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The hazards of time

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Temporal expectations are continuously formed and updated, and interact with expectations about other relevant attributes of events, in order to optimise our interaction with unfolding sensory stimulation. In this paper, we will highlight some evidence revealing the pervasive effects of temporal expectations in modulating perception and action, and reflect on the current state of understanding about their underlying neural systems and mechanisms.

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Increasingly, the brain reveals itself proactive in its interface with external reality. In the past, our conception of the brain changed from that of a mirror to that of an interpreter. Several current lines of research — in fields such as memory, motivation and attentional orienting — now begin to cast the brain as a predictor. The results of experience are integrated over various timescales in order to anticipate events relevant to the current task goals and motivational state of the individual and to tune the relevant perceptual and motor machinery accordingly. In particular, research on attentional orienting has shown how signals coding predictions about the location, identity or simple features of relevant events can influence several stages of neural processing [1]. Recent evidence shows that these predictions are not restricted simply to the contents of events but also extend to their anticipated timing.

Temporal expectations[a] in behaviour
Automatic temporal expectations
Temporal prediction of events is often discussed in terms of 'hazard functions' — the conditional probability of an

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[a] By 'expectation' we mean the state associated with the prediction that something will happen. We use the word devoid of any implication about conscious awareness. Temporal expectations can be either 'automatic' or 'controlled', as is elaborated in the article.

event occurring at a given time given that it has not yet occurred [2]. Several types of motor behaviour exemplify ongoing predictive temporal tuning. Learning in classical conditioning depends upon temporal regularities between conditioned and unconditioned stimuli, and the resultant learned responses become finely tailored to the timing of the unconditioned stimulus [3]. In reaction-time tasks, the interval between a warning signal and an imperative stimulus, the 'foreperiod', is a major determinant of response speed [4]. Studies manipulating foreperiod variability have shown that detection and discrimination responses become faster as temporal variability and uncertainty between events decrease [5•]. The active and continual temporal anticipation of events based on prior experience is made plain during behaviours towards regular and predictable moving stimuli, such as when gaze anticipates targets during smooth pursuit [6]. Recent studies have shown that smooth-pursuit behaviour in humans, as well as monkeys, shows rapid learning of temporal regularities [7,8]. Similarly, temporal regularity between events can shorten saccade latencies or trigger anticipatory saccades to predicted targets [9,10].

Effects of temporal prediction are not confined to motor behaviours. The temporal certainty between events can modulate perceptual thresholds for luminance, orientation and stereoscopic discriminations [11,12] and can increase perceptual discriminability of visual stimuli [13]. Perceptual studies comparing feature discriminations after regular (isochronous) versus irregular temporal rhythms have also shown rapid and flexible temporal 'entrainment' of information processing. Perceptual judgements are enhanced for stimuli occurring in trials with regular rhythm and at the expected moment [14•,15•,16,17•], with accuracy decreasing exponentially as the stimulus precedes or exceeds the predicted moment [18]. Interestingly, this effect generalises for events occurring after two periodic cycles of the temporal interval [14•,15•]. This rhythmic entrainment suggests that temporal expectations are not punctate, but instead involve oscillatory mechanisms [19]. Temporal alignment of perception is not limited to simple isochronous rhythms, but can also follow complex hazard functions. In macaques, accuracy of motion detection was strongly determined by an alternating temporal hazard function such that the target would occur in one of two locations [20]. In humans, implicitly learned complex temporal sequences also provide effective contextual cues that facilitate target identification in visual search tasks [21•]. If oscillatory mechanisms are indeed involved in temporal expectations, then multiple rhythms would be required to create such complex temporal hazard functions [22•].

Controlled temporal expectations

Attentional orienting tasks adapted to the temporal domain have revealed that temporal expectations can be placed under dynamic cognitive control [23]. Symbolic cues, which predict the temporal interval of task-relevant events, confer significant behavioural advantages in speeded detection and discrimination tasks [23–26]. 'Temporal orienting' has been found to operate within multiple sensory modalities, as well as across modalities [27–29]. Importantly, the effects of temporal orienting are independent of sequential foreperiod effects [26,30,31] and cannot be explained solely on the basis of automatic processes, such as an unintentional tendency to respond according to the previous interval [32]. In most studies to date, different temporal cues can be conceived as being associated with a given hazard function, between which participants can switch dynamically. However, it is also possible for participants to orient attention to a specific, task-relevant time interval independently of hazard-function manipulations [33].

Most temporal orienting studies have relied on measures of speeded reaction times, but a few experiments have indicated that temporal expectations can influence perceptual and cognitive stages of processing independently of motor control. Correa et al. [34•] showed that temporal orienting improves perceptual discriminability (d′) when stimuli appear in rapid serial visual presentation (RSVP) and no speeded responses are required. Temporally predictive cues also override the tendency to miss targets occurring shortly after another target event (attentional blink [35,36]). Another intriguing set of RSVP studies have shown that orienting attention to the time that a subliminal stimulus is presented is necessary for unconscious semantic priming [37•,38,39].

Temporal expectations around the brain

The neural mechanisms by which temporal expectations affect perception and action remain largely unknown. Much of the relevant research is scattered in the literature and is fragmented by a lack of cross-referencing. When brought together, the papers attest to widespread effects of temporal prediction upon neural processing and begin to uncover some of the putative cellular mechanisms.

Temporal expectations in action

Electrophysiological recordings in monkeys have shown systematic changes in neural firing patterns as a function of temporal expectation in motor regions. In primary motor cortex, neurons become more synchronised around the expected time of an imperative go-signal [40•] and firing patterns correlate with subjective measures of temporal expectations [41]. In lateral and medial premotor areas, the onset of anticipatory neuronal firing to go-signals adapts to the temporal regularity between stimuli [42]. During smooth pursuit, firing rates in supplementary eye fields and supplementary motor area are

higher for predictable, rather than random stimulus motion, and peaks of neuronal firing shift to coincide with the expected time of motion onset [43•]. Finally, in the lateral intraparietal area (LIP) saccade-related activity varies according to the evolving temporal conditional probability for the appearance of the task-relevant target [44,45•].

In humans, recordings of event-related potentials (ERPs) during performance of speeded response tasks have also shown that motor-related activity varies as a function of temporal expectation. The contingent negative variation (CNV), a component generated in motor-related areas [46] that occurs in anticipation of stimuli or responses [47], is strongly correlated with the temporal predictability of events and concomitant preparation of responses. During cued stimulus or response tasks, in which automatic temporal expectations develop, the CNV ramps up gradually after the temporally predictive event and peaks at the anticipated time of the relevant target or response [48,49]. Manipulations of the hazard function between events strongly influence both the amplitude and the timecourse of the CNV [50]. ERP recordings during temporal orienting tasks also show modulation of the CNV slope and amplitude according to controlled temporal expectations triggered by informative cues [24,51]. Modulation of potentials linked to preparation and execution of responses after the appearance of target events, such as the P300 and lateralised readiness potential, shows that these motor stages of processing are accelerated by automatic temporal expectations in foreperiod paradigms [51–53] and by controlled temporal expectations in orienting paradigms [15•,24,29,33,54].

Brain imaging and lesion data defining the set of brain regions participating in temporal expectations remain scarce. The neuroimaging studies so far confirm the involvement of action-related circuits. Specifically, paradigms using either predictable foreperiods [55,56] or temporally informative cues [23,57] engage inferior parietal and premotor areas. Lesion and TMS studies have only just started to test for brain areas critically involved in temporal expectations and have recently implicated the right prefrontal cortex in foreperiod effects [58–60].

Temporal expectations in perception

Temporal prediction is not an exclusive property of motor areas. Electrophysiological recordings in monkeys show that modulation of neuronal firing rates by spatial attention in visual area V4 is strongly determined by temporal hazard functions [61•]. In humans, perceptual discrimination paradigms have revealed modulation of potentials linked to visual analysis (N1) and lateralised attentional selection (N2PC) by the duration of a foreperiod, as well as inhibition of low-frequency alpha oscillations (8–12 Hz) over the occipital region synchronised to the predicted interval for target appearance [17•,53].

Controlled temporal expectations in temporal orienting tasks have also been shown to enhance perceptual potentials evoked by visual, auditory and somatosensory stimuli [15•,27–29,54], though the findings are not consistent [24,33]. The discrepancies may help specify the mechanisms involved. Perceptual modulation occurs when stimuli appear at predictable spatial locations (including foveally) and in tasks taxing perceptual discrimination. Moreover, although the early visual P1 potential is not modulated by temporal expectation alone, the effect of spatial expectation on the P1 potential is augmented when both spatial and temporal expectations occur together [15•]. The finding suggests that temporal expectations interact synergistically with predictions about stimulus location or other stimulus features to boost the top-down biasing of the relevant location-related or feature-related receptive fields at the predicted time. Perceptual influences of temporal expectations may therefore be dependent upon other receptive-field properties of neurons, though the existence of general perceptual effects of temporal expectation cannot be ruled out at this stage.

Temporal expectations in learning and motivation

The sphere of influence of temporal expectations also reaches beyond sensory and motor areas. Within classical conditioning, it is well known that cellular activity triggered by the conditioned stimulus becomes exquisitely timed to anticipate the unconditioned stimulus. For example, during delay and trace conditioning of the rabbit eye-blink response, the neuronal firing rate in the cerebellum and in the hippocampus gradually shifts until its peak coincides with the onset of the air puff [62,63]. Temporal predictions are also important in reward processing. Reward-related activity of dopaminergic neurons in the substantia nigra and ventral tegmental area is strongly modulated when reward occurs when unexpected, or is omitted when expected [64,65]. In addition, activity of these cells rises monotonically in anticipation of the predicted time of an uncertain reward occurrence or magnitude [66]. Reward-related activity in several other regions, such as prefrontal and orbitofrontal cortex, is also systematically modulated by temporal predictions and temporal discounting of reward value [67,68]. Surprisingly, this effect was even observed in the primary visual cortex of rats [69].

The 'clock(s)' behind the expectations

These initial glimpses of the widespread dynamic temporal adjustments of behaviour and neural activity naturally invite us to ponder on the nature of timekeeping mechanisms driving these temporal expectations. If temporal expectations are to optimise behaviour successfully, the passage of time must first be accurately estimated. The mechanisms underlying the timing of intervals that are relevant for the dynamic control of behaviour ('interval timing') are currently a matter of heated debate [70,71]. Traditionally, time estimation was thought to rely upon an internal clock mechanism [72,73], which keeps time and allows for retrieval and comparison of stored time intervals. More recently, time has been suggested to be represented either by state-dependent changes in network dynamics [71] or by oscillatory or periodic activity in neural circuits [70]. Moreover, either mechanism may be instantiated within a dedicated timing network (e.g. the fronto-striatal motor control loop), or may be more widely distributed, as a common property of many or all neural systems [71,74].

The evidence remains inconclusive. Several lines of evidence support a dedicated timing system linked to motor control. As reviewed above, neuronal activity in motor areas shows temporal prediction. In turn, patients with conditions that compromise the cerebellum or fronto-striatal circuits have deficits in temporal perception and production [75–77]. Disruptions in explicit timing tasks are also observed after transient or short-term disruption to these regions with TMS [78–80]. When brain-imaging studies have succeeded in controlling for spurious variables involved in comparing timing to other 'control' tasks (e.g. sustained attention, motor preparation, task difficulty), these have also pointed to a specific contribution of motor-related frontal-striatal circuits to timing [81,82].

Other emerging lines of evidence support a distributed view. As reviewed above, temporal prediction characterises neuronal activity in brain areas linked to perception, learning and motivation, as well as to motor areas. Recent psychophysical studies have supplied compelling support for highly local and spatially specific timekeeping mechanisms within vision. Significant compression of temporal estimation occurred for events appearing around the time of saccades [83•] or after adaptation to high-frequency motion (or flicker) [84•]. These effects were further shown to be specific for the task-relevant visual stimuli and the relevant spatio-topic location [83•,84•,85]. These tantalising discoveries warrant much wider testing for the crucial participation of specialised perceptual areas in local timing mechanisms. Imaging studies that contrast timing versus non-timing conditions across tasks with different goals, stimulus modalities and motor effectors should prove instructive.

Arbitrating between dedicated versus distributed timing mechanisms may prove tricky, since it is difficult to separate neural activity related to timekeeping from its downstream consequences. Highly localised timing effects could result from the interaction between a dedicated timing system and distributed, task-specific neuronal assemblies. Alternatively, naturally occurring, inherent temporal dynamics of distributed neural circuits could simply engage activity in the motor circuits that are essential for most performance measures. As a speculation, we believe it will pay off to give consideration to contemporary theories emphasising the importance of oscillatory activity

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and synchronisation of neuronal activity across neural networks of different scales [22•,86,87]. These provide an intuitive and plausible framework for embedded timing mechanisms and for fine temporal adjustment of active top-down predictive signals that help construct our experience with reality.

Future directions

The neural basis of timing is currently enjoying a research boom. As the field develops, we must agree on a clear, shared taxonomy and improve cross-referencing between related works carried out with different methods or theoretical perspectives. Findings from both psychology and neuroscience are consonant and adamant about the strong and pervasive influence of the fourth dimension in shaping our behaviour. The next phase requires a concerted and open-minded wave of investigation into the neural mechanisms shaping temporal expectations and their consequences.

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