Naming vs knowing faces in primary progressive aphasia

A tale of 2 hemispheres

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ABSTRACT

Objectives: This study examines the anatomical correlates of naming vs recognizing faces using a novel measure that utilizes culturally relevant and age-appropriate items, the Northwestern University Famous Faces (NUFFACE) Test, in primary progressive aphasia (PPA), a syndrome characterized by progressive language deficits and associated with cortical atrophy in areas important for word and object representations.

Methods: NUFFACE Test performance of 27 controls (mean age 62.3 years) was compared with that of 30 patients with PPA (mean age 62 years). Associations between NUFFACE Test performance and cortical thickness measures were quantified within the PPA group.

Results: Patients with PPA displayed significant impairment on the NUFFACE Test, demonstrating that it is a useful measure of famous-face identification for individuals with relatively young-onset dementias. Despite widespread distribution of atrophy in the PPA group, face naming impairments were correlated with atrophy of the left anterior temporal lobe while face recognition impairments were correlated with bitemporal atrophy.

Conclusions: In addition to their clinical relevance for highlighting the distinction between face naming and recognition impairments in individuals with young-onset dementia, these findings add new insights into the dissociable clinico-anatomical substrates of lexical retrieval and object knowledge. *Neurology*® 2013;81:658–664

GLOSSARY

FDR = false discovery rate; **NUFFACE Test** = Northwestern University Famous Faces Test; **PPA** = primary progressive aphasia; **PPA-S** = semantic subtype of primary progressive aphasia.

Difficulty recalling names of people is a common symptom of advancing age. More severe deficits, especially when accompanied by face recognition impairments, arise as part of neurodegenerative diseases that damage language and object recognition networks. Although several tests assess knowledge of famous faces, none were designed recently and therefore contain stimuli unfamiliar to younger individuals (i.e., aged 40–65 years) who are seeking neurologic assessment and treatment. Furthermore, these tests rarely differentiate face naming from recognition, a distinction of major neurologic significance regarding the locus of the underlying impairment. The current study was based on the Northwestern University Famous Faces (NUFFACE) Test, which addresses the aforementioned concerns by using stimuli relevant for individuals younger than 65 years, and explores the anatomical substrates of face naming and recognition.

Participants included individuals with a diagnosis of primary progressive aphasia (PPA) and healthy controls of a similar age. PPA is a predominantly young-onset clinical dementia characterized by selective language disruption and relative preservation of other cognitive abilities during the initial disease stages.¹ Atrophy in PPA is initially asymmetrically concentrated within the language-dominant (usually left) hemisphere but eventually extends to adjacent and contralateral areas with individual variations from patient to patient. Although the most severe face identification impairments in PPA are encountered in its semantic subtype, this study included all subtypes, thereby providing a subject group with a spectrum of deficits and atrophy sites so

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that the anatomical substrates of face naming and recognition deficits could be explored more objectively.

METHODS Participants. Thirty patients with a root diagnosis of PPA^{1,2} and 27 cognitively healthy controls of similar age and education participated in the study. An independent group of 35 healthy volunteers was recruited as part of the MRI control group to be used in group-based cortical thinning analysis; there were no statistically significant differences in sex, age, or education between the PPA and control groups. Patients with PPA received diagnoses based on their progressive language impairment, and their profiles were characterized as semantic (PPA-S), agrammatic, or logopenic following recently established international consensus criteria.² Two subjects were classified as mixed PPA based on the presence of both grammar and single-word comprehension deficits.³ All participants were right-handed.

Standard protocol approvals, registrations, and patient consents. All participants were recruited from the Language in Primary Progressive Aphasia Research Program, funded by the National Institute on Deafness and Other Communication Disorders, and evaluated at the Cognitive Neurology and Alzheimer's Disease Center at Northwestern University's Feinberg School of Medicine. Written informed consent was obtained from all subjects (or other legal representatives, as appropriate) participating in the study, and the Northwestern University Institutional Review Board approved the study.

Assessment of general cognition, language functions, and facial identification. Psychometric tests of cognition and language. The Mini-Mental State Examination⁴ was administered to assess global cognition, and the aphasia quotient of the revised Western Aphasia Battery served as a measure of global aphasia severity.⁵ The Northwestern Anagram Test⁶ was administered to assess for grammaticality of sentence production. The Boston Naming Test⁷ was used to measure confrontation object naming and comprehension was measured using a subset of moderately difficult items (157–192) of the Peabody Picture Vocabulary Test, fourth edition.⁸

To ensure that within the PPA group lowest scores on the NUFFACE Test were not confounded by an apperceptive agnosia that would affect face perception, we analyzed performance on the Benton Facial Recognition Test–Short Form, a measure of face perception, free of identification. With the exception of one patient who scored in the “borderline range,” just one point below the normal cutoff score on the Benton Test (41/54), all other patients with PPA scored within normal limits on this test, demonstrating that an apperceptive agnosia did not have a role in their facial recognition impairments.

NUFFACE Test. Twenty images of famous faces printed in black and white were downloaded freely from the Internet, and selected for the NUFFACE Test. Stimuli were chosen based on criteria including 1) popularity and celebrity status of famous person in visual media and press, 2) race and sex, and 3) time epoch in which the person was famous. To ensure appropriate level of difficulty, the selected images were tested on approximately 30 cognitively healthy individuals with an approximate mean age of 45 years, and all subjects had greater than 90% accuracy on both naming and recognition portions. Errors were not systematic, thus all items were retained for evaluation of our patient and demographically matched control cohort. Approximately half of the famous persons were still alive at the time of test construction; 65% were male, and 25% were of African-American descent. All famous persons were considered cultural icons: persons were entertainers,

politicians, or internationally acknowledged leaders in various disciplines. Seventy-five percent of famous persons had reached the height of their fame in 1970 or later, with peak fame ranging from 1920 (i.e., Albert Einstein) to current times (i.e., George W. Bush). See appendix e-1 on the *Neurology*® Web site at www.neurology.org for a list of the 20 selected famous persons. Appendix e-1 and associated information about the NUFFACE Test is also available at <http://www.brain.northwestern.edu/>.

Procedures and scoring. There were 2 parts to the NUFFACE Test: 1) accuracy of naming, and 2) accuracy of recognition. Participants could earn a maximum 2 points for each item on each part of the test. For the naming score, faces were presented one at a time and the subject was asked to name the famous face. A 2-point score was given if the full name of the famous person was provided; 1 point was given if either the first *or* last name was uttered. If the subject could not name the face, he or she was asked to identify the famous person through description; responses that included at least 2 relevant details were considered to be a full 2-point “recognition” score. If only one detail could be provided, the subject was given 1 point toward the NUFFACE Test recognition score. Details constituted facts about the famous person that were beyond what could be obviously perceived in the picture, such as sex or race. A recognition score of 2 was automatically credited if the participant named the face (first, last, or both). See table 1 for description of scoring procedures and examples of responses.

Imaging methods. MRI acquisition parameters. T1-weighted, 3-dimensional, magnetization-prepared rapid-acquisition gradient echo sequences (repetition time = 2,300 milliseconds, echo time = 2.91 milliseconds, flip angle = 9°, field of view = 256 mm), recording 176 slices at a slice thickness of 1.0 mm, were acquired on a 3-tesla Siemens TRIO system (Siemens AG, Erlangen, Germany) using a 12-channel birdcage head coil. Imaging was performed at the Northwestern University Center for Translational Imaging.

Image processing and cortical thickness measurements. MRIs were processed using the image analysis suite FreeSurfer (version 5.1.0), which is documented and freely available for download online (<http://surfer.nmr.mgh.harvard.edu/>). This software provides estimates of cortical thickness by measuring the distance between representations of the white-gray and pial-CSF boundaries across each point of the cortical surface. Procedures are described in a prior publication.⁹ This method was demonstrated to be reliable across scanning protocols and platforms in a series of healthy elderly participants when examining general cognitive performance and cortical thickness.¹⁰

Statistical analyses. Independent samples *t* tests were conducted to compare NUFFACE Test recognition and naming scores between patients with PPA and controls. Statistical surface maps were generated using a general linear model that displayed differences in cortical thickness between the PPA group (*n* = 30) and the MRI healthy control group (*n* = 35) for each vertex along surface representations of the entire neocortex. Using the FreeSurfer toolkit, separate statistical analyses were used to identify significant regions of cortical thickness-by-cortical hemisphere correlated with performance for naming and recognition on the NUFFACE Test within the PPA group. The false discovery rate (FDR), which controls for the expected proportion of false positives in a statistical test, was applied at 0.05 to adjust for multiple comparisons, unless stated otherwise.¹¹ Statistical analyses were performed using PASW 18.0 (SPSS Inc., Chicago, IL).

RESULTS Subject demographics and group differences in cognitive measures. Demographic information is

Table 1 Summary of NUFFACE Test scoring procedures^a

Score #1: Naming of famous face (total = 40)	
0 points = incorrect name, don't know, or no response	
Albert Einstein = "I don't know ... scientist ... E = MC ² "	
1 point = response that includes either the first name or the last name	
Lucille Ball = "I love Lucy"	
2 points = response that includes the first and last name of the famous face	
Mohammed Ali = "Cass-iel ... Cassius ... Clay"	
Score #2: Recognition of famous face (total = 40)	
0 points = subject describes irrelevant or incorrect details pertaining to person	
Barbra Streisand = "She's a politician. Maybe in the court."	
1 point = subject describes at least one relevant detail pertaining to person	
Humphrey Bogart = "He was on TV ... I doubt he's alive now, but not sure."	
2 points = image correctly named (even if incomplete OR distorted) or subject describes 2 or more relevant details pertaining to person	
Albert Einstein = "Scientist ... E = MC ² "	

Abbreviation: NUFFACE = Northwestern University Famous Faces.

^a Examples of responses are in quotation marks.

presented in table 2. The mean age of patients with PPA was 62 (± 7.1) years and mean education level was 16.3 (± 2.1) years. Forty percent of the PPA sample was male. Mean age of control subjects was 62.33 (± 6.6) years and mean education level was 16 (± 2.5) years; 51.85% of the control subject group was male. There were no statistically significant differences between patients and control subjects in age,

education, or sex distribution. As reported previously in a smaller sample study examining lexical and non-verbal deficits in PPA,¹² control subjects performed almost at ceiling on language and cognitive measures, whereas PPA subjects demonstrated significantly reduced performance in measures that assess specialized language domains (e.g., grammar and naming) and global cognition (see table 2).

Table 2 Demographics and cognitive testing performance, including the NUFFACE Test, by group

	All PPA patients	Controls
No.	30	27
Age, y, mean (SD)	62.0 (7.14)	62.3 (6.64)
Sex, % male	40.00	51.85
Education, y, mean (SD)	16.3 (2.10)	16.0 (2.50)
Symptom duration at time of visit, y, mean (SD)	3.9 (1.98)	—
NUFFACE Test naming^a	46.4 (0.07) ^b	93.4 (0.02)
NUFFACE Test recognition^a	78.5 (0.05) ^c	96.9 (0.01)
BNT (total 60)^a	62.5 (6.38) ^b	96.9 (0.60)
PPVT-IV^a	78.4 (4.96) ^c	98.0 (0.76)
NAT^a	76.3 (26.91) ^b	99.1 (2.39)
WAB AQ^a	83.1 (2.09) ^b	99.7 (0.16)
Benton FRT-Short Form^a	89.9 (1.36)	86.1 (1.41)
MMSE^a	83.2 (3.08) ^b	98.2 (0.54)

Abbreviations: BNT = Boston Naming Test; FRT = Facial Recognition Test; MMSE = Mini-Mental State Examination; NAT = Northwestern Anagram Test; NUFFACE = Northwestern University Famous Faces; PPA = primary progressive aphasia; PPVT-IV = subset of moderately difficult items (157-192) from the Peabody Picture Vocabulary Test, fourth edition; WAB AQ = aphasia quotient of the Western Aphasia Battery.

^a Mean scores are indicated as percentages of possible total scores per measure, when available, with accompanying standard errors.

^b Significant at $p < 0.0001$.

^c Significant at $p < 0.01$: statistically significant lower means in PPA performance compared with controls.

Interrater reliability of the NUFFACE Test. NUFFACE Test scores from all patients with PPA ($n = 30$) were used to assess interrater agreement of scoring procedures between 2 raters (T.G. and K.W.). The κ statistic was used to determine consistency of scoring for both naming and recognition, independently. Statistical analysis for interrater scoring of naming responses yielded a κ value of 0.93, indicating “very good” agreement ($p < 0.0001$); interrater scoring of recognition responses yielded a κ value of 0.86, representing “very good” agreement ($p < 0.0001$).¹³ In instances of disagreement, scores were discussed and consensus was achieved.

NUFFACE Test performance. On the NUFFACE Test, control subjects performed at ceiling, with average naming accuracy of 93.37%, suggesting that the stimuli were age-appropriate and easily recognized. Group comparisons revealed that the patients with PPA scored significantly worse than controls on both the naming ($p < 0.0001$) and recognition ($p < 0.005$) portions of the NUFFACE Test (table 2). On average, the PPA-S group had the lowest performance on both naming and recognition portions, although there was variability among individual patient scores within PPA-S (NUFFACE Test naming range: 0%–23%; NUFFACE Test recognition range: 5%–85%) (figure). At an individual level, however, performance overlapped among all subtypes, which is consistent with the neurodegenerative nature of PPA. Our results focus on examining performance as a continuous variable within the entire PPA group (rather than generating comparisons of average performance by subtype) because the goal of this study was to examine the face naming and identification deficits and their relationship to atrophy among unselected patients with PPA. Details on PPA subtype scores on cognitive tests, including the NUFFACE Test, are displayed in table 3.

Cortical thickness and correlates of NUFFACE Test naming and recognition. The regional distribution of cortical thinning (atrophy) of the 30 patients with PPA compared with 35 healthy controls (FDR, 0.05) is shown in part A of the figure, and is presented interactively in the video (at www.neurology.org). Cortical thinning was asymmetric and most severe in the perisylvian language regions of the left cerebral hemisphere including peak atrophy of the entire left temporal lobe, as well as the supramarginal, angular, inferior frontal gyri, and insular regions. Although not as prominent as in the left hemisphere, peak thinning of the right hemisphere was primarily in the temporoparietal junction and anterior temporal lobe. This distribution of cortical thinning is consistent with previous reports of atrophy in patients with PPA.³

Correlations between vertex-based whole-brain cortical integrity and NUFFACE Test naming and

recognition performance were examined in a separate analysis using the PPA group as a whole rather than by subtype, because the range of performance overlapped among subtypes.

NUFFACE Test naming performance was positively correlated (FDR, 0.05) with cortical thinning in the left temporal cortex, including anterior portions of the superior, middle, and inferior temporal gyri as well as the anterior fusiform (figure, B). That is, worse naming performance was associated with greater atrophy in these particular regions in all PPA subjects. Scatterplots in part B of the figure provide correlation data at an individual subject level, labeled by subtype.

In contrast, correlations between NUFFACE Test performance and vertex-based whole-brain analysis revealed that NUFFACE Test recognition performance was positively correlated (FDR, 0.05) with bilateral atrophy in the anterior temporal lobe including anterior portions of the superior, middle, and inferior temporal gyri as well as the fusiform gyrus (figure, C). Scatterplots in part C of the figure demonstrate these relationships for both the left and right hemisphere at an individual subject level, labeled by subtype. These results demonstrate that naming and recognition deficits can be dissociated behaviorally as well as by their neuroanatomical substrates. Because recognition impairments occurred for faces that also failed to be named and because we did not have patients with asymmetric right hemisphere atrophy, the possibility that the critical substrate of recognition is predominantly right-sided rather than bilateral cannot be ruled out.

DISCUSSION This study of facial recognition and naming impairments yielded 3 major findings. First, it demonstrated that the NUFFACE Test is a convenient clinical tool for the assessment of face naming and recognition in individuals currently 40 to 65 years of age, a period during which age-related changes in cognition and neurodegenerative dementias are being diagnosed with increasing frequency. Second, findings demonstrated that patients with PPA can have face identification impairments that differentially reflect naming vs recognition deficits. Third, our findings shed additional light on the differential anatomical substrates of face naming and face recognition.

The ability to name faces is an exceedingly complex process of great relevance to everyday life. Face identification deficits are among the most common experiences of otherwise cognitively normal older individuals.^{14–16} In age-related dementias such as typical forms of Alzheimer disease, and in some of the younger-onset dementias related to frontotemporal lobar degeneration, such impairments may be particularly severe.^{16,17} Face identification is vulnerable to disruptions at the level of perceptual encoding (as in apperceptive prosopagnosia), associative elaboration (as in associative prosopagnosia),

A Cortical thinning: PPA vs Controls

B NUFACE naming correlations in PPA

C NUFACE recognition correlations in PPA

(A) Distribution of cortical thinning on the pial surface in patients with PPA compared with controls. (B and C) Colored areas highlight regions on pial surface that show a significant positive correlation between cortical thickness and performance on the NUFACE naming (B) and recognition (C) tests. Lateral (top) and ventral (bottom) views are provided for each hemisphere and each comparison. Significance is displayed as $-\log_{10}(p)$ value on the flame scale. Accompanying scatterplots illustrate the relationship between NUFACE performance and mean cortical thickness for the significant regions from the general linear model analysis. Different shapes are used to indicate the clinical subtype of each participant. LH = left hemisphere; NUFACE = Northwestern University Famous Faces Test; PPA = primary progressive aphasia; PPA-G = agrammatic subtype of PPA; PPA-L = logopenic subtype of PPA; PPA-M = mixed subtype of PPA; PPA-S = semantic subtype of PPA; RH = right hemisphere.

Table 3 Demographics and cognitive testing performance, including the NUFFACE Test by PPA subtype

	PPA-G	PPA-L	PPA-S
No.	11	8	9
Age, y, mean (SD)	61.7 (6.93)	65.9 (7.06)	57.6 (4.39)
Sex, % male	54.5	37.5	22.2
Education, y, mean (SD)	16.5 (2.54)	16.0 (1.60)	16.4 (2.19)
Symptom duration at time of visit, y, mean (SD)	3.8 (1.31)	3.5 (2.07)	4.0 (1.66)
NUFFACE Test naming ^a	73.6 (6.9)	59.7 (10.6)	3.9 (2.5)
NUFFACE Test recognition ^a	94.6 (1.2)	94.7 (1.9)	45.0 (11.9)
BNT (total 60) ^a	76.7 (7.04)	90 (1.91)	18.7 (6.61)
PPVT-IV ^a	95.4 (1.85)	96.0 (2.17)	45.5 (8.11)
NAT ^a	59.7 (7.71)	88.1 (4.65)	94.9 (3.69)
WAB AQ ^a	77.3 (3.89)	91.1 (2.21)	81.9 (3.57)
Benton FRT-Short Form ^a	90.7 (2.09)	85.2 (1.71)	82.4 (2.47)
MMSE ^a	83.3 (5.76)	85.3 (4.43)	78.89 (6.60)

Abbreviations: BNT = Boston Naming Test; FRT = Facial Recognition Test; MMSE = Mini-Mental State Examination; NAT = Northwestern Anagram Test; NUFFACE = Northwestern University Famous Faces; PPA = primary progressive aphasia; PPA-G = agrammatic subtype of PPA; PPA-L = logopenic subtype of PPA; PPA-S = semantic subtype of PPA; PPVT-IV = subset of moderately difficult items (157-192) from the Peabody Picture Vocabulary Test, fourth edition; WAB AQ = aphasia quotient of the Western Aphasia Battery.

^aMean scores are indicated as percentages of possible total scores per measure, when available, with accompanying standard errors. Note that separate subtype scores from subjects with a diagnosis of "mixed subtype of PPA" (n = 2) are not shown.

or the linkage between percepts and corresponding verbal labels (as in anomic aphasia). It may be difficult to determine the principal locus of vulnerability because patients who complain of forgetting faces do not distinguish between naming and recognition deficits, a distinction of high clinical relevance. Indeed, what is reported as "forgetting" the identity of a face frequently turns out to reflect impairment of lexical retrieval rather than of semantic memory. The current study, aiming to differentiate the lexical retrieval (anomic) from the recognition (semantic) components of face identification failures, documents the usefulness of the NUFFACE Test for making this distinction. It remains to be seen whether this approach will prove as useful in the evaluation of patients with other neurodegenerative syndromes.

Numerous tests have been designed to assess face identification deficits. Sanders and Warrington (1971) introduced one of the first tests of this type, based on famous personalities in the United Kingdom. Similar tests were developed for use in the United States, but most measures use stimuli that have since become outdated and inappropriate for use in the younger generation of individuals affected by atypical dementias such as PPA. To our knowledge, there are no updated famous-faces tests for a US population that allow for the quantitative discrimination of naming from recognition deficits using the type of detailed scoring criteria provided by the NUFFACE Test.

Patients with all forms of PPA were included in this study to achieve a broad range of clinical impairment severity and atrophy distribution. In fact, the distribution of peak atrophy in the whole PPA group encompassed extensive parts of the temporal lobes and temporoparietal junctions in both hemispheres (figure, A). Despite this widespread distribution of cortical thinning, the correlations with face identification impairments were highly selective and revealed differential anatomical substrates for naming and recognition failures. The current results showed that face naming impairments were associated with the degree of atrophy in the left anterior temporal lobe whereas face recognition impairments were associated with bilateral anterior temporal lobe atrophy, a pattern that is also consistent with previous observations in patients with semantic dementia.¹⁸ Prior findings from our group¹² demonstrated that left anterior temporal atrophy impairs object naming but not object recognition. These complementary findings suggest that the neural substrates of face naming and recognition may parallel those of object naming and recognition.

Other investigations on patients with semantic dementia, many of whom had bilateral anterior temporal lobe atrophy, have postulated that the anterior temporal lobe contains an amodal representation of objects and faces.¹⁹⁻²¹ The current findings are more consistent with a dual-route model according to which face naming is dependent on the integrity of a left

hemisphere language network, whereas face recognition is dependent on the integrity of a bilateral or predominantly right-sided object recognition network.^{12,22,23} In addition to its practical value for the neuropsychological characterization of patients, the NUFFACE Test thus has the added potential to help disentangle the anatomical substrates of large-scale distributed networks underlying word and object knowledge.

AUTHOR CONTRIBUTIONS

Tamar Gefen, Sandra Weintraub, Christina Wieneke, and Emily Rogalski contributed to the study conceptualization and design. Tamar Gefen, Christina Wieneke, Adam Martersteck, Kristen Whitney, and Emily Rogalski contributed to the acquisition of data and generation of images. Tamar Gefen, Sandra Weintraub, Marsel Mesulam, and Emily Rogalski analyzed and interpreted data. Tamar Gefen, Sandra Weintraub, Marsel Mesulam, and Emily Rogalski edited and revised the manuscript for important intellectual content and data accuracy. Emily Rogalski, Sandra Weintraub, and Marsel Mesulam supervised the study from initiation to completion.

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