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Following a stroke a natural stress response occurs which reflects a disruption of the hypothalamic-pituitary-adrenal (HPA) axis in humans (O'Connell & Gray, 1991). This disruption typically results in elevated cortisol, the endpoint of the HPA axis and a reflection of the physiologic stress response, during the acute post-stroke phase. Subsequently, higher cortisol levels have been linked to higher morbidity, cognitive dysfunction, and poorer functional recovery in stroke patients (e.g., Feibel et al., 1977; Marklund et al., 2004; Makikallio et al., 2007), however, evidence contradicting these findings has emerged. Inconsistencies in findings related to cortisol levels and stroke may be a function of subject sampling. The heterogeneity of stroke patients used in each of the samples, specifically the grouping of right and left hemisphere patients together may confound the results of these studies (e.g., Feibel et al., 1977; Murros et al., 1993; Schwarz et al., 2005). Combining left and right hemisphere stroke patients in one group may be problematic because the control of cortisol secretion is believed to be lateralized. Control of tonic cortisol secretion has long been considered to be managed by the right hemisphere in right-hand dominant individuals (Wittling & Pfluger, 1990; Wang et al., 2005); though evidence also indicates either left hemispheric control of cortisol secretion or no difference in hemispheric laterality and tonic cortisol secretion (Tchiteya, 2003; Lueken et al., 2009). Consequently, it is important to examine and compare variability in cortisol release among right and left hemisphere stroke independently.

In addition to the contribution of laterality and neurological damage to alterations in cortisol secretion, the stress response in stroke patients may also be influenced by the need of the patient to cope with the multiple behavioral changes resulting from neurological damage. One discrete exemplar of post-stroke behavioral change is aphasia which affects 20-38% of stroke patients (Pederson et al., 1995; Warlow et al., 2000). Given the human need to express and understand language and the sudden inability to do so, the reaction to experiencing aphasia may contribute to the natural stress response occurring as a result of the neurological disruption. With the exception of Olsson (1991) who included one patient with aphasia in his sample and Tchiteya et al. (2003) who included 10 patients with aphasia in their sample, the majority of studies have either excluded patients with language disorders (Lueken et al., 2009), grossly estimated the amount of aphasia and added it to a composite score, such as with the SSS (Fassbender et al., 1994; Johansson et al., 2000; Christensen et al., 2004), or ignored language as an outcome, concentrating instead on motor impairments (O'Neill et al., 1991; Murros et al., 1993). To better understand behavioral recovery after stroke, it may be beneficial to tease apart discrete behaviors, such as language disorders post-stroke, and explore their relation to cortisol levels.

Understanding the complex interactions between unilateral stroke, salivary cortisol secretion over time, and language changes during recovery may help explain observed differences in recovery patterns and response to rehabilitation among stroke patients. Therefore, the objectives of this study were as follows: 1) to evaluate differences in salivary cortisol levels between right and left hemisphere stroke patients; and, 2) to determine the association between language skills over time and salivary cortisol levels during the subacute recovery stage.

## Methods

*Participants and testing.* Nineteen individuals with aphasia (IWA) following a left-hemisphere stroke (8 males, 11 females) and 12 individuals with right hemisphere stroke (RBD) (8 males, 4 females) were included in this study. Mean age was 55.7 years (*SD* = 9.1) for IWA and 58.5years (*SD* = 8.4) for the RBD group. All participants began the study between 1-6 months post onset of their stroke. See Tables 1 and 2 for participant description.

Both groups participated in language testing monthly. All aphasia participants were given the *Western Aphasia Battery* (*WAB*; Kertesz, 1982) and the *Boston Naming Test (BNT,* Kaplan, Goodglass, & Weintraub, 2001*)* four times over three months (0, 4, 8, 12 weeks post enrollment in the study). Mean time between administration of testing was 30 days (*SD* = 3.23 days). Individuals with right brain damage were administered the *BNT* and *Mini-Inventory of Right Brain Injury-2* (*MIRBI-2*; Pimental & Knight, 2000) a total of four times over the course of three months. Mean time between administration of testing was 29.8 days (*SD* = 4.32 days).

*Salivary cortisol sampling.* All participants were seen for saliva sampling biweekly for three months for a total of six samples (0, 2, 4, 6, 8, 10 weeks following enrollment into study). As there were occasional scheduling conflicts the mean time between samples across all participants was 14.8 days (*SD* = 4.37). Participants were seen between 1600 and 1800 hours (average sampling time was 1637 hours) either in their home or in the Aphasia and Motor Speech Disorders Laboratory at Georgia State University. One sample per day was chosen to decrease sampling burden on the participant (Ice et al., 2004). Afternoon measurement was chosen as it tends to be a more stable time period for diurnal variation of salivary cortisol and has been used previously for measurement of stress in IWA (Anders, 1982; Laures-Gore et al., 2003; Laures-Gore et al., 2007). Following a ten minute relaxation period (participants were instructed to sit quietly and relax), each participant chewed on a Salivette (Sarstedt, Rommelsdorf, Germany) for one minute until saturation of the Salivette occurred.

## Results

An independent groups t-test showed there was not a significant difference in cortisol levels between groups at $p \leq .05$ (t=1.603; df=28.9). While not statistically significant, we did observe that IWA had consistently higher salivary cortisol levels than did the RBD group (See Figure 1). As might be expected, significant differences between groups on the *BNT* [$F(1,25) = 6.58$, $p < .017$], changes in *BNT* scores over time [$F(3,23) = 4.00$, $p < .020$], and significant differences in changes between groups in BNT scores over time [$F(3,23) = 4.00$, $p < .021$] were found. Within the aphasia subjects, a significant change over time in the *WAB AQscore* [$F(3, 15) = 17.1$, $p < .001$] was found. Within the RBD subjects, no significant change in *MIRBI* scores over time [$F(3,8) = 3.44$, $p < .072$] were found. Pearson's correlation analyses of the sum of salivary cortisol levels over time and the sum of language scores indicate no significant relation in IWA (*BNT*, $r = .547$, $p = .04$ ; *WAB AQ*, $r = .26$ , $p = .28$ ), however, the RBD group showed a relation between naming and cortisol (*BNT*, $r = -.64$, $p = .03$), but did not for overall language scores (*MIRBI*, $r = -.50$, $p = .10$). See Tables 3 and 4 for group means of each test.

## Discussion

The current findings suggest that language skills in left hemisphere stroke patients are independent of afternoon salivary cortisol levels, however, naming skills in right hemisphere stroke patients are related to salivary cortisol levels. Stroke laterality did not differentially influence afternoon levels of salivary cortisol secretion during the subacute stage of recovery. These findings and their clinical implications will be discussed within the context of previous findings by Laures-Gore and colleagues (Laures-Gore, Odell, & Coe, 2003; Laures-Gore, Heim, & Hsu, 2007; Laures-Gore, DuBay, Duff, & Buchanan, 2010).

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Table 1. Description of Participants with Aphasia

| Subject | Gender | Age | Ethnicity | Site of Stroke | MPO | WAB AQ | Initial Aphasia type |
|---|---|---|---|---|---|---|---|
| 1 | F | 60.3 | C | L MCA | 1.00 | 85.5 | Anomic |
| 2 | M | 70.1 | C | L MCA | 1.25 | 14.1 | Broca's |
| 3 | F | 55.7 | AA | L Parietal | 1.50 | 77.3 | Anomic |
| 4 | M | 41.9 | C | L MCA | 1.25 | 63.5 | Transcortical Sensory |
| 5 | F | 52.3 | C | L MCA | 1.00 | 34.2 | Broca's |
| 6 | F | 52.3 | C | L MCA/ACA | 2.00 | 17.6 | Broca's |
| 7 | F | 40.8 | C | L MCA | 0.50 | 88.6 | Anomic |
| 8 | F | 55.5 | C | L MCA | 2.25 | 89.6 | Anomic |
| 9 | F | 47.3 | AA | L MCA with thrombus | 1.25 | 82.6 | Anomic |
| 10 | M | 62.5 | C | L MCA | 2.25 | 68.5 | Transcortical Motor |
| 11 | M | 53.5 | AA | L Anterior, Temporal, Mid-Parietal | 3.50 | 13.2 | Global |
| 12 | F | 74.3 | C | L MCA | 4.50 | 42.1 | Broca's |
| 13 | F | 62.8 | C | L Basal Ganglia | 5.00 | 64.6 | Broca's |
| 14 | F | 46.1 | C | L ICA with aneurysm | 2.00 | 84.8 | Anomic |
| 15 | M | 51.0 | C | L MCA/PCA | 2.00 | 19.5 | Broca's |
| 16 | F | 55.7 | C | L MCA | 3.25 | 36.9 | Broca's |
| 17 | M | 66.3 | C | L ICA | 3.50 | 87.6 | Anomic |
| 18 | M | 61.7 | C | L ICA | 4.75 | 93.0 | Anomic |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| 19 | M | 48.8 | AA | L MCA/ICA | 3.50 | 35.8 | Broca's |

*MCA = Middle Cerebral Artery; ICA = Internal Carotid Artery; PCA = Posterior Cerebral Artery; MPO= months post onset; WAB= Western Aphasia Battery; MIRBI= Mini Inventory of Right Brain Injury; M/F= Male/Female; C/AA= Caucasian/African-American.

Table 2. Description of Participants with Right Hemisphere Stroke

| Subject | Gender | Age | Ethnicity | Site of Stroke | MPO | MIRBI |
|---|---|---|---|---|---|---|
| 1 | M | 66.5 | C | R frontal, occipital | 1.50 | 4 |
| 2 | M | 47.8 | AA | R watershed MCA | 1.75 | 4 |
| 3 | F | 61.7 | AA | R MCA/ACA | 1.75 | 6 |
| 4 | F | 57.2 | AA | R MCA/ACA | 2.25 | 6 |
| 5 | F | 61.7 | AA | R MCA | 1.75 | 7 |
| 6 | M | 59.5 | AA | R MCA/PCA | 1.25 | 4 |
| 7 | M | 63.1 | C | R MCA/ACA | 1.25 | 6 |
| 8 | M | 54.3 | C | R basal ganglia | 2.25 | 5 |
| 9 | M | 43.8 | C | R pontine | 4.50 | 7 |
| 10 | F | 50 | AA | R MCA | 6.75 | 6 |
| 11 | M | 63 | C | R MCA | 1.50 | 7 |
| 12 | F | 73.8 | C | R frontal, parietal, temporal | 2.00 | 6 |

- MCA = Middle Cerebral Artery; ACA = Anterior Cerebral Artery; PCA = Posterior Cerebral Artery; MPO= months post onset; WAB= Western Aphasia Battery; MIRBI= Mini Inventory of Right Brain Injury; M/F= Male/Female; C/AA= Caucasian/African-American.

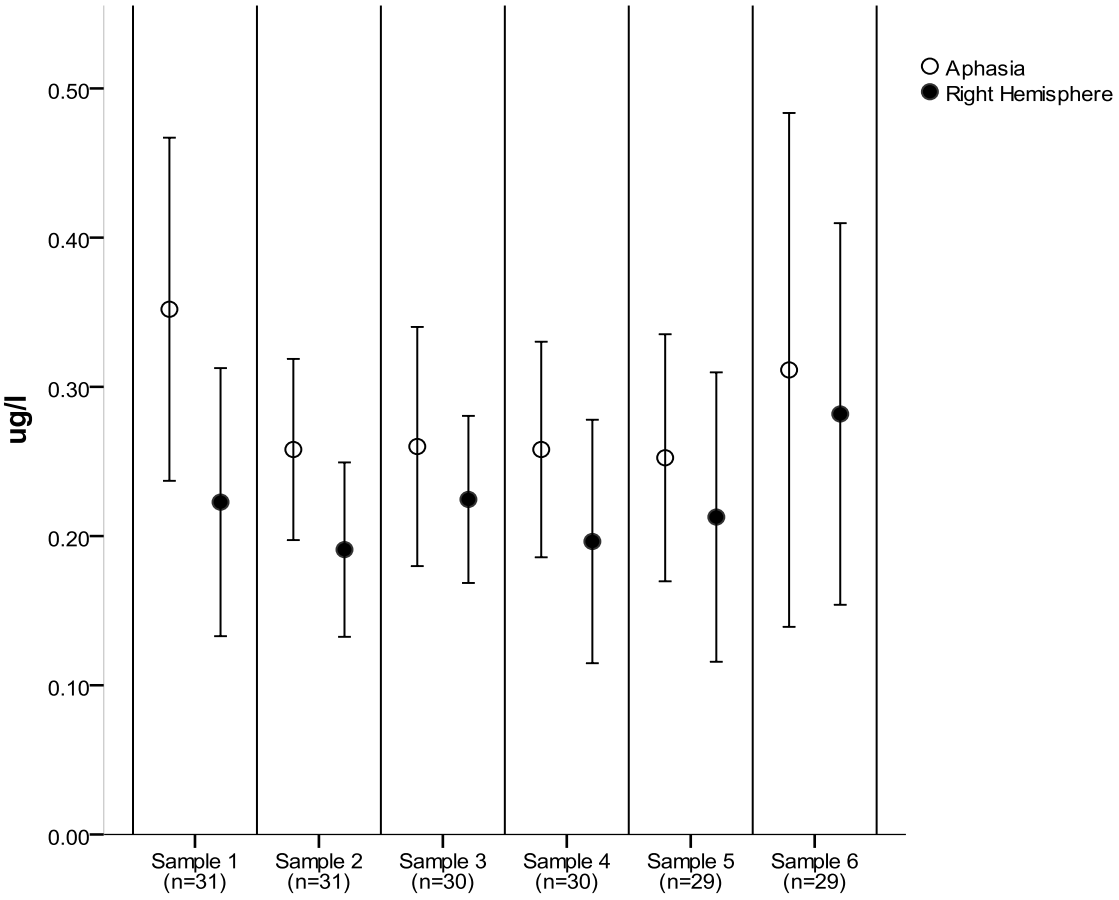
Table 3. Test Scores Over Time for Individuals with Aphasia

| | Time 1<br>Baseline | Time 2<br>4 weeks | Time 3<br>8 weeks | Time 4<br>12 weeks |
|---|---|---|---|---|
| WAB-AQ | 57.8 (29.3) | 63.8 (31.4) | 64.7 (32.2) | 72.6 (27.9) |
| BNT | 29.0 (22.0) | 36.37 (22.9) | 36.0 (22.7) | 38.6 (22.1) |

*Note: Time points present time from enrollment in study, participants averaged approximately 2.4 months post-stroke before enrollment.

Table 4. Test Scores Over Time for Individuals with Right Hemisphere Stroke

| | Time 1<br>Baseline | Time 2<br>4 weeks | Time 3<br>8 weeks | Time 4<br>12 weeks |
|---|---|---|---|---|
| BNT | 52.9 (6.6) | 55.0 (6.0) | 55.8 (4.7) | 54.6 (6.2) |
| MIRBI | 5.7 (1.2) | 6.3 (1.5) | 6.3 (1.4) | 6.3 (1.3) |


Aphasia
Right Hemisphere
ug/l
0.50
0.40
0.30
0.20
0.10
0.00
Sample 1 (n=31)
Sample 2 (n=31)
Sample 3 (n=30)
Sample 4 (n=30)
Sample 5 (n=29)
Sample 6 (n=29)