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Review

More attention must be paid: The neurobiology of attentional effort

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ABSTRACT

Increases in attentional effort are defined as the motivated activation of attentional systems in response to detrimental challenges on attentional performance, such as the presentation of distractors, prolonged time-on-task, changing target stimulus characteristics and stimulus presentation parameters, circadian phase shifts, stress or sickness. Increases in attentional effort are motivated by the expected performance outcome; in the absence of such motivation, attentional performance continues to decline or may cease altogether. The beneficial effects of increased attentional effort are due in part to the activation of top-down mechanisms that act to optimize input detection and processing, thereby stabilizing or recovering attentional performance in response to challenges. Following a description of the psychological construct "attentional effort", evidence is reviewed indicating that increases in the activity of cortical cholinergic inputs represent a major component of the neuronal circuitry mediating increases in attentional effort. A neuronal model describes how error detection and reward loss, indicating declining performance, are integrated with motivational mechanisms on the basis of neuronal circuits between prefrontal/anterior cingulate and mesolimbic regions. The cortical cholinergic input system is activated by projections of mesolimbic structures to the basal forebrain cholinergic system. In prefrontal regions, increases in cholinergic activity are hypothesized to contribute to the activation of the anterior attention system and associated executive functions, particularly the top-down optimization of input processing in sensory regions. Moreover, and influenced in part by prefrontal projections to the basal forebrain, increases in cholinergic activity in sensory and other posterior cortical regions contribute directly to the modification of receptive field properties or the suppression of contextual information and, therefore, to the mediation of top-down effects. The definition of attentional effort as a cognitive incentive, and the description of a neuronal circuitry model that integrates brain systems involved in performance monitoring, the processing of incentives, activation of attention systems and modulation of input functions, suggest that 'attentional effort' represents a viable construct for cognitive neuroscience research.

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Contents

1. Introduction

Increasing attentional 'effort' as a result of challenging circumstances, and as a function of the motivation to maintain or recover attentional performance, represents an everyday experience. To paraphrase and modify a famous statement: *every one knows what increases in attentional effort are*. For example, consider your drive home from work; yesterday it was uneventful and you used a well-practiced route that makes minimal demands on your attentional resources; indeed, you do not even recall whether the traffic light actually was on green as you made it through that intersection. But today, you did not sleep much last night, you had an exhausting day, or you feel that you are getting sick, and you are having trouble concentrating, but the last thing you need is another ticket. You will increase your attentional 'effort' to ensure that you will not miss a red light or a sign, and you will also closely monitor your speed, while looking out for that police car.

However, theoretically and experimentally, 'attentional effort' has remained an undefined concept. Indeed, James (1890) dismissed the issue outright, concluding that "…the notion that our effort in attending is an original faculty, a force additional to the others of which brain and mind are the seat, may be an abject superstition" (p. 452). "Attentional effort" typically has been cited in the literature in order to explain the performance in difficult tasks, or in tasks involving attentional shifts or switching modalities. Thus, 'attentional effort' has been generally considered a function of task difficulty. An arguably more useful conceptualization of attentional effort, as a function of the subject's motivation to perform, particularly following performance challenges, is proposed below. Furthermore, we present a model that describes the interactions between cortical, mesolimbic and cholinergic systems considered essential for activating attentional systems and resources as a result of performance challenges and the subjects' motivation to recover performance or limit performance decline. This model also provides avenues toward the dissociation between attentional processes and changes in reward contingencies (Maunsell, 2004).

2. Attentional effort as a cognitive incentive

The role and function of increases in attentional effort have been captured in the context of two major theoretical perspectives, (1) capacity models of attention and (2) top-town regulation of attentional functions. Because of the limited capacity for attentional processing, Kahneman (1973) suggested that the "mobilization of effort in a task is controlled by the demands of the task rather than by the performer's intentions" (p. 17). However, this focus on task demands as the main determinant of attentional effort remains insufficient. For example, the increases in attentional effort required to slow the decline in performance, to 'stay-on-task', or to regain performance following a detrimental event (e.g., the presentation of a distractor), appear to be controlled to a lesser degree by the demands of the task than by the performer's motivation to maintain performance. Indeed, allowing performance to degrade further, or even to terminate, represent possible and plausible outcomes, specifically in laboratory settings where the costs for such outcomes remain relatively insignificant. This is not to say that task demands and task performance would be without significance, as increases in attentional effort typically are triggered as a result of the subjects' detection of performance errors or of a declining reward rate. In other words, information about non-compliance with task

demands represents the critical stimulus for potentially adjusting levels of attentional effort; however, such an adjustment depends on the costs and benefits associated with a continuing decline in performance versus the stabilization of residual performance or even performance recovery (see Fig. 1). If the driver in our introductory illustration knew for sure that the police were not around, driving performance very likely would deteriorate. Thus, increases in attentional effort do not represent primarily a function of task demands but of the subjects' motivation to perform.

In order to arrive at a constrained and useful definition of the construct 'attentional effort', we will describe 'attentional effort' as a cognitive incentive (Berridge and Robinson, 2003). Increases in attentional effort serve to optimize goal-directed behavioral and cognitive processes. Such a definition integrates explicit and implicit motivational forces with attentional performance and implies that attentional effort is a function of such motivations.

The focus on attentional 'effort' as a cognitive incentive limits our primary discussion to scenarios characterized by "active endogenous control considerations" (Gopher et al., 2000) in order to maintain or regain attentional performance under challenging conditions. This constrained perspective on attentional effort allows us to avoid complex considerations about single versus multiple resources, commodities, or energies available to optimize attentional performance under challenging conditions (e.g., Gopher, 1986). As will be discussed further below, the consideration of attentional effort as a cognitive incentive has defined implications for models of the neuronal circuitry mediating the initiation and effects of increases in attentional effort.

Experimental research on attention appears to have had little interest in actively varying attentional effort, perhaps because the construct has remained undefined, and because standard task and test paradigms for measuring the effects of increased attentional effort do not appear to be in place. There are some instructive exceptions. An unpublished thesis (Collyer, 1968; discussed in Pashler, 1998) describes evidence indicating incentive-induced increases in response speed and accuracy in a choice reaction time task. Pashler (1998) concludes that "people are sometimes capable of exerting continuous control over levels of performance" (p. 384). Furthermore, Tomporowski and Tinsley (1996) observed that young adults who were not paid for performing a 60-min sustained attention task exhibited a significant decline in performance over time-on-task ('vigilance decrement') when compared with paid subjects' performance. Thus, their experiment generated robust evidence for the role of motivational factors in maintaining attentional performance. Presumably, the paid subjects resisted the potential decline in performance by initiating top-down mechanisms (see below) which acted to counter declining attentional performance. Finally, it is not unexpected that in the more applied domain of human factors, research on the role of effort as a cognitive incentive has been studied somewhat more explicitly. This research demonstrated that measures of workload rating indicate the effects of increased incentives, and that such increased workload ratings predict enhancement in performance produced by increased incentives (Vidulich, 1988).

However, and to reiterate, the paucity of laboratory evidence is in stark contrast to the very common experience of being motivated to increase "attentional effort" in order to perform better, or to continue performing under challenging conditions. Likewise, the potentially dramatic consequences of having failed to increase attentional effort in challenging situations represents a familiar experience and indicates that subjects are capable of estimating – validly or not – their capacity for modifying attentional performance.

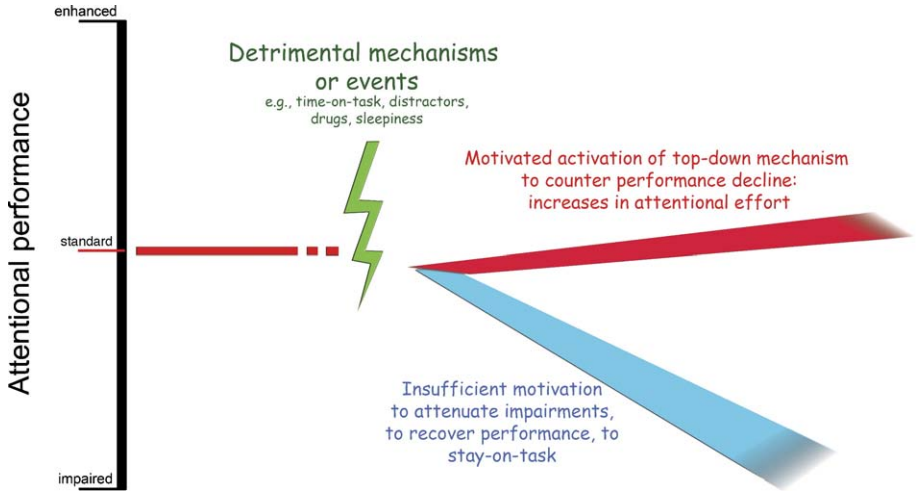


Fig. 1 – Illustration of the role of 'attentional effort', defined as a cognitive incentive, on attentional performance. Various detrimental manipulations, processes or events, including distractors, prolonged time-on-task, drugs or stress potentially result in the deterioration of attentional performance. In the absence of incentives acting toward limiting the decline in performance or recovering from impairments in performance, performance is likely to decline further or the subject will cease performing (in blue). Alternatively, and depending on motivational contingencies, top-down mechanisms are initiated to counteract declining input processing and to optimize attentional resource allocation in order to slow the decline in performance, maintain residual performance, or even attenuate impairments in attentional performance (in red). (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

3. Top-down mechanisms mediate the effects of attentional effort

The recovery or stabilization of attentional performance under challenging conditions, or the enhancement of attentional processes in response to increased incentives, requires mechanisms which act to optimize input processing, noise filtering, and the redistribution and focusing of processing resources. Such functions have been conceptualized as being orchestrated by "supervisory attentional systems" (Norman and Shallice, 1986; Stuss et al., 1995), a 'central executive control' (Baddeley, 1986), or the anterior attention network (Posner, 1994; Posner and Dehaene, 1994). Prefrontal and anterior cingulate regions, interacting with parietal areas, have been routinely demonstrated to represent the core components of the brain's circuitry that executes top-down control (see also Friedman-Hill et al., 2003; Gehring and Knight, 2002; Hopfinger et al., 2000; Pessoa et al., 2003; Serences et al., 2004).

Based on largely undefined neuronal circuits (but see below), frontoparietal networks act to optimize, for example, receptive field properties of sensory neurons in cortical and subcortical regions (Corbetta and Shulman, 2002; Reynolds et al., 2000; Shomstein and Yantis, 2004; Treue, 2001; Treue and Martinez Trujillo, 1999; Wager et al., 2004), or to suppress activity in regions which process irrelevant or competing inputs (Shulman et al., 1997; Smith et al., 2000). Table 1 provides additional illustrations of top-down effects. Importantly, such top-down mechanisms consume cognitive resources as demonstrated, for example, by the increased processing of distractors or irrelevant information in situations in which such resources are highly taxed by extensive demands on cognitive control processes (Lavie, 2005; O'Connor et al., 2002).

The activation and orchestration of such top-down mechanism are assumed to underlie the ability to stabilize or regain attentional performance under challenging conditions and as a function of incentives (Butter, 2004; Small et al., 2005). Below, we will discuss the evidence that suggests a prominent role of cortical cholinergic inputs to prefrontal regions in activating such top-down mechanisms, indicating the possibility that prefrontal modulation of cholinergic activity in somatosensory cortical regions contributes to the mediation of top-down effects, particularly if such effects serve to optimize input processing as a function of increases in attentional effort.

Table 1 – Top-down regulation: synopsis of main neuronal effects

Top-down control of attentional processing generally refers to the biasing of attentional resources toward the detection and processing of target stimuli, based on expectations concerning stimulus modality, features and location, cognitive strategies, and motivational variables. Neurophysiological and neuroimaging research documented a diverse range of top-down mechanisms, primarily in visual and auditory sensory systems. Depending on the experimental methods used, the effects of top-down control can be summarized as follows.

(1) Modification of neuronal firing rate. Attention to stimuli causes an increased response of sensory neurons to these stimuli. For example, attention to low luminance contrasts was demonstrated to increase the responses of V4 neurons in monkeys; such increases were equivalent to a 51% increase in contrast (Treue and Maunsell, 1996). Enhancing the excitability of target-representing neurons therefore may represent a mechanisms designed to enhance the detection and discrimination of stimuli selected top-down (Engel et al., 2001; Fries et al., 2001; Niebur and Koch, 1994; Steinmetz et al., 2000).

(2) Synchronized neuronal firing. Top-down modulation of the degree to which neurons fire in a synchronized fashion may serve as a mechanisms to control the attentional significance of a stimulus (e.g., Fries et al., 2001; Moran and Desimone, 1985).

(3) Modification of receptor field properties: Receptive fields of neurons in primary sensory and sensory associational regions of monkeys trained to detect targets and to discriminate distractors were demonstrated to undergo modification indicative of optimized detection and processing of target stimuli, and optimized suppression of the detection and processing of distractors or 'noise' (e.g., Weissman et al., 2002).

(4) Modulation of activity in attended target stimuli-processing regions and circuits. fMRI studies demonstrated that the activity or cortical regions involved in the detection and discrimination of attended target stimuli is increased (e.g., Serences et al., 2005). Distractors that capture attention cause increases in visual cortical regions representing their location (e.g., Kastner et al., 1999). Likewise, cortical regions representing locations for expected and attended stimuli exhibit increased activity prior to stimulus onset (O'Connor et al., 2002). Such top-down activation extend to subcortical regions, such as the lateral geniculate nucleus (Smith et al., 2000).

(5) Attenuation of activity in cortical regions representing non-target features, modality, or space. Evidence indicating suppression of basal cortical activity in fMRI studies has remained scarce, in part for experimental and methodological reasons (e.g., Treue, 2001; Vanduffel et al., 2000). However, attenuation of activity in regions representing unattended stimulus features has been frequently observed (e.g., O'Connor et al., 2002) and reflects attentional load and resources available for the filtering of unattended stimuli (e.g., Shulman et al., 1997). Furthermore, neuronal activity in areas representing irrelevant modalities can be suppressed. Thus, it is conceivable that top-down imposed attenuation of the excitability of a cortical or subcortical region serves to suppress the detection and processing of unattended stimuli.

4. Brain systems mediating increases in attentional effort

4.1. *Evidence from human imaging studies*

Human neuroimaging data from studies in which attentional effort was considered a cognitive incentive and varied systematically do not appear to be available. However, a relatively rich literature describes brain metabolic correlates of increases in task difficulty, switching between tasks and/or shifts between stimulus modalities. As subjects typically comply with such challenges in laboratory settings, increases in attentional effort may be speculated to mediate the continuing, even if residual, performance, or to recover from the effects of task switching or shifts between modalities. As attention can be shifted to new locations, responses, or

stimulus attributes, and as a multiple or different cognitive operations underlie different types of shifts, it is perhaps not unexpected that a recent meta-analysis of neuroimaging studies on attention shifting concluded that such shifting is associated with increases in activity in a distributed network that includes medial, superior and ventral prefrontal, medial premotor and posterior parietal circuits (Wager et al., 2004; see also Nagahama et al., 2001; Serences et al., 2005; Shomstein and Yantis, 2004; Yantis et al., 2002). Furthermore, several studies suggested that "good" attentional task performance, or attentional performance over extended periods in time, which may involve increases in attentional effort, are associated with activation of frontoparietal regions specifically in the right hemisphere (Coull et al., 1998; Lawrence et al., 2003).

4.2. *Prefrontal cholinergic inputs mediating increases in attentional effort*

4.2.1. *Anatomical organization of the basal forebrain cholinergic system*

All cortical areas and layers are innervated by cholinergic neurons which originate in the nucleus basalis of Meynert (nbM), substantia innominata (SI), the horizontal nucleus of the diagonal band (HDB), and the preoptic nucleus (collectively termed 'basal forebrain'; BF). The organization of these projections follows a rough rostrocaudal/mediolateral topographic organization (Woolf, 1991). In the rat, pre- and infralimbic and cingulate regions receive a strong cholinergic input from the HDB and from anterior portions of the SI and the ventral nbM (Luiten et al., 1987). Additionally, cingulate and medial prefrontal regions may also receive a minor cholinergic projection from the pontine tegmentum (Satoh and Fibiger, 1986; Woolf et al., 1984). Cholinergic projections of the BF to the cortex are not, or only to some very limited degree, collateralized (Semba, 2000).

Zaborszky (2002) suggested that the cortically projecting neurons in the BF form distinct bands and that the basal forebrain projection system therefore may be described as a modular system. Such an organization of this projection system would indicate that cholinergic neurotransmission can be modulated in a cortical area-, modality-, and thus task-specific manner.

Basal forebrain neurons are innervated by numerous telencephalic, diencephalic and brain stem projections, and the differential contributions of these inputs to the behavioral and cognitive functions of basal forebrain cholinergic projections have been conceptualized (Sarter et al., 1999). Notably, prefrontal neurons project back to the basal forebrain (Gaykema et al., 1991; Sesack et al., 1989; Zaborszky et al., 1997), thereby allowing the prefrontal cortex to 'employ' the cholinergic projection system to other cortical regions for the mediation of top-down mechanisms (below; Sarter et al., 2001, 2005a).

4.2.2. *General attentional functions of the cortical cholinergic input system*

Experiments which assessed the effects of selective lesions of the BF cholinergic projection system on attentional performance or monitored cortical ACh efflux in attention task-performing animals generated extensive evidence in support of the hypothesis that the cortical cholinergic input system represents an essential component of neuronal systems mediating attentional functions and capacities (Chiba et al., 1995; Dalley et al., 2001; Everitt and Robbins, 1997; McGaughy et al., 1996; 2000, 2002; Mesulam, 1990; Sarter and Bruno, 1997, 2000; Sarter et al., 1999, 2001; Voytko, 1996). The contributions of cortical cholinergic inputs to these functions have been specified with regard to their role in signal-driven (or bottom-up) versus task-driven or cognitive (or top-down) modulation of signal detection. In this context, the term 'detection' refers to a cognitive process which consists of "…the entry of information concerning the presence of a signal into a system that allows the subject to report the existence of the signal by an arbitrary response indicated by the experimenter" (Posner et al., 1980).

The cortical cholinergic input system generally acts to optimize the processing of thalamic inputs in attention-demanding contexts (Sarter et al., 2005a). Neurophysiological studies demonstrated that increases in cholinergic transmission in sensory areas enhance the cortical processing of thalamic inputs (Edeline, 2003; Weinberger, 2003). Such inputs, if novel, salient, or unexpected, 'recruit', via activation of BF cholinergic projections to the cortex, the cortical attention systems, thereby directly amplifying the detection of such inputs and ensuring their attentional significance.

The activity of cortical cholinergic inputs is also modulated based on direct prefrontal projections to the BF and on multisynaptic prefrontal connections with the cholinergic system via limbic regions including the nucleus accumbens, ventral tegmental area and the amygdala. The prefrontal cortex may also modulate the activity of cholinergic terminals elsewhere in the cortex via cortico-cortical (or associational) projections (Nelson et al., 2005). Prefrontal modulation of the activity of cholinergic inputs to sensory and sensory-associational regions has been suggested to represent a component of the efferent network of the anterior attention system mediating top-down effects (Sarter et al., 2005a). Thus, depending on the quality of stimuli and task characteristics, cortical cholinergic activity reflects the combined effects of signal-driven and task-driven modulation of detection (Bentley et al., 2004; Sarter et al., 2001, 2005a). As discussed next, the cholinergic inputs to the prefrontal cortex are particularly active in situations that require the initiation of top-down mechanisms to cope with impairments in attentional performance or, in short, in situations characterized by increases in attentional effort.

4.2.3. *Prefrontal cholinergic inputs and increases in attentional effort*

Studies designed to measure cortical ACh efflux in attentional task-performing animals consistently demonstrated relatively stable performance-associated increases in ACh efflux (Arnold et al., 2002; Dalley et al., 2001; Himmelheber et al., 2000b; McGaughy et al., 2002; Passetti et al., 2000). Importantly, following completion of the task, ACh efflux typically returns to pre-task baseline levels.

In a recent experiment, we measured the release of ACh in the medial prefrontal cortex in animals while they performed a sustained attention task and following a manipulation that produced limited yet distinct impairments in performance.

The task rewarded rats for the detection of signals and the rejection of non-signal events but did not trigger scheduled consequences in response to incorrect responses (misses, false alarms).

We had previously observed that disruption of NMDA receptor signaling in the basal forebrain impaired the animals' ability to detect signals (Turchi and Sarter, 2001a,b). Importantly, the effects of pharmacological blockade of NMDA receptors can be adjusted so that animals do not cease performing but, depending on dose of the NMDA receptor antagonist, exhibit impaired performance which recovers later in the test session. Similar to humans (Tomporowski and Tinsley, 1996), the attentional performance of rats is sensitive to motivational manipulations (Echevarria et al., 2005); therefore, the recovery and perseverance of attentional performance following the pharmacological challenge (see Fig. 2) was not likely to occur in the absence of the reward contingencies; rather, performance would have further declined and most of the trials would have been omitted. In fact, in this experiment, the number of omissions was not affected, suggesting that animals remained motivated to continue performing the task and, in order to maximize the number of rewards, to counteract the detrimental effects of the challenge by activating attentional, including top-down mechanisms.

As illustrated in Fig. 2, prefrontal ACh efflux further increased in response to the challenge, and while the animals' performance remained below baseline levels (for details see Kozak et al., 2006). It is important to note that this effect could not have been a direct consequence of the pharmacological challenge, as NMDA receptor blockade in the basal forebrain in non-performing animals decreases cortical ACh efflux (Fadel et al., 2001; Giovannini et al., 1997; Rasmusson et al., 1996). Thus, in response to the performance challenge, and presumably in order to mediate increases in attentional effort, cholinergic projections to the prefrontal cortex received sufficient stimulation to not only attenuate the effects of blockade of their NMDA receptors, but to increase further the level of cholinergic transmission, to a level significantly above the extracellular ACh concentrations observed during normal performance. The circuitry mediating the 'import' of this stimulation is unclear but, as will be described in more detail below, there is sufficient evidence and conceptual background to hypothesize that the effects of incentives on attentional performance are mediated via prefrontal–mesolimbic regulation of the excitability of basal forebrain cholinergic neurons.

The evidence described in Kozak et al. (2006) suggests that increases in prefrontal ACh efflux, beyond the elevated levels observed during normal, unchallenged attentional performance, mediate increases in attentional effort. The data did not suggest that such augmented increases are correlated with levels of performance or, more specifically, the degree of performance impairment produced by the challenge. This finding may indicate that increases in attentional effort are not related in a simple (linear) fashion to levels of (residual) performance. Passetti et al. (2000) likewise did not observe relationships between prefrontal ACh efflux and measures of response accuracy following variations in the attentional demands of their task. However, they documented a positive correlation between ACh efflux levels and the number of trials completed. As the number of completed trials reflects primarily the

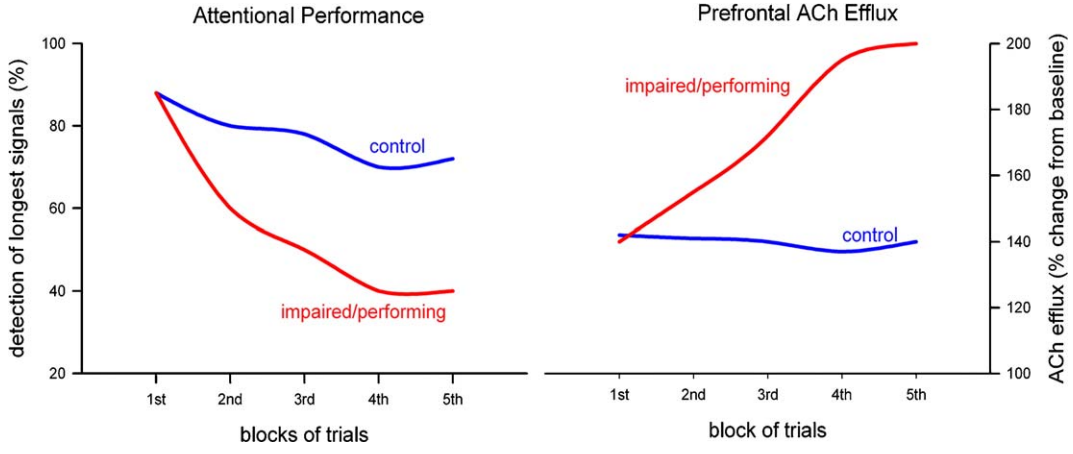


Fig. 2 – Schematic illustration of the main findings described in Kozak et al. (2006). Animals performing the standard sustained attention task exhibit relatively stable levels of performance across the 4 blocks of trials (8 min each) as indicated, for example, by the hit rates to longest (500 ms) signals (left blue line). Performance-associated ACh efflux has been repeatedly shown to be relatively stable across blocks (right blue line; see also Arnold et al., 2002; Dalley et al., 2001; Passetti et al., 2000; Reynolds et al., 2000; Worgotter and Eysel, 2000). Following infusions of an NMDA receptor antagonist, the animals' hit rates were impaired (left red line). Importantly, the number of omissions remained unchanged, suggesting that animals remained motivated to continue performing and earn rewards. Moreover, following a lower dose of drug, performance levels recovered 2 blocks after drug infusion, further supporting the speculation that animals recruited cognitive mechanisms in order to counteract the detrimental effects of the performance challenge. As indicated in the right plot, such increases in attentional efforts were associated with augmented increases in prefrontal ACh efflux. These augmented increases in medial prefrontal ACh efflux were observed while animals' performance remained below pre-challenge baseline. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

animals' motivation for continued attentional performance, this number also serves as an indicator of the levels of attentional effort. Therefore, the finding by Passetti et al. (2000) corresponds with the present hypothesis that increases in PFC ACh efflux mediate increases in attentional effort.

5. Linking motivation with attention: mesolimbic regulation of prefrontal ACh efflux

Collectively, the evidence and hypotheses discussed above form the basis for the following main hypotheses:

(1) Increases in attentional effort are a function of the subjects' motivation to recover from the performance effects of detrimental manipulations and/or to maintain residual performance.
(2) Increased activity of prefrontal cholinergic inputs represents an essential component of the neuronal mechanisms mediating increases in attentional effort. Increased prefrontal cholinergic activity contributes to the recruitment of top-down mechanisms which act to attenuate the effects of detrimental manipulations on input processing.

In accordance with a simplified sequence of events and processes, spanning from the detection of degrading attentional performance to the motivation-driven activation of the prefrontal cholinergic input system and the prefrontal efferent mediation of top-down effects, and based on the available knowledge concerning the mediation of these converging processes by prefrontal/anterior cingulate – mesolimbic – basal forebrain–cortical circuitry, below we will conceptualize a model of the neuronal circuitry mediating increases in attentional effort.

5.1. *The detection of errors and reward loss by frontal, particularly anterior cingulate regions*

The effects of attentional effort are seen in those cognitive control processes that adapt performance to challenging task demands and motivational incentives (Botvinick et al., 2001). The trigger for such effortful cognitive control is a signal of deteriorating performance[1]. Hence, a precondition for successful control is a performance monitoring system that signals when attentional effort is needed. Several events and processes are capable of triggering or advancing a decline in attentional performance, including prolonged time-on-task, distractors, sleepiness, and shifts of circadian periods, or sickness. Depending on individual task parameters and outcome contingencies, the detection of errors and associated reward loss represent the main indicators of deteriorating performance.

Neuroimaging and electrophysiological studies in humans have consistently implicated the medial frontal cortex, in particular the anterior cingulate cortex (ACC), in processing errors, response conflict, losses of reward, and other negative events such as pain perception (Botvinick et al., 2004; Brown and Braver, 2005; Carter et al., 1998, 2000; Gehring and Taylor, 2004; Holroyd and Coles, 2002). Many of the circumstances that invoke ACC activity also cause activity of the lateral prefrontal cortex (LPFC), leading to the view that these structures operate as part of a system for effortful cognitive control (Kerns et al., 2004; MacDonald et al., 2000). One version of this view is that the ACC detects negative events, whereas the LPFC implements control. For example, prefrontal regions have been hypothesized to maintain task representations necessary for control (MacDonald et al., 2000). An alternative view is that the ACC itself may act as a controller. The basal ganglia could be involved in detecting the error or reward loss, with the ACC using the resulting error signal to modify response strategies (Holroyd and Coles, 2002), perhaps dependent on task representations maintained by the LPFC (Gehring and Knight, 2000).

A key aspect of the view of attentional effort as a cognitive incentive is the idea that motivation determines the degree of effort; thus, brain activity reflecting effortful cognitive control should be affected by incentive/motivational manipulations. The clearest tests of this prediction are found in studies that manipulate the incentive associated with task performance and show variation in neural activity associated with effortful cognitive control. Electrophysiological and neuroimaging studies show enhancements of ACC activity associated with errors, particularly when the costs associated with errors increase (Falkenstein et al., 1995; Gehring et al., 1993; Hajcak et al., 2005; Ullsperger and von Cramon, 2004).

The link between aversive response outcomes and effortful changes in response strategy is supported by findings that the ACC appears to be critical for changes in behavioral strategy only when the reward associated with a response signals a behavioral change. Studies in macaques with lesions of the ACC substantiated the hypothesis that ACC circuitry specifically processes action–outcome relationships, as opposed to relationship between stimuli and reward (Hadland et al., 2003). Moreover, studies of single-unit activity and lesion effects in both macaques (Shima and Tanji, 1998) and humans (Williams et al., 2004), as well as an fMRI study in humans (Bush et al., 2002) all indicate that the ACC is implicated when changes in response strategy are signaled by reward loss but not when such changes are signaled by task cues.

The notion that attentional effort must be involved to recruit the cognitive control functions of the ACC may help to explain findings that individuals with damage to the ACC fail to show deficits in some types of cognitive control, such as performance in conditions of response conflict (Fellows and Farah, 2005), despite the large number of neuroimaging studies showing ACC activity in such conditions. The ACC should be critical for cognitive control only when processing of the incentive properties of an aversive event (such as a reward loss) is necessary to instigate control. Other forms of cognitive control may proceed unimpaired without a functioning ACC. A better disconfirmation of our view would consist of findings

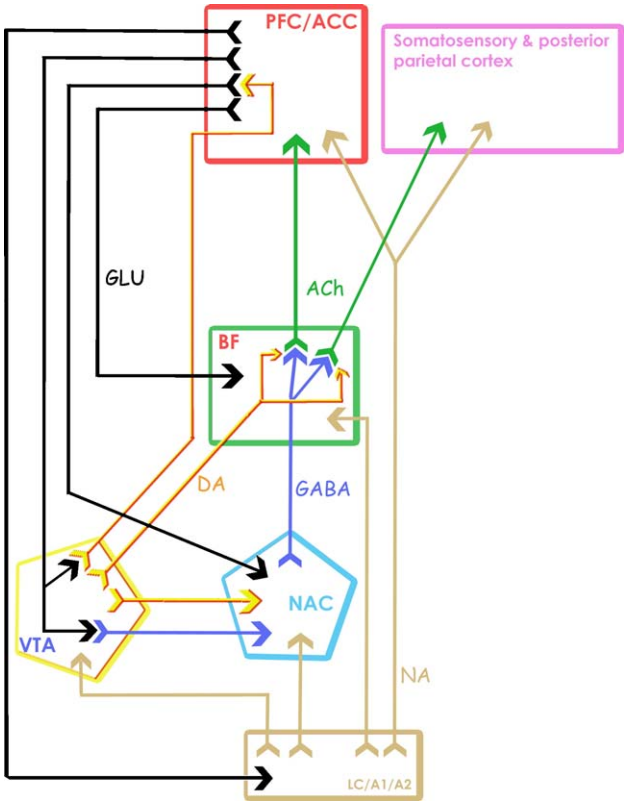
[1] Here we use the term "effortful cognitive control" purposely, as an alternative to the terms "cognitive control" or "executive control." Many kinds of cognitive control can take place without aversive circumstances triggering them. Effortful cognitive control as we define it here is limited to those kinds of cognitive control that are engaged when negative events signal that goals are not being achieved, making effort necessary.

that incentive manipulations influence behavior to the same degree when the ACC is damaged as when it is intact.

Error detection, reward loss, and/or other aversive outcomes associated with incorrect responses are closely associated events and represent conceptually overlapping constructs. Thus, it is not unexpected that evidence indicates that the ACC is also recruited by aversive outcomes (Bush et al., 2002; Gehring and Willoughby, 2002). Therefore, the recruitment of the neuronal circuitry mediating increases in attentional effort as a result of worsening performance begins with error detection and the processing of performance-associated reward loss, based on interactions between the ACC and other prefrontal regions (see also Ridderinkhof et al., 2004).

5.2. *Integration of information about performance deterioration with motivational variables by prefrontal–mesolimbic circuitry*

The failure to detect an attentional signal, or the absence of such a signal, yields a prediction error, as the actual outcome (no reward) differs from the expected outcome (Schultz and Dickinson, 2000). Midbrain dopaminergic neurons code such prediction errors; for example, omitted rewards are associated with reduced dopaminergic activity (Fiorillo et al., 2003; Schultz, 1998; Tobler et al., 2003, 2005). As schematically illustrated in Fig. 3, prefrontal projections contact with two populations of midbrain ventral tegmental (VTA) neurons, (1) with dopaminergic neurons which project back to the medial prefrontal cortex (Carr and Sesack, 2000) where they contact efferents to the nucleus accumbens (NAC) (Carr et al., 1999), and (2) with GABAergic neurons projecting directly to the NAC (Carr and Sesack, 2000).



Given the prominent role of prefrontal–ACC interactions in error detection and, more generally, performance monitoring, prefrontal projections to the NAC, directly or via the VTA, are likely to import critical information about prediction errors and reward to the NAC (Fig. 3). The NAC has long been considered as a link between neuronal circuits processing motivational information and generating behavior and behavioral change. This literature has been extensively reviewed (e.g., Robbins and Everitt, 1996); however, certain issues deserve brief reiteration as they are of immediate relevance for understanding the nature of the motivational activation of behavior via NAC circuitry. Accumulating evidence indicates that positive motivational processes can be separated, behaviorally and with respect to NAC circuitry, into 'wanting' and 'liking'. Importantly, a 'wanted' reward does not necessarily represent a 'liked' reward (see Berridge, 2003, 2004; Berridge and Robinson, 2003). Data from behavioral experiments can be interpreted as suggesting that, based on the interactions between NAC afferents originating from the VTA, prefrontal and other telencephalic regions, and intra-NAC circuitry, the

Fig. 3 – Schematic illustration of the main components of a neuronal network mediating the motivated activation of the cortical cholinergic input system in order to counteract the effects of detriemental manipulations, processes or events on attentional performance. The illustration depicts and emphasizes certain direct synaptic contacts on the basis of anatomical evidence and importance with respect to the main functions of this model (such as the direct VTA projections onto prefrontal efferents to the NAC, or the direct contacts between NAC GABAergic projections with BF cholinergic neurons projecting to the cortex; references in text). Information indicating performance decline (error detection, including prediction errors, reward loss) is generated on the basis of interactions between prefrontal (PFC) and anterior cingulate (ACC) circuits. Via glutamatergic (GLU) projections to midbrain dopamine (DA) cell groups, particularly the ventral tegmental area (VTA) and the nucleus accumbens (NAC), indicators of performance decline are integrated with incentive information. The VTA, directly and indirectly via projections to the NAC, activates cholinergic projections to the cortex. Activation of cholinergic projections to prefrontal regions is hypothesized to contribute to the activation of the anterior attention system and associated executive functions. Multi-synaptic prefrontal efferent networks mediate the optimization of input processing in somatosensory regions. In part based on prefrontal projections to the BF, cholinergic activation in the posterior cortex contributes directly to such top-down effects. The combined effects of increased cholinergic activity in the cortex is to enhance the detection and discrimination of target stimuli and to suppress the effects of distractors and context, thereby stemming further decline in attentional performance and fostering performance recovery. The contributions of ascending noradrenergic (NA) projections originating from the locus coeruleus (LC) and the catecholaminergic cell groups in the medulla (A1/A2) to the mediation of increases in attentional effort are less clear (see text).

output of the nucleus accumbens serves to initiate or sustain instrumental actions (Salamone and Correa, 2002) as a function of 'wanted' outcomes (see also Knutson et al., 2001, 2005; Shidara et al., 1998). In the present context, this would mean that NAC outputs are capable of activating circuitry, depending on the subjects' motivation, that is involved in the mediation of attentional performance (Christakou et al., 2004; Himmelheber et al., 2000a; Miner and Sarter, 1999) and, more importantly, that entails activation of the top-down effects required to protect attentional performance in order to obtained the associated reward. As will be discussed below, evidence indicates that the NAC potently influences the activity of cortical cholinergic inputs, and thereby is positioned to activate the neuronal circuitry that mediates the effects of increased attentional effort.

5.3. *Recruitment of basal forebrain cholinergic neurons by mesolimbic systems*

The main output pathway of the NAC is a GABAergic projection to the basal forebrain. This GABAergic projection direct contacts the cortically projecting cholinergic neurons of this region (see Fig. 3; Zaborszky, 1992; Zaborszky and Cullinan, 1992). Mogenson and colleagues originally indicated that increased NAC dopaminergic transmission reduces the GABAergic inhibition of basal forebrain neurons (Yang and Mogenson, 1989). Although more recent evidence on the essential interactions between glutamatergic and dopaminergic afferents in the NAC suggested a more complex modulatory influence of NAC dopamine on NAC projection neurons (Brady and O'Donnell, 2004; Floresco et al., 2001a,b; Meredith, 1999; Mulder et al., 1998; Nicola et al., 2000; O'Donnell, 1999; O'Donnell and Grace, 1993), several experiments illustrated the role of the NAC, and of NAC dopaminergic mechanisms, in regulating the cortical cholinergic input system.

Blockade of dopamine D2 receptors in the NAC attenuates increases in cortical ACh efflux (Moore et al., 1999). In these studies, the negative GABA modulator FG 7142 (FG) was administered systemically to activate cortical ACh efflux (Moore et al., 1995). The effects of FG on cortical ACh release may be associated with the increases in DA efflux in the medial prefrontal cortex and NAC also triggered by FG (Bassareo et al., 1996; Bradberry et al., 1991; Brose et al., 1987; McCullough and Salamone, 1992; Murphy et al., 1996; Tam and Roth, 1985). Moore et al. (1999) demonstrated that infusions of the D2 receptor antagonist sulpiride or haloperidol into the NAC, but not the D1 antagonist SCH 23390, significantly attenuated ACh efflux. Although the circuitry underlying the NAC dopaminergic regulation of cortical ACh efflux may involve multisynaptic circuits including, for example, the amygdala, these data illustrate that NAC dopaminergic mechanisms influence cortical ACh efflux.

The essential role of NAC neurotransmission in influencing cortical ACh efflux was also demonstrated in behavioral experiments (Neigh et al., 2004). These experiments utilized a complex behavioral procedure that combined motivational processes with events that elicited attentional mechanisms. While performing this procedure, increases in NAC dopamine release and cortical ACh release occurred. Attenuation of neurotransmission in the NAC, by perfusing tetrodotoxin (TTX), a potent blocker of voltage-regulated sodium channels, through the dialysis probe, completely attenuated the performance-associated increases in cortical ACh efflux (Neigh et al., 2004). These results confirmed that NAC neurotransmission is necessary for the demonstration of behavior-associated increases in mPFC ACh efflux.

As illustrated in Fig. 3, mesolimbic dopaminergic neurons also make direct contacts with basal forebrain cholinergic neurons (Gaykema and Zaborszky, 1996; Rodrigo et al., 1998; Smiley et al., 1999) and therefore, the VTA exerts direct influence, in addition to indirect routes via the NAC and the amygdala (not shown), over the excitability of cholinergic projection neurons. Evidence indicates increases in neuronal activity of basal forebrain neurons as a result of D1 stimulation, while the majority of these neurons exhibited D2 receptor-induced decreases in firing rate (Napier, 1992). Dopaminergic inputs to the basal forebrain may also, via D1 receptors, modulate the glutamatergic and GABAergic control of projection neurons (Johnson and Napier, 1997; Momiyama and Sim, 1996; Momiyama et al., 1996).

Thus, mesolimbic dopaminergic systems directly and indirectly control the excitability of the cortical cholinergic input system. The link between these two neuronal systems is hypothesized to mediate the motivational activation of attentional systems in order to counteract attentional performance decrements. As will be discussed next, increases in cholinergic activity as a result of motivational/mesolimbic processes contribute in two major ways to the effects of increases in attentional effort.

5.4. *Increases in cortical ACh efflux in response to challenges on attentional performance: error detection/reward loss or initiation of top-down processes?*

As discussed above, increases in prefrontal ACh efflux have been observed in animals whose attentional performance following a challenge suggested efforts to stay-on-task or even recover from impairments in performance. Thus, increases in prefrontal ACh efflux have been hypothesized to play an essential role in the mediation of increases attentional effort. In light of the extensive evidence indicating that the ACC plays a critical role in the detection of performance decrements (above), and suggestions that the rat's medial prefrontal cortex is homologous to the primate ACC (Preuss, 1995; but see Brown and Bowman, 2002), increases in ACh in this region may either contribute to the mediation of the processes involved in the detection of performance decline (above) or to the activation of the top-down mechanisms by prefrontal regions in order to counteract such decline, or both.

There is evidence to suggest that increases in medial prefrontal ACh release contribute to the activation of mechanisms designed to counter deterioration of attentional performance. Recording from prefrontal neurons in rats while they performed a version of the operant sustained attention task described above, presentation of a distractor, as opposed to the delivery of reward or non-reward, triggered extensive and reliable changes in neuronal firing rate. Moreover, loss of cholinergic inputs specifically to the population of neurons recorded resulted in the attenuation of the neurophysiological

effects of the distractor (Gill et al., 2000). These data suggest that cholinergic inputs play a role primarily in the processing of the distractor while contributing to a less significant degree to the processing of the outcome of trials. The distractor-associated neuronal activity changes in prefrontal cortex presumably reflect the involvement of these cholinergically-driven neurons in mechanisms designed to suppress the detection and processing of distractors. This issue requires more research, and the conclusive dissociation between the contributions of increased prefrontal ACh efflux to performance monitoring versus activation of top-down mechanism requires the measurement of ACh efflux at high temporal resolution in behaving animals (Parikh et al., 2004).

Muscarinic receptor stimulation in the prefrontal cortex activates ACh efflux in the posterior parietal cortex (Nelson et al., 2005), either via direct projections to the BF (Fig. 3; Sarter and Bruno, 2002; Zaborszky et al., 1997) and/or via more distributed circuits. This observation suggests that the level of cholinergic transmission elsewhere in the cortex is modulated by prefrontal regions and therefore corresponds with the view that increases in prefrontal cholinergic activity are involved in the recruitment of top-down mechanisms. This view does not exclude the possibility that increases in ACh efflux in the prefrontal cortex, such as those observed during un-challenged attentional performance (Arnold et al., 2002; Dalley et al., 2001; Passetti et al., 2000), also mediate aspects of performance monitoring, including detection of errors and reward loss; however, augmented increases that are observed as a result of performance challenges in animals motivated to continue performing appear more likely to contribute to the activation of the anterior attention system (Posner and Dehaene, 1994) and thus of top-down mechanisms.

5.5. *Top-down effects of increases in cholinergic transmission in sensorimotor and sensory-associational regions*

Our hypothesis suggests that the effects of increases in attentional effort are achieved in part via activation of the cortical cholinergic input system, primarily based on mesolimbic–basal forebrain circuitry as illustrated in Fig. 3. It is not clear whether such increases in cortical cholinergic activity exhibit cortical region-specific characteristics, or whether they occur cortex-wide; it is also possible that both region-specific, phasic increases in cholinergic transmission and more global, slower, or tonic changes in cholinergic activity occur in a correlated fashion (Sarter and Bruno, 1997). As discussed above, increases in ACh efflux in the prefrontal cortex are hypothesized to contribute to the activation of the anterior attention system and the recruitment of top-down mechanisms. Elsewhere in the cortex, particularly in somato-sensory regions, cholinergic mechanisms optimize input processing characteristics, thereby contributing to the enhancement or stability of attentional performance (Sarter et al., 2001, 2005a). The effects of cholinergic mechanisms on receptive field properties, synchronized firing, enhancement of thalamic inputs, suppression of associational inputs, and other mechanisms designed to amplify and specify input processing have been extensively discussed in the literature (e.g., Hasselmo, 1995; Rasmusson, 2000; Sarter et al., 2005a; Weinberger, 2003). This evidence collectively indicates that increases in cholinergic activity are potentially responsible for, or at least contribute to the mediation of, the top-down mechanisms summarized in Table 1.

Two recent studies serve to illustrate the cholinergic mediation of enhanced input processing in sensory regions. Roberts and colleagues applied ACh iontophoretically to neurons of the visual cortex of marmosets. They demonstrated that ACh specified and facilitated the receptive field properties of a majority of neurons (Roberts et al., 2005). The authors interpreted the effects of ACh as a shift towards a more accurate processing of stimuli, associated with a decreased influence of contextual information. Such a facilitation of input processing is key to performance stabilization and recovery following challenges, and thus represents an essential component of increases in attentional effort.

Bentley and colleagues administered the cholinesterase inhibitor physostigmine to healthy humans and assessed effects on attentional and working memory performance, the performance in visual control tasks, and brain activity using fMRI (Bentley et al., 2004). Physostigmine enhanced attentional but not working memory performance. Specific attentional performance-related activity increases were found in prefrontal and extrastriate visual regions. Overlapping activity changes associated with working memory performance were interpreted as indicating that increases in cholinergic activity enhances both stimulus-driven and task-driven sensory processes.

Thus, recent neurophysiological and imaging studies substantiated the hypothesis that, in sensory regions, cholinergic transmission facilitates input processing and suppresses the influence of, or interference by, contextual or associational information (Hasselmo and McGaughy, 2004; Sarter et al., 2005a). The beneficial performance effects of increases in attentional effort are hypothesized to be due in part to increases in cholinergic activity in sensory regions, as a result of the motivational activation of this system via mesolimbic circuits, and moderated by prefrontal projections to cholinergic neurons (Fig. 3). Thereby, the prefrontal cortex utilizes cholinergic inputs to sensory regions as part of the prefrontal efferent circuitry mediating top-down effects (Sarter et al., 2005a).

5.6. *Arousal effects via activation of ascending noradrenergic projections*

In addition to the motivation-driven activation of the basal forebrain cholinergic projection system, a more generalized increase in arousal may interact with cholinergic mechanisms to counteract declining input processing. Such general arousal effects have been typically attributed to the activation of ascending noradrenergic systems (e.g., Cohen et al., 2000). However, the particular step in the process from the detection of declining performance to the motivation-driven recruitment of top-down mechanisms that is primarily supported by increases in noradrenergic transmission is less clear. It is also important to note that the neuronal mechanisms underlying sensations of increased

arousal and energy that have remained unclear. Related complexities result from the undefined concept 'arousal' (Sarter et al., 2002).

Ascending noradrenergic projections from the medullary catecholaminergic cell groups and the locus coeruleus (LC; e.g., Delfs et al., 1998) modulate all major neuronal populations that are part of the 'attentional effort'-circuitry illustrated in Fig. 3, including basal forebrain cholinergic neurons (Berntson et al., 2003; Fort et al., 1995; Knox et al., 2004; Zaborszky et al., 1993). Moreover, the LC receives an excitatory input from the medial prefrontal cortex (Jodo et al., 1998) and thus can be potentially recruited in response to the detection of performance decline and/or as part of the prefrontal efferent network that is activated in order to combat further performance decline (Riba et al., 2005). Aston-Jones et al. (1997) demonstrated that LC activity in monkeys performing attention tasks codes information about the target, and that target switches are rapidly processed by LC neurons. Furthermore, they have suggested that LC activity facilitates the execution of a behavioral response once the animals made a decision (Clayton et al., 2004). In the cortex, the potential contributions of noradrenergic mechanisms to input processing are complex and depend on the overall activity of the noradrenergic system and/or state of arousal (Coull et al., 1997; Coull et al., 2001). Collectively, it is certainly likely that there is a noradrenergic contribution to the mechanisms of increased attentional effort, but the available evidence remains insufficient to specify such a role.

6. Conclusions

Attentional effort is conceptualized as a motivated activation of attention systems in order to stabilize or recover attentional performance in response to the detection of errors and reward loss or, more generally, deteriorating attentional performance. Furthermore, a necessarily simplistic neuronal circuitry model is described that links performance monitoring with motivational systems which, in turn, activate basal forebrain cholinergic projections to the cortex. Evidence indicates that highest levels of attentional performance-associated ACh efflux are observed in prefrontal regions following a performance challenge and while animals continue performing or regain pre-challenge performance levels. Such increases in ACh efflux are hypothesized to contribute to the activation of the anterior attention system and, via its efferent networks, to the recruitment of top-down mechanisms that act to enhances sensory input processing. In sensory regions, the effects of increases in cholinergic transmission account for a wide range of changes in receptive field properties and neuronal firing properties traditionally described as top-down effects.

Given the central role of cortical cholinergic inputs in the mediation of increases in attentional effort, the cognitive consequences of abnormal regulation or even disintegration of this neuronal system appear readily deducible. For example, dysregulation of the cortical cholinergic input system in aging and patients with precursor symptoms of Alzheimer's disease (Mesulam, 2004; Sarter and Bruno, 2004) would be predicted to suffer from impairments in their ability to increase attentional effort (e.g., Chao and Knight, 1997). Moreover, the disintegration of the cholinergic system in Alzheimer's disease disrupts attentional performance particularly in situations that require the division of attention and thus increases in attentional effort (e.g., Perry et al., 1999).

There is accumulating evidence indicating a dysregulated cortical cholinergic input system in patients with schizophrenia. The exact nature of this dysregulation remains unclear but may involve an abnormal reactivity of cortical cholinergic inputs (Raedler et al., 2003; Sarter et al., 2005b). Patients reported enhanced perception of stimulus characteristics ("Colors seem bright now…"; p. 52; McGhie and Chapman, 1961). However, at the same time, their attentional performance is exquisitely vulnerable to the effects of distractors or changes in the qualities of target stimuli (e.g., Ferstl et al., 1994; Grillon et al., 1990; Spring et al., 1989). The cognitive and neural origin of these deficits remain speculative but almost certainly is associated with an inadequate activation or efficacy of top-down mechanisms. Furthermore, abnormalities in the mesolimbic dopamine systems have been demonstrated in these patients (e.g., Laruelle, 2000; Laruelle et al., 1996), suggesting that BF cholinergic neurons are also dysregulated (Fig. 3). Thus, the regulation of critical attention systems, specifically the performance- and motivation-dependent activation of attention systems, would be expected to be severely impaired in these patients (e.g., Gorissen et al., 2005; Maruff et al., 1996). Impairments in the ability to comply with greater demands on attentional effort have also been documented in patients with affective disorders (Cohen et al., 2001).

Little is known about the regulation of attentional effort in neuropsychiatric disorders, and about the consequences of impairments in this process on the overall cognitive abilities of patients. Likewise, our understanding of the fundamental cognitive and neuronal mechanisms underlying increases in attentional effort remains rudimentary. However, as stressed in the introduction, subject-driven adjustment of attentional effort is a robust everyday experience. We hope that this article assists in introducing 'attentional effort' as a productive research subject to cognitive neuroscience.

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