are found] as well as in insect testis (*15*) where a blood-germ cell barrier occurs. Other investigators who have not found insect tight junctions, possibly because they are difficult to detect by virtue of their relative simplicity, have suggested that septate junctions are the basis of all occluding phenomena in invertebrates (*10, 16*). However, I have found that tracers are able to move completely through septate junctions, and comparable events also occur in such insect tissues as Malpighian tubules, where inulin (molecular weight, 5200) readily traverses the septate junctions between adjacent cells (*17*). The tight junctions observed appear to prevent the inward movement of lanthanum as they do in the insect CNS (*5, 6*) and so may be presumed to be the structures which impede the inward diffusion of molecules, forming a blood-basal rectal cleft barrier.

It would be premature, however, to generalize from these observations that the role of the septate junctions in controlling transepithelial permeability has been completely eliminated in all situations. Studies of more primitive systems such as coelenterates and planarians (*18*) strongly implicate septate junctions as a barrier to the paracellular flow of water and small molecules across epithelia in their tissues.

In summary, this report presents another example of tight junctions in arthropods, which strengthens the case for their existence in invertebrates; it also weakens the argument that septate junctions are the invertebrate equivalent of the vertebrate tight junctions in forming the structural basis of permeability barriers. Moreover, the restriction of occluding tight junctions to the basal region of a fluid-transporting epithelium involved in water and ion resorption, wherein the luminal clefts are open to inward diffusion of tracers, suggests the possibility that the junctions are actively involved in the regulation of unidirectional fluid flow in a way that would permit intercellular transport of the water flowing into and through the system.

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Brain Norepinephrine and Dopamine in Schizophrenia

Farley *et al.* (*1*) reported that increased levels of norepinephrine (NE) were found in certain limbic regions of schizophrenic brain. However, we offer a word of caution about using small numbers of cases from a heterogeneous population. We have measured dopamine (DA) and NE in the striatum and three limbic regions in more than 50 patients who died with a hospital diagnosis of schizophrenia (Table 1). We found a significant increase in DA concentration in the nucleus accumbens, confirming our finding reported in an earlier, smaller series (*2*). In addition, the DA concentration in the anterior perforated substance was significantly increased (Table 1). Although we, like Farley *et al.*, found that the NE concentration was increased in the nucleus accumbens, this result was not statistically significant. Similarly, the apparent increase in NE in anterior perforated substance was not statistically significant when analyzed by a nonparametric test (since the NE values show a skew distribution the Student's *t*-test is not applicable). When the NE values obtained by Farley *et al.* in the nucleus accumbens are compared with our own, it seems likely that differences in defining this anatomical region may exist between our laboratories. Although the NE values they report for the ventral septum and hypothalamus are in accord

Table 1. Norepinephrine and dopamine in limbic and basal ganglia regions of postmortem brain from psychotic patients and controls. The statistical significance was determined with a two-tailed *t*-test; S.E.M., standard error of the mean; *N*, number of brains.

Brain region	Norepinephrine (μg per gram of protein)		Dopamine (μg per gram of protein)	
	Mean ± S.E.M.	*N*	Mean ± S.E.M.	*N*
Nucleus accumbens				
Controls	1.3 ± 0.13	40	12.2 ± 0.95	46
Psychotic	1.8 ± 0.18*	47	16.3 ± 1.03†	51
Anterior perforated substance				
Controls	0.7 ± 0.11	25	1.9 ± 0.3	32
Psychotic	1.4 ± 0.24‡	35	3.7 ± 0.58§	37
Ventral septum				
Controls	4.2 ± 0.71	35	1.4 ± 0.14	35
Psychotic	4.2 ± 0.10	32	1.6 ± 0.15	32
Caudate				
Controls	0.7 ± 0.10	47	17.3 ± 1.27	51
Psychotic	0.5 ± 0.06	44	19.7 ± 1.35	50
Putamen				
Controls			22.0 ± 2.3	29
Psychotic			22.9 ± 2.2	37

*P = .129, Mann-Whitney U test. †$P < .005$ when compared with control, Student's *t*-test or Mann-Whitney U test. ‡P = .067, Mann-Whitney U test. §$P < .02$, when compared with control, Student's *t*-test or Mann-Whitney U test.

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with ours, those in the nucleus accumbens are about ten times higher than the values we obtain. This therefore stresses the need for standardized dissection of the human brain or an anatomical description of a region to accompany neurochemical data. Such differences in dissection procedure and other possible technical factors (*3*) may explain our failure to confirm the increase in NE content of ventral septum in schizophrenia reported by Farley *et al.* (*1*). Since three of their four cases had committed suicide their results may not be typical of the larger psychotic population that we have sampled. We concur with the suggestion of Farley *et al.* that it will be important to examine a larger series of cases and agree about the difficulties of interpreting changes in catecholamine content in the brains of patients with schizophrenia who have received long-term treatment with neuroleptic drugs.

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3. Our results are expressed per gram of protein, since we find variable water content in paraventricular regions in frozen brain tissue.

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The report by Farley *et al.* (*1*) on the norepinephrine patterns in four brains from patients they diagnosed as paranoid schizophrenic is clinically an anachronism. Diagnosis was made by Bleuler's criteria, which are really no criteria at all as they have no reported reliability or validity. It is also unlikely that of four "schizophrenics" three committed suicide, a sequela more suggestive of affective disease. Farley *et al.* could have used one of several sets of modern research criteria (*2*), each supported by reliability and validity data. Their failure to do so has left us with a non sequitur of "hard data."

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We fully agree with Taylor (*1*) that criteria other than Bleuler's could have been used in classifying our psychotic patients. We doubt, however, that this would have influenced the significance of our biochemical study (*2*). The fact that in all of our four patients the direction as well as pattern of limbic norepinephrine (NE) changes was the same strongly argues in favor of diagnostic homogeneity of the patient material studied. This is all that a valid clinical classification, be it Bleulerian or otherwise, can possibly be expected to provide—considering the arbitrary nature of all presently available diagnostic criteria for schizophrenia. In respect to Taylor's remark on suicide and schizophrenia, we fully disagree. First, it is textbook knowledge that in schizophrenia suicide is not uncommon, with "more schizophrenics than manic-depressives commit[ting] suicide" (*3*). Second, and more to the point of studies such as ours, postmortem brain studies in a per se nonlethal illness such as schizophrenia heavily depend on suicide material that is autopsied in the medical examiner's office and therefore more readily available (and in a better condition for postmortem studies) than cases dying of natural causes in chronic psychiatric institutions.

We could not agree more with Bird *et al.* (*4*) regarding the need for a standardized dissection procedure of human brain as the basis for meaningful comparisons of biochemical data obtained in different laboratories. As they correctly observe, their and our areas of nucleus accumbens almost certainly represent two anatomically different entities; this also applies to the area of ventral septum, which, in our dissection, is identified by its characteristic topographic relation to what we define as nucleus accumbens. In view of these crucial differences regarding anatomical definitions, the failure of Bird *et al.* to find significant changes in NE levels in these two regions, as defined in their dissections, has no bearing on our positive results (*2*). Although our sample size of schizophrenics was small, it was diagnostically homogeneous (as discussed above). Most important, the measured differences, especially in the bed nucleus of the stria terminalis and the ventral septum, were large and statistically highly significant. Although using large numbers of cases may make small deviations from normal statistically significant [as the relatively small increase of dopamine in nucleus accumbens in schizophrenics shown by Bird *et al.* in their table 1 (*4*)] the pathophysiological significance of a given (biochemical) alteration is not determined by sample size but by the degree of the observed change. We enviously congratulate Bird *et al.* on the large number of schizophrenic cases that they had been able to collect and analyze. Since the hospital diagnosis of schizophrenia was sufficient for inclusion in their study, their case material, in sharp contrast to our material, probably represented a highly interesting collection of several subtypes of schizophrenic illness. It would not be surprising if by appropriate subgrouping of their case material, a different and more interesting biochemical picture emerged than that shown in their table 1. In this respect, it may be relevant that Kleinman *et al.* (*5*) reported above-normal NE levels in the nucleus accumbens of two paranoid schizophrenics; similarly, Carlsson (*6*) observed highly significant above-normal mesencephalic NE levels in three cases of paranoid schizophrenia. Neither group found any NE abnormalities in nonparanoid schizophrenics or other psychotics.

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