Genetic Marker for Depression Reported

It is not surprising that many neuroscientists and psychiatrists believe that some types of emotional depression are inherited. A growing number of studies — most recently, Seymour S. Kety's results with adoptees in Denmark (SN: 10/7/78, p. 244) — indicate a significant incidence of depression among the offspring of depressed parents.

But it is one thing to cite statistical, if impressive, evidence, and quite another to actually identify biochemical proof that psychological characteristics are inherited. The first molecular evidence of a genetic link — which has eluded researchers until now — is being reported by David E. Comings of the City of Hope National Medical Center in Duarte, Calif.

Comings, a medical geneticist, reports in the Jan. 4 NATURE that he has pinpointed "the major gene in depressive disease." The discovery constitutes "the first basis for a biochemical abnormality found in individual psychotic depression," Comings told SCIENCE NEWS. Work has already begun on the search for an antibody to the abnormal substance, he added.

But while acknowledging that Comings's work is important, some scientists say they are skeptical of the results. Frederick K. Goodwin, chief of the National Institute of Mental Health's Clinical Psychobiology Branch, said the results are "provocative and potentially very exciting." But he said that Comings's conclusions may represent an "over-interpretation of the findings" at this stage.

Comings said in an interview, however, that "there is no question in my mind about [the existence of] a mutant protein." The protein, called Pc 1 Duarte, was found in slightly fewer than one-third of the autopsied brains of 152 persons who did *not* suffer from depression. (That control group included persons who had Huntington's disease.) The incidence of the protein was no greater among the brains of persons with schizophrenia — a condition for which there is even greater statistical indication for inheritance than there is for depression.

However, in the brains of 28 diagnosed depressives — including those with alcoholic and suicidal tendencies — Comings discovered that Pc 1 Duarte was present in 64.2 percent of the cases. He also found the protein in the brains of 21 of 40 persons who had suffered from multiple sclerosis. Throughout the study, the presence of the chemical was distributed equally among the brains of males and females and blacks and whites.

Using a technique called two-dimensional gel electrophoresis, Comings examined the proteins from microscopic slivers of the brains' caudate and putamen areas — regions believed to contain many cells that produce dopamine, a neurochemical implicated in schizophrenia and other disorders. He looked specifically for Pc 1 Duarte because he had stumbled upon that chemical several years before while searching for a cause of Huntington's disease. Though it apparently is not associated with Huntington's disease, the fairly "common" occurrence of the mutant brain protein intrigued the geneticist. He wondered "if Pc 1 Duarte was associated with any of the major psychoses."

Comings not only found the protein present more than twice as often in depressives as in "normals," but he found a "double dose" (indicating a gene from both parents, rather than one) in 18 percent of the depressives and in 20 percent of suicidal persons, compared with less than 3 percent of the control group. Kety had reported statistical evidence for genetic factors in 15 of the 18 suicides that occurred among the families of adoptees. "There may be a genetic predisposition [to suicide] among those exposed to certain life situations," he suggested.

And despite the biochemical indication for a genetic link to depression, Comings agrees that environmental stresses or life situations appear to play a significant role in whether or not the depression will actually surface. "Because it [Pc 1 Duarte] is so prevalent in the general population [who do not exhibit depressive symptoms], there must be environmental as well as genetic factors," he says. "There may be other proteins involved as well," he says. For instance, he notes, something has to account for the greater reported incidence of depression among women — estimated to be three times as great as in men. Since Pc 1 Duarte appears to be no more prevalent in women than in men, Comings suggests that environmental stresses or other chemicals may also be at work.

The main reservations about Comings's work, says NIMH's Goodwin, concern the sampling techniques and methodology. Goodwin notes that various regions of the United States differ greatly in their heritage and genetic mix — a factor that could color the results. (The brains of the depressed and suicidal persons came from St. Louis.) In addition, various chemical changes and breakdowns could affect the tissue samples and conceivably yield deceiving pictures of brain proteins, he adds. For example, depressed persons' brains may contain drug residues, and suicide victims often are not found for days, meaning the dead brains would be at room temperature for a considerable length of time.

Comings responds that the brains were frozen "as fast as humanly possible" after death, and adds that he has "done enough brains" — a total of 276 in the study — to minimize chances of procedural problems. He says that previous findings with dopamine and other neurotransmitters have been, at best, "conflicting." But in the Pc 1 Duarte work, "we've looked at the mutant protein itself," he says.

Goodwin concurs that Comings's techniques are "standard" and that the statistics he reports are "highly significant." And Goodwin says that proteins do not break down as readily as some other brain chemicals during brain decomposition. "But," he emphasizes, "this is the type of work that especially needs more replication."

Comings remains essentially at a loss to explain the correlation with multiple sclerosis, and plans further investigation of that link. The apparent incidence of Pc 1 Duarte with alcoholism as well as depression, he says, seems to fit with the association between the two as well as with previous indications that alcoholism runs in the family.

There is currently "no way" that the mutant protein can be diagnosed in a living person, Comings stresses. He and his colleagues are working with rabbits in hopes of finding an antibody to the mutant protein. □

Voiceprints: Hearing for those who can't?

They said it was impossible. But Victor Zue did it. Now he's teaching others to read voiceprints in the same way he taught himself.

A voiceprint is essentially a spectrogram that displays a plot of the sound frequency of speech (in hertz) against time. Beginning in 1971, Zue, an electrical engineer and expert phoneticist at the Massachusetts Institute of Technology, spent an hour a day learning to discriminate between the different phonetical segments of speech as represented in the spectra.

His technique involves first dividing a spectrogram into obviously definable segments. Then he searches for spectral discontinuities over time which might represent the most basic phonetical units — phonemes. It's a very imprecise business since the range of spectra representing the same sound can differ widely. What's more, while spaces separate words on the page, there are seldom spaces between the words we speak. The voiceprint of "What are you doing?" will appear as a continuous but changing signal. Because, as often as not, people actually say "Whaddarya doin" or "whatcha doin," the