Atypical brain laterality in adults with ADHD during dichotic listening for emotional intonation and words

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Abstract
Few studies directly examined the nature of hemispheric specialization and interaction in ADHD. The present experiment investigated left/right brain dynamics in unmedicated right handed adults with ADHD (n = 19) and in controls (n = 19), using a dichotic listening task to assess hemispheric differences in word and emotion recognition. We also assessed how focusing attention on a single ear modulated lateralized performance and affected cross-callosal interference effects. Analysis of variance indicated that ADHD subjects showed reduced left hemisphere specialization, were better at processing emotions, and worse at processing words compared to controls. These differences were eliminated during focused attention. Finally, during presumed right hemisphere processing of linguistic stimuli, subjects with ADHD showed reduced left hemisphere interference. We concluded that ADHD subjects demonstrated greater right hemisphere and reduced left hemisphere contribution during this task relative to controls. We posit that these hemispheric differences were due to management or use of available cognitive resources rather than inherent capacity.

Keywords: Emotion; Language; Hemisphere; ADHD; Laterality; Emotion

1. Introduction
A number of studies have helped to establish the validity of the diagnosis of adult attention-deficit/hyperactivity disorder (ADHD) (Biederman et al., 1993; Bush et al., 1999; Castellanos, 1996; Ernst, Zamekin, Phillips, & Cohen, 1998; Filipek et al., 1997; Holdnack, Moberg, Arnold, Gur, & Gur, 1995; Raba et al., 1999; Seidman, Biederman, Weber, Hatzi, & Farzaneh, 1998; Zamekin et al., 1990). Longitudinal studies indicate that childhood ADHD persists into young adulthood in 60–70% of the cases when defined relative to same-age peers and in 58% of the cases when DSM-IV criteria and parental reports are used (for review, see McGough & Barkley, 2004). A recent review by Harpin (2005) indicates that adult ADHD is associated with multiple adverse outcomes. For instance, adults with ADHD are more likely to be fired and are often characterized as exhibiting lateness, absenteeism, excessive errors, and an inability to accomplish expected workloads. At home, relationship difficulties and break-ups are more common and the risk of drug and substance abuse is significantly increased in those who have persistent symptoms but do not receive medication. Still, compared to studies of children with ADHD, relatively few investigations have examined basic neurocognitive differences between adults with ADHD and controls, and what core deficits in cognitive processing exist, remains unclear. Thus, more studies of adult ADHD are needed to help clarify processes that underlie the disorder.

Multiple reports utilizing a broad range of techniques, in both child and adult samples, strongly suggest that ADHD involves atypical cerebral asymmetries and that this is a topic deserving further investigation (for review, see Bradshaw & Sheppard, 2000; Grodd, Blumenthal, Molloy, & Castellanos, 2001; Hale, Hariri, & McCracken, 2000; Reid & Norvilitis, 2000; Stefanatos

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McCracken (1991) has suggested that ADHD may be associated with a dysregulation of the brain stem nucleus locus coeruleus, which is thought to produce 80% of the largely right lateralized norepinephrine projections to the cerebral cortex. This system has been shown to play a key role in regulating arousal, vigilance or sustained attention, sleep, autonomic function, and emotion (Aston-Jones, Foote, & Blissom, 1984). Furthermore, abnormal R > L asymmetries in brain activity have been previously reported in both child and adult ADHD samples during studies of resting-state brain activation (Chabot & Serfontein, 1996; Ernst, Zametkin, Matochik, Jons, & Cohen, 1998; Ernst et al., 1999; Seig, Gaffney, Preston, & Jellings, 1995; Zaidel, 1976). Thus, one potential component of ADHD is an ‘over-aroused’ RH is one potential component of ADHD. Importantly, this notion is not at odds with Burkey’s (1997) model of ADHD, which highlights impaired behavioral inhibition and executive functions as core features of the disorder. Indeed, a disregulated/over-aroused RH may be directly contributing to such deficits.

To investigate hemispheric specialization in adults with ADHD we used a modified version of dichotic listening for emotions and words developed by Bryden & MacRae, 1988. This task requires subjects to detect an emotional tone of voice or to identify a word during dichotic presentations of four words (bower, dower, power, tower) spoken in four different emotional tones (happy, sad, angry, neutral). Thus, stimuli for the ‘word’ and ‘emotion’ tasks are identical and only the instructions to the subjects differ. During dichotic listening for emotional tones, the stimuli in each ear are presented simultaneously to the opposite hemisphere via fibers that cross at the superior olive and ipsilateral auditory channels, the stimuli in each ear project to the contralateral hemisphere (i.e. left hemisphere for words, right hemisphere for emotions). According to these findings, under normal task conditions (i.e. words are spoken in different emotional tones), words are processed bilaterally, although more accurately in the LH, while the emotional tone is processed exclusively in the RH.

To study whether words and emotions were processed exclusively in a single hemisphere or bilaterally. They also explored whether the semantic or emotional nature of word stimuli affected the relative contribution of each hemisphere during word processing and whether different word and emotion targets showed varying degrees of hemispheric specialization. They found that the word ‘bower’ and the emotion ‘sad’ showed the strongest left and right hemisphere specialization, respectively. They found that RH processing of word targets was more accurate with words spoken in a negative emotional tone compared to words that had no affective component. In fact, when subjects processed words with negative emotional tone, the typical LH advantage was significantly attenuated due to a decrease in LH and an increase in RH performance. Furthermore, by looking at performance for ‘non-words’ with emotional tone, they found that affect alone was not sufficient to involve the right hemisphere in linguistic processing. They concluded that both the emotional and the lexical nature of linguistic stimuli acted to prime the RH and lead to its participation in word processing. According to these findings, under normal task conditions (i.e. words are spoken in different emotional tones), words are processed bilaterally, although more accurately in the LH, while the emotional tone is processed exclusively in the RH.

Based on these results, we chose to use a signal detection version of this task with nominated targets ‘bower’ and ‘sad’ in order to maximize the chances of independently tapping left and right hemisphere processing. Furthermore, manual responses were utilized to avoid possible confounds associated with verbal responses, given that expressive language is left lateralized. Lastly, our version also required subjects to try and detect the nominated targets in either both ears (attention divided), in just the left ear (focused left), or just the right ear (focused right) during blocked trials of each condition.

During the focused attention conditions, subjects were instructed to ignore information presented to the unattended ear. This was done in order to determine whether subjects modulated their performance with changing attention and to investigate intrusion errors. An intrusion error is when a subject is not able to inhibit a ‘yes’ response when the ‘correct target’ occurs in the ear they are instructed to ignore. Laterality of intrusion errors provides a sensitive measure of hemispheric specialization in that more intrusions are expected to occur via the ear projecting to the hemisphere that is specialized for the task.

The assertions of Grimshaw et al. (2003), although requiring further validation, do provide a useful conceptual framework for our study. For instance, it seems reasonable to expect that focused attention conditions should produce more symmetrical performance benefits during conditions of bilateral compared to unilateral processing. Furthermore, if each hemisphere simultaneously processes task-relevant and yet different stimuli, some form of interhemispheric conflict during stimulus processing and/or response programming might occur. This could limit subjects’ ability for careful and controlled responding and increase errors of commission. Based on these assertions and a model of bilateral word and unilateral emotion processing, we expect more symmetrical benefits of focused attention, as well as,
increased false alarms and intrusions during the word task compared to the emotion task.

One of the goals of the current study was to assess the effects of focused attention in both groups and to evaluate whether these results supported a model of bilateral word and unilateral emotion processing. However, our primary goal was to investigate whether adults with ADHD would exhibit atypical cerebral asymmetry, particularly, an increased RH and a reduced LH contribution. If present, this pattern of asymmetry is expected to result in: (1) enhanced overall and left ear performance during the emotion task and (2) impaired overall and right ear performance during the word task.

2. Methods

2.1. Task

After receiving a full verbal explanation of all study requirements and procedures, subjects provided written informed consent approved by the UCLA Institutional Review Board. Subjects were paid US$15.00 for participation.

Subjects with ADHD were recruited through community advertisements and outpatient clinic outreach efforts. ADHD subjects met full DSM-IV diagnostic criteria for both current and childhood ADHD (inattentive or combined subtypes) as assessed by a board-certified research psychiatrist using the Behavioral Disorders section of the Schedule for Affective Disorders and Schizophrenia for School-Age Children—Present and Lifetime Version (K-SADS-PL) (Kaufman et al., 1999), following procedures outlined by Biederman et al. (1993). Other current psychopathology was assessed with the Structured Clinical Interview for DSM-IV Axis I Disorders (SCID) (First, Gibbon, Spitzer, & Williams, 2000).

Non-ADHD control subjects were recruited from postal community advertisements and word-of-mouth referrals. Control subjects demonstrated an absence of ADHD currently and in childhood. This was established by having three or fewer inattentive and three or fewer hyperactive–impulsive symptoms both currently and in childhood, as assessed by a board-certified research psychiatrist using the K-SADS-PL interview. As with ADHD subjects, the SCID was used to assess other concurrent psychopathology.

All subjects were administered a shortened version of the Edinburgh handedness inventory (Oldfield, 1971). This version involved an 11-point Likert-type scale with potential scores ranging from 1 (left hand dominance) to 10 (right hand dominance). The Edinburgh handedness inventory was included in the study to assess handedness. A score of 10 indicates a strong right hand dominance, while a score of 0 indicates ambidextrous status. Estimated full scale IQs were obtained using the block design and vocabulary subtests of the Wechsler Adult Intelligence Scale–Revised (WASI-R) or the Kaufman Brief Intelligence Test (KBH). Subjects were excluded if any of the following conditions were present: significant neurological or medical disorders, drug and/or alcohol abuse within the past 6 months; use of psychotropic medication within the last 2 weeks (within the last month for neuroleptics and long half-life agents), a known diagnosis of a learning disorder, estimated full scale IQ < 80; non-right handedness (as indicated by scoring less than 11 on the handedness inventory), impaired vision. All subjects learned English as their first language. Control subjects were required to be free of any current or past Axis I psychiatric disorder.

Subjects comprised 22 adults with ADHD and 22 controls. Two controls and one ADHD subject were eliminated because their overall performance was 2 or more standard deviations below the mean for their group. Additionally, one control and two ADHD subjects were eliminated because it was clear that they did not follow instructions and were not performing the task (these subjects were also outliers). Demographic and diagnostic information is summarized in Table 1. ADHD subjects were significantly older than control subjects, but did not statistically differ on mean IQ or education level (i.e., attending at least 1 year of college). All subjects were free of psychotropic medication, including stimulants, a minimum of 2 weeks prior to testing. Five of 19 ADHD subjects that were included in the study were previously treated with psychostimulants.

Numerical average of Clinical Global Impression Severity Rating (CGI-S) were available for all but two ADHD subjects. All ADHD subjects received severity ratings of 4 or 5. The mean CGI-S was 4.12 indicating moderate or greater severity in our ADHD sample. All subjects were right handed (as indicated by scoring a minimum of 11 points on the handedness inventory).

2.2. Task

Subjects listened to digitalized CD quality dichotically presented stimuli on headphones (Sony Digital Reference Dynamic Stereo–MDR CD 160) via a stereo amplifier. To avoid confounds associated with potential variability in auditory sensitivity, subjects were allowed to adjust their own volume setting during a portion of the study where they were first introduced to the stimuli. Responses were registered with a specially designed microswitch situated so that response choices were vertically oriented (rather than left and right). The order of presentation of task (emotion, word) and attention condition (divided, focused left; focused right) was counterbalanced across all subjects. Due to time limitations, response hand could not be counterbalanced within subjects and so was alternated between subjects with half the participants using their left hand and half using their right hand to respond. Subjects were instructed to respond on every trial with their index finger if the target was present and their middle finger if the target was absent.

Each block consisted of 48 trials, which resulted in a total of 288 trials per subject, half of which contained the target. Target presentations were divided equally between both ears, for a total of 12 target presentations per ear. The remaining 24 trials that
did not contain the target for a given block were divided equally among the remaining stimuli. The same stimuli never occurred simultaneously in each ear. This experiment took approximately 15 min to administer. Stimulus introduction and practice sessions were provided for each task.

2.3 Data analysis

Note: The original stimulus list included trials with identical sounds in both ears. In order to prevent the occurrence of such trials the program discarded any redundant pairs from the newly randomized list for each subject. These omitted trials were not replaced, and therefore, this resulted in an unequal number of trials per block. The omission of these trials was random, and therefore, in theory, equally expressed across both groups; both tasks; all block types; and all trial types. On average, 1.9 (out of 48) trials were omitted per block with a standard deviation of (.62) and a range of 0–5. In order to compensate for this error, all performance measures were calculated as the percent correct of the total number of each trial type that actually occurred for each subject.

Our data analysis is comprised of three main components and a secondary analysis. First, we address the subjects’ ability to accurately determine the absence of a signal on a given trial. Because false alarms occur in the absence of a signal, this does not provide a laterality measure, but it does provide a rudimentary indication of response bias. Next, we address how often subjects correctly detect targets and how quickly they respond on such trials (hits). Finally, we address the number of times subjects failed to inhibit their responses when the ‘correct’ target was presented in the wrong ear during focused attention conditions (intrusions). The secondary analysis addresses concerns regarding the potential effects of comorbidity in our ADHD sample.

For each dependent variable, analysis of variance (ANOVA) was performed with task (emotion; word); attention (divided; focused); or (divided; focused left; focused right); and ear (left; right) as within-subject factors. Diagnosis (controls; ADHD) was the only between-subject factor. Gender, age, and response hand were initially included as between-subject factors. None showed main effects or interacted with diagnosis and were removed from the analysis. For each ANOVA, we will first report significant results that do not interact with diagnosis, after which we will address significant group differences. Simple effects for all significant interactions were assessed and reported.

3. Results

3.1 False alarms

All subjects made more false alarms during the word than the emotion task (emotion: 4%; word: 11%) [task: F(1,36) = 34.02, p ≤ .0001]. There was no main effect or interactions for diagnosis.

3.2 Percent hits

Overall performance improved during focused attention conditions (divided: 66%; focused: 78%) [attention: F(1,36) = 44.33, p < .0001]. An interaction of task × attention × ear [F(1,36) = 4.64, p = .038] showed that during divided attention we obtained the canonical result of a left ear advantage (LEA) for emotions (p = .013) and right ear advantage (REA) for words (p < .0001). Focused attention attenuated this LEA for emotions by disproportionately benefiting right ear trials whereas the REA for words remained unchanged (p = .057). During divided attention, all subjects were much better at processing emotions than words in the left ear (p < .0001) but in the right ear there was no difference. During focused attention, emotions were processed significantly better than words in both ears.

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**Fig. 1.** Significant three-way interaction of task × attention × ear [F(1,36) = 4.64, p = .038]. "Significant two-way interaction; "significant differences between means; shows how subject performed under divided vs. focused attention conditions.

There was no main effect for diagnosis. The interaction of attention × diagnosis was not significant (p = .27). An interaction of task × diagnosis [F(1,36) = 4.52, p = .04] showed that ADHD subjects were better than controls at the emotion task overall and, while both groups performed better for emotions than words, this difference was more pronounced in subjects with ADHD. An interaction of ear × diagnosis [F(1,36) = 4.6, p = .039] showed that an overall REA was only significant for controls (controls: p < .0001; ADHD: p = .08). Finally, an interaction of task × attention × diagnosis [F(1,36) = 12.99, p = .0009] indicated that during divided attention, adults with ADHD performed better than controls for emotions (p = .036) and poorer for words (p = .029). Each group showed a significant advantage for the emotion task throughout, but it is clear that during divided attention this advantage is more pronounced in subjects with ADHD (p = .002). Focused attention eliminated group differences that occurred during divided attention (Fig. 2).

Two post hoc analyses were performed to explore specific predictions. During the emotion task, ADHD subjects were significantly better at processing emotions in the left ear [diagnosis:
3.3. Latency for hits

A task × attention interaction [F(1,36) = 7.25, p = .01] showed that during divided attention, all subjects were faster with words than emotions (p = .007) whereas during focused attention there was no difference (p = .36). This occurred because focused attention significantly increased the speed of responses for the emotion task (p = .01) but not the word task (p = .32). An interaction of task × attention × ear [F(1,36) = 4.7, p = .037] demonstrated the canonical result that during divided attention, words were processed more quickly in the right than left ear (p = .0006) and emotions were processed more quickly in the left than right ear (p = .045). Also, during divided attention, words in the right ear were processed faster than emotions (p < .0001) while in the left ear there was no significant difference. During focused attention, not only did responses to emotion become faster but the LEA for emotions remained (p = .046). The REA for words, seen during divided attention, was eliminated during focused attention, reflecting a trend (p = .07) for right ear word responses to become slower under focused conditions (Fig. 3).

There was no main effect for diagnosis. An interaction of ear × diagnosis [F(1,36) = 8.95, p = .005] showed that ADHD subjects were significantly slower in the right ear than controls. Groups did not differ in the left ear. There were no significant interactions of [diagnosis × task] in latency.

3.4. Intrusions

All subjects made more intrusion errors during the word task than the emotion task [task: F(1,36) = 60.6, p < .0001]. All subjects had more intrusions during focused left than focused right condition [attention: F(1,36) = 6.27, p = .017]. A task × attention interaction [F(1,36) = 18.73, p < .0001] showed that during the emotion task there was an equal number of intrusions in either focus conditions whereas during the word task there were significantly more intrusions during focused left.

There was no main effect for diagnosis with respect to number of intrusion errors. An interaction of task × diagnosis [F(1,34) = 5.75, p = .02] indicated that while both groups had significantly more intrusions during the word task than the emotion task, this difference was much larger for controls. An interaction of attention × diagnosis [F(1,36) = 5.48, p = .025] indicated that controls made significantly more intrusions during the focused left than the focused right condition while adults with ADHD showed no differences as a function of direction of focus. An interaction of task × attention × diagnosis approached significance [F(1,36) = 3.41, p = .073] and suggested that group differences were largely due to differences in the number of intrusions that occurred during focused left while performing the word task. Post hoc analysis supported this conclusion. During focused left there was a significant interaction of task × diagnosis [F(1,36) = 10.07, p = .003] showing that controls had more intrusions during the word task than adults with ADHD (p = .01) and that during the emotion task there was no group difference. This same analysis showed that although both groups had significantly more intrusions during the word task than the emotion task, this difference was more pronounced for controls. There was no task × diagnosis interaction nor any group differences with either task during focused right (Fig. 4).

3.5. Secondary analyses

To explore whether an undetected language impairment contributed to our results, we examined correlations between LH word processing and (1) overall emotion processing, (2) RH emotional processing and (3) ‘word’ intrusion errors during the focused left condition in the word task (i.e. RH word processing while attempting to ignore potential intrusions stemming from the LH). There were no significant correlations.

To assess the effects of co-morbid anxiety in our ADHD sample we re-analyzed our main findings with comorbid subjects (n = 7) removed. All but two effects remained significant. The effects that did not reach significance were the word impairment
During the word task, intrusions were most prevalent while trying to ignore the language dominant LH, whereas during the emotion task, the direction of focus had no effect. Although speculative, our results appear to be well explained by a model asserting that, during this paradigm, words are processed bilaterally and emotions exclusively in the RH (Grimshaw et al., 2003).

It should be noted that there is ongoing debate regarding whether or not the LH plays a fundamental role in emotion processing, especially for positive affect, linguistically associated forms of emotion processing, or emotional expression (Aboitiz, Scheibel, Fisher, & Zaidel, 1992; Borod, Bloom, Brickman, Nakhutina, & Kurko; Compton, Heller, Banich, Palmieri, & Miller, 2000; Van Strien & Boom, 1997; Wexler, Schwartz, Warrenburg, Servis, & Tzotzis, 1986). Our task, being a signal detection paradigm, specifically assesses perceptual processing of stimuli. We suggest that characterizing hemispheric specialization of perceptual mechanisms requires placing minimal demands on linguistic and other more complex cognitive functions, and may partly explain existent controversy regarding the lateralization of emotional processing.

4. Discussion

Subjects, in both groups, exhibited the standard pattern of results, i.e. a RH advantage in both response time and accuracy during the emotion task, along with a LH advantage in response time and accuracy during the word task (Bryden & MacRae, 1988).

The previous study by Grimshaw et al. (2003) suggested that words were processed bilaterally and emotions exclusively in the RH. We hypothesized that bilateral processing should be associated with more symmetrical benefits of focused attention, as well as, less careful or controlled responses due to both hemispheres being simultaneously engaged in processing and/or generating response programming for unique and task-relevant stimuli. Several results appear fit this description.

All subjects were less accurate, made more false alarms, and more intrusion errors during the word task compared to the emotion task. Focused attention improved accuracy for both tasks, but with respect to laterality, only trials targeting the purportedly ‘non-competent’ LH showed improvement during the emotion task, while symmetrical benefits were observed during the word task. Furthermore, in the RH, there was no latency difference between words and emotions, whereas in the LH, words were processed faster. This pattern is consistent with the view that the RH is processing both words and emotions while the LH only processes words and has to transfer sensory information of emotions to the RH.

If words are processed bilaterally during our task, it is interesting to consider that ongoing interhemispheric conflict may be limiting each hemisphere’s performance. Whereas, focused attention may create a processing advantage for the hemisphere contralateral to the attended ear, perhaps, reducing interhemispheric conflict and allowing that hemisphere to perform to its potential. With emotions, if the RH is exclusively specialized, it may automatically perform at a maximum, and so, focused attention only benefits trials targeting the ‘non-competent’ LH hemisphere; perhaps, by increasing the efficiency of callosal transfer of sensory information to the RH.

In addition to there being more intrusion errors during the word task, all subjects had more ‘word’ intrusion errors when potentially ‘intruding’ stimuli were processed by the language dominant LH (i.e. when trying to ignore the LH). During the emotion task, whether the subjects focused attention on the left or right ear had no effect. This again seems consonant with the view that during the emotion task, a single RH mechanism generates all response programming, and so, the direction of focus has no bearing on the incident of intrusions.

In summary, our data showed the expected pattern of a RH advantage for emotions and a LH advantage for words, across both groups. Also, focused attention differentially modulated performance for words and emotions and subjects were more prone to intrusions errors and false alarms during the word task. During the word task, intrusions were most prevalent while trying to ignore the language dominant LH, whereas during the emotion task, the direction of focus had no effect. Although speculative, our results appear to be well explained by a model asserting that, during this paradigm, words are processed bilaterally and emotions exclusively in the RH (Grimshaw et al., 2003).
Although subjects with self-reported learning disorders were excluded, we did not directly assess for dyslexia in our sample. ADHD subjects did not differ from controls in IQ or in percent of subjects who attended at least 1 year of college. To explore whether undetected comorbid language impairments in our ADHD sample contributed to our findings, we examined correlations between ADHD subjects’ LH word performance and their: (1) overall emotion processing, (2) RH emotional processing and (3) ‘word’ intrusion errors during the focused left condition in the word task. There were no significant correlations. Although this analysis cannot definitively assess the potential effects of undetected reading disability in our sample (if present), it does strongly suggest that atypically assess the potential effects of undetected reading disability in our ADHD sample contributed to our findings; we excluded, we did not directly assess for dyslexia in our sample. ADHD subjects have smaller regions of the corpus callosum in addition to over-emphasizing a RH strategy during lateralized lexical decision tasks (submitted). Furthermore, abnormal R > L asymmetries in our ADHD sample suggest that adult ADHD subjects had enhanced RH and reduced LH function during our task. Furthermore, our results demonstrate that under conditions of focused attention, both groups performed equally, importantly suggesting that differences between adult ADHD subjects and controls, in this case, are related to the management and utilization of available resources rather than reflecting inherent ability. Further investigation of atypical lateralization of processing in ADHD may prove critical in helping us to better characterize the neural substrates of ADHD pathology. For instance, disregulation of RH arousal mechanisms, as well as, what may prove to be, LH or language mediated executive function deficits, could be indicative of atypical R > L cerebral asymmetry of function in this population.

Future studies should explore the effect of ADHD subtype and gender, include more extensive assessment of language abilities, as well as, aim to determine whether the current findings generalize to younger populations. Also, it is important to consider that the type of processing required by the current study occurs rapidly and so may represent relatively brief cognition. Tasks involving more complex executive processes may present a qualitatively different challenge to the use and management of relevant left/right brain resources and should be independently addressed. Nonetheless, our results suggest that further investigation of the neurobiology, which underlies hemispheric specialization and interaction is warranted among subjects with ADHD and may ultimately help us to better understand and perhaps generate novel treatments for the disorder.

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