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Differential Effects of Lowered Arousal on Covert and Overt Shifts of Attention

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Abstract

Based on previous studies demonstrating detrimental effects of reduced alertness on attentional orienting our study seeks to examine covert and overt attentional orienting in different arousal states. We hypothesized an attentional asymmetry with increasing reaction times to stimuli presented to the left visual field in a state of maximally reduced arousal. Eleven healthy participants underwent sleep deprivation and were examined repeatedly every 4 hr over 28 hr in total with two tasks measuring covert and overt orienting of attention. Contrary to our hypothesis, a reduction of arousal did not induce any asymmetry of overt orienting. Even in participants with profound and significant attentional asymmetries in covert orienting no substantial reaction time differences between left- and right-sided targets in the overt orienting task could be observed. This result is not in agreement with assumptions of a tight coupling of covert and overt attentional processes. In conclusion, we found differential effects of lowered arousal induced by sleep deprivation on covert and overt orienting of attention. This pattern of results points to a neuronal non-overlap of brain structures subserving these functions and a differential influence of the norepinephrine system on these modes of spatial attention. (*JINS*, 2015, *21*, 545–557)

Keywords: Attention, Arousal, Sensory neglect, Reaction time, Sleep deprivation, Norepinephrine

INTRODUCTION

Numerous studies in patients and controls have demonstrated a predominant role of the right cerebral hemisphere in alertness and visuo-spatial attention (Asanowicz, Marzecová, Jaśkowski, & Wolski, 2012; Bartolomeo & Chokron, 2002; Chica et al., 2012; Corbetta & Shulman, 2011; Doricchi, Thiebaut de Schotten, Tomaiuolo, & Bartolomeo, 2008; Fellrath, Blanche-Durbec, Schnider, Jacquemoud, & Ptak, 2012; Fink, Marshall, Weiss, & Zilles, 2001; Hildebrandt, Giesselmann, & Sachsenheimer, 1999; Petersen & Posner, 2012; Sturm & Willmes, 2001; Vallar, 2001). Whereas right hemisphere lesions (RHL) lead to a reduction of alertness (Robertson, Mattingley, Rorden, & Driver, 1998), increased fatigue, a prolongation of reaction times (RTs) and left-sided neglect in a significant portion of patients compared to left-sided lesions (LHL), imaging studies consistently showed fronto-parietal attentional networks subserving alertness (Corbetta & Shulman, 2011; Coull, 1998; Petersen & Posner, 2012; Posner, 2008; Sturm & Willmes, 2001) and subprocesses of visuo-spatial attention (Hopfinger, Camblin, & Parks, 2010; Shulman & Corbetta, 2012; Vossel, Weidner, Driver, Friston, & Fink, 2012). One line of research focused on the potential overlap and resulting interactions of these networks within the right hemisphere. Indeed, Robertson et al. were able to alleviate neglect symptoms in RHL patients by increasing their alertness level with different interventions comprising passive movements of their left upper limbs (Robertson, Hogg, & McMillan, 1998), alerting self-instructions ("be alert!") preceding reactions to lateralized stimuli (Robertson, Tegner, Tham, LO, & Nimmo-Smith, 1995) and alerting stimuli preceding bilaterally presented visual stimuli (Robertson, Mattingley, Rorden, & Driver, 1998). These studies impressively confirmed modulation of visuo-spatial attention by the alertness network. Furthermore, it could be demonstrated that this modulation is not necessarily restricted to patients with gross neuropsychological impairments but can also be observed in controls. Thus, Fimm, Willmes, and Spijkers (2006) investigated a group of young participants every 4 hr over a total period of 28 hr applying a covert shift paradigm. Their sleep-deprived participants consistently

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showed prolongation of RTs to left-sided targets in a state of maximally reduced arousal at 5:00. This effect mainly represented a deficit in reorienting attention to the left hemispace. Thus, a strong reduction of arousal in normal participants led to specific left-sided visuo-spatial impairments resembling the neglect phenomenon in patients, albeit to a much lesser extent, confirming the dominant role of the right hemisphere. There is converging evidence from other studies in normal participants describing time-on-task effects and left-sided deficits with increasing fatigue (Bareham, Manly, Pustovava, Scott, & Bekinschtein, 2014; Benwell, Harvey, Gardner, & Thut, 2013; Newman, O'Donnell, & Bellgrove, 2013; Matthias et al., 2009; Dodds et al., 2008; Dufour, Toulazin, & Candas, 2007; Manly, Dobler, Dodds, & George, 2005b). Newman et al. (2013) additionally demonstrated changes in hemispheric activation asymmetry going along with the rightward behavioural shift in visuo-spatial orienting over time. Participants were asked to distribute their attention across both hemifields in anticipation of peripheral targets and α-band activity became more prominent over the right hemisphere relative to the left hemisphere as the task progressed. In a recent study, Bareham et al. (2014) extended research on attentional asymmetries with decreasing alertness to the auditory modality. In their study, volunteers performed an auditory spatial localization task while transitioning in and out of sleep. In particular, normal drowsiness was linked with a unidirectional tendency to mislocate left-sided acoustic stimuli to the right. Another line of research was mainly concerned with pseudoneglect, that is, the tendency of participants to show a left-sided shift in bisecting lines. This was repeatedly replicated in numerous studies (see Jewell & McCourt, 2000, for a review of modulating factors) and considered to be based on overattention to the left hemispace due to right-hemisphere dominance for visuo-spatial attention. This left-sided bias was shown to be reduced after sleep deprivation when circadian-based sleep propensity and accumulating sleep pressure coincided at 5:00 AM and led to a maximally reduced arousal level (Schmitz, Deliens, Mary, Urbain, & Peigneux, 2011).

The above-mentioned studies with normal participants demonstrating a detrimental effect of reduced alertness level on attentional orienting to the left mainly focused on covert shifts of attention and did not examine respective effects on overt orienting of attention, that is, the preferential processing of stimuli that have to be responded to following eye movements or visual search. Even if Posner (1980) and others demonstrated that covert shifts do not necessarily precede saccades but can be uncoupled from eye movements (irrespective of the kind of cue – exogenous or endogenous) it seems to be commonly accepted that neuronal networks presenting overt and covert attention do overlap to a large extent (Nobre, Gitelman, Dias, & Mesulam, 2000; Corbetta & Shulman, 1998; Beauchamp, Petit, Ellmore, Ingeholm, & Haxby, 2001; de haan, Morgan, & Rorden, 2008). However, this would suggest comparable effects of reduced arousal in both types of attentional orienting. To date, this has not been examined. A differential effect would suggest a more complex interaction between the alertness network and orienting beyond the assumption of nearly identical neuronal representations of covert and overt attentional shifts. Rather, this would suggest subtle differences between these attentional subprocesses as regards their modulation.

Therefore, our study sought to examine covert and overt attentional orienting repeatedly over 28 hr in total in a sample of normal participants who underwent sleep deprivation. We were not primarily interested in chronobiological aspects per se, such as the course of attentional processing by day. Rather, the repeated measures design of the study aimed at identifying intraindividual time points of maximum and minimum arousal within the 28 hr. All dependent measures were then analyzed with respect to these extreme levels of arousal. Some results on covert orienting of these participants have been published already (Fimm et al., 2006). In the present study, additional overt attention results and statistics on covert orienting as well as a single-case analysis in two participants are presented. Furthermore, we implemented a modified multivariate procedure (based on subjective and objective parameters) to identify time points of maximum and minimum state of arousal within the single case. Based on the literature, we hypothesized comparable effects on covert as well as on overt shifts of attention.

METHODS

Participants

Eleven participants (3 female, 8 male; 10 right-handed and 1 left-handed) without any neurological or psychiatric history with an age range of 26–34 years took part in the study. They were instructed to sleep between 6 and 8 hr in the night preceding the study. Furthermore, they were asked not to take any coffee or other stimulating substances after 11:00 on the first day of assessment which was obeyed by the participants. None of the participants took any medication with sedating or stimulating effect. The participants were not paid for taking part in the study.

Experimental Tasks

Overt orienting of attention

The task was presented on a 15 inch computer screen with the participants sitting at a distance of 50 cm in front of the screen. Each trial consisted of two stimuli presented either on the left or right side of a fixation point (unilateral presentation) located 2.9° and 5.2° from the middle of the screen or on both sides of the fixation point (bilateral presentation) both stimuli either 2.9° or 5.2° from the fixation point FP). Overall, two target and two distractor stimuli were used. There were trials with one target and one distractor or without targets (catch trials). Participants were instructed to fixate until the stimuli were presented. Peripherally presented targets could only be detected and discriminated by moving gaze to the target position as maintaining central fixation did not permit to identify the stimuli. The stimuli were presented for a duration of 3 s (non-critical trials) or until the subject detected the target and pressed a response button with the right hand in critical trials. Stimulus presentation was followed by an ISI of 3 s. The task consisted of 12 test conditions (8 critical conditions and 4 catch trial conditions) with 10 trials each leading to a total of 120 trials. With respect to the critical test conditions 3 factors have to be distinguished: SIDE of target (left *vs.* right hemifield), mode of PRESENTATION (unilateral *vs.* bilateral) and target DISTANCE from fixation point (near *vs.* far). Figure 1 gives an overview of the various test conditions.

Covert orienting of attention

The task had previously been described in detail (Fimm et al., 2006). On both sides of the fixation point two squares with a white outline against a black background were displayed and arranged horizontally (4.2 and 7.8 degrees of visual angle from the fixation point). After a fixed time interval the frame of one of the squares was lit up for 100 ms ("Cue"). Then, after a pseudo-randomized time delay of 50, 100, 150, 200, or 250 ms the target, a white oblique cross ("X") against a black background placed inside one of the squares together with a lighting-up of its frame appeared. The task was to press a button with the right hand as quickly as possible as soon as the target appeared. Following the participant's response the next trial began after a variable time interval of 1500 to 2500 ms. The probability of valid trials (cue and target in the same position) was 60 % with 40 % invalid trials, 200 trials were presented per session. One restriction was introduced: In invalid trials with bilateral presentation (cue and target in different hemifield), the distance of both cue and target from the fixation point was identical, that is, both would be far away or close to the fixation point. Thus, four factors were integrated in the experimental setup: VALIDITY of the cue (valid/invalid), SIDE of the target (left or right hemifield), DISTANCE of the target (far or close from the fixation point), and PRESENTATION (cue and target in the same or in a different hemifield). Eye movements between or during test trials were observed by the experimenter (sitting opposite the participant in a 45° angle without distracting him) and

	Fixation	Target side	Presentation	Distance from FP
1	+	Left	Bilateral	Near
2	+	Right	Bilateral	near
3	+	Left	Bilateral	Far
4	+	Right	Bilateral	Far
5	+	Left	Unilateral	Near
6	+	Left	Unilateral	Far
7	+	Right	Unilateral	Near
8	+	Right	Unilateral	Far
9	+	Catch trial		
10	+	Catch trial		
11	+	Catch trial		
12	+	Catch trial		

Fig. 1. Test conditions of the overt attention task with sample stimuli per condition. "10" and "01" are the target stimuli that have to be responded to by a button press with the right hand.

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registered *via* button press. These latter trials were excluded from subsequent analyses.

Design of the study

The participants were examined every 4 hr (9:00, 13:00, 17:00, 21:00, 1:00, 5:00, 9:00, 13:00) in a standardized setting under control of the examiner and with each session lasting approximately 30 min; none of them fell asleep. The order of administration of the overt and covert orienting tasks was counterbalanced between testing session and between participants. In addition to the computerized tasks, the peripheral body temperature (ear) was measured at the beginning of each session and the participants were subsequently asked to rate their state of health on four bipolar 7-point rating scales with the endpoints (a) relaxed *versus* anxious, (b) awake *versus* tired, (c) free of *versus* strong complaints, and (d) pleasant *versus* unpleasant.

All persons gave their informed consent for participation in the study, which was approved by the local ethics committee of the medical faculty in accordance with the declaration of Helsinki.

Statistical Analysis

The data were analyzed with IBM SPSS statistics version 20 using Repeated Measures Analysis of Variance and effect sizes (η_p^2) were reported. In a former study (Fimm et al., 2006), participants' performance in the covert orienting task at time points of presumed maximal and minimal arousal (17:00 *vs*. 5:00) was compared. In our present study, we applied a much more elaborate factor analytic procedure to determine individual points of minimal and maximal arousal per subject based on body temperature, subjective rating of fatigue and overall RTs in the covert and overt orienting tasks (see results section).

RESULTS

Body Temperature, Subjective Tiredness, and Overall RT in the Experimental Tasks

Figure 2a displays the course of the body temperature at the different time points indicating a maximum at 17:00 and a minimum at 5:00. Furthermore, interindividual differences in body temperature are minimal at 17:00 and maximal at 5:00 suggesting that states of low arousal seem to vary considerably, presumably caused by chronotype (Schmidt, Collette, Cajochen, & Peigneux, 2007). In fact, only five participants showed minimal body temperature at 5:00, whereas other participants exhibited their lowest temperature at 9:00 or 1:00 on the first day or even 9:00 or 13:00 on the second day of examination. Such remarkable interindividual variability can also be observed in the participants ratings of tiredness (Figure 2b). Individual points of maximum tiredness can be found at time points 4 and 6–8 with only four participants reporting maximum tiredness at 5:00. The same holds true for the course of RT in the experimental tasks showing remarkable interindividual variability. The longest intraindividual RTs in the covert attention task (see Figure 2c) could be found at 9:00 (first day; 6 participants), 5:00 (4 participants), and 9:00 (second day; 1 subject). In the overt attention task (see Figure 2d), one subject showed

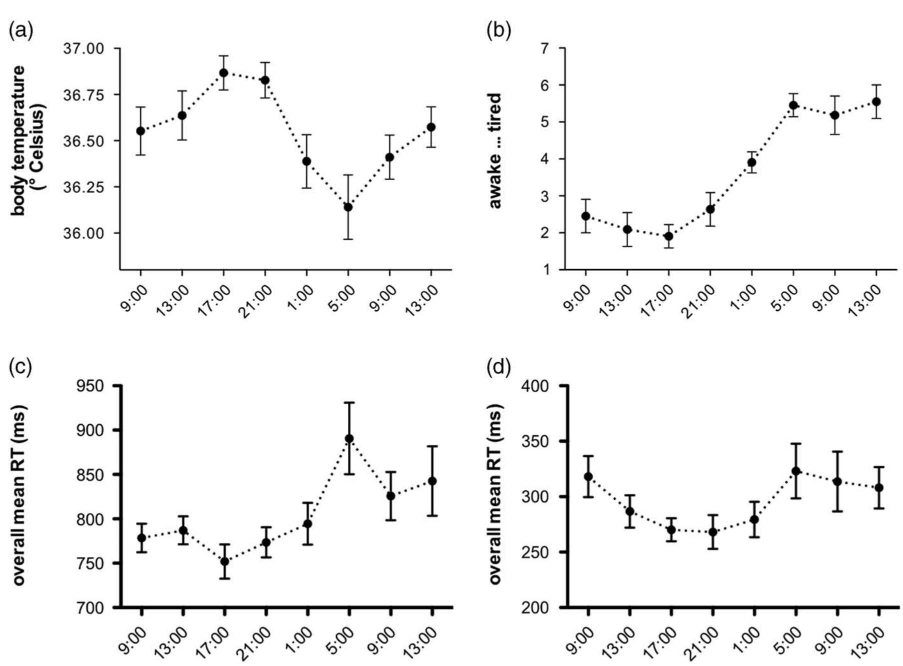

Fig. 2. Course of (a) body temperature, (b) estimated tiredness, (c) overall mean RT in the overt attention task, and (d) overall mean RT in the covert attention task. Error bars represent standard errors of the mean.

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his longest RT on 13:00 (first day), one subject at 21:00, four participants at 5:00, two participants at 9:00 (second day), and three participants at 13:00 (second day).

Determination of Individual Points of Minimal and Maximal Arousal

Because a descriptive analysis of physiological, subjective and performance measures revealed substantial inter-individual differences in (a) the profile per time point across these measures and (b) in the course of the study, making it difficult to determine arousal level, we tried to use a rational multivariate procedure. Using (1) body temperature, (2) subjective ratings of fatigue, (3) the mean of the median RTs in the eight test conditions of the overt orienting task, and (4) the mean of median RTs of the valid-cue conditions in the covert orienting task as variables, we performed a principal component (PCA) factor analysis within every subject, using the Kaiser-Guttman criterion (eigenwert >1) for deciding on the number of principal components to be extracted. Thus, four variables with eight replications each (for each time point) entered the PCA. In case of high inter-correlations between the four measures, a one-factor solution resulted, in other cases two-factor solutions emerged. Two-factor solutions were Varimax-rotated for simple structure and to facilitate interpretation. Subsequently, factor scores based on the regression method were computed. In some cases, factor scores had to be inverted (multiplied by "−1") to achieve homogeneous polarity of all factors. Thus, high positive factor scores represent minimal arousal, high negative values indicate maximal arousal. With two-factor solutions, the sum of both factor scores was computed with high positive values again representing low arousal and high negative values indicating high arousal. One-factor solutions were found in participants showing parallel arousal variation in all variables, two-factor solutions could be observed, when arousal induces differential effects on the variables. Figure 3 exemplifies the procedure with two participants (subject 1 with a one-factor and subject 2 with a two-factor solution). The raw data of both participants can be seen on the left hand side, factor loadings of the variables are displayed in the middle, factor scores are presented on the right-hand side. Regarding subject 1, there is a negative loading of temperature (−.872; low temperature is associated with low level of alertness) and high positive loadings of the subjective rating (high rating = very tired = low arousal) and the RTs of both tasks (large number = slowed RTs = low arousal). Subject 11 shows a somewhat different picture with high positive loadings of subjective tiredness and Covert orienting RT on factor 1 and a highly negative loading of temperature as well as a highly positive loading of overt orienting RT on factor 2 indicating a dissociation of physiological, subjective and performance measures in the course of the study. Figure 4 displays the raw data of both participants and illustrates this dissociation in subject 11 and the high correlations of the four measures in subject 1.

Raw data

Subject 1	Body temperature	Subjective rating „awake vs. tired"	Covert orienting RT	Overt orienting RT
9:00	36,82	1	334,75	815,25
13:00	36,80	4	306,38	863,38
17:00	36,88	3	289,50	808,19
21:00	36,69	4	343,00	812,31
1:00	36,43	4	344,38	956,19
5:00	36,36	7	427,00	1061,50
9:00	36,55	7	370,50	1027,10
13:00	36,68	6	369,50	1141,20

Subject 11	Body temperature	Subjective rating „awake vs. tired"	Covert orienting RT	Overt orienting RT
9:00	36,42	2	296,50	849,00
13:00	36,27	2	256,00	823,69
17:00	36,57	1	246,13	815,00
21:00	36,19	1	239,75	848,06
1:00	36,13	5	297,50	830,00
5:00	36,01	6	337,63	872,00
9:00	36,45	7	298,50	796,19
13:00	36,52	6	305,25	801,88

Factor structure (PC-analysis; Eigenwert-Criterion; Varimax rotation)

Subject 1	Factor
	1
Temperature (°C)	-,872
Subjective tiredness	,900
Covert orienting RT (ms)	,920
Overt Orienting RT (ms)	,897

Subject 11	Factor	
	1	2
Temperature (°C)	-,194	-,904
Subjective tiredness	,975	-,123
Covert orienting RT (ms)	,926	,244
Overt orienting RT (ms)	-,089	,958

Factor scores per time point and factor

Subject 1	Factor score	
9:00	-1,063	
13:00	-,717	
17:00	-1,199	maximal arousal
21:00	-,422	
1:00	,269	
5:00	1,557	minimal arousal
9:00	,830	
13:00	,746	

Subject 11	Factor score		Sum	
	1	2		
9:00	-,313	,281	-,032	
13:00	-,757	,022	-,735	
17:00	-1,159	-,873	-2,033	max.
21:00	-1,287	,742	-,545	
1:00	,504	,447	,951	
5:00	1,162	1,670	2,832	min.
9:00	1,005	-1,151	-,146	
13:00	,845	-1,137	-,292	

Fig. 3. Overview of the sequential procedure to determine points in time of minimal and maximal arousal with two sample participants. The raw data of both participants (four variables; left hand side) enter a PC-analysis with Varimax-rotation if more than one factor is extracted according to the eigenwert-criterion. Factor values (or sum of factor values in the case of two factors) are computed in a final step with maximum values indicating minimal (low) arousal and vice versa.

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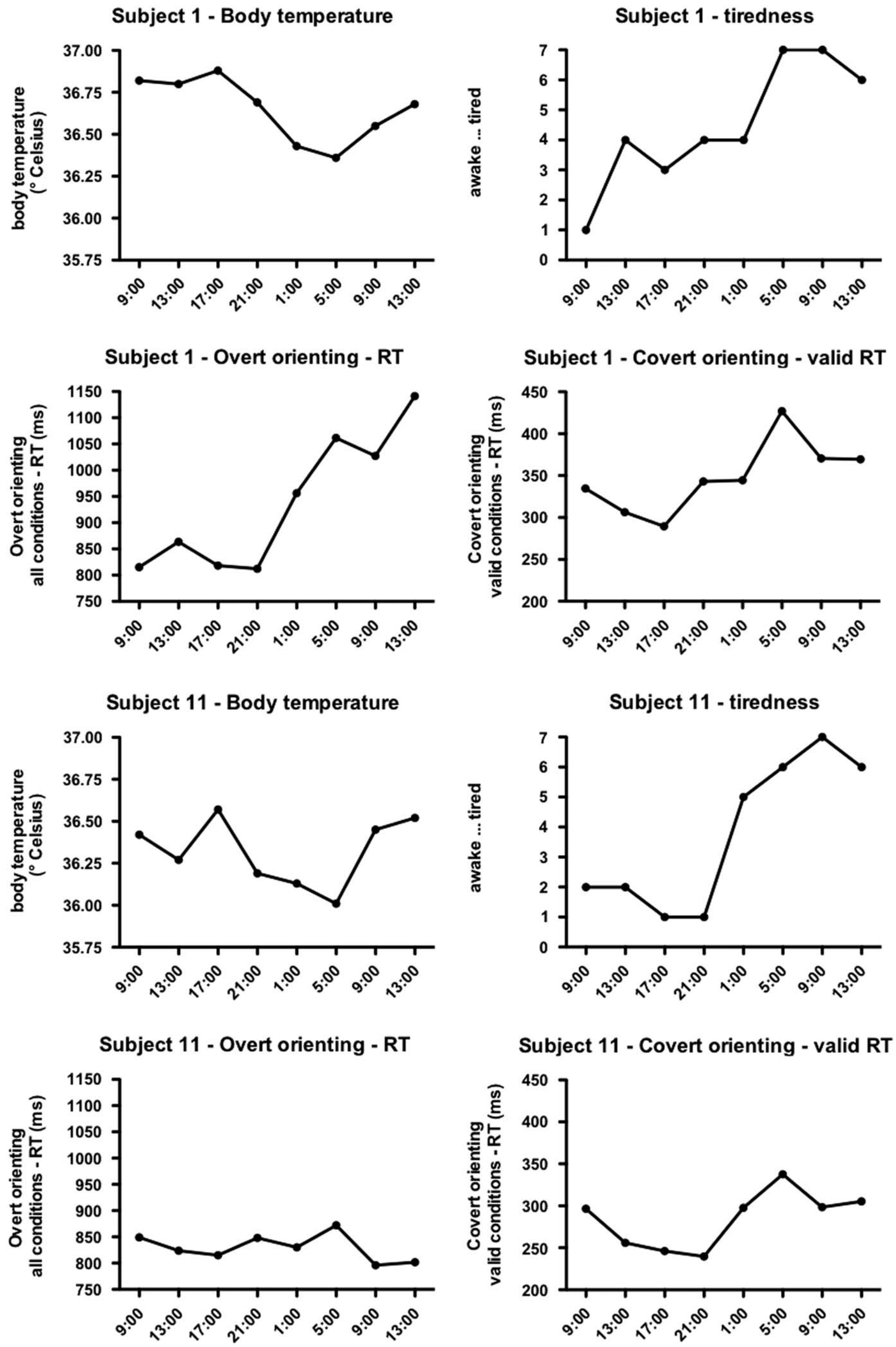

Fig. 4. Participants 1 and 11: data on body temperature, subjective rating of tiredness, overall RT in the overt orienting task, and RT in the valid-cue-conditions of the covert orienting task. In subject 1, the four measures highly correlate, in subject 11 overt and covert orienting dissociate.

Table 1 summarizes the results of the PC analyses for all subjects individually. In subsequent repeated measures analyses of variance (ANOVA), both (individually defined) time points of minimal and maximal arousal will be compared with respect to covert and overt orienting of attention.

Overt Orienting of Attention

A repeated measures ANOVA including the within-subject factors AROUSAL (max. *vs*. min.; representing time points of individual maximum and minimum arousal), SIDE OF TARGET (left *vs*. right hemifield), PRESENTATION (bilateral *vs*. unilateral presentation of stimuli), and DISTANCE (distance of target from fixation point) was applied. To correct for (a) correlation of cell means and standard deviations and (b) skewed distribution of the dependent measure, RTs were log-transformed according to Kirk (2012). Omissions were not analyzed, because only two participants showed isolated omissions with low arousal whereas nine participants detected all targets.

Significant effects of AROUSAL ($F(110) = 21.67$; $p = .001$; $\eta_p^2 = .68$), PRESENTATION ($F(1,10) = 69.55$;

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Table 1. Time points of minimal and maximal arousal

Subject	Minimal (low) arousal	Maximal (high) arousal
1	5:00	17:00
2	21:00	9:00 (2nd day)
3	5:00	21:00
4	9:00 (first day)	21:00
5	5:00	17:00
6	13:00 (2nd day)	17:00
7	5:00	13:00
8	13:00 (2nd day)	13:00
9	5:00	21:00
10	5:00	17:00
11	5:00	17:00

Note. Determined by factor values resulting from the individual Principal Component Analysis and subsequent Varimax rotation of extracted factors (if number of factors >1) based on body temperature, subjective rating of tiredness, and reaction times in the covert and overt experimental paradigms.

$p < .001$; $\eta_p^2 = .87$), and DISTANCE ($F(1,10) = 56.10$; $p < .001$; $\eta_p^2 = .85$) were found. RTs were longer at time points of minimal arousal, with bilateral presentation of stimuli, and in test conditions with targets being presented far from fixation. Furthermore, the PRESENTATION by DISTANCE interaction ($F(1,10) = 22.87$; $p = .001$; $\eta_p^2 = .70$; see Figure 5) was significant. RTs to bilaterally presented stimuli and targets at the "near" position were prolonged (compared to unilaterally presented "near" targets; $t(10) = 10.13$; $p < .001$; cohen's $d = 1.5$) irrespective of AROUSAL. However, there was no significant difference between bilaterally and unilaterally presented stimuli at far positions ($t(10) = 1.94$; $p = .081$).

Additionally, the AROUSAL by PRESENTATION by DISTANCE interaction ($F(1,10) = 4.51$; $p = .06$; $\eta_p^2 = .31$; see Figure 6) was marginally significant indicating a prolongation of RTs to far and a reduction of RTs to near targets with low arousal. However, no SIDE-effects in relation to arousal and overt orienting of attention could be observed.

Covert Orienting of Attention

Again, a repeated measures ANOVA with the within-subject factors AROUSAL (max. *vs*. min.; representing time points of individual maximum and minimum arousal), SIDE OF TARGET (left *vs*. right hemifield), VALIDITY (valid *vs*. invalid cue; only invalid trials with bilateral presentation of cue and target, that is, cue and target in different hemifields), and DISTANCE (far *vs*. near target distance from fixation point) was used. The significant main effects AROUSAL ($F(1,10) = 13.07$; $p = .005$; $\eta_p^2 = .57$), SIDE ($F(1,10) = 8.31$; $p = .016$; $\eta_p^2 = .45$), and DISTANCE ($F(1,10) = 5.15$; $p = .047$; $\eta_p^2 = .34$) indicate longer RTs with low arousal, with left-sided targets, and with far targets. The significant AROUSAL by VALIDITY by DISTANCE interaction ($F(1,10) = 8.71$; $p = .015$; $\eta_p^2 = .47$) indicates a greater validity effect at near locations in a state of low arousal, irrespective of the side of the target (see Figure 7).

We subsequently focused exclusively on all invalid conditions (bilateral AND unilateral presentation of cue and target) and applied a repeated measures ANOVA with the factors AROUSAL, SIDE OF TARGET, and DISTANCE. This approach revealed significant main effects of AROUSAL ($F(1,10) = 9.00$; $p = .013$; $\eta_p^2 = .47$), SIDE OF TARGET ($F(1,10) = 5.60$; $p = .039$; $\eta_p^2 = .36$), and a significant AROUSAL by SIDE OF TARGET interaction ($F(1,10) = 5.60$; $p = .04$; $\eta_p^2 = .36$) caused by prolongation of RTs to left-sided targets in a state of low arousal (see Figure 8). The distance of the target to the fixation point does not seem to play a role when comparing different invalid conditions.

For the four target positions (left side – far from fixation point (FP), left side – near FP, right side – near FP, right side – far from FP) the mean re-orienting costs are 20.98 ms (*SD*: 63.81 ms), 33.00 ms (67.74 ms), 23.25 ms (38.72 ms),

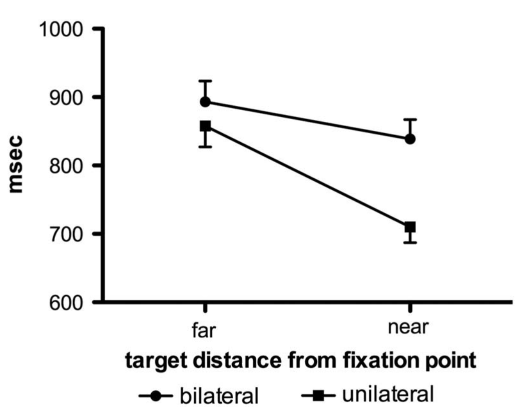

Fig. 5. Overt orienting of attention: PRESENTATION by DISTANCE interaction based on median RTs. Unidirectional error bars represent standard errors of the mean.

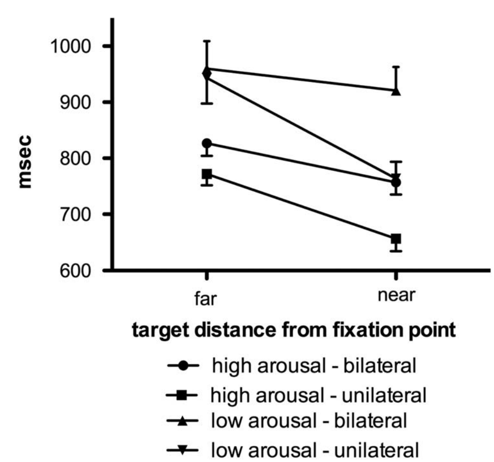

Fig. 6. Overt orienting of attention: AROUSAL by PRESENTATION by DISTANCE interaction based on median RTs. Unidirectional error bars represent standard errors of the mean.

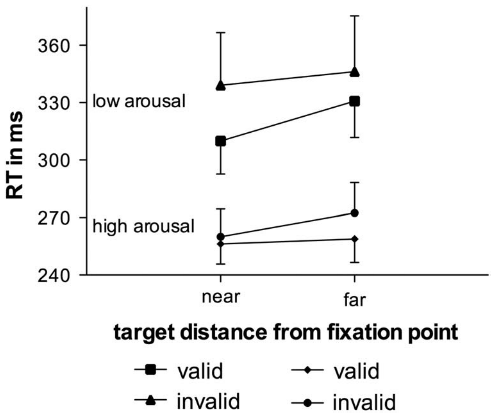

Fig. 7. Covert orienting of attention: AROUSAL by VALIDITY by DISTANCE interaction based on median RTs. Unidirectional error bars represent standard errors of the mean.

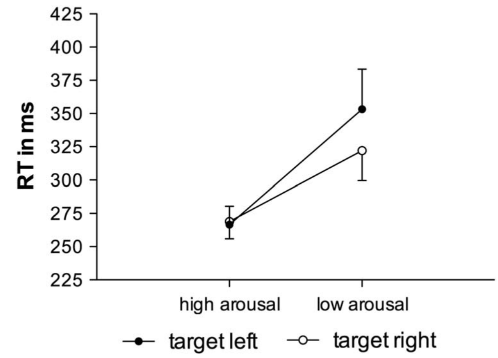

Fig. 8. Covert orienting of attention: AROUSAL by SIDE OF TARGET interaction based on median RTs in all invalid test conditions. Unidirectional error bars represent standard errors of the mean.

and −8.27 ms (35.27 ms) for low arousal and 7.84 ms (23.62 ms), 7.00 ms (28.21 ms), 12.07 ms (19.91 ms), and 14.00 ms (18.89 ms) for high arousal. A repeated measures ANOVA with the factors AROUSAL, SIDE OF TARGET, and DISTANCE resulted in a significant TIME by DISTANCE interaction ($F(1,10) = 15.30$; $p = .003$; $\eta_p^2 = .61$) with greater re-orienting costs to targets near fixation point in a low arousal state. AROUSAL ($F(1,10) = .40$; $p = .54$; $\eta_p^2 = .04$), SIDE ($F(1,10) = 2.18$; $p = .171$; $\eta_p^2 = .18$) and TIME by SIDE ($F(1,10) = 2.14$; $p = .174$; $\eta_p^2 = .18$) are not significant. It is assumed, that computing the difference between invalid and valid conditions eliminates substantial AROUSAL and SIDE effects as these also exist in valid conditions (see repeated measures ANOVAs mentioned above with main effects of AROUSAL and SIDE). Thus, arousal effects are not confined to re-orienting of attention but also influence orienting with valid cues.

Relation of Covert and Overt Attention with Low Arousal

A single-case analysis of attentional asymmetries with low arousal adds further information on the relation of covert and overt attentional orienting. The results of the two participants with most prominent arousal-dependent asymmetries of attentional orienting are displayed in Figure 9, contrasting covert and overt orienting. A two-condition randomization test (Edgington & Onghena, 2007) based on median RTs in the eight invalid test conditions of the covert orienting task revealed a significant (70 permutations; one-tailed $p = .029$) prolongation of RTs to left-sided targets *versus* right-sided targets in both participants. In contrast, comparison of RTs to left- and right-sided targets in the eight overt orienting test conditions *via* randomization test does not show any significant difference (as can easily be gleaned from Figure 9). It is striking that even such strong asymmetries of covert attentional orienting are not associated with respective overt asymmetries.

DISCUSSION

In our study we investigated the effect of lowered arousal induced by sleep deprivation on covert and overt attentional orienting. Based on the assumptions of (1) interactions of the neural networks of alertness and orienting, and (2) neural overlap of areas representing covert and overt attentional orienting we expected comparable results in both attentional orienting domains. More specifically, we hypothesized attentional asymmetry with increasing RTs to stimuli presented to the left visual field in a state of maximally reduced arousal after sleep deprivation. In previous work, we were able to demonstrate asymmetries of covert orienting in sleep deprived healthy participants. The current study now extends our findings (Fimm et al., 2006) by using a more elaborate strategy to identify individual points of minimum and maximum arousal and by analyzing both covert and overt orienting of attention.

Participants responded more slowly to left-sided-targets in the covert orienting task at points of minimal arousal. Thus, we not only replicated our previous finding of an asymmetry of covert orienting, but we were able to show that the strategy to compare individual time points of minimal and maximal arousal (and not just fixed time points as we did in a previous study) is feasible to minimize interindividual differences in chronobiology and renders more precise conclusions about the role of the alertness network in attentional orienting.

Contrary to our hypothesis, sleep deprivation did not induce any asymmetry of overt orienting. Even in participants with profound (and significant) attentional asymmetries in covert orienting, no substantial RT differences to left- and right-sided targets in the overt orienting task could be observed. However, we found a large effect on overall detection times when overtly orienting to peripheral targets more distant from a central fixation point. Furthermore, and not surprisingly, overt RTs to targets, which are located in the same visual field as the distractors (unilateral presentation), were significantly shorter than to targets in the bilateral presentation condition. In the former situation no choice

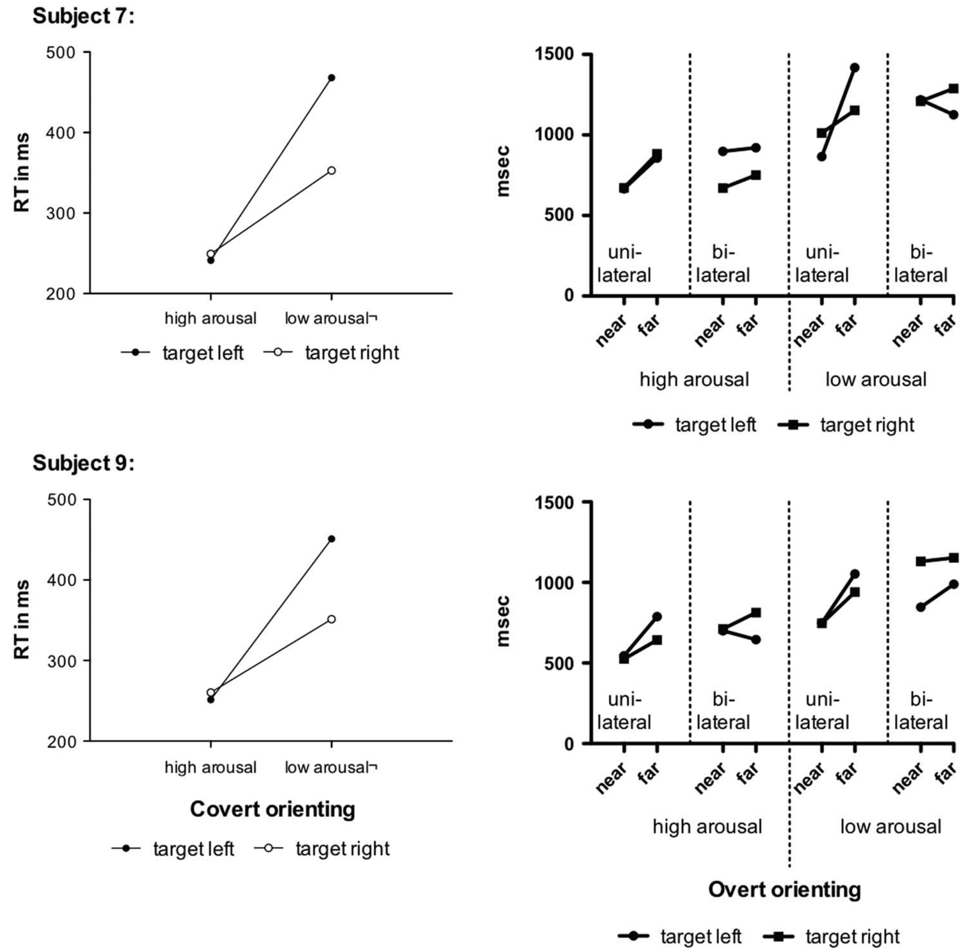

Fig. 9. Covert and overt orienting in two participants with most prominent and significant (one-tailed $p < .05$; two-condition randomization test) attentional asymmetries between left- and right-sided targets in the covert orienting task. There are no horizontal attentional asymmetries in the overt orienting task.

according to the direction of the saccade (left or right) has to be made thus speeding up target search.

Our study primarily suggests a dissociation of overt and covert orienting of attention in participants without any cerebral lesion undergoing sleep deprivation. Whereas significant reduction of arousal leads to an asymmetry of covert orienting, namely a prolongation of RTs to left-sided targets, no asymmetry of overt orienting could be observed. Rather, target detection times (after having initiated a saccade to the target and/or distractor) are increased irrespective of the side of the stimulus. This result is not in line with assumptions of a tight coupling of covert and overt attentional processes. The alertness network seems to exert a differential influence on covert and overt orienting processes.

A closer look at the studies reporting effects of activation or increasing alertness level on neglect symptoms (Robertson et al., 1995; Robertson, Mattingley, et al., 1998; Robertson, Hogg, et al., 1998) shows that mainly complex behavioral measures and complex visual displays or scenarios such as the Baking Tray Task (Robertson et al., 1995; Robertson, Hogg, et al., 1998; Thimm, Fink, Küst, Karbe, & Sturm, 2006), letter cancellation (Manly, Cornish, Grant, Dobler, & Hollis, 2005a; Robertson, Mattingley, et al., 1998), balloons and star cancellation tasks (Dobler, Manly, Verity, Woolrych, & Robertson, 2003), or a combing and a navigation task (Robertson, Hogg, et al., 1998) were used. These tasks heavily rely on both overt and covert attention. Studies implementing experimental methods trying to disentangle the attentional components primarily focus on covert attention such as Robertson, Mattingley, et al. (1998), whose right-hemisphere neglect patients had to judge, whether a visual stimulus on the left of fixation preceded or followed a comparable stimulus on the right. Furthermore, Thimm et al. (2006, 2009) reported positive effects of alertness training on neglect symptoms by using a computerized detection task (with no eye movements and no cues included) as performance measure, a computer-based visual search task and cancellation tests. Pharmacologically increasing alertness by use of psychostimulants leads to similar effects in normal participants, that is, increasing bias to the left (Dodds, Müller, & Manly, 2009). It could even be demonstrated that short-lived phasic alerting effects lead to an improvement of covert attentional orienting to the left side in patients with right hemisphere lesion and signs of visual hemineglect (Chica et al., 2012). In another study applying Bundesens Theory of Visual Attention (Bundesen, 1998) and

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examining the effect of alerting stimuli on attentional orienting, neglect patients showed a redistribution of attentional weights from the pathological rightward bias to a normal, more balanced distribution of visual attention after a phasic alerting cue (Finke et al., 2012).

The impact of reduced arousal on oculomotor parameters has been investigated in a range of sleep deprivation studies. The main results point to deteriorating saccadic velocity and smooth pursuit gain (De Gennaro, Ferrara, Urbani, & Bertini, 2000; Fransson et al., 2008; Russo et al., 2003), whereas accuracy in general seemed to be largely preserved. Interestingly, accuracy was only impaired for highly autonomic reflexive saccades but not for voluntary antisaccades or memory-guided saccades (Zils, Sprenger, Heide, Born, & Gais, 2005). Unfortunately, none of these studies differentiated between eye movements to the left or to the right, thus making it impossible to check for directional effects of reduced arousal.

The dissociation of overt and covert orienting of attention with respect to arousal points to a neural non-overlap of brain structures subserving these functions, an assumption in conflict with studies reporting substantial overlap (de Haan, Morgan, & Rorden, 2008; Nobre et al., 2000) and with accounts treating covert and overt orienting as sequential processes with saccades being preceded by a preliminary covert orienting process (Rizzolatti, Riggio, Dascola, & Umiltà, 1987). These views are challenged by our study in that the modification of the alertness network only leads to covert (left-sided) but not overt attentional asymmetries. However, both attentional processes are slowed with reduced alertness irrespective of the direction of orienting, but covertly orienting is additionally biased to the disadvantage of left-sided targets. Klein and Lawrence (2012) raise three issues on the relation of covert and overt attention. First, attending without looking is always accomplished by an inhibition of oculomotor networks and current neuroimaging methods might be too insensitive to distinguish between neural activity designed to inhibit versus to enable behavior. Second, there is considerable non-overlap, being partly responsible for the ability to shift attention independently of gaze, and third, endogenous covert and overt spatial attention may be mediated by different neural circuits in the same neural structures, making it difficult to differentiate them by neuroimaging methods. The third argument is illustrated by recent findings from single-unit recordings focusing on the frontal eye fields (FEF). According to Schall and Thompson (2012) the FEF is composed of morphologically diverse neurons that have different functions derived from different inputs, outputs and intrinsic processes. For instance, they distinguish neurons shifting gaze from neurons contributing to attentional selection. Whereas the former project to the superior colliculus (Sommer & Wurtz, 2000) and the brainstem, the latter project to extrastriate visual cortex (Pouget et al., 2009). Both populations of neurons are non-overlapping as shown by tracer studies (Pouget et al., 2009). Thus, Schall and Thompson (2012) concluded that shifting attention and saccade preparation are subserved by different neural populations, speaking against the premotor theory of attention (Rizzolatti et al., 1987), which states that shifts of attention are identical to processes of saccade preparation. These attentional and movement neurons in the FEF are located in different FEF layers and can only be separated in single-unit recordings (Schall & Thompson, 2012). This might explain the different effects observed for reduced alertness on covert and overt orienting.

The alertness network has repeatedly been associated with activity of the locus coeruleus, being the main source of norepinephrine innervation of the cortex (Aston-Jones & Cohen, 2005; Corbetta & Shulman, 2011; Petersen & Posner, 2012; Samuels & Szabadi, 2008). On the basis of numerous behavioural, lesion, and imaging studies, a right hemisphere dominance for alertness has been stated (Corbetta & Shulman, 2011; Coull, 1998; Mesulam, 1999; Petersen & Posner, 2012; Sturm & Willmes, 2001) and a corresponding asymmetric organization of the locus coeruleus/ norepinephrine system in animal studies has been reported (Robinson, 1985). As we found non-spatial (prolonged RTs in all test conditions of the covert and overt orienting tasks) and spatial effects (slowed RTs when covertly reorienting to left-sided stimuli) after sleep deprivation, we assume an effect of the norepinephrine/locus coeruleus system on both the dorsal attention network (with orienting to attended stimuli being one of its main tasks) and the ventral attention network (being right-hemisphere dominant and mainly activated by reorienting to unattended, behaviorally relevant stimuli), which have been described in detail by the group of Corbetta (Corbetta & Shulman, 2011; Shulman & Corbetta, 2012; Shulman et al., 2010). The dorsal attention network comprising the medial intraparietal sulcus (mIPS), the superior parietal lobe, precuneus, supplementary eye fields, and frontal eye fields (Corbetta & Shulman, 2011) is assumed to function in a symmetric way, that is, each hemisphere controls the contralateral space, wheras the ventral attention network, consisting of the temporo-parietal junction, the supramarginal gyrus, the superior temporal gyrus, and the ventral frontal cortex, is considered to be lateralized with a right hemisphere dominance (Corbetta & Shulman, 2011; Shulman & Corbetta, 2012). The results of our study can be interpreted in the sense of a closer link between the norepinephrine system and the ventral attention network.

Another explanation refers to the comparability of the covert and overt paradigms. Whereas the covert orienting task is a pure Posner-type cueing task with two target positions in each visual hemifield and orienting/re-orienting conditions, the overt orienting paradigm is a kind of search and detection task, requiring voluntary shifts of attention and eye movements as well as the detection of targets in the presence of a distractor. It can be assumed that this task relies more heavily on the dorsal attention (and not the ventral) network, since targets do not appear unexpectedly at "unattended" positions. Thus, it would not be surprising that no attentional asymmetry can be observed with reduced arousal and the dissociation between overt and covert orienting in our study would consequently be related to task properties alone. However, we included some test conditions in the overt orienting paradigm, in which distractor and target were bilaterally presented, requiring saccades to the left or right visual field. In case of "correct" initial saccades to the target side we would have expected an increasing asymmetry of detection times to the disadvantage of left-sided targets in a situation of low arousal, reflecting a decreased probability to begin searching on the left and an increased probability to start searching on the right, when alertness is reduced. This asymmetry of visual search has been reported in numerous studies on cancellation tasks in neglect patients and can hardly be associated with the ventral attention network, as no unexpected and "unattended" stimuli are used, but targets and distractors are presented bilaterally. Accordingly, neglect patients showed impaired saccades into the neglected field with multi-stimulus (including distractors) displays but not when the stimulus was presented alone (Harvey, Olk, Muir, & Gilchrist, 2002; Olk, Harvey, & Gilchrist, 2002), or they exhibited abnormally speeded saccades to ipsilesional targets (Natale, Marzi, Bricolo, Johannsen, & Karnath, 2007). Such left–right asymmetries were not observed in our overt attention task irrespective of alertness level, further indicating a differential influence of arousal level on covert and overt orienting of attention.

In conclusion, we found differential effects of lowered arousal induced by sleep deprivation on covert and overt orienting of attention. An attentional left–right asymmetry was only observed with covert shifts of attention, whereas overt orienting did not show any comparable attentional bias. This points to a neural non-overlap of brain structures subserving these functions and a differential influence of the norepinephrine system on these attentional domains. Furthermore, a closer link is assumed between the alertness network and the ventral attentional network.

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