for white light and 9 percent for blue light at 5 days and 4 percent for white and 2 percent for blue light at 11 days. These findings correspond to a previous report (*13*) of light transmission through the crania of human infants, and may explain why blue light does not affect calcium.

Our results indicate that phototherapy-induced hypocalcemia is not related to bilirubin metabolism and can be prevented by occipital shielding, exogenous melatonin, or inhibition of corticosterone synthesis. Melatonin blocks the hypocalcemic effects of exogenous corticosteriod. We postulate that inhibition of melatonin synthesis results from transcranial illumination of the pineal, and that hypocalcemia ensues when bone calcium uptake is increased by the unopposed action of endogenous steroid.

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Increased Pyrophosphate in Fibroblasts and Lymphoblasts from Patients with Hereditary Diffuse Articular Chondrocalcinosis

Abstract. *The metabolic and genetic factors leading to deposition of calcium pyrophosphate crystals in cartilage of patients with chondrocalcinosis are not well understood. Analysis of cultured fibroblasts and lymphoblasts from 12 affected members of a large kindred showed a mean concentration of intracellular inorganic pyrophosphate two times greater than that in cells from unaffected family members or normal, unrelated volunteers. Increased intracellular pyrophosphate may, therefore, be a biochemical marker for the heterozygous expression of the chondrocalcinosis gene.*

In chondrocalcinosis, crystals of calcium pyrophosphate dihydrate are deposited in cartilage, leading to severe arthritis. The disease is found at autopsy in about 5 percent of the population. Chondrocalcinosis has been described in families in Czechoslovakia (*1*), Holland (*2*), Chile (*3*), France (*4*), Spain (*5*), and the United States (*6*). A dominant pattern of inheritance has been found in some families (*2, 4, 6*); in others the pattern of inheritance is less clear (*1, 3, 5*).

An increased concentration of inorganic pyrophosphate was previously reported in synovial fluid (*7–11*) in articular cartilage and in cultured chondrocytes and fibroblasts (*12*) from an affected patient, but not in plasma or urine (*7–13*). We now report an increased concentration of pyrophosphate in cultured fibroblasts and lymphoblasts from affected members of a large family with hereditary diffuse articular chondrocalcinosis (*4*).

Cells from three groups of subjects were cultured. The experimental group comprised 12 family members (seven females and five males 35 to 74 years of age), eleven of whom had had diffuse articular chondrocalcinosis for at least 10 years as confirmed clinically and radiologically. For one control group we selected unaffected siblings or close relatives of both sexes and 45 to 63 years of age. Unaffected, unrelated volunteers were used as a second control group.

As determined by the coupled enzymatic procedure (*14*), lymphoblasts and fibroblasts from affected family members had a substantially higher mean concentration of intracellular inorganic pyrophosphate than did cells from the control

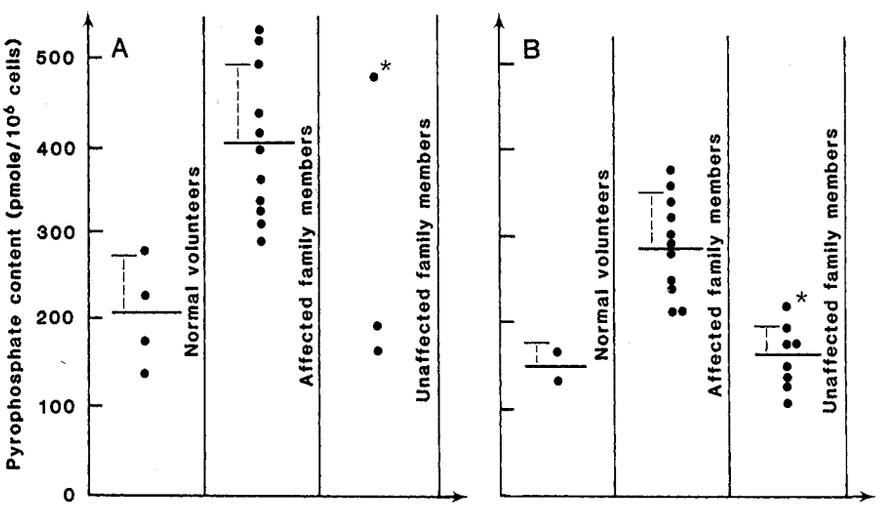

Fig. 1. Pyrophosphate content of fibroblasts (A) and Epstein-Barr–transformed lymphoblasts (B) from 12 affected family members, unaffected family members, and unrelated, unaffected volunteers. The mean concentration of intracellular inorganic pyrophosphate is 65 to 80 percent higher in affected family members than in the control groups. Fibroblasts were cultured in Eagle's minimal essential medium with 10 percent fetal calf serum, penicillin (50 U/ml), and streptomycin (50 μg/ml); the antibiotics were omitted after the first passage. The cells were then harvested and analyzed for pyrophosphate (*12*). Permanent lymphoblast lines were established by separating lymphocytes from peripheral blood by gradient density centrifugation in Ficoll Hypaque, adding Epstein-Barr virus, and culturing the cells in RPMI 1640 medium with 20 percent fetal calf serum (*17*). Asterisks indicate the subject who initially was classified as unaffected, but whose high pyrophosphate values prompted a clinical reexamination that produced x-ray evidence of chondrocalcinosis. The long horizontal lines denote means and the short horizontal lines show the magnitude of the standard deviations.

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subjects (Fig. 1). These results agree with our previous finding that the pyrophosphate content of fibroblasts cultured from skin and fibrocartilage of a chondrocalcinosis patient was twice that of fibroblasts from two gouty patients and two normal volunteers (*12*). The fibroblasts of one family member with no overt symptoms had a pyrophosphate content similar to that of fibroblasts from the experimental subjects, and detailed reexamination revealed clinical signs in the knee and radiological evidence of calcified cartilage in the knees, pubic symphysis, and coxofemoral joints. Thus the high value indicated the presence of the gene for chondrocalcinosis before its clinical expression was noted.

This demonstration of a deranged pyrophosphate metabolism in a large kindred is in keeping with the genetic nature of chondrocalcinosis and is correlated with the demonstration by x-ray diffraction of calcium pyrophosphate in triclinic crystalline form in two affected family members (*15*). The presence of a high pyrophosphate content in fibroblasts may explain the calcification found in tendons, joint capsules, and fibrocartilage (*16*). The severity of the disease in this family, in which only one of the parents was affected, raises questions about the clinical features that might be found in families in which both parents are affected. Finally, the finding of this metabolic abnormality in lymphoblasts suggests that lymphoblast cell lines, particularly those cultured from the homozygote, might be used to further study the metabolic derangement underlying chondrocalcinosis.

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Different Command Neurons Select Different Outputs from a Shared Premotor Interneuron of Crayfish Tail-Flip Circuitry

Abstract. *In the crayfish a bilateral pair of interneurons (the I3's) are involved in the generation of two types of tail-flip escape responses, one mediated by giant neurons and the other by nongiant circuitry. The I3's make a variety of output connections with the motoneurons and with other interneurons involved in tail flipping. The motoneuronal outputs include strong synapses on telson flexor motoneurons, whose activity during tail flips mediated by lateral giant fibers would be maladaptive. The lateral giants always drive the I3's, but also drive inhibitory neurons that prevent the undesirable outputs of the I3's while permitting their adaptive outputs to be expressed. It is often adaptive for tail flips initiated by nongiant circuitry to utilize the telson flexor muscles that I3 strongly excites. During such tail flips I3 is often fired, and this firing is important in driving the telson flexors.*

Great economies in the amount of nerve circuitry needed to generate behavior can be achieved by systems of hierarchical control in which complex movements are synthesized from a basic set of movements of rather general utility. Still greater economy could be attained if these basic motor patterns, rather than being fixed and merely callable by higher level controllers, were altered somewhat by those controllers to produce a range of movements. Thus one flexible movement-producing subroutine could play the role of many fixed ones (*1*). However, evidence for alteration of subroutines—in particular, evidence for alterations in their "logical structure" (alterations in what effectively drives or suppresses what)—has mostly been indirect (*2*).

Here we provide direct evidence for such alteration by reporting the discovery of a pair of crayfish motor interneurons that are used in the production of several types of tail-flip escape responses and whose pattern of effective outputs is adaptively altered according to the type of tail flip being produced. This bilateral pair of neurons, the I3's, was discovered as an apparent participant in the production of tail flips mediated by the crayfish's medial giant and lateral giant command neurons (*3*). These escape reactions are rapid, stereotyped responses to sudden stimulation. The medial giants respond to rostrally located stimuli and command a pattern of abdominal phasic flexor muscle contraction that jerks the crayfish rapidly backward. The lateral giants respond to caudally located stimuli and evoke a pattern of muscular contraction that thrusts the abdomen upward in the start of a forward somersault (*4, 5*).

The I3 of each side has its soma and dendrites in the third abdominal ganglion, where it is strongly excited by medial and lateral giants bilaterally; its axon projects to the last abdominal (sixth) ganglion (*3*). When the I3's are directly stimulated to fire bilaterally, the most conspicuous consequence is contraction of the ventral and posterior telson flexors, two tail fan muscles innervated by motor nerves of the last ganglion. Often a single I3 suffices to produce the same effects. These contractions are the result of apparently monosynaptic connections between I3 and posterior and ventral telson flexor motoneurons in the last ganglion (*3*).

These connections were surprising, because in healthy preparations firing of the lateral giants always recruits both I3's (*3*), yet it has been reported that the posterior and ventral telson flexor muscles do not contract during lateral giant-mediated tail flips (*5*). Indeed, it is believed that were they to contract, the animal's trajectory would be more backward than upward and the animal would tend to move toward the stimulus it should be evading (*4, 5*). We have confirmed that firing of the I3's alone causes telson flexor muscles to contract, whereas firing of the lateral giants, which

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