COGNITIVE–ENERGETIC MECHANISMS AND NEURAL BASIS OF ALERTNESS REGULATION

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Every day you may make progress. Every step may be fruitful. Yet there will stretch out before you an ever-lengthening, ever-ascending, ever-improving path. You know you will never get to the end of the journey. But this, so far from discouraging, only adds to the joy and glory of the climb.

-- Winston Churchill, *Thoughts and Adventures*

SUMMARY

Human cognition is influenced by "energetic" factors like effort or fatigue. Interestingly, seemingly easy or well-practiced tasks that still require a continuous attentional engagement, have been found especially susceptible to the effects of such energetic variables. Particularly in monotonous and cognitively little challenging tasks, impaired performance, from reduced efficiency to catastrophic errors, often results from temporary deficits in sustaining attention.

A classic paradigm with minimal cognitive demands that is used for examining the most basic form of sustained attention is simple reaction-time tasks. These tasks require a rapid motor response to predefined stimuli. The reaction upon stimulus detection is always the same, and the only unknown variable is the exact moment of stimulus occurrence. Attaining and maintaining a state of readiness to respond in such tasks has been termed "alertness." This thesis investigates cognitive-energetic mechanisms that contribute to alertness and its decrease over time as well as the neurobiological basis of alertness regulation.

The first investigation (*Study 1*) examined in three 25-min simple reaction-time tasks, which posed different demands on attention via manipulations of stimulus salience, whether performance decrements with time on task can be better explained with increasing drifts of the attentional focus away from the task (distraction hypothesis) or with a depletion of attentional resources (mental-fatigue hypothesis). The performance and questionnaire data largely corroborated the latter explanation, since decrements and subjective fatigue increased more with higher attentional demands. The increase of self-reported task-unrelated thoughts over time, however, provided some evidence for the distraction hypothesis as well. Based on these findings, an approach is developed that incorporates both explanations in a hierarchical model of self-regulation.

Study 2 examined the question as to what extent the mechanisms of temporal preparation under time uncertainty, which contribute to optimal performance in simple reaction-time tasks, suffer from exhaustion after prolonged continuous demands. In a 50-min simple reaction-time task, we found the typical reaction-time slowing with time on task but no change in parameters of temporal preparation (i.e. the so-called variable and sequential foreperiod effects, respectively). This suggests (a) that cognitive processes of temporal preparation do not significantly contribute to alertness decrements with time on task and (b)

that the mechanisms underlying temporal preparation are processes that are hardly susceptible to mental fatigue, such as nonintentional associative learning.

The third experiment (*Study 3*) investigated the brain network subserving alertness regulation — independent of the sensory modality of the response signals. We used functional magnetic resonance imaging to measure brain activity during simple reaction-time performance in tasks with auditory, tactile or visual stimuli. The results revealed a supramodal (i.e. modality-independent) brain network consisting of predominantly right-lateralized cortical areas as well as brainstem and cerebellar structures. This corroborates the modality independence of previous findings from single-modality studies that used positron emission tomography and demonstrates that the notion of a right-lateralized network for alertness regulation can be generalized to tactile stimuli.

Taken together, the results of the thesis show that a variety of – fatigable as well as non-fatigable – processes contribute to maintaining response readiness in simple reaction-time tasks, which appear to be subserved by a widespread supramodal brain network. These findings raise the question for future research and application to what extent the construct “alertness” may be segregated into useful subcomponents to achieve a refined differentiation in diagnostic contexts.

KURZFASSUNG DER DISSERTATION

Die menschliche Kognition wird von „energetischen“ Faktoren wie Anstrengung oder Müdigkeit beeinflusst. Interessanterweise finden sich deutliche Effekte gerade bei scheinbar einfachen oder überlernten kognitiven Aufgaben, die eine andauernde Aufmerksamkeitszuwendung erfordern. Viele Leistungseinbußen und Fehler, von verminderter Effizienz bis zu katastrophalen Unfällen, lassen sich besonders bei monotonen und kognitiv wenig herausfordernden Aufgaben auf Daueraufmerksamkeitsdefizite zurückführen.

Ein klassisches Paradigma, mit dem die Daueraufmerksamkeitsleistung bei gleichzeitig minimalen kognitiven Anforderungen untersucht wird, sind Einfachreaktionsaufgaben. Bei diesen soll schnellstmöglich auf vorbestimmte Reize reagiert werden, wobei die Entdeckung eines Reizes stets dieselbe Reaktion erfordert. Die einzige Unbekannte in diesem Paradigma ist der genaue Zeitpunkt des Auftretens der Reize. Die Herstellung und Aufrechterhaltung einer hohen Reaktionsbereitschaft in solchen Aufgaben wird als „Alertness“ bezeichnet. Diese Arbeit beschäftigt sich zum einen mit den kognitiv-energetischen Mechanismen, die zu einer hohen Alertness beitragen bzw. ihre Abnahme über die Zeit bedingen, zum anderen mit der neurobiologischen Grundlage der Alertness-Regulation.

Die erste Studie untersuchte in drei 25-minütigen Einfachreaktionsaufgaben, die via Manipulation der Stimulussalienz unterschiedlich hohe Anforderungen an die Aufmerksamkeit stellten, ob Leistungsseinbußen über die Zeit eher mit einem zunehmenden Abschweifen des Aufmerksamkeitsfokus (Distraktionshypothese) oder mit einer Erschöpfung attentionaler Ressourcen (Ermüdungshypothese) zu erklären sind. Die erhobenen Verhaltens- und Fragebogendaten sprachen überwiegend für letztere Erklärung, da Leistungseinbußen und subjektive Erschöpfung bei höheren Aufmerksamkeitsanforderungen stärker anstiegen. Die Zunahme selbstberichteter aufgabenirrelevanter Kognitionen über die Zeit lieferte aber auch einen Beleg für die Distraktionshypothese. Basierend auf diesen Befunden wird ein Ansatz entwickelt, der beide Erklärungen in einem hierarchischen Selbstregulationsmodell vereint.

Die zweite Studie ging der Frage nach, inwieweit Mechanismen der zeitlichen Vorbereitung unter Unsicherheit, die zu einer optimalen Effizienz in Einfachreaktionsaufgaben beitragen, bei Daueranforderung ermüden. In einer 50-minütigen Einfachreaktionsaufgabe fand sich eine typische allgemeine Reaktionszeitverlangsamung

über die Zeit, aber keine Veränderung in Parametern der zeitlichen Vorbereitung (d. h. im so genannten variablen sowie sequentiellen Vorperiodeneffekt). Das lässt zum einen den Schluss zu, dass kognitive Prozesse der zeitlichen Vorbereitung nicht wesentlich zum Leistungsabfall über die Zeit beitragen, und zum anderen, dass der zeitlichen Vorbereitung unter Unsicherheit zumindest teilweise unbewusste, wenig ermüdbare Prozesse (z. B. assoziatives Lernen) unterliegen.

Die dritte Studie beschäftigte sich mit der Frage, welches Netzwerk im Gehirn der Alertness-Regulation zugrunde liegt – und zwar unabhängig von der Sinnesmodalität der Reize. Die kernspintomographische Messung der Hirnaktivität bei der Bearbeitung von Einfachreaktionsaufgaben mit auditiven, taktilen oder visuellen Reaktionssignalen ergab übereinstimmend ein Netzwerk aus vorwiegend rechtshemisphärischen kortikalen Arealen sowie mesenzephalen und zerebellären Strukturen. Dies belegt die Modalitätsunabhängigkeit früherer Befunde aus positronenemissionstomographischen Studien und zeigt, dass die bisherigen Erkenntnisse auch auf taktile Reize generalisierbar sind.

Insgesamt zeigt die Arbeit, dass verschiedene – ermüdbare wie nicht ermüdbare – kognitive Prozesse zur Aufrechterhaltung einer hohen Reaktionsbereitschaft beitragen, die von einem umfangreichen supramodalen zerebralen Netzwerk geleistet werden. Weiterführend stellt sich die Frage, inwieweit das Konstrukt „Alertness“ in sinnvolle Subkomponenten zerlegt werden könnte, um für diagnostische Fragestellungen einen höheren Differenzierungsgrad zu erreichen.

TABLE OF CONTENTS

1. GENERAL INTRODUCTION

1.1. Theoretical Background

The ability to remain attentive to sensory information over extended periods of time is crucial for many everyday behaviours, such as talking with other people or reading a book. During time-critical interactions with machines, it can even become vital. In a review paper on sustained attention, Ian Robertson (2003) relates two catastrophic traffic accidents. One involved a train driver who missed a critical stop signal, which caused a devastating train crash; the other one involved a sleep-deprived, tired driver whose car plunged from the motorway down onto a railroad track and caused the derailment of a train, which subsequently smashed into another train and killed several people. Common to both accidents is their occurrence during the prolonged performance of routine behaviours that require the continuous maintenance of attention. In these cases, a single lapse of attention had disastrous consequences. Research shows that such failures in sustaining attention are the most common cause of accidents on railways (Edkins & Pollock, 1997). In the second case, driver fatigue has certainly contributed to the fatal incident, and according to Wickens, Gordon and Liu (1998, p. 397), fatigue is estimated to be a causal factor in about 200,000 car accidents per year.

These incidents are forceful examples for the influence of “energetic” factors on human cognition (cf. Hockey, Coles & Gaillard, 1986; van der Molen, 1996). They show that in states of boredom, fatigue or sleepiness the efficiency of information processing can deteriorate substantially. Strangely, modern cognitive psychology has been predominantly concerned with the “computational” side, or architecture, of information processing. The above examples, however, add to existing evidence which demonstrates that energetic variables cannot be ignored when aiming to explain human performance and its failures (e.g. Berlyne, 1960; Broadbent, 1971; Eysenck, 1982; Hockey, Gaillard & Coles, 1986; Humphreys & Revelle, 1984; Kahneman, 1973; Matthews, Davies, Westerman & Stammers, 2000; Pfaff, 2006; Sanders, 1983, 1998). Many insights into interactions between computational and energetic aspects of human behaviour have also been gained from research in applied areas like clinical neuropsychology or human factors, which aim to understand how cognition is influenced by pathologies or environmental stressors that affect energetic mechanisms.

One link between computational and energetic aspects of human performance is provided by attention, which modulates and biases computational processes by mediating motivational forces and overcoming energetic obstacles like fatigue in order to reach behavioural goals (cf. H. A. Simon, 1994). A basic attentional function is to establish a level of alertness that is sufficient for task performance. Alertness, sometimes referred to as "vigilant attention," "attentional state" or "attentiveness," has been defined as the readiness to respond to external signals (Posner, 1978). As such, alertness represents a basic intensity aspect of attention, in contrast to attentional selectivity aspects such as orienting, focusing or dividing attention (Sturm, 2003; van Zomeren & Brouwer, 1994). The concept has been further differentiated into phasic, tonic and intrinsic alertness (Sturm et al., 1999; Sturm & Willmes, 2001). Accordingly, phasic alertness refers to short-term response readiness following a warning signal, with peak readiness only lasting for time periods in the millisecond range. Tonic alertness refers to states of alertness that change slowly over minutes to hours, mainly driven by physiological factors like the circadian rhythm or the sleep–wakefulness cycle. Finally, intrinsic alertness refers to voluntary alertness changes within the range of seconds to minutes. As such, intrinsic alertness is closely related to what Requin, Brener and Ring (1991) called "tonic response preparation."

Alertness is typically operationalized as response speed in simple reaction-time (SRT) tasks, which require a rapid and invariable response to stimuli presented at random intervals over a relatively long time; high speed is taken to reflect a high level of alertness (Buck, 1966; Posner, 1978; Sturm, 2006; Sturm et al., 1999; Zimmermann & Fimm, 1993). SRT tasks are chosen because they constitute one of the most basic input–output translations and, thus, pose only relatively little computational processing demands, minimizing variance due to irrelevant factors like strategy or practice (e.g. Blatter & Cajochen, 2007; Lim & Dinges, 2008). Hence, SRT tasks are thought to be especially sensitive to the effects of energetic variables that influence the efficiency of information processing. This view was confirmed in many studies demonstrating profound effects of energetic variables on SRT performance. These variables included sleep deprivation (van Dongen, Maislin, Mullington & Dinges, 2003), circadian rhythmicity (Wyatt, Ritz-De Cecco, Czeisler & Dijk, 1999), stimulating drugs (Wesensten et al., 2002), and time on task (Lisper & Ericsson, 1973).

In comparison to energetic variables, however, it is the influence of stimulus characteristics on computational processes during SRT performance that has been studied much more systematically. In fact, this was a topic since the early days of experimental psychology (e.g. Cattell, 1886). For instance, it is well established since long that SRT decreases with increasing stimulus size, intensity or duration (see Woodworth, 1938, for an early review). Based on these and other findings, several elaborate theories and models have been developed to explain the computational mechanisms underlying SRT performance (e.g. Miller & Ulrich, 2003; Ollman & Billington, 1972; Raab, 1962; P. L. Smith, 1995).

For instance, Miller and Ulrich (2003) proposed a race-like model and the principle of statistical facilitation (cf. Raab, 1962) to account for the effects of various experimental manipulations on mean SRT. In brief, the model assumes that a stimulus reaching the brain leads to the parallel activation of a variable number of “grains” (arbitrary neural units) within a variable time interval, depending on stimulus characteristics like size, intensity and duration. This activation is then transmitted to a decision centre within a variable time interval (due to neural noise), and stimulus detection occurs as soon as the number of transmitted grain activations satisfies a decision criterion. After detection, a command is sent to the motor system to initiate and execute the response. Miller and Ulrich only mentioned in passing that changes in energetic factors like arousal or attention were likely to produce fluctuations in parameter values of the model. Since energetic factors are not included in the model, any intraindividual variability in response speed that might be caused by them is considered “noise.”

However, in keeping with others (e.g. Flehmig, Steinborn, Langner, Scholz & Westhoff, 2007; Stuss, Murphy, Binns & Alexander, 2003), we argue that a substantial part of this “noise” may be due to the systematic influence of energetic variables. In this thesis, we further explore such cognitive-energetic interactions in SRT performance. The thesis consists of three studies. Two of them are behavioural studies, the first of which investigated energetic mechanisms that may underlie the failure to maintain alertness (i.e. stable SRT performance) over extended periods of time. The second study dealt with the question of whether cognitive processes of timing and expectancy during an alertness task also deteriorate over time. The third study explored the brain systems that enable the endogenous maintenance of alertness, with a focus on the influence of stimulus modality.

1.2. Outline of the Research Questions of the Thesis

1.2.1. Study 1: Fatigue and Mindlessness in Time-Related Alertness Decrements

For optimal (i.e. consistently fast and correct) SRT performance, attentional and cognitive-control processes are necessary (Frith & Done, 1986; Goodrich, Henderson & Kennard, 1989). They include the facilitation of task-relevant perceptual, decisional, and motor processes as well as the monitoring and adjustment of performance level (Stuss, Shallice, Alexander & Picton, 1995). We suggest that attentional control signals can be thought of as modulators influencing the parameters of the above-mentioned computational model of Miller and Ulrich (2003): the number of grains activated by a given stimulus, the time it takes for the activation to occur, and the time it takes for the activation to be transmitted to the decision centre. Furthermore, attention may influence where the decision criterion is set as well as the time it takes for the motor command to proceed from the decision centre to the motor system and for the motor response to be initiated (Los & Schut, 2008, p. 22; Niemi & Näätänen, 1981, pp. 152-153). Further beneficial top-down control processes comprise the inhibition of premature responses and the prevention of distraction, which includes suppressing awareness of task-irrelevant thoughts (Goldberg, Harel & Malach, 2006) or stimuli (Mennemeier et al., 1994) as well as goal shielding (Dreisbach & Haider, 2007).

As already indicated by the introductory examples, decrements in alertness with time on task (TOT) may occur when these top-down control processes are not implemented appropriately anymore, either because of insufficient attentional effort or because of a misallocation of attentional resources. Therefore, the first study tested whether the decline in SRT performance with TOT can be better explained with a depletion of attentional resources (i.e. mental fatigue) or with a drifting of the attentional focus away from the task due to monotony and boredom (i.e. mindlessness).

1.2.2. Study 2: Mental Fatigue and Temporal Preparation

In SRT tasks, all computational processes can potentially be prepared before stimulus onset, since there is no uncertainty about the kind of response required. Apart from specific preparatory attentional processes that facilitate necessary computations and inhibit irrelevant ones (e.g. Jennings & van der Molen, 2005), preparation is also assumed to act in a nonspecific way, “energizing” computational processes (e.g. Los & Schut, 2008; Stuss et al., 2005; see also Requin et al., 1991). The beneficial effects of preparatory activity on performance can be seen when varying the level of preparedness, for instance by manipulating the temporal distance between subsequent stimuli. In unwarned SRT tasks, this time period is usually termed “interstimulus interval” (ISI), whereas in forewarned SRT tasks, the time between warning stimulus and response signal is typically called “foreperiod” (FP). To avoid confusion, we will generally refer to both kinds of interval as “foreperiod” (cf. Näätänen, 1971). When the FP is fixed within a block of trials and varies between blocks, mean reaction time (RT) has been found to be decreasing from FPs of 0 to about 250-300 ms and slowly increasing thereafter (e.g. Müller-Gethmann, Ulrich & Rinkenauer, 2003). The decrease indicates that it takes some time to reach optimal preparedness, and the increase is thought to reflect that optimal preparedness is hard to maintain and dissipates as a result of the growing subjective uncertainty about the moment of stimulus occurrence (cf. Los & Schut, 2008, p. 22; see also Niemi & Näätänen, 1981). Analogously, it can be assumed that performance decrements with TOT occur when optimal preparedness at the moment of stimulus occurrence cannot be achieved anymore. Now, the question arises whether or not the processes that underlie the timing of preparation contribute to the decline in preparedness and, thus, performance. Therefore, employing a variable-FP design, the second study tested whether indices of temporal preparation change over time along with global performance parameters.

1.2.3. Study 3: A Supramodal Brain System Subserving Intrinsic Alertness

Neuroimaging and neuropsychological studies provide evidence that the brain systems subserving the endogenous control of alertness and sustained attention are mainly located in right-hemisphere prefrontal and parietal areas, anterior cingulate cortex, thalamus, and brainstem (see Figure 1; Drummond et al., 2005; Howes & Boller; 1975; Kinomura, Larsson, Gulyas & Roland (1996); Lawrence, Ross, Hoffmann, Garavan & Stein, 2003; Lewin et al., 1996; Pardo, Fox & Raichle, 1991; Paus et al., 1997; Rueckert & Grafman, 1996, 1998; Schmidt et al., 2009; Sturm et al., 1999, 2004, 2006; Sturm & Willmes, 2001; Wilkins, Shallice & McCarthy, 1987).

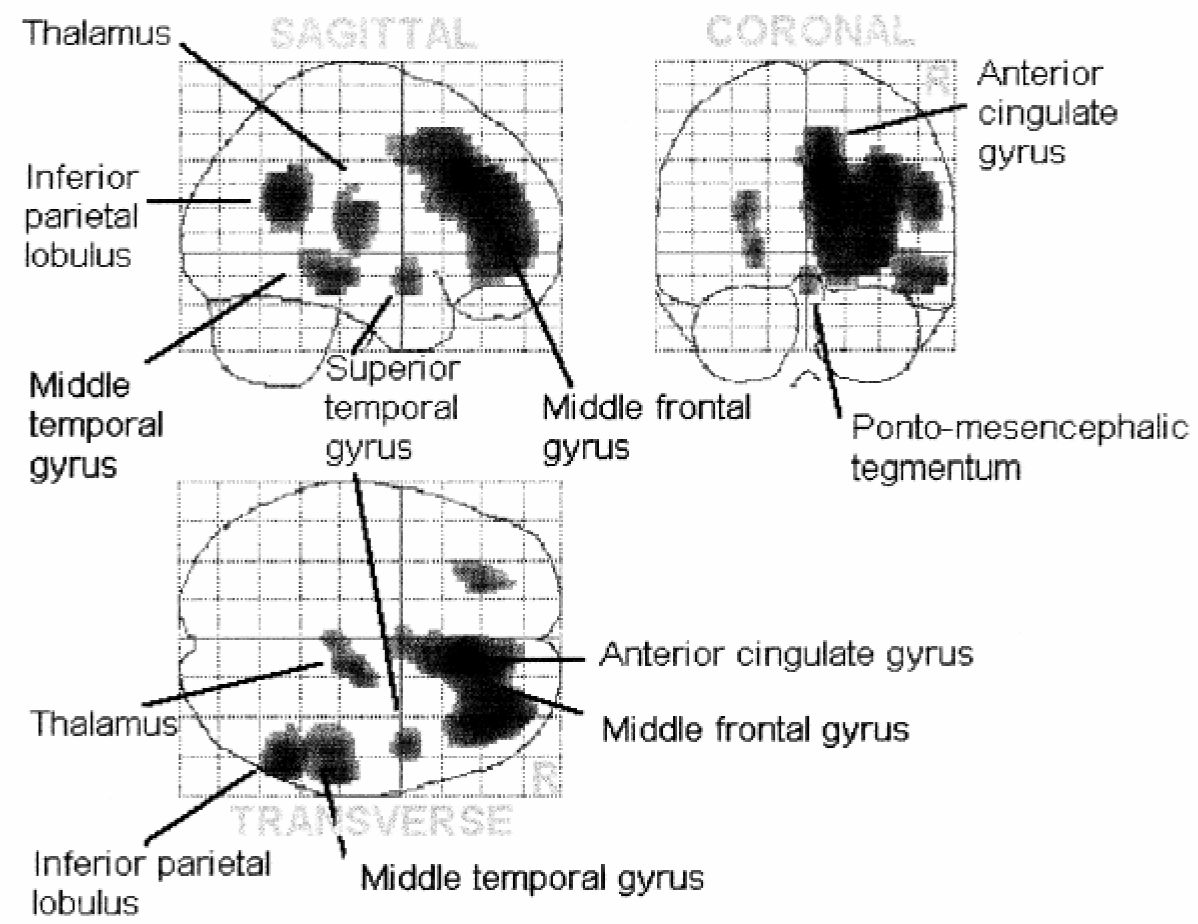

Figure 1. Brain activity related to visual intrinsic alertness (from Sturm et al., 1999).

Also, neuropsychological research employing RT paradigms with lateralized stimulus presentation found evidence for the crucial role of the right hemisphere in maintaining an alert state, with healthy participants (Dimond & Beaumont, 1973; Fimm, Willmes & Spijkers, 2006; Heilman & van den Abell, 1979; Sturm, Reul & Willmes, 1989) as well as split-brain patients (Dimond, 1979). So far, however, no study has tested this right-lateralized network's independence of the sensory modality of the stimuli. To answer this question, we used functional magnetic resonance imaging (fMRI) to measure brain activity during the performance of auditory, tactile and visual SRT tasks. Additionally, we included a condition in which stimulus modality was unpredictable to test the effect of increased monitoring demands.

2. STUDY 1

ENERGETIC EFFECTS OF STIMULUS INTENSITY ON PROLONGED SIMPLE REACTION-TIME PERFORMANCE

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2.1. Introduction

Human behaviour is influenced by energetic factors such as fatigue, arousal, effort or circadian rhythms, which produce variation in the efficiency of information processing (Eysenck, 1982; Hockey, Coles et al., 1986; Sanders, 1983; van der Molen, 1996). Major impulses for studying the impact of energetic factors on human cognition have come from applied areas like clinical neuropsychology (cf. van Zomeren & Brouwer, 1994) or human-factors research (cf. Hancock & Desmond, 2001). This research revealed problems with translating models of cognition devoid of energetic considerations into real-world settings. Peter Hancock remarked in 1987: “It is the inability to incorporate these energetic aspects of behavior […] into linear processing models that has rendered the latter somewhat sterile and potentially misleading when applied simplistically to actual operational systems” (pp. 170-171).

An example for this problem is provided by computational models of simple reaction-time (SRT) performance (e.g. Miller & Ulrich, 2003; Ollman & Billington, 1972; P. L. Smith, 1995). In such models, energetic factors are usually considered noise, although many studies have demonstrated systematic effects of energetic variables such as sleepiness (van Dongen et al., 2003), circadian rhythmicity (Wyatt et al., 1999) or stimulating drugs (Wesensten et al., 2002). Indeed, in neuropsychology and sleep-deprivation research, SRT tasks are used to measure alertness (also termed psychomotor vigilance; cf. Lim & Dinges, 2008; Sturm & Willmes, 2001), which is an energetic, nonselective component of attention defined as the ability to achieve and maintain the readiness to respond to incoming information (Posner, 1978).

2.1.1. The Resource Theory of Sustained Performance

Another well-known energetic factor that affects SRT performance is time on task (TOT). It has often been reported that SRT slows down over time (e.g. Buck, 1966; Gustafson, 1986; Langner, Steinborn, Chatterjee, Sturm & Willmes, in press; Lisper & Ericsson, 1973; Lisper, Melin, Sjödén & Fagerström, 1977; Sanders, Wijnen & van Arkel, 1982; van den Berg & Neely, 2006). The mechanism behind this performance deterioration is not fully understood yet, but earlier studies implicated reduced attentional control because of mental fatigue. For instance, Lisper, Kjellberg and Melin (1972) used randomly mixed auditory stimuli of four intensities in a 2-hour SRT task and reported a general RT increase over time, which was, at least in the longest RT range, significantly larger for near-threshold than higher-intensity stimuli. This intensity-dependent effect suggests a specific impairment of top-down attentional control, on which the efficient processing of near-threshold stimuli presumably relies to a larger extent than the processing of salient, high-intensity stimuli.

The assumption of fatigue-related decreases in attentional control receives further support from a study in which the regularity of the interstimulus interval (ISI) was manipulated (constant 7.5 s vs. randomly varied 4-11 s) (Lisper & Törnros, 1974). This study revealed a significantly larger RT increase over time in the *irregular*-ISI than in the *regular*-ISI condition. The latter condition should be less demanding for the controlled-attention system and thus less fatiguing: during regular ISIs it should be easier to take short breaks from sustaining attention and maintaining preparedness, processes which are effortful (Gottsdanker, 1975; Näätänen, 1972).

Which are the mechanisms assumed to underlie the development of mental fatigue during prolonged SRT performance? Even seemingly very easy tasks like the speeded detection of single predefined stimuli require the top-down control of attention in order to be performed optimally (Frith & Done, 1986; Henderson & Dittrich, 1998). Because such attentional control processes are transient (Smallwood & Schooler, 2006; Weissman, Roberts, Visscher & Woldorff, 2006; West, 2001), prolonged performance requires a mechanism that stabilizes or reactivates these processes to ensure continuous task engagement (Banich et al., 2000, 2009). This stabilization is an active, effortful process (Mulder, 1986; Posner, Cohen, Choate, Hockey, & Maylor, 1984; Sarter, Gehring & Kozak, 2006). Prolonged exertion of effort, however, is assumed to deplete limited attentional resources (Grier et al., 2003; Smit, Eling & Coenen, 2004; R. A. Wright, Stewart & Barnett, 2008). The result of this resource depletion is a state of mental fatigue, which is characterized by a failure to further exert appropriate top-down control to maintain a stable allocation of cognitive resources to the task at hand (Hockey, 1997; Lorist et al., 2000; Matthews & Desmond, 2002; van der Linden, Frese & Meijman, 2003; R. A. Wright et al., 2007). As a consequence, when fatigued, the implementation of task-specific cognitive processes cannot be maintained at optimal levels, and performance declines.

These conclusions are supported by studies on vigilance, which typically employ a similar paradigm: prolonged go/no-go tasks with many more no-go than go stimuli (see Davies & Parasuraman, 1982, for a review). The hallmark of vigilance tasks is a time-related performance decrement, just like that observed during prolonged SRT tasks. Analyses based on signal detection theory indicated that the time-related vigilance decrement is due to a reduction in perceptual sensitivity, which has been interpreted as a depletion of limited attentional resources (Helton & Warm, 2008; Temple et al., 2000; Smit et al., 2004). This view is also consistent with the finding that maintaining vigilance poses substantial attentional demands and is perceived to be stressful (Grier et al., 2003; Szalma et al., 2004; Warm, Parasuraman & Matthews, 2008).

2.1.2. Mindlessness Theory — A Challenge to the Resource-Depletion Account

Recently, the explanation of time-related performance decrements in terms of attentional resource depletion has been challenged: Robertson and collaborators (Manly, Robertson, Galloway & Hawkins, 1999; Robertson, Manly, Andrade, Baddeley & Yiend 1997) suggested an account that is based on the concept of understimulation, i.e. suboptimal levels of workload or cognitive demand. Accordingly, the repetitive nature of typical vigilance assignments induces participants to withdraw their attentional effort from the task and perform it in an increasingly mindless, routinized manner. Thus, the monotony of the situation is assumed to lead to the disengagement of conscious awareness of the task (including a preoccupation with task-irrelevant thoughts; Smallwood et al., 2004), resulting in a decline of performance (cf. Pattyn, Neyt, Henderickx & Soetens, 2008).

This mindlessness model of time-related performance decrements during continuous tasks is mainly based on studies using the Sustained Attention to Response Task (SART). In the SART, the go/no-go trial ratio of typical vigilance tasks is inverted: observers have to respond as quickly as possible to the majority of the regularly presented stimuli and to withhold their response to infrequently interspersed non-targets. This design was chosen to promote the rapid routinization of the sensorimotor response over time. In support of the model it was found that RT in target trials prior to inhibition failures is decreased compared to successful inhibitions, indicating that failures to maintain attention are preceded by periods of increased routinization (Dockree et al., 2004; Manly et al., 1999; but see Dockree, Kelly, Robertson, Reilly & Foxe, 2005). Further, participants who reported to commit more absent-minded errors in everyday life also made more errors in the SART (Manly et al., 1999; Robertson et al., 1997). Another study reported that occasionally reminding participants of the task goal by means of “content-free” auditory cues improved SART performance significantly (Manly et al., 2004). Finally, the mindlessness model is also consistent with the finding that participants consider vigilance tasks as boring (Scerbo, 1998) and with a study showing that the vigilance decrement is associated with a decrease in task-related effort as indexed by physiological measures of sympathetic and parasympathetic tone (Pattyn et al., 2008).

In conclusion, accumulating mental fatigue and growing mindlessness emerge from earlier studies as two candidate mechanisms that may be involved in the decrement of sustained performance with TOT. Here we investigated the generalizability of both accounts by testing which of them might best explain time-related performance decrements in prolonged SRT tasks. To this end, we manipulated stimulus intensity and stimulation monotony to observe the effect of high versus low stimulus intensity in pure versus mixed blocks of trials on the time-related decline in performance. It is well established that SRT is longer with lower stimulus intensities (see Nissen, 1977, for a review) or when stimuli of different intensities are presented in a randomly mixed manner (see Los, 1996, for a review). In the present study, however, we focused on non-cognitive (energetic) effects of stimulus intensity and presentation mode. Below we will explain our rationale and predictions in detail.

2.1.3. Experimental Approach and Predictions

Several lines of research suggest that attentional top-down control processes get increasingly more involved with increasing encoding difficulty (i.e. decreasing intensity or salience) of the target stimulus: First of all, attention enhances effective stimulus strength (Reynolds, Pasternak & Desimone, 2000), which would be most important for speeded detection when stimulus intensity is low. Further, in various paradigms used to study the interaction of top-down and bottom-up processes in the control of attention, stimulus salience has been shown to facilitate encoding by driving bottom-up attention — a phenomenon called attentional capture (Turatto & Galfano, 2000). These capture effects of highly salient stimuli can either support or challenge the top-down control of attention, depending on whether it is the target or irrelevant stimuli that are especially attention-grabbing. For instance, visual search is much more easily performed when the target is salient; conversely, search is substantially slowed by salient distractors (Nothdurft, 2006; Treisman & Gormican, 1988). This difference has been interpreted as reflecting the need for top-down attentional control when searching for low-salience targets. Furthermore, patients with attentional deficits (unilateral neglect) had greater impairments in effortful visual search for nonsalient targets than in search for salient ones (Aglioti, Smania, Barbieri & Corbetta, 1997).

These findings taken together suggest that the efficient processing of task-relevant low-salience stimuli puts stronger demands on attentional top-down control processes. Therefore, from the perspective of the resource model, *low* stimulus intensity should lead to a stronger depletion of attentional resources over time, thus producing a stronger performance decrement over time. In contrast, from the perspective of the mindlessness model, *high* stimulus intensity should induce a steeper vigilance decline over time, since high-intensity stimuli are easy to detect and should thus facilitate routinization and promote mindlessness.

To manipulate the monotony of the situation, which is a pivotal variable in the mindlessness model, we varied the presentation mode of the two different stimulus types. In two "pure" experimental blocks, only high- *or* low-intensity stimuli were presented (highly monotonous conditions); in a third "mixed" experimental block, stimuli of both intensities were presented in a randomly mixed fashion (less monotonous condition). The unpredictability of stimulus type on any given trial in the mixed condition objectively reduces monotony. Furthermore, it somewhat increases task difficulty (as reflected by the typically increased RT compared to non-mixed conditions; cf. Los, 1996), which in turn should interfere with routinization and mindlessness. Therefore, from the view of mindlessness theory, we would predict that the mixed presentation entails smaller performance decrements for high- and low-intensity stimuli alike, as compared to the "pure" conditions.

In contrast, from the view of resource theory, the mixed presentation should have a different effect on responses to high- versus low-intensity stimuli. The time-related increase in RT to *high*-intensity stimuli should be *larger* under the mixed than under the pure condition. This is because the interspersed low-intensity stimuli of the mixed condition pose higher demands on the top-down attention system, which, in turn, should lead to a stronger resource depletion over time. Conversely, the time-related increase in RT to *low*-intensity stimuli should be *smaller* under the mixed than under the pure condition. This is because the interspersed high-intensity stimuli of the mixed condition pose lower demands on the top-down attention system, which, in turn, should mitigate the depletion of attentional resources.

In sum, mindlessness theory predicts main effects of stimulus intensity (i.e. a smaller performance decrement with hard-to-detect low-intensity stimuli) and presentation mode (i.e. a smaller performance decrement with the less monotonous mixed presentation), whereas resource theory predicts no such main effects but a cross-over interaction: the performance decrement over time should be smaller under the pure *high*-intensity than *low*-intensity condition, and under the mixed condition the decrement should worsen for high-intensity stimuli but lessen for low-intensity ones. Additionally, we expected that mean RT, irrespective of any time-related changes, should be shorter in high- versus low-intensity trials (cf. Nissen, 1977) as well as in pure- versus mixed-presentation trials (cf. Los, 1996). We also expected an overadditive interaction between intensity and presentation mode, resulting in a larger effect of mixing on low- than on high-intensity stimuli, which, according to Sanders (1977), would indicate an effect of immediate arousal that offsets the effect of lower stimulus predictability in the mixed-presentation condition (see Los, 1996, for a detailed discussion).

In addition to the SRT task, we used two questionnaires to assess task-related changes in subjective state. These self-report measures comprised the Short Questionnaire for Current Strain (KAB; Müller & Basler, 1993), a measure of subjective strain, and the Dundee Stress State Questionnaire—Short Version (DSSQ-S; Matthews, Emo & Funke, 2005; Matthews et al., 2002), which assesses subjective perceptions of task engagement, energetic arousal, distress, and worry. Both questionnaires were given before and immediately following the tasks. According to the mindlessness model, one would expect that the mixed condition is associated with less subjective strain and worry (i.e. task-irrelevant thoughts) and stronger self-reported task engagement. In contrast, according to the resource model, one would expect that conditions containing low-intensity stimuli induce stronger feelings of strain, and conditions containing high-intensity stimuli lead to a smaller decrease in self-reported energetic arousal (i.e. perceived mental fatigue).

2.2. Method

2.2.1. Participants

The sample comprised 42 (15 female, 27 male) volunteers, aged 20 to 30 (*M* = 23.6, *SD* = 2.9) years, who were university students recruited via advertisements on campus. They were paid 15 € for their participation. The study was performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki; all participants gave their informed consent prior to their inclusion in the study. The data of one participant were excluded from analysis, since they revealed a continuous, rhythmical response pattern against instructions. The majority (*n* = 38) of the sample was right-handed (as determined with the Edinburgh Inventory, Oldfield, 1971), and all participants had normal or corrected-to-normal vision.

Self-reports indicated that no-one had slept unusually little the night before or had consumed substantial amounts of alcohol the day before or unusual amounts of nicotine or caffeine on the day of testing.

2.2.2. Apparatus and Task

The experiment was carried out in a dimly lit and quiet room. The task was presented via a standard IBM-compatible computer using the software Presentation 10.0 (Neurobehavioral Systems Inc., Albany, CA, USA). Participants were seated approximately 60 cm in front of the computer screen. The task was to respond as fast as possible to a square appearing at the centre of the screen. There were large, high-intensity squares (19.85° visual angle; 23.9 cd/m^2) and small, low-intensity squares (0.96° visual angle; 5.5 cd/m^2); the background colour was dark-grey (5.0 cd/m^2). Participants used an in-house-built optical response button for responding to the stimuli with the index finger of their dominant hand. The stimuli were presented for 50 ms; the duration of the interstimulus interval varied randomly and was sampled from an exponential distribution with a mean of 900 ms plus a constant period of 2100 ms. Reaction time was measured as the temporal difference between stimulus onset and response.

2.2.3. Self-Report Measures

The Short Questionnaire for Current Strain (KAB; Müller & Basler, 1993) was administered to assess subjective perceptions of strain and fatigue. This self-report measure comprises eight pairs of adjectives on 6-point Likert-type rating scales describing opposite endpoints of different strain dimensions (e.g., stressed vs. relaxed; languid vs. fresh). Task-induced mental fatigue was assessed by comparing the KAB total scores from before and after the sessions.

Subjective state was further assessed by means of four scales of the Dundee Stress State Questionnaire—Short Version (DSSQ-S; Matthews et al., 2002; Matthews et al., 2005): Task Engagement, Energetic Arousal, Distress, and Worry. The DSSQ-S consists of 30 items, which assess aspects of arousal, motivation, affect and cognition on 5-point Likert-type rating scales. In fact, Energetic Arousal is a subscale of Task Engagement, which we decided to report separately, because it captures a facet of subjective state which, according to resource theorists, reflects mental fatigue and resource depletion (Matthews et al., 2000). In contrast, other, more cognitive items of the Task Engagement scale assess aspects of self-perceived motivation and concentration. The Distress scale comprises items related to tension, negative mood, and cognitions of low confidence and control. The Worry scale assesses self-focused attention and cognitive interference by task-unrelated thoughts about personal concerns, motives and previous experiences. The DSSQ-S was administered before and after the session; changes in subjective state were assessed by comparing pre- with post-task scores. These data were available from 31 participants only.

2.2.4. Design and Procedure

In one part of the experiment, only high-intensity squares were used ("Pure-High" condition); in a second part, only low-intensity squares were used ("Pure-Low" condition); in a third part, high- and low-intensity squares were presented in a randomly mixed way, creating two conditions: a mixed, high-intensity ("Mixed-High") condition that included all trials with high-intensity stimuli, and a mixed, low-intensity ("Mixed-Low") condition that included all trials with low-intensity stimuli. Each of the three parts lasted 25 min; their order was counterbalanced across participants.

Before the task, participants answered a socio-demographic and a handedness questionnaire (Oldfield, 1971), a current-state questionnaire asking for health status, alcohol, nicotine, and caffeine intake and amount of sleep during the night before, as well as the KAB and DSSQ-S. Then, participants received written task instructions, after which the first part of the task started, including 10 practice trials at the beginning. Each part was followed by a break, which lasted 10-15 min and started by answering the KAB and DSSQ-S to receive post-task measures of subjective state. During the breaks, full light was switched on and participants were encouraged to move around to minimize transfer effects by providing time and distraction to recover from fatigue and decreased arousal.

2.3. Results

2.3.1. Behavioural Data

Before analysing the data, half the trials of the Pure conditions were removed to approximate the number of trials (and the reliability of RT measures based on them) to the level of the Mixed conditions. This was done by randomly dropping one member of a pair of successive Pure-condition trials. Mean RT based on all trials and adjusted mean RT based on the remaining trials after removal were highly correlated across participants in each of the four conditions (all $r = .99$, $p < .001$). The trials of each run's first minute were considered practice and were not included in the analysis. Furthermore, trials with RT shorter than 120 ms (0.15 % on average) were discarded, since they were not considered responses to experimental stimuli. Responses more than 550 ms after stimulus onset were coded as errors of omission

The analysis of TOT effects was based on individual mean RT of consecutive 4-min time bins[1]. Group averages for all six time bins of all four conditions are shown in Figure 2. Lines of best fit using least-squares estimation were calculated for each participant for the six time bins. The slope of the fitted line indicated the overall linear trend of RT over time. This strategy enabled us to specifically test linear changes in performance over time (the slope, or RT increase function; cf. Helton & Warm, 2008). Since the linear trend only reflects RT variance that is explained by the global linear change in RT, the measure is relatively insensitive to varying short-term influences on performance (e.g. motivational shifts), which would not so much impact the slope of the linear increase function but rather the goodness of its fit to the data. Nevertheless, a quadratic term was included in the least-squares fitting model to capture nonlinear changes that take a normal or inverted U-shaped form. This way we quantified deviations from the linear change of RT like levelling off or even reversing the trend towards the end of the task, since such nonlinear changes can have some impact on the linear trend measure and might thus artificially inflate or reduce differences between experimental conditions.

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[1] All major analyses were repeated based on individual median RT as the dependent variable, which yielded comparable results.

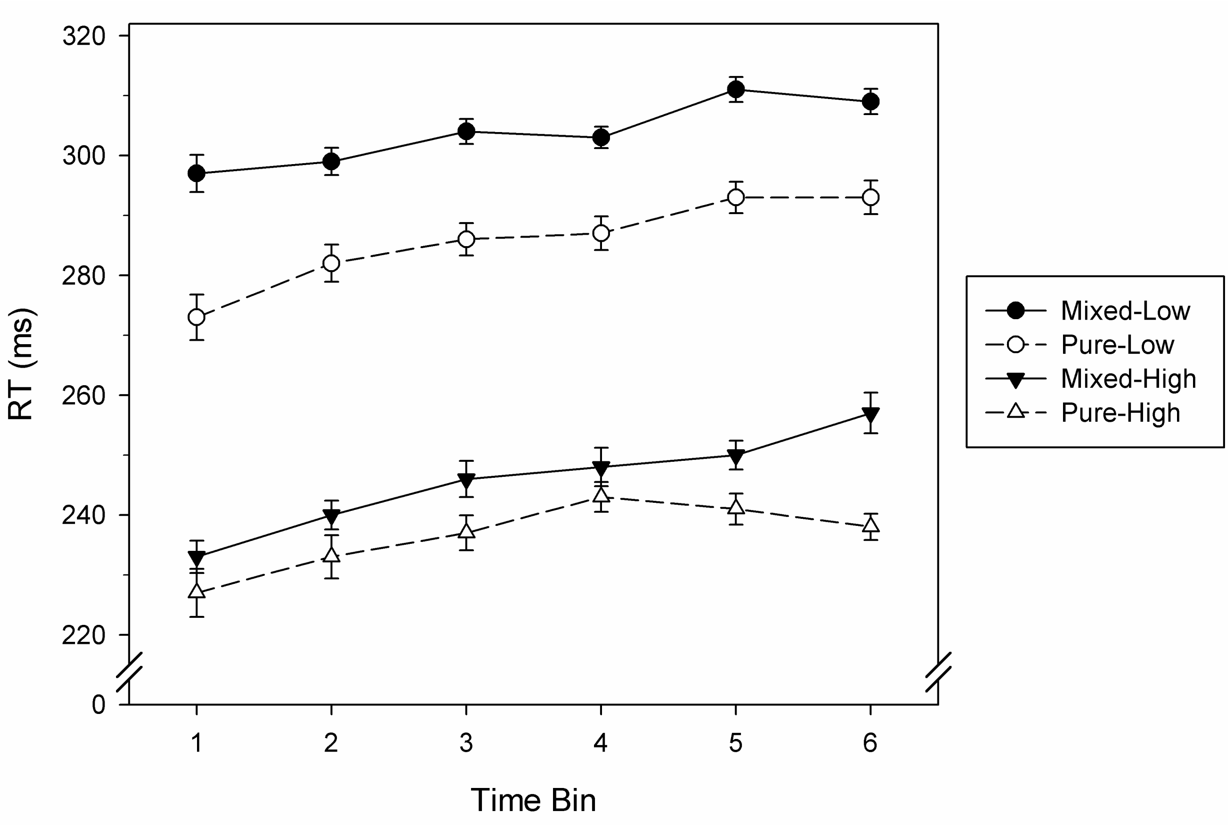

Figure 2. Mean reaction time (RT) across all six time bins for each condition (see text for further explanation). Error bars represent standard errors of the mean adjusted for within-subject designs (cf. Cousineau, 2005). Connecting lines between data points were added for illustrative purposes.

The average goodness of fit (as indicated by the coefficient of determination) across conditions and participants was $M = 0.380$ ($SD = 0.293$) for the linear model and $M = 0.565$ ($SD = 0.286$) for the linear-plus-quadratic model. Repeated-measures analyses of variance (ANOVAs) indicated for both models that the goodness of fit did not differ significantly between the four conditions [all $F(3, 120) < 0.25$]. In addition to the linear trend over time, we calculated the RT difference between the first and last time bin for each participant (cf. Szalma et al., 2006). Although this approach only takes into account performance during two of the six time periods (Rogosa, 1995), this measure was taken to provide additional evidence for the robustness of our findings. Group averages of individual RT slopes and differences between the first and last time bin for all four conditions are given in Table 1.

Table 1

Means and Standard Deviations of Measures of Performance Change with Time on Task

Measure of Change	Experimental Condition			
	Pure-High	Mixed-High	Pure-Low	Mixed-Low
	M (SD)	*M (SD)*	*M (SD)*	*M (SD)*
Linear RT slope	2.4 (5.5)	4.2 (4.9)	3.8 (5.2)	2.8 (4.3)
RT difference (ms)	11.2 (27.3)	23.5 (29.1)	19.7 (27.8)	12.4 (23.0)
Quadratic RT slope	-1.3 (2.0)	-0.3 (3.2)	-0.7 (2.5)	-0.1 (2.2)
Difference in missings (%)	1.0 (2.6)	1.1 (3.9)	0.7 (4.1)	2.4 (8.7)

Note. RT = reaction time. Linear RT slopes of the lines of best fit represent RT increases in ms per 4 min; RT difference is the difference in mean RT, Difference in missings the difference in the percentage of trials without response, between the last and first time bin, respectively. Generally, positive values reflect increases with time on task. For quadratic RT slopes, however, negative values indicate inverted U-shaped trends with time on task.

The relationship between stimulus intensity (high vs. low), presentation mode (pure vs. mixed) and performance was tested at the group level with repeated-measures ANOVAs. Initial analyses based on mean RT of the first and last time bin (instead of RT slope or difference score) revealed significant main effects for stimulus intensity, presentation mode, and time on task: RT was significantly shorter for high- intensity vs. low- intensity stimuli [$F(1, 40) = 458.52$, $p < .001$, partial $\eta^2 = .92$], stimuli presented in pure vs. mixed blocks [$F(1, 40) = 41.50$, $p < .001$, partial $\eta^2 = .51$], and stimuli presented at the beginning vs. the end of each run [$F(1, 40) = 43.03$, $p < .001$, partial $\eta^2 = .52$]. The only significant interaction was the three-way interaction between stimulus intensity, presentation mode, and time on task: $F(1, 40) = 8.07$, $p < .01$, partial $\eta^2 = .17$.

Figure 3 summarizes the main results showing the average RT slopes for all four conditions. The ANOVA of RT slopes yielded no significant main effects for stimulus intensity or presentation mode but, importantly, a significant crossed interaction between both factors [$F(1, 40) = 4.68$, $p < .05$, partial $\eta^2 = .11$], resulting in a larger slope for the Mixed-High compared to the Pure-High condition but a smaller slope for the Mixed-Low compared to the Pure-Low condition (see Table 1). An ANOVA based on individual RT differences between the first and last time bin confirmed this pattern of results [$F(1, 40) = 8.07$, $p < .01$, partial $\eta^2 = .17$; see Table 1].

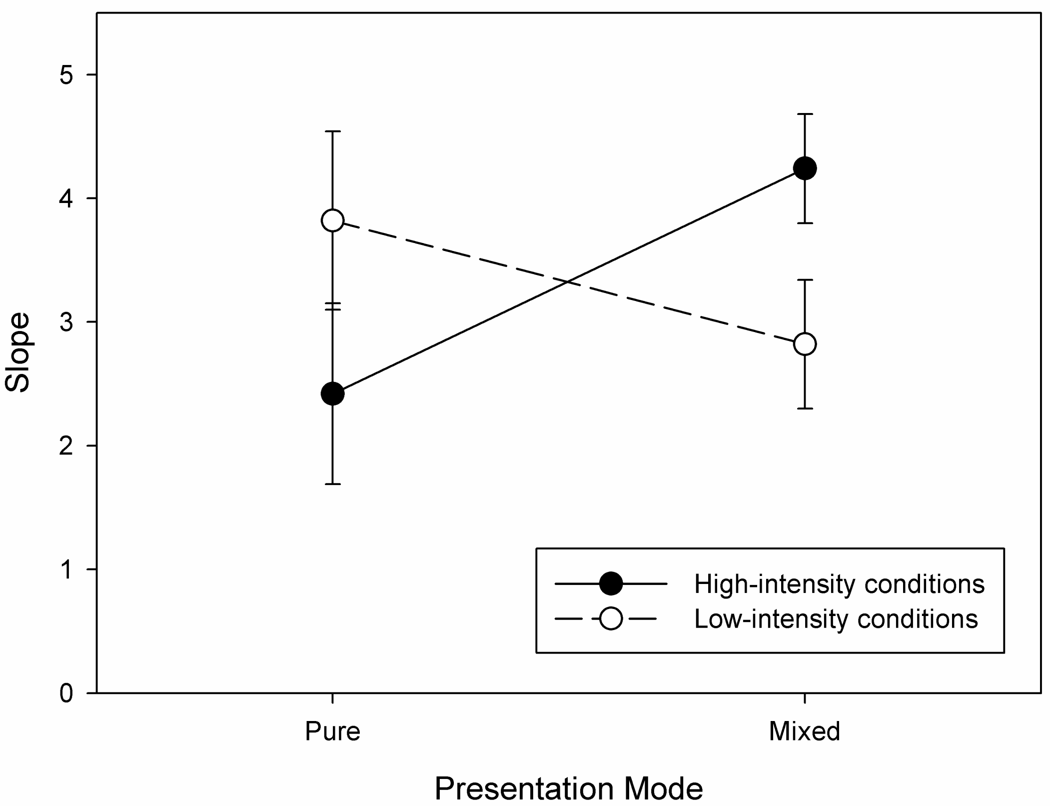

Figure 3. Mean slopes of the lines of best fit across all six time bins, representing reaction-time increase with time on task for each condition (see text for details). Error bars represent standard errors of the mean adjusted for within-subject designs (cf. Cousineau, 2005). Connecting lines between data points were added for illustrative purposes.

Subsequently, simple main effects were tested separately for both high- and low-intensity stimuli using paired t-tests with p-values adjusted for one-sided testing. The tests revealed that the difference in mean RT slopes, which were numerically steeper in the Pure-Low than the Pure-High condition, did not reach significance [$t(40) = -1.15$, $p = .13$]. When using mean RT difference scores as dependent variable, the numerical tendency approached significance [$t(40) = -1.41$, $p = .08$]. Further, the tests revealed that mean RT slopes for high-intensity stimuli were significantly larger in the mixed- than in the pure-presentation condition [$t(40) = -1.80$, $p < .05$]; for low-intensity stimuli, the numerical difference in the expected direction did not reach significance [$t(40) = 0.94$, $p = .18$]. This pattern was confirmed when tests were repeated using mean RT difference scores as dependent variable: for high-intensity stimuli, a significant difference between mixed- and pure-presentation was found [$t(40) = -2.20$, $p < .05$]; for low-intensity stimuli, the expected numerical difference approached significance [$t(40) = 1.28$, $p = .10$].

As can be seen in Table 1, all mean quadratic RT slopes have small negative values, which indicates a slight inverted U-shaped trend in RT over time across conditions. Subjecting the quadratic RT slopes of all four conditions to a repeated-measures ANOVA yielded neither significant main effects for stimulus salience [$F(1, 40) = 1.18$, ns.] or presentation mode [$F(1, 40) = 3.28$, ns.] nor a significant interaction [$F(1, 40) = 0.44$, ns.]. It should be noted, though, that the effect of presentation mode approached significance ($p = .08$, partial $\eta^2 = .08$).

Potentially confounding effects of condition order were tested by including it as a between-subject factor in the ANOVA. Importantly, no significant three-way interaction was found between order of condition, stimulus salience, and presentation mode [for RT slopes: $F(5, 35) = 1.90$, ns.; for RT difference scores: $F(5, 35) = 1.33$, ns.], and the two-way interaction between stimulus salience and presentation mode remained essentially unaffected [for RT slopes: $F(1, 35) = 4.58$, $p < .05$, partial $\eta^2 = .12$; for RT difference scores: $F(1, 35) = 7.71$, $p < .01$, partial $\eta^2 = .18$].

For testing dependencies between initial response speed and performance change over time, we calculated Pearson correlation coefficients between intercept and slope of the fitted line and between mean RT of the first time bin and RT difference score separately for each condition. Results are shown in Table 2. Correlation coefficients significantly different from zero were only found for the Pure-High condition.

Trials with missing responses were generally rare (Pure-High: 1.7 %; Mixed-High: 1.2 %; Pure-Low: 3.1 %; Mixed-Low: 3.8 %). Time-related increases in the relative number of missings are shown in Table 1. Owing to the relative rarity of missings, we did not calculate individual slopes for estimating linear increases in the number of missings over time. A repeated-measures ANOVA of the arcsine-transformed percentage of missed trials in the first and last time bins of each condition yielded significant main effects for stimulus intensity [$F(1, 40) = 38.56$, $p < .001$, partial $\eta^2 = .49$) and TOT ($F(1, 40) = 9.78$, $p < .01$, partial $\eta^2 = .20$). No other effect reached statistical significance.

Table 2

Pearson Correlation Coefficients Between Measures of Initial Response Speed and Measures of Change of Response Speed with Time on Task

Measures	Experimental Condition			
	Pure-High	Mixed-High	Pure-Low	Mixed-Low
Intercept × linear RT slope	-.53*	.05	-.14	-.22
Mean RT × RT difference	-.49*	.07	-.15	-.22

Note. RT = reaction time. Mean RT refers to the first time bin; RT difference refers to the difference between the last and first time bin. *Correlations significantly deviating from zero (p < .05).

An additional ANOVA of the data collapsed across time bins (mean RTs: Pure-High = 236 ms; Mixed-High = 245 ms; Pure-Low = 286; Mixed-Low = 304 ms) confirmed both main effects of stimulus intensity [$F(1, 40) = 542.08$, $p < .001$, partial $\eta^2 = .93$] and presentation mode [$F(1, 40) = 38.20$, $p < .001$, partial $\eta^2 = .49$] and also yielded a significant interaction [$F(1, 40) = 5.05$, $p < .05$, partial $\eta^2 = .11$], showing that the difference in mean RT between the mixed- and pure-presentation conditions was larger for low- than for high-intensity stimuli.

2.3.2. Questionnaire Data

The KAB pre- and post-task scores were compared by means of paired *t*-tests for all three sessions. The KAB pre-task score ($M = 19.4$, $SD = 5.4$) was significantly lower than each post-task score [Pure-High: $M = 23.6$, $SD = 6.2$, $t(40) = -4.6$, $p < .001$; Pure-Low: $M = 26.6$, $SD = 8.1$, $t(40) = -5.8$, $p < .001$; Mixed: $M = 26.1$, $SD = 8.5$, $t(41) = -5.0$, $p < .001$]. A subsequent ANOVA comparing pre- and post-task differences between sessions yielded a significant global effect of session [$F(2, 80) = 7.1$, $p = .002$, partial $\eta^2 = .15$]. Simple contrasts revealed that the pre–post KAB score differences for both the Pure-Low and the Mixed sessions were significantly larger than for the Pure-High session [Pure-Low vs. Pure-High contrast: $F(1, 40) = 14.0$, $p = .001$, partial $\eta^2 = .26$; Mixed vs. Pure-High contrast: $F(1, 40) = 6.1$, $p = .017$, partial $\eta^2 = .13$]. This shows that mental fatigue increased generally with time on task, but did more so over the presumably more demanding Pure-Low and Mixed conditions compared to the Pure-High condition.

Initial multivariate ANOVAs of the four DSSQ-S scale scores yielded a significant effect of time of administration (pre- vs. post-task) for the Pure-High session [Pillai's trace = 0.64, $F(4, 27) = 11.9$, $p < .001$]. Subsequent univariate analyses revealed that Task Engagement decreased significantly [$F(1, 30) = 45.6$, $p < .001$, partial $\eta^2 = .60$] from pre-task ($M = 20.7$, $SD = 3.9$) to post-task ($M = 14.2$, $SD = 5.9$). Not surprisingly, there also was a significant decrease in Energetic Arousal [pre-task: $M = 7.9$, $SD = 1.9$; post-task: $M = 5.3$, $SD = 3.2$; $F(1, 30) = 35.7$, $p < .001$, partial $\eta^2 = .54$]. At the same time, we found a significant increase in Distress [pre-task: $M = 7.9$, $SD = 3.2$; post-task: $M = 9.6$, $SD = 3.6$; $F(1, 30) = 4.9$, $p = .035$, partial $\eta^2 = .14$] and Worry [pre-task: $M = 9.4$, $SD = 5.4$; post-task: $M = 12.4$, $SD = 5.9$; $F(1, 30) = 5.5$, $p = .026$, partial $\eta^2 = .16$].

For the Pure-Low session, the pattern of state change was similar: the multivariate analysis indicated a global effect of time of administration [Pillai's trace = 0.81, $F(4, 27) = 29.3$, $p < .001$]. Also, Task Engagement again decreased over time [pre-task: $M = 20.7$, $SD = 3.9$; post-task: $M = 12.8$, $SD = 2.8$; $F(1, 30) = 98.9$, $p < .001$, partial $\eta^2 = .77$]; Energetic Arousal decreased as well [pre-task: $M = 7.9$, $SD = 1.9$; post-task: $M = 3.9$, $SD = 2.4$; $F(1, 30) = 92.8$, $p < .001$, partial $\eta^2 = .76$]; and again, the Distress score increased [pre-task: $M = 7.9$, $SD = 3.2$; post-task: $M = 9.7$, $SD = 2.9$; $F(1, 30) = 4.7$, $p = .038$, partial $\eta^2 = .14$]. The modest increase in the Worry score [pre-task: $M = 9.4$, $SD = 5.4$; post-task: $M = 10.6$, $SD = 6.2$] did not reach significance, however [$F(1, 30) = 1.1$, $p = .297$, partial $\eta^2 = .04$].

Finally, a slightly different pattern was found for the Mixed session [Pillai's trace = 0.73, $F(4, 27) = 18.2$, $p < .001$]. Here again, both Task Engagement [pre-task: $M = 20.7$, $SD = 3.9$; post-task: $M = 13.2$, $SD = 5.8$; $F(1, 30) = 46.0$, $p < .001$, partial $\eta^2 = .61$] and Energetic Arousal [pre-task: $M = 7.9$, $SD = 1.9$; post-task: $M = 4.9$, $SD = 3.2$; $F(1, 30) = 26.0$, $p < .001$, partial $\eta^2 = .46$] decreased. The numerical increase in the Distress score, however, failed significance [pre-task: $M = 7.9$, $SD = 3.2$; post-task: $M = 9.4$, $SD = 3.7$; $F(1, 30) = 2.8$, $p = .102$, partial $\eta^2 = .09$], whereas the Worry score increased significantly [pre-task: $M = 9.4$, $SD = 5.4$; post-task: $M = 13.0$, $SD = 5.9$; $F(1, 30) = 6.0$, $p = .005$, partial $\eta^2 = .24$].

Subsequent ANOVAs comparing the size of the time-related state changes (pre–post differences) between the three sessions for each of the four DSSQ-S scales yielded an overall effect of session only for Energetic Arousal [$F(2, 60) = 3.6$, $p = .035$, partial $\eta^2 = .11$] and Worry [$F(2, 60) = 4.0$, $p = .023$, partial $\eta^2 = .12$]. Time-related changes in Task Engagement and Distress scores were not significantly different between sessions (all Fs < 1). Simple contrasts revealed that the pre–post decrease in the Energetic Arousal score during the Pure-

Low session was significantly larger than during the Pure-High session [*F*(1, 30) = 5.8, *p* = .023, partial $\eta^2 = .16$] and tended to be larger than during the Mixed session [*F*(1, 30) = 3.7, *p* = .064, partial $\eta^2 = .11$]. Energetic Arousal decreases during Mixed and Pure-High sessions did not differ significantly ($F < 1$). Furthermore, simple contrasts showed that the increase in the Worry score during the Pure-Low session was significantly smaller than during the Mixed session [*F*(1, 30) = 9.3, *p* = .005, partial $\eta^2 = .24$] and tended to be smaller than during the Pure-High session [*F*(1, 30) = 3.2, *p* = .082, partial $\eta^2 = .10$]. Worry score increases during Mixed and Pure-High sessions did not differ significantly ($F < 1$).

2.4. Discussion

Our results revealed a significant overall increase in mean RT with TOT in three 25-min continuous visual SRT tasks, confirming earlier studies (e.g. Lisper & Ericsson, 1973; Lisper & Törnros, 1974; Sanders et al., 1982, Exp. 2). Since there was a parallel increase in the (overall rather negligible) number of missed responses, this RT increase cannot be attributed to a shift of the speed–accuracy trade-off towards higher accuracy, thereby sacrificing speed. More importantly, the results corroborated the predictions derived from the resource-depletion theory of vigilance (Grier et al., 2003; Helton & Warm, 2008; Smit et al., 2004) but not those derived from the mindlessness model of performance decrements during sustained attention (Manly et al., 1999; Robertson et al., 1997): Although the numerically larger time-related RT increase for low- compared to high-intensity stimuli in pure presentation conditions did not reach significance, it still tended toward the opposite of what was predicted based on mindlessness theory. Even stronger support for resource theory comes from the cross-over interaction between stimulus intensity and presentation mode: for high-intensity stimuli, the time-related RT increase became larger during the mixed presentation compared to the pure one, whereas for low-intensity stimuli it became smaller. Subsequent comparisons of simple main effects largely confirmed this result.

Examining potential quadratic trends over time (i.e. RT changes of a U-shaped form) revealed that all coefficients had a small negative mean value. This might reflect a slightly accelerated RT increase early in the task or a small "final spurt" RT decrease towards the end or both. Importantly, the coefficients did not significantly differ between conditions, ruling out the possibility that the observed differences in linear RT trend between conditions were due to the differential impact of quadratic changes. This also disconfirms the visual impression (cf. Figure 2) that the difference between Pure- and Mixed-High conditions is mainly driven by the stabilization of RT during the last eight minutes of the Pure-High condition.

The significant changes in subjective-state measures indicate that our TOT manipulation was successful in producing mental fatigue, broadly supporting resource theory. The overall increase in the KAB score demonstrates that our cognitively little demanding SRT task elicited perceived strain over time. This is consistent with a previous study that used a forewarned SRT task (Langner et al., in press). It also corresponds to the results of a study which reported elevated levels of subjective strain after performing a very simple, monotonous simulated driving task in combination with a highly compatible choice RT task over 25 min (Fischer, Langner, Birbaumer & Brocke, 2008). Further, the larger increase in the KAB score during the Pure-Low and Mixed sessions compared to the Pure-High session shows that the former were perceived to induce more strain (i.e. mental fatigue) over time than the latter. We argue that this finding supports the assumption of resource theory that both sessions containing hard-to-detect low-intensity stimuli (i.e. the Pure-Low and Mixed sessions) require more top-down attentional control and, thus, induce more resource depletion and feelings of strain.

The DSSQ-S findings largely match those of previous studies assessing subjective-state changes during prolonged SRT or vigilance tasks using the long or short version of the DSSQ (Helton & Warm, 2008; Langner et al., in press; Szalma et al., 2004; Temple et al., 2000): Participants reported feeling less energetically aroused after the session than before its start, and task engagement was perceived to be higher before the session than at its end. Both effects agree well with the resource-depletion account. The elevation of self-reported distress is consistent with studies demonstrating that participants perceive prolonged monotonous RT tasks as stressful (Hancock & Warm, 1989; Langner et al., in press; Szalma et al., 2004). Only the increase in self-reported worry (i.e. task-unrelated thoughts) is at odds with findings from previous vigilance studies, which either reported no increase (Szalma et al., 2004) or a decrease (Helton & Warm, 2008; Temple et al., 2000) in such interfering task-irrelevant cognitions. Their significant increase over time in this study is evidence for “absent-mindedness” during performance, i.e. mindlessness theory. The difference compared to previous findings might be related to the higher cognitive demands of the vigilance tasks used previously, which required not only stimulus detection but also stimulus discrimination, possibly preventing mind-wandering more than the easier SRT tasks do. Alternatively, the difference might also be related to using the short version of the DSSQ and associated differences in item content in our study (cf. Matthews et al., 2005).

Apart from these global changes in subjective state, two significant differences between the sessions emerged: First, energetic arousal was perceived to decrease more strongly during the Pure-Low session than during both the Pure-High and Mixed sessions, although the latter difference just failed significance. This pattern indicates that our intensity manipulation had a modest effect on perceived energetic arousal, such that arousal was reported to be somewhat lower when no high-intensity stimuli were present, that is, when attentional demand was constantly high. Second, task-unrelated thoughts were reported to have increased less during the Pure-Low session than during both the Pure-High or Mixed sessions, although the former difference just failed significance. This pattern of results is neither fully consistent with mindlessness nor with resource theory. The easier of the two highly monotonous conditions (i.e. Pure-High), which should promote routinization and mindlessness more than the more difficult Pure-Low condition, indeed showed a tendency for a larger increase in perceived absent-mindedness. The report of less task-irrelevant thoughts during the highly monotonous Pure-Low session than during the objectively less monotonous Mixed session may appear at odds with mindlessness theory, but this finding might be due to an overcompensation of the mindlessness-promoting effect of monotony by the mindlessness-preventing effect of attentional demand. This demand was objectively higher during the Pure-Low condition, which contained only hard-to-detect low-intensity stimuli. In conflict with mindlessness theory, however, is the absence of any difference in self-reported task-irrelevant thoughts between the highly monotonous, easy Pure-High and the objectively less monotonous and more difficult Mixed session, since the former condition should definitely promote more routinization and mind-wandering.

All data taken together, we argue that the steeper RT increase in Mixed-High compared to Pure-High trials is attributable to the resource-demanding effect of the interspersed hard-to-detect low-intensity stimuli. Alternatively, it might be argued that this difference may be due to the lower stimulation level in the Mixed-High condition, since there obviously were only half as many more arousing high-intensity stimuli compared to the Pure-High condition. However, the immediate-arousal effect of the high-intensity stimuli (cf. Sanders, 1977) would probably have offset any of these subtler context effects present at the time of the response. Also, the unpredictability of stimulus type in the mixed condition is a source of arousal itself, which additionally counteracts the smaller stimulation effect in the mixed condition (see

Berlyne, 1960, or Pfaff, 2006, for detailed discussions of the relationship between uncertainty and arousal).

In a similar vein we argue that the smaller RT increase in Mixed-Low compared to Pure-Low trials is attributable to the resource-saving effect of the interspersed easy-to-detect high-intensity stimuli. Although the higher initial RT levels in the Mixed-Low compared to the Pure-Low condition might also suggest a regression-to-the-mean artefact as a possible cause for the smaller RT increase in the Mixed-Low condition, this explanation can be excluded, since initial RT scores were not inversely correlated with measures of performance change (Rogosa & Willett, 1985). In sum, the pattern of our results provides strong evidence in favour of the resource-depletion model as an explanation of the performance decline during continuous SRT tasks. Nevertheless, some of the self-report data also attest to an increase in task-unrelated thoughts (i.e. mindlessness) during sustained SRT performance.

The interpretation of our results in terms of resource theory agrees well with research on vigilance, which demonstrated that conditions placing higher demands on attention (e.g. high event rates or degraded stimuli) lead to stronger performance decrements over time (Parasuraman, 1979; Nuechterlein, Parasuraman & Jiang, 1983; Smit et al., 2004). A meta-analysis (See et al., 1995) confirmed that the likelihood of a vigilance decrement increases with task difficulty. Low conspicuity, or salience, of targets turned out to be the strongest predictor for a large decrement (see also Helton & Warm, 2008; Temple et al., 2000). The study by Temple et al. (2000) also revealed that decreased target salience is associated with elevated ratings of perceived workload and distress in comparison to a high-salience condition.

2.4.1. Are Resource Depletion and Mindlessness Related to Each Other? — A Conjecture

The results of our study support the hypothesis that the efficiency of information processing even in elementary cognitive tasks gets compromised over time if the continuous allocation of attention is required. In line with earlier studies, our data suggest that the performance decrement with TOT is related to demands on top-down attentional control. A unified explanation of time-related decrements in various cognitive processes that rely on top-down control is offered by assuming a limited mental resource that is essential to all these control processes but gets depleted with prolonged continuous use. This notion is inspired by recent conceptualizations of self-regulatory strength as a depletable mental resource (R. F. Baumeister, Vohs & Tice, 2007; Muraven & Baumeister, 2000). In fact, efforts to sustain attention towards a monotonous task over extended periods of time may be considered a prime example of self-regulation. Thus, we propose that prolonged effortful attention leads to reduced self-regulatory power, which we consider a hallmark of mental fatigue.

Can this proposal also help to explain findings that support mindlessness theory? After all, there is good evidence for either model in the literature. In fact, even though our results strongly argue for the resource-depletion model, they do not completely refute mindlessness theory, since it may still be argued that our manipulations were not strong enough to elicit reliable differences in the processes deemed relevant in the mindlessness model. The self-reported increase in task-irrelevant thoughts in our study provides some support for mindlessness theory, too. Of course, different findings in different studies can always be explained away by more or less subtle methodological differences. This provides an easy but often unsatisfactory solution. We argue instead that both theories are not so contradictory after all, but rather complementary. That is to say, both phenomena, mental fatigue and mindlessness, are associated with sustained performance and can explain certain aspects of performance decline over time.

We suggest that our above assumption that reduced self-regulatory power underlies the failure to maintain optimal performance via destabilizing cognitive control helps to reconcile the two theoretical positions. Their seeming contradiction dissolves when adopting the self-regulation perspective, from which both phenomena can be explained as consequences of the decrease in self-control strength with TOT: On the one hand, reduced self-control strength presumably results in diminished goal maintenance, leading to "absent-mindedness." Recent research indicates that goal maintenance may be especially challenged under "simple" task conditions without interference, conflict or dual-task demands, as is characteristic of SRT tasks (Dreisbach & Haider, 2008; Goschke & Dreisbach, 2008; Kane & Engle, 2003). There, individuals are assumed to need more effortful control to "stay on the job," which would render SRT tasks especially susceptible to reduced self-regulatory power (cf. Walker, Muth, Odle-Dusseau, Moore & Pilcher, 2009). These findings also agree with the proposal of Hockey (1986) that the vigilance decrement may be at least partially due to difficulties in maintaining a specific task set.

On the other hand, reduced self-control strength presumably results in exerting less attentional effort, leading to a diminished efficiency of task-relevant computational processes (cf. Hockey, 1997; Sarter et al., 2006). This conjecture implies a subtle qualitative difference in how mindlessness and reduced attentional effort affect performance: the former reflects an impaired allocation of attention, whereas the latter reflects a deficit in the intensity of allocated attention. Thus, both mind-wandering and the unstable allocation of attentional effort may be two sides of the same coin — depletion of self-regulatory power. Further research is needed to test this conjecture with different, possibly parametric manipulations of attentional demand and independent measures of self-control strength.

2.4.2. Limitations of the Study

There might be some potential methodological concerns related to the comparison of pure with mixed blocks of trials: For instance, the significantly longer mean RT in mixed versus pure conditions could be taken as evidence for increased computational difficulty that could possibly entail higher energetic costs, too, as would be reflected in a steeper time-related RT increase. The potential computational processes underlying this TOT-independent mean RT difference (i.e. “mixing costs”) are comprehensively discussed by Los (1996). However, regarding energetic modulations reflected in the time-related RT increase, our data reveal opposite effects for high- versus low-intensity stimuli in the mixed compared to the pure conditions, whereas the assumption of higher energetic costs associated with mixing per se would predict an intensity-independent effect of mixing. This provides evidence against the assumption of generally increased energetic costs associated with the mixed presentation and has implications for theories about the cognitive mechanisms that underlie intensity-mixing costs in SRT tasks, since this result is more consistent with notions of automatic, stimulus-driven processes that pose little attentional demands.

Further, the different number of stimuli with the same intensity in the pure versus mixed conditions might have entailed differential effects of stimulus-specific practice or habituation or both. These effects cannot be completely excluded, but the following arguments may show that these potential confounds are unlikely to undermine the interpretation of our results: First of all, practice and habituation have been previously shown to have no substantial impact on prolonged SRT performance (Lim & Dinges, 2008; Lisper & Törnros, 1974). Further, if still present to some degree, practice and habituation should work in opposite directions, and their small effects may thus cancel each other out or at least diminish each other further. More importantly, differential practice and habituation effects between mixed and pure blocks could not explain why in the mixed condition the time-related performance decline for low-versus high-intensity stimuli should change in opposite directions compared to the pure conditions. Finally, and more generally, these potential confounds are inherent to all blocked-mixed designs and can only be avoided by introducing other confounds (e.g. presenting twice as many trials in the mixed compared to the blocked conditions; see Los, 1996, p. 163, for a related discussion). Nevertheless we think that this slight uncertainty does not outweigh the potential usefulness of the blocked-mixed design, given that the potential confound is taken into consideration.

A further limitation is the availability of DSSQ-S data for only about three quarters of the sample. For the remainder of the sample, the effects of our manipulations on self-reported task engagement, energetic arousal, distress and worry can only be assumed to be similar. Since all participants were sampled from the same population, this assumption may be warranted.

2.4.3. Conclusions

Our results largely support the resource-depletion theory of SRT performance decline with TOT and disconfirm predictions derived from mindlessness theory: First, the time-related performance decrement was not smaller (as predicted from mindlessness theory) but tended to be larger for attentionally demanding low-intensity stimuli. Second, contrary to the prediction from mindlessness theory, the time-related decrement did not become generally smaller when stimuli of both intensities were presented in a less monotonous, randomly intermixed fashion. Instead, the decrement for high-intensity stimuli worsened when attentionally demanding low-intensity stimuli were introduced, whereas the decrement for low-intensity stimuli lessened when attentionally undemanding high-intensity stimuli were introduced. These effects argue for a model that regards time-related decrements in SRT performance as mediated by resource depletion (i.e. mental fatigue), induced by prolonged attentional demands. A conjecture that explains both resource depletion and mindlessness as consequences of reduced self-regulatory power was suggested but needs empirical testing. This conjecture might also apply to other cognitive tasks that show a performance decline over time, particularly vigilance tasks and other tasks involving continuous top-down control.

Taking a more general perspective, our data confirm the significant influence of energetic variables on elementary cognitive processes. These results should encourage theorists to consider the impact of energetic factors on the behaviour under scrutiny more systematically. In keeping with Hockey, Coles et al. (1986) we maintain that including energetic variables in models of human cognition is an important and necessary step towards better understanding the workings of the human mind. This approach may also improve translating basic research findings into real-world applications, for instance by defining energetic boundary conditions for the applicability of cognitive models or including energetic factors as model parameters. This appears even more important when considering today's automated world and its job demands, which, in many cases, have moved away from physical work towards cognitive tasks like sustained monitoring and decision making.

3. STUDY 2

MENTAL FATIGUE AND TEMPORAL PREPARATION IN SIMPLE REACTION-TIME PERFORMANCE

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3.1. Introduction

Fatigue from prolonged mental work has been found to impair performance in a variety of cognitive tasks (e.g. Bills, 1931; Helton & Warm, 2008; Kraepelin, 1902; Lorist et al., 2000; Sanders & Hoogenboom, 1970). The state of mental fatigue is characterized by the inability to allocate sufficient processing resources to the task at hand (Matthews & Desmond, 2002; Smit et al., 2004). Frequently, fatigued participants are still able to perform highly over-learned, automated tasks, whereas their performance significantly deteriorates when tasks require the voluntary allocation (i.e., top-down control) of attention (e.g., Boksem, Meijman & Lorist, 2005, 2006; Lorist, Boksem & Ridderinkhof, 2005; Lorist et al., 2000). Because top-down control processes are transient (Smallwood & Schooler, 2006; Steinborn, Flehmig, Westhoff & Langner, 2008; Stuss et al., 2003; West, 2001), maintaining performance at optimal levels requires a mechanism that stabilizes control and ensures continuous task engagement. This stabilization is considered an effortful mechanism vulnerable to mental fatigue (e.g., Lorist et al., 2005; Sarter et al., 2006; Smit et al., 2004; R. A. Wright et al., 2008).

Our study examined effects of mental fatigue on speeded performance in a forewarned SRT task. Various studies have demonstrated that SRT performance substantially deteriorates over time (e.g., Buck, 1966; Lisper & Ericsson, 1973; Lisper, Melin & Sjödén, 1973; Sanders et al., 1982; van den Berg & Neely, 2006). It is not yet clear, however, whether this effect only results from an overall effect of fatigue on response speed or whether it also involves more specific fatigue-related changes in the timing behaviour under temporal uncertainty.

3.1.1. Strategic Accounts of Temporal Preparation in Variable-Foreperiod Designs

Preparation enhances performance, for example, by speeding up responses to an imperative signal in simple and choice RT tasks (Jennings & van der Molen, 2005). Here, we only deal with purely temporal (i.e. nonspecific) preparation, which is based on the temporal contingencies between experimental events. In tasks involving nonspecific preparation, participants use temporal information to optimise performance by anticipating the imperative moment (i.e. the moment of target occurrence) (Coull, 2004). Typically, a warning signal (WS) precedes the imperative stimulus (IS), enabling nonspecific preparation for the impending IS. This usually improves RT substantially (e.g. Hackley & Valle-Inclan, 2003; Los & Schut, 2008).

The delay between WS and IS is called foreperiod (FP). When FP duration is variable within a block of trials, participants remain uncertain about the exact moment of IS occurrence on any given trial and thus cannot exactly synchronize their preparation with IS occurrence. In this variable-FP setting, responses are typically found to be relatively slow at early imperative moments but to become faster at later imperative moments during the FP interval (cf. Los, Knol & Boers, 2001; Niemi & Näätänen, 1981; Woodrow, 1914). This phenomenon, termed the variable-FP effect, has been traditionally explained by assuming that participants exploit the gradual increase in conditional probability of IS occurrence during the FP and transform them into a state of preparation (Niemi & Näätänen, 1981, p. 137).

To illustrate this point, consider an RT experiment in which the IS is presented with an equal a-priori probability at three imperative moments, say 1000, 3000, or 5000 ms after the WS. At the first imperative moment (i.e. 1000 ms after the WS), the probability of IS occurrence is 33 % (and 66 % that the IS will be presented later). In trials where the first imperative moment is bypassed, the probability that the IS will occur at the next one (i.e. 3000 ms after the WS) increases to 50 %. When this moment is also bypassed, participants will then have full certainty that the IS will be presented at the latest imperative moment (i.e. 5000 ms after the WS). In this situation, the typical finding is a decrease in RT with increasing FP length. That is, the fastest responses in this example occur with FPs of 5000 ms. The resulting downward-sloping FP–RT function has traditionally been taken to reflect a strategic process by which participants convert the objective increase in the conditional probability of IS occurrence into a subjective expectation. This strategic account assumes that participants actively track the flow of time after the WS and intentionally monitor the changing conditional probability to use this information for top-down regulation of their preparatory state (e.g. Näätänen & Merisalo, 1977). This top-down control of preparation is considered an effortful process since it arises from voluntarily orienting attention to specific moments in time after the WS (e.g. Correa, Lupiáñez & Tudela, 2006; Coull, Frith, Büchel & Nobre, 2000; Lange, Krämer & Röder, 2006; Nobre, 2001). The degree to which attention is directed to a specific time point during the FP is assumed to be directly related to the subjective probability (expectancy) of IS occurrence at this time point (e.g. A. A. Baumeister & Joubert, 1969; Karlin, 1966). Furthermore, studies have shown that a state of peak preparation can hardly be maintained for long, which underscores the importance of exact temporal predictions for being optimally prepared at the right time (e.g. Gottsdanker, 1975; Näätänen, 1972).

This strategic account, however, cannot explain sequential FP effects: Analyses that also considered FP length on the previous trial (FP_{n-1}) as a determinant of RT revealed that responses are relatively *fast* when the previous trial's FP was *short* but are relatively *slow* when the previous trial's FP was *long*. (e.g. Alegria & Delhaye-Rembaux, 1975; Karlin, 1959; Steinborn, Rolke, Bratzke & Ulrich, 2008, 2009; Vallesi & Shallice, 2007; van der Lubbe, Los, Jaskowski & Verleger, 2004; Woodrow, 1914). These sequential FP effects are usually asymmetric, since RT is more strongly affected in trials with short FPs compared to trials with longer FPs, producing a typical $FP_{n-1} \times FP_n$ interaction (see Fig. 1). To explain these asymmetric sequential FP effects within the traditional account (e.g. Alegria, 1975; Drazin, 1961; Klemmer, 1957), it has been argued that individuals expect a repetition of FP_{n-1} on the current trial, so that optimal preparedness is reached at the same moment as on the preceding trial. If FP_n is shorter than FP_{n-1}, then optimal preparedness will not yet have been reached at IS occurrence, and RT will be relatively slow. If instead FP_n is longer than FP_{n-1} and the repetition-expectancy-based moment of optimal preparedness is bypassed without IS occurrence, then it is assumed that individuals extend the period of optimal preparedness or cyclically re-prepare at later moments. Thus they achieve relatively fast responses in long-FP_n trials even after short-FP_{n-1} trials (i.e., in non-repetition trials), which accounts for the asymmetry in the sequential effects (cf. Vallesi & Shallice, 2007; van der Lubbe et al., 2004, for a discussion). This asymmetry, in turn, has the potential to also explain the FP_n effect, although it is as yet unclear to what extent. The assumption of two different processes for explaining the FP_n effect and the asymmetric sequential FP effect is, however, a general disadvantage of the strategic account.

3.1.2. The Conditioning Account of Temporal Preparation in Variable-Foreperiod Designs

Los and co-workers (e.g. Los et al., 2001; Los & Heslenfeld, 2005; Los & van den Heuvel, 2001) have recently challenged the strategic view by proposing a unified and parsimonious account for both effects. They argued that response-related temporal preparation is driven by trace conditioning, a nonstrategic process of trial-to-trial associative learning that determines preparatory behaviour across subsequent trials (see also Gallistel & Gibbon, 2000; Machado, 1997). The conditioning account of temporal preparation maintains that the FP_n and the asymmetric FP_{n-1} effects are two outcomes of one process. Specifically, it is assumed that the asymmetry of the sequential effect drives the FP_n main effect. That is, the $FP_{n-1} \times FP_n$ interaction is considered responsible for the negatively accelerating slope of the FP_n–RT function.

Thus, the asymmetric $FP_{n-1} \times FP_n$ interaction is at the core of the conditioning model, and it is explained as follows: In cases where FP is repeated, fast responses occur, because responding was just previously reinforced at the same imperative moment. In cases where FP alters from long on the preceding trial to short on the current one, slow responses occur, because the imperative moment was just previously bypassed. This bypassing without response is thought to extinguish previous moment–response associations or at least to reduce the strength of their association. Finally, in cases where FP alters from short to long, again fast responses occur, because later imperative moments were not just previously bypassed, and, thus, their response associations were not extinguished or loosened. As a result, responses in trials with the longest FP_ns are predicted to be consistently fast and not subject to sequential effects. In sum, the conditioning account predicts asymmetric sequential FP effects, since a long FP_{n-1} slows RT on a short-FP_n trial but not on a long-FP_n trial. A short FP_{n-1}, however, should not produce any slowing, neither on short- nor on long-FP_n trials. According to this model, the strength of the association between any given imperative moment and a response should increase with increasingly long FP_ns and should be maximal at the latest imperative moment. The strength of this moment–response association is assumed to be directly related to the preparatory state at this moment, which, in turn, is thought to facilitate responding (Los & Heslenfeld, 2005; Van der Lubbe et al., 2004).

3.1.3. Present Study

As mentioned above, mental fatigue from prolonged time on task (TOT) has been shown to impair SRT performance. Previous research, however, mainly focussed on effects of TOT on overall RT performance. To our knowledge, only one study has investigated TOT modulations of FP effects so far: Björklund (1992) reported that RT after long FP_ns increased more over 80 min than did RT after short FP_ns. Unfortunately, he did not analyse sequential FP effects. Here we explored whether TOT-induced mental fatigue affects the complex sequential dependencies within RT patterns, which are typical of temporal preparation in variable-FP designs. Based on the premises (1) that TOT-induced mental fatigue mainly impairs tasks involving top-down attentional control, (2) that the processes underlying temporal preparation according to the strategic view *do* involve top-down attentional control, and (3) that the processes underlying temporal preparation according to the conditioning view *do not* involve top-down attentional control but rather bottom-up learning, we derived the following hypothesis: If the typical RT pattern in variable-FP experiments were mainly based on strategic, top-down attentional processes, it should suffer from mental fatigue, whereas if it were mainly based on trace conditioning, it should remain rather unaffected by fatigue.

Specifically, from a strategic view of temporal preparation (e.g. Näätänen & Merisalo, 1977), one would predict that mental fatigue reduces or even eliminates the FP_n effect and subtly changes the asymmetric sequential FP effect: regarding the FP_n effect, a strategic view would predict that TOT impairs the ability to increase preparation with an increase of the conditional probability of IS occurrence in long-FP_n trials, since this requires an effortful process of conditional probability monitoring during the FP interval (cf. Vallesi & Shallice, 2007, for a recent discussion). As a result, RT in long-FP_n trials would increase, and the typical downward slope of the FP_n–RT function would dwindle or even vanish. This prediction is consistent with the results of Björklund (1992). Analogously, regarding the asymmetry of the sequential FP effect, a strategic view would predict that TOT impairs the maintenance or restoration of a prepared state when imperative moments occur later than expected (in long-FP_n trials following a shorter FP_{n-1}). Further, it can be reasonably assumed that the FP-repetition expectancy does not change with TOT, since expecting a repetition appears to be the rather effortless default option. In sum, TOT-induced fatigue should bereave later imperative moments of their benefit from increased preparation after FP repetitions or maintained/restored preparation after shorter FP_{n-1}s, whereas it should spare the benefits of a short-FP repetition as well as the costs of an earlier-than-expected imperative moment (see Figure 4, Panel C, for an idealized visualization of the predicted outcome pattern). In contrast, from the perspective of the trace-conditioning model (Los et al., 2001; Los & van den Heuvel, 2001), no significant changes in the RT pattern with TOT would be predicted, since the mechanisms assumed to underlie temporal preparation in this model do not involve top-down control processes. Instead, the model is solely based on the associative learning of temporal contingencies between warning signals and imperative stimuli. Accordingly, both the FP_n effect and the asymmetry of the sequential FP effect result from effortless, automatic processes and should not be affected by fatigue (see Figure 4, Panel B, for an idealized visualization of the predicted outcome pattern).

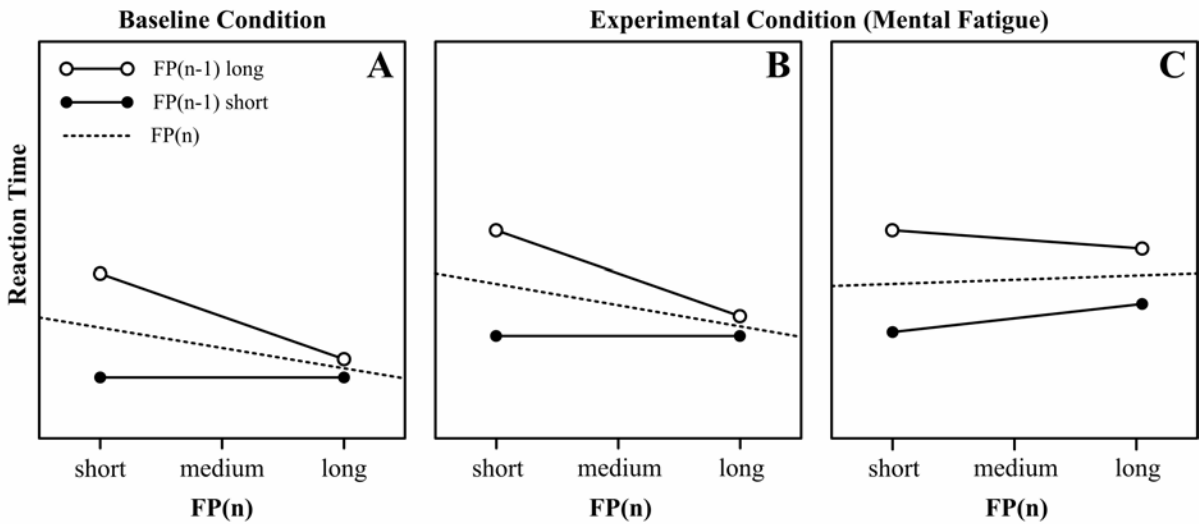

Figure 4. Idealized hypothetical effects of time on task on the pattern of response timing in a simple reaction-time (RT) task with two variable foreperiods (FPs): panel A displays the baseline condition (non-fatigued state) at the beginning of the task; panel B displays the RT pattern at the end of the work period (fatigued state) as predicted from the conditioning view of temporal preparation; panel C displays the RT pattern at the end of the work period (fatigued state) as predicted from the strategic view of temporal preparation (see text for details).

To summarize, we investigated whether or not TOT-induced mental fatigue influences temporal preparation under time uncertainty. We derived two competing predictions based on two different explanations for the RT pattern typically found in variable-FP tasks: The traditional, strategic account, assuming top-down guidance of preparation, would predict a pronounced TOT-related RT increase at late imperative moments (in long-FP_n trials); the conditioning account, assuming bottom-up trial-to-trial learning, would predict no such interaction with TOT. To test these predictions, we conducted an experiment in which a warned SRT task with variable FPs was performed over a time period of about 50 min.

3.2. Method

3.2.1. Participants

Thirty students (24 females and 6 males; mean age = 22.6 years, *SD* = 3.3) took part in the experiment in return for course credits. All participants but one were right-handed and all of them had normal or corrected-to-normal vision.

3.2.2. Apparatus and Stimuli

The experiment was run in a dimly lit and noise-shielded room. It was controlled via a standard personal computer with colour display (19”, 150 Hz refresh rate) and programmed in Matlab (The MathWorks, Inc., Sherborn, MA, USA) using the Psychophysics Toolbox extension (Brainard, 1997). Participants were seated at a distance of about 60 cm in front of the computer screen. A dot (0.5° × 0.5° visual angle) in the middle of the screen served as fixation point and was constantly present throughout the experimental session. A 1000-Hz tone (70 dB SPL), presented binaurally via headphones, served as WS. The letter “X” (1.14° × 0.86° visual angle), displayed in blue (7.1 cd/m^2) at the centre of the screen, served as the IS.

3.2.3. Task and Design

Participants performed a forewarned SRT task and were required to respond as quickly as possible to the IS by pressing the right Shift key with their right index finger. A trial started with the presentation of the WS for 200 ms, followed by a blank FP interval, after which the IS occurred. We used FPs of 1000, 3000 and 5000 ms length, which were randomly chosen with equal probability for each trial. The IS was terminated either by response or when the response interval expired after 2000 ms. Subsequent trials were separated by a constant intertrial interval of 1500 ms. Feedback was given only when the response interval had expired without response; then the German phrase “zu langsam” (“too slow”) was presented for 300 ms. Participants performed 48 practice trials and 600 experimental trials, amounting to about 51 minutes of testing time. Reaction time was computed as the temporal distance between IS onset and response. We used a 3 × 3 × 3 within-subject design with the factors time on task (TOT: first 17 min vs. second 17 min vs. last 17 min), previous FP length (FP_{n-1}: short vs. medium vs. long) and current FP length (FP_n: short vs. medium vs. long), and RT as the main dependent measure.

3.2.4. Self-Report Measures

Two subjective measures of mental fatigue were available from 15 participants: The Short Questionnaire for Current Strain (KAB; Müller & Basler, 1993) was administered before and after the experimental session to assess subjective perceptions of strain and fatigue. This self-report measure comprises eight pairs of adjectives on 6-point Likert-type rating scales describing opposite endpoints of different strain dimensions (e.g., stressed vs. relaxed; languid vs. fresh). Task-induced mental fatigue was assessed by comparing the KAB total scores from before and after the session.

Subjective state was further assessed by means of three scales of the Dundee Stress State Questionnaire–Short Version (DSSQ-S; Matthews et al., 2005; Matthews et al., 2002): Energetic Arousal, Task Engagement, and Distress. The questionnaire consists of 30 items, which assess different facets of mental fatigue on 5-point Likert-type rating scales. The DSSQ-S was administered before and after the session; changes in subjective state were assessed by comparing pre- with post-task scores.

3.3. Results

Responses with an RT between 100 and 1000 ms were considered correct and used for computing mean RT. Responses slower than 1000 ms (0.3 % on average) were considered outliers and discarded from the analysis. Trials with premature responses (button presses between WS and IS or earlier than 100 ms after IS onset) were used to compute the percentage of anticipatory responses. Trials without response within 2000 ms after IS onset were counted as errors of omission. For a more fine-grained description of the overall TOT effect on response speed, we averaged individual mean RT of six successive 8.5-min time bins (containing 100 trials each), yielding the following values: 312, 331, 334, 332, 332 and 337 ms. That is, overall RT slowed over time by 25 ms. Note that the statistical analysis of TOT effects was based on three successive 17-min time bins (containing 200 trials each). Group averages of RT and percentage of anticipatory responses for the three time bins of all experimental conditions are depicted in Figure 5. Additionally, group averages including standard deviation and standard error of mean RT are given in Table 3. Trials with missing responses were extremely rare (0.1 % on average) and were not further analysed.

3.3.1. Standard RT Analysis

Repeated-measures analyses of variance (ANOVAs) were performed on RT and percentage of anticipatory responses. When necessary, the Greenhouse–Geisser correction was used to compensate for violations of sphericity. The ANOVA results are listed in Table 4. As expected, all three factors had significant main effects: RT increased significantly with

TOT [*F*(2, 58) = 8.0, $p = .001$, partial $\eta^2 = 0.22$] and FP_{n-1} length [*F*(2, 58) = 67.1, $p < .001$, partial $\eta^2 = 0.69$]; it decreased significantly with FP_n length [*F*(2, 58) = 15.7, $p < .001$, partial $\eta^2 = 0.35$]. Also, there was the typical asymmetric $FP_{n-1} \times FP_n$ interaction [*F*(4, 116) = 28.7, $p < .001$, partial $\eta^2 = 0.49$], revealing that the increase in RT after a long FP_{n-1} trial was greatest in short FP_n trials. Crucially, there was no interaction of FP_n or $FP_{n-1} \times FP_n$ with TOT (all $F < 1$; see Table 2). There was, however, a significant interaction of FP_{n-1} with TOT [*F*(4,116) = 28.7, $p < .001$, partial $\eta^2 = 0.50$].

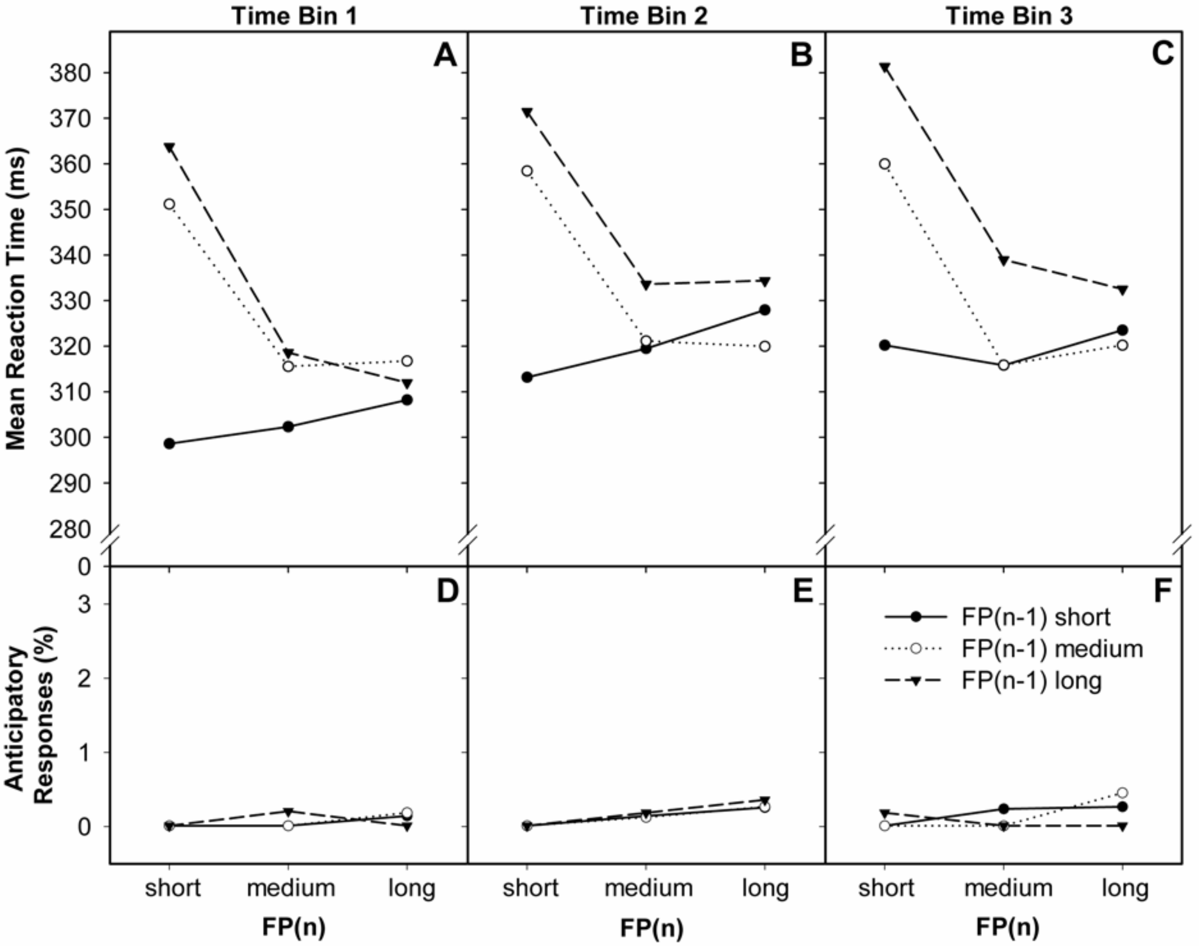

Figure 5. The effects of time on task (TOT), preceding foreperiod length (FP_{n-1}), and current foreperiod length (FP_n) on task performance. The upper panels (A, B, C) display the effects on reaction time (RT); the lower panels (D, E, F) display the effects on the percentage of anticipatory responses. Connecting lines were added for illustrative purposes.

Table 3

Group Averages, Standard Deviations, and Standard Errors of the Mean of Individual Mean Reaction Time (in ms) as a Function of Current Foreperiod Length (FP_n), Previous Foreperiod Length (FP_{n-1}), and Time on Task (Successive 17-min Periods)

	Time Bin 1			Time Bin 2			Time Bin 3		
Foreperiod	*M*	*SD*	*SE*	*M*	*SD*	*SE*	*M*	*SD*	*SE*
Short FP_{n-1}									
Short FP_n	299	56	4.8	313	64	5.1	320	66	6.0
Medium FP_n	302	46	3.8	320	55	4.7	316	50	5.8
Long FP_n	308	47	5.2	328	60	5.3	324	47	6.5
Medium FP_{n-1}									
Short FP_n	351	71	7.5	358	74	6.6	360	64	5.9
Medium FP_n	316	57	4.6	321	49	2.7	316	47	4.4
Long FP_n	317	56	5.0	320	57	4.3	320	66	6.0
Long FP_{n-1}									
Short FP_n	364	70	6.0	371	83	8.1	381	77	8.3
Medium FP_n	319	47	4.0	334	55	3.9	339	47	4.8
Long FP_n	312	52	4.5	334	55	5.1	333	51	4.7

Note. Standard errors of the mean are adjusted for within-subject designs (cf. Cousineau, 2005).

3.3.2. Post-hoc RT Analysis

Simple post-hoc contrasts were computed for significant TOT-related effects. They revealed that the main effect of TOT was mainly driven by a significant RT increase between the first and second time bin [$F(1, 29) = 12.3$, $p = .001$, partial $\eta^2 = 0.30$]; the increase between the second and third time bin was not significant [$F(1, 29) < 1$]. Further, the TOT × FP_{n-1} interaction was shown to be driven by a smaller RT increase between time bins 1 and 2 on trials with a preceding FP of medium length compared to trials with a short preceding FP [$F(1, 29) = 6.1$, $p = .019$, partial $\eta^2 = 0.17$] or with a long preceding FP [$F(1, 29) = 6.2$, $p = .019$, partial $\eta^2 = 0.18$].

Table 4

Results of the Analyses of Variance for Mean Reaction Time and Percentage of Anticipatory Responses

			Reaction Time			Anticipatory Responses		
	Source	*dfs*	*F*	*p*	η^2	*F*	*p*	η^2
1	TOT	2,58	8.0	.001	0.22	0.3	.780	0.01
2	FP_{n-1}	2,58	67.1	.000	0.69	3.7	.045	0.11
3	FP_n	2,58	15.7	.000	0.35	1.0	.383	0.03
4	$TOT \times FP_{n-1}$	4,116	4.1	.009	0.12	1.6	.196	0.05
5	$TOT \times FP_n$	4,116	0.9	.405	0.03	1.7	.176	0.06
6	$FP_{n-1} \times FP_n$	4,116	28.7	.000	0.49	1.2	.331	0.04
7	$TOT \times FP_{n-1} \times FP_n$	8,232	0.4	.818	0.02	1.6	.178	0.05

Note. Effect size: partial η^2; factors: time on task (TOT: Time Bin 1 vs. Time Bin 2 vs. Time Bin 3); previous foreperiod (FP_{n-1}: short vs. medium vs. long); current foreperiod (FP_n: short vs. medium vs. long). Effects of interest are denoted in grey.

3.3.3. Extreme-Group Analysis

To further test whether the non-modulation of the FP_n effect or the $FP_{n-1} \times FP_n$ interaction by TOT is because of an insufficient increase in mental fatigue over time, we repeated the ANOVA but only included the participants with the largest performance decrement. To this end, we did a median split of the sample according to the individual mean RT increase over time (i.e., the difference between mean RT of time bins 1 and 3) and selected the 15 participants above the median. For descriptive comparison, we averaged individual mean RT of six successive 8.5-min time bins, which yielded: 291, 320, 320, 326, 325 and 337 ms. That is, in the subsample of strong decrementers, overall RT became slower over time by 46 ms. As expected, the ANOVA yielded significant main effects of TOT [$F(2, 28) = 13.7$, $p < .001$, partial $\eta^2 = 0.49$], FP_n [$F(2, 28) = 5.7$, $p = .026$, partial $\eta^2 = 0.29$] and FP_{n-1} [$F(2, 28) = 38.2$, $p < .001$, partial $\eta^2 = 0.73$] as well as the typical $FP_{n-1} \times FP_n$ interaction [$F(2, 28) = 14.0$, $p < .001$, partial $\eta^2 = 0.50$]. However, the analysis revealed no effect of TOT on FP_n, FP_{n-1} or $FP_{n-1} \times FP_n$ (all $F < 1.1$). Thus, the previously found TOT × FP_{n-1} interaction did not show in the subsample (partial $\eta^2 = 0.07$). The results are depicted in Figure 6, which provides additional visual evidence that there is absolutely no TOT effect on the latest imperative moment, as would be predicted from the strategic account of temporal preparation.

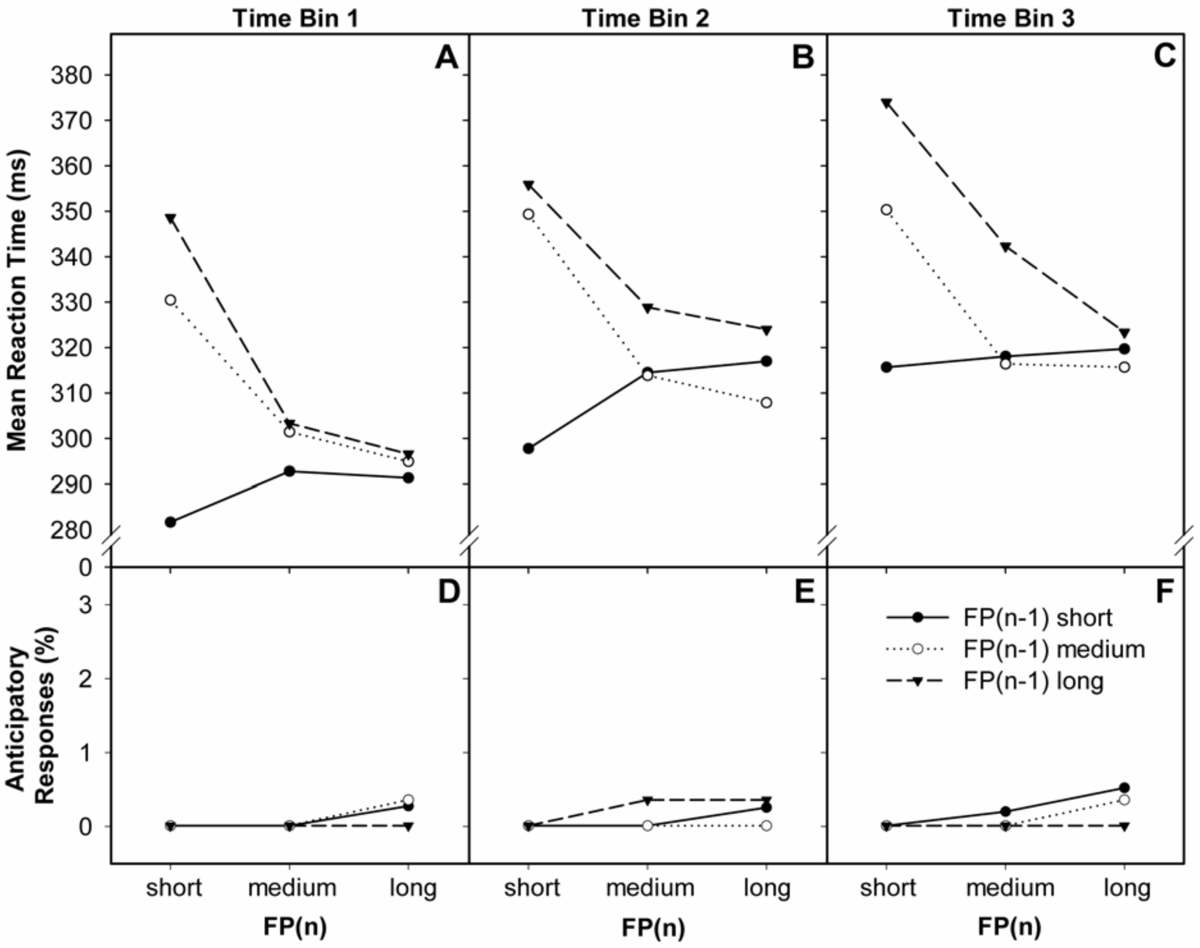

Figure 6. Separate results for the 15 participants with the largest overall performance decrement. Effects of time on task (TOT), preceding foreperiod length (FP_{n-1}), and current foreperiod length (FP_n) on task performance, The upper panels (A, B, C) display the effects on reaction time (RT); the lower panels (D, E, F) display the effects on the percentage of anticipatory responses. Connecting lines were added for illustrative purposes.

3.3.4. *Analysis of Anticipatory Responses*

Premature button-presses were generally rare and therefore arcsine-transformed before submitting them to an ANOVA. The only significant effect was an increase in the percentage of anticipatory responses with increasing length of FP_{n-1} [$F(2, 58) = 3.7$, $p = .045$, partial $\eta^2 = 0.11$]. Notably, the analysis did not yield any significant interactions with TOT (all $F < 1.8$; see Table 4 for details).

3.3.5. Subjective Measures

The questionnaire pre- and post-task scores were compared by means of paired *t*-tests. The KAB score after the session (*M* = 26.3, *SD* = 6.1) was significantly higher than before the session (*M* = 20.5, *SD* = 7.1) [*t*(14) = -4.4, *p* = .001]. The analysis of the three DSSQ-S scale scores revealed that energetic arousal decreased significantly [*t*(14) = 3.4, *p* = .004] from pre-task (*M* = 6.1, *SD* = 3.2) to post-task (*M* = 2.9, *SD* = 2.6). Further, there was a significant decrease [*t*(14) = 4.1, *p* = .001] in task engagement (pre-task: *M* = 19.6, *SD* = 6.2; post-task: *M* = 11.9, *SD* = 5.5) and a significant increase [*t*(14) = -4.2, *p* = .001] in distress (pre-task: *M* = 9.0, *SD* = 3.5; post-task: *M* = 13.9, *SD* = 4.5).

3.4. Discussion

Our study investigated whether mental fatigue from prolonged work affects temporal preparation under time uncertainty in a SRT task. To this end, we examined potential interactions of TOT with the effects of the current and previous FPs on RT, using a variable-FP paradigm with three equiprobable FPs of 1000, 3000 and 5000 ms. The significant changes in subjective-state measures indicate that our TOT manipulation was successful in producing mental fatigue. The increase in the KAB score demonstrates that the cognitively little demanding SRT task elicited perceived strain over the course of the session. This corresponds to the results of a previous study, which revealed higher levels of subjective strain after performing a monotonous low-demand condition of a simulated driving task compared to a high-demand racing condition (Fischer et al., 2008). Our DSSQ-S findings match those of previous studies assessing subjective-state changes during vigilance tasks using the long version of the DSSQ (Helton & Warm, 2008; Temple et al., 2000). Participants reported feeling less energetic after the session than before its start; similarly, task engagement was perceived to be higher before the session than at its end. Decreasing energetic arousal and decreasing task engagement indicate mental fatigue or resource depletion. The elevation of distress is consistent with studies demonstrating that participants perceive long-duration monotonous RT tasks as stressful (Hancock & Warm, 1989; Szalma et al., 2004).

As expected, we found a significant slowing of mean RT over the course of 51 min of task performance. There were, however, no specific effects of TOT on indices of temporal preparation: neither the effect of FP_n nor the asymmetrical $FP_{n-1} \times FP_n$ interaction was modulated by TOT. It should be noted that the non-significance of the TOT × FP_n and TOT × $FP_{n-1} \times FP_n$ interactions can hardly be explained by a lack of statistical power, since their effect sizes were very small (partial η^2 = 0.03 and 0.02, respectively). Fig. 2 confirms visually that the RT pattern remained about the same over time. An extreme-group analysis, which included only the 15 participants with the largest TOT decrement, also did not demonstrate any modulation of FP effects by TOT (cf. Fig. 3). Also, the TOT × FP_{n-1} interaction found for the whole sample was not present in the subsample of TOT decrementers, which suggests that this effect was not due to an increase in mental fatigue. This reasoning is supported by the fact that in decrementers a larger RT increase over time corresponded to a reduction of this interaction's effect size (whole sample: partial η^2 = 0.12; decrementers: partial η^2 = 0.07).

3.4.1. Mental Fatigue Affects Overall Processing Speed but Not Temporal Preparation

The significant overall RT slowing with TOT replicates previous results (Björklund, 1992; Lisper et al., 1973, 1977) and provides further evidence for the impact of energetic variables on performance efficiency in elementary cognitive tasks. A shift of the speed–accuracy trade-off towards a stricter criterion can be excluded as an explanation, since no concomitant decrease in the number of errors (anticipatory responses or errors of omission) was observed. If anything, the number of anticipatory responses tended to increase over time (cf. Figure 5). Previous research supports the notion that mental fatigue may be a major cause for this performance deterioration (e.g. Boksem et al., 2005; Smit et al., 2004; R. A. Wright et al., 2008), but a decrease in arousal may also play a role, especially in highly repetitive, monotonous situations like SRT tasks (Dirnberger, Duregger, Lindinger & Lang, 2004). Although the effect of TOT on overall RT was modest (i.e., on average ca. 25 ms RT increase across six 8.5-min time bins), our study is one of the first to report a clear-cut performance decrement in a variable-FP experiment.

We suggest that the use of a WS may have contributed to the rather small decrement with TOT, since a WS may somewhat counteract the time-related performance decline typically found in unwarned SRT tasks (cf. Lisper & Ericsson, 1973; Sanders et al., 1982). This assumption is supported by earlier studies using a paired-stimulus paradigm (Lisper et al., 1973, 1977), which reported a smaller time-related RT increase to the second (and therefore forewarned) stimulus than to the first one of a pair. Lisper et al. (1973) suggested that different rates of habituation to the two stimuli of a pair were responsible for their differential RT increase, but other explanations are possible as well: For instance, the individuals might get some relief from short relaxation pauses that are possible during the intertrial interval, that is, the time between response and next WS (cf. Wilkinson, 1990). Also, the WS provides additional stimulation that might be beneficial for maintaining arousal in monotonous tasks (Hackley et al., 2009). In addition, the WS event might act as a memory cue that reactivates the task goal (Steinborn, Rolke et al., 2009).

In contrast to the overall slowing, temporal preparation (i.e. the effects of FP_n or the asymmetrical $FP_n \times FP_{n-1}$ interaction) was not modulated by TOT. Thus, according to our reasoning that only processes relying on top-down control should be affected by mental fatigue (see Introduction), the purely additive effect of TOT on performance speed is more consistent with the view that temporal preparation under time uncertainty results from a bottom-up trace-conditioning process rather than from top-down-guided conditional probability monitoring and voluntary temporal (re)orienting. From the perspective of the strategic account of temporal preparation, RT would be expected to especially increase at late critical moments during the session. Obviously, this was by no means the case in this study. According to the trace-conditioning view, FP effects result from trial-to-trial reinforcement or extinction of moment–response associations. This learning process generates (and continuously updates) representations of temporal contingencies between WS and IS and its associated response. We consider this forming of representations an automatic, effortless process that does not suffer from a decline of top-down attentional control processes due to TOT-induced mental fatigue.

As mentioned in the introduction, there is one earlier study (Björklund, 1992) that reported an interaction between the effects of FP and TOT. This seemingly contradictory finding might be related to differences in the FP distribution: Björklund used five different FPs (500, 889, 1581, 2812, and 5000 ms). That is, a higher number of different FPs with a wider range was used, and FPs were spaced logarithmically rather than symmetrically. All these factors might have contributed to Björklund’s finding the typical FP effect on RT only for the shorter FPs, which may be due to a relatively less precise time estimation at remote critical moments. This, in turn, might have rendered Björklund’s FP distribution sensitive to TOT in that the already compromised time estimation at late critical moments became even more impaired by fatigue than that at early critical moments. Also, unlike in our study, Björklund used a double-response paradigm to measure movement time between two button presses. This more complex motor response probably evokes more preparatory activity, which might have somehow interacted with temporal factors and mental fatigue.

3.4.2. Sources of the Time-Related Response Slowing in SRT Tasks

One question remains to be answered: What processes in SRT performance are slowed by mental fatigue? Although temporal preparation is an integral part of any SRT task, there must be distinct subprocesses other than the ones subserving timing aspects that are sensitive to mental fatigue. According to our rationale, it should be processes relying on top-down control. Hence, the additive RT increase over time could be interpreted as less efficient information processing that results from a reduced allocation of attentional resources to task-relevant cognitive processes. Effortful top-down control is needed to "stay on the job," that is, to maintain attention to the task over time, enabling the efficient processing of task-relevant information (Sarter et al., 2006; Stuss et al., 2005). Recent models of controlled attention argue that it is the cognitively little demanding tasks (in contrast to more demanding, intrinsically interesting ones) that most require the active control of attention when their performance needs to be sustained over prolonged time. These models have been successfully applied to explain the high vulnerability of simple, monotonous tasks to fatigue from sleep deprivation (Pilcher, Band, Odle-Dusseau & Muth, 2007; Walker et al., 2009). This might similarly apply to the effects of fatigue from prolonged mental work.

Mental fatigue may affect all stages of information processing that receive modulatory top-down input, from stimulus processing to response execution. Of course, this study cannot determine the exact locus (or loci) of fatigue effects within a stage model of information processing, since this would require additional manipulations. Efficient SRT performance has been shown to involve top-down control to facilitate stimulus detection and to specify and prepare the response in advance (Frith & Done, 1986; Goodrich et al., 1989; Henderson & Dittrich, 1998). It is these top-down modulations that potentially are vulnerable to mental fatigue. This notion is supported by studies that examined the effects of mental fatigue on preparatory processes in different cognitive tasks. Boksem et al. (2006) reported a TOT-induced decrease in the amplitude of the contingent negative variation, which is a slow cortical potential that globally reflects preparatory activity. Lorist (2008) showed that the facilitation of performance by response-related advance information diminished with increasing mental fatigue. We interpret these and our findings as indicating that it was not the timing under temporal uncertainty produced by variable FPs but rather the efficiency of processing stimulus information and initiating the motor response that was affected by mental fatigue.

To be quite explicit, we propose a dissociation between nonspecific temporal preparation and specific, attentionally guided perceptual and motor aspects of preparation, the temporal aspect being insensitive, the attentional aspect being sensitive, to mental fatigue. Such a dissociation has been suggested before regarding choice RT performance (e.g. Brown & Robbins, 1991; Holender & Bertelson, 1975). A crucial question for future research concerns how both nonspecific and specific aspects of preparation combine to produce efficient processing at the imperative moment. We conjecture that the representational strength of different moment–response associations, as determined by previous experiences, forms a kind of temporal salience map that is unintentionally used to time the allocation of attentional resources to task-specific perceptual and motor processes. This idea is akin to the concept of exogenous temporal expectations (cf. Coull & Nobre, 2008).

3.4.3. Limitations of the Study

A limitation of our study concerns the modest effect of TOT, which might not have been powerful enough to modify FP effects. This argument implies that top-down control processes potentially involved in temporal preparation might be less affected by fatigue than those processes that led to the observed decrement. This possibility cannot be completely ruled out. It is, however, made implausible by the results of the extreme-group analysis which showed that there was no modulation of the RT pattern (especially at the latest imperative moment), even when the effect of TOT on overall RT was almost twice as large. Future studies should test whether stronger fatigue-related decrements (e.g., with longer or attentionally more demanding tasks) produce different results. Furthermore, settings that encourage top-down strategies in temporal preparation (e.g., the use of explicit temporal cues or non-uniform, peaked FP distributions) may be used to contrast the sensitivity to mental fatigue of different mechanisms potentially contributing to temporal preparation.

Apart from the power issue, it cannot be excluded completely that an interaction between fatigue and temporal preparation was absent only because it was masked by either of two well-known factors opposing the effects of time-related performance decrements: practice and compensatory effort. Practice-related masking effects are unlikely, since SRT tasks have been found insensitive to repeated administration, which is why they are a favourite tool to assess alertness/fatigue in neuropsychology (Sturm & Willmes, 2001) as well as in chronobiological (Blatter & Cajochen, 2007) and sleep-deprivation (Lim & Dinges, 2008) research. Also, any practice effects that selectively affect temporal preparation would imply that, over time, a preparation-related strategy shift occurs from controlled to automatic processing, i.e. from intentional, repreparation-based to nonintentional, conditioning-based timing behaviour. This may not be impossible but it is improbable, since the main effect of both strategies cannot necessarily be assumed to be equal, which it is. A similar reasoning applies to potentially counteracting effects of compensatory effort: it seems highly unlikely that a time-related increase in effort exertion would selectively affect the timing of preparatory behaviour, thereby masking fatigue effects only on indices of temporal preparation but not overall RT. Nevertheless, we would like to emphasize that our study was not undertaken to unequivocally “decide” between alternative accounts of temporal preparation phenomena. Rather, it was done to contribute a further piece of evidence and to broaden the basis for a future evaluation of these phenomena.

Finally, another limitation is the availability of subjective-state measures for only half the sample. For the other half, the subjectively perceived effectiveness of our TOT manipulation in producing mental fatigue can only be assumed. Since all participants were sampled from the same population, this assumption may be warranted.

3.4.4. Conclusions

In sum, we observed that TOT-induced mental fatigue did not influence the pattern of response timing in a variable-FP paradigm. Based on our assumption that mental fatigue primarily impairs cognitive processes relying on top-down control, we infer that temporal preparation under time uncertainty is primarily guided by bottom-up processes such as trace conditioning. This provides further support for the conditioning account of temporal preparation (Los et al., 2001; Los & van den Heuvel, 2001), generalizing the body of evidence to a manipulation of TOT. Future studies should test whether this interpretation holds true for manipulations of other energetic variables such as sleep deprivation and circadian rhythms. By analysing intertrial sequential effects, we extend previous research on TOT-induced mental fatigue, which often only considered effects on overall RT performance. In general, the examination of sequential effects may provide a means to gain additional insights into how mental fatigue affects different cognitive processes underlying human performance.

4. STUDY 3

A SUPRAMODAL BRAIN NETWORK FOR THE CONTROL OF ALERTNESS

(Co-authored with T. Kellermann, S. B. Eickhoff, F. Boers, A. Chatterjee, K. Willmes and W. Sturm)

4.1. Introduction

Attention is a mental function that uses modulatory top-down signals to selectively prioritize information processing. An important dimension of attention, apart from its selectivity, is its intensity, i.e. the strength of its modulatory influence (Spitzer, Desimone & Moran, 1988). Here we investigated brain systems that control attentional intensity in situations that put little demand on attentional selectivity but still require high levels of attentiveness. In keeping with several taxonomies of attentional functions, we refer to this nonselective attentiveness as "alertness" (cf., e.g., Posner & Boies 1971; Raz & Buhle 2006; Sturm & Willmes, 2001). Alertness has been defined as responsiveness to external stimulation (Posner & Boies, 1971; Thiel & Fink, 2007). Short-term ("phasic") increases in alertness after warning cues have been differentiated from "intrinsic" alerting, which refers to the voluntary (endogenous) control of response readiness over seconds to minutes without the help of cues (Sturm et al., 1999; Sturm & Willmes, 2001). As such, intrinsic alertness is the most basic form of sustaining attention. The level of alertness is usually assessed with simple stimulus-detection tasks that require an unchanging, speeded response to stimuli that occur at unpredictable times.

Which mechanisms contribute to a self-generated, sustained state of maximal readiness in such SRT tasks? First, in these tasks, all perceptual and motor processes can be prepared before stimulus onset, since there is no uncertainty about the stimuli and the response they require (Jennings & van der Molen, 2005; Requin et al., 1991). For sustained readiness, maintaining (or repeatedly reactivating) this task-specific preparatory set over time is essential. This includes maintaining the relevant stimulus–response mapping, sustained sensory anticipation, and maintaining a balance between motor preparation and inhibition to avoid premature responding. Second, response speed in SRT tasks with variable interstimulus intervals benefits from building implicit temporal expectations based on the temporal structure of previous stimuli (Coull & Nobre, 2008; Langner et al., in press). Finally, preparation for speeded action is assumed to include the regulation of arousal, which determines the general responsiveness of the brain and "energizes" cognitive processes (Pfaff, 2006; Sturm et al., 1999; Stuss, 2006). The optimal interplay of these processes should result in maximal response readiness (i.e. high alertness).

Studies in patients suffering from brain damage revealed a dominant role of the right hemisphere (RH) in the control of alertness. For instance, Howes and Boller (1975), Ladavas

(1987), as well as Posner, Inhoff, Friedrich and Cohen (1987) reported a substantial increase in simple visual and auditory RT following RH lesions. However, when testing phasic alerting with *forewarned* SRT tasks, RH patients showed much smaller performance deficits (Posner et al., 1987; Tartaglione, Bino, Manzino, Spadavecchia & Favale, 1986). This suggests that RH lesions mainly impair the control of intrinsic, and not phasic, alertness.

The number of brain imaging studies on alertness is rather limited, but their results point to a comparable differentiation between brain mechanisms underlying warning-cue-induced (phasic) versus self-regulated (intrinsic) alertness. For instance, Sturm and colleagues (Sturm et al., 1999, 2004) found in two studies with positron emission tomography (PET) a predominantly RH network subserving *intrinsic* alertness. The network included right anterior cingulate cortex (ACC), right dorsolateral prefrontal cortex, right inferior parietal lobule as well as thalamic and brainstem structures (possibly including the locus coeruleus) for both visual and auditory intrinsic alertness tasks. In contrast, studies on *phasic* alerting revealed (additional) left-hemisphere activity: Using functional magnetic resonance imaging (fMRI), Sturm and Willmes (2001) reported right and additional left frontal and parietal activations in forewarned auditory detection tasks. Bilateral activity was also reported in other fMRI studies on phasic alerting (Fan, McCandliss, Fossella, Flombaum & Posner, 2005; Konrad et al., 2005; Thiel & Fink, 2007; Thiel, Zilles & Fink, 2004). Mainly left-sided activity related to phasic alerting was found in anterior insula, dorsal premotor cortex, and superior and inferior parietal cortex in a study by Coull, Nobre and Frith (2001).

Left-hemisphere activity related to phasic alerting has been explained by increased demands on selective attention arising from the need to distinguish warning stimuli from imperative ones (cf. Sturm & Willmes, 2001). Recently, Jaffard, Benraiss, Longcamp, Velay and Boulinguez (2007) pointed to another confound inherent to phasic-alertness studies that present cued and uncued trials in the typical randomly mixed fashion (see, e.g., Fan et al., 2005; Thiel & Fink, 2007; but see Sturm & Willmes, 2001, for a non-mixed approach): According to Jaffard and coworkers, this mixing leads to sustained proactive inhibition to prevent erroneous responding to cues, which is only briefly released after the imperative stimulus has been identified. The authors showed that this process modulates responses to both cued and uncued imperative stimuli. They argued convincingly that relative RT improvements in cued trials, which are usually attributed to performance gains from alerting, should rather be attributed to inhibition-related performance losses in uncued trials. Therefore, results from studies on phasic alerting using composites of randomly intermixed cued and uncued stimuli may be of limited use for answering questions related to the neural basis of the control of self-generated (i.e. intrinsic) alertness.

The modality independence of brain activity related to intrinsic alertness has not been tested systematically yet. To our knowledge, there is only one study (Kinomura et al., 1996) that tested intrinsic alerting with stimuli of different modalities (visual and tactile) in the same participants. This pioneering study had some limitations, though: first, alertness and sensorimotor-control tasks were performed by two different and rather small samples (n = 9 each); second and more importantly, the study focused on subcortical areas only; no cortical activity was reported.

To our knowledge, there is only one other imaging study that investigated the modality specificity of alertness-related brain activity (Thiel & Fink, 2007). The authors, however, focused on phasic alertness: they contrasted cued with uncued trials of SRT tasks with visual or auditory stimuli and found the only modality-independent activity in the posterior part of the right superior temporal gyrus. The relevance of this finding for defining a supramodal network that controls *intrinsic* alertness is at least debatable, since it is still unclear to what degree short-term, externally triggered increases in alertness can be likened to longer-term, self-generated alertness maintenance. Also, according to Jaffard et al.'s (2007) reasoning (see above), in tasks with randomly mixed cued and uncued trials as used by Thiel and Fink, brain activity related to uncued trials is affected by the sheer presence of unpredictably interspersed cued trials. This difference to standard intrinsic-alertness tasks complicates comparisons.

In conclusion, the question as to the modality independence of brain activity subserving alertness still has to be considered open. Our study aimed to test this modality independence using auditory, tactile, and visual stimuli in simple, uncued RT tasks performed by the same participants. Additionally, we were interested in the effects of increased monitoring demands, which were manipulated by introducing a condition in which the modality of the upcoming stimulus was unpredictable.

4.2. Method

4.2.1. Participants

Twenty (9 female) healthy, right-handed university students (mean age = 24.0 years, *SD* = 3.5) were recruited via advertisements on campus and were paid for their participation in the experiment. The study was approved by the Ethics Committee of the RWTH Aachen University Hospital. All participants gave written informed consent before entering the study.

4.2.2. Tasks and Procedure

The experiment was run on a standard IBM-compatible computer using the software Presentation 10.0 (Neurobehavioral Systems, Inc., www.neurobs.com). The experiment comprised four experimental (auditory, tactile, visual, and mixed) and three sensorimotor control (auditory, tactile, and visual) conditions. In all experimental conditions, the task was to respond as fast as possible to the imperative stimulus by a button press with the right-hand index finger. All imperative stimuli were bilaterally presented for 500 ms with a frequency of 10 Hz (five 50-ms-on/50-ms-off cycles each). In the auditory condition, the imperative stimulus was a 1000-Hz sine tone (70 dB), presented binaurally via noise-shielded, MRI-compatible headphones. The tactile imperative stimulus was generated by the 1-mm extension of eight blunt plastic rods (each generating a force of about 5 mN) from two MRI-compatible Braille stimulators strapped to the inner side of each ring finger's upper phalanx. The visual imperative stimulus consisted of two white squares (5.7° visual angle each) to the left and right of a central fixation cross, presented via MRI-compatible goggles. In the mixed condition, stimuli of all three modalities were presented in an unpredictably mixed way. The interstimulus intervals in all experimental conditions varied randomly between 1350 and 5100 ms (mean = 2785 ms), sampled from an exponential distribution.

In the three sensorimotor control conditions (auditory, tactile, and visual), the same stimuli were used but were presented continuously throughout. Participants were instructed to perceive the stimulation passively and press the response button with their right index finger approximately every 2 s in a self-paced manner (cf. Sturm et al., 2004). This was done to capture the purely sensory and motor aspects of the experimental conditions. The continuous high-rate stimulation was necessary to prevent participants from synchronizing their button presses with the stimuli, which would have rendered this task another alertness task (cf. Sturm et al., 1999). The button-press rate of about 0.5 Hz was chosen to approximately match the response rate during the experimental tasks and to induce some automaticity in responding, thereby minimizing alertness demand.

All conditions were presented in separate sessions, each consisting of six 20-s task blocks and seven 20-s resting-baseline blocks. Each experimental task block contained seven imperative stimuli. Throughout all task blocks, a central fixation cross was presented; its disappearance indicated the beginning of a baseline block. Toward the end of each baseline block (between 1500 and 3500 ms before task-block onset), an auditory 2000-Hz sine tone was presented as a warning signal indicating the imminent beginning of the next task block. This was done to help participants relax their alertness during the resting blocks. Before each session, the type of condition was announced by the experimenter. Condition order was chosen at random for each participant. Prior to the experiment, participants were given 10 practice trials of each experimental condition.

4.2.3. fMRI Data Acquisition

Brain imaging data were obtained with a 3-T MRI scanner (Philips Achieva, Philips Medical Systems, Best, The Netherlands) with a SENSE head coil. Participants lay supine in the scanner, and their heads were immobilized with cushions to minimize movements. A T1-weighted structural image was used for anatomical reference (TE = 2.3 ms, TR = 506 ms, flip angle = 80º, matrix size = 240 × 240, 32 sagittal slices, voxel size = 0.94 × 1.17 × 4 mm^3, 1 mm gap between slices). Blood oxygenation level-dependent (BOLD) signals were acquired using echo-planar imaging (EPI) covering the whole brain in 28 transverse slices parallel to the AC/PC line (TE = 32 ms, TR = 2.0 s, flip angle = 80º, SENSE factor = 1.3, matrix size = 64 × 74, field of view = 192 × 228 mm^2, voxel size = 3 × 3 × 3.6 mm^3, 0.8 mm gap between slices, interleaved slice acquisition). During each run, 133 volumes were acquired, preceded by seven dummy scans.

4.2.4. fMRI Data Analysis

Data were analyzed with the SPM5 software package (Wellcome Department of Imaging Neuroscience, London) implemented in Matlab 7.2 (The MathWorks, Inc., Sherborn, MA, USA). After discarding the dummy scans, all images were realigned to the mean image of the first run to correct for movement artifacts. Spatial normalization into standard stereotaxic anatomical MNI space was achieved by applying the unifiedsegmentation procedure of SPM5 to the mean EPI of all runs using the segmented structural SPM5 template image as tissue probability map and then applying the normalization parameters to all EPIs (resliced voxel size: 2 × 2 × 2 mm^3). The normalized EPI data were smoothed with an isotropic Gaussian filter of 8 mm to accommodate interindividual variation in brain anatomy.

The statistical analysis of the data was done according to a block-design approach: The expected hemodynamic response for each block was modeled by a canonical hemodynamic response function (HRF; Friston et al. 1998). This function was convolved with block onsets and durations to create predictors in a general linear model. We also modeled the parametric modulation of task-related hemodynamic activity by mean-centered reaction time (mean RT of each experimental block). In order to reduce residual variance in the time series (induced, e.g., by head movements), a dispersion measure of each volume from the respective mean of the time series was entered as covariate of no interest (see Stöcker et al., 2005, for details). After correction of the time series for dependent observations according to an autoregressive first-order correlation structure, parameter estimates of the HRF regressors were calculated from the least-mean-squares fit of the model to the time series. Group analysis was done by entering parameter estimates of all 11 regressors of interest (four experimental task conditions and their parametric modulations plus three sensorimotor control conditions) into a random-effects repeated-measurement analysis of variance (ANOVA). Alertness-related activity was analyzed by contrasting activity in experimental task conditions with activity in sensorimotor control conditions. Activity differences were considered significant when surviving a single-voxel threshold of $p < .001$ and a cluster-level threshold of $p < .05$, family-wise error (FWE) corrected for multiple comparisons across the whole brain.

4.3. Results

4.3.1. Behavioral Data

Mean reaction time (standard deviation) was 272 (49) ms in the auditory condition, 274 (45) ms in the visual condition, 240 (46) ms in the tactile condition, and 313 (52) ms in the mixed condition. A repeated-measures ANOVA yielded a significant effect of condition on mean RT [$F(3, 57) = 30.6$, $p < .001$]. Simple contrasts revealed that this effect was driven by both significantly faster responses to tactile stimuli than to auditory ones [$F(1, 19) = 19.6$, $p <$

.001] and significantly slower responses in the mixed condition than in the visual one [*F*(1, 19) = 18.8, $p < .001$]. The RT values lie in the typical range of SRT tasks, confirming that our participants responded as instructed. Also, the longer RT in the mixed condition attests to the higher processing load imposed by monitoring three sensory input channels simultaneously.

4.3.2. Imaging Data

Baseline contrast. To examine general task-induced activity, we contrasted the main effect across all three unimodal experimental conditions against resting-baseline activity (see Table A1 and Figure A1 in Appendices A and C). Results were filtered to ensure that voxels were included only if their activation during each of the three unimodal conditions was stronger than during baseline. Significant task-related activity was found in the left pre- and postcentral gyri, posterior motor cingulate cortex (rostral BA 23), middle and posterior insula, putamen, and pallidum. Bilateral activity was found in anterior motor cingulate cortex [caudal Brodmann area (BA) 24], dorsal premotor cortex (dPMC), supplementary motor cortex (SMA; BA 6), anterior insula, inferior parietal lobule, supramarginal gyrus, temporo-parietal junction, posterior superior temporal gyrus, middle and inferior occipital cortex, thalamus, midbrain (in the vicinity of substantia nigra and red nucleus), pons (in the vicinity of locus coeruleus, reticular formation and ventral pontine nuclei), and medial cerebellum (vermis and intermediate hemispheres). Right-sided activity was found in inferior frontal cortex, pre-SMA, posterior middle temporal gyrus, and anterior cerebellar lobe.

Relative contrasts. To identify supramodal alertness-related activity, the main effect across all three unimodal experimental conditions was contrasted against the main effect across all three sensorimotor control conditions, applying a filter to retain only voxels whose activation during each single experimental task was stronger than during both baseline and their respective sensorimotor control task. Results are presented in Table 5 and Figure 7. The analysis revealed significant right-sided activity in the SMA, pre-SMA, dPMC, anterior cingulate cortex (ACC), inferior frontal cortex (pars opercularis and pars triangularis), anterior insula, and temporo-parietal junction. Further significant alertness-related activity was found in bilateral rostral motor cingulate areas and left medial cerebellum. The cerebellar cluster extended into the brainstem (pontine reticular formation). Finally, a subcortical cluster comprised activity in bilateral rostrodorsal pons (possibly locus coeruleus) and midbrain (vicinity of nucleus ruber, ventral tegmental area, and substantia nigra).

Table 5

Supramodal Alertness-Related Brain Activity

Cluster/Area	x, y, z	z-score
Cerebellum/pons (k = 772, p < .001)		
L cerebellar vermis	-6 -48 -24	5.84
R dorsal pons (reticular formation)	14 -34 -32	4.34
L cerebellar intermediate hemisphere	-18 -50 -24	4.21
R medial pons (reticular formation)	6 -22 -34	3.86
Medial frontal/cingulate cortex (k = 706, p < .001)		
R supplementary motor area (BA 6)	8 18 50	4.60
R anterior cingulate cortex	4 38 24	4.01
L middle cingulate cortex	-2 6 34	3.84
R pre-supplementary motor area (BA 8)	10 32 46	3.82
R middle cingulate cortex	6 -6 34	3.62
L middle cingulate cortex	-6 16 32	3.44
L anterior cingulate cortex	-1 24 30	3.40
Temporo-parietal junction (k = 593, p < .001)		
R inferior parietal cortex	50 -50 22	4.11
R superior temporal gyrus	50 -46 14	3.73
R superior temporal gyrus	56 -42 12	3.43
Precentral gyrus (k = 204, p = .024)		
R dorsal premotor cortex (BA 6)	36 -4 46	4.45
Inferior frontal/insular cortex (k = 189, p = .031)		
R inferior frontal gyrus (pars triangularis)	42 22 4	4.15
R anterior insula	39 24 0	3.70
Midbrain/brainstem (k = 179, p = .038)		
R substantia nigra	16 -14 -10	3.85
R nucleus ruber	10 -18 -12	3.74
R rostrodorsal pons (locus coeruleus)	2 -28 -18	3.71
L rostrodorsal pons (locus coeruleus)	-4 -26 -18	3.46
L nucleus ruber	-6 -20 -12	3.37
L ventral tegmental area	-4 -16 -14	3.30

Note. L = left; R = right; BA = Brodmann area. Coordinates x, y, z refer to MNI space; k = number of voxels in cluster; p-value represents cluster-level error probability corrected for multiple comparisons.

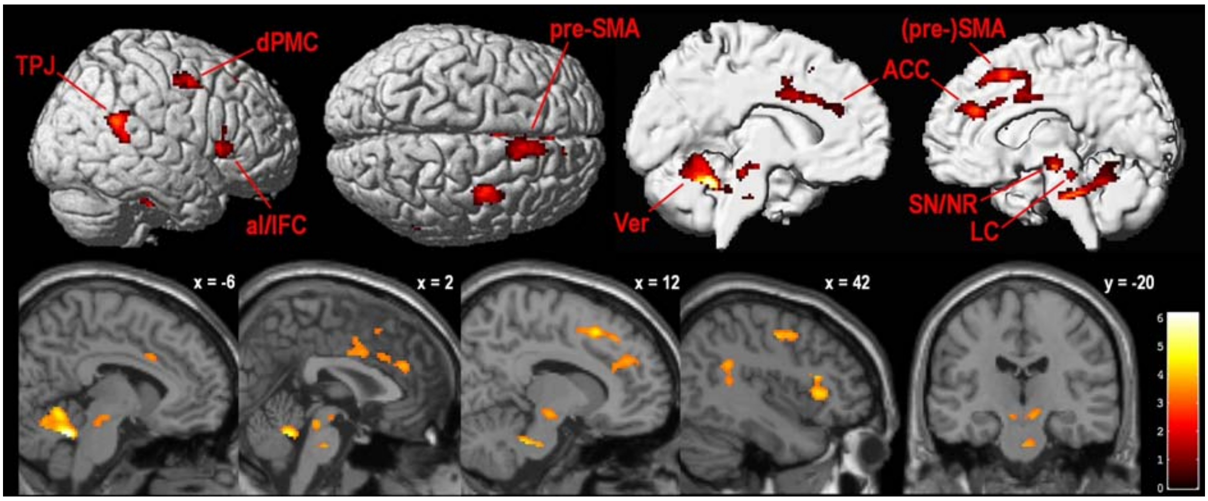

Figure 7. Supramodal alertness-related brain activity (averaged unimodal alertness conditions vs. averaged control conditions, masked to include only voxels that show stronger activity during each unimodal experimental condition than resting baseline as well as during each unimodal experimental condition and its respective control condition). TPJ = temporo-parietal junction; dPMC = dorsal premotor cortex; aI/IFC = anterior insula/inferior frontal cortex; pre-SMA = pre-supplementary motor area; Ver = cerebellar vermis; ACC = anterior cingulate cortex; SN/NR = substantia nigra/nucleus ruber; LC = locus coeruleus. Parasagittal slices show activity overlaid over the SPM5 single-subject template brain; coordinates refer to MNI space; color codes t-values; voxel-wise $p < .001$ & FWE-corrected cluster-level $p < .05$.

Modality-specific alertness-related activity was analyzed by calculating balanced contrasts between one unimodal task condition and the other two conditions. These contrasts were masked to include only voxels that showed stronger activity during the experimental task condition than during both baseline and their respective sensorimotor control condition. The results of these analyses are reported in Figure 8 and Table 6. Generally, modality-specific activity was found only in areas specialized in processing signals of a given sensory modality: Contrasting auditory with somatosensory and visual alertness revealed stronger bilateral activity in posterior aspects of the superior and middle temporal gyri (BAs 41, 42 and 22; see Figure 8*A*). These areas correspond to primary and secondary auditory cortices. Comparing somatosensory with auditory and visual alertness revealed stronger bilateral activity in the postcentral gyrus (BAs 1 and 2), parietal operculum, and supramarginal gyrus, with activity being more pronounced in the right hemisphere (see Figure 8*B*). These regions correspond to primary (S1), secondary (S2) and higher-order somatosensory cortices. Finally, contrasting visual with auditory and somatosensory alertness revealed stronger bilateral activity in superior, middle, and inferior occipital gyri, fusiform gyrus, caudal superior and inferior parietal lobules, and inferior temporal gyrus (see Figure 8*C*). Additionally, activity was found in right cuneus (BAs 18 and 19) and lingual gyrus. These regions correspond to secondary and higher-order visual association areas of both the dorsal and ventral visual-processing streams.

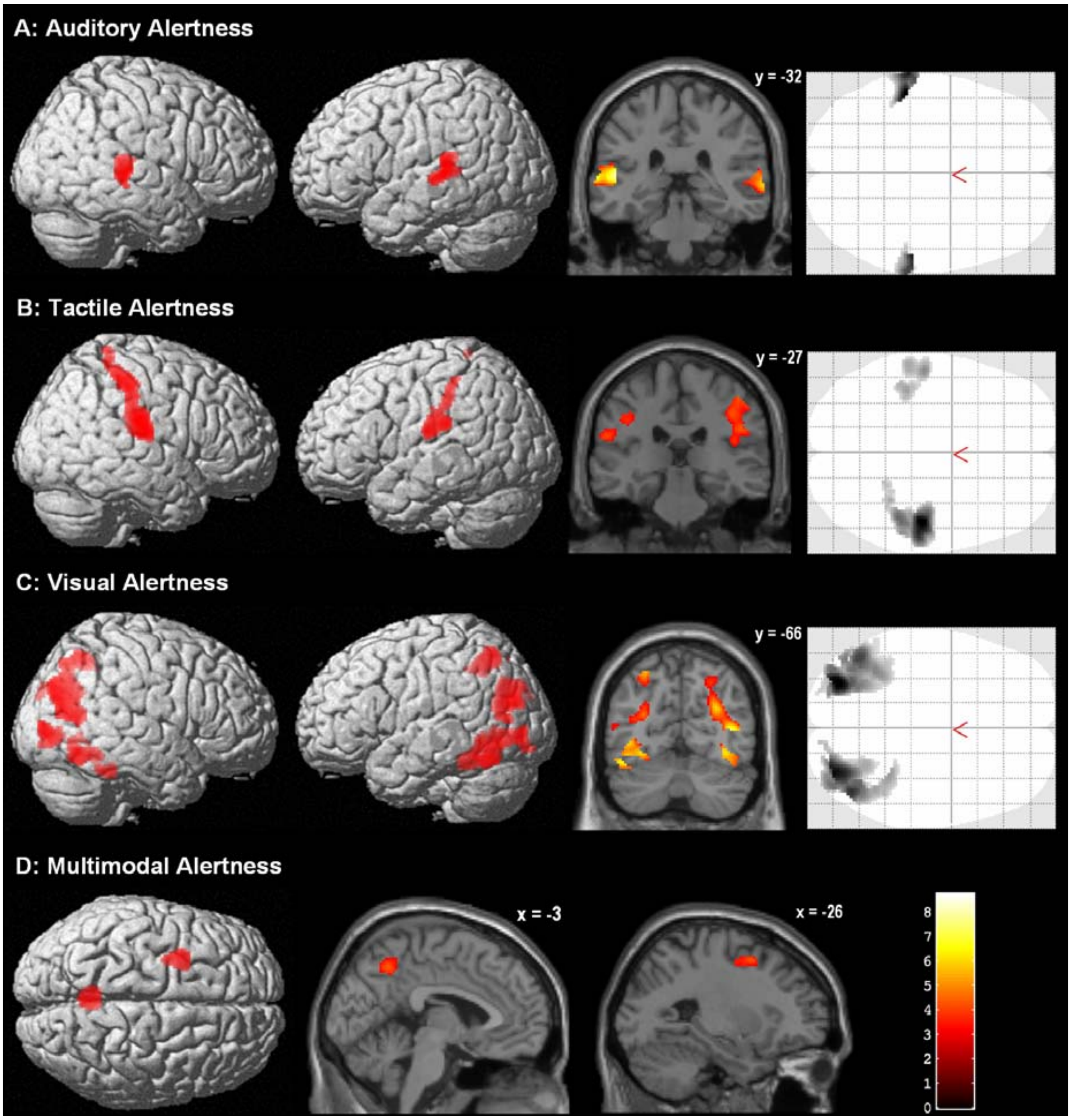

Figure 8. **(A-C)** Modality-specific alertness-related brain activity during the three unimodal conditions (one unimodal alertness condition vs. the other two unimodal alertness conditions, respectively; masked to include only voxels that show stronger activity during each unimodal experimental condition than resting baseline as well as during each unimodal experimental condition and its respective control condition). **(D)** Alertness-related brain activity specific to the unpredictably mixed presentation of stimuli of different modalities (mixed condition vs. all three unimodal alertness conditions, masked to include only voxels that show stronger activity during the mixed condition than during baseline as well as during the mixed and each single unimodal condition). Coronal and parasagittal slices show activity overlaid over the SPM5 single-subject template brain; coordinates refer to MNI space; color codes t-values; voxel-wise p<.001 & FWE-corrected cluster-level p<.05.

Table 6

Modality-Specific Alertness-Related Activity

Cluster/Area	x, y, z	z-score
Auditory Alertness		
Cluster 1 (k = 306, p = .004)		
L posterior superior temporal gyrus	-52 -30 8	7.73
L posterior middle temporal gyrus	-66 -28 6	7.03
L posterior superior temporal sulcus	-54 -30 4	6.38
Cluster 2 (k = 169, p = .047)		
R posterior superior temporal gyrus	62 -26 4	6.50
R posterior middle temporal gyrus	64 -30 -2	4.68
R posterior superior temporal sulcus	50 -30 0	3.57
Tactile Alertness		
Cluster 1 (k = 1043, p < .001)		
R Rolandic operculum (S2)	46 -20 16	6.18
R postcentral sulcus (BA 2/5)	44 -36 56	4.72
R supramarginal gyrus	54 -34 48	4.21
R postcentral sulcus (BA 2/40)	44 -26 40	4.09
R postcentral gyrus (BA 1; S1)	32 -42 66	3.86
Cluster 2 (k = 405, p = .001)		
L Rolandic operculum (S2)	-54 -18 18	4.22
L postcentral gyrus (BA 2/7)	-40 -30 46	3.95
L supramarginal gyrus	-56 -28 22	3.85
L postcentral sulcus (BA 2/5)	-44 -34 52	3.75
L postcentral sulcus (BA 2/40)	-36 -32 40	3.62
Visual Alertness		
Cluster 1 (k = 1174, p < .001)		
R middle occipital gyrus	30 -80 24	7.58
R lateral middle occipital gyrus	42 -68 10	6.80
R superior parietal lobule (BA 7A)	26 -60 52	4.35
R superior parietal lobule (BA 7P)	26 -74 48	3.98
R cuneus (BA 19) (V3)	12 -86 28	3.95
R cuneus (BA 18) (V2)	10 -90 24	3.80

Table 6 (continued)

Modality-Specific Alertness-Related Activity

Cluster/Area	x, y, z	z-score
Cluster 2 (k = 995, p < .001)		
L fusiform gyrus	-46 -62 -16	6.48
L middle occipital gyrus	-38 -80 2	5.64
L inferior occipital gyrus (V4)	-30 -86 -12	3.68
L inferior temporal gyrus	-56 -52 -16	3.18
Cluster 3 (k = 578, p < .001)		
L middle occipital gyrus	-30 -78 20	Inf.
L lateral middle occipital gyrus	-44 -72 10	5.22
Cluster 4 (k = 372, p = .001)		
R inferior occipital gyrus	38 -66 -8	5.80
R inferior temporal gyrus	42 -52 -14	4.49
R fusiform gyrus	32 -42 -20	3.32
Cluster 5 (k = 292, p = .005)		
L superior parietal lobule (BA 7A)	-26 -64 56	5.38
Cluster 6 (k = 262, p = .008)		
R inferior occipital gyrus	34 -76 -4	5.74
R middle occipital gyrus	40 -80 2	5.60
R lingual gyrus	24 -84 -4	5.23

Note. L = left; R = right; BA = Brodmann area. Coordinates x, y, z refer to MNI space; k = number of voxels in cluster; p-value represents cluster-level error probability corrected for multiple comparisons.

Alertness-related activity under increased monitoring demand was examined via a balanced contrast between the mixed-modalities condition and all three sensorimotor control conditions, using a filter to include only voxels with more activity during the experimental task than during baseline. Results are shown in Table A2 and Figure A2 (see Appendices B and D). In general, the pattern of results was similar to the supramodal network described above but included additional foci of significant activity. The analysis revealed bilateral activity in dPMC, precuneus, and posterior aspects of middle and superior temporal gyri, which at the right side extended into inferior parietal cortex. Right-sided activity was found in inferior frontal cortex (pars opercularis and pars triangularis), inferior parietal lobule and angular gyrus. Activity in right pre-SMA was found to be slightly above our cluster threshold (corrected cluster-level $p = .085$). Other areas with significant supramodal alertness-related activity reported above (right SMA, anterior insula, and ACC; left medial cerebellum; bilateral mid-cingulum, midbrain, and brainstem) were only active at a lower level (uncorrected voxel-wise $p < .01$).

To directly test for differences between the network identified in the mixed condition and the supramodal network identified across unimodal conditions, we computed a balanced contrast between both, again applying a composite filter to retain only voxels with more activity during the mixed condition than during baseline and each of the three unimodal conditions. Only two areas survived this direct test: bilateral precuneus (BA 7; MNI coordinates: 4/-56/46; $z = 4.15$) and left dPMC (BA 6; -28/6/52, $z = 4.40$; -28/-4/50, $z = 3.80$; see Figure 8*D*). Conversely, contrasting all three unimodal against the mixed condition yielded a significant difference in the bilateral anterior medial cerebellum (-8/-50/-6, $z = 4.31$; 10/-48/-8, $z = 3.99$).

When analyzing modulatory effects of the parametric RT regressors, it turned out that blockwise averaged response speed was not significantly associated with brain activity in any of the four experimental task conditions. Thus, mean RT per block appears not to explain any additional variance in alertness-related brain activity beyond the task regressors themselves.

4.4. Discussion

We examined the influence of stimulus modality on the brain network activated when maintaining a highly alert state, that is, high responsiveness to temporally unpredictable stimuli. First, we tested the modality independence versus modality specificity of this network by comparing activity in response to auditory, tactile, and visual stimuli. Second, we explored the effect of further increasing monitoring demands by making stimulus modality unpredictable. Our results provide evidence for a mainly right-lateralized supramodal core network controlling intrinsic alertness. This network, identified across all three sensory modalities (alertness conditions contrasted against sensorimotor control conditions), consisted of right dPMC, SMA, pre-SMA, ACC, inferior frontal cortex, anterior insula, and temporo-parietal junction as well as left medial cerebellum, bilateral motor cingulate areas, midbrain, and brainstem areas. These findings are generally in agreement with previous studies on intrinsic alertness using only one sensory modality (auditory or visual; cf. Sturm et al., 1999, 2004; Sturm & Willmes, 2001). In the following, we will discuss possible contributions of the network's parts to maintaining an alert state (see Supplementary Material for a brief discussion of the results of the baseline contrast).

4.4.1. Maintaining the Preparatory Set: Stimulus–Response Mapping, Motor Preparation, and the Prevention of Premature Responses

Lesion studies in non-human primates (Halsband & Passingham, 1985; Petrides, 1985) and human patients (Petrides, 1997) showed that the dPMC is essential for learning and using arbitrary stimulus–response associations. Evidence for a crucial role of the dPMC in such sensorimotor mapping is also provided by electrophysiological recordings in monkeys (Hoshi & Tanji, 2006). Dorsal PMC also has a role in preparatory motor processes: Transcranial magnetic stimulation (TMS) revealed dPMC involvement in using cue information for the preparatory scaling of grip force (Chouinard, Leonard & Paus, 2005). This area also processes information provided by spatial cues to direct movements, regardless of the cue's sensory modality (Weinrich & Wise, 1982). Further, there is electrophysiological evidence for sensory functions of dPMC (Wise, Boussaoud, Johnson & Caminiti, 1997), and a recent fMRI study (Kansaku, Hanakawa, Wu & Hallett, 2004) reported bilateral (more pronounced on the right side) dPMC activity when participants attended to auditory, tactile or visual stimuli without any response requirement. This was assumed to reflect a role of dPMC in facilitating cue detection. This non-motor function of dPMC is also supported by an fMRI study of S. R. Simon et al. (2002), who found increased dPMC activity related to spatial attention and memory. Non-motor, detection-related activity in the vicinity of the right dPMC was also reported in an earlier PET study on sustained attention, in which participants were required to count infrequent somatosensory or visual targets without any overt response (Pardo et al., 1991).

At the same time, dPMC has been found to be directly involved in motor control (Geyer, Matelli, Luppino & Zilles, 2000; Graziano, Taylor & Moore, 2002), via direct connections to the primary motor area (M1) and the spinal cord (Barbas & Pandya, 1987; Dum & Strick, 1991). Thus it can be argued that bilateral activation of dPMC in our task vs. baseline contrast reflects both (i) maintaining the mapping between stimuli and instructed motor response (including the facilitation of stimulus detection) and (ii) sending motor-execution signals further down the motor hierarchy. Both functional aspects have been proposed to be differentially localized in more rostral vs. caudal subdivisions of dPMC, respectively (reviewed in Picard & Strick, 2001, see also Chouinard & Paus, 2006; S. R. Simon et al., 2002). In fact, our baseline contrast shows a somewhat more rostral focus of dPMC activity at the right compared to the left side (see Appendix C, Figure A1). This may explain why only right dPMC survived the comparison with the sensorimotor control tasks: Both experimental and control tasks required the repeated execution of button presses, to which caudal dPMC may contribute equally in both tasks, resulting in elimination by subtraction. Sustained stimulus–response mapping and signal detection, however, were only required in the experimental tasks. This differential processing demand might be preferably subserved by the contralateral rostral dPMC.

A similar logic may apply to alertness-related right-sided SMA activations. Unilateral movements usually activate bilateral SMA (e.g. Naito et al., 2000), which is supposed to be involved in initiating and executing movements (Cunnington Windischberger, Deecke & Moser, 2003). This notion is supported by recent effective-connectivity studies (Eickhoff et al., 2008; Grefkes, Eickhoff, Nowak, Dafotakis & Fink, 2008; Grefkes, Nowak et al., 2008) that revealed strong context-specific influences of SMA on M1, promoting ipsilateral and suppressing contralateral M1 activity during unilateral hand movements. Picard and Strick (1996) suggested that SMA proper is more active in simple, automatic tasks and pre-SMA is more active in complex, cognitively controlled ones (cf. Jakobs et al., 2009). Recently it has been proposed that functional differences between SMA proper and pre-SMA follow a caudal–rostral continuum rather than a discrete parcellation (Nachev, Kennard & Husain, 2008). This approach is also reflected in another function ascribed to SMA and, to a greater extent, pre-SMA: the preparation of movements (Cunnington, Windischberger & Moser, 2005; Hülsmann, Erb & Grodd, 2003). The role of pre-SMA in voluntary movement preparation is also supported by its connectivity pattern in monkeys, where it receives afferents from the inferior parietal lobule (Luppino, Matelli, Camarda & Rizzolatti, 1993), supplying it with integrated sensory input and motor plans; efferents are predominantly sent to dPMC. We argue that maintaining a preparatory set for a given movement is subserved by rostral SMA and its anterior continuation, pre-SMA. In contrast, more basic processes related to response initiation/execution may be localized more caudally. Since the latter are shared by our experimental and control tasks, caudal SMA activity is eliminated by the subtraction of activity during sensorimotor control tasks.

The ACC has been found involved in a wealth of motor, cognitive, and affective processes (reviewed in Devinsky, Morrell & Vogt, 1995). Motor functions have been associated with different cingulate motor zones, among them caudal BA 24, which has been found active during simple movements (Picard & Strick, 1996). The stronger activation of caudal ACC during intrinsic alerting, compared to our repetitive motor control tasks, might reflect a preparatory attentional modulation that facilitates the generation of motor output. This notion is supported by a study showing that ACC activity is closely related to the generation of the contingent negative variation, an electrocortical potential indicating top-down preparatory activity following a warning signal that announces an impending imperative stimulus (Nagai et al., 2004).

Maintaining a preparatory set for a given movement involves motor preparation as well as motor inhibition, largely implemented in parallel (Davranche et al., 2007; Duque & Ivry, 2009; Hasbroucq et al., 1999; Jennings & van der Molen, 2005). Motor preparation results in increased readiness to respond in a predefined way upon occurrence of a signal. The resulting “urge to move,” however, must be held in check to prevent premature responding. Also, competing action tendencies need be suppressed while preparing for a given motor response (Jennings et al. 2009). Here, inhibitory processes come into play, which are presumably subserved by pre-SMA and right inferior frontal gyrus (BA 44). In their review, Picard and Strick (1996) argued for an important role of pre-SMA in higher motor control including motor inhibition. This assumption is corroborated by a patient study showing that lesions in pre-SMA and SMA were selectively associated with deficits in response inhibition (Picton et al., 2007). Further support comes from a recent experiment using the stop-signal paradigm, in which the deactivation of pre-SMA by means of TMS disrupted the ability to suppress responses after stop signals (Chen, Muggleton, Tzeng, Hung & Juan, 2009). Since our temporally unpredictable experimental conditions required a rapid stimulus-contingent implementation of motor plans, alertness-related pre-SMA activity may reflect increased demands for preparatory motor control to hold motor plans on line for rapid use as well as to mediate constraints on excitatory activity to prevent the premature release of motor plans.

There is evidence that these constraining signals may originate from inferior prefrontal cortex (BA 44). Lesions in this area were accompanied by disturbed inhibition of initiated movements (Aron, Fletcher, Bullmore, Sahakian & Robbins, 2003), and TMS over right BA 44 impaired the ability to stop a motor act (Chambers et al., 2006). Similarly, Brass, Derrfuss and von Cramon (2005) concluded from an fMRI experiment comparing the inhibition of imitative and overlearned responses that BA 44 generates stop signals for the control of action. It has been suggested (Jakobs et al., 2009) that BA 44 acts as a hold-and-release switch in situations of temporal uncertainty about the moment of movement execution. Direct anatomical connections between pre-SMA and right BA 44 have been shown with diffusion tensor tractography (Aron, Behrens, Smith, Frank & Poldrack, 2007; Johansen-Berg et al., 2004), and fMRI revealed common activity of both areas during response inhibition (Coxon, Stinear & Byblow, 2009; Xue, Aron & Poldrack, 2008). Further, a recent study (Duann, Ide, Luo & Li, 2009) reported substantial effective connectivity between both regions during stop-signal performance, with greater connectivity during successful response inhibition. Based on these studies and our results we suggest that BA 44 modulates pre-SMA activity to bias the balance (or permanent conflict) between "going" and "withholding" according to current task demands.

4.4.2. The Timing of Preparation

It has been postulated that the brain constantly predicts future events based on previous experiences in order to minimize computational load and to disambiguate incoming information — a feature that has been labeled "predictive coding" (Creutzig & Sprekeler, 2008; Summerfield et al., 2006). Situations with uncertainty result in frequent prediction errors and constant updating of beliefs to improve the accuracy of future predictions (Behrens, Woolrich, Walton & Rushworth, 2007; Kilner, Friston & Frith, 2007). Under such circumstances, computational activity should increase in areas that subserve predictive coding. With respect to uncertainty about action parameters (type and onset of responses), the right temporo-parietal junction (TPJ) has recently been implicated to play a central role in predictive motor coding (Jakobs et al., 2009). The function of the TPJ has been proposed to involve the updating of action expectations and/or the comparison of prepared motor programs with current requirements. In RT tasks involving temporal uncertainty such as our experimental conditions, participants develop temporal expectations about the onset of the next stimulus and its associated response (Coull & Nobre, 2008; Langner et al., in press). We propose that the activity in right TPJ observed in our study reflects such temporal predictions and their updating. This is consistent with recent theories of trial-to-trial conditioning processes governing temporal preparation in RT tasks under temporal uncertainty (Los et al., 2001; Steinborn, Rolke et al., 2008).

The interpretation of a role of the TPJ in facilitating the speeded detection of stimuli by predictive coding is in line with previous studies on stimulus-driven attention (Corbetta and Shulman 2002; Downar, Crawley, Mikulis & Davis, 2000), which reported increased activity in the TPJ region during disruptions in expectation about incoming visual stimuli (i.e. increasing prediction error) or detection of sensory changes in the environment (i.e. updating the present prediction). A role of the right TPJ in establishing and updating implicit models of the temporal structure of sensory input under time uncertainty may also be inferred from Kansaku et al.'s (2004) study, in which right TPJ activity was observed during both monitoring of, and speeded responding to, temporally unpredictable stimuli of different modalities. Right TPJ activity was also observed during phasic alerting (Fan et al., 2005; Thiel & Fink, 2007), which involves a similar situation at a smaller time scale: a warning cue facilitates detecting a stimulus after a variable delay.

Another brain region associated with temporal preparation under time uncertainty is the cerebellum (Courchesne & Allen, 1997), which showed modality-independent alertness-related activity in the anterior vermis and left intermediate hemisphere. This finding agrees well with other reports of cerebellar activity during alertness, sustained attention, and SRT performance (Kansaku et al., 2004; Lawrence et al., 2003; Sturm et al., 2004; Sturm & Willmes, 2001). Our results are also consistent with a recent study showing that the absence of the cerebellar vermis because of a congenital dysplasia is related to deficits in endogenously maintaining responsiveness to visual signals (Michael, Garcia, Bussy, Lion-Francois & Guibaud, 2009). It should be noted, though, that the chosen field of view of our fMRI measurement only allowed us to image the superior cerebellum, precluding inferences on its lower parts.

Cerebellar involvement in precise motor timing has long been known from lesion studies (Ivry, 1996; Sailer, Eggert & Straube, 2005). Other studies demonstrated a specific role of the cerebellum in preparation. For instance, increased activation of the cerebellum in random compared to fixed timing in a task-switching experiment was observed by Dreher and Grafman (2002). Martin et al. (2006) showed with magnetoencephalography (MEG) that cerebellar activity predicted response speed in temporally unpredictable SRT tasks. Another recent MEG study (Pollok, Gross, Kamp & Schnitzler, 2008), which analyzed functional connectivity in a cerebello-diencephalic-parietal network, suggested that the cerebellum is involved in both anticipatory motor control and mismatch-contingent updating of an internal model, which is in line with the predictive-coding framework outlined above (cf. Nixon &

Passingham, 2001; Trillenberg, Verleger, Teetzmann, Wascher & Wessel, 2004). Elaborating on the potential mechanism that mediates the cerebellar contribution to preparation, Courchesne and colleagues (Allen, Buxton, Wong & Courchesne, 1997; Courchesne et al., 1994; Courchesne & Allen, 1997) suggested that the cerebellum shifts excitability thresholds in task-relevant neurons toward optimal levels, thereby continuously updating and adjusting patterns of responsiveness.

4.4.3. Arousal Regulation

Apart from the cingulate motor zones, controversy surrounds the function of the ACC. Paus (2001) argued that the ACC is the place where motor control, executive attention, and arousal regulation interface. This is in line with our data and previous studies on intrinsic alertness or vigilance, which consistently found ACC activity related to maintaining responsiveness (Paus et al., 1997; Sturm et al. 1999, 2004; Sturm & Willmes, 2001). One role of the ACC in simple tasks requiring fast responding under temporal uncertainty might be the regulation of nonspecific arousal via top-down influences on midbrain and brainstem arousal systems in order to maintain optimal efficiency of information processing (Aston-Jones & Cohen, 2005; Critchley et al. 2003; Fischer et al., 2008; Sturm et al., 1999). This notion is corroborated by a PET study (Paus et al., 1997), in which the decline of arousal during a 60-min vigilance task covaried with activity in ACC and midbrain structures. Further support comes from an effective-connectivity analysis of brain activity during intrinsic alerting (Mottaghy et al., 2006), which revealed top-down influences of the ACC on thalamus and brainstem structures associated with arousal regulation. Also, ACC activity has been repeatedly shown to increase with preparatory attention (Luks, Simpson, Feiwell & Miller, 2002; Murtha, Chertkow, Beauregard, Dixon & Evans, 1996) and attentional effort (Mulert, Menzinger, Leicht, Pogarell & Hegerl, 2005; Walton, Bannerman, Alterescu & Rushworth, 2003). Along these lines we suggest that in tasks that demand intense attentiveness, the ACC is important for initiating and maintaining efficient goal-directed behavior by “energizing” cognition (see also Stuss, 2006).

This energizing is thought to be mediated via input from midbrain and brainstem arousal systems (for reviews, see Jones, 2003; Pfaff, 2006). These systems employ various neurotransmitters, such as noradrenalin, dopamine, acetylcholine, or serotonin, which innervate large parts of the cortex. In their target zones, they modulate computational processes and thus control the efficiency of information processing (Hasselmo, 1995;

Grefkes, Wang, Eickhoff & Fink, 2009). These neuromodulatory systems originate in subcortical regions, some of which correspond to activity foci of our study, such as the ventral tegmental area and substantia nigra (dopamine) or the locus coeruleus (noradrenalin). Furthermore, midbrain structures like the substantia nigra as well as the pons are implicated in the control of sympathetic autonomic arousal (Critchley, Melmed, Featherstone, Mathias & Dolan, 2002). We are aware that fMRI cannot localize these structures with certainty, since its spatial resolution is too coarse. Nevertheless, our data provide further evidence that distinct midbrain and brainstem structures involved in neuromodulation contribute to voluntarily maintaining an alert state.

The network of ACC and midbrain/brainstem regions, mediating cerebral and bodily arousal, is also tightly connected with another area of the supramodal alertness network: the anterior insula, an area that has been found involved in representing bodily states (Craig 2002; Critchley, Wiens, Rotshtein, Öhman & Dolan, 2004). There are strong anatomical connections between anterior insula and ACC (Augustine, 1996; Mesulam & Mufson, 1982), and a recent fMRI study measuring resting-state connectivity provided evidence for a functional anterior-insula–cingulate system (Taylor, Seminowicz & Davis, 2009). Similar to ACC, anterior insula activity has not only been found in *response* to stimulus events but also in *preparation* for expected ones. For instance, a meta-analysis revealed that anterior insula activation increases prior to both expected losses and expected gains and correlates with both self-reported negative and positive arousal (Knutson & Greer, 2008).

Thus, during intrinsic alerting, right anterior insula might feed integrated information on bodily states to ACC, which monitors and, if necessary, adjusts arousal to maintain optimal readiness in body and brain. This assumption is supported by the finding that activity in right anterior insula, right ACC, cerebellum and brainstem covaries with peripheral cardiovascular arousal (i.e. sympathetic autonomic activity) induced by mental or physical stressors (Critchley, Corfield, Chandler, Mathias & Dolan, 2000; see also Pollatos, Schandry, Auer & Kaufmann, 2007). In line with this notion is another recent study (Eckert et al., 2009) that reported significant functional connectivity between right anterior insula and ACC across different attention-demanding tasks, leading to the conclusion that the right anterior insula may be especially critical for modulating cognitive control systems under challenging conditions. Apart from *cognitive* challenges, this might also, or even particularly, apply to very simple tasks like ours, which are challenging, because they are repetitive and ultimately boring but still require the continuous, effortful maintenance of attention (cf. Fischer et al., 2008; Walker et al., 2009).

4.4.4. Unimodal Alertness-Related Activity

Maintaining alertness involves sustained (preparatory) attention to sensory input, which facilitates subsequent processing. Our findings corroborate the hypothesis that modality-specific attentional modulations should be found in areas that process sensory information of the given modality. Indeed, the only unimodal components of the alertness-related network corresponded to primary and secondary auditory cortex, primary and higher-order somatosensory cortex, and visual association cortex, respectively. The absence of increased alertness-related activity in primary visual cortex during visual alertness is most likely due to the processing of some visual input (fixation cross) in all three unimodal alertness conditions. It should be noted that the unimodal alertness-related activity is not due to simple stimulus processing, since the outcome included only voxels that showed higher activity during alertness than during the sensorimotor control tasks, which actually provided much more sensory stimulation.

In general, our modality-specific results show remarkable overlap with findings from a study that had its participants attend to auditory, somatosensory and visual stimulation, each of which randomly alternated between two modes (Downar et al., 2000). This suggests that change detection is subserved by cortical modules that are also the target of attentional modulation in tasks like ours, which require detecting the mere presence of stimuli of a given modality. Since Downar et al. did not find change-related effects in primary somatosensory cortex, this overlap might not apply to tactile stimulation. We conclude that modality-specific activity is related to stimulus anticipation and attentional enhancement of stimulus processing during the alertness conditions. This again implicates that other subprocesses during intrinsic alerting, e.g. related to motor preparation, timing, or arousal, are independent of stimulus modality.

4.4.5. Additional Alertness-Related Activity With Unpredictable Stimulus Modality

In the mixed condition, in which stimulus modality was unpredictable, the pattern of activity showed large overlap with the network shared by all three unimodal conditions. Two additional foci of activity emerged for the mixed condition when it was directly compared against the unimodal conditions: left dPMC and bilateral precuneus. We suggest that the additional left-sided dPMC activity reflects (i) increased demands on signal detection because of the larger number of input channels to be monitored and (ii) the associated more complex stimulus–response mapping to be maintained. This interpretation is in line with findings from other studies requiring attention to be divided between different sensory modalities (Lewis, Beauchamp & DeYoe, 2000; Saito et al., 2005; Vohn et al., 2007).

Precuneus activation has been previously shown during voluntary attentional shifts between spatial (Krumbholz, Nobis, Weatheritt & Fink, 2009) and non-spatial (Le, Pardo & Hu, 1998) features of auditory and visual stimuli as well as between auditory and visual stimulus modalities (Shomstein & Yantis, 2004). Although our mixed condition did not require voluntary shifts of attention between modalities, the participants might have adopted a resource-saving strategy of cyclically or probabilistically shifting their attention between the three modalities instead of being prepared for all of them all the time. Trials in which preparation was not directed toward the correct modality would then have provided some room for stimulus-driven reorienting to the modality of the current stimulus (see Appendix E for supplemental discussion).

4.4.6. Conclusions

We performed one of the first fMRI studies on the brain network that supramodally controls intrinsic alertness (i.e. the readiness to respond in unwarned situations). To induce intrinsic alerting, we used non-cued SRT tasks with variable interstimulus intervals and three different stimulus modalities. Regardless of sensory modality, intrinsic alerting was subserved by a mainly right-hemisphere network, which confirms findings of earlier unimodal PET studies and extends them to the somatosensory modality. We identified multimodal brain regions which have been associated with different subprocesses of alerting, such as maintaining the stimulus–response mapping, balancing motor preparation and inhibition, building temporal expectations, and regulating arousal. In this supramodal alertness network, the ACC might be the central coordinating structure for readying body and brain for action. Modality-specific activity, presumably related to anticipating the response signal, was confined to sensory cortices. When monitoring demands were increased by making stimulus modality unpredictable, additional left frontal and medial parietal areas were recruited. The challenge for the future is to further specify the functional significance of each identified brain region by delineating the neurocomputational operations these regions and their interplay subserve during intrinsic alerting. This endeavor has also direct relevance for the treatment of impaired alertness regulation in various neurological and psychiatric patient groups, since understanding the neural basis of specific cognitive subprocesses offers the chance for more focused diagnostic and therapeutic approaches with substantially improved outcome.

5. GENERAL DISCUSSION

Apart from a summary of the main findings and conclusions of the three studies, the general discussion will focus on aspects of the studies that were omitted from the papers for reasons of space. Further, the discussion will deal with implications of the findings for future research and applications.

5.1. Summary of Main Findings and Conclusions

The first study dealt with the question of whether the well-known decrement of continuous SRT performance with TOT is due to mental fatigue or mindlessness. To this end, we manipulated stimulus intensity and stimulation monotony and observed the effect on performance change over time. The pattern of results argued strongly for the mental-fatigue hypothesis, supporting resource theory, which assumes that the depletion of attentional resources underlies such time-related deterioration (e.g. Grier et al., 2003; Helton & Warm, 2008; Smit et al., 2004). Taking others' and our results together, we conclude that the prolonged performance of computationally easy SRT tasks is increasingly impaired by growing mental fatigue and that the amount of fatigue and impairment accumulating over time appears to depend on the demands placed on attentional systems. Nevertheless, our self-report data also showed that task-unrelated thoughts increased during SRT performance, which suggests that increasing mindlessness (e.g. Pattyn et al., 2008; Robertson et al., 1997) might also contribute to performance decrements in SRT tasks.

This led us to propose a hierarchical model of performance decrements with TOT, which incorporates both aspects, resource depletion and mindlessness. Briefly, on the top level, the model assumes self-regulatory power as the basic driving force behind the sustained performance of an – arguably – boring and not intrinsically rewarding task like the continuous SRT task. Close connections between attentional control and self-regulation have already been proposed earlier (e.g. Posner & Rothbart, 1998; Tang et al., 2008). Recent research considers self-regulation a limited resource that gets depleted with prolonged use (R. F. Baumeister et al., 2007; Muraven & Baumeister, 2000). This so-called "ego depletion" has been observed across a wide range of tasks that require active volition or the inhibition of prepotent actions or both, for example making personally meaningful choices, restraining emotional impulses or resisting temptations (e.g. R. F. Baumeister, Bratslavsky, Muraven & Tice, 1998; Vohs et al., 2008; Vohs & Heatherton, 2000). Our model proposes that the depletion of attentional resources as well as absent-mindedness follow from a reduction of self-control strength over time. We interpret the depletion of attentional resources as a decrease in the intensity of top-down attentional modulations that normally facilitate task-relevant computational processes to optimize performance (Spitzer et al., 1988). That is, attentional effort is diminished with reduced self-regulatory power. At the same time, our model assumes that the task goal cannot be maintained constantly when self-control strength decreases. That is, the number of attentional lapses increases, since internal or external distractors draw attention away from the task with increasing ease, producing phenomena such as mind-wandering (Smallwood et al., 2004; Smallwood & Schooler, 2006). Of course, the proposed model requires empirical testing with different and possibly parametric manipulations of attentional demand and independent measures of self-control strength. Also, RT analysis may be refined by including different measures such as RT variability (cf. Flehmig et al., 2007) and the number of extra-long responses (cf. Bills, 1931), since they might be differentially sensitive to the various processes presumably underlying performance change over time (Steinborn, Flehmig, Westhoff & Langner, 2009).

The second study explored whether mental fatigue from prolonged TOT also impacts alertness by impairing processes of temporal preparation. Using a forewarned SRT task with three different foreperiods that varied randomly from trial to trial, we found the typical time-related increase in overall RT but no time-related modulation of indices of temporal preparation (i.e. the variable-FP effect and the asymmetrical sequential FP effect). This shows that the cognitive processes underlying the timing of preparatory attention under temporal uncertainty do not contribute significantly to the alertness decrement with TOT. This result also has implications for the nature of the timing processes: since mental fatigue primarily affects top-down control processes, our finding is more consistent with a recent bottom-up associative-learning account of temporal preparation (Los et al., 2001; Steinborn, Rolke et al., 2008) than a strategic account based on intentional conditional probability monitoring and endogenous temporal orienting (Näätäänen & Merisalo, 1977; Nobre, 2001).

In the third study, we tested to what extent the activity of the brain network subserving intrinsic alertness depends on the sensory modality of the stimuli presented. To this end, we measured brain activity with fMRI during tasks requiring the speeded detection of auditory, vibrotactile, or visual stimuli presented at unpredictable times. The effect of increased monitoring demand was tested in a fourth condition in which stimulus modality was unpredictable. In contrast to sensorimotor control tasks, all three unimodal alertness conditions showed stronger activity in the right temporo-parietal junction, inferior frontal cortex, anterior insula, dorsal premotor cortex, and anterior cingulate cortex as well as bilateral mid-cingulum, midbrain, brainstem and medial cerebellum. Modality-specific alertness-related activity was confined to respective sensory areas. With unpredictable stimulus modality, additional activity was found in left dorsal premotor cortex and bilateral precuneus. These findings corroborate the modality-independence of a predominantly right-lateralized core network for maintaining a highly alert state and extend previous results to the tactile modality. Increasing the monitoring demand through uncertainty about stimulus modality appears to induce additional processing in left frontal and medial parietal cortex, which might be related to maintaining the more complex stimulus–response mapping and orienting attention to a given sensory modality.

In the following, we will discuss several aspects of the three studies that touch upon broader issues of interest, which space limitations precluded from being considered in the Discussion sections of the respective papers.

5.2. Arousal and Performance Decline

In addition to mental fatigue or mindlessness, some theorists have proposed that a decrease in arousal may be one of the reasons for the time-related deterioration of performance in vigilance tasks (Heilman, 1995; Loeb & Alluisi, 1984; Koelega, 1996). This might also apply to SRT tasks, since they are similar to typical vigilance paradigms. Indeed, prolonged SRT tasks usually are even more repetitive and predictable and, therefore, monotonous and de-arousing. For example, Dirnberger et al. (2004) observed that a repetitive simple motor task was accompanied by a reduction of movement-related electrocortical activity over time, which has been taken to reflect a decline of arousal-related cortical excitability. Low arousal has often been found to be associated with decreased cognitive efficiency (see, e.g., Eysenck, 1982, for a review), and manipulations that reduce general arousal have been shown to impair SRT task performance. For instance, Lisper and Kjellberg (1972) and Maruff, Falleti, Collie, Darby & McStephen (2005) found a significant SRT increase after 24 hours of sleep deprivation. Increases in SRT have also been reported as a consequence of prolonged partial sleep deprivation (Dinges et al., 1997) or sedative drugs (e.g. Wesensten, Balkin et al., 2005). Administering arousal-enhancing drugs (e.g. caffeine or amphetamines) or physical stimulation (e.g. bright light) has been shown to improve SRT performance and to attenuate sleep deprivation deficits (e.g. K. P. Wright et al., 1997; Wesensten, Killgore & Balkin, 2005). Taken together, SRT performance correlates with general arousal level, but the question remains whether the performance decline with TOT is related to a decrease in arousal.

Indirect support for this assumption has come from studies on vigilance showing that a performance decline can be ameliorated by extraneous or self-generated stimulation (e.g. Davies, Land & Shackelton, 1975; Mackworth, 1956; Randel, 1968; Zuercher, 1965) or stimulant drugs such as caffeine (Koelega, 1993; Temple et al., 2000). In fact, the results of Study 1 are also consistent with an arousal explanation of SRT performance decline, since the low-intensity stimuli are not only harder to detect and therefore attentionally more demanding than high-intensity stimuli but also provide less stimulation and therefore induce less arousal.

Arousal is evoked by sensory input via excitatory collateral projections of sensory pathways to brainstem arousal systems and/or their “continuations” in thalamic nuclei (Foote, Aston-Jones & Bloom, 1980; Grunwerg & Krauthamer, 1992; Sarter, Givens & Bruno, 2001; Schiff, 2008; Vandewalle et al., 2006). Arousing effects of sensory stimulation and their positive associations with different measures of cognitive efficiency have been demonstrated across several stimulus modalities, including the effects of noise (e.g. Brocke, Tasche & Beauducel, 1997; A. Smith & Nutt, 1996), odours (e.g. Hiruma, Yabe, Sato, Sutoh & Kaneko, 2002; Warm, Dember & Parasuraman, 1991), or light (e.g. Badia, Myers, Boecker, Culpepper & Harsh, 1991; Phipps-Nelson, Redman, Dijk & Rajaratnam, 2003). Generally, the more intense a stimulation, the more arousing it is (Geen, 1984; Uno & Grings, 1965). Sanders (1983) suggested that stimulus intensity determines the magnitude of the “immediate arousal” accompanying sensory input, which, in turn, increases “activation,” the readiness to respond. Similarly, it has been suggested by Posner (1978) that the automatic change in arousal brought about by sensory stimulation is mediated by the same pathways that are responsible for maintaining response readiness (see also Whitehead, 1991). Studies on reflex pathway reactivity showed that neural excitability (as expressed by reflex amplitude) increased unspecifically after sensory input (for a review, see Requin et al., 1991, pp. 424-425). This effect “was found to be an enhancement of the general arousal effect of any stimulus without warning significance, and depended on its intensity” (ibid., p. 425).

The concept of general arousal has a long history in psychology and related fields and has faced many criticisms (see, e.g., Hockey, 2008; Neiss, 1988, but see Anderson, 1990, for a reply). Although some critics questioned the explanatory value of a general arousal concept (e.g. Hancock, 1987; Hanoch & Vitouch, 2004; Hockey, 1997; Robbins & Everitt, 1995), evidence supporting the usefulness of this concept has accumulated across various research domains, including cognition (e.g. Steinborn, Rolke et al., 2008), emotion (e.g. Keil et al., 2008; Russell, 2003), cognitive-emotional interactions (e.g. Bradley, Greenwald, Petry & Lang, 1992; Mather, 2007), personality factors (e.g. Beauducel, Brocke & Leue, 2006), and developmental aspects (e.g. Mayes, 2000). Also, research in neuropsychology (e.g. Whyte, Polansky, Fleming, Coslett & Cavallucci, 1995), neurology (e.g. Schiff, 2008) and cognitive neuroscience (e.g. Coull, 1998; Gobbelé et al., 2000; Gonzáles & Aston-Jones, 2006; Hackley et al., 2009; Oken, Salinsky & Elsass, 2006; Paus, 2000; Robbins & Arnsten, 2009) has found merit in using this concept to describe global changes in the functional state of patients or participants.

In response to past criticisms, earlier views of arousal as a one-dimensional concept have been abandoned in favour of compound views that consider arousal to consist of a generalized component and context-specific ones (Garey et al., 2003; Pfaff, 2006; Pfaff, Ribeiro, Matthews & Kow, 2008). For instance, Pfaff (2006) maintained that the "activation of brain and behavior depends on a compound function of a primitive brainstem system common to many states *combined with* neural and hormonal forces that arise from specific biologic needs" (p. 7). Similarly, Robbins and Arnsten (2009) stated in a recent review on neuromodulation of fronto-executive functioning: "These different [arousal] levels may reflect fluctuations in the sleep–wake cycle, motivation, mood, and stress, which, while constituting distinct processes, may have a common currency through PFC [prefrontal cortex] arousal" (p. 268). According to such current views, generalized arousal reflects the general responsiveness of the brain and is considered a prerequisite for, and a modulator of, the activation of specific cognitive systems (Fischer et al., 2008; Pfaff et al., 2008).

Neurobiologically, arousal is assumed to reflect the excitability of cortical neurons (Elbert, 1993; Elbert & Rockstroh, 1987; Fischer et al., 2008), which is modulated via input from several distinct neuromodulatory arousal systems originating in the brainstem and other subcortical areas and innervating large parts of the cortex (Pfaff, 2006; Jones, 2003). In their target zones, input from these arousal systems leads to changes in the functional state of cortical neuronal cell assemblies, for instance by enhancing the signal-to-noise ratio, thus facilitating cortical information processing in a rather nonspecific way (Hasselmo, 1995).

The neurobiological findings agree well with an influential theory about how general arousal may exert its influence on performance: Kahneman (1973) and Humphreys and Revelle (1984) have argued that arousal determines the availability of cognitive resources (see also Matthews, Davies & Lees, 1990; Thiffault & Bergeron, 2003). This notion is also reflected in the fact that the Energetic Arousal dimension of the Dundee Stress State Questionnaire (DSSQ) is considered to represent a subjective estimate of resource availability (Helton & Warm, 2008; Matthews et al., 2000). The exact mechanisms through which arousal may influence resource availability have not been explicated yet, but Kahneman's original proposal is consistent with neuroimaging studies that reported interaction effects of arousal and attentional manipulations in specific brain areas (e.g. Coull, Jones, Egan, Frith & Maze, 2004; Fischer et al., 2008; Foucher, Otzenberger & Gounot, 2004; Portas et al., 1998). In addition to assuming that more resources are available with increased arousal, we suggest that the hypothesized or perceived enhanced resource availability with higher arousal might also reflect a reduced resource demand for a given piece of information to be processed. This might result from an arousal-induced increase in the speed of information processing, by which stable representations of stimuli and task rules may be achieved earlier and with consuming less resources. In sum, arousal appears to be positively correlated with the general efficiency of cognitive processes, mediated via its impact on the availability of, or demand for, cognitive resources.

According to this reasoning, it is plausible to assume that a decrease in arousal over time contributes to time-related SRT performance decrements. Conversely, it is also plausible to assume that mitigating a decrease in arousal with external stimulation can diminish performance decrements associated with suboptimal arousal. Therefore, the finding reported in Study 1 that the increased stimulation during the Mixed compared to the Pure-Low condition supports the efficient processing of low-intensity stimuli could also be explained within the framework of arousal theory. This explanation is also consistent with results from Matthews and Davies (1998), who manipulated event rate and target salience and found beneficial effects of high arousal only on more demanding vigilance tasks. Still, an explanation of the entire pattern of results in Study 1 based solely on arousal theory is rather improbable, since it has been repeatedly shown that visual stimuli induce reliable arousal effects only with extreme intensities (Jaskowski & Włodarczyk, 2006; Niemi & Lehtonen, 1982; Sanders, 1975). It should also be noted that the arousal theory of the vigilance decrement has been criticized before. Several theorists concluded that arousal, at least when viewed as a unidimensional concept, cannot explain all of the changes with TOT observed in vigilance situations (e.g. Loeb & Alluisi, 1984; Parasuraman, Warm & See, 1998; Warm, Matthews & Finomore, 2008).

To disentangle effects of attentional resource depletion and arousal decrease, future research needs to employ tasks with independent manipulations of attentional demand and environmental stimulation (i.e. arousal), if possible in combination with subjective reports and physiological measures. This issue becomes even more complex when considering arousal not only as a passive entity evoked by external or internal stimulation but as a variable that can also be controlled voluntarily. Neurophysiological correlates of compensatory arousal regulation have begun to be investigated (e.g. Fischer et al., 2008). Since this kind of top-down regulation is also considered effortful, mental fatigue might also include a reduced capacity to endogenously up-regulate arousal in monotonous, de-arousing situations.

5.3. Mechanisms Underlying Temporal Preparation

In Study 2, we found no evidence for a change of the variable-foreperiod (FP) effect or the sequential FP effect with TOT. This was interpreted as support for an explanation of FP effects that is based on associative learning (i.e. trace conditioning) instead of intentional probability monitoring and temporal orienting. The learning account maintains that the variable-FP effect is an emerging property of the asymmetry of the sequential FP effect, which, in turn, is based on a trial-to-trial update of associations between warning signal and critical moments (Los et al., 2001; Los & van den Heuvel, 2001). It has become clear, however, that this learning mechanism can hardly account for the entire phenomenon of temporal preparation under time uncertainty (Los & Agter, 2005). For instance, Vallesi and colleagues (Vallesi et al., 2007; Vallesi & Shallice, 2007) have reported dissociations between the variable and the sequential FP effects in developmental and neuropsychological populations. As a solution, a dual-process model was proposed that combines intentional preparatory processes with sequential effects of arousal level. In this model, arousal is assumed to decrease during FPs, naturally more so during long than short ones (Vallesi & Shallice, 2007). Without going into the details of this account, it is quite clear, however, that the postulation of an energetic variable like arousal playing a pivotal role in timing aspects of preparation is rather inconsistent with not finding any interaction between TOT-induced mental fatigue and indices of temporal preparation in our study.

According to our rationale, a potential solution would need to involve a mechanism that is based on nonintentional, automatic processes, which pose little demands for attentional control and are thus less affected by energetic factors. In fact, such a mechanism is not too hard to be imagined. All it needs is reframing the traditional intentional probability-monitoring account as a set of nonintentional processes that compute an anticipation function, that is, the subjective hazard rate. This hazard rate reflects the probability that a stimulus occurs at a given time, given that is has not yet occurred (Luce, 1986). For the computation of the hazard rate, the brain needs a representation of the passage of time and a representation of the probabilistic time schedule of stimulus occurrence (Janssen & Shadlen, 2005). It can be assumed that both representations do not necessarily rely on top-down control (cf. Nobre, Correa & Coull, 2007). Similar to moment–response associations modulated by a trial-to-trial conditioning processes as suggested by Los and colleagues (e.g. Los et al., 2001), the subjective hazard rate may then automatically guide the allocation of attentional resources within time. Anticipation based on a subjective hazard function can, however, not explain sequential FP effects. Therefore, we assume that a trial-to-trial learning process runs in parallel, which modulates the outcome of the hazard-related computations. This conjecture of course needs empirical testing, ideally involving computational modelling of the two processes to compare their explanatory power.

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5.4. The Neurobiology of Alertness Regulation

In the following section, some further thoughts on the roles of the anterior cingulate cortex (ACC) and anterior insula for maintaining alertness will be discussed. In Study 3, we discussed the non-motor function of the ACC in terms of a coordinating structure that controls the level of arousal (cf. Sturm et al., 1999; Mottaghy et al., 2006). The function of the anterior insula was regarded as representing the state of bodily arousal and feeding this information to the ACC as well as being part of the circuit that regulates peripheral arousal (Craig, 2002; Critchley et al., 2002). In light of Study 1, it seems reasonable to assume that maintaining the task set (e.g. goal-shielding) is important for maintaining high performance levels in SRT tasks, i.e. for maintaining alertness. Recent studies suggest that task-set maintenance might be subserved by a functional ACC–insula system. For instance, Dosenbach et al. (2006) found across ten different tasks and 183 subjects that dorsal ACC and bilateral anterior insula showed reliable start-cue and sustained activations across tasks. This was taken as evidence that these regions form a core system for implementing task sets. The notion that an ACC–anterior-insula network is involved in the maintenance of task sets is further supported by a study using resting-state fMRI (Dosenbach et al., 2007).

How might task sets be implemented and how could this process be related to arousal regulation? There might be a direct influence of ACC/insula on computational processes in other cortical regions via cortico-cortical interactions (e.g. connections between ACC and mid-cingulate motor zones), but there might also be an indirect influence mediated via subcortical loops that involve brainstem arousal centres (Corbetta, Patel & Shulman, 2008). The locus coeruleus (LC), a major brainstem arousal centre that innervates large parts of the cortex via widespread noradrenergic projections, receives input from ACC and insula (Aston-Jones & Cohen, 2005; Ongur, Ferry & Price, 2003). These inputs might transmit control signals through which ACC and insula regulate LC output. Apart from its role in mediating transitions between arousal-related behavioural states (e.g. sleep, alert wakefulness) through a change in its tonic firing mode (cf. Aston-Jones & Cohen, 2005), the LC system might also contribute to implementing task sets through its phasic burst activity, which has been interpreted as a “network reset” signal (Bouret & Sara, 2005) driving the (re)configuration of target networks after a target is detected and maybe when a target is expected, too. Since Study 3 found alertness-related activity in the vicinity of the LC, efficient SRT performance might depend on a repeated, ACC/insula-initiated and LC-mediated reset of the task-relevant brain network to “stay on the job” continuously.

This conceptualization of ACC control over subcortical arousal structures is also consistent with inferences drawn from behavioural deficits in patients with lesions in the ACC and medial frontal cortex: Stuss and colleagues (Picton, Stuss, Shallice, Alexander & Gillingham, 2006; Shallice, Stuss, Alexander, Picton & Derkzen, 2008; Stuss, 2006; Stuss et al., 1995, 2005) proposed that these regions subserve the “energization” of cognition, that is, they activate specific task schemata or task sets. This assumption is supported by the substantially slowed performance of patients with such lesions in various RT tasks (Alexander, Stuss, Shallice, Picton & Gillingham, 2005; Stuss et al., 2005; Stuss, Binns, Murphy & Alexander, 2002) as well as by their deficits in non-motor tasks of sustained attention (Shallice et al., 2008). Taking these findings together, we suggest the allocation of attentional resources, which according to Study 1 gets impaired with TOT, might be a metaphor for a network reset, and the dependence of the phasic LC mode on the underlying tonic mode (cf. Aston-Jones & Cohen, 2005) might constitute one of the neural underpinnings of the influence of arousal on the availability of such resources, as suggested by Kahneman (1973) or Humphreys and Revelle (1984). The ACC then might exert control over both LC firing modes, adaptively adjusting LC activity according to task demands as well as behavioural goals. This view of ACC function is also consistent with studies that argue for a general role of the ACC in self-regulation (Posner & Rothbart, 1998; Posner, Rothbart, Sheese & Tang, 2007), which agrees with our proposal of a hierarchical model of depletable self-regulatory power underlying performance decrements in tasks that require sustained attention.

Finally, there is a new, alternative but complementary hypothesis as to what kind of information might be processed in the anterior insula: recently, it has been suggested (Craig, 2009) that the anterior insula uses the representation of bodily states to perceive time. Specifically, this hypothesis assumes that through temporally integrating successive signals from within the body, a series of “emotional moments” is produced, which brings about the perception of duration. Therefore, based on this proposal, it might be speculated whether in RT tasks with variable interstimulus intervals, such as the one used in Study 3, anterior insula integrates information on elapsed time after each response and sends it to the temporo-parietal junction, where it is then used, together with probability representations, for the preparatory timing of the allocation of attentional resources. This fits nicely with our above conjecture regarding the computation of a subjective hazard rate based on representations of elapsed time and the probability schedule of expected events.

5.5. Implications for Future Research and Applications

The findings of this thesis demonstrate that alertness as measured with SRT tasks is far from being a unitary entity. The main reason for this state of affairs lies in the differences between the theoretical concept and its operationalization. It is generally assumed that every operationalization is only an impure reflection of the concept it purports to measure. This concerns the well-know issue of construct validity, which is never perfect, since any transition from the level of abstract, latent concepts to concrete, manifest measures introduces factors that are specific to the given operationalization and diminishes conceptual overlap between the latent construct and its manifest indicator. As already mentioned in the introduction, alertness is usually measured by means of SRT tasks. It is defined, however, as readiness to respond to external events (cf. Posner, 1978). Therefore, the aspect of motor activity in its operationalization via SRT tasks is a component that goes beyond the theoretical definition, since response readiness does not necessarily include responding, at least not only overt responding. This means the motor part of SRT tasks constitutes a specific factor unrelated to the theoretical concept. The problem for diagnostic applications that results from this is that differences in SRT performance between people might not be related to true differences in alertness (in its theoretical meaning) but to differences in computational processes related to producing rapid stimulus-contingent motor output.

Therefore it may be advisable for future research as well as applications to employ several different operationalizations of alertness. Apart from SRT tasks, this could be tasks that require a high sensory responsiveness without involving a fast motor response. These tasks should also reflect (aspects of) the construct “alertness” validly. Such a task could, for example, require participants to mentally count slight deviations in a given feature of stimuli that are presented only very briefly. Or, the task could require the detection of subtle differences in the onset of two stimuli presented (nearly) in parallel. Since all these potential operationalizations in principle suffer from the same limitation of incomplete overlap with the latent construct, future research or applied testing may consider using more than just one task to measure alertness. In fact, this notion is an extension of the approach adopted in Study 3. However, instead of using different modalities to investigate the core brain network subserving alertness, the proposed method would entail using different types of task to get down to the core. This approach is not new; for instance, research on sustained attention has employed a variety of paradigms that differ in their task-specific additional factors, such as the continuous performance task (which itself is used in several versions), the rapid visual information-processing task, sustained counting, or serial mental addition, just to name a few.

In addition to this “conjunction” approach it might be worthwhile to study SRT tasks more systematically. Since they constitute the primary operationalization of alertness and are widely used in applied neuropsychological settings (e.g. Sturm, 2006; Zimmermann & Fimm, 1993), it might be advantageous to learn more about the different component processes of this task. This would comprise (a) applying manipulations that specifically target one of the assumed subprocesses; (b) delineating the specific computational contributions of each part of the brain network involved; and (c) using sophisticated ways of RT and error analysis that go beyond means or medians (e.g. distributional analyses) to develop indices that specifically reflect changes in one of the contributing subprocesses. These developments are hoped to improve both the understanding of the specific mechanisms through which different factors affect alertness and the diagnosis of specific deficits in various patient populations.

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APPENDIX

Appendix A

Table A1

Supramodal General Task-Related Activity

Cluster/Area	x, y, z	z-score
Cluster 1 (k = 19110, p < .001)		
L SMA (BA 6)	-6 -8 54	Inf.
R cerebellar vermis	6 -58 -18	Inf.
R anterior cerebellar lobe	20 -48 -26	Inf.
R anterior cerebellum (vermis)	14 -50 -22	Inf.
L precentral gyrus	-30 -26 56	Inf.
L thalamus	-16 -16 4	7.80
L dorsal premotor cortex (BA 6)	-38 -18 52	7.75
L precentral gyrus	-32 -24 66	7.49
L frontal operculum	-46 2 0	7.44
L posterior STG	-48 -26 14	7.03
L middle insula/claustrum	-32 0 -4	6.71
L anterior insula	-30 16 10	6.57
L posterior insula	-42 -30 20	6.39
R inferior frontal gyrus/anterior insula	44 20 2	6.16
L middle insula/Rolandic operculum	-40 -2 12	5.89
R thalamus	10 -14 4	5.80
R dorsal premotor cortex (BA 6)	44 0 50	5.30
R anterior cingulate cortex (BA 32)	4 16 40	5.13
R pre-SMA (BA 8)	8 16 48	4.95
L precentral gyrus	-56 -22 42	4.89
L posterior cingulate cortex (BA 31)	-10 -26 48	4.78
R subthalamic nucleus	16 -10 -6	4.67
L posterior cingulate cortex (BA 23)	0 -24 28	4.62
L temporo-parietal junction (BA 40/22)	-60 -38 24	4.55

L inferior parietal lobule	-52 -38 48	4.53
R ventral premotor cortex (BA 44)	52 8 6	4.50
L nucleus ruber	-8 -18 -14	4.49
R putamen	28 0 6	4.46
L rostrodorsal pons (locus coeruleus)	-6 -26 -18	4.40
Cluster 2 (k = 483, p < .001)		
L middle/inferior occipital gyri	-28 -90 -4	Inf.
Cluster 3 (k = 604, p < .001)		
R middle/inferior occipital gyri	32 -88 -4	Inf.
R inferior occipital gyrus	38 -68 -6	3.61
Cluster 4 (k = 3218, p < .001)		
R posterior STG	60 -36 14	7.14
R temporo-parietal junction (BA 40/22)	54 -38 22	6.77
R inf. parietal lobule	48 -48 44	5.81
R posterior MTG	66 -34 0	5.34
R inferior parietal lobule	46 -42 40	5.29
R posterior MTG	54 -38 2	4.98
R posterior insula	36 -34 20	4.30
R intraparietal sulcus	30 -50 40	4.29
R posterior STS	52 -24 -10	3.95
R posterior STG	64 -16 8	3.44

Note. L = left; R = right; BA = Brodmann area; (pre-)SMA = (pre-)supplementary motor area; STG/MTG = superior/middle temporal gyrus; STS = superior temporal sulcus. Coordinates x, y, z refer to MNI space; k = number of voxels in cluster; p-value represents cluster-level error probability corrected for multiple comparisons.

Appendix B

Table A2

Alertness-Related Activity in the Mixed Condition

Cluster/Area	x, y, z	z-score
Cluster 1 (k = 338, p = .002)		
L posterior STS (TPJ)	-58 -46 10	5.53
Cluster 2 (k = 435, p < .001)		
R precentral gyrus (dPMC)	36 0 48	5.07
R middle frontal gyrus	32 10 48	4.56
Cluster 3 (k = 623, p < .001)		
L middle frontal gyrus	-30 2 52	4.90
L precentral gyrus (dPMC)	-28 -4 50	4.86
L superior frontal gyrus	-20 2 56	4.43
Cluster 4 (k = 800, p < .001)		
R middle precuneus	0 -58 48	4.83
L anterior precuneus	-8 -48 56	3.98
L middle precuneus	-12 -70 44	3.65
L anterior precuneus	-8 -46 48	3.60
R middle precuneus	6 -68 42	3.21
Cluster 5 (k = 363, p = .002)		
R posterior STG (TPJ)	52 -46 14	4.47
R posterior STS (TPJ)	46 -44 14	4.33
Cluster 6 (k = 286, p = .005)		
R inferior frontal gyrus (pars triangularis)	40 20 18	4.42
R inferior frontal gyrus (pars triangularis)	40 14 24	4.01
R inferior frontal gyrus (pars opercularis)	36 6 24	3.42
Cluster 7* (k = 140, p = .085)		
R pre-SMA (BA 8)	6 30 46	4.17
R pre-SMA (BA 6)	8 22 50	4.16

Cluster 8 (k = 232, p = .014)		
R angular gyrus	34 -62 40	3.86
R angular gyrus	36 -58 46	3.84

Note. L = left; R = right; BA = Brodmann area; TPJ = temporo-parietal junction; dPMC = dorsal premotor cortex; pre-SMA = pre-supplementary motor area. Coordinates x, y, z refer to MNI space; k = number of voxels in cluster; p-value represents cluster-level error probability corrected for multiple comparisons.

* significant only at corrected cluster-level p < .1

Appendix C

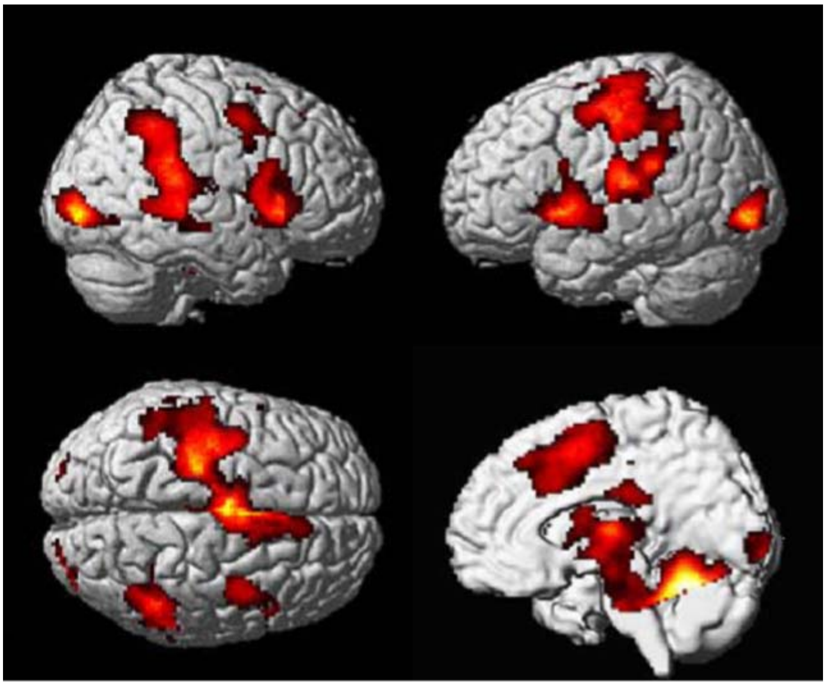

Figure A1. General task-related brain activity across all three unimodal conditions (alertness tasks vs. resting baseline).

Appendix D

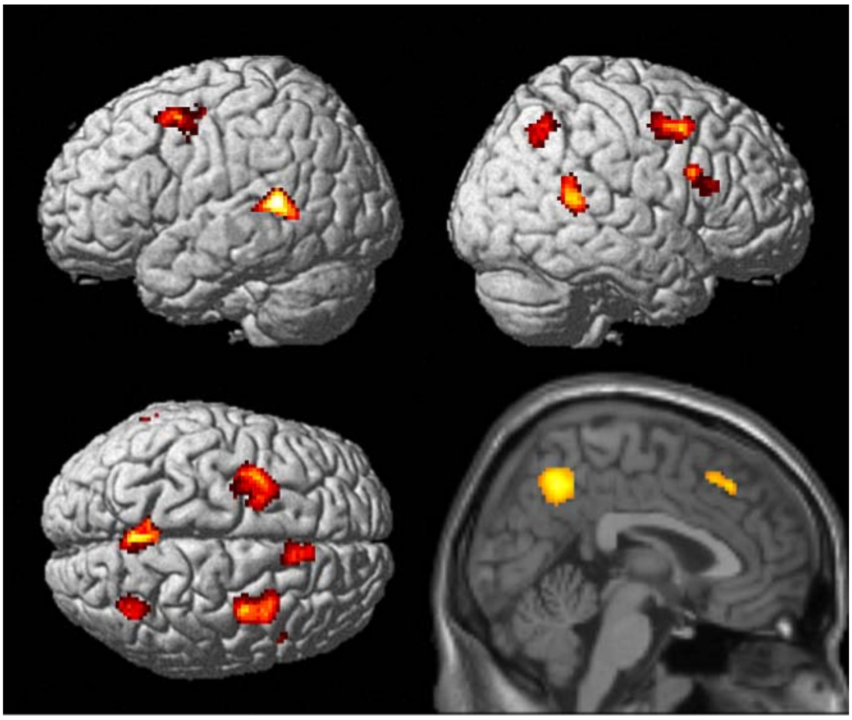

Figure A2. Alertness-related brain activity in the mixed condition with unpredictable stimulus modality (alertness task vs. unimodal control tasks)

Appendix E

Supplemental Discussion

General Task-Related Brain Activity

The comparison of brain activity during task versus baseline revealed a widespread network shared between all three unimodal task conditions, comprising foci in all lobes of the brain as well as in midbrain, brainstem, and cerebellar structures (see Table A1 and Figure A1). This finding replicates and extends results of earlier studies that explored supramodal brain activity elicited by simple reaction-time tasks using stimuli of the same three sensory modalities (Kansaku et al., 2006; Naito et al., 2000). Activity foci not previously reported in those studies as belonging to a modality-independent network might have been detected here because of the higher sensitivity of our study resulting from more trial replications (task duration per modality: Naito et al.: 200 ms; Kansaku et al.: 3 x 27 ms) and from the larger sample size (Naito et al.: n = 9; Kansaku et al.: n = 10). As expected, the general task-related network mainly consisted of areas controlling attention and motor output. Primary sensory cortices commonly activated comprised left-sided somatosensory and occipital areas. The former finding most likely reflects processing of sensory input elicited by pressing the response button; activity in occipital cortex may be the result of asking participants to fixate a small cross in all three unimodal conditions.

Reorienting to Stimulus Modality During the Mixed-Modality Condition

The assumed reorienting of attention might be subserved by right posterior parietal cortex, which showed significantly increased activity in the alertness vs. control comparison but did not survive the direct comparison between mixed and unimodal alertness conditions (see Figure A2). This parietal region (right angular gyrus) has been associated with stimulus-driven attentional shifts to a given stimulus location if the stimulus is task-relevant (Indovina & Macaluso, 2007). In our experiment, similar stimulus-driven shifts may have occurred between modalities when the participant was prepared for a different modality at the time of stimulus occurrence.

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