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13. ABSTRACT (Maximum 200 words)

Our primary objective is to carry out a cellular and computational analysis of operant conditioning of the headwaving response in Aplysia. Progress has been made in four areas: (1) We have now unequivocally identified the neural pathway essential for reinforcement: a bilateral set of nerves from the oral veil. (2) We have achieved reliable stimulus control over the operant response (headwaving) by our discovery that Aplysia shows a strong positive phototaxis to a directional light source. (3) We have identified the neural pathway necessary for phototaxis: the nerves from the primary visual organs (the eyes and rhinophores). (4) We have preliminary evidence that headwaving motor neurons can be operantly conditioned (by direct injection of hyperpolarizing or depolarizing current, paired with reinforcement) to increase or decrease their spontaneous firing rate. These findings suggest that a co-variance principle may be operating in identified neural circuits of Aplysia.

14. SUBJECT TERMS

Operant Conditioning, Circuit analysis, Neurocomputation, Aplysia

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ANNUAL TECHNICAL REPORT

Thomas J. Carew

AFOSR-89-0362

A. OBJECTIVES

The overall research project has three primary objectives:

1. **The first objective is to carry out a detailed circuit analysis of the neural networks underlying operant conditioning in Aplysia.**

To perform a complete circuit analysis of operant conditioning we are specifying: a) the operant response circuitry; b) feedback circuitry; and c) reinforcement circuitry involved in the learning.

2. **The second objective is to analyze the expression of operant conditioning in identified neural circuits.**

Three experimental strategies are being used: a) We are examining neural correlates of the conditioning in previously trained animals; b) we are producing the operant conditioning *in vitro* while recording from relevant circuit elements; and c) we are examining neural analogues of the conditioning by direct activation of relevant circuitry.

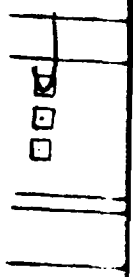
3. **The third objective is to generate a quantitative computational model of operant conditioning.**

An essential feature of the computational model we plan to generate is that it will use empirically derived biophysical parameters, synaptic weights and circuit properties in its construction. The modelling analysis will be carried out at three levels: a) individual circuit elements; b) restricted neural networks; and c) simulations of adaptive changes within elements and networks.

B. STATUS OF THE RESEARCH EFFORT

In the first year of this award we have made significant progress towards achieving the first two research objectives described above. Thus we are on schedule for the overall project, since we plan to begin our efforts towards the third objective (computational modelling) in Year 2, and be actively engaged in it by Year 3. In the first 12 months of this award, important strides have been made in four areas, which I will discuss in the paragraphs that follow.

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1. We have identified the neural pathway mediating reinforcement in operant conditioning of Aplysia.

Aplysia rapidly learn to operantly modify their headwaving response when headwaving to one side of their body is punished with whole-field bright light, which the animals find aversive. In a previous study (Cook and Carew, 1989) we found to our surprise that input from the primary visual structures of the animal (the eyes and rhinophores) was not necessary for operant conditioning; animals with chronic transections of the optic and rhinophore nerves conditioned perfectly well. This finding raised two questions: a) What are the eyes and rhinophores used for? (see below); and b) If these pathways do not mediate reinforcement, what pathways are critical? We have now identified the essential reinforcement pathway for the conditioning: it is comprised of a bilateral set of nerves (nerves C1-C3) from the oral veil, a facial structure of the animal. Chronic transection of the oral veil nerves abolishes the ability of animals to be conditioned, while a number of sham-operated controls learn perfectly. Thus we now have in hand a specific neural pathway mediating reinforcement, a major advance in our circuit analysis. We are currently examining neurons that process this photic input and project to the operant response pathway.

2. We have achieved stimulus control over the head-waving response.

In order to quantitatively analyze the operant response in both cellular and modelling studies, it is critical to have stimulus control over the behavior. We have recently discovered a means of achieving such control. Specifically, we have found that *Aplysia* show a clear positive phototaxis toward a directional light source. (Kuenzi et al, 1989; Kuenzi and Carew, 1990). We have characterized the behavior fully, and find it is primarily achieved by superimposing a directional posture on the ongoing oscillatory motor response of headwaving (essentially, biasing the oscillator). This response will prove extremely valuable in behavioral and especially cellular studies of the operant response.

3. We have identified the neural pathway mediating phototactic modulation of headwaving.

In our initial studies designed to characterize the phototactic response (described above) on a cellular level, we have found that the pathways from the primary visual structures (the eyes and rhinophores) are essential for phototaxis (Kuenzi and Carew, 1990). Recall that these pathways are not required for operant conditioning (see point #1 above). Thus we have discovered that *Aplysia* has two functionally opposite visual systems: one (eyes and rhinophores) mediates approach responses to directional light, the other (oral veil) mediates avoidance behavior during operant conditioning. We are now analyzing the cellular organization of these opposing visual processing systems.

4. We have preliminary evidence that headwaving motor neurons can be operantly conditioned by direct injection of current paired with reinforcement.

One of our main objectives is to directly produce conditioning-specific changes in motor neurons of the operant response pathway. We had previously found that the spontaneous baseline firing rate of motor neurons could be operantly modified by presenting bright-light in a semi-intact preparation (Cook and Carew, 1988). We have now obtained preliminary evidence in the isolated CNS that these same neurons can be operantly conditioned by direct injection of hyperpolarizing or depolarizing current, paired with electrical stimulation of the oral veil nerves, to increase or decrease their spontaneous firing rate. These findings suggest that a co-variance principle similar to that described for LTP in the mammalian hippocampus may be operating in a form of associative learning in an identified neural circuit of *Aplysia*.

C. PUBLICATIONS

1. Cook, D.G. and Carew, T.J. (1989a) Operant conditioning of head-waving in *Aplysia* I: Identified muscles involved in the operant response. *J. Neuroscience* 9: 3097-3106.
2. Cook, D.G. and Carew, T.J. (1989b) Operant conditioning of head-waving in *Aplysia* II: Contingent modification of electromyographic activity in identified muscles. *J. Neuroscience* 9: 3107-3114.
3. Cook, D.G. and Carew, T.J. (1989c) Operant conditioning of head-waving in *Aplysia* III: Cellular analysis of possible reinforcement pathways in *Aplysia*. *J. Neuroscience* 9: 3115-3122.
4. Baxter, D.A., Buonomano D.V., Raymond, J.L., Cook, D.G., Kuenzi, F.M., Carew, T.J. and Byrne, J.H. (1989) Empirically derived adaptive elements and networks simulate associative learning; In *Quantitative Analysis of Behavior Volume XII: Neural Network Models of Conditioning and Action*. Hillsdale: Lawrence Erlbaum & Assoc (in press).
5. Cook, D.G., Stopfer, M. and Carew, T.J. (1990) Identification of the neural pathway mediating reinforcement in operant conditioning of head-waving in *Aplysia*. (in preparation for *Behavioral Biology*).
6. Kuenzi, F.M. and Carew, T.J. (1990) Identification of the neural pathway mediating phototactic modulation of head-waving in *Aplysia*. (in preparation for *Behavioral Biology*).

7. Cook, D.G. and Carew T.J. (1990) Operant conditioning of single identified neurons in *Aplysia* (in preparation for *Science*).

D. PERSONNEL

1. David Cook, graduate student (Ph.D. expected Fall, 1990)
2. Frederick Kuenzi, graduate student (Ph.D. expected Spring, 1991)
3. Kent Fitzgerald, graduate student (third year)
4. Diana Blazis, Ph.D., post doctoral fellow (beginning July 1, 1990)

E. INTERACTIONS

Papers at scientific meetings

1. Kuenzi, F.M., Cruikshank, S., Storer, A.M.B., and Carew, T.J. (1989) Identification of neural pathway mediating positive phototaxis in *Aplysia*. *Soc. Neurosci. Abst.* **15**, 1285.
2. Cook, D.G. and Carew, T.J. (1989) Identification of reinforcement pathways necessary for operant conditioning in *Aplysia*. *Soc. Neurosci. Abst.* **15**, 1265.

Invited colloquia and plenary presentations

1. International Society for Neuroethology, Berlin (Fall 1989)
2. Royal Society, London (Winter 1990)
3. University of Southern California Medical School (Spring 1990)

F. DISCOVERIES, INVENTIONS, PATENTS

not applicable