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Analyzing Behavior-Related Neural Activity Via Correlation of Distribution Shape: Part 1

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INTRODUCTION

A main goal of the behavioral neuroscientist is to demonstrate the existence of meaningful relationships between neural activity and the behavior of an organism. In pursuit of this goal researchers typically make multiple- and single-unit neural recordings from an aggregation of neurons, while the subject of the recordings learns or performs some task. Peri-stimulus time histograms of discriminated action potentials are then compared to time lines of task-related events, including stimulus presentation, delays, and response initiation. Significant neural-behavioral relationships are apparent in time-locking between task-related events and increased neural firing (e.g., Eichenbaum, et.al, 1989; Goldman-Rakic, 1985; Mountcastle, et.al, 1987; White, et.al., 1994).

This technique encounters one main limitation, in that it reduces ongoing behavior to a simple series of events. By treating each behavior as either occurring or non-occurring at each time point, typical analyses necessarily ignore response topography-the qualitative shape of the behavior. It would be useful, given an appropriate preparation, to go one step beyond the correlation of neural and behavioral timings, in order to more precisely relate neural activity to associated behaviors.

The rabbit conditioned eyeblink preparation (Gormezano, et.al., 1962; Steinmetz & Thompson, 1991) provides just such an opportunity. Specifically, this preparation allows researchers to characterize the shape of the eyeblink response-its amplitude over time. These data can then be directly related to the peri-stimuli time histogram of action potentials, also describable in terms of amplitude over time. This report describes the procedures, based on techniques developed by Berger and Thompson (1978), by which our lab analyzes data collected in the rabbit eyeblink preparation. Procedures that will be described include: 1) the within-trial normalization of spike counts; and 2) the cross-correlation of behavioral and neural distributions at various time-lags. These analyses enable us to state concretely the relationship between activity in the selected structures and the classically conditioned eyeblink.

The rabbit eyeblink preparation

A brief puff of air directed at the cornea will cause an animal to blink reflexively. The air puff is an unconditioned stimulus (US); the reflexive blink is an unconditioned response (UR). A tone conditioned stimulus (CS) can be paired with the air puff such that the CS always precedes the US by a consistent temporal interval. The conditioning paradigm typically involves 750 msec trials that are divided into three periods: a 250 msec pre-CS baseline period (see below), a 250 msec CS period between CS onset and US onset, and a 250 msec US period after US onset. Normally, the CS and US coterminate sometime during the US period. After 100 to 400 of these trials, most rabbits develop conditioned eyeblink responses (CRs), blinks that precede the presentation of the US by 50 to 150 msec. In essence, the rabbit learns to anticipate and avoid the air puff.

Fifteen years of research, some of it from this lab, have identified the neural system underlying learning of the CR (e.g., Berthier & Moore, 1986; Chapman, *et.al.*, 1990;

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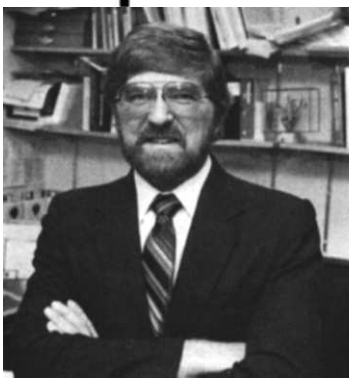

Editor's Column

It is springtime in the US heartland. Somehow, however, it seems like it is not quite as nice as usual. It isn't the fact that we have had a cool spring, or that there has been a lot of rain. It is the fact that 167 people died in a bomb blast in Oklahoma City just 3 weeks ago, as I write this. We could go a long time now without something like this happening again, and not miss it. The problem for me is not that it happened fairly near here, or that it was the worst US terrorist (or criminal, or both) activity on record. The worst part is that it happened at all. Why should people anywhere think they can or have to do this sort of thing? What happens to people thinking about other people as people, rather than objects? We are now "celebrating" the end of World War II. Another example of the way people can see other people as objects rather than people who have dreams, hopes, fears, and more importantly, rights and dignity. Many other recent examples, including the "Una-bomber" come to mind. Even the acts of the "animal rights" activists often fall in this category.

I guess all of us take ourselves and our ideas too seriously at times. Could we help the flow of ideas, the dignity of each other, and the way the world works by recognizing that other people have a right to their ideas and ways of life, and even to their scientific theories, and that because they do, that doesn't make them bad people, or objects? I hope so. Remember, getting to know someone is the best way to find out they are people, not objects.

On the bright side, my wife and I even found a few morel mushrooms in the woods behind our home this spring. There must have been a lot of them out, because we usually are very poor at finding them. They were delicious.

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Lavond, Hembree, & Thompson, 1985; Sears & Steinmetz, 1991; Steinmetz, 1990; Steinmetz, Lavond, & Thompson, 1989; Steinmetz, et.al., 1992; Thompson, 1988). In brief, we have hypothesized that information pertaining to the US is relayed to the cer-ebellar cortex via climbing fibers from the inferior olive. Information pertaining to the CS, meanwhile, is relayed to the cerebellar cortex from the pontine nucleus via the mossy fibers. Both pathways send collaterals to the interpositus nucleus, which also serves as the output structure for the cerebellar cortical portion of the circuit. Plastic processes in cortex and interpositus, brought on by activity in the converging CS-US pathways, are hypothesized to be the mechanisms of the CR acquisition and expression. Importantly, the interpositus nucleus seems to serve as a 'bottleneck' in this circuit. As such, it is vital to the expression of the learned response.

Datasets collected in the process of unveiling this fairly complex circuit have involved neural recordings (Gould, Sears, & Steinmetz, 1991) and records of eyelid movements (in the form of smoothed output from EMG recordings, photoelectric measurements of reflectance changes, or mechanical deflection of potentiometers) taken during trials. Figure 1 shows such a dataset. In Figure la, the untrained animal blinks after the US delivery (note that an upward deflection of the line denoting eyelid activity represents eye closure). In Figure Ib, the trained animal now begins closing its eye well before the air puff comes on. In both cases, the discriminated action potentials recorded from the interpositus are displayed in a peri-stimuli time histogram below the eyelid activity line. Informal scrutiny suggests that the neural activity is somehow related to the CR; action potentials 'pile up' near the end of the CS period. The reality of this appearance, and its specific relationship to the conditioned eyeblink, is the subject of the procedures explained in the second part of this article which will appear in the next edition of the Carrier.

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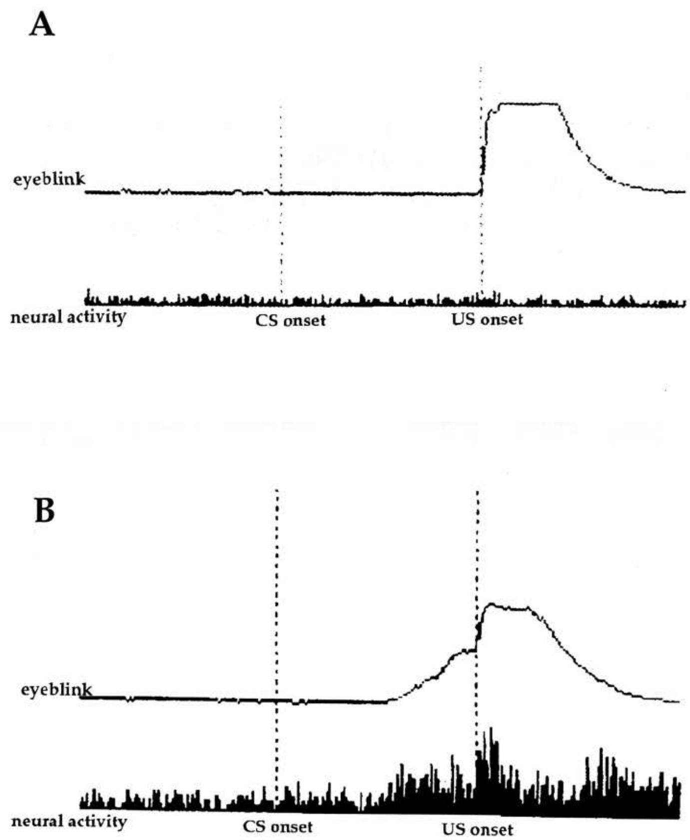

Figure 1. Representative examples of single blocks of data. The top trace is averaged eyelid activity, with an upward deflection denoting eyelid closure; the bottom histogram is summed discriminated action potentials. Time is represented along the horizontal axis, with presentation time of CS and US noted. **A.** A block during the first session of training. The animal is not conditioned-the eyeblink begins when the air-puff strikes the cornea. No learning-related activity is apparent in the neural data. **B.** A block from a later session. The eyeblink CR begins well before the airpuff was delivered. The neural activity seems to resemble the eyeblink in shape, but slightly precedes it in time.

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