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ined, NRG-1 heterozygous mutant mice have reduced numbers of AChRs, thus providing support for this model[14]. However, Yang and colleagues analyzed a new transgenic mouse that inactivates NRG-1 specifically in sensory and motor neurons. These new data indicate that NRG-1 is not necessary for the refinement of AChR expression during synapse formation (arrival of the nerve), nor is it necessary for synapse-specific AChR transcription itself. When NRG-1 was selectively eliminated in sensory/motoneurons, the zone of AChR transcription at the endplate not only was normal, but this zone was as narrow as that observed at innervated wild-type muscle. This indicates that the nerve could still refine the broader pre-patterned zone of AChR transcription in the absence of NRG-1 and could also maintain subsynaptic AChR transcription. In these experiments, there remains the formal possibility, although it seems unlikely, that very low levels of NRG-1 were produced before gene inactivation occurred and that these low levels of NRG-1 were sufficient to induce synapse specific gene expression of AChRs at the endplate.

Three simple models follow the new NRG-1 genetic data. One possibility is that a signal other than neural agrin refines the pattern of AChR synthesis during synapse formation. A second possibility is that neural agrin, requiring MuSK activation, leads to synapse-specific transcription that is independent of NRG-1. Finally, it is known that agrin can cluster muscle-derived NRG-1 (ref. 15). Thus, nerve-derived agrin may refine the pattern of AChR expression by stabilizing synaptic muscle-derived NRG-1 (ref. 7). By extension, the activity of NDF may not only contribute to the dissolution of the non-stabilized, pre-patterned AChR clusters, but may dissolve all aspects of pre-patterning that are not stabilized by innervation including aneural AChR expression.

Many new questions are raised concerning the mechanisms by which the pre-patterning of muscles can be achieved, maintained and then disrupted in a precisely regulated manner. Pre-pattern formation might be initiated during early myoblast fusion by signaling derived from the muscle founder cells. Given that a founder cell might initiate this process, several other questions arise. How is the pre-pattern maintained until the time of innervation and, for that matter, how are even small AChR clusters formed during this process of pre-patterning? It is now clear that MuSK is necessary for the pre-patterning of AChR synthesis and clustering, but the precise involvement that MuSK has in this process remains to be determined. The regulated disruption of the pre-patterning mechanism will also need investigation. Does it involve a novel nerve-derived factor—NDF—or an activity-dependent program initiated upon arrival of the nerve and release of transmitter? Finally, there are larger questions regarding the importance of pre-patterning. Is pre-patterning of the muscle necessary for synapse formation? This seems unlikely given that synapse formation occurs *in vitro*, where pre-patterning is not observed[3]. Nevertheless, pre-patterning of the muscle fiber could be involved in targeting of axons to the endplate region of the muscle fiber, if molecules involved in target recognition were similarly pre-patterned.

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Brain at work: play by play

Frank Tong

A functional magnetic resonance imaging (fMRI) study reveals areas of the human brain that are activated during the perception of boundaries between events.

In the game of soccer, the players never stop running. The sport consists of non-stop action as twelve players battle for control of the ball. But through the eyes of the commentator, every dribble, pass, shot at the goal or block by the goalkeeper, is broken down—play by play. From this breakdown of the game into each meaningful event, fans listening to the radio can translate the commentator's words back into a dynamic mental 'movie' of the ongoing game.

Many everyday activities, such as making a bed or ironing a shirt, also consist of a continuous stream of actions. Yet what we tend to perceive is a series of discrete, meaningful events. How does the human brain parse the dynamic flow of action in the world into distinct perceptual events?

A functional brain imaging study by Zacks and colleagues[1] in this issue provides important new clues to this question. The authors first had subjects in an MR scanner passively watch movies of an actor performing an everyday activity such as ironing a shirt (**Fig. 1**) or playing the saxophone (Fig. 2). In two later scans, the same movies were shown again, but this time, subjects were instructed to press a button whenever they perceived the end of one event and the beginning of another. In one of these later scans, subjects were asked to divide the movie into the largest units that seemed natural and meaningful; in the other, the smallest units. This experimental design allowed the authors to look at brain activity during coarse and fine event boundaries and to test whether similar activity occurred in the earlier passive viewing scans when no task was required. Activation during the passive viewing scans might indicate that the brain automatically parses events in the absence of any explicit instructions to do so.

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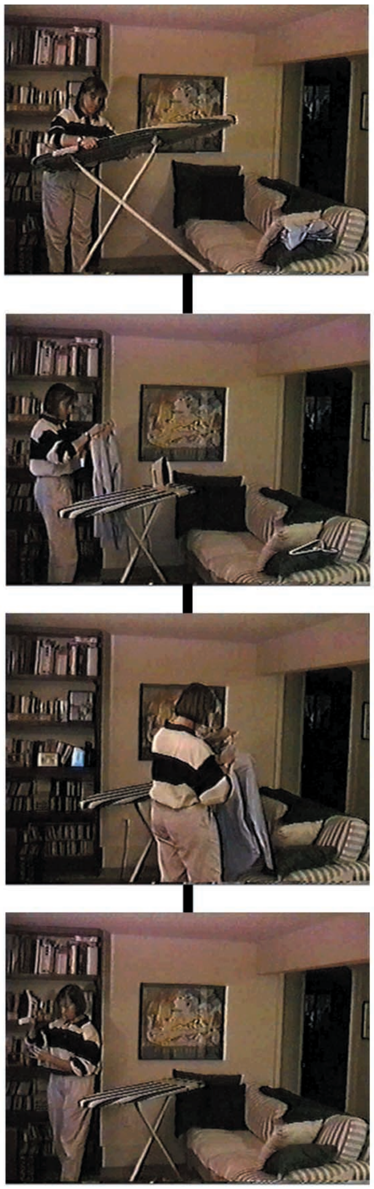

Fig. 1. Four example images from one of the movies shown to subjects in the Zacks *et al.* study. How does the brain parse activities in the world into discrete perceptual events?

Functional MRI activity recorded during the active tasks revealed transient activation in two brain areas around the time of reported event boundaries. These areas corresponded well to the typical location of two well-known functional regions: the extrastriate motion area MT (or V5) and the frontal eye fields (FEF). Several aspects of the results suggest that the activity in these regions was linked to the perception rather than the report of event boundaries. First, fMRI activity began to rise several seconds before the subject's actual report. It is unlikely that brain activity caused by response preparation would start so early. Second, fMRI activity was stronger when subjects reported perceiving coarse event boundaries than fine event boundaries, suggesting that perceptual differences between these boundaries led to differential activation. Third, the authors used the event boundaries reported by subjects in the later scans to test if similar patterns of fMRI activity occurred in the first scan when subjects viewed the movies passively. The putative MT region showed similar (although weaker) responses during the passive viewing task, indicating that this region responds during event boundaries even in the absence of a task. Taken together, these findings suggest that the observed neural responses were closely tied to event perception itself.

What do these brain activations reveal about how we perceive event boundaries? There are at least two candidate explanations for how events are parsed: a top-down knowledge-based interpretation and a bottom-up stimulus-driven interpretation.

The authors favor a top-down interpretation in which event segmentation is determined by one's knowledge of the actor's plans, goals and repertoire of possible actions. For example, during the ironing movie, an event boundary might be perceived just after the actor places the shirt on the ironing board and just before she finishes reaching for the iron. According to the top-down story, an event boundary is perceived here because of our knowledge that the actor is about to begin a qualitatively different action with a qualitatively different purpose: placing the iron on the shirt. The activation of the frontal eye fields and MT may thus reflect top-down modulation of these regions in segmenting events. Previous studies have shown that the frontal eye fields respond not only to overt eye movements but also to covert shifts of spatial attention[2]. Likewise, area MT can be modulated by attention[3] and activated by implied human movement in static images[4]. The activation of these areas may therefore reflect the attentive monitoring of events in response to knowledge-based expectations. This view is supported by the finding that stronger fMRI activations occurred during the event segmentation task than the passive viewing task, suggesting that the activations were in part due to attention to event boundaries. The putative contribution of top-down knowledge to event segmentation could be tested directly by comparing experts with novices. For example, would a soccer commentator show a different pattern of brain activity than a naive soccer spectator? How would brain activity change as a function of visual experience with an initially unfamiliar sequence of events? Future studies along these lines could help clarify how knowledge can influence event segmentation.

An alternative explanation is that bottom-up cues present in the stimulus are predictive of event boundaries, independent of their high-level interpretation. Event boundaries might involve, for instance, changes in the motion of the actor or of other relevant objects as one event is finished and the next started. This possibility is also consistent with the data. It is well known that motion area MT is highly responsive to image motion. Thus, the MT activation at event boundaries could easily be due to changes in image motion alone, irrespective of their semantic significance. Several things could be done to test this account. One option would be to analyze the image motion surrounding reported event boundaries. Standard optic flow algorithms could be applied to the movies, and the amount of motion at event boundaries compared with that elsewhere in the movies. One could also test if the disruption of motion perception, say via stroboscopic illumination, selectively impairs the perception of events.

The activation of the frontal eye field region may suggest a role for eye movements in event perception. One interpretation is that enhanced image motion around the time of event boundaries leads to more eye movements as the subject follows these changes, and thus leads to greater FEF activity. Alternatively, eye movements may have a more predictive and interpretive involvement in event perception. Recent behavioral studies have shown that eye movements are highly predictive of a subject's next action during familiar tasks such as making a cup of tea[5]. Moreover, the efficiency of eye movements may be related to a person's ability to predict dynamic events such as the final destination of a ball thrown in the game of cricket[6]. It would be useful to monitor the eye movements and fMRI activity of subjects while they freely view everyday activities. Would the same predictive eye movements occur when one is trying to predict the actions of another person? If so, then would steady fixation reduce frontal eye field activity or impair behavioral performance in the event segmentation task? If FEF activity still occurred with steady eye fixation, this would instead suggest that FEF activations are due to spatial shifts of attention that occur when subjects perceive event boundaries.

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Fig. 2. Images from another movie shown to subjects by Zachs *et al.*

Impaired behavioral performance during steady fixation might indicate that the eyes do not simply follow the internal predictions of the subject, but have a more active role in gathering relevant information and generating new predictions about events.

Ultimately, top-down versus bottom-up accounts of event perception may not prove to be mutually exclusive. In some situations, physical stimulus changes may be highly predictive of an event, such as when a soccer ball shoots across the field during a pass. In other situations, however, bottom-up cues may be too ambiguous, and top-down knowledge may be required. Behavioral studies have shown that a movie of randomly arranged images can eventually be perceived as a coherent event after it is repeatedly seen in different contexts surrounded by other random movie sequences[7]. These top-down effects of knowledge likely contribute to our perception of real-world events, as do bottom-up processes.

Regardless of the dependence of event perception on high-level knowledge or low-level stimulus changes, this study provides the intriguing suggestion that the encoding of event boundaries might occur automatically whenever people attend to action in the world. Before the initial scan in which subjects passively viewed the movies, subjects were merely instructed to pay attention to the movies and to try to understand them. No mention was made of the purpose of the study or of any requirement to attend to part structure in the movies. Thus, the fact that MT tended to be active at points that were later labeled as event boundaries indicates that the event boundaries in the stimuli were registered in the brain independent of any outside motivation to do so. Whether subjects were aware of the event boundaries as such during passive viewing is another matter; it could be that the stimulus changes at event boundaries produced brain activity without concomitant awareness of the part structure, and it is less clear how to probe this without contaminating the passive viewing scan with a task of some sort. But the event boundaries did produce changes in the brain during passive viewing, leaving open the possibility that they are extracted automatically as part of normal perception.

Zacks and colleagues have tapped into a network of brain processes that seem to involve spatial attention, top-down expectation, bottom-up motion cues and eye movements. All these processes may contribute to our ability to form perceptual boundaries between events, helping us to understand soccer games and other complex activities, and may also facilitate the representation of events themselves.

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