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Olfactory identification and Stroop interference converge in schizophrenia

Scot E. Purdon, PhD

Department of Neuropsychology, Alberta Hospital Edmonton, and Department of Psychiatry and Psychology, University of Alberta, Edmonton, Alta.

Objective: To test the discriminant validity of a model predicting a dissociation between measures of right and left frontal lobe function in people with schizophrenia. **Participants:** Twenty-one clinically stable outpatients with schizophrenia. **Interventions:** Patients were administered the University of Pennsylvania Smell Identification Test (UPSIT), the Stroop Color-Word Test (Stroop), and the Positive and Negative Syndrome Scale (PANSS). **Outcome measures:** Scores on these tests and relation among scores. **Results:** There was a convergence of UPSIT and Stroop interference scores consistent with a common cerebral basis for limitations in olfactory identification and inhibition of distraction. There was also a divergence of UPSIT and Stroop reading scores suggesting that the olfactory identification limitation is distinct from a general limitation of attention or a dysfunction of the left dorsolateral prefrontal cortex. Most notable was the 81% classification convergence between the UPSIT and Stroop incongruous colour naming scores compared with the near-random 57% classification convergence of the UPSIT and Stroop reading scores. **Conclusions:** These data are consistent with a right orbitofrontal dysfunction in a subgroup of patients with schizophrenia, although the involvement of mesial temporal structures in both tasks must be ruled out with further study. A multifactorial model depicting contributions from diverse cerebral structures is required to describe the pathophysiology of schizophrenia. Valid behavioural methods for classifying suspected subgroups of patients with particular cerebral dysfunction would be of value in the construction of this model.

Objectif : Vérifier la validité discriminante d'un modèle prédisant une dissociation entre des mesures de la fonction des lobes frontaux gauche et droit chez des personnes atteintes de schizophrénie. **Participants :** Vingt-et-un patients atteints de schizophrénie, stables et traités en service externe. **Interventions :** On a administré aux patients le test d'identification des odeurs de l'Université de la Pennsylvanie (UPSIT), le test des mots et couleurs de Stroop (Stroop) et l'échelle des syndromes positifs et négatifs (PANSS). **Mesures de résultats :** Résultats obtenus à ces tests et relation entre les résultats. **Résultats :** On a constaté, entre les résultats du test UPSIT et les résultats d'interférence du test Stroop, une convergence conforme à une cause cérébrale commune de limitations de l'identification olfactive et de l'inhibition de la distraction. On a constaté aussi une divergence entre les résultats du test UPSIT et les résultats de lecture du test Stroop qui indique que la limitation de l'identification olfactive est distincte d'une limita-

Correspondence to: Dr. Scot E. Purdon, Neuropsychology - 9 Building, Alberta Hospital Edmonton, Box 307 17480 Fort Rd., Edmonton AB T5J 2J7; fax 403 472-5398; spurdon@gpu.srv.ualberta.ca

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tion générale de l'attention ou d'une dysfonction du cortex préfontal dorsolatéral gauche. On a remarqué surtout la convergence de classification, établie à 81 %, entre les résultats du test UPSIT et les résultats de la désignation incongrue des couleurs du test Stroop comparativement à la convergence de la classification quasi aléatoire, qui a atteint 57 %, des résultats obtenus au test UPSIT et des résultats de lecture obtenus au test Stroop. **Conclusions :** Ces données sont conformes à une dysfonction orbitofrontale droite chez un sous-groupe de patients atteints de schizophrénie, même s'il faut exclure au moyen d'une étude plus poussée l'atteinte des structures mésio-temporales dans le cas des deux tâches. Il faut un modèle multifactoriel décrivant les contributions de diverses structures cérébrales pour décrire la pathophysiologie de la schizophrénie. Des méthodes comportementales valides permettant de classer des sous-groupes de patients chez qui l'on soupçonne une dysfonction cérébrale particulière seraient utiles pour construire ce modèle.

Introduction

The heterogeneity of clinical syndromes and the myriad of potential etiologies have hampered efforts to come to a consensus on the principal cerebral pathology of schizophrenia. Although cognitive impairment and cerebral anomalies are readily demonstrable in samples of people with schizophrenia, the pathophysiological relevance of these aberrations has remained elusive. The confusion is clearly evident at the gross level of cerebral lateralization of pathology. Early models postulating left hemisphere involvement[1,2] were initially supported by neuropsychological impairment,[3,4] and subsequently by left hemisphere anomalies found on single photon emission computed tomography (SPECT), positron emission tomography (PET) regional cerebral blood flow (rCBF), functional PET (F-PET) and topographic electroencephalography.[5–10] However, recently a number of authors have advanced arguments for a right hemisphere contribution as well,[11,12] and the pathophysiological exclusivity of the left hemisphere has been challenged by right hemisphere dysfunction suggested by psychometric data, guanosine triphosphate binding irregularities, neurological soft signs in early development, and PET rCBF.[3,13–15] Thus, there is considerable disagreement about the primary cerebral pathology of schizophrenia even at the gross level of the cerebral hemispheres. A rapprochement may be achieved by considering a model that posits unique contributions from each cerebral hemisphere to the clinical symptoms and cognitive impairments evident in schizophrenia.

The relative contributions of the right and left cerebral hemispheres to variants of personality structure and psychopathology have been discussed in the literature for many years and recently generalized to schizophrenia. In the original formulations, a right orbitofrontal dysfunction was related to a syndrome of pseudopsychopathy characterized by disorganized affect, speech and behaviour, whereas a left dorsolateral prefrontal dysfunction was related to a syndrome of pseudodepression characterized by a poverty of affect, speech and behaviour.[16,17] The model was extended to schizophrenia in a series of creative studies by Liddle and colleagues[18–22] implicating structures in the region of the right prefrontal and mesial temporal cortex in a disorganized syndrome and the left dorsolateral prefrontal cortex in a psychomotor poverty syndrome. The clinical syndromes were defined by factor analysis of a multitude of symptoms resulting in the extraction of 3 syndrome variants, 2 of which were subsequently related to the prefrontal cortex.[18] The disorganization syndrome was associated with an interference score on the Stroop Color-Word Test.[19] The Stroop Color-Word Test interference score has been linked to the integrity of the right orbitofrontal cortex in healthy normal people in 1 study demonstrating PET activation of this region with the Stroop test,[23] although the precise selectivity of the Stroop test for the integrity of a circumscribed region of the right frontal cortex has been questioned by evidence of PET activation of the right superior mesial cortex[24] and the bilateral anterior cingulate.[25,26] The preliminary evidence of right cerebral hemisphere involvement in the disorganization syndrome provided by the Stroop test was supplemented by evidence of PET rCBF hypoperfusion in similar regions.[20,21] In contrast, the psychomotor poverty syndrome was associated with Stroop Color-Word Test reading score.[19] Verbal production has long been associated with left dorsolateral prefrontal cortex,[27,28] suggesting that the association between Stroop reading scores and the psychomotor poverty syndrome may represent left dorsolateral prefrontal cortical dysfunction, a postulate that was also recapitulated in PET

rCBF hypoperfusion.[20–22] There has been 1 independent replication of the association between psychomotor poverty and left dorsolateral prefrontal dysfunction, but this study did not confirm the association between disorganization and right orbitofrontal cortex.[29] The original work, however, raises the possibility of bilateral cerebral pathology in schizophrenia with discrete contributions from each hemisphere to the cognitive impairments and perhaps the clinical manifestation of symptoms. The difficulty replicating the original observations may well result from the paucity of valid behavioural measures that are selective for right orbitofrontal cortical activity, a methodological limitation that may be improved by considering olfactory identification.

A series of studies by Kopala et al[30–33] has underscored the potential relevance of the right orbitofrontal cortex with a large subgroup of men with schizophrenia who showed olfactory identification impairment on the University of Pennsylvania Smell Identification Test (UPSIT). With only 1 exception,[34] the olfactory identification impairment has been replicated in a number of independent laboratories.[12,35,36] The olfactory system emanates from each nostril in a predominantly ipsilateral fashion along the olfactory bulb within 3 layers, with the medial layer projecting to the contralateral anterior olfactory nucleus, the intermediate layer projecting to the ipsilateral olfactory tubercle, and the lateral layer projecting ipsilateral to a variety of mesial temporal structures including the pyriform, amygdaloid complex and entorhinal cortex.[37] The orbitofrontal cortex, in turn, receives direct input from the olfactory tract, as well as secondary inputs from the mesial temporal structures and indirect input from the pyriform via the medial dorsal nucleus of the thalamus.[38,39] The significance of this convergence of olfactory information on the right orbitofrontal cortex has been suggested from a series of ablation and PET studies.[38–40] For example, the greatest impairment in UPSIT performance was shown with orbitofrontal cortex or right frontotemporal lesions, when compared with lesions involving the temporal lobe or with lesions of frontal cortex that did not impinge upon the orbitofrontal region.[39] A deficit in olfactory identification in schizophrenia could thus implicate pathology in the right orbitofrontal cortex or in the afferent and efferent projection fibres involved in this region. This hypothesis has received support recently from an association between olfactory identification deficits and smooth pursuit eye movement (SPEM) abnormalities[41] and from a dissociation between olfactory identification deficits and perseverative errors on the Wisconsin Card Sort Test (WCST).[12] Ocular pursuit is a classic measure of bilateral frontal integrity[42] and hence provides compelling preliminary evidence to implicate prefrontal cortical dysfunction in the olfactory limitation in schizophrenia. WCST perseveration has been linked to dorsolateral prefrontal cortical dysfunction by both PET rCBF and lesion studies,[43–46] as well as to predominant left hemisphere involvement by studies of missile wounds and lobectomy.[47,48] When considered with the absence of an association between the UPSIT and WCST perseveration, the presence of an association between the UPSIT and SPEM may represent a predominantly right hemisphere orbitobasal dysfunction that is distinct from left dorsolateral prefrontal involvement.

Along with the indirect evidence of an association between olfactory identification limitations and right orbitofrontal function in people with schizophrenia, there is some indication that the olfactory limitation cannot be entirely attributed to the peripheral effects of smoking or medication, nor is it easily attributed to a general attention deficit. Smoking and a wide range of medications have been shown to influence olfactory identification performance, likely by compromising the epithelial surface.[49,50] Although only 1 prospective control-group study has been published on smoking,[35] the results support other post-hoc comparisons and analyses of covariance that have suggested that the olfactory identification limitations in people with schizophrenia do not depend entirely on whether a person smokes.[12,33,51] Further, a medication hypothesis is insufficient to account for observations from controlled studies of people with schizophrenia not taking medication who also exhibit impaired olfactory identification.[33,36] The olfactory identification deficit is no less susceptible than other cognitive measures to the confounding effects of a general attention deficit expounded by Chapman and Chapman[52] and reiterated by others.[53,54] However, there are reports of a dissociation between olfactory identification performance and colour identification,[55] as well as a dissociation between olfactory identification and perseveration on the WCST,[12] both of which argue against general attention deficit being sufficient to account for the olfactory deficit. The exclusion of peripheral and attentional deficits in the olfactory identification limi-

tation raises the possibility that it may provide a sensitive and selective measure of right frontal dysfunction in people with schizophrenia.

The utility of the olfactory identification impairment for isolating right frontal cortical dysfunction in people with schizophrenia is contingent on the discriminant validity of the putative association. There is direct evidence to suggest that the olfactory impairment is not entirely the result of peripheral damage or psychometric artifact, but there is a lack of empirical evidence to implicate this limitation in the delineation of right orbitofrontal cortical dysfunction. As reviewed above, previous investigations have linked the olfactory identification limitation to right orbitofrontal dysfunction by an association with SPEM and a dissociation from perseveration, but there has, as yet, been no direct test of cerebral specificity. This study examined the discriminant validity of the olfactory identification deficit by directly testing a predicted convergence with Stroop interference scores and a predicted divergence from Stroop reading scores.

Method

Thirty-one clinically stable outpatients who gave signed consent were recruited from the Royal Ottawa Hospital, Ottawa, Ont. The protocol was reviewed and accepted by an institutional ethics review panel. Diagnosis was based on chart documentation and independent clinical examinations by psychiatry and clinical psychology staff. Eliminated from the group were 4 patients with recent electroconvulsive therapy, 1 patient with chronic alcohol abuse, 2 patients with mental retardation and 3 patients for whom there were incomplete data. One person reported remote previous cocaine use and 4 people reported remote previous hashish and marijuana use but they were not excluded from the analysis. Three people who reported significant trauma to the nasal region were excluded for other reasons. The presence of a previous head injury was not adequately assessed and hence was not used to exclude anyone. Of the remaining 21 people, 18 were men and 3 were women, with an average age of 37.14 years (standard deviation [SD] 9.60), education of 12.07 years (SD 2.27), and age of onset of 20.94 years (SD 4.12). Nineteen participants were receiving routine neuroleptic treatment and the remaining 2 were not taking any medication. Most of the sample (14/21) were chronic smokers of approximately 20 to 25 cigarettes per day, with a duration ranging from 2 to 38 years.

Each participant was administered an olfactory dysfunction questionnaire to eliminate obvious peripheral contributions before completing the UPSIT[30] and the Stroop Color-Word Test.[56,57] With assistance from nursing staff, a clinician who was blind to the psychometric results administered the Positive and Negative Syndrome Scale (PANSS), a standard rating tool for the symptoms of schizophrenia.[58] Detailed results from the PANSS assessment have been submitted in a supplementary report. The Stroop test was administered in 3 phases as described by Golden,[57] with scores provided for reading lists of colour words in black ink (RCW), naming the colour of a series of Xs (NCX), and naming the ink colour of incongruous colour words (NCW). Dependent variables were the number of items achieved over 45-second intervals (i.e., RCW, NCX, NCW), as well as an index of interference (Stroop II) corrected for speed by subtracting from the observed incongruous colour naming score (NCW) a predicted score derived from naming colours and reading words. Hence, Stroop II = NCW – (NCX + RCW / NCX × RCW). Performance on the interference measure is deemed to represent response conflict created by a rapid processing of the colour word, which interferes with the naming of an incongruous colour. The UPSIT was also administered and scored according to standard convention.[30] It is a 40-item, multiple-forced-choice test in which subjects scratch an area containing a micro-encapsulated odour and match the exuding smell to 1 of 4 given alternatives. Participants were classified using the Doty[30] criteria applied to the total correct scores, with malingering in the 0 to 5 range, anosmia in the 6 to 19 range, microsmia in the 20 to 33 (men) or 20 to 34 range (women), and normosmia at 34 to 40 (men) or 35 to 40 (women).

Results

Ratings of psychopathology documented a mild severity of positive and global symptoms and a mild to moderate severity of negative symptoms (PANSS positive mean 12.76, SD 4.70; global mean 29.43, SD 9.29; negative mean 17.43, SD 5.90) consistent with a clinically stable sample of outpatients with residual negative symptoms.

Olfactory identification impairment was evident

with an overall mean in the microsmic range (mean 31.00, SD 5.92, range 17 to 38). Classification revealed 5% (1/21) with anosmia, 43% (9/21) with microsmia, and 52% (11/21) with normosmia. The person who was anosmic and all those who were normosmic were men. The 2 people who were not taking any medication were both classified as normosmic. Age and smoking status accounted for a small (5% and 6%, respectively) and statistically nonsignificant proportion of the variance in UPSIT scores, which also showed no difference between smokers (mean 31.27, SD 6.56) and nonsmokers (mean 31.40, SD 3.85). The observed proportion of participants with hyposmia (48%) is consistent with previous reports of samples in which patients were not receiving medication (e.g., 42% in the study by Kopala et al[32]). The minute effects of smoking and age also replicate earlier findings.[12,33] The observed normosmia in people not taking any medication is inconsistent with previous reports of olfactory impairment in patients who were not receiving medication.[33,36]

Age-corrected standardized Stroop T scores, which have a normative average of 50 and SD of 10, showed mild to moderate impairment of colour naming (NCX mean 34.29, SD 9.65) and incongruent colour naming (NCW mean 36.24, SD 11.9), mild impairment of colour reading (RCW mean 39.10, SD 9.41), and no impairment of the interference index (Stroop II mean 47.05, SD 8.50). Thus, these results replicate earlier demonstrations of colour naming and incongruent colour naming impairment in patients with schizophrenia,[19,59] as well as an interesting normalization of interference scores across the sample after correction for reading speed and colour naming.

The predicted convergent and divergent discrimination pattern between olfactory identification and Stroop Colour-Word Test performance was confirmed. The UPSIT total score was significantly correlated with colour naming speed ($r = 0.57$, $p = 0.006$), incongruous colour naming speed ($r = 0.63$, $p = 0.002$), and the interference index ($r = 0.44$, $p = 0.047$) and no statistical association was observed with colour reading speed ($r = 0.22$, $p = 0.33$). This pattern is particularly striking when considered within the context of the sample stratified by UPSIT status (normosmic versus hyposmic UPSIT scores are less than 34 for men and less than 35 for women) and Stroop status from incongruent colour naming (spared versus impaired defined by performance less than 1.50 SDs below the mean given by NCW T scores of less than 35). The UPSIT and Stroop scores converged on impairment in 43% of the sample and converged on spared function in 38% of the sample, for an 81% classification agreement. There was only 1 false-positive result on the UPSIT (i.e., hyposmic with spared Stroop score) and 3 false-positive results on the Stroop test (i.e., normosmic with impaired Stroop score), for a 19% classification disagreement. In contrast, minimal evidence for convergence was obtained between UPSIT and the Stroop colour reading scores. Convergent impairment was observed in only 14% and convergent sparing in 43%, yielding a false-positive rate of 33% on the UPSIT and of 9% on the Stroop test, for a total of 57% agreement and 42% disagreement, which is clearly no better than chance. Thus, there is a strong association between UPSIT and Stroop incongruous colour naming score that cannot be attributed to a generalized decrement in performance.

Discussion

The scientific pursuit of reliable neuroanatomical and neurophysiological anomalies in people with schizophrenia has been arduous and, for the most part, ungratifying. This is readily apparent when considering the lateralization of cortical dysfunction, which cannot be specifically related to either a discrete left or right hemisphere pathologic process. Recent syndrome studies, however, have provided evidence of apparently discrete and dissociable contributions from each hemisphere. This might offer a model for the assimilation of the apparent discrepancies between previous laterality studies. The original work by Liddle et al[18] linking a disorganization syndrome to right frontal dysfunction has proven difficult to replicate, possibly due to limitations in the *a priori* identification of people with discrete lateralized impairment. Olfactory identification may facilitate this delineation because it is sensitive, although not entirely specific, to damage in the right orbitofrontal cortex. Previous research has indirectly implicated olfactory identification for this purpose through its association with eye movement and its dissociation from perseveration on the WCST.

These results provide the first direct evidence to suggest the discriminant validity of olfactory identification as a measure of circumscribed cerebral pathology in people with schizophrenia. Thus, it contradicts attributions of the impairment to peripheral factors or

a general attention deficit. The olfactory identification deficit was linked to right orbitofrontal function by an effective discrimination between convergence on a putative measure of right orbitofrontal or anterior cingulate integrity (i.e., the Stroop incongruous colour naming test and Stroop interference index) and divergence from a putative measure of left dorsolateral prefrontal function (i.e., Stroop colour reading test). The magnitude of the association is evident in the remarkable 81% classification convergence between olfactory identification and incongruous colour naming, compared with the diminished and near-random convergence of 57% between olfaction and a measure of left dorsolateral prefrontal function. The association between olfactory identification and incongruous colour naming is strong and cannot easily be attributed to a deficiency of attention. These results represent an opening bid in the effort to fill the gap in our knowledge about the potential value of the olfactory identification limitation to investigations of cerebral pathology in people with schizophrenia.

The olfactory identification deficit in people with schizophrenia is a stable phenomenon that cannot be easily attributed to a generalized attention deficit. This study revealed such a deficit in 48% of the sample, very similar to that reported in a previous study of similar patients receiving neuroleptic medication (i.e., 42% in Kopala et al[32]). It is also unlikely that the olfactory limitation is a consequence of general attentional factors alone because it was dissociated from reading speed, a result that is consistent with previous demonstrations of a dissociation between olfactory identification and attention measured by the WCST.[12] Moreover, the general-attention-deficit argument is prefaced on the expectation that people with schizophrenia would show more impairment on tests with heightened sensitivity to differences in normal people,[52,54] an assumption that cannot be easily generalized to colour naming or colour reading and is contradicted by the similarity of statistical variance on these tasks in our study (i.e., Stroop word SD 9.41; interference SD 8.50; incongruent colour naming SD 11.90). It may be difficult to rule out sensitivity or ceiling effects from the differential deficits observed in previous studies of attention and the olfactory identification deficit,[36,60] but such artifacts provide a less compelling account of our findings.

The pathognomonic specificity of the olfactory identification limitation to people with schizophrenia remains to be determined. In particular, despite assurances from previous studies that smoking and medication status cannot account for the olfactory limitations, there have been few controlled investigations of these potential confounding factors. Comparisons among studies show only slightly more diminution of the olfactory limitation in patients not receiving medication (30%; Kopala et al[32]) than in those receiving medication (25%; Kopala et al[33]), suggesting that the identification limitation as a central marker is prone to occasional false-positive errors. The normosmia observed in both subjects not receiving medication in our study is consistent with this view and underscores the need for additional controlled investigations of medication effects. Although most of the sample was receiving neuroleptic treatment, it is unlikely that medication contributed to the convergence of impairment because there is no documented evidence of a negative effect of neuroleptic treatment on Stroop test performance but there is evidence of a potential facilitative effect.[61,62] A similar argument applies to the confounding effect of cigarette smoking, which is common in people with schizophrenia and has a robust association with olfactory identification in normal people.[30] The people in the sample reported here showed a minor effect of smoking, consistent with results from the only controlled study demonstrating olfactory impairment among nonsmokers with schizophrenia,[35] and with the results from other investigations that have drawn similar conclusions from post-hoc comparisons and analyses of covariance.[12,33] Thus, although smoking likely contributes to the false-positive error rate in the delineation of an olfactory deficit group, this effect may be relatively minor. Moreover, studies of smoking effects on the Stroop Color-Word Test show either that smoking has no effect or that nicotine has a facilitative effect on performance.[63,64] It is unlikely, therefore, that the convergence between olfactory identification and Stroop test limitations can be attributed to peripheral effects from either medication or smoking. This study did not exclude people who had suffered head injuries. Hence, the possibility that trauma accounted for the impairment cannot be ruled out.

One deviation from previous reports on olfaction in people with schizophrenia was the observation that all 3 women had olfactory identification limitations, an effect out of keeping with previous demonstrations of relatively intact olfactory identification among women (i.e., normosmia in 14/15 of women in the

study by Kopala et al[32] and 9/10 of those in the study by Kopala et al[33]). This finding may relate to the relatively advanced age of the women in this study (40, 48 and 50 years), given recent evidence suggesting diminished postmenopausal olfaction in women with schizophrenia.[60] A sensitive measure of olfactory acuity was not included in this study, but an attribution of the anomalous effect of sex to a peripheral detection deficit is unlikely, given the fact that all 3 women were also classified as deficient on the Stroop incongruent colour test. An attribution of these effects to a general attention factor is equally unlikely, given that all 3 women were within normal limits on the Stroop colour reading test. The effect of sex does, however, require additional investigation, particularly given that premenopausal young women with schizophrenia consistently outperform men on the olfactory identification test,[60] and that young normal women not only outperform men on the Stroop test but also show monthly variations, with a midcycle peak in performance.[65] Together, these effects may suggest a right orbitofrontal interaction between neuroendocrine and cerebral function, with considerable relevance to the onset and course of cerebral pathology in people with schizophrenia.

The convergence on right orbitofrontal dysfunction provides another step toward solving the perennial problem posed by the clinical and cognitive heterogeneity of the disorder and may provide an indication of relevant cerebral structures. Considerable work remains, however, before we can conclude that a combination of test scores provides a definitive index of right orbitofrontal dysfunction in schizophrenia. A replication of our findings is essential, and additional multimeasure data will be necessary from psychometric investigation, functional neuroimaging and structural neuroimaging before declaring a neuroanatomical or neurophysiological mechanism for the deficits. Moreover, additional emphasis on the apparent normalization of the interference index in people with schizophrenia with corrections for processing speed will be required to further disentangle the relative contributions of lateralized cortical activity. The current data, however, suggest a valid method for the *a priori* selection of people with schizophrenia who are most likely to show anomalies in the right orbitofrontal regions. The confidence with which such a classification scheme is applied, and the relevance of such an application to an understanding of cerebral structure and function, is also contingent on additional documentation that the olfactory limitation in schizophrenia is not the product of peripheral sensory dysfunction in the nasal cavity, the epithelial surface or the olfactory receptor cells. Subsequent research must also emphasize and rule out paleo- and neocortical pathology in the olfactory bulb, the anterior olfactory nucleus, the olfactory tubercle, the pyriform cortex, the amygdaloid complex, the entorhinal cortex and the thalamus. All of these structures have been implicated in the pathology of schizophrenia, but they also have bilateral representation. Continued documentation of the relevance of right cerebral dysfunction will allow additional confidence in attributing the prefrontal cortex to the cerebral localization of the olfactory limitation in schizophrenia. This research is necessary to delineate reliable parameters in a model of schizophrenia that recognizes the diverse — but not amorphous — range of neural circuitry involved in the clinical symptoms and cognitive impairments associated with this often devastating disorder.

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