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Research Report

# Hyperfamiliarity for faces: Preserved core face processing with altered medial temporal lobe connectivity in a single case study

*Kira N. Noad* [a,*,e], *Marie Kieseler* [c,d,e], *David M. Watson* [b], *Brad Duchaine* [c] and *Timothy J. Andrews* [b]

[a] Mathematisches Institut, Justus-Liebig-Universität Gießen, Gießen, Germany
[b] Department of Psychology, University of York, York, UK
[c] Department of Psychological and Brain Sciences, Dartmouth College, New Hampshire, USA
[d] Department of Psychology, University of Fribourg, Switzerland

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ABSTRACT

Hyperfamiliarity for faces (HFF) is a rare condition in which unfamiliar faces evoke an abnormal sense of familiarity. We present a case study of Nell, a 49-year-old woman who developed hyperfamiliarity following a severe migraine. Using a combination of behavioural and neuroimaging approaches, we investigated the cognitive and neural mechanisms underlying her condition. Behaviourally, Nell demonstrated accurate recognition of famous and personally familiar faces, but frequently misclassified unfamiliar faces as familiar. Structural MRI scans revealed no overt abnormalities, and functional imaging showed a typical pattern of face-selective activation within the core face-processing regions. To probe familiarity-related neural responses, Nell viewed movie clips from *Game of Thrones*, a series she had never seen. A whole-brain analysis showed that neural activity in her medial temporal lobe (MTL) more closely resembled control participants who were familiar with the series than those who were unfamiliar. Moreover, functional connectivity analyses revealed that her core face-processing regions exhibited connectivity patterns with the MTL that were similar to familiar controls. These findings suggest that HFF may arise from atypical functional connectivity between the core face network and memory-related regions in the MTL, leading to a spurious sense of familiarity in the absence of recognition. This case offers novel insights into the neural systems supporting face familiarity and highlights the dissociability of familiarity and identification processes in face perception.



* *Corresponding author.*
E-mail address: kira.n.noad@gmail.com (K.N. Noad).
[e] Joint first authors.

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## 1. Introduction

Hyperfamiliarity for faces (HFF) is a rare condition in which unfamiliar faces evoke an abnormal sense of familiarity, despite intact recognition of known individuals and preserved visual processing (Vuilleumier et al., 2003; Young et al., 1993). This phenomenon can lead to the mistaken feeling that unfamiliar faces have been previously encountered. Although prior studies have linked HFF to damage in the temporal lobe (Amlerova et al., 2012; Devinsky et al., 2010; Michelucci et al., 2010; Negro et al., 2015; Vuilleumier et al., 2003), the precise neural mechanisms underlying this condition remain unclear. HFF provides a unique opportunity to investigate how the brain generates a sense of familiarity and to clarify the neural distinction between familiarity and recognition.

Cognitive models propose that familiar face recognition occurs in a sequence of serial processing stages (Bruce & Young, 1986). Faces are initially processed in an image-dependent manner before being transformed into an image-invariant representation of identity, if the face is familiar (Burton et al., 1999; Hancock et al., 2000; Young & Burton, 2017). The activation of these image-invariant representations, known as face recognition units (FRUs), is believed to trigger the sensation of familiarity. Familiarity is thought to precede recognition because it is possible to perceive a face as being familiar without recalling the identity of the person, but never the reverse (Young et al., 1985).

The neural basis of familiar face recognition begins with the core face-processing network (Duchaine & Yovel, 2015; Haxby et al., 2000; Ishai, 2008). The occipital face area (OFA) encodes early facial features, before information is projected to the fusiform face area (FFA) to generate a stable, identity-specific representation. However, the extent to which familiarity modulates activity in core face regions remains debated. Some studies report stronger FFA responses to familiar faces (Deen et al., 2024; Sergent et al., 1992; Weibert & Andrews, 2015), while others find no such effect (Gobbini et al., 2004; Gorno-Tempini & Price, 2001; Leveroni et al., 2000). However, the neural processing of familiar faces continues beyond the core network, engaging an extended face network responsible for retrieving person-related semantic, episodic, and affective information (Gobbini & Haxby, 2007; Haxby et al., 2000; Ishai, 2008; Kovács, 2020). This network includes medial temporal and frontal regions that integrate non-visual knowledge associated with the face.

Here, we investigate the neural correlates of familiarity for faces by assessing behavioural and neural responses in a single case study of HFF. First, we examine recognition and familiarity judgments for faces in HFF to determine whether impairments stem from deficits in face recognition or from the misattribution of familiarity to unfamiliar faces. Next, we use fMRI to assess whether visual face processing remains intact despite the disorder. Finally, we investigate fMRI responses to unfamiliar faces in a naturalistic viewing paradigm. This study shows that HFF is accompanied by disrupted connectivity between the core face-processing regions in the visual brain and memory-related regions in the medial temporal lobe and provides new insights into the processes underlying familiarity and identification of faces.

## 2. Methods

### 2.1. *Case history*

Nell is a 49-year-old woman from the United Kingdom who developed hyperfamiliarity for faces (HFF) following a severe migraine in August 2020. Prior to this episode, she typically experienced two migraines per year. The migraine preceding the onset of HFF produced pain on the right side of the head. Since then, Nell has reported persistent HFF, with two further atypical migraines eliciting transient increases in perceived facial familiarity. While the intensity of these symptoms diminished over time, she continues to experience HFF with all faces.

Nell describes her condition as highly distressing and reports employing compensatory strategies, such as focusing on individuals' gaits, voices, or associated contextual cues (e.g., dogs) to determine whether someone is truly known to her. She particularly relies on these strategies in ambiguous cases, such as encounters with acquaintances. After five years, she reports having adjusted to the condition, reframing it positively as a sense of being surrounded by familiar individuals. A CT scan (June 2021) revealed no evidence of active bleeding, and a structural MRI scan conducted at the York Neuroimaging Centre, University of York (February 2022), showed no structural abnormalities.

### 2.2. *Behavioural assessment*

#### 2.2.1. *Participants*

We compared Nell's behaviour with age-matched control participants recruited through advertisements in local newsletters and tested online. Comparisons between Nell and control participants were conducted using one-tailed *t*-tests adapted for single-case studies, effect sizes are reported as $z_{cc}$ (*Singlims_ES.exe*, Crawford et al., 2010). Written informed consent was obtained from all participants, and the study was approved by the Committee for the Protection of Human Subjects at Dartmouth College.

#### 2.2.2. *Basic visual processing test*

Nell's basic visual functions were assessed using the Hanover Early Vision Assessment (HEVA; Kieseler et al., 2022). This battery comprises five tasks requiring discrimination of circle size, ellipse size, angular size, line length, and dot spacing. Twenty-one participants (mean age = 47.6, SD = 6.1, range = 39–58; 10 female) served as controls for the basic visual assessment.

#### 2.2.3. *Old/new face recognition test*

To objectively quantify HFF, Nell completed the Old/New Face Recognition Test (Duchaine et al., 2006). During the learning phase, she was instructed to memorize 10 sequentially presented unfamiliar faces, each displayed twice for 3 sec (3° × 3° visual angle). In the test phase, 50 faces were presented sequentially for up to 10 sec each. Nell was instructed to indicate via button press whether each face was “old” (previously seen) or “new.” The test set comprised the 10 studied faces (each repeated twice) and 30 novel unfamiliar faces.

Signal detection (measured with A-prime) was used to assess the ability to discriminate between old and new faces. Reaction time was also measured. Ten control participants tested at Dartmouth College (USA) (mean age = 56.2 years, SD = 6.25, range = 46–63; 8 female) completed the Old/New Face Recognition Test and served as control participants for the Doppelganger Test and the Cambridge Face Memory Test.

#### 2.2.4. Face recognition tests

To assess long-term recognition of famous faces, Nell completed two tasks. In the Famous Faces Test, 60 celebrity photographs cropped to remove hair and background information were presented sequentially for 5 sec each ($13^\circ \times 17^\circ$ visual angle), and Nell was asked to provide either the name or a unique identifying detail. Five age-matched participants from the UK (mean age = 56.6, SD = 5.5) completed the Famous Faces Test.

In the Doppelganger Test, 60 trials presented the written name of a celebrity along with two photographs: the actual celebrity and a visually similar "doppelganger." Images were shown for 2 sec (~$24^\circ \times 13^\circ$ visual angle), and Nell was asked to indicate which was the famous person. Accuracy and reaction time were measured. For the Personally Familiar Face Recognition Test, 13 personally familiar images were selected of family, friends, and acquaintances. These were shown with 100 AI-generated unfamiliar faces (https://generated.photos/) degraded to match the quality of the personally familiar faces. Each of the 13 familiar faces was presented once in upright orientation and once in an inverted orientation. In addition, 50 unfamiliar faces were presented upright and 50 unfamiliar faces were presented inverted. Across 126 randomized trials, each image was displayed for 2 sec (~$13^\circ \times 17^\circ$ visual angle), and Nell judged whether the face was personally familiar.

Short-term face recognition was evaluated using the Cambridge Face Memory Test (CFMT; Duchaine & Nakayama, 2006). Participants learned six male target faces and subsequently completed 72 three-alternative forced-choice trials requiring identification of the target face (stimuli subtending ~$17^\circ \times 9^\circ$ visual angle). Accuracy and reaction time were measured.

#### 2.2.5. Voice recognition

To determine whether Nell's hyperfamiliarity extended to non-facial stimuli, we administered a voice recognition battery (Garrido et al., 2009; (Jiahui et al., 2018). Participants were first introduced to six female British English speakers by name. In three learning blocks, they heard sentences spoken by each speaker and were asked to match the voice to the corresponding name. The first learning block consisted of six sentences per speaker for a total of 36 trials, the second and third learning blocks consisted of ten sentences per speaker for a total of 60 trials per block. Following this familiarization, participants completed a recognition test that required them to identify which of the six speakers had spoken on each trial. Each speaker spoke ten sentences in this test, for a total of 60 trials. Finally, an old/new test was administered, in which participants judged whether each voice belonged to one of the original six speakers or to one of the nine novel speakers. The test consisted of 36 trials for the six "old" speakers (six trials each), and 36 trials for nine "new" speakers (four trials each), for a total of 72 trials. Control data for this test battery were taken from Garrido et al. (2009) and consist of eight UK participants (mean age = 56.6, SD = 5.5, range = 46–64; all female).

### 2.3. MRI analysis

To determine the neural correlates of hyperfamiliarity, we compared fMRI responses in Nell with 45 control participants (median age: 19 years, age range: 18–32, 15 male) previously reported in Noad et al. (2024) (https://openneuro.org/datasets/ds004848). All control participants were neurologically healthy, right-handed, had normal or corrected-to-normal vision, and reported no issues with face recognition. 23 of the control participants had watched the TV series Game of Thrones, while the remaining 22 control participants had not watched Game of Thrones. Written informed consent was obtained for all participants, and the study was approved by the York Neuroimaging Centre Ethics Committee. All participants performed a face-localizer scan and a movie-watching scan to measure the neural response to faces.

#### 2.3.1. fMRI data acquisition

All scanning was completed at the York Neuroimaging Centre using a 3T Siemens Magnetom Prisma MRI scanner and a 64-channel phased array head coil. A gradient-echo echo-planner imaging (EPI) sequence was used to collect data from 60 axial slices (TR = 2 sec, TE = 30 ms, FOV = 240 × 240 mm, matrix size = 80 × 80, voxel dimensions = 3 × 3 × 3 mm, slice thickness = 3 mm, flip angle = 80°, phase encoding direction = anterior to posterior, multiband acceleration factor = 2). T1-weighted structural images were acquired from 176 sagittal slices (TR = 2300 ms, TE = 2.26 ms, matrix size = 256 × 256, voxel dimensions = 1 × 1 × 1 mm, slice thickness = 1 mm, flip angle = 8°). Field maps were collected from 60 slices (TR = 554 ms, short TE = 4.90 ms, long TE = 7.38 ms, matrix size = 80 × 80, voxel dimensions = 3 × 3 × 3 mm, slice thickness = 3 mm, flip angle = 60°).

The fMRI data were analysed using FSL's FEAT v6.0 (http://www.fmrib.ox.ac.uk/fsl; (Jenkinson et al., 2012). Motion correction (MCFLIRT) (Jenkinson et al., 2002), temporal high-pass filtering (Gaussian-weighted least squares straight line fittings, sigma = 50 sec) and slice timing correction were applied. Spatial smoothing (Gaussian) was applied at 6 mm FWHM. Removal of non-brain material was performed with BET (Smith, 2002). Functional data were first registered to a high-resolution T1-anatomical image via boundary-based registration (Greve & Fischl, 2009), and then onto the standard MRI brain (MNI152) via a non-linear registration computed via FNIRT. Field maps were used to apply correction to distortion of functional images as part of the registration step.

#### 2.3.2. Face-localizer scan

A face-localizer scan was used to define face-selective regions. There were 3 stimulus conditions: faces, scenes, and phase-scrambled faces. Face stimuli had three viewpoints (−45°, 0°, 45°) and were taken from the Radboud database of face stimuli (Langner et al., 2010). Faces were presented on a greyscale 1/f amplitude-mask background. Scrambled faces were created by randomising the phase spectra while maintaining the amplitude spectra of the face images including the amplitude mask background. Scenes were indoor, outdoor man-made, and outdoor natural stimuli from the SUN database (Xiao et al., 2010). 4 images (8.4° × 8.4° visual angle) from each condition were presented in 3 sec blocks, in which each image was shown for 600 ms, with a 200 ms ISI. A fixation cross on a grey screen was presented for 6 sec between blocks. 9 blocks were presented for each condition in a pseudorandomized order, for a total scan time of 244 sec. To maintain attention, participants performed an orthogonal task detecting periodic colour changes in the fixation cross, responding via a button press.

Data from the localizer scan were used to define face-selective regions of interest (ROIs) from control participants, and to establish whether Nell showed typical responses to static unfamiliar face stimuli. Boxcar models of each stimulus block were convolved with a single-gamma haemodynamic response function to generate regressors for each condition. These were then entered into a first-level GLM analysis (Woolrich et al., 2001) alongside their temporal derivatives plus confound regressors for 6 head motion parameters. Individual participant data from the controls were entered into a higher-level group analysis using a mixed-effects GLM using FLAME (Woolrich et al., 2004). Face-selective regions were then defined using the contrast of the response to faces to both other conditions (faces > scenes + scrambled face). To define ROIs, we used a clustering algorithm that iteratively adjusted the statistical threshold to grow clusters of 250 spatially contiguous voxels (2000 $mm^3$) around seed voxels within each region.

To determine whether Nell demonstrated typical face-selective responses, a first-level analysis of Nell's localizer scan was performed using methods identical to those used with the scans from the control participants. To make a direct comparison between Nell and control participants, we compared face-selectivity in face regions. A Crawford–Howell *t*-test was used to test for differences in the magnitude of response in Nell compared to controls.

### 2.3.3. *Movie-watching scan*

Participants viewed and listened to a movie that was constructed with audio-visual segments from Seasons 3 and 4 of Game of Thrones (Fig. 1a). The selected scenes consisted predominantly of close-up and mid-shot views of characters' faces as they engaged in dialogue, social interactions, and dynamic actions, providing consistent exposure to facial information throughout the clips. There were 10 distinct scenes that ranged in length from 50 to 117 s, for a total movie length of 12 min 58 s (778 sec). Each scene depicts an independent and coherent narrative. The movie was projected onto an in-bore screen at a distance of 57 cm from the participant with the image subtending approximately 38.7 × 22.3 degrees of visual angle. Accompanying audio was also played to participants in the scanner. The movie was presented using PsychoPy (Peirce et al., 2019).

First, we compared functional responses between Nell and control participants who were familiar or unfamiliar with Game of Thrones. The time series from each voxel in each participant was converted to % signal change, 6 head motion parameters were regressed out of the data, and the data were aligned into a standard space (MNI152). We calculated the intersubject correlations (ISCs) using Pearson's *r* between Nell and each participant from both groups (Fig. 1b). For each voxel in the brain, the timecourse of response in Nell was correlated with the timecourse from the corresponding voxel in a control participant. This was repeated across all voxels for all combinations of Nell with control participants in a pairwise approach, leading to 23 correlations for Nell's similiarity to the familiar group (one correlation per familiar control) and 22 correlations for Nell's similarity to the unfamiliar group (one correlation per unfamiliar control). A Fisher's *z* transform was applied to the correlations prior to statistical testing. To determine whether the ISCs were greater between Nell and the familiar group compared to Nell and the unfamiliar group, a one-tailed Welch's independent-samples *t*-test was performed on each voxel in the brain. This produced whole-brain *p*-statistic maps for each contrast (Nell correlated with familiar controls *vs* Nell correlated with unfamiliar controls, and vice versa). Statistical maps were thresholded at $p < .001$, uncorrected for multiple comparisons.

Next, we compared functional connectivity between regions in Nell and the familiar or unfamiliar control participants. The time course of the responses of all voxels within a region was averaged in each participant. To measure connectivity, pairwise correlations (Pearson's *r*) of timeseries were computed between regions for each participant (Fig. 1c). A Fisher's z transform was applied to all correlations prior to any statistics. To test whether Nell was significantly different from unfamiliar but not familiar participants in average connectivity between these functional regions, we performed Crawford–Howell *t*-tests (Crawford & Howell, 1998) on the Fisher's *z* average connectivity scores for Nell versus the familiar participants and Nell versus the unfamiliar participants. We compared functional connectivity within early visual regions (Wang et al., 2015) and face-selective regions. Finally, we measured functional connectivity between the face regions and a network of non-visual regions that have been previously linked to familiarity (Noad et al., 2024).

All participants performed a behavioural test to determine their familiarity with Game of Thrones before undergoing the MRI experiment. Understanding of the narrative was tested using a set of 14, 4-alternative, multiple-choice questions. Next, we tested the ability to recognize the faces of key people from Game of Thrones. Participants viewed faces and were asked to name the person or provide relevant information about them. Finally, we tested the ability to recognize key places or landmarks. Participants viewed scenes and were asked to provide the name or key information about the scene that was relevant to Game of Thrones. When participants provided key information rather than the name of the face or scene, two independent observers who were familiar with Game of Thrones had to both agree that the information provided was sufficient to show

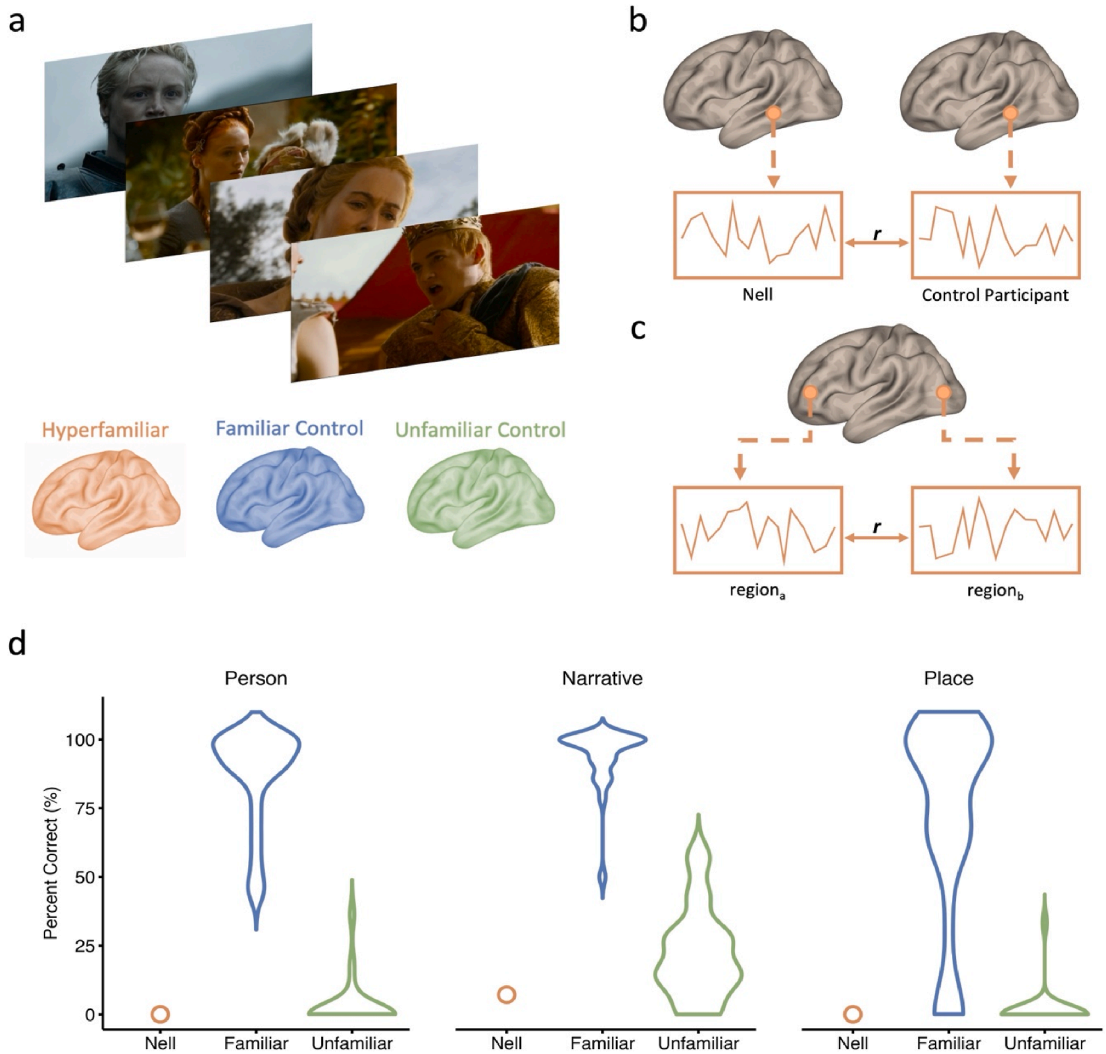


**Fig. 1 – Natural viewing fMRI paradigm a) Nell, familiar control participants, and unfamiliar control participants watched a movie containing clips from the TV show Game of Thrones while neural responses were measured using fMRI. b) Neural responses were compared using intersubject correlation, in which the time-course of response in each voxel of Nell was correlated with the time-course of response of each corresponding voxel in control participants. c) Functional connectivity was calculated within each participant by correlating the time-course of response of one region with the time-course of response of another region. d) Participants completed a behavioural test to demonstrate their familiarity with Game of Thrones. Nell is unfamiliar with the TV series Game of Thrones, and shows a similar behavioural performance to unfamiliar control participants on the test about the show.**

familiarity. All tests were self-paced. Differences between Nell and familiar and unfamiliar control participants were tested using Crawford–Howell tests.

## 3. Results

### 3.1. *Behaviour*

#### 3.1.1. *Basic visual processing tests*

On the Hanover Early Vision Assessment (HEVA), Nell achieved an overall accuracy of 87.5%, comparable to control participants tested online (control mean ± SD = 76.0 ± 13.6%; $t(20) = .83$, $p = .209$; chance = 33%, $z_{cc} = .8$ (95% CI: .3–1.3).

#### 3.1.2. *Old-new face recognition test*

Nell's performance on the Old/New Face Recognition Test confirmed her self-reported hyperfamiliarity for faces (HFF). Accuracy was significantly lower than controls (Nell A′ = .84 *vs* control A’ = .96 ± .05; $t(9) = -2.29$, $p = .023$, $z_{cc} = -2.4$ (95% CI: −3.6 to −1.1; Fig. 2a). This was due to Nell making substantially more false alarms than controls (19 *vs* 2.7 ± 2.5; $t(9) = 6.34$, $p < .001$, $z_{cc} = 6.7$ (3.6–9.7). Signal detection analysis further indicated a markedly liberal response bias (C = −1.71) relative to controls (mean C = −.39 ± .54; $z = -2.33$, $p = .022$, $z_{cc} = -2.4$ (−3.7 to −1.2). Reaction times for correct responses did not differ from controls (Nell = 1.37 sec; control mean = 1.32 ± .53 ms; $t(9) = .11$, $p = .459$, $z_{cc} = .1$ (−.6 − .7).

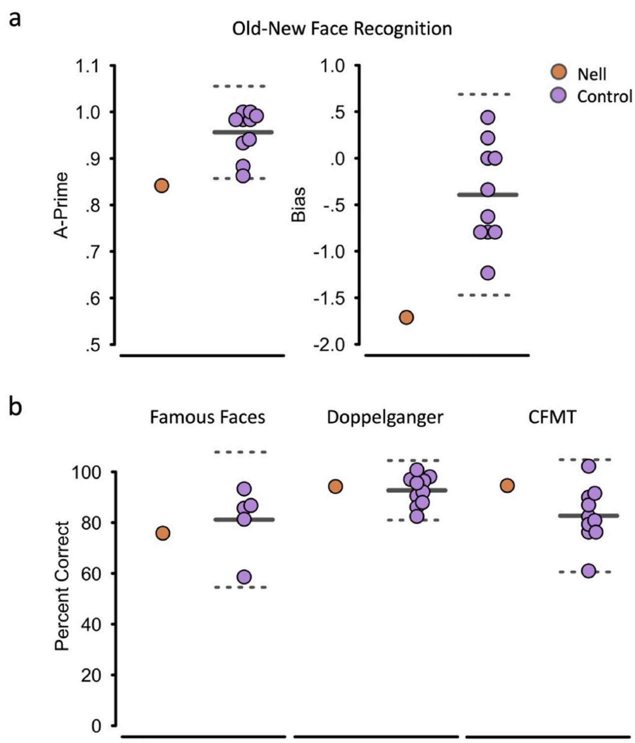


**Fig. 2 – Face recognition and face perception in Nell (orange circle) and control participants (purple circles). a) Performance on an old/new face recognition test. Nell showed reduced accuracy for judging whether faces have been seen before, due to the miscategorization of new faces as old, consistent with HFF. b) Nell demonstrates typical performance on tests of face recognition including a Famous Faces Test, a Doppelganger test and the Cambridge Face Memory Test, showing that she can accurately determine the identity of faces. Solid lines denote the control mean, dashed lines denote 2 standard deviations above and below the mean.**

#### 3.1.3. *Face recognition tests*

Despite HFF, Nell's performance on tests of familiar face recognition fell within the normal range (Fig. 2b). On the Famous Faces Test, she correctly identified 75.6% of faces from people she was familiar with (control mean = 81.2 ± 13.3%; $t(4) = -.38$, $p = .360$, $z_{cc} = -.4$ (95% CI: −1.3 – .5). On the Doppelganger Test, she correctly selected the celebrity image in 85.7% of trials from people she was familiar with (control mean = 84.3 ± 5.3%; $t(9) = .25$, $p = .403$, $z_{cc} = .3$ (−.4 – .9)). However, although accuracy was preserved on this test, reaction times were significantly longer (Nell = 5.56 sec; controls = 2.13 ± .40 sec; $t(9) = 8.20$, $p < .001$, $z_{cc} = 8.6$ (4.7–12.6)). On the Personally Familiar Faces Test, Nell correctly recognized all 13 personally familiar faces (100%). However, she also misclassified 32 of 50 upright unfamiliar faces as personally familiar (36% correct). Only 7 of 13 inverted familiar faces were reported as familiar (54%), but she correctly rejected 49 of 50 inverted unfamiliar faces as being familiar. Post-test, Nell reported that inverted faces did not evoke the abnormal sense of familiarity typically triggered by upright faces. Control comparisons were not possible for this task, as it was designed specifically around Nell's social network.

On the Cambridge Face Memory Test (CFMT), Nell's accuracy (86.1%) was not statistically different from controls (75.3 ± 10%; $t(9) = 1.02$, $p = .165$, $z_{cc} = 1.1$ (.3–1.9). However, reaction times on correct trials were slower (Nell = 4.64 sec; controls = 3.06 ± .80 sec; $t(9) = -1.90$, $p = .046$, $z_{cc} = 2.0$ (.9–3.1).

#### 3.1.4. *Voice Recognition Test*

Nell's performance on the voice recognition battery indicated no evidence of hyperfamiliarity for voices. She outperformed controls on Learning Test 1 (86.1% *vs* 71.6 ± 4.1%; $t(7) = 3.32$, $p = .006$, $z_{cc} = 3.5$ (95% CI: 1.6–5.4) and Learning Test 2 (86.7% *vs* 74.4 ± 5.3%; $t(7) = 2.20$, $p = .032$, $z_{cc} = 2.4$ (.9–3.7), but did not differ significantly on Learning Test 3 (86.7% *vs* 78.1 ± 5.5%; $t(7) = 1.48$, $p = .091$, $z_{cc} = 1.6$ (.5–2.6) or on the Voice Recognition Test (55% *vs* 35.6 ± 10.9%; $t(7) = 1.67$, $p = .070$, $z_{cc} = 1.770$ (.6–2.9)). On the Voice Old/New Test, Nell's performance ($A' = .85$) was within the normal range (control mean = .80 ± .04; $t(7) = 1.25$, $p = .125$, $z_{cc} = 1.3$ (.3–2.3). These results align with her self-report that HFF does not extend to the auditory domain.

### 3.2. *MRI*

#### 3.2.1. *Structural MRI*

We performed T1 and T2 structural scans. Neither of these scans revealed any structural abnormalities (Fig. 3).

#### 3.2.2. *Face-localizer scan*

To investigate how hyperfamiliarity manifests in face-selective regions of the brain, the response to unfamiliar faces was compared to scenes and scrambled faces using a face-localizer scan. Fig. 4a shows a comparison of face-selectivity in neurotypical controls and Nell. Nell showed a similar pattern of face-selective regions when compared to neurotypical controls. We directly compared the magnitude of the face-selective responses across different regions in Nell and controls (Fig. 4b). In face-selective regions, Nell showed a similar selectivity to faces compared to controls (lOFA: $M_C = .54$, $SD_C = .35$, $M_{Nell} = 1.28$, $t(44) = 2.09$, $p = .042$; rOFA: $M_C = .62$, $SD_C = .33$, $M_{Nell} = .63$, $t(44) = .03$, $p = .973$; lFFA: $M_C = .55$, $SD_C = .30$, $M_{Nell} = .36$, $t(44) = .63$, $p = .533$; rFFA: $M_C = .63$, $SD_C = .32$, $M_{Nell} = .48$, $t(44) = .46$, $p = .650$; lSTS: $M_C = .18$, $SD_C = .16$, $M_{Nell} = .14$, $t(44) = .22$, $p = .829$; rSTS: $M_C = .20$, $SD_C = .15$, $M_{Nell} = -.01$, $t(44) = 1.42$, $p = .163$).

#### 3.2.3. *Movie-watching viewing*

We measured knowledge of the TV series Game of Thrones in Nell, and control participants who were either familiar or unfamiliar with the show (Fig. 1d). Nell is unfamiliar with Game of Thrones and, as expected, performed worse than familiar controls on the narrative test ($M_C = 93.8\%$, $SD_C = 11.5\%$, $M_{Nell} = 7.1\%$, $t(22) = 7.4$, $p < .001$), person recognition test ($M_C = 87.0\%$, $SD_C = 17.9\%$, $M_{Nell} = 0\%$, $t(22) = 4.75$, $p < .001$) and place recognition test ($M_C = 71.0\%$, $SD_C = 38.0\%$, $M_{Nell} = 0\%$, $t(22) = 1.83$, $p = .081$). However, there was no difference between Nell and the unfamiliar controls (narrative: $M_C = 22.1\%$, $SD_C = 16.6\%$, $M_{Nell} = 7.1\%$, $t(21) = .88$, $p = .390$, person: $M_C = 2.9\%$, $SD_C = 8.6\%$, $M_{Nell} = 0\%$, $t(21) = .31$, $p = .745$, place:

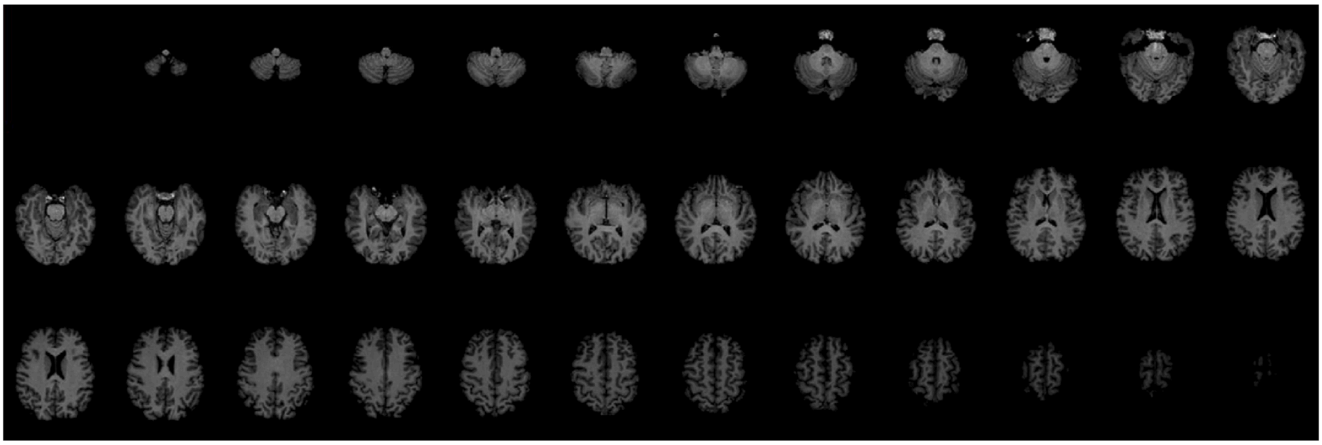

**Fig. 3 – T1 MRI Structural Scan did not reveal any obvious structural abnormalities in Nell that could explain her hyperfamiliarity for faces.**

$M_C = 1.5\%$, $SD_C = 7.1\%$, $M_{Nell} = 0\%$, $t(21) = .21$, $p = .837$). On the person recognition questions, Nell made responses that are characteristic of her HFF. For example, one character was thought to be a friend of the family, or her yoga teacher.

To determine how Nell responded to faces during naturalistic viewing, we compared the time course of neural response from Nell with control participants who were familiar, or unfamiliar, with Game of Thrones. We then

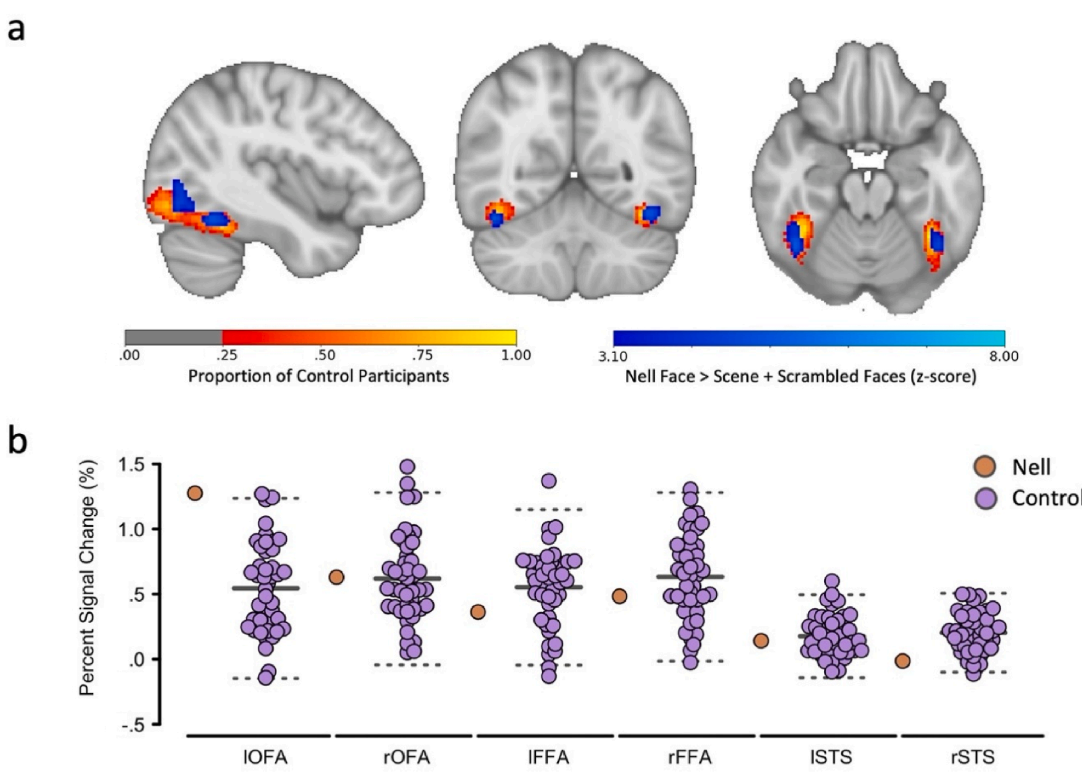


**Fig. 4 – Nell shows normal category-selective responses to faces. a) Face-selective regions in Nell and control participants. Red-orange demonstrates the proportion of control participants showing face-selective activity of Z > 3.1. Blue-light blue shows the face-selective activity in participant Nell thresholded at Z > 3.1 (voxel coordinates, −40, −56, −20). b) Differences in fMRI response to face images compared to scene and scrambled face images in face-selective regions in Nell (orange circle) and control participants (purple circles). Solid lines denote the control mean, dashed lines denote 2 standard deviations above and below the mean.**

compared these correlations across all voxels in the brain. Fig. 5a shows voxels where ISCs were significantly greater between Nell and familiar participants than between Nell and unfamiliar participants (red-yellow). Nell shows significantly greater similarities with familiar participants in the medial temporal lobes bilaterally, overlapping with the hippocampus (Table 1). Despite being unfamiliar with Game of Thrones, Nell does not show any significantly greater neural similarities with unfamiliar participants compared to familiar participants.

Next, we investigated whether functional connectivity in Nell would be more similar to familiar or unfamiliar participants when watching Game of Thrones. To do this, we measured functional connectivity between regions in Nell and then compared that to functional connectivity in familiar and unfamiliar controls. We compared connectivity between regions in early and high-level visual cortex. The magnitude of connectivity between early visual regions was similar in Nell and both familiar and unfamiliar controls (Nell *vs* familiar: $M_C = 1.50$, $SD_C = .22$, $M_{Nell} = 1.47$, $t(22) = .45$, $p = .659$; Nell *vs* unfamiliar: $M_C = 1.42$, $SD_C = .13$, $M_{Nell} = 1.47$, $t(21) = 1.34$, $p = .195$). There was also no significant difference in magnitude of connectivity between Nell and unfamiliar controls ($M_C = .58$, $SD_C = .10$, $M_{Nell} = .74$, $t(21) = 1.59$, $p = .127$) or between Nell and familiar controls ($M_C = .68$, $SD_C = .12$, $M_{Nell} = .74$, $t(22) = .48$, $p = .639$) in the core face-selective regions.

**Table 1 – Regions showing higher ISC between Nell and familiar controls compared to Nell and unfamiliar controls. The maximum p- and t-value are shown for each region.**

| | x | y | z | $-\log_{10}(p)$ | t |
|---|---|---|---|---|---|
| Right hippocampus | 40 | 60 | 24 | 4.19 | 4.22 |
| Left hippocampus | 57 | 60 | 23 | 3.48 | 3.67 |

In a previous study, we found that overall connectivity between core face-selective regions and an extended network of regions beyond the visual brain was greater in familiar compared to unfamiliar participants (Noad et al., 2024). This network of regions is predominantly non-visual, and includes the superior frontal gyrus, superior parietal lobule, medial frontal gyrus, post–central gyrus, precuneus, intraparietal lobule, post–central gyrus, posterior cingulate, supramarginal gyrus, precentral gyrus, temporoparietal junction, superior temporal gyrus, occipital pole, inferior frontal gyrus, frontal pole, retrosplenial cortex, middle temporal gyrus, superior temporal sulcus, medial prefrontal cortex, hippocampus,

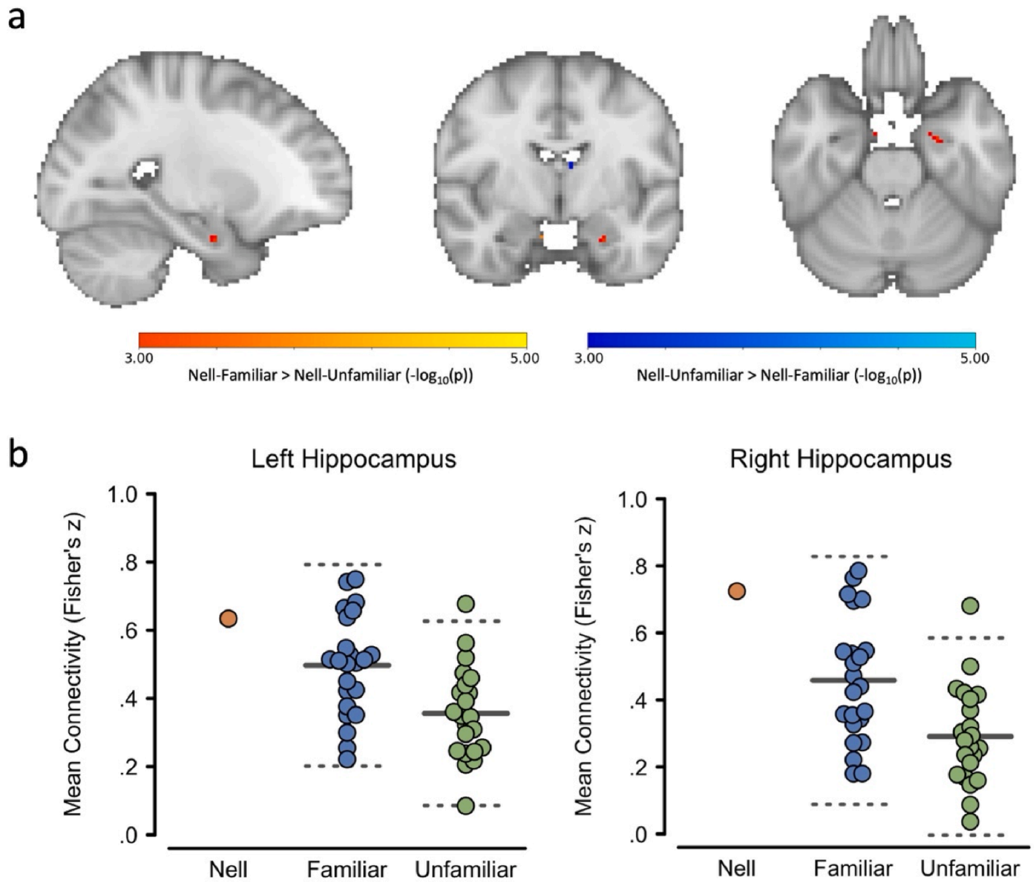


**Fig. 5 – Neural correlates of HFF in the medial temporal lobe. a) In bilateral medial temporal regions, Nell's responses are more similar to those of familiar controls (red–yellow) than to those of unfamiliar controls (blue–light blue) thresholded at $p < .001$, uncorrected for multiple comparisons (MNI coordinates −24, −6, −26). b) Functional connectivity between the core face regions and the hippocampus is similar to familiar controls but significantly different from unfamiliar controls. Solid lines denote the control mean, dashed lines denote 2 standard deviations above and below the mean.**

inferior temporal gyrus, fusiform gyrus and temporal pole. Given her HFF, we tested whether Nell would also show greater overall connectivity between these regions and core face-selective regions compared to unfamiliar controls. Consistent with this prediction, Nell showed significantly greater connectivity than unfamiliar controls ($M_C = .36$, $SD_C = .10$, $M_{Nell} = .65$, $t(21) = 2.92$, $p = .008$) but not familiar controls ($M_C = .50$, $SD_C = .12$, $M_{Nell} = .65$, $t(22) = 1.09$, $p = .236$).

Finally, since Nell showed greater ISC in the medial temporal lobe with familiar compared to unfamiliar participants, we looked at connectivity specifically between the hippocampus and face-selective regions (Fig. 5b). Here, Nell showed significantly greater connectivity than unfamiliar but not familiar controls in both the left (Nell *vs* unfamiliar: $M_C = .36$, $SD_C = .14$, $M_{Nell} = .63$, $t(21) = 2.10$, $p = .048$; Nell *vs* familiar: $M_C = .50$, $SD_C = .15$, $M_{Nell} = .63$, $t(22) = .95$, $p = .354$) and right hippocampus (Nell *vs* unfamiliar: $M_C = .29$, $SD_C = .15$, $M_{Nell} = .72$, $t(21) = 3.02$, $p = .007$; Nell *vs* familiar: $M_C = .46$, $SD_C = .18$, $M_{Nell} = .72$, $t(22) = 1.47$, $p = .155$).

To determine whether the observed differences in functional connectivity could be explained by differences in activation between Nell and the control groups, we conducted two further analyses. First, we compared temporal signal-to-noise ratio (tSNR) between Nell and the control group across the brain during the movie-watching scan. A higher tSNR could lead to higher correlations. However, this showed no significant differences ($M_C = .63$, $SD_C = .20$, $M_{Nell} = .54$, $t(44) = -.48$, $p = .634$). This shows that signal variance across the whole brain was not different between Nell and the control group. Next, we examined mean hippocampal activation in response to faces > scenes + scrambled faces in the localiser scan. Nell showed no significant difference in activation to controls in the left hippocampus ($M_C = .03$, $SD_C = .24$, $M_{Nell} = -.15$, $t(44) = -.75$, $p = .455$), and a significantly decreased activation in the right hippocampus ($M_C = -.09$, $SD_C = .35$, $M_{Nell} = -.94$, $t(44) = -2.42$, $p = .020$). This shows that there was no hyperactivity in the response to faces in the hippocampus that might give rise to higher functional connectivity values.

## 4. Discussion

This study provides novel insights into the cognitive and neural mechanisms underlying hyperfamiliarity for faces (HFF), a phenomenon in which unfamiliar faces persistently evoke feelings of familiarity despite the knowledge that these faces are unfamiliar. Behavioural results confirmed that our single case, Nell, exhibited a marked tendency to categorize unfamiliar faces as familiar, despite intact recognition of genuinely familiar faces. Voice tests confirmed that Nell's hyperfamiliarity does not extend to the auditory domain. Neuroimaging analyses further elucidated the neural underpinnings of this condition, revealing that while early perceptual processing of faces appeared normal, atypical functional connectivity with the medial temporal lobe (MTL) played a crucial role in the manifestation of HFF.

Nell's performance on an old/new face recognition task provided a clear behavioural demonstration of her hyperfamiliarity for faces (HFF). She showed a markedly elevated false-alarm rate relative to control participants, indicating a bias to judge unfamiliar faces as familiar (Young et al., 1993). A similar pattern emerged in a second task involving both personally familiar and unfamiliar faces: Nell again exhibited a high rate of false alarms for unfamiliar faces. In contrast, her performance on the CFMT was within the normal range. This discrepancy likely reflects differences in task design. The old/new test requires familiarity judgements for individual faces and is therefore susceptible to response-criterion shifts, whereas the CFMT uses a three-alternative forced-choice format that minimises criterion effects. Consistent with this interpretation, Nell's recognition of genuinely familiar individuals was intact, as shown by her normal performance on two famous-face recognition tests. Her normal accuracy on voice-recognition tasks further indicates that the hyperfamiliarity effect is restricted to the visual modality. Together, these findings suggest that HFF does not reflect a fundamental deficit in face recognition per se, but rather an aberrant attribution of familiarity.

To investigate potential structural abnormalities underlying HFF in Nell, we examined her structural MRI scans. We found no overt structural abnormalities. This contrasts with previous reports that have linked HFF to lesions in the temporal lobe (Negro et al., 2015; Vuilleumier et al., 2003). For example, HFF has been associated with temporal epileptiform abnormalities (Amlerova et al., 2012; Bujarski & Sperling, 2008) and amygdalo-hippocampal lesions (Michelucci et al., 2010). Nell's HFF onset coincided with a migraine episode, a condition known to induce neurological, vascular, and neurochemical alterations that may not always manifest as structural changes detectable via MRI (Goadsby et al., 2017). Therefore, while no structural abnormalities were observed, this does not preclude the presence of subtle functional or microstructural alterations contributing to the emergence of HFF.

To determine if the neural correlates of Nell's HFF were evident in the visual processing of faces, we examined functional responses in face-selective regions of the occipital and temporal lobes (Haxby et al., 2000; Kanwisher et al., 1997). The fusiform face area (FFA), a key component of the core face-processing network, plays a critical role in representing facial features necessary for familiar face recognition (Weibert & Andrews, 2015). Our analysis confirmed that Nell's core face-selective regions, including the FFA, were intact and showed a similar selectivity to faces compared to control participants. These findings suggest that early visual processing of faces remains intact in Nell despite the presence of HFF.

To further investigate the neural mechanisms underlying HFF, we examined neural responses to faces during naturalistic viewing. Nell and control participants, who were either familiar or unfamiliar with the TV series Game of Thrones (GoT), watched movie clips from the show. As Nell had never seen GoT, her ability to recognize characters was comparable to that of unfamiliar controls and far lower than that of familiar controls. Nevertheless, we hypothesized that brain regions implicated in Nell's hyperfamiliarity would be more similar to familiar participants than they would be to unfamiliar participants. The only brain regions showing this predicted difference in intersubject correlation were in the right and left medial temporal lobe (MTL) in the location of the hippocampus. Prior research has identified the MTL as critical for the recognition of familiar identities (Nielson et al., 2010; Quiroga et al., 2009; Weibert et al., 2016), and disruptions in MTL function have also been linked to HFF (Michelucci et al., 2010). These findings suggest a role of the MTL in the anomalous familiarity experiences characteristic of HFF.

To further examine the neural basis of HFF, we analyzed functional connectivity between core face-selective regions, including the FFA, and a broader network implicated in face familiarity. Previously, we demonstrated increased functional connectivity within this network in individuals familiar with GoT compared to those unfamiliar (Noad et al., 2024). Despite the fact that Nell was unfamiliar with GoT, we found that Nell exhibited functional connectivity between core face-processing regions and the extended familiarity network that was similar to familiar control participants. Notably, this effect was evident in the connectivity between the face-selective regions and the hippocampus. These findings align with prior studies indicating that connectivity between face-selective cortical areas and MTL structures contributes to face memory (Ramot et al., 2019).

Our findings are consistent with other neurological conditions in which the sense of familiarity for faces can be dissociated from explicit recognition. For example, in prosopagnosia individuals can exhibit preserved physiological responses to familiar faces despite impaired recognition (Bobes et al., 2004; Tranel & Damasio, 1988). Additionally, disorders such as Capgras and Fregoli syndromes demonstrate pathological dissociations between familiarity and identity recognition (Ellis & Lewis, 2001; Hirstein & Ramachandran, 1997) and include delusions which are not present in HFF. Capgras syndrome involves a disruption of familiarity, whereby patients can recognize a person's identity but do not experience the usual sense of familiarity. This often leads to the belief that a close relative or friend has been replaced by an imposter. In contrast, Fregoli syndrome involves an abnormal sense of familiarity in the absence of true recognition, such that patients feel that strangers are familiar people in disguise. The pattern observed in Nell's HFF aligns more closely with Fregoli syndrome, suggesting that an imbalance between face memory networks can lead to aberrant familiarity attributions.

A potential concern in interpreting neural data is the age difference between Nell and the control participants. Although age-related changes in neural processing could make older adults appear more similar to familiar viewers, evidence from our previous study indicates that this is unlikely (Noad et al., 2024). In a whole-brain analysis, we failed to find voxels in which ISC was predicted by participant age. We also found overall signal variance, which could affect functional connectivity, was not significantly affected by age. Together, these results suggest that age is unlikely to be a major contributor to the effects of HFF observed in the present study.

In conclusion, these results suggest that HFF arises from altered functional connectivity between core face-processing regions and the MTL. Despite intact early visual processing, Nell exhibits an abnormal sense of familiarity accompanied by heightened MTL activity and connectivity with face-processing regions. This supports the notion that familiarity perception is mediated by a dynamic interplay between visual and non-visual brain networks. Understanding the neural mechanisms underlying HFF not only sheds light on face familiarity processing and its interplay with face recognition, but also provides insights into broader memory and recognition systems.

## Declaration of competing interest

The authors declare no competing financial interests.

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## Scientific transparency statement

DATA: Some raw and processed data supporting this research are publicly available, while some are subject to restrictions: https://osf.io/3e5sq, https://doi.org/10.18112/openneuro.ds004848.v1.0.1

CODE: All analysis code supporting this research is publicly available: https://osf.io/3e5sq

MATERIALS: Some study materials supporting this research are publicly available, while some are subject to restrictions: https://osf.io/3e5sq

DESIGN: The authors indicated that reporting the sample size determination, data exclusions, and inclusion and exclusion criteria was not applicable to this research. They provided the following justification: '*This is a single case study*'.

PRE-REGISTRATION: No part of the study procedures was pre-registered in a time-stamped, institutional registry prior to the research being conducted. No part of the analysis plans was pre-registered in a time-stamped, institutional registry prior to the research being conducted.

For full details, see the *Scientific Transparency Report* in the supplementary data to the online version of this article.

## Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.cortex.2026.02.003.

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