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Short communication

Eye movements as a measure of word comprehension deficits in primary progressive aphasia

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ABSTRACT

Introduction: Eye movement studies can uncover subtle aspects of language processing impairment in individuals with primary progressive aphasia (PPA), who may have difficulty understanding words. This study examined eye movement patterns on a word-object matching task in response to varying levels of word-knowledge in PPA.
Methods: Participants with semantic and non-semantic PPA completed an object-matching task, where a word was presented and participants then selected the corresponding pictured object from an array. Afterwards, participants defined words for trials to which they incorrectly pointed. Linear mixed-effects analyses examined fixation differences on targets and related and unrelated foils.
Results: On incorrectly-pointed trials, participants demonstrated greater fixation duration on related foils, demonstrating intra-category blurring. For words that could not be defined, there was similar fixation duration on related and unrelated foils, demonstrating inter-category semantic blurring.
Discussion: This study demonstrated that fixation patterns reflect varying levels of word knowledge in PPA.

1. Introduction

Primary progressive aphasia (PPA) is a dementia syndrome characterized by early, selective, and progressive language impairment, including difficulties with finding words, grammar, naming objects, and word comprehension (Mesulam et al., 2001). PPA is a result of a neurodegenerative disease (i.e. Alzheimer's disease or frontotemporal lobar degeneration) that selectively targets the left-hemisphere language network. The most common feature for all pathologies is the asymmetric prominence of atrophy, neuronal loss, and disease-specific proteinopathy in the language-dominant (usually left) hemisphere (Mesulam et al., 2014). Within the language network, patterns of atrophy vary and are typically related to symptom presentation (Rogalski et al., 2011). There are different profiles, or variants, of PPA, that are typically distinguished by their most prominent impairment (Gorno-Tempini et al., 2011; Mesulam et al., 2014). In the semantic variant, the central impairment is single word comprehension, and naming is also severely impaired. The other two variants present with non-semantic language deficits. In logopenic PPA, there is impaired word retrieval in spontaneous speech and naming. In the agrammatic profile of PPA, the most pronounced feature is impaired grammatical structure of spoken or written language and low fluency.

Because individuals with PPA may have language output difficulties, and also because off-line tests do not capture the more dynamic aspects of language, a tool that bypasses the need for language output and that offers real-time assessment of language function is desirable. One such approach is based on the tracking of eye movements during language-based tasks. Prior studies have demonstrated the usefulness of eye

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tracking to detect subtle or early impairments in PPA by examining patterns of eye movements in response to naming or object-matching tasks (Reilly et al., 2020; Faria et al., 2018).

Our laboratory developed a paradigm where a word (e.g. animals, clothes, fruits-vegetables, and manipulable objects) is presented visually and aurally, and the participant subsequently chooses the matching pictured object from a 16-item array (Seckin et al., 2016a). Participants with semantic PPA tended to look more towards semantically related foils during their search compared to controls and participants with non-semantic variants of PPA. These findings demonstrated that foils from the same category may have acquired a stronger association with the word probe compared to the foils from different categories, a phenomenon known as taxonomic interference. We speculated that this pattern reflects a blurring of meaning boundaries among words denoting exemplars of the same semantic category (Mesulam et al., 2013; Hurley et al., 2012; Seckin et al., 2016, Seckin et al., 2016b; Rogalski et al., 2007). In a case report for example, a participant with PPA demonstrated greater time viewing foils when an object could be pointed to but not named, and even greater time viewing unrelated foils when the object could not be named or pointed to (Seckin et al., 2016b). This study suggested that retrieval deficits (identified by correct pointing but failed naming) may also result in abnormal eye movement patterns, though not as severe as in instances where anomia is accompanied by word comprehension impairment identified by mispointing. A more recent study utilizing this paradigm found that even phonemic paraphasias during object naming were related to increased taxonomic interference in PPA-G, indicating subtle differences in the word-object linkages underlying phonemic paraphasias, differences that could not be detected by off-line tests (Nelson et al., 2020). These eye movement paradigms provide a clue into the distinctions underlying object naming and word recognition failures. Specifically, one may be unable to name an item due to difficulties with lexical access, but not semantic loss of word knowledge, as represented by poor naming but relatively intact comprehension of the word denoting the object. Conversely, one may have difficulty naming an item, primarily due to semantic loss, resulting in failure to name the object because the knowledge of the word that denotes the object is distorted.

The goal of the present study is to examine patterns of eye movements in response to varying levels of word-knowledge, as defined by the ability to define a word. To do so, we used a word-object matching task, where participants are asked to point to a pictured object matching a previously presented word probe, from a 16-tem array of the target and related and unrelated items (Seckin et al., 2016). Participants were then asked to define words that elicited incorrect word-picture matching. Eye movement patterns were then examined, to determine if fixation patterns differed between targets versus related and unrelated foil items depending on the accuracy of their word knowledge via definitions.

2. Methods

2.1. Participants

Participants with a diagnosis of PPA were recruited from a larger longitudinal study of PPA at Northwestern University. Ten participants with semantic PPA (PPA-S) and 23 participants with non-semantic (PPA-L, PPA-G, or logopenic/agrammatic; Mesulam & Weintraub, 2014) PPA (PPA-NS) completed the study. All participants were right-handed and were native English-speakers. The root diagnosis of PPA was based on the original 2001 criteria described by Mesulam (2001). Subsequent subtyping followed the guidelines in Gorno-Tempini et al., 2011 & Mesulam, et al., 2012 with methods described in Mesulam et al., 2012. Diagnosis was determined by the study's principal investigator (author M.M.M) based on detailed clinical evaluation, including laboratory studies, and stringent criteria. Participants completed the Western Aphasia Battery (Kertesz, 2006) to characterize aphasia. PPA-S classification was based on the presence of severe anomia and impaired single-word comprehension, as measured by the Boston Naming Test (BNT; Goodglass et al., 1983) and Peabody Picture Vocabulary Test (PPVT), respectively but intact fluency and grammar. Participant demographics and clinical characteristics are listed in Table 1.

Table 1
Study Sample Characteristics.

	PPA-S (n = 10)	PPA-NS (n = 23)	Test Statistic (t or χ^2)
Age, Mean (SD)	63.0 (3.8)	66.8 (7.2)	1.6
Sex, M:F	5:5	15:8	0.7
Years of Education, Mean (SD)	16.1 (2.6)	16.1 (2.6)	0.3
Symptom Duration Years, Mean (SD)	5.2 (2.7)	5.3 (2.7)	0.1
WAB-AQ, Mean (SD)	73.8 (19.1)	77.5 (14.6)	0.6
BNT Score, Mean (SD)	8.7 (9.2)	29.8 (18.0)	4.4***
PPVT Score, Mean (SD)	18.9 (7.4)	30.1 (5.6)	4.6***

*p <.05, *p <.01, *p <.001.

2.2. Eye movement procedures

Participants completed a word-object matching task, in which they were presented with a word in auditory and written format simultaneously followed by an elliptical array including 16 pictured objects presented on a touchscreen monitor. Participants were instructed to point to the pictured object that corresponded to the word cue. Twelve items from each category including animals (e.g. zebra), clothes (e.g. skirt), fruits-vegetables (e.g. apple), and manipulable objects (e.g. wrench) were used to create a total of 48 trials. Each picture array on each trial included the target, seven related foils from the same category as the target, and eight unrelated foils from different categories. Targets and foils on each trial were matched for psycholinguistic and visual characteristics (i.e. visual saliency, visual complexity, lexical frequency, and phonological neighborhood density). The objects were shaded gray scale drawings (Rossion & Pourtois, 2004) from the Snodgrass and Vanderwart (1980) image set and were scaled to 122 × 122 pixels (visual angle 3.4°). Stimuli were presented on a 20.5 × 11.5″ monitor (1920 × 1080 resolution), using the Presentation experimental software package (Neurobehavioral Systems, Inc., Albany, CA, US). For more detailed information regarding task parameters, refer to Seckin et al., 2016.

Eye tracking procedures were completed using the Eyelink 1000 (SR Research, Mississauga, ON, Canada) tracking system, using a tower mount set-up. Calibration was completed using a nine-point calibration procedure prior to the start of the task. Eye movements were recorded at a sampling rate of 500 Hz. Recording of eye movements on each trial included the epoch between the appearance of the object array on the screen and the touch response. Fixation durations were determined by the EyeLink DataViewer software algorithm; fixations less than 40 ms were discarded. Each object probe was surrounded by a trapezoidal area of interest. Only fixations on these areas of interest were included. Duration of gaze on each category was divided by total viewing time on each trial to calculate percent viewing time on targets, related foils, and unrelated foils.

2.3. Word definitions

Following completion of the task, participants were asked to define word items for trials to which they incorrectly pointed. Participants were shown visual text form of the word on a computer monitor and were asked to define the word and to include details that define the item. A fully correct response was operationalized as spontaneous generation of the category and at least two specific descriptors (for example, zebra = animal, black and white stripes, at the zoo). A partially correct response included the generation of the category or two specific descriptors. An incorrect response included a response of "I don't know" or incorrect categorical or descriptor information.

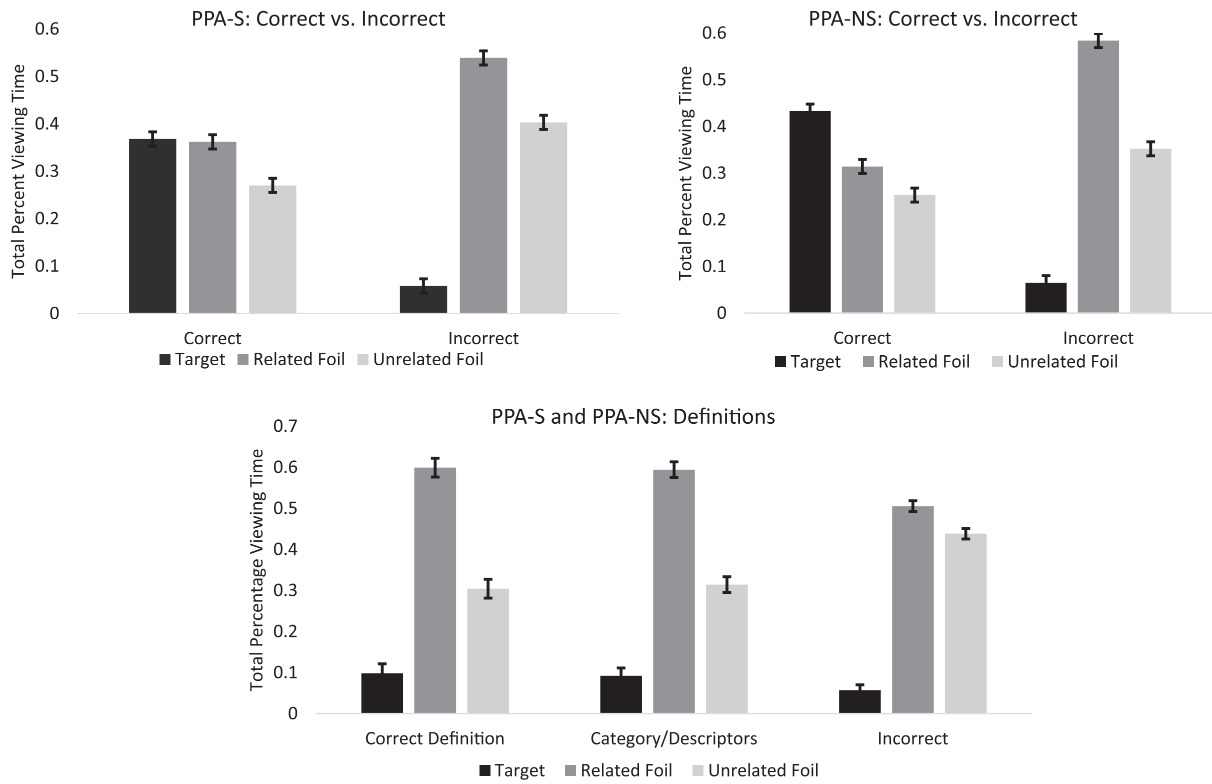

Fig. 1. (Top) On correct trials, the PPA-S group spent a similar amount of time fixating on targets and related foils, while the PPA-NS group spent a greater time fixating on targets. On incorrect trials, there was a preference for looking at the related versus unrelated foils, which was similar for both groups. (Bottom) For fully or partially defined items, there was greater time viewing related foils, while on items that could not be defined, there was little differentiation between related and unrelated foils.

2.4. Data analysis

Differences in participant demographics and clinical characteristics were tested using independent-samples t-tests or chi-squared tests. Linear mixed-effects analyses examining differences in percent viewing time were used on trial-wise data due to varying total valid trials across definition types across subjects. First, differences in percent fixations on correct and incorrect pointing trials on targets, related foils, and unrelated foils were assessed across groups. This analysis included the effects of fixation type (target, related foil, unrelated foil), accuracy (correct or incorrect), and group (semantic or nonsemantic), as well as their interactions as fixed effects, and with subject included as a random effect. The need for interaction terms was verified using a likelihood ratio test comparing this model to the simpler model containing only main effects. A separate second analysis examined differences in correct, partially correct, and incorrect definitions. Due to a limited number of valid trials across definition types, as well as a relatively similar pattern across the PPA-S and PPA-NS groups, groups were pooled in this analysis. This analysis included effects of fixation type and definition accuracy (correct, partially correct, or incorrect), as well as their interactions as fixed effects, with subject included as a random effect.

3. Results

Participant demographics are listed in Table 1. The PPA-S and PPA-NS groups did not differ with respect to age, gender, race, years of education, symptom duration, WAB-AQ (ps > 0.05). As expected, the semantic group had lower scores on the PPVT and BNT (all p values less than 0.001). One participant in the PPA-S group was excluded due to poor eye tracking trace that resulted in no valid trials.

Fig. 1 summarizes the main findings. Specifically, in PPA-NS, where word comprehension is relatively intact, correct trials were characterized by a hierarchy of gaze preference that was highest for the target, less for the related foils, and least for the unrelated foils (Target – Related: $\beta = 0.12$, Related – Unrelated: $\beta = 0.06$; $p < .001$). However, even in trials where the word was accurately matched to the object, PPA-S displayed less differentiation of the target from the related foil (i.e., less preference for viewing the target) (Target – Related: $\beta = 0.01$, $p > .05$; Related – Unrelated: $\beta = 0.09$, $p < .001$). This indicates the presence of subtle blurring of semantic mapping even in trials where pointing is accurate, demonstrating the advantage of eye tracking as a tool for probing more subtle aspects of word recognition integrity. Furthermore, in trials on which pointing failed (i.e., the word or object was not recognized), the overall pattern of gaze preferences was similar in PPA-S and PPA-NS, which implicates a similar mechanism of impaired word-object matching in all forms of PPA. Interestingly, even in these incorrect trials, there was a preference for looking at the related versus unrelated foil (PPA-NS, Related - Unrelated: $\beta = 0.23$, PPA-S, Related – Unrelated: $\beta = 0.14$; $p < .001$), reflecting a subtle residual recognition that this method can reveal.

The only instance where the related versus unrelated foil differentiation disappeared was when the word-object matching failure was accompanied by a failure of word definition, a combination that reflects a severe loss of word knowledge. For fully or partially defined items, there was greater fixation time for related foils (Fully-defined items, Related-Unrelated: $\beta = 0.30$, Partially-defined items, Related-Unrelated: $\beta = 0.28$; $p < .001$), while on items that could not be defined, there was little differentiation between viewing related versus unrelated foils (Incorrectly-defined items, Related-Unrelated: $\beta = 0.07$).

In summary, eye movements revealed a complex landscape of semantic mapping, based on the differential gaze directed to the target, related foil, and unrelated foil. The target > related foil > unrelated foil gaze hierarchy that characterized intact word comprehension was distorted into patterns of impairment that progressively lost the distinction first of target from related foil, and then the distinction of related from unrelated foil at the most severe stage of word comprehension impairment where definitions were also incorrect.

4. Discussion

This study investigated eye movement patterns on a word-object matching task in individuals with Primary Progressive Aphasia. Specifically, we examined gaze patterns in relation to both pointing accuracy and to word knowledge accuracy. In PPA-NS, percent viewing time was greatest for targets, followed by related foils, and unrelated foils. This represented the pattern characteristic of relatively intact word knowledge. However, PPA-S displayed less fixation differentiation between the target and related foil, demonstrating some degree of intra-category semantic blurring even on correctly matched trials, a distortion that could not have been detected by off-line name-object verification tasks. On incorrect pointing trials, both groups showed enhanced fixation on related foils, a pattern indicative of intra-category blurring in semantic mapping (Seckin et al., 2016, Mesulam et al., 2013), where individuals have difficulty differentiating words denoting items from the same category (Mesulam et al., 2009).

Pointing errors can reflect impairment in either word or object knowledge. In order to probe the selective influence of word knowledge on pointing accuracy, participants were asked to define the meaning of words corresponding to trials where pointing had been incorrect. An analysis of gaze patterns stratified by word definition accuracy showed that there was greater time viewing related foils for fully or partially defined words across participants. However, for words that could not be defined, there was similar fixation duration on related and unrelated foils, demonstrating not just intra-category but also inter-category semantic blurring. Eye movement patterns are therefore sensitive to and provide a window into word knowledge. These results indicate that this method is useful for dissociating contributions of impaired word knowledge from those of impaired object knowledge in name-object verifications tasks.

Eye movement measures can detect subtle deficits in semantic processing and word comprehension, particularly in participants with reduced verbal output. Furthermore, eye movements are particularly useful for mapping the multiple cognitive components of object naming (Meyer et al. 1998). Eye movements may also be influenced by word frequency and may be used to show that aphasics compensate for reading comprehension difficulties by utilizing sentence context (Huck et al., 2017). Eye movement studies have also highlighted other subtle language impairments in PPA, including distorted verb-argument integration (Mack et al., 2019). Distinct patterns of eye movements in a word-picture matching task have been shown to predict participants who would go on to develop anomia or semantic PPA (Faria et al., 2018; Reilly et al., 2020). The present study provides further evidence that eye movement patterns provide real-time gauges of distinctive patterns of word comprehension impairments in PPA. Given the fact that most patients with PPA-S, including the ones in this study, have asymmetrical left anterior temporal lobe neurodegeneration (Mesulam et al., 2021), an approach based on eye movements can also help to disentangle the mechanisms through which this component of the language network links word-forms to object representations.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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