Impact of structural/functional lesions in the ventral stream on online semantic integration

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Background: Semantic integration (SI), the ability to combine the meaning of words to form more complex representations, is central to rapid, auditory processing of sentences. Prior neuroimaging research has suggested that SI involves widespread left hemisphere activation of cortical regions within the ventral stream (VS) including the anterior middle temporal gyrus (ATL) and the angular gyrus (AG)[1,2,3,4,5]. However, the necessity of each of these areas within the network to support SI is not clear. One way to investigate their functional role is to identify how damage (structural or functional) to any of these regions impacts the SI process. Post-stroke individuals with chronic aphasia (IWA; a language impairment that typically results from damage to the language dominant hemisphere of the brain) can provide insight into this issue. Structural lesion information is commonly used to map out the association between structural damage and resulting behavior. However, structural damage may not capture underlying alterations to brain function. Following a stroke, cerebral blood flow (CBF) may be hypoperfused (i.e., reduced) in regions of the brain that otherwise appear structurally intact, which can lead to language impairments that would not be predicted by location of structural brain damage alone[6]. One way to capture these functional impairments is through the use of perfusion imaging, which measures CBF of neural tissue[7].

Current Study: This study investigates the role of regions within the left VS network that have been implicated in SI. We present preliminary evidence for the role of ATL and AG. For this study, we grouped IWA into two groups based on their structural and functional lesion characteristics, those with VS damage (vs-IWA) and those without VS damage (nvs-IWA). We then examined SI using an eye-tracking while listening paradigm (ETL). We predicted that only those with functional or structural damage to ATL or AG within the VS network will exhibit impaired SI abilities.

Participants: 11 neurotypical age-matched controls (AMC) and 11 chronic IWA (>1-year post-stroke) participated in the ETL study. Thus far, 5/11 IWA contributed CBF data in this within-subjects study and are used for analysis to determine compromised brain regions (see Table 1).

Behavioral Task: Using ETL, we tested SI during real-time sentence processing in a group of AMC and our two groups of IWA with CBF data (vs-IWA and nvs-IWA). Here, we operationalized SI as a process by which information from a semantic cue facilitates access of an upcoming noun <u>before</u> it is heard (i.e., anticipation)[1,8]. In the experimental sentences, semantically biased adjectives (“venomous”) were uniquely associated with the target noun (“snake”), whereas unbiased adjectives (“voracious”) in the control sentences were not (Fig. 1[a]).

Neuroimaging: Using a 3T GE MRI scanner, we investigated both structural and functional brain damage; using <u>structural MRI</u> to determine size and location of lesioned tissue and <u>perfusion MRI</u> to determine the extent of neural integrity in our regions of interest (ATL, AG).

Results: Fig. 1[b] shows the time course of proportion of gazes to the target noun in biased and unbiased conditions for AMC and IWA. Separate multilevel group analyses were conducted to show which participants demonstrated SI, as indexed by rate of lexical access in the biased versus unbiased conditions. Results (Fig. 2) revealed that AMC and IWA were able to access the target lexical item, but IWA demonstrated different anticipatory gaze patterns. The nvs-IWA participants used the semantically biased adjective to anticipate the upcoming noun, whereas the vs-IWA participants did not.

Conclusion: Preliminary results thus far suggest that the ATL and AG play a functional role in SI, by facilitating the use of semantic cues for on time lexical access. When either of these areas become impaired (as measured by structural or functional lesions), semantic cues may no longer be efficiently integrated into the ongoing auditory sentence stream. As will be discussed in the presentation, these effects could be linked to reports of delayed lexical access in aphasia[11] and underscore the importance of considering functional and structural brain damage in IWA when mapping the association between brain and behavior.

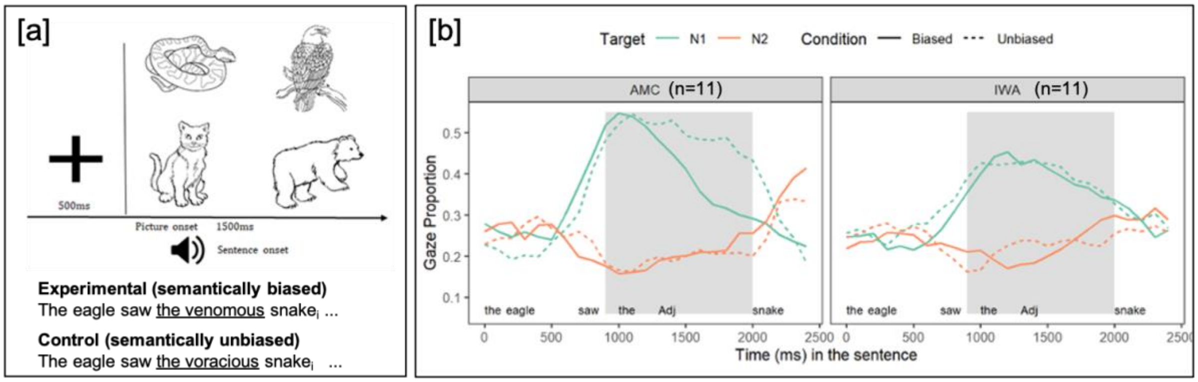

Figure 1. [a] Visual world eye-tracking paradigm. Adjectives (adj) were matched for syllable length and lexical frequency. The time window of interest (underlined) begins at the average onset of the second determiner until the end of the adj (across all items). Follow-up analysis included an extended time window to the end of the second noun (*snake*). [b] Time course depiction of looks to the first and second noun (N1 and N2) as the sentence is heard. Looks to distractor items are excluded from this plot. The shaded region represents the time window of interest for statistical analysis, which captures looks to N2 after hearing the adj.

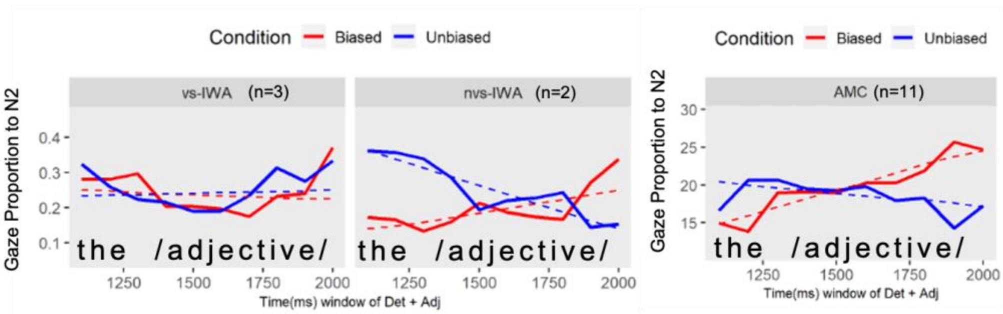

Figure 2. Time course analysis of gaze proportion to N2 in the window of interest [the + Adj] for both IWA groups and AMC across conditions. The dashed line represents the model fit and the solid lines represent the raw data for each condition. Increase in gazes to N2 in the biased versus unbiased condition reflect anticipation of the target noun. The AMC group (rightmost panel) used the biased adjective to access the target noun (ES = -0.2, SE = 0.09, t = -2.6, p = 0.008). Similarly, the nvs-IWA participants showed anticipatory access to N2 in the biased versus unbiased condition. This contrasts with the vs-IWA participants (ES = -0.7, SE = 0.3, t = -2.7, p = 0.007) indicating that individuals with VS damage do not integrate the semantic properties of the adj to anticipate N2.

Group	IWA	Sex	Years Post-Stroke	Age at Testing (Years)	Education (Years)	Aphasia Subtype	BDAE-3 Severity[9]	WAB-AQ[10]	Lesion Location	% Damage in L ATL	CBF in L ATL	% Damage in L AG	CBF in L AG
vs-IWA	009	M	15	55	17	Mixed non-fluent	2	67.7	Large L lesion, IFG (BA 44/BA45) w/ posterior extension	56%	18.73	5%	20.65
vs-IWA	169	M	4	59	12	Broca	2	28.2	L posterior IFG (BA 44) w/ posterior extension	0%	**32.38***	33%	49.95
vs-IWA	190	F	6	76	12	Broca	3	88.2	Left superior temporal lobe	0%	**22.64***	9%	68.15
nvs-IWA	101	M	9	67	20	Broca	3	82.6	Large L lesion posterior IFG (BA 44) w/ posterior extension	0%	43.55	2%	79.13
nvs-IWA	151	F	7	65	16	Anomic	4	95.8	L MCA infarct with subcortical extension	0%	39.30	0%	56.83
AMC	Ages 57-66 years (mean = ~61.9); 7 females, 4 males; Education 14-18 years (mean = ~15.7)*						--	--	--	--	--	--	--

Table 1. Participant Demographics. IWA = individual with aphasia; vs-IWA = ventral stream damage; nvs-IWA = no ventral stream damage; AMC = Age-matched neurotypical controls; BDAE-3 = Boston Diagnostic Aphasia Examination v 3 (1=Severe, 5=Mild); WAB-AQ = Western Aphasia Battery - Aphasia Quotient (<50=severe, 51-70=moderate, >71=mild); L ATL = left anterior temporal lobe; CBF = cerebral blood flow (mL/100g/sec); L AG = left angular gyrus; *Hypoperfusion in the left hemisphere was based on CBF values that were at least 2 standard deviations below each participants right hemisphere mean. Bolded values represent functional lesions (hypoperfused regions). *Missing education data for four AMC

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