INTENSITY AND DURATION IN BRAIN-STIMULATION REWARD

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DECLARATION

I declare that no part of this thesis has been accepted or presented for the award of any degree or diploma by any University, and that to the best of my knowledge, the thesis contains no material previously published or written by any other person, except where due reference is given to that author by direct credit in the text or bibliography.

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Abstract

Electrical stimulation of certain regions of the vertebrate brain produces behaviour analogous to a powerful motivational state. The electrical stimulation that produces this behaviour is described as rewarding brain stimulation. When an animal is placed in a situation in which it can control both the initiation and termination of rewarding brain stimulation, an alternation often occurs between periods of stimulation and periods of no stimulation which has been termed shuttling behaviour. The research program reported here examined the relationship between shuttling behaviour and the intensity and duration of rewarding brain stimulation.

Shuttling behaviour has been argued as capable of yielding valid measures of the rewarding effect produced by this type of stimulation. As a result, measures that are available from a consideration of the self-regulation of stimulation have found an increasing use in pharmacological studies. However, some of the assumptions and theoretical interpretations on which such arguments rest have not been adequately examined. In particular, the assumption that the two durations are independent and may be consistently interpreted in terms of reward and aversion have not received sufficient attention. The series of experiments reported here examined in detail the relationship between the selected durations and the intensity of stimulation, and also evaluated hypotheses concerning the termination response in terms of how well the observed relationships may be explained.

The literature review shows that the selected durations of stimulation (ON time) and the selected durations of no stimulation (OFF time) are both decreasing functions of the intensity of stimulation. Evidence also indicates that there is no significant correlation between these two durations. However, for several reasons, existing evidence could not be accepted with confidence: including, a considerable range in the reported correlation (-0.47 to $+0.79$), considerable differences in how the correlation was calculated, and a failure to consider the possible effect of intensity on the correlation.

In the present study, the correlation between ON and OFF time was examined in several ways, including the correlation between mean ON and OFF time, the correlation between within-trial ON time and the immediately preceding OFF time, the correlation between within-trial ON time and the immediately following OFF time. Within-trial correlations were also calculated after differencing and after time series methods had been used.

The decrease in OFF time that occurs as intensity is increased may be caused directly by the increase in intensity, or may occur indirectly as a result of the concurrent decrease in the duration of stimulation. Three experiments are reported which attempt to dissociate the effects of intensity of stimulation from the effects of duration of stimulation on OFF time under continuous reinforcement. The statistical relationship between ON and OFF time was examined throughout all experiments.

The results indicated that the intensity of stimulation was the major determinant of OFF time. An increase in the intensity of stimulation produces highly significant decreases in both ON and OFF time, whereas an increase in the duration of stimulation produces small, but significant, increases in OFF time.

The correlation between ON and OFF time varied markedly depending on whether mean values were correlated (across animals or trials), or whether the within-trial ON and OFF times were correlated. Correlation between mean values at low to moderate intensities were significantly positive, but at higher intensities, nonsignificant, near-zero correlation were found. Within-trial correlations were not significant at any intensity level once a tendency for linear trend in the data was accounted for. Particular animals in particular trials can show significant correlations between ON and OFF time but correlation across animals or across trials was not consistent.

An analysis from a time series perspective indicated that except for the tendency for linear trend, each ON time and each OFF time is generated independently and stochastically; past durations of stimulation have little or no effect on the determination of the immediate duration of stimulation.

Two models that satisfactorily accommodate the main features of shuttling behaviour are discussed in relation to how the behaviour might be produced. The results supported a two system substrate for brain stimulation reward, which, in turn, could support either a reward/aversion or a reciprocal inhibition model. From a neurophysiological point of view, the interaction of the two systems and the timing of the termination response might be best interpreted in terms of adaptation and the arousal of an inhibitory system. The timing of the initiation response appears to

depend on several factors including the presence of various stimulus contingencies.

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