The Predictive Brain State: Asynchrony in Disorders of Attention?

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Hypothesis

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It is postulated that a key function of attention in goal-oriented behavior is to reduce performance variability by generating anticipatory neural activity that can be synchronized with expected sensory information. A network encompassing the prefrontal cortex, parietal lobe, and cerebellum may be critical in the maintenance and timing of such predictive neural activity. Dysfunction of this temporal process may constitute a fundamental defect in attention, causing working memory problems, distractibility, and decreased awareness.

Keywords: attention; working memory; anticipatory timing; self agency; variability.

> *"Who would deny that the present has no temporal extension, passing away as it does in a moment? But the attention, through which what arrives hastens to depart, endures and remains." Augustine, The Confessions, Book Eleven, AD 397*

The concept of attention has been applied to a broad array of control processes including arousal, intent, selection, execution, error checking, working memory, and vigilance. Attention, by definition, implies a fixed capacity, frequently assessed in experiments in which the cognitive load is manipulated, or where attention must be divided between multiple locations and/or tasks. The limited capacity of attention is manifest by increases in reaction time, errors, distractibility, reduced awareness, and increased variability when cognitive capabilities are taxed. These effects are readily observed in healthy individuals under laboratory conditions. They are also quite prevalent in fatigued and aged individuals and, indeed, a core component of several neurological and psychiatric pathologies including traumatic brain injury (Ghajar and Ivry 2008). These deficits have a significant impact on the daily activities of these individuals.

We postulate that one function of attention, distinct from arousal and intention, involves the generation of moment-to-moment expectancies of sensory input. It is not that sensory expectancy requires attention of this form; many expectancy effects can be observed in the absence of attention (Naatanen and others 2007). Rather, we emphasize that attention in its role of generating time-based expectancies of sensory information may be essential for ensuring the fluid operation of a range of cognitive operations, allowing these operations to be predictive rather than reactive. One consequence of sensory prediction is that performance becomes less variable because the performer is less likely to be distracted by irrelevant information and make errors. By predicting and successfully synchronizing with selective sensory input, the individual is "paying attention," creating a future-oriented brain state. Such predictive brain states likely involve an optimal and relatively restricted time frame. Although we are certainly capable of long-term planning (an issue we do not address in this article), the neural dynamics that underlie sensory predictions operate on a relatively small time scale (Karmarkar and Buonomano 2007).

We hypothesize that these moment-to-moment sensory predictions emerge from the interactions of a network involving frontal, parietal, and cerebellar areas. Disruption of this connectivity by trauma, degeneration, fatigue, or even developmental changes may underlie deficits in certain aspects of goal-oriented behavior.

Cortical Activation and Coherence in the Predictive State

Prediction is crucial for organizing motor and cognitive functions. Indeed, one could argue that the brain is essentially in a predictive state, anticipating and synchronizing with the immediate future. Could one prominent source of performance variability be related to a deficiency in the temporal generation and/or maintenance of such a predictive state? One way to examine the neural architecture of prediction and synchronization is to study

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not only the activation of brain regions associated with attentional anticipation but also the coherence between these regions. These patterns have been examined extensively in neuroimaging studies involving the presentation of attentional cues or during the maintenance phase of working memory tasks.

Imaging Studies

Studies of spatial attention frequently use a cue that may indicate the probable location of a stimulus or serve as a more generic alerting signal. This cue is typically followed after a short delay by an imperative stimulus. Neuroimaging studies consistently reveal that, following the cue, a network is engaged that encompasses the dorsolateral prefrontal cortex (PFC) and the parietal lobe, most prominently in the right hemisphere (Posner and others 1984; Knight 1997; Nagai and others 2004; Thiel and others 2004; Naghavi and Nyberg 2005; Wiese and others 2005; Grent-'t-Jong and Woldorff 2007). The frontal and parietal responses are not dependent on the presentation of a cue at the to-be-attended location; it is also observed when attention is directed covertly (Kastner and others 1999). Awareness is associated with greater activation in frontal and parietal regions (Carmel and others 2006). Within the PFC, activation on spatial cueing tasks is correlated with performance (Lutz and others 2002).

The same network identified for spatial attention is also activated in working memory tasks (LaBar and others 1999). In one study, the magnitude of this activation during initial encoding did not correlate with performance unless there was strong sustained activity of both the PFC and inferior parietal lobe (IPL) during the delay or maintenance period (Pessoa and others 2002). Similarly, activation of the IPL was found for a verbal short-term memory task during the maintenance period prior to the presentation of the probe (Majerus and others 2006), and again, the strength of this signal can predict performance (Sapir and others 2005). In terms of development, adults show stronger activation in the PFC and IPL compared to children, a difference that may help account for why the children are more distractible and make more errors (Olesen and others 2007). Maturation of the white matter tracts running between the PFC and IPL, identified with MRI-based diffusion tensor imaging (DTI), is correlated with performance in working memory tasks (Klingberg 2006). Covariation of signals in the PFC and IPL are also observed prior to voluntary movement (Ball and others 1999; Filipovíc and others 2001).

Electrophysiological Studies

Electrophysiological markers of anticipation associated with the PFC include the readiness potential (RP) (Cunnington and others 2003), observed when the movement is self-initiated, and contingent negative variation (CNV) (Walter and others 1964), observed when the response is initiated following an imperative stimulus. The early phase of the CNV is associated with the cue, whereas the later phase is associated with the response (Hillyard 1969, 1973). The amplitude of the CNV just prior to the imperative signal is correlated with faster reaction times and improved accuracy on a wide range of tasks (Morgan and others 1992; Filipovíc and others 2001; Padilla and others 2006). Moreover, the CNV amplitude increases as learning occurs, generally associated with further reductions in reaction time (Jongsma and others 2006). Although one cannot directly relate the electrophysiological and hemodynamic signals, CNV amplitude is correlated with the BOLD signal in PFC. The prominent EEG correlate of expectancy over the IPL is desynchronization in the alpha range (Foxe and others 1998; Small and others 2003; Babiloni and others 2004). EEG and magnetoencephalography (MEG) studies in working memory for visual or auditory tasks show preparatory activation in IPL (Lang and others 1992; Martin and others 2007).

Combining EEG and fMRI data, resting state brain networks have been identified that confirm the robust nature of PFC and IPL coherence (Mantini and others 2007). These findings suggest that the PFC and IPL interact to maintain information during delay periods in which the participants can predict forthcoming events, either related to the expectation of an imperative stimulus or the retrieval of information from working memory. Models of these interactions suggest a synchronization process that enables an expectancy to be maintained and compared with incoming sensory information.

Cerebellar Role in Prediction

In addition to the cortical network described above, prediction also engages the cerebellum. fMRI studies consistently show activation of the cerebellum during the interval following attentional cues (Kim and others 1994; Macar and others 2004; Tomasi and others 2004) (Fig. 2). This activation is not dependent on movement, although it may require the preparation of a potential response (Ivry and Fiez 2000; Bischoff-Grethe and others 2002).

Anticipatory Signals in the Cerebellum

Event-related functional MRI studies of the period before a movement show that activation changes in the cerebellum and PFC occur several seconds before movement onset. Physiologically, a few studies have attempted to specify the relationship between the cerebellum and cortical areas in terms of this predictive activity. Using coherence analysis methods, the degree

Table 1. Attentional Processes

Attention
- The process of alerting (cueing), selection (orienting), execution, and error checking
- Analogous to Ready (alerting), Get Set (selection), Go (execution) (Fig. 1)
- Successful performance is achieved by strong coherent anticipatory neural activity in the PFC and IPL during the Get Set period.

Expectancy Period of Attention (Get Set)
- The period between cueing and execution
- A feed-forward process to reduce performance variability by generating timed expectancies to synchronize with the to-be-acted-upon sensory input
- Neural components of the feed-forward process and postulated interactions are:
  - Delay of PFC response by the IPL (measured as coherence) to synchronize with sensory input
  - Feed-forward timing of delay (PFC-IPL coherence) is mediated by the cerebellum
  - Timing delay period is acquired by the cerebellum through associative learning
  - Optimal delay period for maximal reduction in performance variability is about 2.5 seconds

Ready, Get Set, Go Terms in Attention and Working Memory

Ready - arousal (A), start (A), cue (A), encode (WM)

Get Set - timed delay (A), maintenance (WM)

Go - execute (A), release (A), retrieve (WM)

Note: PFC, prefrontal cortex; IPL, inferior parietal lobe; WM, working memory functions; A, attention functions.

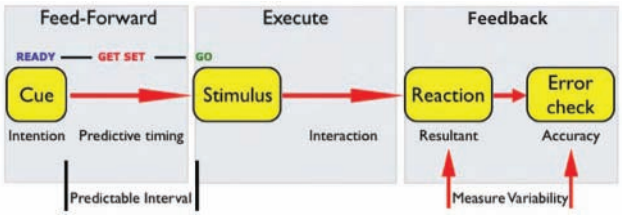

Figure 1. Diagram Showing How Anticipatory Timing Can Facilitate Performance in a Simple Cueing Task When the Time of a Stimulus Occurs after a Known Interval. Predictive timing allows the participant to anticipate the stimulus and generate an expectancy of the resulting feedback. Accurate predictive timing ensures synchronization of the predictions, in this example, generated in anticipation of the "Go" stimulus.

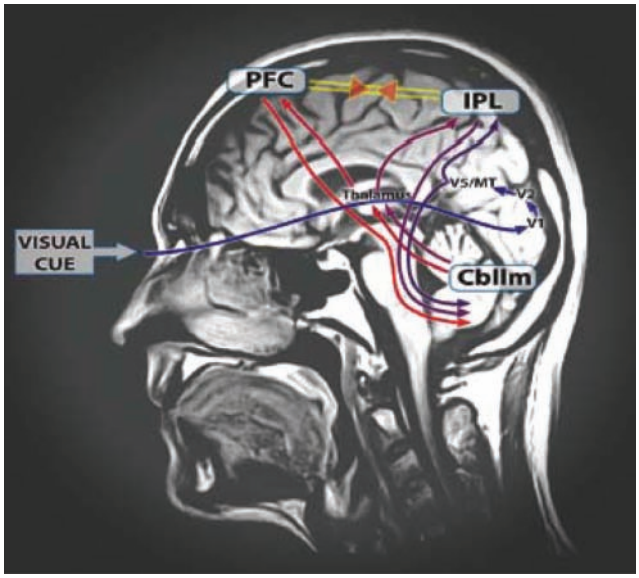

Figure 2. Predictive Neural Network That Is Activated in Cued, Learned Attention Tasks in the Time Period before Task Presentation. The sensory cue (CUE), with a visual cue as an example, activates the cerebellum (Cbllm) to delay motor or cognitive action to coincide with onset of the cued task. This learned delay, mediated by the cerebellum, synchronizes expectancy with actual sensory input. The timed expectancy is manifested by a mainly right-sided coherence (large gray arrowheads) between the dorsolateral prefrontal cortex (PFC) and inferior parietal lobe (IPL).

of cerebellar activation has been found to correlate with that observed in dorsolateral prefrontal and inferior parietal cortices (Allen and others 2005). Higher cortical areas are sequentially activated in tandem with an intracerebellar shift from lateral to medial zones before voluntary movements. In the case of voluntary movements performed at a slow rate, PFC activation is observed first, followed by lateral cerebellar activation, and then up to 2 to 3 seconds later by activation in the motor cortex (Hulsmann and others 2003) and medial aspects of the cerebellum. Similar patterns have been observed in cognitive tasks involving preparatory periods (Allen and others 1997).

Patients with cerebellar lesions restricted to the dentate nucleus show a marked attenuation of the readiness potential for self-initiated movements (Kitamura and others 1999), indicating that the cerebellum may be the origin of the temporal delay necessary to maintain anticipatory PFC-IPL activity. Task-to-task variability in this delay period, perhaps resulting from cerebellar signals, may result in decreased PFC-IPL coherence (Carmel and others 2006). Moreover, variability of preparatory activity for movement is predictive of performance variability, supporting a central source for variability rather than variability in execution (Churchland, Afshar, and Shenoy 2006; Churchland, Santhanam, and Shenoy 2006).

A striking example of the predictive nature of cerebellar activity comes from a MEG study in which tactile inputs were periodically applied to the finger (Tesche and Karhu 2000). In the primary somatosensory cortex, the responses were strictly tied to the stimulus with an onset time right around the time of the stimulus. If the expected stimulus was omitted, this response was absent. In contrast, the cerebellar response in the .25 to 2 Hz range was as strong on trials in which the expected stimulus was omitted compared to when the stimulus actually occurred. Two other features of the MEG results should be noted. First, the cerebellar signal was evident prior to the expected time of the stimulus, underscoring the anticipatory nature of this activity. Second, the expectancy signals were not evident when the interstimulus interval was greater than 4 seconds, suggesting that cerebellar prediction has temporal limits (discussed below).

Errors, or violations of expectancies, produce significant increases in cerebellar activation, perhaps because of the powerful effects of climbing fiber responses on the BOLD signal (Lauritzen 2001). Such activations are observed in tasks in which temporal regularities are disrupted (Dreher and Grafman 2002), as well as during tasks in which participants gradually learn to anticipate forthcoming events (Doyon and others 2002). Deficits in error-based learning are widely documented in patients with cerebellar pathology (Ivry and others 2002; Diedrichsen and others 2005), although there remains considerable debate over whether this operation is limited to certain types of prediction. Cerebellar lesions have also been associated with impairments on tasks requiring rapid shifts in attention (Fiez and others 1992; Riva and Giorgi 2000; Gottwald and others 2004; Molinari and others 2004), although these deficits may be related to a resource allocation problem given the increased demands on these patients to prepare and produce responses (Ravizza and Ivry 2001). In addition, patients with cerebellar or cerebellar outflow tract lesions show an attenuation of the readiness potential or the CNV (Ikeda and others 1994; Kitamura and others 1999), as well as a reduction in activity in the contralateral parietal cortex (Lauritzen 2001).

The Cerebellum and Forward Models of Action and Cognition

It has been hypothesized that the cerebellum generates forward models related to the consequences of planned actions and the resultant changes in sensory feedback (Blakemore and Sirigu 2003). Within the context of a sensory synchronization network that includes the prefrontal and parietal cortex, the specialized role of the cerebellum might be to help code the precise timing of predictions to achieve sensory synchronization. Increases in variability could be a consequence of deficits in feed-forward or feedback control (Mauk and others 2000; Mehta and Schaal 2002).

The cerebellum's role in reducing movement variability, specifically temporal variability, has been studied over a range of task domains (Ivry and Spencer 2004). In rapid movements, the temporal patterning of the biphasic response of agonist and antagonist muscles is planned in advance of the movement (Manto and others 1998). A hallmark of cerebellar ataxia is the increased variability of the onset of the antagonist, which normally delays the agonist movement, resulting in dysmetria and intentional tremor (Timmann and others 2001). Thus, predictions, especially for motor control, not only require that we represent what to expect in the future; to be adaptive, it is usually essential that the timing of this prediction be accurate. When lifting an object, the anticipatory adjustment of grip force occurs just prior to lifting an object, thus ensuring that the object does not slip (Witney and Wolpert 2003). By generating well-timed predictions, the cerebellum would keep performance variability low.

Indeed, the predictive nature of the cerebellum may not be limited to the synchronization of actions with their sensory consequences, but may reflect a more general capability that extends to more abstract predictions (Schmahmann and Sherman 1998; Parsons 2004). An example of abstract (language) synchronization in interaction (conversation):

> When conversing with another on the phone, there is an expectancy of when the other person will pause and when that person is about to speak. When this timing is disrupted by variable transmission in the cell phone signal, the person on the receiving end has a great deal of difficulty in attending to the conversation.
>
> A similar result might occur if the variability is internally generated, resulting in temporal variability in terms of sensory expectations. This would lead to a defect in synchronization and difficulty in attending to the conversation.

The expanded size of the cerebellum in humans, especially the neocerebellum and dentate nucleus, parallels the phylogenetic development of prefrontal (Weaver 2005) and parietal lobes and corresponding capacity for goal-oriented behavior. This suggests a conservative process in which predictive functions derived for reducing motor variability have also come to be exploited in a more general manner. Polysynaptic tracers have identified cortical targets of the deep cerebellar nuclei in the monkey. This work has shown that in addition to the projections to primary and secondary motor areas, there are significant projections, via the thalamus, to the prefrontal and parietal cortex (Middleton and Strick 2001; Dum and Strick 2003). These anatomical connections most probably subserve predictive neural activity in the PFC-IPL-cerebellum network.

Timed Delay of Motor or Cognitive Action as a Synchronization Mechanism

What is the neural process that synchronizes expectancy with sensory input? To achieve synchronization between the expected sensory consequences of action or cognition and actual sensory feedback, motor or cognitive function would have to be timed accurately to occur so that the desired (synchronized) sensory state is achieved. One possible method is to generate appropriately timed sensory expectations that coincide with the desired sensory state. This is essential in interactions where the sensory input timing cannot be controlled, as in listening to another person's speech. One must time (delay) the cognitive expectancy of another person's speech to coincide with the auditory input. This presumes that an attentional cue immediately generates anticipatory signals. If sensory delays were not anticipated, the expectation would not match sensory input.

If one takes this mechanism a step further and cognition is considered a "motor" act, then the cerebellum could hypothetically reduce performance variability through feed-forward activation of the IPL. The cerebellum could reduce variability by coordinating in time the interactions between the IPL and PFC. This postulated mechanism has an antecedent in the cerebellar control of movement variability. Cerebellar control of the timing of the conditioned eye blink appears to be mediated by inhibition or damping of the facial motor nucleus (Delgado-Garcia and Gruart 2006). Following learning of the conditioned reflex, lesions of the cerebellar interpositus nucleus, which mediates eye-blink conditioning, produces early (not delayed) and variable eye-blink responses corresponding to an undelayed imperative motor response.

We suggest a similar process may occur for higher-order cortical processes. Some studies support a role for IPL in operating as a delay, or gating mechanism, to synchronize the action of PFC to the onset of the task. Parietal activation is in some cases antecedent to PFC in attention tasks (Corbetta and others 2000; Green and McDonald 2008), marked by a desynchronization in the alpha range of the EEG signal and subsequent increase in gamma frequency over PFC (Fan and others 2007). Parietal activation is seen before PFC in bottom-up processing versus top-down processing where the reverse is reported (Buschman and Miller 2007). An MEG study, in a working memory task, showed parietal activation 60 ms before PFC activation (Martin and others 2007). Using a 13 Hz visual flicker probe to detect cortical excitation/inhibition, decreased EEG amplitude (inhibition) in PFC and increased amplitude in the parietal region was observed in a spatial working memory n-back task (Ellis and others 2006). Although external cues suggest that parietal activation may precede PFC, at least in spatial attention tasks, the time course and cerebellar role in these interactions requires further study.

Optimal Time Frame for Reducing Performance Variability

As discussed in this review, variability in performance is related to attention: A result of successful attending is a reduction in variability. Accepting that coherence between PFC and IPL is necessary to pay attention, is there an optimal time frame or delay period for PFC-IPL coherence that will maximally reduce variability and is this timed delay dependent on inputs from the cerebellum? Can the time frame for such synchronization be related to the perceived, specious present and our sense of self-agency?

Time Frame of 2.5 Seconds for Minimizing Variability

Neural preparatory activity (cognitive or motor) is initiated generally about 2 to 3 seconds before execution, especially in self-initiated actions. The time frame for generation of the CNV seems to have a maximum of approximately 2.5 seconds. When the preparatory interval exceeds this duration, the peak of the CNV is observed at 2.5 seconds and then decays (Macar and Vidal 2003). Further EEG evidence suggests that anticipatory components weaken rapidly beyond a few seconds (Morgan and others 1992). Interestingly, performance declines for preparatory intervals that exceed 2.5 seconds (Macar and Vidal 2003; Macar and others 2004). A similar window has been suggested from studies of motor and perceptual timing, although the upper bound estimate tends to be between 1 and 2 seconds (Grondin and others 2004). Activation of the cerebellum begins approximately 3 seconds before self-initiated voluntary movements (Hulsmann and others 2003). A similar duration is observed in which people can integrate information to produce anticipatory eye movements (Barnes and Marsden 2002).

Working memory tasks also point to an optimal time frame of a few seconds (Pöppel 1994). For delay periods up to 4 seconds, the information can be maintained without requiring refresh processes or active rehearsal, suggesting a buffer that operates on a time scale consistent with the immediate present (Tulving 1989; Baddeley 2000). This time frame of approximately 2.5 seconds may reflect an upper bound for generating moment-to-moment predictions that allow the integration or synchronization of immediate goals or expectancies with sensory and motor events.

Pöppel and colleagues (Pöppel 2004) have proposed that the immediate present corresponds to an interval of approximately 2 to 3 seconds. Events within this interval are temporally bound (Fraisse 1963). We postulate that this time frame engages awareness due to its comparatively low variability and that it reflects

processing constraints imposed by the cerebellum (Dragoi and others 2003).

> Given the ability to attend to any time interval, one perceives events being contiguous within a time frame that attention generates the lowest variability—the specious present.

This attraction of awareness to repeating time frames about 2.5 seconds has been well capitalized by the television industry, which has a practice of "jump cuts" or camera switches that occur approximately every 2.5 seconds. The neural work of extracting the temporal period for synchronization is done for the viewer, freeing up cognitive resources for the TV show's content.

Awareness of Self-Agency: Distractibility as a Function of Variability

What about the relationship of variability and awareness of one's own actions? Awareness is, of course, a component of paying attention; moreover, awareness of self-agency during selective attention is likely a by-product that results from the synchronization of expectancy with sensory input (Jeannerod 2003). Cerebellar-parietal interactions have been posited as the axis of sensorimotor prediction (Blakemore and Sirigu 2003). Disruption of synchronization, either artificially as in delaying sensory feedback (Blakemore and others 1999) or clinically as in schizophrenia (Posada and others 2001) and autism (Schmitz and others 2003), lead to a decreased awareness of self-agency.

The impact of synchronization variability on awareness and self-agency is also evident in right parietal lesion patients with left-sided neglect—less attention or awareness is directed toward the left side. Spatial neglect may arise from reduced synchronization of one's own actions and their consequences, and as a consequence, a loss of self-awareness occurs in that spatial field. The patients are biased to orient their attention in the ipsilesional direction, to regions of space in which synchronization is less variable (Anderson and others 2000).

Similarly, the high individual variability and distractibility that occurs in normal fatigue (Maruff and others 2005) or in clinical conditions such as in traumatic brain injury (TBI) (Prigatano 2005) are associated with decreased selective attention and reduced awareness of self-agency. Indeed, a hallmark of TBI is the lack of awareness of the cognitive deficits. Rather than assuming an additional neural process that reduces distractibility, we posit that because awareness is enhanced in interactions characterized by low variability, distractors will have lower salience, allowing for better maintenance of attention.

Accurate anticipation, resulting in synchronization of external and/or self-generated events, produces lower performance variability, a heightened focus of attention, and enhanced self-agency. Under such conditions, performance will be less prone to interference or distraction. The better one attends, the more one is aware of one's self interacting with the object of attention.

Individual Variability and Disorders of Attention

Although we have emphasized how failures of prediction can lead to attention deficits, a lack of preparation can arise from many causes. For example, performance will be variable if an alert person is unable to maintain the current goal. However, the importance of well-timed predictions for optimizing goal-directed behavior has been underappreciated, especially when considering individual performance. In most studies, performance variability is considered at the group level. Individual variability tends to be ignored, with the various observations in each condition collapsed into a single mean. However, in terms of the study of attention and anticipation, intraindividual variability (IIV) is likely to prove quite informative. Interestingly, variability has frequently been the primary dependent variable in studies of temporal processing.

Increased IIV goes hand in hand with increases in distractibility in studies that measure both. Are the two parameters linked? Distractible individuals obviously perform tasks with higher IIV. But increased IIV may also make individuals prone to distractibility. Distractibility increases with IIV in attention loading tasks (Lavie 2005). Children who have higher performance variability than adults are more distractible and show weaker PFC-IPL coherence on working memory tasks that have distracters (Olesen and others 2007). Measurement of IIV can be extended to neural structures involved in reducing variability. Decreased variability in the parietal BOLD signal is correlated with improved arithmetic performance (Menon and others 2000). Although low IIV is useful in maintaining concentration, it may hinder switching to a new task when the information for the new task had previously been used as a source of distraction. However, high IIV may disrupt normal day-to-day function because distracters are disproportionately salient compared to task-relevant information.

Clinical Disorders and Normal Variants

With respect to the prediction attention network, lesions of the cerebellum, IPL, and PFC result in increased individual variability on a wide range of tasks. Cerebellar pathology is associated with impairments on a range of tasks that require precise timing, but this impairment is

manifest as an increase in IIV in both perceptual timing tasks and also attention tasks (Ivry and others 2002). Similar increases in IIV have been associated with lesions of the prefrontal cortex (Stuss and others 2003), parietal lobe (Anderson and others 2000), and the basal ganglia (Spencer and Ivry 2005). Lateral but not inferior medial PFC lesions produce increased IIV and reduced performance on cognitive tasks (Stuss and others 2003). Right IPL lesions produce neglect of the contralateral hemifield. But even here, a gradient of IIV can be observed with performance variability greatest for the most eccentric locations (Anderson and others 2000; Bartolomeo and others 2001).

A recent review (MacDonald and others 2006) and other studies have demonstrated high IIV in TBI (Stuss and others 1994; Collins and Long 1996) and ADHD (Castellanos and others 2005; Klein and others 2006). In chronic fatigue syndrome, there is increased IIV associated with attention, memory, and concentration difficulties and longer reaction times (Fuentes and others 2001). TBI patients have a well-documented increase in IIV (Stuss and others 1994; Burton and others 2002), longer reaction times (Hetherington and others 1996; Segalowitz and others 1997), distractibility (Mangels and others 2002), and difficulty in sustaining attention (Whyte and others 1995). They may require greater involvement of the PFC to compensate for damaged attention processes. This concept is supported by an fMRI study of TBI patients during a working memory task showing increased prefrontal cortical recruitment compared to a normal control group (McAllister and others 2001). Similar findings are reported for older individuals who have increased individual variability yet show increased prefrontal cortical activation on a working memory task (Cabeza and others 1997; Strauss and others 2002).

In normal fatigued individuals, there is an increase in IIV (Fuentes and others 2001; Adam and others 2006; Bliese and others 2006), cognitive IIV (Maruff and others 2005), with corresponding problems in performance (Martin and Hofer 2004). The very young and the very old have high IIV (Williams and others 2005). Aging studies (Hultsch and others 2002; Martin and Hofer 2004; Nesselroade and Salthouse 2004; Gorus and others 2006) show increasing IIV accounts for most of the group variance in cognitive performance (Strauss and others 2002). In addition, IIV is one of the better predictors of cognitive decline (MacDonald and others 2003).

Variability as a Metric of Attention

If one consequence or function of attention is to reduce performance variability, then variability can be used as a metric to reflect attention accuracy and capacity. Traditionally, discrete responses have been used in most studies that assess IIV (Stuss and others 1994; Segalowitz and others 1997), allowing measurements, at best, every few seconds. Such measures would not detect momentary lapses in attention. Yet attention varies over time; thus, relatively continuous and extended measures of performance should be used to gauge moment-to-moment fluctuations in attention within individuals.

We have used circular smooth pursuit eye movements, measuring target-eye position variability with a high-resolution camera that allows data collection every 2 milliseconds. Subjects view a red dot on a computer screen moving in a circle at 0.4 Hz (completing a full circle in 2.5 seconds) with a 500 Hz infrared camera eye-tracking system. This task engages a network spanning the prefrontal cortex, parietal lobe, and the cerebellum, presumably reflecting the operation of an anticipatory network. Using this technique, measures of variability related to the difference in eye-target position and velocity correlate with performance on a working memory task in normal and TBI subjects (Suh, Basu, and others 2006; Suh, Kolster, and others 2006).

This eye-tracking technique may be useful in rapidly assessing attention following mild TBI, sports concussion, and attention disorders, and in evaluating normal levels of fluctuating attention. Variability measures can also be calculated from simple reaction time testing; however, the temporal sampling rate is significantly lower (at best 2 data points per second versus 500–1000 data points per second in eye-target tracking, depending on the eye-tracking camera resolution), leading to long duration testing and missed moment-to-moment fluctuations in attention. For rehabilitation, the question remains whether reducing timing variability by, for example, a continuous feedback method could help alleviate attention and working memory deficits.

Questions for Future Investigation

Answers to the following questions could bridge current gaps in our knowledge:

PFC-IPL Coherence in Attention

- What are the temporal dynamics?
- What are the subcortical (cerebellar/thalamic/basal ganglia) contributors to initiating, sustaining, or terminating coherence?
- What is the relationship of the CNV and RP to PFC-IPL coherence?
- Do patients with cerebellar dentate lesions have contralateral disturbances in PFC-IPL coherence (variable coherence)?
- Is there a correlation between fatigue, variability, and PFC-IPL coherence in normal individuals?
- How is PFC compensation of timing variability detected?

Variability Relationship to Distractibility

- Is performance variability a primary cause of distraction or is it governed by a separate process (filter)?
- Could emotional states, say anger, be construed as a dual task and cause increased variability and distraction on tasks requiring attention?

- What is the level of variability required for sustained attention or task switching?
- Are there normal cycles of low and high variability? If so, are these windows of potential distraction?
- Is self-agency and awareness correlated with PFC-IPL coherence? States of meditation and voluntary suspension of the predictive state may disrupt this coherence leading to an absence of self-agency leaving only sensory awareness.

Cerebellum as a Time Delay for Sensorimotor Synchronization

- What is the nature of cerebellar interaction with PFC-IPL coherence?
- How is the temporal delay between cue and execution learned?
- Is temporal delay learning implicit or explicit?
- Is eye-blink trace conditioning the evolutionary basis for cerebral cortical predictive timing?
- What are the behavioral effects of selective damage to feed-forward or feed-back tracts from cerebellum to parietal and PFC areas?
- Why is the temporal delay interval optimal at 2 to 3 seconds? What are the inherent cerebellar circuitry properties that would yield such limits?
- What produces variability in the cerebellar timed delay output?
- Does rest or sleep restore accurate cerebellar timing delays and if so what is the role of REM sleep?
- How does early postnatal cerebellar granule cell synaptogenesis during the period of experimental interactions (play) produce temporal frameworks for learning and synchronization?

Summary

The evolutionary expansion of the human brain occurred with the development of language and abstract thinking and the appearance of sustained attention. The temporal processing requirements of such higher cognitive processes demand that the brain adopt a predictive state. This predictive capability is an important part of what we experience as perceived present, allowing moment-to-moment synchronization of sensory predictions with task relevant information. Selective attention, as part of this predictive process, reduces performance variability, minimizes distractibility, and as a consequence increases awareness (self-agency).

We propose that the prefrontal and parietal cortices, in concert with the cerebellum, are essential for the generation and utilization of these real-time predictions. This system operates within a limited time frame, what has been called the immediate present, a temporal window that spans approximately 2.5 seconds. The limitation here may reflect a boundary for optimal reduction in the variability of real-time feed-forward predictions. With learning, this system allows behavior to shift from reactive to predictive. We attend by accurately predicting.

The inability to efficiently and consistently use predictive mechanisms is hypothesized to be a major cause of disability in attention disorders. High variability leads to distractibility (and, as a consequence, decreased awareness) and reduced cognitive performance. Permanent increased variability can originate from damage to the prefrontal cortex, parietal cortex, the cerebellum, or to the fiber tracts that link these regions. We propose that the cerebellum is involved in producing the requisite timing required to synchronize sensory predictions with the consequences of motor and cognitive interactions. In the absence of this timing, or as a consequence of elevated variability, the PFC operates on the immediate state of neural activity, leading to reactive responses. This leads to high variability in performance, errors, reduced self-agency, as well as a proclivity for distraction.

Defining attention as a process to reduce variability in the synchronization of expected and actual sensory input over a time frame determined by cognitive and motor temporal constraints allows objective scientific study that can lead to useful diagnostics and therapeutics.

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