the field in this area.

The paper by Kohler and colleagues extends previous work on affect recognition deficits in schizophrenia by using a set of photographs of facial expressions of both high and low intensity from an ethnically diverse set of subjects. Patients performed worse than comparison subjects for all emotional and neutral stimuli. Of interest is that while healthy subjects improved in their affect recognition performance with the higher intensity expressions, the patients with schizophrenia did not, especially for fearful expressions. The latter is particularly noteworthy given that in a previous study, this research group had demonstrated a deficit in amygdala activity among patients with schizophrenia in response to these same emotional stimuli. Furthermore, the degree of impairment in facial recognition was positively correlated with negative symptoms, establishing an important link between the experimental finding and the clinical phenomenology of schizophrenia. The authors caution that the demographic differences between the patients and comparison subjects (e.g., differences in race, age, sex distribution) could contribute to the findings. Nevertheless, the observation that schizophrenic subjects do not benefit from higher intensity expressions may reflect a more pervasive affect deficit. The perception of facial expressions itself can induce an emotional response in the viewer, and this internal response may aid in the identification of the facial expression. People with schizophrenia may have a deficit in this automatically generated emotional response, thus limiting the availability of another source of information about the meaning of facial expressions. In addition to the implications of these results for impairment in social interaction and maintenance of interpersonal relationships, the findings from this paper support the hypothesis that arousal mechanisms may be abnormal in schizophrenia.

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Brewer and colleagues report on a unique sample of patients at high risk for developing psychosis who performed an olfactory identification test that was then used to predict future clinical course. These investigators found that the patients who went on to develop schizophrenia or schizophreniform disorder performed most poorly on the olfactory test, including in comparison with patients who went on to develop other (often affective) psychoses. Ever since Kraepelin distinguished between schizophrenia and manic-depressive illness,

psychiatrists have longed for a marker or predictor of who would go on to develop one disorder or the other. Given the central importance and yet the differing nature of the affective disturbance in the two disorders, it is difficult to imagine a more useful goal for clinical emotion research than to create a method for predicting (and ultimately preventing) onset of either disorder. The method used by Brewer et al. likely will not do that, since other studies by this group indicate that patients with psychotic disorders other than schizophrenia have an impairment on this olfactory test. Furthermore, the patients in this study had psychotic symptoms (attenuated or brief limited) that were already rather advanced. Thus, this study may be revealing a marker of change already set in motion as opposed to a truly premorbid marker. The authors plausibly suggest that the incipient onset of schizophrenia compromises normal frontal lobe development. Given that much is known about the neural basis of olfactory processing, the findings extend what is known about the nature and timing of frontal lobe dysfunction in schizophrenia.

The study by Moberg and colleagues involved use of one odorant in different concentrations in healthy subjects and patients with schizophrenia. They found that in healthy men and women and in women with schizophrenia, the self-reported pleasantness of this odorant increased as the concentration of the odorant decreased. In men with schizophrenia, however, the highest concentration of odorant was rated as very pleasant, and the typical increase in pleasantness with decreasing concentration was not observed. The authors label this as an impairment in odor hedonics. Although the unusually high pleasantness ratings are not consistent with anhedonia, they do suggest that there is alteration in the usual modulation of affective response in relation to variations in stimulus intensity. A correspondence with the paper by Kohler and colleagues implicating abnormal arousal mechanisms is schizophrenia is therefore apparent. It is also noteworthy that the study by Brewer and colleagues revealed an impairment in odor identification in male subjects that is consistent with this finding. Given that the clinical manifestations of schizophrenia differ in men and women (women have a later onset, milder course, and more affective symptoms), this finding provides a potential window into the neural basis of the sex difference in schizophrenia that may have an affective basis.

The paper by Paradiso et al. breaks new ground by performing imaging of healthy subjects and patients with schizophrenia who had not been taking neuroleptic medications for at least 3 weeks. Patients viewed highly arousing pleasant and unpleasant pictures during scanning and were later asked to rate the pleasantness of the stimuli. Results showed that the patients rated the negative pictures comparably to the healthy subjects and rated the pleasant stimuli as less pleasant. The brain imaging data revealed that a widely distributed network of structures involved in affect processing was activated to a greater extent in healthy subjects than in the schizophrenia patients. The self-reported ratings of the pictures provided critical corroborative evidence that the patients were attending to the stimuli. The authors argue persuasively that the decreases in neural activity among the patients correspond to clinical observations of anhedonia and affective blunting. One concern is that the schizophrenia group consisted of 16 male and two female patients and the comparison group consisted of seven male and nine female subjects, raising the question of whether the greater proportion of women in the healthy group may have contributed to the findings. It would be important to corroborate these findings using a sex-matched control group and using eye-tracking measures and autonomic indi-

ces to prove that patients and healthy subjects attended to the stimuli equally. Nevertheless, the current study extends that of previous work by this group and others and provides further support for the model implicating dysfunction of a cerebello-thalamo-frontal circuit in schizophrenia.

Emotion research is complicated enough when studying healthy subjects. In the clinical context, the research becomes that much more complex, as one must take into account and control where possible the use of medications, the severity of symptoms to permit adequate task performance, the duration of illness, the presence of comorbid conditions, and general cognitive ability. Each study has made an admirable attempt to deal with these issues and collectively have moved us closer to the goal of identifying the neural basis of the abnormality in affect in schizophrenia.

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