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Eye Movements as Probes of Lexico-semantic Processing in a Patient with Primary Progressive Aphasia

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Abstract

Eye movement trajectories during a verbally-cued object search task were used as probes of lexicosemantic associations in an amnestic patient with primary progressive aphasia. Visual search was normal on trials where the target object could be named but became lengthy and inefficient on trials where the object failed to be named. The abnormality was most profound if the noun denoting the object could not be recognized. Even trials where the name of the target object was recognized but not retrieved triggered abnormal eye movements, demonstrating that retrieval failures can have underlying associative components despite intact comprehension of the corresponding noun.

Keywords

eye movements; aphasia; anterior temporal lobe; single-word comprehension; object naming

Anomia, the inability to name objects verbally, is one of the most common symptoms in disorders of language known as aphasias. This is true for aphasias caused by both cerebrovascular injury and neurodegenerative disease, the latter known as primary progressive aphasia (PPA) (Budd et al., 2010; Jefferies & Lambon Ralph, 2006). Two types of naming failures are commonly described in aphasic patients. In one type, anomia is based on a failure to recognize or comprehend the noun that denotes the object. In practice, this is detected when a patient fails to match a noun to the corresponding object embedded among an array of foils (M.-M. Mesulam et al., 2009). In the second type of naming failure the ability to match the noun to the object is preserved, despite inability to name the object aloud, and the anomia is attributed to a block at the stage of word retrieval (Dell, Schwartz, Martin, Saffran, & Gagnon, 1997). Recent evidence from PPA indicates that retrieval anomia can also be based on a disruption of the associative lexico-semantic linkage between objects and words (Hurley, Paller, Rogalski, & Mesulam, 2012).

Eye movements generated during “visual world” paradigms are sensitive to psycholinguistic factors relevant to object naming and word comprehension (Cooper, 1974; Tanenhaus, Spivey-Knowlton, Eberhard, & Sedivy, 1995). In these paradigms, participants are provided with a verbal cue and tasked with finding the corresponding object from among an array of object foils. Lexical frequency, which is closely related to the ease of word recognition and retrieval, has been shown to modulate viewing behavior in the visual world paradigm. Healthy adults are able to find (fixate) targets with high frequency names quicker than those with low frequency names (Magnuson, Dixon, Tanenhaus, & Aslin, 2007). The visual world paradigm has also been applied to psycholinguistic study of patients with aphasia caused by cerebrovascular injury. Yee and colleagues (2008) found that aphasic patients were slower than controls to fixate a target object, while Mirman and Graziano (2012) found that they spent a smaller proportion of time viewing a target object (and conversely more time viewing foils).

Previous investigations of eye movements in PPA have focused on non-linguistic domains including oculomotor functioning and visuospatial attention. Measurement of saccadic amplitude towards basic stimuli (dots, crosshairs, etc), cued antisaccadic movements away from such stimuli, and smooth pursuit revealed that, in general, PPA patients of the agrammatic and logopenic subtypes showed abnormal performance on at least one of these tasks. The oculomotor dysfunction in these studies was attributed to atrophy in the frontal and cingulate eye fields and the pre-supplementary motor area (Boxer et al., 2006; Coppe, Orban de Xivry, Yuksel, Ivanoiu, & Lefevre, 2012; Garbutt et al., 2008). Given the utility of visual world and similar paradigms for psycholinguistic assessment, it is surprising that eye tracking has not been applied to the study of language impairment in PPA.

In order to better understand how word-object associations may be disrupted in PPA, we developed a variant of the visual world eye-tracking paradigm where participants are given a verbal cue and asked to point to a target object embedded in an elliptical array containing the target and seven other object foils. In order to complete this task the verbal cue must elicit relevant representations in visual long-term memory, and those representations must be compared against incoming visual sensory patterns as participants actively search the array for the correct match (Fan & Turk-Browne, 2013). Monitoring eye movements will allow covert mental processes related to these word-object associations to be probed with an on-line task that does not require overt verbal responses.

The goal of this report is to establish whether visual world paradigms are sensitive to the associative mechanisms of anomia and comprehension impairments in PPA. To this end, we examined eye movements of a patient with primary progressive aphasia (PPA) and four healthy controls while they completed the matching paradigm. The patient was able to name some objects but not others, and his anomic errors included some instances where word-object matching was intact and others where it was impaired. Through an item-by-item analysis we examined whether the architecture of oculomotor scanning reflected the nature of the naming process, specifically, whether eye movements have a normal pattern in trials that involved an object that the patient subsequently was able to name. Secondly, we wanted to delineate the type of abnormality in the speed and distribution of visual search in trials where the patient could neither verbally name the item nor match the word to the object (i.e.

where the word is not recognized or understood). Finally, we wondered whether instances of ‘retrieval’ anomia would also reveal visual search abnormalities, as markers of partial impairments in the formation of lexico-semantic associations.

CASE REPORT

A 61-year old patient with a clinical diagnosis of PPA and four cognitively healthy control participants of comparable age and education were tested (Table 1). All participants were right-handed, native English-speaking males.

Symptom onset occurred at the age of 55 years, by history, beginning with word-finding difficulties followed by progressive impairments in word comprehension, spelling, and reading. The diagnosis of PPA was made using established guidelines (Gorno-Tempini et al., 2011). The neuropsychological assessment showed a prominent aphasia, as indicated by the WAB Aphasia Quotient of 47/100 (Kertesz, 2006). He was profoundly anomic, as demonstrated by a score of 4/60 on the Boston Naming Test (Kaplan, Goodglass, & Weintraub, 1983). He had single-word comprehension impairments as shown by a score of 36/60 on the WAB Auditory Word Recognition subtest, and also poor grammaticality as shown by a score of 3/10 on the Northwestern Anagram Test (Weintraub et al., 2009). The clinical presentation therefore fulfilled the criteria for the “mixed” subtype of PPA (Mesulam, Wieneke, Thompson, Rogalski, & Weintraub, 2012).

The patient showed relatively intact performance on tests of other cognitive domains including executive and visuospatial functions as shown in Table 1. Based on this neuropsychological profile, any abnormalities in the patient’s performance in the current study would be properly attributed to a language impairment (aphasia) rather than to executive, visuospatial (i.e. neglect), or object recognition (i.e. agnosia) impairments.

Structural magnetic resonance images (MRI) of the patient’s brain were acquired using a Siemens Trio 3 tesla scanner. A T1-weighted 3D MPRAGE sequence was used (repetition time, 2300ms; echo time, 2.91ms; flip angle, 9°; field of view, 256mm) recording 160 slices at a thickness of 1.0mm. Cortical thickness analyses were conducted using FreeSurfer software (<http://surfer.nmr.mgh.harvard.edu/>). Thickness values at each vertex of the cortex were contrasted against values from a normative group of healthy adults with similar demographic properties to PPA patients (Rogalski et al., 2011). The patient showed significantly thinner cortex in the left temporal lobe and insula (Figure 1), with peak atrophy on the anterior section of the temporal lobe (ATL) extending posteriorly along the middle-temporal gyrus. This pattern is common among PPA patients with prominent semantic deficits (M. Mesulam et al., 2009). An ¹⁸F-FDG PET scan obtained two years prior to the current study showed peak hypometabolism not only in the left anterior temporal lobe but also in the frontal and temporoparietal components of the left-hemispheric language network, consistent with the atrophy pattern described for the mixed aphasia subtype in PPA.

METHODS

Apparatus

A 20.5×11.5" touchscreen monitor was used to present visual stimuli and to collect touch responses. Participants were placed approximately 22" in front of the monitor. Eye movements were monitored using an Eyelink 1000 system (SR Research, Mississauga, ON, Canada). Eye and head movements were simultaneously monitored and accounted for as part of the calibration procedure.

Stimuli

The stimuli consisted of 24 items divided equally into four semantic categories: animals, clothes, fruits-vegetables, and manipulable objects (e.g. tools, utensils). Word cues consisted of the lowercase written name of each item, presented in the center of the screen. Object probes consisted of shaded gray-scale drawings of each object, adapted from the Snodgrass and Vanderwart (1980) image set (Rossion & Pourtois, 2004). Each drawing was scaled to 122×122 pixels (visual angle 3.4°), and presented on a white background.

Experimental paradigm

On each trial, participants were first presented with a word cue for 2.5 seconds in the center of the screen, followed by a fixation cross for 2 seconds. A blank screen was then followed by an elliptical array of eight object probes including the target object and seven foils (Figure 2a). Three of the seven foils were from the same taxonomic category as the target (e.g. other animals for target dog), and the remaining four were evenly distributed across other categories. The object array remained on the screen until a touch response was detected. Participants were instructed to read each word and to then point to the corresponding object. After each word-to-object pointing trial, participants were asked to rate how confident they were that they had selected the correct object, on a 4-point scale (Figure 2a).

There were 24 trials in total, with each item appearing once as a word cue and as a corresponding target object. Object probes were placed equidistantly from each other along an ellipse with a horizontal axis of 1152 pixels (31.4°) and a vertical axis of 878 pixels (24.2°). This aspect ratio equates all object positions for the quality of visual acuity when fixating the center of the screen (Iordanescu, Grabowecky, & Suzuki, 2011). Finally, after completion of the visual world task, participants completed a confrontation naming procedure. Participants were shown each of the 24 object pictures again, one at a time, and were asked to name each one aloud. Items were then sorted into those that were successfully named versus misnamed.

Classification of trial types

We sorted the patient's behavioral and eye gaze data from each of the 24 visual world trials into one of three categories, based on accuracy in matching the written word cue with the target object (by pointing to it), and on success in verbalizing the object's name during the subsequent confrontation naming procedure. One third of the visual world trials (8/24) included a target object that the patient was able to name by confrontation. He correctly

pointed to all of these named object targets, on what are henceforth referred to as N^+P^+ trials (an abbreviation for “*correctly named, and correctly pointed to*”). On roughly another third of the trials (7/24), the patient correctly pointed to the target object, but was later unable to name that same object aloud, referred to as N^-P^+ trials (“*incorrectly named, but correctly pointed to*”). Finally, on the remaining trials (9/24) the patient failed to both name and point to the target object, referred to as N^-P^- trials (“*incorrectly named, and incorrectly pointed to*”). N^-P^- trials therefore represent a more severe deficit in comprehension as compared to N^-P^+ trials, which reflect failures attributed to retrieval. The subject could not name any objects the words of which he could not comprehend.

Although controls demonstrated no failures in naming or pointing, their data were still sorted into the same three trial types, based on the patient’s performance on the corresponding trials rather than their own. For example, since the patient correctly pointed to the onion during the eye tracking task but failed to name it aloud afterwards, the data from that trial was assigned to the ‘ N^-P^+ ’ condition for all four controls as well as for the patient. In this way all patient-control comparisons were based on the same subset of trials, controlling for variation in psycholinguistic or perceptual properties of the stimuli across trials.

Acquisition of eye movement data

Eye movements were successfully recorded from all participants at a sampling rate of 500Hz. Eye movements were recorded in epochs beginning with the onset of the object array and ending with each corresponding touch response on each trial. Saccade- and blink-free periods lasting 40ms were categorized as fixations. The space surrounding the object probes was divided into eight trapezoidal areas of interest (AOIs, Figure 1b). Fixations falling outside of these AOIs were excluded from analysis.

Four metrics were used to quantify fixation patterns on each trial. The *total number of fixations* represents a count of all fixations recorded in each epoch, beginning with the onset of the object array and ending with the touch response on each trial. The *number of post-target fixations* reflect a count of all fixations occurring after the participant had already fixated on the target AOI, but prior to the touch response. Post-target fixations are thus particularly significant, as they suggest that the participant did not recognize the target with enough certainty to quit searching. *Percentage of time spent viewing the target* was calculated by taking the duration of time spent viewing the target object AOI on each trial, divided by the total time spent viewing all object AOIs. Finally, the *mean duration of viewing time per foil* was calculated by taking the amount of time spent viewing each individual object foil on that trial, and averaging those values.

Statistical analyses

We hypothesized that the patient would show a linear pattern of performance in terms of both touch behavior and eye movements, with best performance on N^+P^+ trials and performance becoming progressively more impaired on N^-P^+ and N^-P^- trials. In order to test for this predicted pattern of decreasing performance across trial types, behavioral and gaze data from the patient’s N^+P^+ , N^-P^+ and N^-P^- trials were compared via one-way

ANOVA, examining the significance of the linear term in each test (equivalent to a contrast of 1/0/-1 for N^+P^+ / N^-P^+ / N^-P^-).

Linear mixed-models were used for patient-control comparisons. The individual data points from the 24 trials were included as repeated measures. Subject was included as a random factor, and group was included as a fixed factor with two levels (patient and control). Trial type was coded as a continuous variable with three levels, assigning values of 1/0/-1 for N^+P^+ / N^-P^+ / N^-P^- , and included as a covariate in the mixed model. The group by trial type interaction therefore revealed whether the drop in performance across trial types was more extreme in the patient than in controls. Separate mixed-models were also run for each level of trial type, revealing whether the patient performance differed from controls specifically on N^+P^+ , N^-P^+ and N^-P^- trials.

RESULTS

Accuracy in pointing and naming

Controls pointed to the target object with perfect accuracy during the eye tracking task. The patient correctly pointed to the target object on 15/24 trials (62.5% accuracy) and to the foils on the remaining 9 trials. During the subsequent confrontation naming procedure controls successfully named all picture stimuli, but the patient was unable to name 16/24 of the experimental stimuli. In all cases the patient made no response (i.e. “don’t know”) rather than producing paraphasic errors.

As noted above, accuracy in naming (N) and pointing (P) were used to divide performance of the patient into three trial types: N^+P^+ trials ($N = 8$ trials), N^-P^+ trials ($N = 7$ trials) and N^-P^- trials ($N = 9$ trials).

Reaction Times

The patient’s mean reaction times in each of the three trial types (N^+P^+ , N^-P^+ , and N^-P^-) are shown in Figure 3a. Performance of healthy controls on corresponding trials are shown next to each patient. In general the patient’s touch responses were slower ($M \pm SD = 7772 \pm 5671$ ms) than those of controls ($M \pm SD = 2859 \pm 576$ ms; $F_{(1,3)} = 52.238$, $p = .005$). When responses were divided into N^+P^+ , N^-P^+ , and N^-P^- trials, the patient showed differential patterns of reaction times on each trial type (Figure 3a). The patient’s touch responses were slower on N^-P^+ than N^+P^+ trials, and slowest on N^-P^- trials, as shown by a significant one-way ANOVA linear term ($F_{(1,21)} = 18.9$, $p < .001$). Even though controls demonstrated no errors in naming or pointing, their responses were binned according to the patient’s performance on that corresponding trial (e.g. N^+P^+ , N^-P^+ and N^-P^- trials), so comparisons between the patient and controls were always based on the exact same subsets of trials. A significant group by trial type interaction indicated that rate of slowing across trial types was greater in the patient than seen in the control group ($F_{(1,113)} = 67$, $p < .001$). When broken down separately by trial type, the patient’s reaction times did not significantly differ from controls on N^+P^+ trials ($F_{(1,3)} = .007$, $p = .94$), but were significantly slower than controls on N^-P^+ ($F_{(1,3)} = 63.9$, $p = .004$) and N^-P^- trials ($F_{(1,3)} = 199.1$, $p = .001$).

Confidence Ratings

In general the patient's confidence ratings ($M \pm SD = 2.8 \pm 1.372$) were lower than controls ($M \pm SD = 4 \pm 0$), suggesting that he was aware of his difficulties with the task. As with reaction times, his confidence ratings differed by trial type (Figure 3b). On N^+P^+ trials, he gave the highest possible confidence ratings ($M \pm SD = 4.0 \pm 0$). He was less confident on N^-P^+ trials ($M \pm SD = 3.0 \pm 1.4$) and least confident on N^-P^- trials ($M \pm SD = 1.7 \pm 1.4$), with the linear term across trial types significant according to one-way ANOVA ($F_{(1,21)} = 24.2, p < .001$).

Furthermore, the patient pointed to the item located on the bottom of the array on all 9 of the N^-P^- trials, suggesting that he was pointing to the item physically closest to his hand rather than making an "educated guess".

Number of fixations

Consistent with the pattern of reaction times, the patient showed relatively normal gaze patterns on N^+P^+ trials, but showed an increasingly lengthy and inefficient serial search pattern on N^-P^+ and N^-P^- trials. Visual search patterns from representative trials are shown in the form of heat maps in Figure 4. The patient showed similar gaze patterns to controls on N^+P^+ trials, viewing a few objects and then discontinuing visual search by pointing to the target. On N^-P^+ and N^-P^- trials, however, the patient appeared to employ a serial search strategy instead, directing gaze to each object in turn around the elliptical array, eventually viewing all eight objects on most trials.

The inefficiency of the patient's visual search is apparent in the total number of fixations he made compared to controls (Figure 5a). The ANOVA linear term showed that the patient made an increasing number of fixations from N^+P^+ to N^-P^+ to N^-P^- trials ($F_{(1,21)} = 20.5, p < .001$). The patient's fixation patterns were then compared to controls on corresponding trials (even though controls named and pointed to all items successfully). An interaction showed that the effect of trial type ($N^+P^+/N^-P^+/N^-P^-$) was more extreme in the patient than in the controls ($F_{(1,106)} = 50.6, p < .001$). Separate linear mixed-models showed that the patient made a number of fixations equivalent to controls on N^+P^+ trials ($F_{(1,2.8)} = .2, p = .71$), but made more fixations than controls on N^-P^+ ($F_{(1,3)} = 45.7, p = .007$) and N^-P^- trials ($F_{(1,2.5)} = 139.8, p = .003$).

The same pattern emerged when examining a subset of fixations occurring after the target had already been viewed (Figure 5b). The patient made increasingly more post target fixations on N^-P^+ and N^-P^- trials ($F_{(1,21)} = 14.9, p < .001$), and this effect, as expected, was more pronounced than in controls ($F_{(1,106.9)} = 46.5, p < .001$). The patient showed an equivalent number of fixations after target to controls on N^+P^+ trials ($F_{(1,2)} = 4.4, p = .17$), but made more fixations on N^-P^+ ($F_{(1,2.3)} = 508.5, p = .001$) and N^-P^- trials ($F_{(1,2.4)} = 345.7, p = .001$).

Percentage of time spent viewing the target versus foils

The patient spent proportionately less time viewing the target object (and therefore proportionately more time viewing foils) on N^-P^+ compared to N^+P^+ trials, and even less time on N^-P^- trials (Figure 6) ($F_{(1,21)} = 30.5, p < .001$). The group by trial type interaction was significant ($F_{(1,105.9)} = 17.5, p < .001$), and separate linear mixed-models for each trial

type showed that the patient spent proportionately less time viewing the target than controls on N⁻P⁻ trials ($F_{(1,2.5)} = 13, p = .05$), but not on N⁺P⁺ ($F_{(1,2.8)} = .07, p = .81$) or N⁻P⁺ trials ($F_{(1,2.6)} = 3.3, p = .19$).

We were further interested in determining whether the patient spent a greater proportion of time viewing the target object than would expected based on chance alone. Given that there were 8 objects on the screen, if the patient was randomly allocating his gaze across objects then he would be expected to spend 12.5% percent of his time viewing the target. We examined this by comparing his relative viewing times on targets in each trial to a baseline of 12.5% via one-sample t-tests. Results suggest that the patient spent a greater-than-chance proportion of time viewing the target on N⁺P⁺ ($t_{(7)} = 5.5, P = .001$) and N⁻P⁺ trials ($t_{(6)} = 4.4, P = .005$), but not on N⁻P⁻ trials ($t_{(8)} = .6, P = .56$).

Mean duration of viewing time per foil

Figure 6 demonstrates that, compared to controls, the patient spent a greater proportion of time on N⁻P⁺ and N⁻P⁻ trials viewing foils rather than the target. One explanation is that the patient viewed each object for an inordinate duration, requiring more time to recognize and then reject each foil as not matching the verbal cue. We addressed this by calculating the mean duration of viewing time per foil (Figure 7). The patient behaved similar to controls on N⁺P⁺ trials, but spent increasingly longer times viewing each foil on N⁻P⁺ and N⁻P⁻ trials ($F_{(1,108)} = 10.8, p = .001$). The group by trial type interaction was significant ($F_{(1,104.3)} = 37.3, p < .001$), and separate linear mixed-models for each trial type showed that the patient spent more time viewing each foil than controls on N⁻P⁺ ($F_{(1,2.7)} = 33, p = .01$) and N⁻P⁻ trials ($F_{(1,3)} = 41.1, p = .008$), but not on N⁺P⁺ trials ($F_{(1,2.8)} = .01, p = .92$).

DISCUSSION

In the current study we established the validity of a visual world eye-tracking paradigm for revealing differential patterns of disrupted lexico-semantic associations in the anomia of PPA. The patient we investigated clinically had prominent anomia and impaired single-word comprehension and the experimental paradigm revealed similar deficits. Distinctive patterns emerged when the patient's responses were sorted by individual trials. On trials where he was able to verbally name the target object (N⁺P⁺ trials), he was able to visually fixate and manually point to the target as rapidly as controls. Both the patient and controls showed relatively few fixations on these trials, quickly identifying the target and making few unnecessary post-target fixations. In such trials, the patient spent the majority of the time viewing the target object rather than foils and gave the highest possible confidence ratings. Altogether these metrics show that the patient was able to complete the task as effectively as controls when searching for objects he could name. This rules out the possibility that his impaired performance in the other trials could be attributed to deficits in spatial attention or executive functioning.

In contrast to the rapid identification shown on N⁺P⁺ trials, the patient showed a different search strategy on the remaining trials related to unnamed objects. This was true both for cases where he pointed to the target object but could not name it aloud (N⁻P⁺ trials), and on trials where he could neither name nor point to the target object (N⁻P⁻ trials). On both of

these types of trials the fixation patterns revealed a serial and therefore slower search strategy (Treisman & Gelade, 1980), where each object around the elliptical array was sequentially fixated. Consistent with this, he engaged in lengthier visual search on N^-P^+ trials than on N^+P^+ trials, and even longer on N^-P^- trials, as reflected by increasingly longer touch response reaction times and more numerous fixations.

The patient showed the greatest deviation from normal scanning patterns on N^-P^- trials. On each N^-P^- trial he made an average of 20 additional fixations *after* viewing the target object and ultimately pointed to a foil, suggesting a profound failure to recognize the relationship between the verbal cue and target object. On all N^-P^- trials he pointed to the foil at the bottom of the screen, possibly because he had too little information to make an educated guess and instead made a stereotyped response. Consistent with this, his confidence ratings on N^-P^- trials fell between “unsure” and “very unsure” on the rating scale (average of 1.7 out of 4). There is no evidence that he recognized the target on an implicit level either, since he spent no more time viewing the target object than would be predicted based on chance alone, given that there were eight objects in the array.

An associative basis for retrieval failures

The current results provide eye-movement based evidence of associative dysfunction in anomia, complementing previous results from studies using event-related potentials (ERPs). ERPs such as the N400 are sensitive to the predictive coding of words when cued by objects, and vice versa (Federmeier, 2007). In previous studies we found that retrieval anomia in PPA was accompanied by dramatic reductions in N400 amplitude to word targets (Hurley et al., 2012; Hurley et al., 2009). In cases of retrieval failure, where predictive coding may be selectively disrupted, names can still be recognized and matched to the object but the process is less efficient, as reflected by increased reaction times on those trials.

There appears to be an analogous finding in the current study. The patient showed a retrieval anomia for a subset of objects, which were the targets on N^-P^+ trials. On those trials he engaged in a lengthy serial search, which did not cease even after fixating on the target. Thus, on N^-P^+ trials the patient’s knowledge of the association between words and objects appears to be partially distorted. Taken together with the previous ERP findings, this suggests that disruption of the associative component in anomia is graded rather than dichotomous, with milder associative disruption resulting in word retrieval failures (as indexed on N^-P^+ trials), and more severe disruption resulting in overt failures of name recognition (as indexed on N^-P^- trials).

The current visual-world paradigm required the integration of a verbal cue with an object target, and in that sense is more similar to ERP studies employing picture rather than word targets (Federmeier & Kutas, 2001, 2002). Interestingly, in addition to the N400 a number of early “visual evoked potentials” were also modulated by semantic congruency in those studies, indicating that the predictive coding of objects, unlike the predictive coding of words, is instantiated in early stages of the ventral visual stream (Martinez et al., 2006; Schendan & Lucia, 2010).

Inefficient performance of the patient on N⁻P⁺ trials may therefore have been driven by failure to predictively code the target object during visual search. Verbal cueing of objects is theorized to involve access of object “structural” representations (Huettig, Olivers, & Hartsuiker, 2011); for example upon reading the verbal cue “zebra”, features such as stripes become automatically activated. Accessing these structural representations allows target objects to be recognized more readily (i.e. predictively coded), and for foils to be more quickly rejected (Vickery, King, & Jiang, 2005). This is consistent with the performance of the patient in the current study: he only briefly viewed object foils on N⁺P⁺ trials (for about 200ms each), but required three times as much time to reject foils on N⁻P⁺ trials (Figure 7). This finding mirrors those from our previous ERP study (Hurley et al., 2009): when patients fail to generate N400 potentials, suggesting predictive coding did not take place, it is still possible to recognize the relationships between words and objects (i.e. match them accurately), but the process is greatly slowed down. Thus in this independent paradigm using the method of eye tracking rather than ERPs, again retrieval anomia is characterized by inefficiency in matching words with objects. Future studies are required, in order to confirm whether this inefficiency is driven by failure to retrieve and predictively code object features, for example by providing patients with a noun and asking them to draw the relevant object (Bozeat et al., 2003).

Other mechanisms of anomia in PPA

The current results show that the visual world paradigm is sensitive to mechanisms of anomia in a patient with impaired comprehension and associated anterior-to-mid temporal atrophy. Anomia in PPA, however, can result from disruption at any of a number of theoretical processing stages (Hurley et al., 2012; Hurley et al., 2009), and can occur after damage to virtually any area of the language network (Rogalski et al., 2011). By administering this paradigm to a larger heterogeneous group of patients, we hope to explore and characterize other forms of anomia in PPA.

In future studies the visual world paradigm could be used to probe the integrity of lexico-semantic associations in agrammatic and logopenic variants of PPA, who have relatively intact single-word comprehension (Gorno-Tempini et al., 2011; M. Mesulam et al., 2009). Such patients have been shown to have abnormal performance and reduced N400 potentials in verbal conceptual priming paradigms (Hurley et al., 2012; Rogalski, Rademaker, Mesulam, & Weintraub, 2008), suggesting an associative basis for misnaming even among these “non-semantic” variants of PPA. Patients whose dysfunction is limited to a late phonological/articulatory stage of naming may be a possible exception to this pattern. Patients with a block at these final stages of naming can generate intact N400 potentials in response to objects that cannot be named aloud, and may even be able to write those names despite being unable to vocalize them (Hurley 2009). To the extent that lexico-semantic stages of processing are preserved, we would predict those patients to show relatively normal gaze patterns in the visual world paradigm. In sum, we anticipate that future studies with additional patients will further support the close relationship between eye movements in this modified visual world paradigm and lexico-semantic integrity in PPA.

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Figure 1.

Cortical thickness map showing regional distribution of atrophy in the patient with PPA. The pial surfaces of each hemisphere are rendered above, and inflated views revealing areas in sulci and the perisylvian fissure are shown below. Areas where the cortex is significantly thinner than in controls are shown in red-yellow, thresholded to a false discovery rate of 0.05. Atrophy was confined to the left temporal lobe and insula. ^{18}F -FDG PET testing (not shown) showed hypometabolism in additional areas including frontal and temporoparietal components of the language network, and in ATL in the right hemisphere.

Figure 2.

(a) Schematic of the word-to-object pointing paradigm. Word cues were followed by a central fixation point, a blank screen, and then eight objects including the target and seven foils. After a touch response was detected, participants were asked to make confidence ratings on a 4-point scale. (b) Trapezoidal AOIs (not visible during the task) were used to categorize the location of touch responses and eye fixations.

Figure 3.

Reaction times (a) and confidence ratings (b) for touch responses. The performance of the patient (dark bars) is averaged and displayed separately across trials where he could name and point to the target object (N⁺P⁺), where he could not name but could point to the object (N⁻P⁺), and where he could neither name nor point to the object (N⁻P⁻), with standard deviation bars superimposed on each mean. Performance of the four healthy controls (light bars), averaged across trials corresponding to the patient's in each category (as all controls were able to name and point to all items). The means and standard deviations for each control were calculated separately, and then averaged across the four controls to create group means and group standard deviations, which are displayed next to the patient's means and standard deviations. The patient's responses were as fast and as confident as controls on N⁺P⁺ trials. The patient was slower and less confident on N⁻P⁺ trials, and the slowest and least confident on N⁻P⁻ trials.

Figure 4.

Fixation duration heat maps. Representative trials are shown from a control, and from the patient on N⁺P⁺, N⁻P⁺, and N⁻P⁻ trials. On N⁺P⁺ trials the patient showed a gaze pattern similar to controls, identifying the target within the first few fixations. On N⁻P⁺ and N⁻P⁻ trials the patient instead employs a serial search strategy, fixating each object around the array in turn.

Figure 5.

Number of fixations. (a) Total number of fixations prior to touch responses. When the patient named and pointed to the target successfully, the number of fixations that he required to detect the target was comparable to controls. The patient made increasingly more fixations than controls on N⁻P⁺ and N⁻P⁻ trials. (b) The number of post-target fixations. The patient made very few additional fixations after foveating the target on N⁺P⁺ trials. After viewing the target on N⁻P⁺ and N⁻P⁻ trials the patient continued the visual search by viewing additional object foils.

Figure 6.

Percentage of time spent viewing the target. Like controls, on N⁺P⁺ trials the patient spent the majority of the time fixating the target object. On N⁻P⁺ trials the patient spent relatively more time viewing foils rather than the target object. This was even more pronounced on N⁻P⁻ trials, where the patient spent no more time viewing the target object than would be predicted based on chance alone (base rate shown as a horizontal dotted line).

Figure 7.

Mean duration of viewing time per foil. Controls only briefly viewed each foil, as did the patient on N⁻P⁺ trials. On N⁻P⁺ and N⁻P⁻ trials the patient spend increasingly more time viewing each foil, suggesting increased difficulty in rejecting each foil as not matching the verbal cue.

Table 1

Neuropsychological test scores and demographic characteristics. The minimum and maximum scores (range) from the four control participants are listed alongside the patient's scores. Controls were not given the WAB at the time of testing, so do not have Aphasia Quotient or Auditory Word Recognition scores.

Measure (# of Items)	PPA Patient	Control Range
Age	61	59–70
Years of Education	14	14–20
Aphasia Quotient (100)	47	N/A
Boston Naming Test (60)	4	56–60
Auditory Word Recognition (60)	36	N/A
Northwestern Anagrams test (10)	3	9–10
Digit Span, Backwards	4	4–4
Trail Making Part-A (sec)	24	18–23
Trail Making Part-B (sec)	85	47–68
Digit Symbol	47	52–73
Visual Target Cancellation (60)	60	57–60
Judgment of Line Orientation (20)	20	11–20
Facial Recognition (54)	42	44–51
Pyramids & Palm Trees Pictures (52)	46	49–52