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Influence of attentional load on spatial attention in acquired and developmental disorders of attention

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ABSTRACT

Converging evidence suggests that right-hemisphere dominant spatial attention systems can be modulated by non-spatial processes such as attentional capacity. The severity of neglect in right-hemisphere stroke patients for example, is correlated with impairments in non-lateralized attention. Evidence also suggests the coexistence of lateralized inattention and reduced capacity in developmental disorders of attention, such as attention deficit hyperactivity disorder (ADHD), which is marked by cognitive impairments suggestive of right hemisphere dysfunction. These lines of evidence argue against a coincident damage hypothesis and suggest instead a direct modulation of spatial attention by non-spatial processes. Here we sought experimental evidence for this relationship in both acquired and developmental disorders of attention. Six adult stroke patients with focal right brain injury and 19 children with ADHD were studied in comparison to control groups of both healthy older adults and typically developing children. The participants were required to detect transient, unilateral visual targets while simultaneously monitoring a stream of alphanumeric characters at fixation. Load at fixation was manipulated by asking participants either to ignore the central stream and focus on the peripheral detection task (no report condition), or to monitor the central stream for a probe item that was defined by either a unique feature (low load condition) or a conjunction of features (high load condition). As expected, in all participants greater load at fixation slowed responses to peripheral targets. Crucially, in right brain injured patients but not older healthy adults left target detection was slowed significantly more than central and right target detection. A qualitatively similar pattern was seen in children with ADHD, but not in typically developing children. The imposition of load at fixation slowed responses to left compared with right targets, and this response time asymmetry was correlated with the severity of ADHD symptoms. These results suggest that a direct manipulation of non-spatial attention can reveal lateralised attention deficits in both

acquired and developmental forms of inattention. Our findings support the view that spatial attention networks are tightly integrated with non-lateralized aspects of attention.

1. Introduction

Acquired damage to the right cerebral hemisphere, particularly in the region of the temporo-parietal junction, is associated with the syndrome of unilateral spatial neglect, in which stimuli located toward the contralesional side are not consciously perceived despite adequate sensory processing (Driver & Mattingley, 1998). Even in right hemisphere patients with mild or recovered neglect, perception of brief visual targets may follow a spatial gradient; stimuli located further toward the left side are less likely to be detected, and are responded to more slowly, than comparable events located toward the right (Russell, Malhotra, & Husain, 2004; Smania et al., 1998). In addition to their lateralized attention deficits, many right hemisphere patients also have profound impairments in non-lateralized attention, reflecting reduced attentional capacity, independent of their spatial bias (Duncan et al., 1999; Husain & Rorden, 2003; Lavie & Robertson, 2001; Robertson et al., 1997; Wilkins, Shallice, & McCarthy, 1987). For instance, the time required to identify successive visual targets presented within a rapid stream at the fovea is significantly prolonged in patients with right temporo-parietal damage, and this impairment correlates with clinical measures of neglect severity (Husain, Shapiro, Martin, & Kennard, 1997). Right hemisphere patients also experience difficulty when required to intrinsically maintain alertness (Robertson, et al., 1997) yet are able to do so when attention is driven by a random external cue, for example (Posner, Inhoff, Friedrich,

& Cohen, 1987). The co-existence of lateralized inattention and reduced attentional capacity is also evident in neurodevelopmental disorders of attention such as attention deficit hyperactivity disorder (ADHD) (Bellgrove et al., 2009; Geeraerts, Lafosse, Vaes, Vandenbussche, & Verfaillie, 2007; Sheppard, Bradshaw, Mattingley, & Lee, 1999) and dyslexia (Facoetti, Turatto, Lorusso, & Mascetti, 2001). In the case of ADHD numerous structural, functional and molecular imaging studies have documented abnormalities in fronto-parietal and fronto-striatal circuits of the right hemisphere (Castellanos et al., 1994; Konrad, Neufang, Hanisch, Fink, & Herpertz-Dahlmann, 2005; Silk et al., 2005; Spencer et al., 2007; Vance et al., 2007). Moreover, qualitatively similar deficits in left-sided performance have been reported in children with acquired lesions of the right hemisphere and children with developmental hyperactivity (Braun, Archambault, Daigneault, & Larocque, 2000).

Current models of spatial attention assume a dominant role for right-hemisphere networks in shifting and allocating attention to spatial locations (Corbetta, Patel, & Shulman, 2008; Kinsbourne, 1993; Mesulam, 1999), and while there is increasing evidence that similar right-hemisphere regions are involved in non-lateralized aspects of attention, our understanding of how these systems interact is incomplete. Several studies have found that the degree of bias in spatial attention is correlated with the effectiveness of non-lateralized attention, including vigilance (Bellgrove, Dockree, Aimola, & Robertson, 2004; Malhotra, Coulthard, & Husain, 2009; Robertson, et al., 1997), phasic alertness (Finke et al., 2012; Robertson, Mattingley, Rorden, & Driver, 1998), attentional capacity (Bonato, Priftis, Marenzi, Umiltà, & Zorzi, 2010; Russell, et al., 2004; Shapiro, Hillstrom, & Husain, 2002), and spatial working memory (Malhotra, et al., 2009). This relationship is particularly well supported in the case of spatial attention and its association with vigilance and alertness over time. For example, when

patients with right-hemisphere damage engage in continuous performance tasks involving monitoring a series of stimuli presented at fixation, patients with spatial neglect are significantly more impaired on such tasks than those without neglect (Heilman, Schwartz, & Watson, 1978; Malhotra, et al., 2009), and the degree of vigilance impairment predicts the severity of patients' spatial bias on neglect tasks (Hjalton, Tegner, Tham, Levander, & Ericson, 1996; Malhotra, et al., 2009; Robertson, et al., 1998). This same relationship is apparent in patients with ADHD and rightward spatial bias (George, Dobler, Nicholls, & Manly, 2005). Indeed, alertness has a direct influence on spatial biases in attention, and in both ADHD and acquired right-hemisphere damage, presenting an intermittent warning tone designed to alert patients can transiently reduce their ipsilesional bias on spatial attention tasks – an effect that is independent of the location of the warning tones (Dobler et al., 2005; Robertson, et al., 1998). Furthermore, diminishing levels of alertness can lead to a subtle but consistent rightward shift in spatial attention in neurologically healthy adults and children (Bellgrove, et al., 2004). Together, these findings support a modulatory interaction between a non-lateralized component of attention – that of sustained attention – and spatial attention within the right hemisphere.

Although there is growing understanding of the interplay between sustained and spatial attention and its association with right fronto-parietal networks, less is understood about other non-lateralized deficits in attention that co-exist with disorders of spatial attention (Husain & Nachev, 2007). One such example is attentional capacity. Unilateral spatial neglect is thought to arise not only from a lateralized bias in selective attention, but also from a pathological reduction in attentional capacity (Driver & Vuilleumier, 2001). This produces strong competition for attentional resources even in the presence of as few as two stimuli – leading to the 'extinction' or failure to perceive salient, suprathreshold stimuli in relatively

uncluttered displays. Left spatial extinction is a common symptom of right parietal damage (Driver & Mattingley, 1998). In extinction, patients are able to detect isolated stimuli presented to either hemifield, but fail to detect the more contralesional event during bilateral simultaneous stimulation. An emerging literature suggests a link between reduced capacity and spatial bias in extinction and neglect. Several studies have demonstrated that when patients process multiple competing stimuli as a single unit (which presumably overcomes their capacity limitation) extinction is significantly reduced. For example, Mattingley, Davis and Driver (1997) found that low-level perceptual grouping of multiple elements of a visual display into a single object can improve patients' awareness of contralesional items, whereas when the same stimuli are configured such that they are perceived as separate elements, contralesional spatial extinction re-emerges. Similarly, extinction is reduced when patients subitize (or preattentively enumerate) small groups of simultaneous stimuli (Vuilleumier & Rafal, 1999). Thus, extinction is not only a symptom of lateralized bias but also an indicator of reduced attentional capacity – a fundamental component of the neglect syndrome (Driver, Mattingley, Rorden, & Davis, 1997).

The notion that perceptual awareness is dependent on attentional capacity is a central component of Lavie's theory of perceptual load (Lavie & De Fockert, 2005). Normal limitations in attentional resources mean that performing perceptual tasks that are more difficult or attentionally demanding will reduce resources available for processing task irrelevant stimuli. Thus, directly manipulating the attentional demands or 'load' of a perceptual task modulates the resources available for orienting to peripheral, task-irrelevant stimuli. Using this approach, Lavie and Robertson (2001) found that in patients with right brain damage, a small increase in the attentional load of a central task significantly reduced distraction by peripheral, task irrelevant stimuli. This effect was evident for both ipsilesional

and contralesional task-irrelevant stimuli. By contrast, in a follow-up patient study by Snow and Mattingley significant distractor effects were found in both low- and high-load tasks for ipsilesional and contralesional task-irrelevant stimuli (Snow & Mattingley, 2008).

Notwithstanding the different outcomes, in both these studies patients' capacity to orient to the irrelevant stimulus was measured indirectly through compatibility effects on the central task. Furthermore, neither study examined the effect of increasing attentional load on patients' spatial bias in orienting. Previous work has shown that increasing task difficulty (which is assumed to tax attentional capacity) produces a stronger rightward bias in spatial selection (Bonato, et al., 2010; Eglin, Robertson, & Knight, 1989; Peers, Cusack, & Duncan, 2006). These studies, however, manipulated load by increasing the number of items in a display, or by making targets harder to discriminate from distractors, thus confounding any influence of load with perceptual complexity. Russell et al (2004) however demonstrated in 6 right hemisphere stroke patients that increasing perceptual demands at fixation lead to a deterioration in awareness of peripheral events, particularly those located in contralesional space.

Data from neuroimaging studies, where stimulus displays were held constant across different levels of attentional load, indicate asymmetric neural responses to stimulation with increased attentional load, implying an increase in the spatial gradient (or bias) in orienting. For example, Vuilleumier et al. (2008) conducted an fMRI study of patients with right parietal damage but structurally intact early visual areas. Increasing attentional load at fixation caused a reduction in activity within right retinotopic visual areas (corresponding to task-irrelevant stimulation within the left hemifield) but produced no changes in response within left visual areas to stimulation on the right. The effect of increasing task demands produced greater attenuation of stimulus response within the damaged right hemisphere – suggesting that

capacity reduction led to an asymmetric top-down suppression of competing sensory input. In the normal brain, an increase in attentional load leads to bilateral suppression of visual cortex responses to irrelevant peripheral stimulation (Schwartz et al., 2005). The spatially asymmetric top-down effect apparent in unilateral neglect patients may reflect the attentional imbalance created by unilateral right lesions (Corbetta, Kincade, Lewis, Snyder, & Sapir, 2005). In the absence of mutual inhibition, hyperactivity within the intact left hemisphere may lead to increased suppression of visual areas within the opposite right hemisphere, in the context of weak suppression of left visual cortical responses. Although the increase in perceptual load produced spatially asymmetric effects on early visual areas, its implications for conscious perception were not examined. Furthermore, it is not clear how attentional capacity would interact with spatial orienting to *task-relevant* stimuli. In a recent electroencephalographic study, healthy participants were required to detect brief lateralized visual stimuli while simultaneously engaged in a non-spatial perceptual task at fixation (O'Connell, Schneider, Hester, Mattingley, & Bellgrove, 2011). Increasing the processing load of this central task reduced the amplitude of right hemisphere evoked N1 potentials to contralateral stimuli and a concomitant increase in the N1 amplitude elicited by ipsilateral stimuli. This asymmetric effect of attentional load on brain responses to peripheral, task relevant stimuli was not, however, accompanied by a behavioural difference in orienting to the peripheral stimuli.

Here we examined whether the decline in efficiency of spatial selection for more contralesional locations is exacerbated by an increase in central processing load in both acquired and developmental disorders of attention. Although rightward spatial bias is well documented in both right brain damage and ADHD, factors underlying the bias have not previously been examined in both conditions using the same task and stimuli. We tested six

adult patients with confirmed right hemisphere pathology and mild or recovered neglect, all of whom exhibited a rightward bias in spatial selection. Data were qualitatively compared to available data from 23 healthy older adults who had performed the same task. We also tested 19 children with ADHD and 21 typically developing controls to determine whether qualitatively similar asymmetries of spatial attention were unmasked by increasing central processing load. Our results show that increasing central load exacerbates the spatial bias in selective attention characteristic of neglect in patients with right-hemisphere lesions and in children with ADHD.

2. Methods

2.1. Participants

All participants provided written informed consent according to the Declaration of Helsinki, and all procedures were approved by the research ethics committees of the participating hospitals, schools, the University of Melbourne and The University of Queensland.

2.1.1. Right-Hemisphere Patients

Six patients with a first-ever focal right-hemisphere stroke, involving the territory of the middle cerebral artery, participated in the study (4 male, Mean age= 57.8 years, SD=18.2). Data for time since stroke was missing for 1 participant; the remaining 5 patients had a mean time since stroke of 38 days (SD=37). All patients were right-handed and demonstrated left visual extinction on clinical confrontation testing. No patient was tested within 2 weeks of their stroke. The extinction test involved a standard bedside procedure. The patient was asked to fixate the examiner's nose while the examiner positioned his/her index fingers bilaterally in the patients' peripheral visual fields. The patient was asked to detect target stimuli, which consisted of a single movement of either one or both of the examiner's fingers.

A standard administration procedure for extinction was used with all patients, which involved delivering 36 stimuli in random order: 16 bilateral, 8 unilateral left, 8 unilateral right, and 4 catch trials with no stimulus. Each time the examiner moved a finger he/she prompted the patient by saying "Now" and the patient had to respond "left", "right", "both", or "none". Patients were categorised as having extinction if their score on bilateral trials was at least 25% worse than on unilateral left trials. Thus, for example, if a patient scored 8/8 for unilateral left trials, he/she would have to score 12/16 or worse on bilateral trials to have extinction. A further criterion for inclusion in the study was that no patient ever made false positives on catch trials. Raw scores for the extinction test were not retained and patients were simply categorised as +ive or -ive based on the criteria above. Patients were recruited from the Austin Hospital and Royal Talbot Rehabilitation Hospital in Melbourne, Australia. Brain lesions for five of the six patients were manually mapped from clinical CT or MR images onto the T1 weighted MNI template (see Figure 1) using MRIcro software (Rorden & Brett, 2000). MR images for the remaining patient were unavailable but radiological reports indicated a circumscribed right thalamic lesion.

Data were also available for a group of older adults (N=23) who were recruited from retirement villages and newsletter advertisements for qualitative comparison to the right-hemisphere patients. The age range of the participants was 67-79 years (M=74.1, SD=4.2). Visual acuity was checked using a Snellen Chart and eye glasses were worn when required. Mood was assessed using the Geriatric Depression Scale and we screened for dementia using the Mini Mental State Examination (range 27-30; M=29.5, SD=0.8)

2.1.2. Children with and without ADHD

Forty matched children (19 ADHD and 21 typically developing) participated in the study. Children with ADHD were recruited through the Royal Children's Hospital (RCH)

Melbourne, Australia. Typically developing children were recruited through schools of the Anglican School system in Brisbane, Australia. Informed consent was appropriately obtained from the parents of all participants.

Children recruited into the ADHD group had all undergone a full cognitive and behavioural assessment at the RCH within two years of the current study and met criteria for ADHD-Combined type (ADHD-CT) according to DSM-IV criteria (American Psychiatric Association, 1995). Children were excluded if their performance on the Wide Range Achievement Test – Reading Subtest (WRAT-R) was 1.5 SD's or more below normative values, estimated full scale IQ ≤ 80 on the WISC-IV, or if they had previously been diagnosed with impaired sensorimotor skills, learning disabilities or symptoms of psychosis. The exclusion of children with reading impairment is particularly important given evidence that children with reading disorder have impairments of spatial attention (Facoetti, et al., 2001; Franceschini, Gori, Ruffino, Pedrolli, & Facoetti, 2012). Within one week of participating in the current study, parents were required to complete the Parent Conners' ADHD Rating Scale-Revised: Long Version (CPRS-R:L) (Conners, 1997). Any medication was withdrawn at least 24 hours prior to the cognitive assessment. Clinical and demographic information is presented in Table 1.0

The typically developing children had no previous diagnosis of ADHD, had current parent Global Index T-scores on the Conners' of < 60 , and no parent or teacher report of any learning disabilities or psychiatric/psychological problems. At the time of testing, typically developing children were administered a 2-subtest short-form of the Wechsler Abbreviated Scale of Intelligence, which reliably estimates full-scale IQ ($r=0.93$). In addition, all children completed the WRAT Reading (WRAT-R) and Spelling (WRAT-S) subtests, and were required to score in the normative range for reading ability.

The two groups did not differ in terms of age or full-scale IQ but did in terms of reading and spelling ability (Table 1). On all indices of the CPRS-R:L children with ADHD were reported as having significantly greater symptom severity than the control group (all subscales $p < 0.001$; See Table 1). Eighty-four percent ($n=16$) of the children with ADHD and all of the typically developing children were right-handed, as assessed by the Edinburgh Handedness Inventory (Oldfield, 1971).

2.2. Stimuli and Procedures

Participants performed a task in which they monitored a centrally presented rapid serial visual presentation (RSVP) stream for a probe stimulus, while also responding to brief peripheral events. The task was presented on a laptop computer with a liquid crystal display, positioned ~50cm in front of the seated participant. All stimuli were presented in either red or green on a black background (see Figure 2).

The initial display consisted of a central red fixation cross and three peripheral red boxes ($2^\circ \times 2^\circ$) that defined the spatial locations of the peripheral targets (Figure 2). These ‘placeholders’ were positioned to the right, left and directly below the fixation point at a distance of 6.3° from fixation (Figure 2) and remained visible throughout a trial. The use of three peripheral target positions (left, centre and right) enabled spatial attention to be mapped across the visual field and to examine gradients of spatial attention.

At the start of each trial, the central fixation cross was replaced by a stream of eight sequentially presented alphanumeric characters, consisting predominantly of red digits (0 - 9) which acted as distractors. Each character appeared for 400 ms and was immediately replaced by the next character, yielding a presentation frequency of 2.5Hz and a trial duration of 3,200 ms. Participants were asked to fixate the stream of stimuli for a designated probe stimulus,

the identity of which was specified in advance for the two load conditions. In low-load blocks, participants had to report the presence of any green probe character (digits 0 -9, letters A - H) that appeared within the stream of red digits. By contrast, in high-load blocks participants had to report any red probe letter that appeared within the stream of red digits. In each block the designated probe - a green character for low-load trials and a red letter for high-load trials - appeared in 50% of trials, and occurred unpredictably at any temporal position within the central RSVP stream. In both the low- and high-load trials participants were only required to report *if a probe had appeared* (yes/no) and were not required to report the identity of the probe.

While performing the central task at fixation, participants were also required to respond to a brief peripheral target. This peripheral target consisted of a green square ($2^{\circ} \times 2^{\circ}$) that was flashed for 200ms at one of the three peripheral locations defined by the placeholders. The peripheral target appeared with equal probability at each of the three locations and could occur at any time point during the RSVP stream, with the condition that it never coincided with a central probe stimulus. Over the course of a block of trials, 10 peripheral targets appeared in each of the three locations. There were five catch trials in which a peripheral target was never presented.

On each trial participants made a speeded, manual response to the occurrence of any peripheral target (using their right hand), and then made an unspeeded vocal response at the end of the trial to indicate whether a probe had appeared in the central stream. Previous studies have demonstrated that hand of response has minimal impact upon lateralized response times (Peers, et al., 2006). Vocal responses were entered via the experimenter using a separate keyboard. Attentional load at fixation was manipulated via three experimental

conditions, each with identical stimulus displays. Figure 2 displays a schematic of the three attention conditions that were employed. In the *no report* condition, participants were instructed to fixate centrally but to ignore the central stream and to devote their attention exclusively to the peripheral-target detection task. In the *low load* condition participants were required to report the presence of any green letter or digit in the central stream of red digits. As the probe item was defined by its unique feature (colour) it ‘popped out’ of the RSVP stream. In the *high load* condition participants reported the presence of any red letter in the stream of red digits. In this condition the probe item was defined by a conjunction of colour and form, and thus required greater attentional resources to be discriminated than the low-load probe.

The children with ADHD and the typically developing children performed 2 blocks of 35 trials in each load condition in the order: no-report, low-load, high-load, high-load, low-load, no-report. Similarly, the right-hemisphere patients performed 8 blocks of 35 trials in each load condition (i.e, 840 trials per individual) in the order: no-report, low-load, high-load, high-load, low-load, no-report. We note that a larger number of trials were administered to the right-hemisphere group (across multiple sessions) than to the other cohorts under study. This was done to safeguard against the larger error variances that are typical in patient populations, particularly when sample sizes are relatively small, as was the case in the current study. The order of trial blocks within a session for the right-hemisphere patients was always as above. The older adult participants completed 336 trials across each of the no-report, low-load and high-load conditions.

2.3. Statistical analysis

Reaction time and accuracy data for the peripheral target detection task were submitted to a repeated measures ANOVA with within-subjects factors of central task load (no-report, low-load, high-load) and target position (left, centre, right). Central task accuracy was analysed using an analogous repeated measures ANOVA with two levels of central task load (low-load, high-load). Group (ADHD versus control) was entered as a between-subjects factor as appropriate. Interactions were decomposed with analysis of simple main effects with Bonferroni corrections. The Greenhouse-Geisser correction was applied to contrasts in which the assumption of sphericity for within-subjects factors was violated.

3. Results

3.1. Right-hemisphere patients and non-clinical older adults

3.1.1. Effect of Central Load on Peripheral Target Detection

Analysis of reaction times (RTs) to peripheral targets across the three spatial locations revealed a significant main effect of target location, with responses to left events (407 ms) being slower than responses to central (340 ms) and right events (305 ms), $F(2,10) = 48.30$, $p < .001$. There was also a significant main effect of central load, with significantly longer RTs in the high-load condition (427 ms) than in the low-load (358 ms) and no-report conditions (269 ms), $F(2,10) = 23.53$, $p < .001$. Crucially, increasing the central load steepened the spatial gradient for peripheral target detection, as indicated by a significant interaction between target location and central load, $F(4,20) = 5.03$, $p < .05$. The RT cost of increasing central load was greatest for left targets [low-load minus no-report = 102 ms (SE=16.5, $p=0.005$, Bonferroni adjusted); high-load minus no-load = 182 ms, SE=32.8, $p=0.008$],

smallest for right targets [low-load minus no-report = 78 ms (SE=22, $p=0.05$); high-load minus no-load = 127 ms, SE=26.5, $p=0.02$], and intermediate for central targets [low-load minus no-report = 88 ms (SE=20, $p=0.02$); high-load minus no-load = 164 ms, SE=34, $p=0.01$] (see Figure 3).

Importantly the analogous analysis in the sample of non-clinical older adults revealed the predicted main effect of central load, $F(1.47, 32.45)=148.1, p<0.001$ and a main effect of target position, $F(1.71, 37.53)=3.79, p<0.05$. The latter reflected marginally faster RTs for right ($M=383$ ms, SE= 15.3) compared to central targets ($M=405$ ms, SE= 16.4) ($p<0.05$). Importantly, there was no significant interaction between central task load and target position, $F(2.26, 49.72)=0.59, p>0.05$ (Figure 4).

The differential effect of central load on left versus right targets was evident for three of the six right-hemisphere patients in the low-load condition (left minus right in low-load RT minus no-report RT) ($M=24$ ms, S.E=15.2) and for all six patients in the high-load condition (left minus right in high-load RT minus no-report RT) ($M=55$ ms, S.E=10.3) (Figure 5). The finding of a significant influence of load at fixation on spatial selective attention cannot be attributed to a trade-off between speed and accuracy, since the error data for the peripheral target task followed a similar pattern to the RT data.

Overall, significantly more targets were missed by the right-hemisphere patients on the left (24.6%) than in the central (17.9%) and right (16.3%) positions, $F(2,10) = 5.32, p < .05$.

There was also an effect of central load, such that significantly more peripheral targets were missed in the high-load (21.7%) and low-load (20.9%) conditions than in the no-report (16.3%) condition, $F(2,10) = 5.15, p < .05$; but there was no interaction between these factors, $F(4,20) = 1.75, p > .10$.

3.1.2. Central Task Accuracy

Accuracy (% correct) to the central task in each of the low- and high-load central conditions was examined as a function of peripheral target location in the right-hemisphere patients.

Overall, central task accuracy was high ($M=97.7\%$, $SE=0.6$). There was neither a main effect of central task load, $F(1,5)=0.92, p>0.05$ nor target location, $F(2,10)=0.7, p>0.05$. Nor was the interaction between central task load and target location significant, $F(1,1, 5.5)=2.4, p>0.05$.

3.2. Children with and without ADHD

3.2.1. Effect of Central Load on Peripheral Target Detection

There was a significant main effect of group, $F(1, 38)=9.78, p<0.01$ which reflected slower responses to peripheral targets in the ADHD children ($M=357$ ms, $S.E=19$) relative to controls ($M=275$ ms, $S.E=18$). There was also a main effect of central task load, $F(1.5,56.5)=78.9, p<0.001$. Peripheral targets in the no-report condition were responded to more quickly ($M=244$ ms, $S.E=9.7$) than targets in the low-load condition ($M=324$ ms, $S.E=14.9$) ($p<0.001$), which in turn were responded to more quickly than targets in the high-load condition ($M=378$ ms, $S.E=17.8$) ($p<0.001$). There was a significant interaction between group and target location, $F(2,76)=5.42, p<0.01$. This interaction was driven by the slower responses of the ADHD children to left ($p<0.001$) and central targets ($p<0.01$), relative to right targets, whereas the responses of the control children did not differ by target location.

Crucially, there was an interaction between group, central task load and target location, $F(2.5,95.9)=5.99, p<0.01$ (Figure 6). The interaction of group and target location was examined at each level of central task load. Critically, this interaction was apparent at low-

and high-load but not in the no-report condition. In the no-report condition, there was no interaction between group and target location, $F(2,76)=0.21, p>0.05$. An interaction between group and target location was apparent under low-load, $F(2,76)=3.2, p<0.05$ and was driven by an effect of peripheral target location in the ADHD group but not controls. ADHD children were slowest to detect targets on the left, compared with central ($p<0.01$) and right ($p<0.01$) targets. Responses to central and right targets did not differ from each other ($p>0.05$). There was no significant effect of target location in the typically developing children (all pair-wise comparisons $p>0.05$). The interaction between group and peripheral target location was also significant under high-load, $F(2,76)=7.2, p<0.001$. ADHD children responded more slowly than controls to both left ($p<0.01$) and central ($p<0.001$) targets, but not to right targets ($p>0.05$). Further, the ADHD children were slower to respond to left relative to right targets ($p<0.01$), as well as to central relative to right targets ($p<0.01$). Note that the critical interaction between group, central task load and target location remained significant when three left-handed children with ADHD were excluded from the analysis, $F(2.5,85.7)=4.9, p=0.006$, and when reading and spelling ability were covaried, $F(2.45, 85.7)=4.9, p=0.0009$.

The differential effect of central load on left versus right targets was evident for 68% of the ADHD children and 57% of control children in the low-load condition (left minus right in low-load RT minus no-report RT) (ADHD: $M=42$ ms, $S.E=15.6$; controls: $M=9$ ms, $S.E=14.8$) and for 63% of ADHD children and only 24% of control children in the high-load condition (left minus right in high-load RT minus no-report RT) (ADHD: $M=62$ ms, $S.E=24.4$; controls: $M=-26.7$ ms, $S.E=23.2$) (Figure 6). This group effect was not significant for low-load [$F(1,38)=2.4, p>0.05$] but reached significance for the high-load contrast [$F(1,38)=6.9, p<0.05$].

As for the right hemisphere patients, the finding of a significant influence of load at fixation on spatial selective attention cannot be attributed to a trade-off between speed and accuracy. Accuracy of peripheral target detection was examined as a function of central load, target location and group. Overall, ADHD children missed ($M=15\%$, $SE=0.2$) more targets than control children ($M=9.9\%$, $SE=0.2$), $F(1,38)=4.45, p<0.05$. Group and central task load interacted, $F(1.3,49.6)=3.5, p<0.05$. ADHD children missed more targets compared with controls in both the no-report condition ($p=0.05$) and in the high-load condition ($p<0.03$). ADHD children also missed more targets under high- compared with low-load ($p<0.05$), whereas the controls did not differ between these conditions ($p=0.16$). These error data suggest that the lateralized effects observed for peripheral target RTs did not arise because of a speed-accuracy tradeoff.

3.2.2. *Asymmetrical attention deficits correlate with ADHD symptoms*

A partial correlation, controlling for group, revealed that asymmetrical peripheral target responses correlated with dimensional measures of ADHD symptomatology. Specifically, there was a significant positive correlation between the parent-rated ADHD Global Index and the difference in RT between left and right targets under high-load, relative to the no-report condition (left minus right in high-load RT minus no-report RT) ($r=0.39, p=0.014$) (see Supplementary Results for correlation matrix of all Conners' indices). This correlation was not significant for the low-load RT -no-report RT comparison ($p>0.05$). Nor were correlations observed for comparable differences in RT between left and centre ($r=0.09, p>0.05$) or centre and right targets ($r=0.25, p>0.05$) under high-load, relative to the no-report condition (high-load RT minus no-report RT). Thus, differences between left and right response times under high attentional load were maximally sensitive to the severity of ADHD symptomatology.

3.2.3. Central Task Accuracy

Accuracy on the central RSVP task was assessed as a function of target location in the ADHD and typically developing children. Overall, there was no main effect of group for central task accuracy, $F(1,38)=1.45, p>0.05$. The children with ADHD correctly identified 94% ($SE=0.8$) of central probe items as present/absent compared with 95% ($SE=0.8$) in control children. There was, however, a main effect of load, $F(1,38)=4.0, p=0.05$, with better accuracy in the low- ($M=96\%$, $S.E.=0.5$) than in high-load ($M=94\%$, $S.E.=0.84$) conditions. None of the interaction terms was significant [group by target location, $F(2,76)=2.39, p>0.05$, group by load $F(1,38)=0.8, p>0.05$; group by load by target location, $F(2,76)=2.58, p>0.05$]. Thus, the two groups performed at a comparable level on the central RSVP task.

4. Discussion

We investigated the effects of non-spatial attentional load on spatial orienting biases in a novel task that held all visual stimuli constant across the critical experimental conditions. These effects were examined in adults with focal right hemisphere injury and in children with ADHD, a developmental disorder of putative right hemisphere origin. The results indicate that manipulating attentional load at fixation reveals a lateralized visual orienting impairment that is qualitatively similar in both disorders.

Consistent with their attentional bias, the right brain injured patients demonstrated a lateralised spatial gradient for detecting peripheral targets under all three conditions of central load. Thus, responses to leftward targets were slower than for central and right targets. Critically, as the attentional demands of the central task increased, the spatial gradient in responding to peripheral targets became increasingly biased, leading to slower responses to left-sided targets. Increasing attentional load at fixation did not however lead to asymmetrical response times in a healthy sample of older adults. These results represent an important demonstration that the spatial selection imbalance following focal temporo-parietal lesions is directly influenced by non-spatial processing capacity (Bonato, et al., 2010; Russell, et al., 2004). Unlike previous studies (Eglin, et al., 1989; Mattingley, et al., 1997; Peers, et al., 2006), we used an explicit manipulation of attentional capacity and controlled for factors such as stimulus complexity and dual-task demands. Our findings indicate that perceptual processing of lateralized stimuli is asymmetrically modulated by non-spatial load, which conforms with previous findings of load-imposed asymmetry in visual cortical responses to task-irrelevant stimuli in neglect (Vuilleumier, et al., 2008).

Crucially, we also found an analogous effect of attentional load on spatial selectivity in children with ADHD, which was not apparent in children without ADHD. Just as was observed for the right brain injured patients, ADHD children demonstrated a lateralised spatial bias in orienting to peripheral targets, when compared with control children. This bias emerged when the ADHD children had to monitor the central RSVP stream for easy (“pop-out”) probes, and was exacerbated under high load in which probes were defined by a conjunction of colour and form. Interestingly, this load-modulated spatial bias was positively correlated with levels of ADHD symptomatology. Taken together, the findings from right brain injured patients and children with ADHD suggest that the interaction between attentional capacity and spatial orienting in right hemisphere dysfunction is unlikely to be due to coincident damage to structurally distinct attention networks (Husain & Nachev, 2007). Instead, we suggest that neurodevelopmental abnormalities of fronto-parietal attention networks can give rise to similar effects of attentional load on spatial orienting as is evident in patients with focal lesions defined by cerebrovascular territory.

A point of departure between the findings for the right-hemisphere patients and those of the children with ADHD was the slowed response times of the ADHD group to central peripheral targets under high load. For the right-hemisphere patients response times increased monotonically from right targets, to centre targets, to left targets under both low and high central load. Under low load the ADHD children were slowest on the left, whereas response times to central and right targets did not differ. Under high load, however, responses to both left and central targets were slowed compared with right targets. These effects were not apparent in the control children. Although we cannot determine with certainty the reason for this discrepancy between the adult patients and the ADHD children, the difference might

have arisen because central probe items in the low load condition shared a common colour (green) with the peripheral targets, whereas this was not the case for the high load condition in which central probes were always red. Thus, whereas under high load there was colour conflict between central and peripheral targets, no such conflict was present under low load. Since children with ADHD are known to have problems resolving incompatible response contingencies (Bush et al., 1999; Johnson et al., 2008), perhaps this further impaired their performance under high load conditions. Another possibility is that the ADHD participants may have adopted a heuristic in the high load condition such as “respond to lateral green events but don’t respond to midline green events” which may have inadvertently slowed response times for the green midline (i.e., central) peripheral events. Whatever the explanation, we note that although response times at the central position were slowed in children with ADHD, only *lateral differences* in response times correlated with the severity of ADHD symptomatology.

Unlike the ADHD children in our study, a lateralised bias of attention was not influenced by central load in either healthy older adults or typically developing children. These data support our recent findings which indicated that increases in central attentional demands did not differentially affect participants’ ability to respond to peripheral targets on the left and right (O’Connell, et al., 2011). In that study differential effects were, however, observed in the amplitude of stimulus-evoked electrophysiological responses to the peripheral stimuli, with reduced right hemisphere responses to left (contralateral) stimuli when attentional load was increased. Thus, even in the healthy brain, taxing attentional capacity with a non-spatial task evidently reduces the efficiency with which the right hemisphere can re-orient attention to a peripheral stimulus. The severe capacity limitation associated with neglect in both ADHD and right brain injury therefore makes patients more susceptible to the effects of attentional

load, whereas a greater increase in load may be required to challenge the right hemisphere's dominance of lateralised responses in the healthy brain. We note that a limitation of the current study was that we performed a qualitative rather than quantitative, comparison between the right-hemisphere and older adult (but not age-matched) samples. Although future studies could address this limitation explicitly, we note that central attentional load did not impact peripheral target response times in either the typically developing children or the older adults studied here or in our previous report in younger adults (O'Connell, et al., 2011).

Recent functional neuroimaging studies in healthy participants lend support to the notion of overlapping neural substrates for attentional capacity and spatial orienting. Several studies have shown that the level of activation within the intraparietal sulcus (IPS) depends on the number of items held in a short-term store (Sheremata, Bettencourt, & Somers, 2010; Todd & Marois, 2004) , and that this effect is independent of the number of stimuli presented within the visual field (Sheremata, et al., 2010) . Moreover, Sheremata and colleagues have reported that the representation of attended items within the left and right IPS is asymmetric.

Specifically, set-size dependent BOLD responses were found for the left IPS when participants had to remember stimuli presented to the right visual hemifield, whereas the right IPS encoded attentional set size for stimuli presented to either hemifield. Right parietal dominance for visual attention capacity is also suggested by neuropsychological studies, which have shown that lesions of the right IPL and STG cause greater impairments in attending to visual stimuli that are in temporal competition (i.e., presented in rapid sequence) when compared with lesions of the left IPL or right SPL (Shapiro, et al., 2002) . In this study, patients with right IPL/STG damage with concomitant spatial neglect showed the greatest impairment, which is also consistent with our finding of a relationship between spatial bias and non-lateralized attention. Indeed, Husain and Nachev (2007) recently suggested that the

IPL may play a role in both spatial orienting and in non-lateralized processes such as attending to salient stimuli over time. Likewise, attentional capacity is another non-spatial function that may be partly associated with the functional integrity of this region (Sheremata, et al., 2010; Todd & Marois, 2004).

Most current models of spatial attention assume a right-hemisphere-dominant network of frontal, parietal and temporal regions for directing attention to the left or right visual hemifield (Corbetta, et al., 2008; Kinsbourne, 1993; Mesulam, 1999). Recent work suggests that only a small component of this spatial attention network is lateralized to the right, and that this includes regions such as inferior parietal areas and the temporo-parietal junction. Shulman et al (2010) performed an fMRI study in healthy participants, and found that although the dorsal fronto-parietal network for selective attention and spatial orienting was bilaterally represented, the ventral attentional stream (including TPJ and inferior frontal cortex) showed right dominant activation for attention shifts to a previously unattended stimulus (i.e., stimulus-driven reorienting to spatial stimuli). Furthermore, this right dominant activation of the ventral network was associated with both contralateral and ipsilateral spatial shifts in attention. Thus, the ability to shift attention from monitoring the central stream of visual stimuli to detecting a stimulus at an unattended location is dependent on the co-activation of bilateral dorsal fronto-parietal regions as well as (predominantly) right ventral temporo-parietal regions. In the case of damaged or dysfunctional ventral nodes of this network, such as right IPL, TPJ, and inferior frontal regions frequently associated with ADHD (Vance, et al., 2007) and neglect (Corbetta, et al., 2005; Mort et al., 2003), stimulus-driven re-orienting to contralesional space is weakened relative to ipsilesional space, producing a lateralised spatial attention gradient. Presumably, taxing the capacity of this right dominant network leads to reduced efficiency of the same structures involved in re-orienting

attention. Our data suggest that the capacity of the ventral attention system to disrupt dorsal attention processes is dependent on resource allocation. Under conditions of resource depletion, spatial re-orienting becomes less efficient.

In summary, our findings suggest that in both acquired and developmental disorders of right hemisphere function, taxing central attention resources directly modulates lateralized visual orienting and selection. This interaction is apparent in patients with circumscribed lesions defined by cerebrovascular territory, as well as in children with ADHD, a neurodevelopmental disorder of putative right hemisphere origin. The results support neuroimaging data in healthy individuals which have shown overlapping neural substrates for attentional capacity and for the re-orienting of spatial attention. In the context of such findings, our results support a conceptualization of spatial attention networks working in concert with non-lateralized components of attention.

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Table 1: Clinical and demographic data for the children with ADHD and typically developing children

	Typically Developing Children Control (<i>n</i> = 21) M(SD)	Children with ADHD (<i>n</i> = 19) M(SD)	<i>p</i> value
Age in years	11.4 (1.8)	10.1 (2.5)	>0.05
Full-scale IQ	99.8 (8.7)	93 (12.4)	>0.05
WRAT Reading score	117 (18.0)	97 (15.9)	<0.01
WRAT Spelling score	108 (13.3)	92 (16.5)	<0.01
Conners' ADHD Index T- score	48 (4.6)	71.6 (12.9)	< 0.001
Conners' Global Index T- score	48 (4.9)	77.4 (8.4)	< 0.001
Conners' DSM-IV Inattentive T-score	49.1 (5.3)	71.3 (8.9)	< 0.001
Conners' DSM-IV Hyperactive/Impulsive T- score	47.9 (5.4)	82 (7.1)	< 0.001
Conners' DSM-IV Total T- score	48.6 (4.9)	76 (12.6)	< 0.001

FIGURE CAPTIONS

Figure 1. Lesion maps for right brain damaged patients. Reconstruction of lesions in five of the six right hemisphere patients, using MRICro. (MRI scans for one patient, who had a

circumscribed thalamic lesion, were unavailable.) Areas of damage (in red) are superimposed onto the standard MNI-template brain. Numbers in red are z-coordinates. All patients had suffered a first-ever stroke in the territory of the middle cerebral artery.

Figure 2. Presentation conditions for the RSVP task. The “no report” condition required a speeded peripheral target response only. The “low attentional load” condition required a non-speeded response to a centrally presented green probe, as well as a speeded response to the peripheral target. The “high attentional load” condition also required a non-speeded response to a centrally presented red-letter probe as well as a speeded response to the peripheral target.

Figure 3: Central load by target position interaction for response time (ms) in right hemisphere patients. Increasing central load steepened the spatial gradient of selective attention with the effect of load being most pronounced for left targets, least for right targets and intermediate for central targets.

Figure 4: Effect of central load on peripheral target response times (ms) in healthy older adults. Although increasing central load impacted response times for peripheral targets, there was no interaction between this factor and target position.

Figure 5: Response time differences (ms) for left versus right targets under low and high load, relative to the no report condition in right hemisphere patients, presented as

individual and group data.

Figure 6: Central load by target position interaction for response time (ms) in children with ADHD compared to controls. Increasing central load resulted in a marked slowing in response times in the ADHD children particularly for left and central, compared to right targets.

Figure 7: Response time differences (ms) for left versus right targets under low and high load, relative to the no report condition in ADHD children versus controls, presented as individual and group data.

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Highlights

Non-spatial attention load at fixation influenced spatial selective attention

Non-spatial load unmasked a spatial gradient of neglect in right hemisphere patients

A qualitatively similar pattern was observed in children with ADHD

Such that non-spatial load slowed responses particularly for left targets

This response time asymmetry under load was correlated with ADHD symptom severity

Figure 2

Figure 3

Figure 4

Figure 5

Figure 6

Figure 7

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