rights inoculated with media alone did not wilt, and no bacteria were isolated from any of them. In a separate test, sugarcane isolates from Louisiana, Brazil, South Africa, and Japan incited wilting of uprights, but Bermuda grass isolates again did not.

Although no serological relation has been found between the RSD bacterium and numerous other species of bacteria (*13*), including *Corynebacterium tritici*, *C. rathayi*, *C. flaccumfaciens*, *C. michiganense*, *C. nebraskense*, *C. fascians*, and *C. insidiosum*, the sugarcane and Bermuda grass strains morphologically appear to be members of the group of coryneform bacteria pathogenic to plants. All the sugarcane and Bermuda grass isolates were aerobic, nonmotile, Gram-positive, non-acid-fast, catalase-positive, and oxidase-negative. Apparently the two strains are closely related species or are different pathovars of the same species of a xylem-inhabiting pathogen. Cultivation of the RSD causal agent in vitro will greatly enhance efforts to study and control the disease.

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Functional Development of Grafted Vasopressin Neurons

Abstract. *Vasopressin neurons, transplanted from normal rat fetuses into the third ventricle of adult Brattleboro rats, alleviate the polydipsia and polyuria of the hosts. Determination of the antidiuretic activity of grafted neurons in hosts with congenital diabetes insipidus provides a convenient model for analyzing the development, plasticity, and function of transplanted central nervous system neurons in mammals.*

A major problem in neurobiology concerns delineating the neuroplasticity of the central nervous system (CNS). A useful technique for investigating this has been the transplantation of neural tissue (*1*). Although neural transplants often demonstrate the morphological and physiological properties of normal tissue (*2*), their ability to provide appropriate and meaningful input to the host is un-

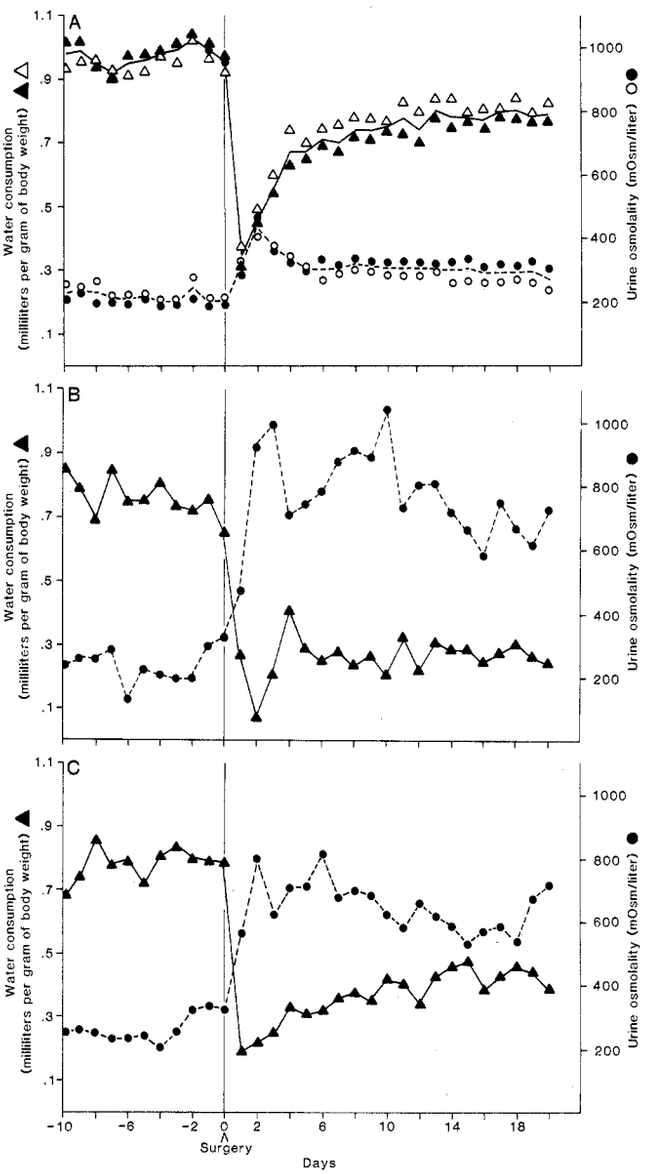

Fig. 1. Effects of surgery and transplantation in the control and experimental rats. (A) The average daily consumption of water by the sham-operated rats (△, $N = 11$) and the control tissue-implanted rats (▲, $N = 18$) is indicated by the solid line. The average osmolality of the urine is plotted on the same graph. Since we did not measure osmolality for all the controls, the sample size is smaller; $N = 8$ for the sham-operated rats (○) and $N = 10$ for the rats with occipital cortex implants (●). The standard error for each daily average was ≤ 0.04 ml for water consumption and ≤ 43 milliosmoles for urine osmolality. In some of the experimental animals [(B) a rat that received vasopressin neurons from a 17-day-old fetus and (C) a rat that received such tissue from a 19-day-old fetus], there were sustained decreases in water consumption and sustained increases in urine osmolality. Changes of these magnitudes were never observed in the control animals.

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clear. To address this issue, we developed a model system for analyzing both the development and the degree of function of neural grafts. Our method involves transplanting vasopressin neurons from the hypothalamic neurosecretory system of normal donors into Brattleboro rats, which congenitally lack vasopressin-producing neurons (*3*). Amelioration of the symptoms of diabetes insipidus in the host is then evaluated as a correlate of the function of the transplant. Due to the lack of vasopressin, Brattleboro rats exhibit pronounced polydipsia and polyuria (*4*). A dose-dependent decrease in water consumption and a concomitant increase in urine osmolality occur when vasopressin is administered to these animals.

It was recently shown that the fetal hypothalamus can survive transplantation (*5*, *6*). The present study was conducted to ascertain the antidiuretic influence of transplanted fetal hypothalamic tissue and to quantify the vasopressin content in the grafts. Adult female Brattleboro rats, homozygous for the diabetes insipidus trait, were divided into three test groups: sham-operated control rats (N = 11), control tissue-implanted rats (N = 18), and anterior hypothalamus-implanted rats (N = 40). Using procedures described elsewhere (*5*), we dissected the anterior hypothalamus from the brains of 17- and 19-day-old Wistar-Lewis rat fetuses. For a tissue control, a block of tissue of the same size was taken from the occipital cortex of the fetuses. The tissue was stereotaxically grafted into the third ventricle of hosts anesthetized with Brevital Sodium (40 mg per kilogram of body weight). Identical surgical procedures were followed with the sham-operated animals, which received no tissue, but rather an injection of physiological saline. All test animals were monitored in metabolism cages for 10 days before surgery and 20 days afterward. The daily water consumption of each animal was measured, and urine volume and osmolality were determined for 8 of the sham-operated controls, 10 of the control tissue-implanted rats, and 32 of the rats with hypothalamic transplants. Between 20 and 22 days after surgery the host animals were decapitated and the region of the diencephalon containing the transplant was dissected out and homogenized for vasopressin radioimmunoassay (*7*) or processed for light microscopic immunocytochemistry (*8*).

Sham-operated rats and occipital cortex recipients showed about the same response to transplantation (Fig. 1A). In both control groups there was a significant decrease ($P < .01$, paired t-test) in water consumption and a significant increase ($P < .01$) in urine osmolality during the 20-day period after surgery; the differences between the control groups in water consumption and urine osmolality were not significant. It is possible that these changes were due to damage caused by the implantation techniques to the periventricular area of the hypothalamus, an area that is important in drinking behavior (*9*).

Based on the responses of the control groups, criteria were established for evaluating host responsiveness to transplantation of vasopressin neurons. A significant response was considered to consist of (i) daily water consumption falling below and remaining below 0.5 ml per gram of body weight for the 20-day period after transplantation and (ii) urine osmolality increasing above and remaining above 500 milliosmoles per liter for the 20-day period. None of the control animals met either of these criteria, while 9 of the 40 experimental rats met criterion (i). Five of the nine also met criterion (ii); two did not (urine osmolality data were not available for the remaining two). The response pattern was similar in the five animals that met both criteria (Fig. 1, B and C). Water consumption decreased markedly on the first day after implantation and remained depressed for the duration of the experiment. The converse was true for urine osmolality, which was above 800 milliosmoles per liter in the first 2 days and remained elevated throughout the experiment.

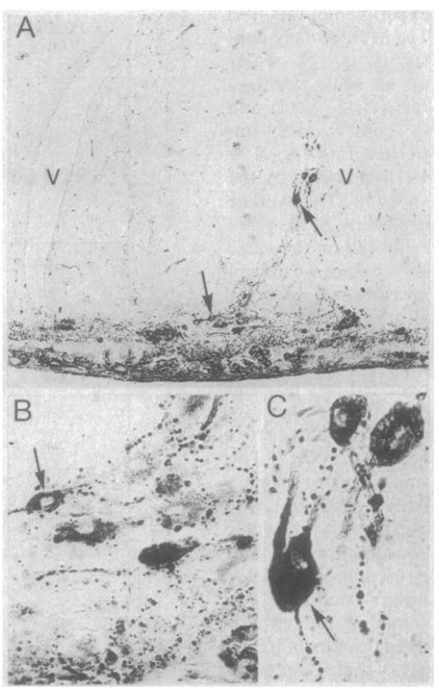

Fig. 2. (A) Coronal section of 17-day-old fetal hypothalamic tissue after immunocytochemical staining for neurophysin. The transplant is located in the distended third ventricle (*V*) of the host's diencephalon, attached to the ventricular surface of the median eminence. Neurophysin-containing perikarya (arrows) are seen at the interface between the median eminence and the transplant. (B and C) Higher magnification views of these neurons (arrows). Neurophysin-positive axonal processes were common features in the transplants and could often be traced to the vicinity of blood vessels. Magnifications: (A) ×60, (B) ×200, and (C) ×260.

The number of animals responding to both criteria was small, making statistical analysis difficult. Thus the issues to be determined were whether the responses in the animals with hypothalamic transplants could be best explained by the action of vasopressin and whether vasopressin was present in the transplanted tissue.

Since the urine of Brattleboro rats becomes more concentrated when they are deprived of water (*10*), it was appropriate to consider whether the changes in urine osmolality observed after transplantation reflect an action of vasopressin or a response to decreased water intake secondary to hypothalamic damage during transplantation. Brattleboro rats dehydrated for 24 hours achieve a urine osmolality of 696 milliosmoles per liter; however, these rats are severely dehydrated, as evidenced by a 20 percent reduction in body weight (*10*). Such dramatic alterations were not observed in the hypothalamic transplant recipients. Thus, the response observed in these animals suggests a functional action of vasopressin. The rapid and sustained response to transplantation indicates that the graft becomes functional in 3 to 4 days.

Vasopressin was identified in the anterior hypothalamus grafts by both immunocytochemistry and radioimmunoassay. Magnocellular neurons staining for neurophysin or vasopressin were identified in five of the nine transplants processed for light microscopic histology and immunocytochemistry (Fig. 2). Radioimmunoassayable vasopressin concentrations of 40 to 300 pg were measured in 9 of 31 grafts. The observation that some vasopressin-containing transplants did not promote antidiuretic changes in the host suggests that survival of the graft is, by itself, not sufficient to guarantee function. The connections that the transplanted vasopressin neurons make in the host brain, whether with blood vessels or other neurons, may be crucial in determining the antidiuretic activity of the graft. It is important to determine whether there are consistent morphological differences between functional and nonfunctional grafts.

The regenerative capacity of damaged adult CNS neurons is limited (*11*). Although regenerative sprouting of severed axons has been observed by many investigators, the formation of appropriate and functional synaptic connections has not been demonstrated and may be rare. The formation of dense connective tissue and neuroglial scars after CNS damage has been regarded as a significant barrier to neural regeneration (*12*). On the other hand, there is evidence that lesioned neonatal CNS neurons can regenerate in a functionally useful way (*13*). In an earlier study (*5*), we found that axons from transplanted vasopressin neurons coursed from the graft into the median eminence of the host. In normal animals, vasopressin is released into the circulation by axons terminating at capillaries in the median eminence and neural lobe (*14*). The presence of vasopressin in the hypothalamic grafts and the increased ability of some of the host animals to conserve water suggest that the axons of the grafted fetal neurons made appropriate and functional connections. Glial scarring in the host brain, resulting from our stereotaxic transplantation procedures, did not prevent functional development.

This study demonstrated that symptoms resulting from a congenital defect in the CNS of an adult mammal can be ameliorated by transplanted neurons. Additional evidence that brain grafts may function in the adult host was recently provided by Perlow *et al.* (*15*). Transplants of fetal dopamine neurons were found to reduce motor abnormalities resulting from lesions of the substantia nigra. The development of the ability to transplant neurons to correct CNS deficiencies, whether due to genetic defects, disease, or trauma, has extraordinary theoretical and clinical implications.

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Mental Symptoms in Huntington's Disease and a Possible Primary Aminergic Neuron Lesion

Abstract. *Monoamine oxidase activity was higher in the cerebral cortex and basal ganglia of patients dying from Huntington's disease than in controls. Enzyme kinetics and multiple substrate studies indicated that the increased activity was due to elevated concentrations of monoamine oxidase type B. Concentrations of homovanillic acid were increased in the cerebral cortex but not in the basal ganglia of brains of patients with Huntington's disease. These changes may represent a primary aminergic lesion that could underlie some of the mental symptoms of this disease.*

Huntington's disease (HD) is an autosomal dominant degenerative disease characterized clinically by mental symptoms including a schizophreniform psychosis and dementia, and the neurological signs of chorea (*1*). The pathophysiology of this disease has some bearing on understanding that of schizophrenia and the primary dementias.

The pathology of the basal ganglia (*1*) includes marked neuronal loss in the caudate nucleus, putamen, and globus pallidus; and relative sparing of the substantia nigra. A reduction in the basal ganglia of the activity of choline acetyltransferase (CAT) and glutamic acid decarboxylase (GAD) (*2, 3*) reflects these morphological changes. Muscarinic cholinergic, γ-aminobutyric acid (GABA), and serotonergic receptor densities are reduced in the basal ganglia (*4*). In contrast, the concentrations in the basal ganglia of norepinephrine, dopamine, and tyrosine hydroxylase are normal (*2, 5*). Drugs that block dopamine receptors, deplete dopamine, or increase acetycholine improve the choreiform movements, while L-dopa and anticholinergics aggravate them (*6*). Work on animals suggests that GABA modulates dopaminergic function in the basal ganglia (*6*). Thus, it is postulated that dopaminergic overactivity, secondary to the loss of the inhibitory restraint of GABA and cholinergic neurons, is responsible for the choreiform movements.

While it is reasonable to assume that the pathology seen in the basal ganglia is responsible for the motor disturbances associated with this disease, the mental symptoms are more likely to be related to changes in the cerebral cortex where degeneration of the third, fifth, and sixth layers occurs (*1*). In contrast to the basal ganglia, the cortex appears to lack a neurochemical counterpart to these histological changes, and pharmacological manipulations aimed at improving cognitive function have been preliminary and desultory. No significant alterations in GAD or CAT activity or in the concentrations of muscarinic or GABA receptors are found in the cerebral cortex (*2, 3, 7*). Decreased [^{3}H]spiroperidol binding is reported in the cerebral cortex of choreics

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