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Neuropsychologia xxx (2004) xxx–xxx

NEUROPSYCHOLOGIA

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Reduced endogenous control in alien hand syndrome: evidence from naturalistic action

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Received 30 July 2003; received in revised form 19 May 2004; accepted 16 June 2004

Abstract

Patients with alien hand (AH) syndrome from medial frontal lesions exhibit involuntary but seemingly purposeful contralesional upper limb movements. Two observations about AH patients have received little, if any, experimental confirmation. The first is that AH is triggered opportunistically by nearby objects. The second is that AH behaviors are increased in conditions of fatigue or anxiety, i.e. under reduced attentional control. A prominent account explains AH as reduced intention-driven (endogenous) executive control. This account predicts that erroneous AH behaviors should be driven by environmental (i.e. exogenous) factors, such as distractor proximity to the hand. AH errors should be less influenced by the intention or action plan (i.e. endogenous factors), such as the semantic relatedness of distractors to targets. Moreover, due to capacity limitations of the endogenous controller, AH behaviors should increase under conditions of secondary task load. We tested these predictions with an AH patient in two experiments using a naturalistic coffee-making task. Experiment 1 demonstrated that the affected hand was highly perseverative and strongly influenced by exogenous but not endogenous factors. The non-alien hand made fewer errors. Experiment 2 showed that there was a disproportionate increase in perseverations and exogenous errors of the affected hand under secondary task load. The non-alien hand was significantly less disrupted by dual task conditions. These data provide experimental support for previous anecdotal observations about AH behavior in naturalistic settings, and are consistent with a unilateral defect in endogenous control.

Keywords: Anarchic hand; Alien hand; Action control; Naturalistic action; Everyday action; Praxis; Apraxia; Callosal apraxia; Dual task; Secondary task; Premotor; Attention

1. Introduction

Patients with alien hand (AH) syndrome exhibit involuntary but seemingly purposive unilateral limb movements following medial frontal and callosal lesions (Della Sala, Marchetti, & Spinnler, 1991; Goldberg & Bloom, 1990; Goldberg, Mayer, & Toglia, 1981). There have been numerous descriptions of the syndrome, many of which emphasize the predilection of AH patients to act opportunistically on nearby objects (Baynes, Tramo, Reeves, & Gazzaniga, 1997; Feinberg, Schindler, Flanagan, & Haber, 1992; Ong Hai & Odderson, 2000; Papagno & Marsile, 1995; and see Feinberg et al., 1992; Gasquoine, 1993a for reviews). Goldberg et al. (1981), for example, reported a patient who would "tend spontaneously to reach out and grasp objects (e.g. door knobs) that she passed" (p. 684). Another patient, described by Della Sala et al. (1991), "took a glass of water in her left [alien] hand while eating a piece of bread in her right and raised both to her mouth simultaneously" (pp. 2711–2712). These behaviors have been described as "compulsive" (McNabb, Carroll, & Mastaglia, 1988; Ong Hai & Odderson, 2000),

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0028-3932/$ – see front matter
doi:10.1016/j.neuropsychologia.2004.06.017

"context-dependent" (Della Sala et al., 1991), and "externally driven" (Goldberg & Bloom, 1990; Goldberg et al., 1981). However, these reports of AH behaviors have been anectodal. As a result, little is known about the factors influencing AH appearance or frequency.

To our knowledge, the only experimental studies of AH behavior were performed by Riddoch and co-workers (Riddoch, Edwards, Humphreys, West, & Heafield, 1998; Riddoch, Humphreys, & Edwards, 2000) with a single patient who was described as having bimanual AH due to corticobasal degeneration. The patient was tested in an experimental apparatus in which two objects were presented in two fixed locations, and the influence of proximity, familiarity, and location uncertainty on object and effector selection was explored. There were effects of stimulus-response compatibility and proximity to path of the action (fewer errors to distractors close to the reach path). Different error patterns emerged with each hand: the right hand was influenced relatively strongly by familiar objects (i.e. objects with associated actions, such as a cup), and the left was influenced by spatial uncertainty (i.e. instances when the position of the target and distractor were not known until a response was required). In general, the patient had greater difficulties with effector selection (i.e. using the hand specified by the examiner) than with object selection.

Several questions are raised by these studies. First, given that the patient presented with an unusual variant of bimanual AH in the context of a progressive disorder, it is not clear how the results bear on unimanual AH seen after medial frontal stroke. Second, the investigators reported that the patient's behavior on the experimental tasks was quite different than the behaviors she exhibited in daily life, and they cautioned against generalizing unduly from the experimental findings (Riddoch et al., 1998, 2000). One important remaining question, then, is how unimanual AH is impacted by task and object factors such as object relatedness and proximity to hand in the context of naturalistic everyday tasks. This question was addressed in the first of the two studies reported here.

Patients with AH characteristically exhibit lesions of the corpus callosum in addition to medial frontal structures (Goldberg & Bloom, 1990; Marchetti & Della Sala, 1998; Papagno & Marsile, 1995; Trojano, Crisci, Lanzillo, Elefante, & Caruso, 1993). Previous work by our group (Buxbaum, Schwartz, Coslett, & Carew, 1995) suggests that patients with callosal disconnection (in the absence of AH) may exhibit distinctive error patterns in naturalistic action with each hand. The patient we reported made more object selection (i.e. semantic) errors with the left hand and more spatial errors with the right hand, suggesting that each hemisphere contributes specialized cognitive processes to the performance of naturalistic action. The relevance of these prior observations for AH syndrome was also tested in the first study.

There is another often-reported aspect of AH that has not, to this point, been subject to experimental investigation. AH behaviors appear to fluctuate. That is, they are apparently subject to intermittent voluntary control, but increase in situations of fatigue or anxiety (Goldberg & Bloom, 1990). This is a provocative observation, suggesting the possibility that AH may be kept partially in check by a system that may (at times) monitor and prevent the alien behaviors. Previous accounts attribute monitoring and error prevention to control systems mediated by the frontal lobe (Shallice, 1988; Slachevsky et al., 2003).

One influential account attributes AH to an imbalance between lateral and medial premotor systems (hereafter, the dual premotor system hypothesis, or DPMS; Goldberg & Bloom, 1990; Goldberg et al., 1981. Following Denny-Brown's (1956, 1958, 1966) notion of interactive, intrahemispheric systems, Goldberg postulates a lateral premotor system in each hemisphere that controls contralateral movements that are triggered by or made in response to sensory stimuli. Medial premotor systems (one in each hemisphere) direct contralateral movements that are directed by an internal action plan (i.e. predictive models of future contingencies). Normally, these systems coordinate actions through mutual inhibition; however, following unilateral damage to the medial system, contralesional limb movements are driven largely by the preserved, externally-triggered lateral system. Consequentially, contralesional movements are perceived to be incongruous with the individual's intentions (Goldberg & Bloom, 1990; Goldberg et al., 1981). Similarly, Frith, Blakemore, & Wolpert, 2000 describe AH as a deficit in the selection of intentional actions and the disinhibition of automatic responses to objects in the environment.

Several other major theories of attention and behavioral control also posit a dichotomy between systems acting in response to external, sensory (i.e. exogenous) stimuli and those operating according to endogenously generated goals or plans. For instance, the posterior attention system proposed by Posner and Petersen (1990) is devoted to orienting attention to the environment, whereas the anterior attention system prioritizes multiple acts in accordance with higher task goals. On the model of Shallice and co-workers (Cooper, Schwartz, Yule, Warrick, & Shallice, in press; Cooper & Shallice, 2000; Norman, 1980; Shallice & Burgess, 1996) the contention scheduling system handles routine actions and "low level" interactions with the environment (e.g. effector selection), whereas the supervisory attention system is called into play to resolve response conflict and select responses in accordance with higher level goals. Importantly, on both of these accounts, the executive system is capacity-limited and subject to disruption when cognitive load is high, as, for instance, under dual task conditions. Under these circumstances, the predilection of the system handling routine or low-level actions to exogenously driven behavior is unmasked. If the medial premotor system of the DPMS is equated to (or comprises part of) a limited-capacity executive system, then we might predict that any residual control over exogenously driven behavior in AH syndrome should be reduced under conditions of cognitive load. This prediction was tested in the second study.

2. Case description

JC is a 56-year-old right-handed man with a 12th grade education who worked as a technical professional. In July 2001, he was admitted to an acute care hospital with right hemiplegia and expressive aphasia. A magnetic resonance image (MRI) of the brain performed 6 months post-stroke showed a left medial frontal lesion extending into the corpus callosum (see Fig. 1).

At MossRehab 2 weeks post-stroke, JC showed decreased motor strength on the left (lower extremity weaker than upper extremity), decreased sensation in the right lower extremity, difficulty performing rapid alternating upper extremity movements, and transcortical motor aphasia. JC and his therapists noted that the right hand uncontrollably reached for, grasped, and used objects, and that the right and left hand sometimes worked at cross-purposes. The right hand showed a strong grasp reflex, and JC often used his left hand to pry objects from the right hand. These disruptive movements continued after discharge to home. For example, JC and his spouse reported that the right hand reached for light switches, repeatedly pressed buttons on the television remote control, and groped for his left hand or face during sleep. JC expressed distress over the actions of the right hand and reported, “the hand does what it wants to” and “it has a mind of its own.”

Experimental testing of JC began in October 2001 (approximately 3–4 months post-stroke). A neurological examination at the onset of the investigation revealed no evidence of cranial nerve damage, motor weakness, or drift. All reflexes were symmetric and there were no pyramidal signs. Sensation was intact to light touch, pain and position, and there were no cerebellar signs.

A brief neuropsychological screening showed that JC was fully alert and oriented. His speech was fluent, with intact comprehension and repetition. He performed within the average to low average range on the Total Scale and all subtests of the Repeatable Battery for the Assessment of Neuropsychological Status (RBANS; Randolph, 1998); Total Scale = 16th percentile; immediate memory = 25th percentile; visuospatial/visuocontructional = 38th percentile; language = 25th percentile; attention = 24th percentile). Performance on

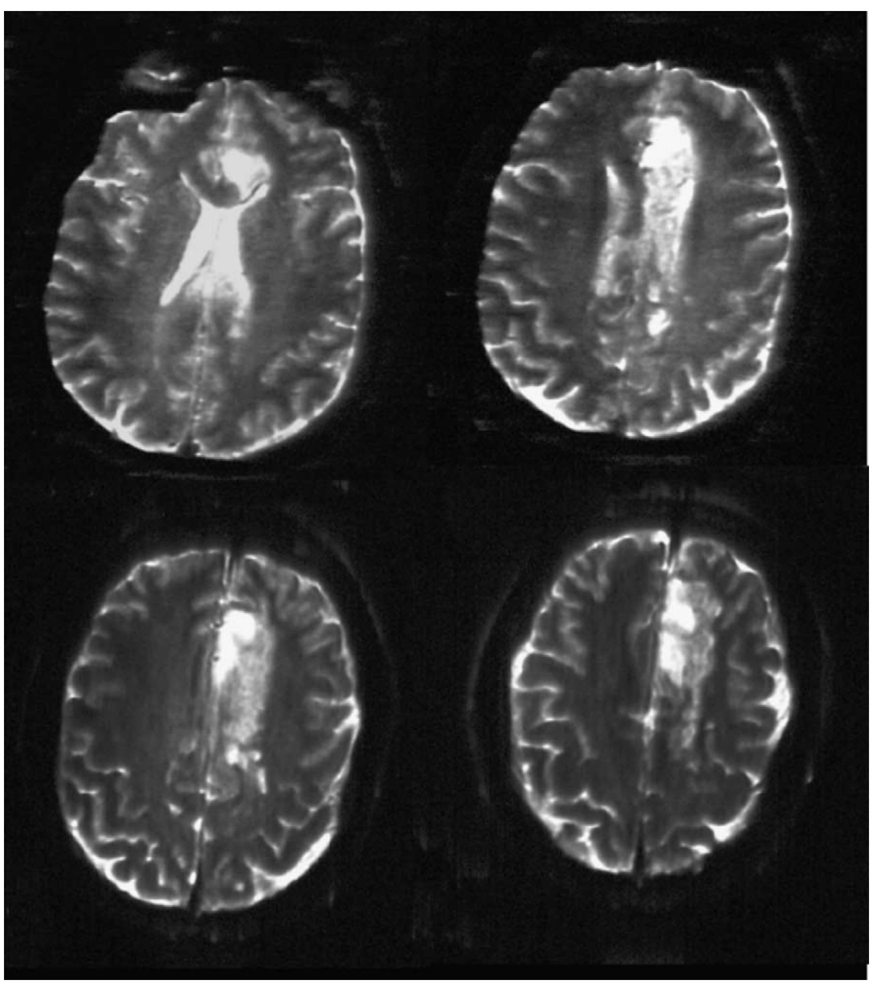

Fig. 1. T2 weighted magnetic resonance images showing JC’s ischemic lesion of the left medial frontal cortex and the corpus callosum. The lesion involves the middle and anterior cingulate (Brodmann’s Area (BA) 24 and parts of 23) as well as parts of BA 6, 8, and 32.

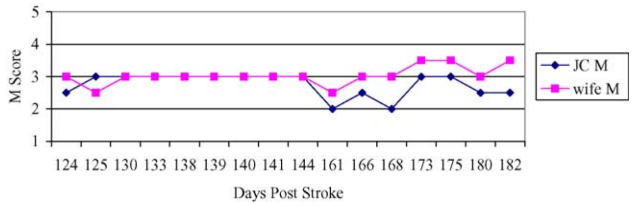

Fig. 2. Mean symptom questionnaire scores for JC and his wife during the course of the study.

the delayed memory scale was in the low average range (10th percentile) due to performance on free recall trials; recognition test performance was intact.

There was no evidence of tactile anomia or agraphia with either hand. To assess apraxia, JC was asked to gesture the use of 10 visually presented objects with the right and left hand separately. Performance was videotaped and each gesture was scored on a 4-point scale[1] by two coders (see Buxbaum, Giovannetti, & Libon, 2000). Coding discrepancies were reviewed and discussed until agreement was reached. JC's performance was compared to normative data from 10 healthy right-handed controls (*M* age = 64.7, range = 43–77; *M* education = 14, range 10–18) tested with their left hands (Buxbaum, 2003). JC performed within the normal range (*M* = 90.4, S.D. = 6.2, 2 S.D. cut off = 78.0) with his dominant (right) hand (*M* = 0.80, S.D. = 0.31), but scored below the cut-off with his non-dominant (left) hand (*M* = 0.65, S.D. = 0.27). Within-subject comparison showed that JC's praxis scores were significantly lower with the left than the right hand (Wilcoxon signed ranks $z = -2.12$, $P = 0.034$). This pattern of performance is consistent with callosal apraxia.

Data for this study were collected during a period of 51 days (26/11/2002 to 15/1/2002). During this time, JC and his spouse completed a brief questionnaire designed to chart the frequency and severity of JC's AH symptoms. The questions were: (1) How many daily activities were disrupted by the right hand? and (2) On average, how severely did the right hand disrupt performance? Response choices were presented on a 5-point scale, with "1" indicating mild or no problems and "5" frequent and severe problems. Results are shown in Fig. 2. Note that although JC endorsed slightly improved performance toward the end of the study, his wife did not corroborate the improvement. Overall, AH symptoms appear to have been relatively stable throughout the study.

3. Study 1: Standard Coffee Challenge

To assess the factors that influence AH behaviors and to examine the effect of callosal apraxia on naturalistic action, JC (and healthy controls) performed the Coffee Challenge (CC). The CC is a standardized naturalistic task that was developed by Giovannetti, Schwartz and Buxbaum (in press) to study naturalistic action errors in healthy (i.e. cognitively unimpaired) participants. The CC incorporates factors known to disrupt everyday action and/or target selection, including time pressure, the presence of multiple functionally and visually similar distractor objects, and object location uncertainty. Details of the original, normative study of the CC are reported in Appendix A.

The CC is especially suitable for the current study because it yields variables reflecting the rate and types of errors and exogenous/endogenous influences on errors. The functional similarity and visual similarity between distractors and targets were considered to reflect endogenous influences on CC errors. If errors are influenced by an internal action plan (or internal object representation), then distractors that are highly similar to targets will be selected over distractors that are dissimilar to targets. Prior evidence with brain-damaged patients attests to an effect of distractor–target similarity on action errors (Cooper & Shallice, 2000; Giovannetti, Libon, Buxbaum & Schwartz, 2002; Reason, 1990; Schwartz et al., 1995). Even more to the point, in healthy adults, the salience of various visual and functional distractor features is modulated by the participant's intention (i.e. action plan; Bekkering & Neggers, 2002; Boutsen & Humphreys, 2003; Pavese & Buxbaum, 2002; Remington & Folk, 2001). For example, handled cups are more distracting when subjects intend to grasp than poke a target (Pavese & Buxbaum, 2002). In a normative study of the CC with healthy participants, distractor–target similarity had a greater effect on errors than chance (see Appendix A).

The proximity of distractors to the acting hand and to the target were assessed as indicators of exogenous influences on CC errors. Selection based on distractor location reflects the influence of the environment or object array (exogenous), not the internal action plan (or object representation). Distractor location has been shown to affect performance in a range of reach-to-target tasks (Buxbaum & Permaul, 2001; Tipper, Howard, & Houghton, 1998; Tipper, Lortie & Baylis, 1992; see also Graziano, Yap & Gross, 1994). Additionally, we have shown that these factors influenced distractor selection more than chance in a normative study of the CC (see Appendix A).

3.1. Method

3.1.1. Participants

JC and four healthy, right handed, age- and education-matched controls (CTLs) were tested (CTL *M* age = 52.3; range 48–60; *M* education = 12.0; range = 10–14). On interview, CTLs denied record of memory/cognitive deficits, neurological or psychiatric illness, substance abuse, or traumatic brain injury.

3.1.2. CC procedures

Participants were asked to make two cups of coffee (one for Joe and one for Martha). As shown in Table 1, eight unique, but similar objects were used for each cup and were

[1] Each gesture was ultimately scored as the percent correct out of four possible points.

Table 1
Objects used in the Coffee Challenge

Object type	Joe's cup	Martha's cup
Coffee maker	Electric drip coffee maker (with glass pitcher)	Hot water pitcher
Filter holder	Basket filter	Manual drip cone filter
Filter paper	Basket filter paper	Cone filter paper
Mug	Green travel mug	White ceramic mug
Coffee	Regular coffee in can	Hazelnut coffee in bag
Sweetener	Artificial sweetener in packet	Sugar in bowl
Creamer	Fresh cream in small pitcher	Non-dairy powder creamer in jar
Stirrer	Spoon	Plastic stirrer

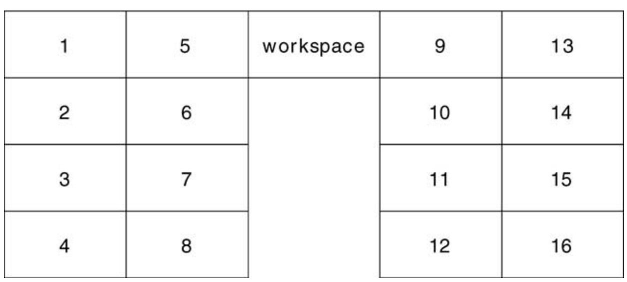

Fig. 3. Schematic of U-shaped testing table sections and workspace. Participants were seating at the center of the table facing the workspace.

present on a U-shaped testing table throughout the task. The tabletop was divided into 16 sections, each containing an object, and a central workspace as shown in Fig. 3.

Object placement was standardized so that the object array was the same across participants, but differed from trial to trial. Prior to each trial, several of the corresponding objects for each cup (e.g. the two mugs; the two sweeteners) switched places. For example, if the mugs for Joe's cup and Martha's cup were on the left and right, respectively, in the first trial, these placements were intermittently reversed in subsequent trials.

Prior to the first trial, the objects used for each cup were reviewed several times and participants were instructed to work as quickly as possible without making errors. The order of the task was not specified, but participants were encouraged to interleave the steps of Joe and Martha's cups to minimize time. Participants were also urged not to touch or move objects until they were ready to use them. At the end of each trial, time to completion was announced, and participants were encouraged to try and outperform their fastest time on the subsequent trial. While data from the normative study indicated that CC performance stabilized by the 10th trial (see Appendix A), we administered 13 trials in the present study to increase the opportunity for JC to reach asymptotic levels of performance. All trials were videotaped for coding.

3.1.3. Performance analysis

3.1.3.1. Frequency of errors and intermanual conflict. For the present study, right (R), left (L), and bimanual errors were summed separately. Intermanual conflict was coded when: (1) the R and L hands worked at cross-purposes (e.g. the R hand closed the coffee can while the L hand attempted to scoop coffee from the can); (2) the R and L hand simultaneously took two different objects that are used for different steps (e.g. the R hand picked up the basket filter while the L hand took the artificial sweetener); or (3) the R/L hand grasped the opposite hand or the object in the opposite hand.

3.1.3.2. Error types. Errors were classified according to the taxonomy described in Table 2.

3.1.3.3. Exogenous/endogenous influences. Distractor proximity to the hand and proximity to the target (exogenous influences) according to the procedures described in Appendix A. For the present study, exogenous influences were assessed for all errors (substitutions, perseverations, and sequence).

The visual similarity and functional similarity between distractors and targets (endogenous influences) were assessed for CC substitutions as described in Appendix A. Ratings were converted to ranked scores for the purpose of statistical analyses.

3.2. Results

3.2.1. Frequency of errors and intermanual conflict

A minority of errors was made by both hands simultaneously (JC −9%; CTLs −11%) or could not be attributed to either hand (e.g. anticipatory errors in which a step was omitted; JC −1% of total errors – controls −13% of total errors). These errors were dropped from further analysis.

Fig. 4 shows the CTL mean R and L errors and JC's total R and L errors on each CC trial. CTL R and L data showed improvement and stabilization over trials. JC's performance

Table 2
Coffee challenge error taxonomy

Error category	Definition	Example
Substitution	A non-target object is substituted for the target	Puts sugar or coffee (instead of artificial sweetener) into green travel mug
Anticipation/omission	Object is used before (or without) completing the necessary preceeding steps	Filter basket placed in coffee machine before (or without) adding coffee
Perseveration	Object is used a second time (or more) after it had been used correctly	Sugar added to the white ceramic mug twice

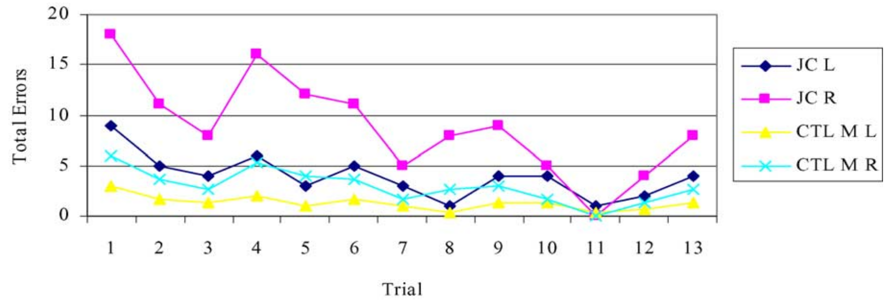

Fig. 4. Total right and left hand errors for JC and mean total errors for the four CTLs across the 13 Coffee Challenge trials in Study 1.

Table 3
Mean right and left errors per trial for JC and controls in Study 1

	JC *M* (S.D.)	Controls *M* (S.D.)
Right errors	13.5 (4.3)	2.9 (1.6)
Left errors	4.3 (2.9)	1.3 (0.71)
Intermanual conflict	10.54 (5.8)	0

also showed some gross improvement over the 13 trials, but the R hand continued to show a high and variable error rate.

JC's mean instances of intermanual conflict per trial along with his (and CTL) mean errors per trial are shown in Table 3. A participant (JC versus CTL) × hand (R versus L) analysis of variance (ANOVA) showed significant main effects, with more errors for JC than CTLs ($F(1, 24) = 61.7$, $P < 0.01$) and more R than L errors ($F(1, 24) = 73.7$, $P < 0.01$). The participant × hand interaction was also significant ($F(1, 24) = 35.7$, $P < 0.01$), indicating that JC made disproportionately more R hand errors.

JC also showed intermanual conflict throughout the CC trials, ranging from 26 instances on the first trial to 5 instances on the final trial. CTLs did not exhibit intermanual conflict.

3.2.2. Error types

Fig. 5 shows means of the 3 error types for JC and CTLs. Between group analyses were performed using Mann–Whitney tests. As compared to CTLs, JC made more R hand errors of all three types ($z < -2.6$, $P > 0.01$ for all) and more L hand substitution errors ($z = -2.8$, $P < 0.01$). No other differences were significant ($z < -1.2$, $P > 0.26$ for all).

Fig. 6 shows JC and CTL total errors (by hand) and the proportion of errors of each type. JC's R hand shows a disproportionate number of perseverations relative to his L hand (and relative to CTLs), while his L hand error pattern is strikingly similar to controls. When the ratio of JC's perseverations to substitutions was compared to that of CTLs, results greatly differed for the R hand (chi-square (1) = 55.0, $P < 0.001$) but not the L hand (chi-square (1) = 0.05, $P = 0.82$).

3.2.3. Exogenous/endogenous influences

Table 4 shows the proportion of errors made to distractors near the acting hand or near the target. There was a significant difference between JC and CTLs for R "near hand" errors and a trend for the L.

The mean rank visual and functional similarity ratings of substitution errors are also shown in Table 4. Substitutions made by JC's R hand were significantly less visually and functionally similar to the target than controls' R hand errors. There were no differences between JC and CTLs with the L hand.

3.3. Discussion

A number of findings permit us to characterize JC's deficits in performing naturalistic action. First, he exhibited frequent intermanual conflict. Second, errors with both the R and L hand were higher than that of healthy participants. Third, the significant participant × hand interaction indicates that JC's R hand performance was disproportionately im-

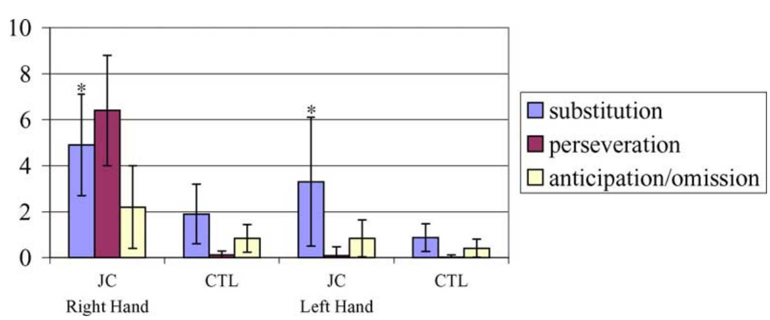

Fig. 5. Mean right and left hand errors per trial for JC and controls (CTLs) in Study 1 (* JC significantly greater than CTLs).

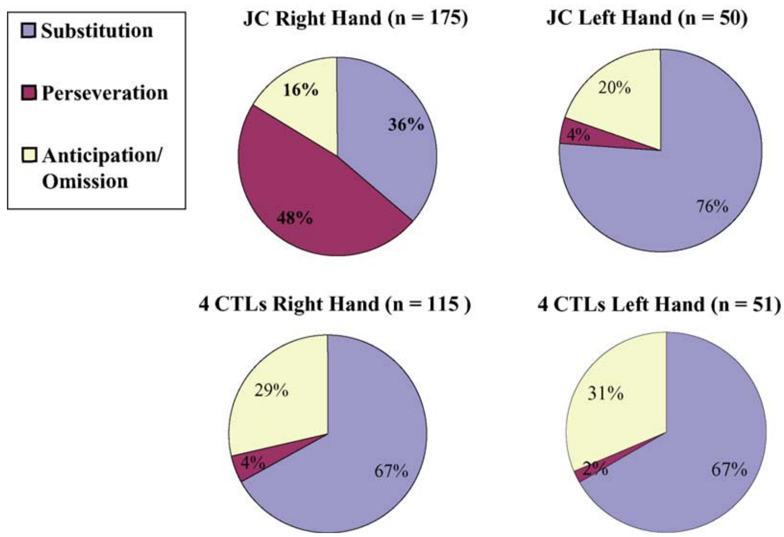

Fig. 6. Right and left hand errors as a proportion of total errors for JC and four CTLs in Study 1.

paired. Fourth, each hand demonstrated a unique pattern of errors.

JC's R (alien) hand was more influenced by an exogenous factor (proximity of distractors to the hand) and less influenced by endogenous factors (perceptual and functional similarity of distractors to targets) than were CTL errors. Although JC's L hand tended to be slightly more influenced by exogenous influences than controls, substitution errors of that hand were no more likely to be influenced by visual and functional similarity than were controls' substitution errors. Thus, the R hand exhibited greater overall abnormality in the relative influence of exogenous versus endogenous factors.

JC's R hand was also abnormally perseverative. Perseveration is a hallmark feature of the AH syndrome, with numerous case reports describing repetitive movement sequences and/or a strong palmar grasp reflex (Ong Hai & Odderson, 2000; Papagno & Marsile, 1995). Liepmann originally termed these clonic/continuous and tonic perseverations, respectively (see Sandson & Albert, 1984). JC demonstrated tonic perseverations on the CC, and frequently used his L hand to release objects from his R hand. Although these behaviors were disruptive, they were not coded as perseverative errors on the CC. The errors we termed perseverations were inappropriate repetitions of actions, which for JC, unlike controls, almost always occurred without interruption (i.e. continuous perseveration). For example, JC's perseverations included cyclically scooping sugar into the mug, repetitively opening and closing the coffee can, and so on. Unlike other forms of perseveration, continuous perseverations are putatively unrelated to failures of episodic memory (Sandson & Albert, 1984). Shallice (1988) has proposed that perseverative errors, in general, are the consequence of reduced endogenous (i.e. supervisory) control. Thus, it is possible that in the absence of strong endogenous control, the action system defaults to the most recently performed action. If this interpretation is correct, it is of interest that in the case of JC, this reversion to recent behavior occurs in only one hand.

JC's L hand made more substitution errors than CTLs; on the other hand, neither overall error proportion nor the influence of endogenous factors significantly differed from

Table 4
Endogenous and exogenous influences in Study 1

	Right hand				Left hand			
	JC (N = 175)	Controls (N = 115)	Chi-square	P-value	JC (N = 56)	Controls (N = 51)	Chi-square	P-value
Exogenous influences on total errors								
Percent of errors near hand	64%	44%	10.1	<0.01	54%	33%	3.7	0.06
Percent of errors near target	42%	37%	0.5	0.48	48%	31%	2.5	0.11
	JC (N = 64)	Controls (N = 77)			JC (N = 43)	Controls (N = 34)		
	M rank	M rank	z	P-value	M rank	M rank	z	P-value
Endogenous influences on substitutions								
Visual rating	94.9	118.3	−2.7	<0.01	38.7	39.5	−0.16	0.88
Functional rating	93.7	120.2	−3.1	<0.01	39.1	38.8	−0.06	0.95

CTLs. The high number of L hand substitutions is consistent with data from our previously reported patient with callosal disconnection syndrome (Buxbaum et al., 1995). This supports our previous claim that in such patients, unimanual substitution errors of the L hand may be attributable to partial disconnection of R hemisphere motor systems from L hemisphere-based semantic and gestural information guiding object selection and use.

4. Study 2: effect of divided attention

If AH behaviors are partially held in check by the residual control of a resource-limited endogenous system, then diverting attentional resources from the primary naturalistic task should have a disruptive effect on the alien hand. This predicts disproportionate increases in R hand errors, and in exogenously-influenced errors more specifically, under secondary task load. We assessed this prediction in the second study.

4.1. Method

4.1.1. Participants

JC and four healthy, right-handed, controls (CTLs) were tested. The CTLs, similar to JC in both age and education (CTL *M* age = 47; range 44–53; *M* education = 13.5; range = 12–16), were drawn from the normative CC study described in Appendix A. Prior to performing the Standard- and Concurrent-CC conditions, CTLs had completed 10 CC "practice" trials. Their performance on these trials (*M* errors per CC trial = 3.45, S.D. = 1.85) was comparable to CTLs in Study1 ($M = 4.0$, S.D. = 2.1; $t\,(21) = -0.68$, $P = 0.50$).

4.1.2. CC concurrent task procedures

The concurrent task was the oral-trail making test (OTMT; (Abraham, Axelrod, & Ricker, 1996; Ricker & Axelrod, 1995; see Appendix A). The OTMT was modified for JC because he was unable to perform the version administered to controls, even following considerable practice. JC was asked to repetitively and rapidly cycle through letter-number pairs from A1 to J10 (i.e. A-1, B-2, C-3, D-4, E-5, F-6, G-7, H-8, I-9, J-10, A-1, B-2, etc.). Twenty-three OTMT practice trials were performed in which JC recited the A-1 thru J-10 sequence twice. JC's performance on these trials was recorded.

Following OTMT practice, all participants performed 4 blocks of 3 CC trials (total 12 trials), alternating (ABAB) between the Standard-CC, performed as in Study 1, and Concurrent-CC, in which the CC and OTMT were performed simultaneously. JC and CTLs were told that performance on both the CC and OTMT tasks would be evaluated for speed and accuracy and that both tasks should be performed simultaneously. Performance was videotaped for analysis.

4.1.3. Performance analysis

All measures collected in Study 1 (i.e. error frequency, intermanual conflict, error types, and endogenous/exogenous influences) were obtained for each hand on Standard- and Concurrent-CC trials. In addition, the average number of seconds to produce a correct OTMT letter & number pair (i.e. time to completion divided by number of correct responses; OTMT RATE) was recorded. A low OTMT RATE reflects better performance than a high OTMT RATE.

4.2. Results

4.2.1. Frequency of errors and OTMT RATE

Fig. 7 shows the mean total errors (R, L and bimanual) for JC and the CTLs across the Standard- and Concurrent-CC conditions. A participant (JC versus CTLs) × condition (Standard-CC versus Concurrent-CC) ANOVA showed significant main effects, with more errors for JC than CTLs ($F(1, 20) = 49.9$, $P < 0.01$) and more errors in the Concurrent-CC than the Standard-CC ($F(1, 20) = 7.7$, $P = 0.01$). The participant × condition interaction was not significant ($F(1, 20) = 0.40$, $P = 0.54$), suggesting that the Concurrent-CC was equally difficult for both JC and CTLs. Moreover, there was no difference in the mean OTMT RATE for Concurrent-CC trials when JC ($M = 3.4$, S.D. = 1.3) was compared to CTLs ($M = 4.1$, S.D. = 0.18; $t = 1.1$, $P = 0.28$), indicating that participants were generating OTMT responses at a comparable rate. Thus, despite the fact that the OTMT procedures differed between JC and CTLs, we were successful in creating an equivalent dual task challenge.

JC's OTMT RATE was significantly higher for the six Concurrent-CC trials than the last six OTMT practice trials ($M = 1.2$, S.D. = 0.09; $t = -4.0$, $P = 0.01$). Thus, both the OTMT and CC task suffered in the concurrent condition.

4.2.2. Frequency of errors by hand and intermanual conflict

As in study 1, a minority of errors was made by both hands simultaneously or could not be attributed to either hand (JC-Standard-CC- 16% of all errors, Concurrent-CC- 10% of all errors; CTLs- Standard-CC- 12%, Concurrent-CC- 18%). These were dropped from subsequent analyses. Mean total R and L errors are shown in Table 5. We performed two participant (JC versus CTL *M*) × hand (R versus L) ANOVAs, the first with Standard-CC errors as the dependent variable and the second with Concurrent-CC as the dependent variable. In the first ANOVA, both main effects were significant, such that JC made more errors than CTLs ($F(1, 10) = 51.8$, $P < 0.01$) and there were more R than L errors ($F(1, 10) = 5.5$, $P = 0.04$) in the Standard-CC condition. The interaction was not significant ($F(1, 10) = 3.3$, $P = 0.10$). In the second ANOVA, however, both main effects and the interaction were significant, indicating that in the Concurrent-CC condition JC made more errors than CTLs ($F(1, 10) = 23.1$, $P < 0.01$), there were more R than L errors ($F(1, 10) = 45.5$, $P < 0.01$), and JC made disproportionately more R errors than

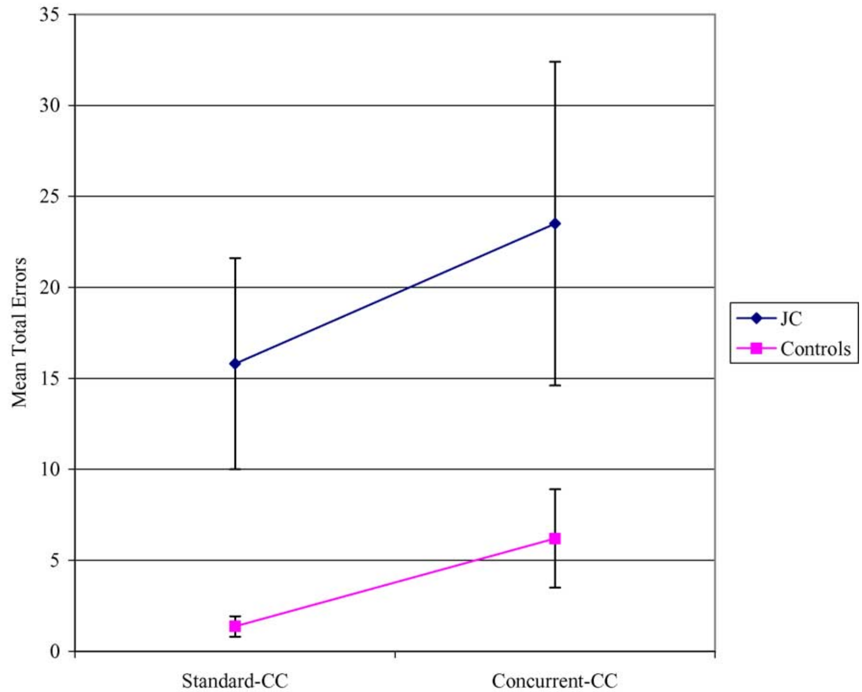

Fig. 7. Mean total CC errors (right, left, and bimanual summed) for JC and CTLs across the Standard-CC and Concurrent-CC in Study 2.

CTLs ($F(1, 10) = 10.5$, $P = 0.01$). Thus, the concurrent task disproportionately disrupted JC's CC performance with the R (alien) hand.

As shown in Table 5, JC also had significantly more instances of intermanual conflict in the Concurrent-CC than the Standard-CC (Mann–Whitney $z = -2.3$, $P = 0.03$). CTLs showed no instances of intermanual conflict in either CC condition.

4.2.3. Error types

Fig. 8 shows the mean total errors of each type by hand in the Standard- and Concurrent-CC conditions. Condition (Standard versus Concurrent) × hand (R versus L) ANOVAs for each error type (substitution, anticipation, perseveration) were performed for JC. The ANOVA for substitutions showed JC made more errors in the Concurrent-CC ($F(1, 20) = 5.7$, $P = 0.03$), and more errors with the R hand ($F = 10.0$, $P < 0.01$), but the condition × hand interaction was not significant ($F = 0.28$, $P = 0.60$). The ANOVA for anticipations showed no significant effect of condition, hand, or condition × hand ($F < 0.63$, $P > 0.43$ for all). The results for perseverations showed significant effects of both condition ($F = 5.6$, $P = 0.03$) and hand ($F = 9.9$, $P < 0.01$), as well as a significant condition × hand interaction ($F = 5.6$, $P = 0.03$), demonstrating a disproportionate increase of perseverative errors in the Concurrent-CC with the R hand.

Table 5
Mean errors per trial for the standard and concurrent conditions of Study 2

	Standard		Concurrent	
	M	S.D.	*M*	S.D.
JC				
R errors	6.8	1.6	11.5	3.2
L errors	4.5	2.6	6	3.2
Intermanual conflict	1.8	1.6	4.3	2.3
Controls				
R errors	0.75	0.55	3.5	1.7
L errors	0.46	0.37	1.6	0.57
Intermanual conflict	0		0	

Condition × hand ANOVAs were not performed for CTL data, as error rates were too low in the Standard-CC for reliable analyses of error types (see Table 5 and Fig. 8). Therefore, we focused on the Concurrent-CC. Participant (JC versus CTL *M*) × hand (R versus L) ANOVAs for each error type (substitution, anticipation, perseveration; see Fig. 8) were performed. The ANOVA for substitutions showed JC made more errors than CTLs ($F(1, 20) = 70$, $P < 0.01$), but there was no effect of hand ($F = 3.2$, $P = 0.09$) and no interaction ($F = 2.7$, $P = 0.12$). There were no significant effects for anticipation errors ($F < 1.8$, $P > 0.19$ for all). However, the ANOVA for perseverations showed significant main effects (participant $F = 21.2$, $P < 0.01$; hand $F = 13.3$, $P < 0.01$) and a significant interaction ($F = 9.5$, $P < 0.01$), indicating that JC made disproportionately more R hand perseverations than CTLs.

4.2.4. Exogenous/endogenous influences

Table 6 shows the proportion of JC's errors influenced by exogenous factors (proximity to hand/target). A greater proportion of R errors were coded as "near the hand" in the Concurrent than the Standard-CC. No other Standard versus Concurrent comparisons were significant. Relative to CTLs

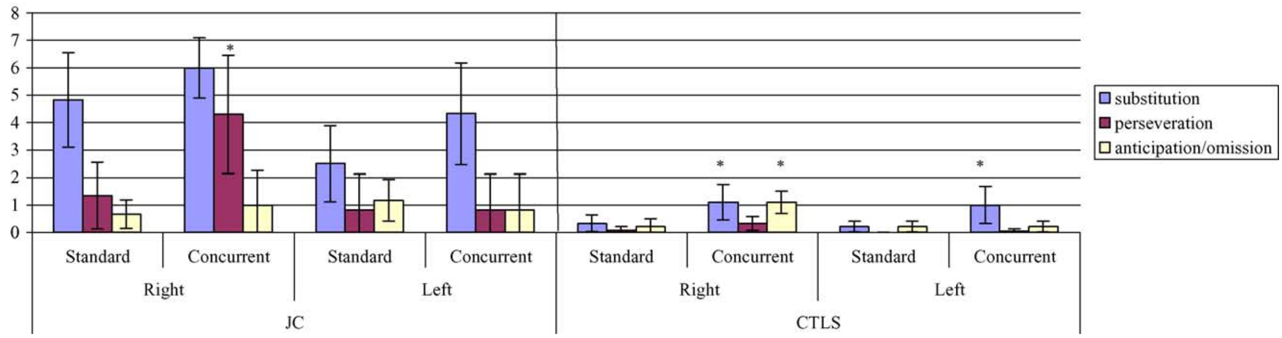

Fig. 8. Mean right and left hand errors per trial for JC and CTLs across the Standard-CC and Concurrent-CC in Study 2.

Table 6
Exogenous influences on total errors across the standard and concurrent conditions in Study 2

	R hand				L hand			
	Standard-CC (n = 41)	Concurrent-CC (n = 69)	Chi-square	P-value	Standard-CC (n = 27)	Concurrent-CC (n = 35)	Chi-square	P-value
Near hand	32%	58%	6.1	0.01	63%	46%	1.2	0.28
Near target	20%	25%	0.18	0.67	33%	17%	1.3	0.24

(near hand: R 42%, L 30%; near target: R 39%, L 30%), JC showed a higher proportion of R “near hand” errors (chi-square (1) = 3.9, P = 0.05) in the Concurrent-CC. No other comparison between JC and CTLs was significant (chi-square (1) < 3.4, P > 0.06 for all).

The influence of endogenous factors (visual and semantic similarity) on substitution errors did not differ across the two CC conditions for either hand (z’s < −1.5, P’s > 0.13 for all). CTLs obtained higher functional similarity ratings than JC in the Concurrent-CC for both the R (z = −3.7, P < 0.01) and the L hand (z = −2.7, P = 0.01). There were no JC versus CTL differences in visual similarity ratings (z < −1.1, P > 0.28 for all).

4.3. Discussion

Performance of a concurrent task along with the naturalistic task resulted in a performance decrement on the CC for both JC and CTLs. For JC, the naturalistic task decrement was quite specific to intermanual conflict and errors with the R (alien hand). Importantly, the R hand did not show a general increase in all error types. Rather, the concurrent task caused a qualitative shift in JC’s R (alien) hand action error pattern, with a disproportionate increase in perseverations and errors influenced by distractors near the acting hand (an exogenous factor). JC’s left hand, in contrast, showed no shift in the error pattern or the factors that influenced errors. Thus, depletion of attentional resources disrupts control of he alien hand, but does not significantly exacerbate callosal apraxia.

One possible objection to the disproportionate impairment of the R hand in the concurrent condition is that the effects are non-specific, and would be observed in any patient with a unilateral motor deficit. We believe that this explanation is unlikely for several reasons. First, the effect of the secondary task on JC’s R hand was specific to perseverations, intermanual conflict, and exogenously influenced errors, all of which are prominent features of AHS. In previous studies of unilateral stroke patients tested with the naturalistic action test (NAT), a standardized test requiring participants to perform a series of everyday tasks, intermanual conflict never occurred, and perseveration errors were so rare that they were combined with anticipation errors and reported together in a general “sequence” category (Buxbaum et al., 1998; Schwartz et al., 1999). In fact, perseverations comprised only 1 and 4% of total errors for LCVA (n = 16; Buxbaum et al., 1998) and R CVA (n = 30; Schwartz et al., 1999), respectively (compare to JC, for whom perseverations comprised 20% of Standard-CC total errors and 38% of Concurrent-CC errors). Thus, stroke patients’ pattern of performance looked qualitatively different than that of JC.

To directly address the possibility that mild contralesional motor deficits in LCVA might be sensitive to exacerbation in executively challenging conditions, we identified three LCVA participants from the NAT database who exhibited mild hemiparesis, used both hands on the NAT, and made errors.[2] We compared performance across NAT items, which increase in difficulty: (Item 1) prepare toast with butter and jelly and prepare coffee with cream and sugar; (Item 2) wrap a gift with related distractor objects (gardening clippers, stapler, etc.) in the array; and (Item 3) pack a lunch box with a sandwich, snack, and a drink and pack a school bag with supplies for school, while holding in mind the fact that several of the necessary objects (knife, thermos lids) are stored out of view in

[2] Participants’ data were selected from our database of patients undergoing rehabilitation for LCVA previously reported by Schwartz et al. (2002).

a drawer along with potentially distracting objects (ice tongs, measuring tape, etc.). In addition, Item 3 also requires participants to hold in mind an instruction to activate a buzzer after completing each main task. Item 3 is more difficult and executively demanding than preceding items (see Buxbaum et al., 1998; Schwartz et al., 1998; 1999): neurologically-impaired patients commit more errors on this item, even after error rates are standardized for differences in the opportunity to make errors at each level (standardized error rates; Schwartz et al., 2002). The three LCVA participants we examined here demonstrated a progressive increase in mean standardized error across the NAT Items (Item 1 M = 2.6, S.D. = 2.9; Item 2 M = 8.8, S.D. = 7.8; Item 3 M = 10.0, S.D. = 9.3). Despite the increase in standardized error rate, there was no evidence for a disproportionate increase in errors with the weak R hand across the NAT Items, and if anything, the increase was somewhat greater for the L hand (R hand: Item 1 M = 1.3, S.D. = 2.3; Item 2 M = 1.9, S.D. = 3.4; Item 3 M = 3.2, S.D. = 4.4; ratio 1/1.5/2.5; L hand: Item 1 M = 0.6, S.D. = 1.0; Item 2 M = 1.9, S.D. = 3.4; Item 3 M = 3.2, S.D. = 3.2; ratio 1/3.2/5.3).

The specific increase in JC's intermanual conflict and R (alien) hand perseverations and exogenously influenced errors under resource limitations is consistent with the notion that AH behaviors may be held in check by a resource-limited endogenous control system. The DPMS account suggests that residual endogenous control of the alien hand occurs through the contralateral mesial premotor area. Other theories of action control posit a more general resource-limited supramodal control system that is not explicitly premotor in nature (Posner & Peterson, 1990; Shallice & Burgess, 1996). This putatively amodal controller is similarly localized to medial prefrontal cortex (Posner & Peterson, 1990). More recently, Frith et al. (2000) propose a model with both a lateralized premotor system that selects action and inhibits responses to external action triggers and a high level system that generates intentions and goals. On this account, AH is attributed to impairment in the premotor system.

The present results suggest an interaction between a unilateral motor control deficit (AH) and executive resources, but do not speak to the question of whether the damaged endogenous control system is specialized for motor actions, or is more broadly applicable to general behavior control. In Section 4.4, we will focus on the behaviors of the alien hand and explore possible underlying mechanisms.

4.4. General discussion

To our knowledge, this is the first systematic investigation of naturalistic action performance in AH syndrome. Consistent with anecdotal reports and theories of executive dyscontrol, alien hand errors reflected triggering of action by an exogenous factor; namely, the proximity of distractor objects to the hand. At the same time, JC's errors were less influenced by the visual and functional similarity between distractors and targets, indicating diminished responsiveness to endogenous (e.g. plan-driven) information. An exogenous–endogenous imbalance of the right (alien) hand was also observed on computerized target detection tasks in a companion study to be reported (Biran, Giovannetti, Buxbaum & Chatterjee, 2002).

Studies with healthy adults (e.g. Tipper et al., 1992, 1998) and patients with neglect (Behrmann & Meegan, 1998; Buxbaum & Permaul, 2001) indicate that visual attention may be "hand centered," in that distractors close to the hand (and close to the intended path of action) compete more strongly for attentional control than distractors further from the hand. In healthy adults, inhibitory processes resolve the competition by suppressing the activation of the close-to-hand distractor objects, and this inhibitory process exerts a cost on reaction time. When inhibitory processes fail altogether, as is likely the case with JC, frank misreaches to distractor objects may occur (see Buxbaum & Permaul, 2001).

This study is also the first to show empirical support for an exacerbation and qualitative shift of AH behaviors under conditions of resource limitations. The R hand showed a disproportionate error rate, with a tendency for perseverative and exogenously-influenced errors on the naturalistic task (Study 1). This disproportionate R hand error rate diminished with practice (Standard-CC, Study 2); but recurred when the secondary task load was imposed (Concurrent-CC, Study 2). Moreover, the concurrent task caused a specific increase in intermanual conflict, R hand perseverative behaviors, and R hand sensitivity to distractors close to the hand. These data are consistent with the proposal that alien behaviors are normally partially suppressed by a limited-capacity endogenous system.

The DPMS account suggests that mesial premotor areas including the anterior cingulate and supplementary motor area are involved in the process of "selection for action," involving gating the access of inputs to motor output. Moreover, the account posits that some degree of volitional control of the AH may be imposed by the preserved ipsilateral (in this case, R) mesial premotor area. Thus, the R mesial premotor area is responsible for controlling the actions of both hands. To explain the specific exacerbation of JC's AH behaviors under secondary task load, this account requires that the medial premotor system is both resource-limited and recruited for verbally-mediated, executive tasks, such as the oral trail making test.

On both accounts of Posner & Peterson, 1990) and Shallice and co-workers (Cooper & Shallice, 2000; Norman, 1980; Shallice & Burgess, 1996) the executive control system of the frontal lobe is not lateralized, and not as explicitly tied to the premotor system. Instead, it is a supramodal system involved in resolving conflict between potential sources of behavioral control, and in prioritizing current goals on the basis of changing environmental events. In their discussion of "utilization behavior" (a tendency to use task-unrelated objects seen in some frontal lobe patients, arguably related to AH behaviors), Shallice and co-workers (Cooper & Shallice, 2000; Norman, 1980; Shallice & Burgess, 1996; Shallice, Burgess, Schon, & Baxter, 1989) describe a mechanism whereby posterior perceptual systems activate schema for low level or routine behaviors, including actions associated with objects. Under normal circumstances, the supervisory (executive) system of the frontal lobes prevents activation of task-irrelevant schema. To explain the findings of an asymmetric increase in contralesional AH behaviors (but not abnormal substitution behaviors of the ipsilesional hand) under secondary task load, these accounts must posit that control of the alien right hand is at baseline more difficult for the supramodal executive system than is control of the substitution errors of the left hand.

More recently, Frith et al. (2000) have proposed an intermediate account, which posits a lateralized medial frontal system (supplementary motor area) involved in selection for action and inhibition of automatic action triggers, and a separate, high level control system that mediates goals and intended actions (analogous to Shallice's supervisory system and localized only generally, to the prefrontal cortex). Based on the observation that patients with AH, unlike those with utilization behavior, perceive a disparity between their actions and intentions, they propose that the premotor system is impaired in patients with AH, while the higher-level system is affected in utilization behavior. The mechanism for intermittent voluntary control of the AH, however, is not specified.

The present results do not adjudicate between these theories of AH, but clearly demonstrate that AH reflects impairment both in selecting targets that are congruent with intentions and in inhibiting automatic responses to distractors close to the hand. The results also show that automatic responses to nearby distractors in AH are suppressed by a resource-limited system that is affected by task load. This rich description of AH behaviors yielded practical rehabilitation recommendations for JC that may apply in the future to other patients with AH. JC's family and rehabilitation therapists were encouraged to keep his environment stark and free of distractor objects, and JC was discouraged from working on more than one task at a time, particularly when he was feeling fatigued. In the case of JC, these recommendations might make a difference between uncontrolled AH behavior and behavior that is purposive.

Acknowledgments

A portion of this study was presented at the 2003 meeting of the Cognitive Neuroscience Society, New York, NY. This research was supported, in part, by the following grants: NIH National Research Service Grant 5132HD07425, NIDRR H133G0169, and NIH R01NS36387. The authors thank JC and his spouse for their participation. We thank Diane Holz for her help with CC data collection and analysis and Mary Ferraro for her help in identifying appropriate comparison subjects. We are also grateful for the collaboration and suggestions of Myrna Schwartz, who is a co-author on the normative CC study that is described in Appendix A.

Appendix A

A.1. Normative data on the coffee challenge

Seventeen healthy participants (*M* age = 35.4 years, S.D. = 9.3; *M* education = 15.1 years, S.D. = 2.7) participated in a normative study of the CC using methods highly similar to those reported here. Details will be reported elsewhere (Giovannetti, Schwartz, & Buxbaum, in press). After practice, participants alternated between Standard-CC and Concurrent-CC conditions (ABAB).

In the Concurrent-CC, participants performed the CC and the oral version of the Trail Making Test (OTMT; Ricker & Axelrod, 1995) simultaneously. The OTMT required participants to alternate between reciting letters and numbers in alphabetical/sequential order. An example was provided (i.e. A1, B2, C3, etc.), and participants were asked to practice the task. The examiner corrected any errors made during practice. Then, prior to each concurrent trial, participants were presented with an arbitrary letter-number pair that indicated where to begin the OTMT task. The following arbitrary letter-number pairs were used for the six concurrent trials with each participant: F-7, R-2, L-11, N-23, J-10, H-4.

Performance was coded for overt errors and microslips (objects reached for and/or touched without being lifted from table). Errors were coded according to the taxonomy presented in Table 2. Substitutions were further coded according to whether they were influenced by exogenous factors (distractor proximity to the acting hand and distractor proximity to the target) or endogenous factors (visual and semantic similarity of distractor to target). Proximity was coded using the table divisions as a distance metric (see Fig. 3). The obtained data was compared to the chance opportunity to commit near-target and near-hand errors.

Distractor–target similarity was based on ratings obtained from an independent participant sample (n = 10; *M* age = 33.9, S.D. = 13.2; *M* years of education = 15.4, S.D. = 1.7). Ratings for all possible distractor–target combinations were made on 4 visual dimensions (i.e. size, shape, color, structural features) and function using a 3-point scale (maximum visual similarity for each distractor–target pair = 12; maximum function similarity = 3). For example, non-dairy creamer and artificial sweetener obtained high function similarity ratings whereas white ceramic mug and stirrer did not. The mean rating for all possible object pairs reflects the visual/functional ratings expected by chance. Ordinal ratings were converted to ranked scores for the purpose of analysis, and mean ranks are reported below.

Results on the Standard-CC and Concurrent-CC are shown in Table A1. Correlation analyses showed no evidence for relationships between CC errors and age or education.

Every participant made more total errors and more errors of each type on the Concurrent-CC compared to the Standard-CC ($P < 0.01$ for all comparisons). There was a tendency for participants who made more errors on the Concurrent-CC to obtain higher OTMT rates, indicating that partici-

Table A1
Total errors, error types, and exogenous/endogenous influences on errors from the normative study of the Coffee Challenge

	Standard-CC *M* (S.D.)	Concurrent-CC *M* (S.D.)
Total errors	12.6 (6.0)	40.0 (26.7)
Error types		
Sequence	6.1 (5.5)	12.4 (6.4)
Substitution	0.9 (1.3)	2.9 (2.6)
Perseveration	6.1 (4.1)	24.9 (17.8)
Exogenous influences on substitutions (%)		
Percent of errors near hand	29	34
Percent of errors near target	43	41
Endogenous influences on substitutions (*M* rank)		
Visual rating	276.6	236.8
Functional rating	266.3	239.2

pants were dividing their attentional resources to both tasks (Table A1).

There was no Standard-CC versus Concurrent-CC difference in spatial scores or functional similarity ratings. Visual ratings were significantly lower in the Concurrent-CC. Errors from the Standard-CC and Concurrent-CC were combined and compared to chance spatial scores and similarity ratings. Substitutions occurred to distractors "near the hand" and "near the target" significantly more than chance, and were more functionally similar and visually similar to the target than expected by chance.

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