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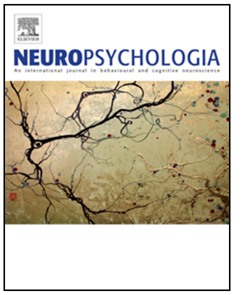

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Angélique Volfart: Data curation, Formal analysis, Methodology, Vizualisation, Writing – original draft, Writing – Review & Editing. **Jacques Jonas:** Conceptualization, Funding acquisition, Investigation, Supervision, Writing – original draft, Writing – Review & Editing. **Louis Maillard:** Funding acquisition, Investigation, Writing – original draft. **Thomas Busigny:** Conceptualization, Methodology. **Bruno Rossion:** Conceptualization, Funding acquisition, Supervision, Writing – original draft, Writing – Review & Editing. **Hélène Brissart:** Conceptualization, Data curation, Supervision, Writing – original draft.

Typical visual unfamiliar face individuation in left and right mesial temporal epilepsy

Angélique Volfart[1,2], Jacques Jonas[1,3], Louis Maillard[1,3], Thomas Busigny[2], Bruno Rossion[1,2,3*], Hélène Brissart[1,3*]

[1] Université de Lorraine, CNRS, CRAN, F-54000 Nancy, France

[2] Université Catholique de Louvain, Institute of Research in Psychological Science, Louvain-La-Neuve, Belgium

[3] Université de Lorraine, CHRU-Nancy, Service de Neurologie, F-54000 Nancy, France

* equal contribution

Corresponding author: Bruno Rossion, bruno.rossion@univ-lorraine.fr

Abstract

Patients with chronic mesial temporal lobe epilepsy have difficulties at identifying familiar faces as well as at explicit old/new face recognition tasks. However, the extent to which these difficulties can be attributed to visual individuation of faces, independently of general explicit learning and semantic memory processes, is unknown. We tested 42 mesial temporal lobe epilepsy patients divided into two groups according to the side of epilepsy (left and right) and 42 matched controls on an extensive series of individuation tasks of unfamiliar faces and control visual stimuli, as well as on face detection, famous face recognition and naming, and face and non-face learning. Overall, both patient groups had difficulties at identifying and naming famous faces, and at explicitly learning face and non-face images. However, there was no group difference in accuracy between patients and controls at the two most widely used neuropsychological tests assessing visual individuation of unfamiliar faces (Benton Facial Recognition Test and Cambridge Face Memory Test). While patients with right mesial temporal lobe epilepsy were slowed down at all tasks, this effect was not specific to faces or even high-level stimuli. Importantly, both groups showed the same profile of response as typical participants across various stimulus manipulations, showing no evidence of qualitative processing impairments. Overall, these results point to largely preserved visual face individuation processes in patients with mesial temporal lobe epilepsy, with semantic and episodic memory difficulties being consistent with the localization of the neural structures (anterior temporal cortex and hippocampus) involved in their epilepsy. These observations have implications for predictive neuropsychological outcomes in the case of surgery, and support the validity of intracranial EEG recordings performed in this population to understand neural mechanisms of human face individuation, notably throughout intracranial electrophysiological recordings and stimulations.

Key words

Mesial temporal lobe epilepsy ; Face individuation ; Neuropsychology

List of abbreviations

BFRT-c: Benton facial recognition test computerized

CFMT: Cambridge Face Memory Test

iEEG: intracranial electroencephalography

fMRI: functional magnetic resonance imaging

FRI: face recognition index

HR: head rotation

LD: lighting direction

MTLE: mesial temporal lobe epilepsy

NAI: name access index

NC: normal controls

RT: response times

SEEG: stereotactic electroencephalography

VOTC: ventral occipito-temporal cortex

WAIS: Wechsler Adult Intelligence Scale

1. Introduction

Face identity recognition is critical for social interactions in the human species and constitutes one of the most impressive functions of the adult human brain. Unfortunately, face identity recognition is also frequently affected in a variety of neurological conditions, e.g. following acquired brain damage (Benton and Van Allen, 1972; Valentine *et al.*, 2006; Barton, 2008), surgery for temporal glioma (Papagno *et al.*, 2017), Alzheimer's disease (Tippett *et al.*, 2003; Pal *et al.*, 2019), fronto-temporal semantic dementia (Luzzi *et al.*, 2017; Pozueta *et al.*, 2019), or temporal lobe epilepsy (Seidenberg *et al.*, 2002; Drane *et al.*, 2013).

Recognizing the identity of familiar people based on their faces requires first and foremost to decode the idiosyncratic visual features of these faces (i.e., face individuation). Efficient face individuation is often required when we first encounter people or when they have not yet been encoded in long-term memory, i.e. when they are unfamiliar. Since most human societies are characterized by the presence of numerous individuals and a tendency to change the number of individuals over time, visual individuation of *unfamiliar* faces occurs frequently and is key to our social interactions (Rossion, 2018).

In neurotypical individuals, the neural basis of visual face individuation has been primarily investigated with functional MRI (fMRI). In particular, fMRI-adaptation studies have found face individuation effects in pre-defined face-selective regions of the posterior ventral occipito-temporal cortex (VOTC) such as the inferior occipital gyrus ("Occipital Face Area", OFA) and the middle fusiform gyrus ("Fusiform Face Area", FFA) (Gauthier *et al.*, 2000; Schiltz *et al.*, 2006; Davies-Thompson *et al.*, 2009; Ewbank *et al.*, 2013; Fox *et al.*, 2013; Hermann *et al.*, 2017; Hughes *et al.*, 2019; Rostalski *et al.*, 2019). These studies usually use pictures of unfamiliar faces in order to rule out the automatic involvement of affective and semantic memory processes, as well as name retrieval. In contrast, the processing of familiar (i.e. famous and personally familiar) faces has been consistently shown to involve more anterior regions of the VOTC, such as the anterior and medial temporal regions (Sergent *et al.*, 1992; Gorno-Tempini *et al.*, 1998; Leveroni *et al.*, 2000; Gorno-Tempini and Price, 2001; Elfgren *et al.*, 2006; Gobbini and Haxby, 2007; Natu and O'Toole, 2011; Sugiura *et al.*, 2011; Von Der Heide *et al.*, 2013; Duchaine and Yovel, 2015; Ramon *et al.*, 2015, Rice *et al.*, 2018*b*), in line with episodic, semantic and emotional contents evoked by familiar faces (Brambati *et al.*, 2010; Sugiura *et al.*, 2011; Ross and Olson, 2012).

Mesial temporal lobe epilepsy (MTLE) is the most frequent focal epilepsy referred for epilepsy surgery (Schuele and Lüders, 2008; Spencer and Huh, 2008; Tatum, 2012; see also Ladino *et al.*, 2014). Intracranial electroencephalographic (iEEG) recordings have shown that MTLE frequently affects the temporal pole, the amygdala, the head and body of the hippocampus, the rhinal cortex, and the ventral anterior temporal cortex (including the anterior parts of the fusiform and inferior temporal gyri) (Maillard *et al.*, 2004). These structures are typically involved in anterior temporal lobectomy, one of the most frequent surgical procedure in refractory MTLE (Brotis *et al.*, 2019). Several studies have shown that patients with MTLE are impaired at recognizing familiar faces (Seidenberg *et al.*, 2002; Viskontas *et al.*, 2002; Glosser *et al.*, 2003; Griffith *et al.*, 2006). More precisely, left-sided MTLE has been more consistently related to difficulties at *naming* famous faces, while right-sided MTLE has been frequently linked to difficulties at *familiarity judgment*, or providing *semantic* information about a face (Gainotti, 2007; Drane *et al.*, 2008, 2013). A similar pattern of famous face identification difficulties has also been found in MTLE patients following ATL resection (Glosser *et al.*, 2003; Drane *et al.*, 2008, 2013; Lambon Ralph *et al.*, 2012, Rice *et al.*, 2018*a*). Additionally, these patients exhibit difficulties at explicitly encoding and subsequently recognizing pictures of unfamiliar faces, regardless of the epileptogenic focus side (Milner, 1968; Chiaravalloti and Glosser, 2004).

The extent to which famous face recognition difficulties in MTLE can be attributed to the process of visual individuation of faces, independently of general explicit learning and semantic memory processes, remains unknown. Clarifying this issue is important both for clinical and fundamental research. From a clinical standpoint, a comprehensive view of the neuropsychological performance of epileptic patients before epilepsy surgery is critical to predict the neurocognitive outcome after surgery (Potter *et al.*, 2009; Sherman *et al.*, 2011; Helmstaedter, 2013). Indeed, post-operative cognitive outcome depends, among other variables, on the relationship between the location of the epileptogenic zone (i.e., the region to be resected to cure the patient) and the pre-operative neuropsychological profile. According to the model of functional adequacy, the postoperative decline is expected to be high when there is an adequacy between the brain region planned to be resected and high pre-operative performance on the cognitive functions supported by this region (Chelune, 1995; Helmstaedter, 2004). At the level of fundamental research, there is increasing evidence for limitations of animal models, in particular the macaque brain, to understand the neural mechanisms of human face (identity) recognition (Rossion and Taubert, 2019; Griffin, 2020). In this context, iEEG recordings of face processing in human epileptic patients may become increasingly informative (e.g. Allison *et al.*, 1999; Davidesco *et al.*, 2014; Jonas *et al.*, 2016; see Rossion *et al.*, 2018 for review). Therefore, a comprehensive view of face recognition performance in these patients is needed to validate the results obtained with iEEG recordings. This issue of potential deficits in visual individuation of faces in MTLE patients remains unsolved, mainly because very few studies have assessed face individuation with unfamiliar faces in these patients (Hermann *et al.*, 1997; Seidenberg *et al.*, 1998; Glosser *et al.*, 2003;

Chiaravalloti and Glosser, 2004; Griffith *et al.*, 2006), and these studies have used only a single test (most often the Benton Facial Recognition Test, BFRT, Benton and Van Allen, 1968). While these studies found that both left and right MTLE patients performed in the normal range at this test, with sometimes a trend towards higher scores for left MTLE patients, they never recorded response times (RT) at this task, an important variable to consider in individual face matching tasks (Delvenne *et al.*, 2004; Rossion and Michel, 2018).

In the present study, we went well beyond the state-of-the art by testing 42 MTLE patients and their matched controls on a series of individuation tasks with unfamiliar faces and control visual stimuli and by reporting both accuracy and response times. The entire cohort of participants was also tested with a face detection task, face and non-face explicit learning tasks, and a famous face recognition and naming task, in order to provide a comprehensive overview of their face recognition performance.

2. Materials and Methods

2.1. Participants

Forty-three consecutive pre-surgical patients with refractory MTLE were prospectively enrolled between 2013 and 2017 at the University Hospital of Nancy. The inclusion criteria were: (1) age above 18 years; (2) left or right MTLE as assessed by non-invasive examinations (structural MRI, EEG-video, PET, SPECT) for all patients and stereotactic-EEG (SEEG) for 24 out of 42 patients (when non-invasive examinations were inconclusive with regard to the location of the epileptogenic focus); (3) normal basic visual functions (as measured by the VOSP, i.e. Visual Object and Space Perception battery).

Among the 43 patients screened, one patient was later excluded because of insufficient data about the location of the epileptic focus. Therefore, 42 patients were included in the subsequent analyses (21 males, 21 females; mean age 37.05 ± 11.68). Thirty-nine patients were right-handed (93%) and three patients were left-handed (7%) as measured by the Edinburgh Handedness Inventory (Oldfield, 1971). All but 2 (left) MTLE patients had their intellectual efficiency assessed through the WAIS-R or WAIS-IV (Wechsler Adult Intelligence Scale) and showed a normal IQ (> 70). All patients gave written informed consent and the study (ATENA-F, trial N°2013-A00515-40, ClinicalTrials.gov identifier NCT02888925) was approved by the local ethical committee (CPP Est III, 13.05.02).

Two groups of patients were distinguished according to the lateralization of the epileptogenic focus: a left MTLE group (17 patients, 9 females; mean age 36.41 ± 12.49) and a right MTLE group (25 patients, 12 females; mean age 37.48 ± 11.34). The side of the epileptogenic focus was assessed by non-invasive examinations (structural MRI, EEG-video, PET, SPECT) and, when available, SEEG recordings (24/42 patients). The two patient groups were not statistically different on gender, age at inclusion, handedness, educational level, age at epilepsy onset, duration of epilepsy, number of antiepileptic drugs, structural status of the hippocampus (presence or not of a hippocampal sclerosis) or total IQ (**Table 1**). However, left MTLE patients were significantly faster in processing speed (as measured by the Coding test from the WAIS) than right MTLE patients (**Table 1**).

Characteristics		**Left MTLE (n=17)**	**Right MTLE (n=25)**	**Statistical comparisons**
Gender	**Male**	8	13	χ=0.099, p=.753 V_{Cramer}= 0.049
	Female	9	12	
Age at inclusion		36.41 ± 12.49	37.48 ± 11.34	t=-0.288, p=.775 d_{Cohen}= 0.135
Handedness (left/right)		2/15	1/24	χ=0.920, p=.338 V_{Cramer}= 0.148
Educational Level	**< 12 academic years**	7	13	χ=2.293, p=.318 V_{Cramer}= 0.234
	12-14 academic years	3	7	

	> 14 academic years	7	5	
Age at epilepsy onset		19.88 ± 16.65	14.56 ± 9.95	U=181, p=.419 d_{Cohen}= 0.251
Duration of epilepsy		16.53 ± 12.8	22.92 ± 13.94	U=157, p=.155 d_{Cohen}= 0.450
Number of anti-epileptic drugs		2.18 ± 1.13	2.28 ± 0.89	U=185.5, p=.440 d_{Cohen}= 0.215
Presence of hippocampal sclerosis (yes/no)		7/10	13/12	χ=0.475, p=.491 V_{Cramer}= 0.106
Total IQ		100.13 ± 17.87	90.28 ± 11.39	U=126, p=.085 d_{Cohen}= 0.565
Processing speed (percentile Coding test)		48.2 ± 32.1	27.4 ± 23.17	**U=117, p=.047** **d_{Cohen}= 0.816**

Table 1. Demographic and clinical characteristics of MTLE patients. Values are shown as mean ± standard deviation or as the number of patients per category. Independent t-tests, Mann-Whitney U and chi-square's results are shown. Statistical comparisons in bold are significant at p < .05.

Patients were matched individually to normal controls (NC) on age range (± 5 years), gender, handedness and level of education (< 12, 12 to 14 or > 14 academic years). Of these 42 NC, 37 were included in the present protocol (ATENA-F, N° 2013-A00515-40) and 5 were controls from a previous single-case study (Jonas *et al.*, 2018) who were tested with the exact same tasks as in the present study. We constituted two NC groups: the left NC group matched to left MTLE patients (17 controls, 9 females; mean age 35.88 ± 12.44) and the right NC group matched to right MTLE patients (25 controls, 12 females; mean age 37.12 ± 11.92). None of the control participants had a history of neurological or psychiatric disease, drug or alcohol abuse, nor did they have cognitive complaints. All participants gave a written consent before their inclusion and received financial compensation for their participation in the study.

2.2. Neuropsychological tests

2.2.1. General procedure

Participants were assessed with a set of seven behavioral experiments. The order of administration was the same for each participant: (1) the electronic version of the Benton Face Recognition Test-computerized (BFRT-c); (2) Old/New face recognition task; (3) Old/New recognition task with birds; (4) Face and car delayed matching task with upright and inverted orientations; (5) Mooney face detection test; (6) Famous face identification test (CELEB); and (7) Cambridge Face Memory Test (CFMT). Testing lasted for approximately two hours.

The behavioral tasks were created and tested using E-prime 1.1, except for the CFMT test, running in Java, and the CELEB task running with its own software (https://www.ipsp.ucl.ac.be/recherche/projets/Celeb/setup.exe). Participants were seated in front of a computer screen, at a distance about 50cm. In all tests but the BFRT-c and CELEB, participants had to respond by pressing a button on the keyboard. In the BFRT-c, participants had to respond by clicking with the mouse on on-screen images. In the CELEB, the experimenter was responsible for pressing a button on the keyboard when the participant correctly named the famous face and for writing down semantic information when the name was not automatically retrieved by the participant.

2.2.2. Face detection

Mooney Face Test. This test assesses the ability to categorize a visual stimulus as a "face" without being able to rely on local features (i.e., requiring to perceive the stimulus as a global configuration; Moore and Cavanagh, 1998; Rossion *et al.*, 2011). Stimuli and procedure were the same as those used in the experiment 16 of Busigny *et al.* (2010).

Stimuli. Eighty Mooney faces (two-tone, thresholded, black and white) were selected from the dataset created by Schurger and colleagues (http://www.princeton.edu/artofscience/gallery/view.php%3Fid=77.html) and based on Mooney's original stimuli (Mooney, 1957). When a Mooney face is presented upside-down, the face is usually not perceived.

Procedure. Mooney faces were individually presented upright and upside-down in the middle of the screen. They were randomly displayed in two blocks of 80 trials. The subject had to decide whether the image depicted a face or not. We considered a correct response when participants pressed the button "yes" for upright Mooney faces (80 trials), and "no" for upside-down Mooney faces (80 trials). Every response was followed by the apparition of a central cross (300 ms) and a grey screen (300 ms).

One control participant (matched with a left MTLE patient) was not tested with this task because of technical issues.

2.2.3. Face and non-face individuation

Benton Facial Recognition Test-computerized (BFRT-c). This test, developed by Benton and Van Allen (1968), is the oldest unfamiliar face matching test in neuropsychology, used in numerous clinical and experimental studies. It requires to match simultaneously presented pictures of unfamiliar faces, against distractor faces. It was performed in a computerized version (Rossion and Michel, 2018).

Stimuli. As in the original test, stimuli were greyscale male or female face photographs with neutral expressions and unfamiliar to the participants.

Procedure. A full-front target was always presented in the upper part of the screen with six probes organized in two rows below it. Participants were instructed to match as fast as possible the face at the top of the screen to the face(s) presented among distractors The experiment was composed of 22 trials split in two parts (6 trials in Part 1 and 16 in Part 2). In Part 1, targets and probes were all full-front stimuli taken under the same lighting conditions, and participants were instructed to match the target face with the same identical face presented among five distractors. In Part 2, targets were full-front while probes were pictures taken under different lighting conditions (8 items, lighting direction or LD items) and head orientations (8 items, head rotation or HR items) and participants were instructed to match the target face to 3 different exemplars of the same face among 3 distractors. Each trial was separated from the following one by a blank interval of 500 ms. Accuracy was scored on a total of 54, and the total time taken by participants to complete the test was measured in seconds (Rossion and Michel, 2018).

Cambridge Face Memory Test (CFMT). The CFMT was originally developed by Duchaine and Nakayama (2006) to evaluate face identity recognition difficulties of developmental origin and has become one of the most widely used test in the literature. It requires to explicitly encode pictures of six individual faces that have to be matched to pictures of the same individuals, against distractor faces. Stimuli and procedure used here were the same as those used in Duchaine and Nakayama (2006).

Stimuli. The stimuli were 52 faces of young men with cropped hair and neutral expressions taken under different viewpoints and lightings. Six individuals were designated as targets (with 12 images for each target face) while other 46 individuals were used as distractors.

Procedure. The CFMT starts with a brief practice (3 trials) followed by a learning step in which participants are asked to learn six unfamiliar target faces. Each target face is first presented under three different viewpoints and participants have to subsequently recognize it among two distractors (6 target faces x 3 trials each, i.e., 18 trials). In this first step, target faces in the forced-choice task are identical to the studied items. In a second step, participants are asked to perform the same task with novel images of the target faces in which viewpoints and lighting conditions are different from the learning step (30 trials). In the last step, participants have to perform the task while Gaussian noise is added on target and distractor faces to obscure facial features (24 trials). Total accuracy on the CFMT is scored on 72. Note that three right MTLE patients were not tested with this task because of time constraints.

Face and car delayed matching task with upright and inverted orientations. This task also requires matching individual face and non-face items against a distractor, across orientation changes, and with a brief delay between the presentation of the stimuli to match. Stimuli and procedure are identical to the experiment 4 in Busigny and Rossion (2010).

Stimuli. One full front and one 3/4 profile greyscale photographs of 36 individuals (18 females) and 36 cars were used. The target picture was always a full front picture, and the probe a left 3/4 profile picture.

Procedure. Each trial began with a white screen (1000 ms), followed by the target (2000 ms) and a blank interval (1000 ms). After this interval, two 3/4 profile probes were presented. Participants were instructed to find the probe that corresponded to the previously shown target. Each trial was presented both at upright and upside-down orientations. In total, the experiment consisted in 144 trials (36 per condition and orientation). As in Busigny and Rossion (2010), an index of inversion effect was computed to quantify the performance decrease related to inversion by combining both accuracy and correct response times. This was done by first calculating the inverse efficiency, i.e. the average response times of the correct trials divided by accuracy in each condition (face upright, face inverted, car upright and car inverted). The index of inversion effect for faces and cars was then calculated using the following formula: (Inverse efficiency Upright - Inverse efficiency Inverted) / (Inverse efficiency Upright + Inverse efficiency Inverted).

2.2.4. Old/New individual recognition tasks with face and non-face items.

These tasks evaluate the ability to encode a series of individual faces, or nonfaces in a separate test, and then to recognize these items against distractors in a subsequent recognition stage.

Old/New Faces. The procedure was identical to the experiment 3 in Busigny *et al.* (2010).

Stimuli. Stimuli were 60 color uncropped unfamiliar face pictures (30 females, 30 males). Thirty faces were selected as targets, while 30 other faces were used as distractors (matched with the target in gender, hairstyle and skin color).

Procedure. Participants were first presented with each of the 30 target faces for 4 seconds and were asked to explicitly learn them. Next, in a forced-choice recognition task, participants were presented with 30 pairs of faces (= 30 trials). For each pair, one face had been learnt during the first step while the other face was a similar-looking distractor. Participants were instructed to select the learnt face.

Old/New birds. The procedure was the same as for the Old/New Faces test except that faces were replaced by images of birds. Birds' images were presented in greyscale to avoid simple matching based on color differences (color varying substantially across birds in the original images). Distractor items were matched with the target in general appearance, all pairs depicting birds from the same bird family, thus making it difficult to rely on a verbal strategy to retrieve the target item.

2.2.5. Famous face recognition and naming

CELEB Test. This test assesses (French) famous face identification through naming, retrieval of semantic knowledge and multiple-choice face-to-name matching (Busigny *et al.*, 2014). An advantage of this test is that it provides two indexes evaluating famous face identification and naming independently. The same procedure was used as in Busigny *et al.* (2014).

Stimuli. Sixty photographs of famous faces without external facial cues were presented. They were mostly from the French speaking community (singers, actors, politicians, etc.). Stimuli were displayed on a black background in the middle of the screen.

Procedure. Each famous face was displayed for 30 seconds and the participant had to name the person (naming step). If naming was correct, the next face was presented; if not, the subject performed 2 additional steps on this face (description and designation steps). First, the subject had 30 additional seconds to give as much information as possible, i.e., occupation, age, nationality, etc. (description step). Second, after these 30 seconds, the participant was provided with a multiple-choice and asked to find the correct name among four distractors (designation step). A face was considered to be correctly identified if the participant correctly named the face (naming step) or if the face was well-described *and* correctly designated. At the end of the task, a final step was performed for all faces that were not correctly identified (knowledge step). Here, the experimenter provided the correct name and asked the participants if they know this person. If the person was not known, it was removed from the calculation of indexes.

Scores and indexes. Three scores were computed. The denomination score was the number of correctly named faces. The recognition score represented the total of recognized faces, i.e., the number of correctly named faces plus the number of faces correctly-described *and* correctly-designated. The knowledge score was the total of famous faces that were really known to participants. Based on these three scores, two indexes were computed. The Facial Recognition Index (FRI), representing the ability to recognize famous people from their face, corresponded to the recognition score divided by the knowledge score (multiplied by 100). The Name Access Index (NAI), representing the ability to retrieve a proper name based on a face, corresponded to the denomination score divided by the recognition score (multiplied by 100) (Busigny *et al.*, 2014). Response times were recorded for the naming step only (faces correctly named).

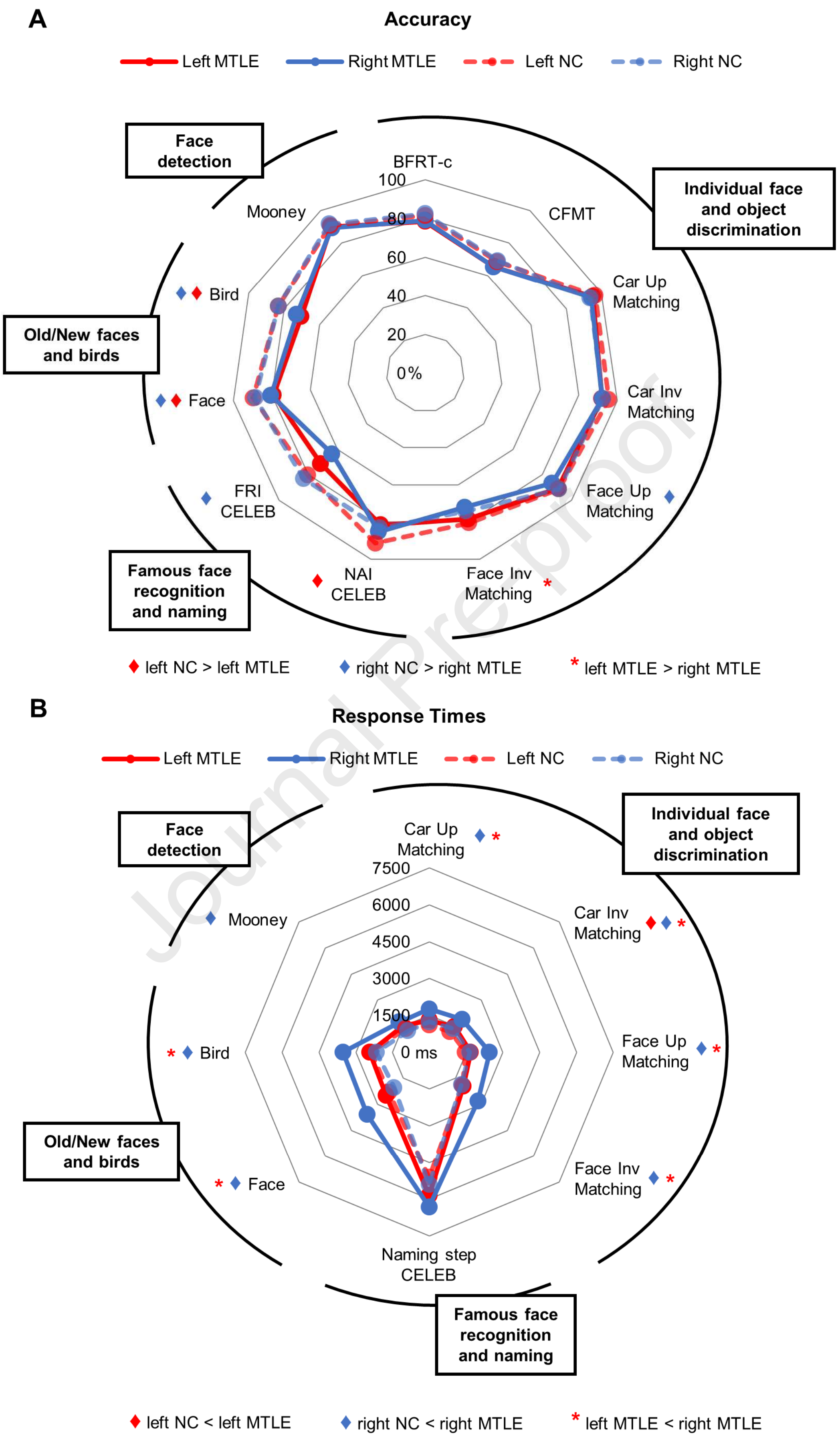
2.3. Statistical analysis

Statistical analyses were conducted using the SPSS software (IBM SPSS Statistics, Version 20.0; Armonk, NY: IBM Corp.). All tests were two-sided, and the alpha-level was set at $p < .05$. Analyses were carried out using chi-square tests for categorical variables and two independent samples t-tests or non-parametric Mann-Whitney U-tests for continuous variables, depending on whether the data were or were not normally distributed (as assessed by the Shapiro-Wilk test). An estimation of effect size is reported using Cramer's V for categorical variables and Cohen's d for continuous variables.

3. Results

3.1. Group level

The results are summarized in **Fig. 1**. All data and statistical results are available in **Table 2**. The following analysis focuses on the comparison of accuracy and correct RT between left and right MTLE patients and their respective normal controls (NC) (**Fig. 1, Table 2**). Direct comparisons between right and left MTLE patients are also reported (**Fig. 1, Table 2**).



A
Accuracy
Left MTLE
Right MTLE
Left NC
Right NC
Face detection
Individual face and object discrimination
Old/New faces and birds
Famous face recognition and naming
BFRT-c
CFMT
Car Up Matching
Car Inv Matching
Face Up Matching
Face Inv Matching
NAI CELEB
FRI CELEB
Face
Bird
Mooney
100
80
60
40
20
0%
left NC > left MTLE
right NC > right MTLE
left MTLE > right MTLE
B
Response Times
Left MTLE
Right MTLE
Left NC
Right NC
Face detection
Individual face and object discrimination
Old/New faces and birds
Famous face recognition and naming
Car Up Matching
Car Inv Matching
Face Up Matching
Face Inv Matching
Naming step CELEB
Face
Bird
Mooney
7500
6000
4500
3000
1500
0 ms
left NC < left MTLE
right NC < right MTLE
left MTLE < right MTLE

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Fig. 1. Accuracy and correct RT of patients and NC in the face and object recognition tasks. Significant differences between patient groups and their respective NC groups, and between left and right patient groups on independent t-tests or Mann-Whitney U tests ($p < 0.05$) are noted with diamonds and asterisks, respectively. **A.** Accuracy is reported in percentages. BFRT-c and CFMT total scores were converted in percentages for visual purposes. **B.** RT are reported in milliseconds. BFRT-c is not represented because response times were measured in seconds.

Cognitive tasks			Left MTLE (n=17)	Left NC (n=17)	Comparison MTLE / NC	Right MTLE (n=25)	Right NC (n=25)	Comparison MTLE / NC	Comparison left/right MTLE
Mooney Face Test		**Acc (%)**	90.08 ± 4.7	90.76 ± 5.8	U=116.5, p=.482 d_{Cohen}= 0.246	89.27 ± 7.1	91.64 ± 4.7	U=246.5, p=.200 d_{Cohen}= 0.368	U=212.5, p=1 d_{Cohen}= 0
		RT (ms)	1528 ± 749	1364 ± 913	U=99, p=.183 d_{Cohen}= 0.477	1728 ± 725	1232 ± 671	**U=176, p=.008** d_{Cohen}= 0.808	U=164.5, p=.219 d_{Cohen}= 0.387
BFRT		**Acc (/54)**	42.35 ± 2.4	44.06 ± 2.9	t=-1.821, p=.078 d_{Cohen}= 0.624	42.64 ± 4.8	44.56 ± 3.4	t=-1.631, p=.110 d_{Cohen}= 0.461	t=-0.255, p=.800 d_{Cohen}= 0.080
		RT (s)	275 ± 81	243 ± 80	t=1.176, p=.248 d_{Cohen}= 0.403	397 ± 255	246 ± 82	**U=176, p=.008** d_{Cohen}= 0.808	U=148.5, p=.101 d_{Cohen}= 0.523
Delayed Matching Task	**Cars**	**Acc Up (%)**	95.09 ± 8.0	96.55 ± 3.3	U=131.5, p=.637 d_{Cohen}= 0.154	94.34 ± 3.9	93.55 ± 7.9	U=278.5, p=.501 d_{Cohen}= 0.187	U=146.5, p=.082 d_{Cohen}= 0.541
		Acc Inv (%)	92.15 ± 9.4	95.58 ± 4.0	U=113.5, p=.276 d_{Cohen}= 0.373	92.32 ± 6.3	92.55 ± 10.2	U=256.5, p=.267 d_{Cohen}= 0.311	U=200.5, p=.755 d_{Cohen}= 0.095
		RT Up (ms)	1305 ± 528	1096 ± 227	U=118, p=.361 d_{Cohen}= 0.317	1756 ± 785	1238 ± 279	**U=151, p=.002** d_{Cohen}= 0.989	**U=97, p=.003** d_{Cohen}= 1.027
		RT Inv (ms)	1469 ± 563	1188 ± 258	**U=77, p=.020** d_{Cohen}= 0.870	1887 ± 799	1360 ± 298	**U=159, p=.003** d_{Cohen}= 0.929	**U=117, p=.014** d_{Cohen}= 0.816
		Index	8.39 ± 5.5	4.68 ± 3.8	**t=2.277, p=.030** d_{Cohen}= 0.781	5.49 ± 4.3	5.42 ± 4.7	t=0.057, p=.955 d_{Cohen}= 0.016	t=1.900, p=.065 d_{Cohen}= 0.597
	Faces	**Acc Up (%)**	90.51 ± 8.3	91.32 ± 5.3	U=139, p=.848 d_{Cohen}= 0.065	86.79 ± 7.5	91.32 ± 7.9	**U=193, p=.02** d_{Cohen}= 0.694	U=145.5, p=.084 d_{Cohen}= 0.549
		Acc Inv (%)	78.43 ± 10.7	80.55 ± 6.9	t=-0.687, p=.497 d_{Cohen}= 0.236	72.10 ± 9.0	74.22 ± 8.6	t=-0.843, p=.403 d_{Cohen}= 0.238	**t=2.064, p=.046** d_{Cohen}= 0.649
		RT Up (ms)	1682 ± 605	1475 ± 550	U=110, p=.235 d_{Cohen}= 0.416	2463 ± 2298	1649 ± 480	**U=178, p=.009** d_{Cohen}= 0.794	**U=124, p=.023** d_{Cohen}= 0.747
		RT Inv (ms)	1958 ± 715	1909 ± 713	U=133, p=.692 d_{Cohen}= 0.136	2814 ± 2324	1856 ± 394	**U=174, p=.007** d_{Cohen}= 0.144	**U=119, p=.017** d_{Cohen}= 0.796
		Index	14.34 ± 6.2	15.35 ± 10.7	t=-0.336, p=.740 d_{Cohen}= 0.115	16.44 ± 9.9	16.53 ± 10.1	t=-0.031, p=.975 d_{Cohen}= 0.009	t=-0.846, p=.403 d_{Cohen}= 0.266
CELEB		**FRI (%)**	71.27 ± 20.2	80.29 ± 19.1	U=102, p=.143 d_{Cohen}= 0.519	63.65 ± 24.3	83.15 ± 17.2	**U=150.5, p=.002** d_{Cohen}= 0.993	t=1.065, p=.293 d_{Cohen}= 0.335

		NAI (%)	81.65 ± 18.0	91.41 ± 5.7	**U=85.5, p=.042** d_{Cohen}= 0.744	85.20 ± 9.1	83.31 ± 13.4	U=311, p=.977 d_{Cohen}= 0.008	U=205, p=.847 d_{Cohen}= 0.059
		RT (ms)	5848 ± 2809	5117 ± 1148	U=136, p=.770 d_{Cohen}= 0.101	6321 ± 2447	5409 ± 1992	t=1.444, p=0.155 d_{Cohen}= 0.408	U=177, p=.363 d_{Cohen}= 0.284
CFMT	**Intro**	**Acc (/18)**	17.00 ± 1.8	17.76 ± 0.6	U=122.5, p=.308 d_{Cohen}= 0.262	16.90 ± 2.1	17.44 ± 1.1	U=232, p=.289 d_{Cohen}= 0.270	U=167, p=.516 d_{Cohen}= 0.366
	No Noise	**Acc (/30)**	18.24 ± 4.4	19.18 ± 4.4	t=-0.621, p=.539 d_{Cohen}= 0.213	17.95 ± 5.4	18.96 ± 5.0	t=-0.661, p=.512 d_{Cohen}= 0.193	t=0.173, p=.863 d_{Cohen}= 0.056
	Noise	**Acc (/24)**	11.94 ± 4.1	12.35 ± 4.0	t=-0.294, p=.771 d_{Cohen}= 0.101	12.20 ± 4.7	13.40 ± 4.2	t=-0.905, p=.370 d_{Cohen}= 0.264	t=-0.200, p=.843 d_{Cohen}= 0.064
	Total	**Acc (/72)**	47.18 ± 9.1	49.41 ± 8.0	t=-0.759, p=.453 d_{Cohen}= 0.260	47.10 ± 10.9	49.80 ± 8.8	t=-0.945, p=.350 d_{Cohen}= 0.276	t=0.026, p=.979 d_{Cohen}= 0.008
Old/New Tasks	**Faces**	**Acc (%)**	79.12 ± 11.5	89.66 ± 7.2	**t=-3.206, p=.003** d_{Cohen}= 1.099	80.40 ± 10.8	88.54 ± 8.3	**U=170.5, p=.005** d_{Cohen}= 0.846	U=197.5, p=.699 d_{Cohen}= 0.119
		RT (ms)	2484 ± 1184	2325 ± 900	U=142, p=.931 d_{Cohen}= 0.030	3583 ± 2114	2034 ± 549	**U=131, p<.001** d_{Cohen}= 1.149	**U=128, p=.030** d_{Cohen}= 0.709
	Birds	**Acc (%)**	70.39 ± 8.2	83.34 ± 6.5	**t=-5.099, p<.001** d_{Cohen}= 1.749	72.92 ± 8.4	83.37 ± 9.1	**t=-4.208, p<.001** d_{Cohen}= 1.190	t=-0.964, p=.341 d_{Cohen}= 0.303
		RT (ms)	2433 ± 710	2374 ± 1029	U=119, p=.380 d_{Cohen}= 0.305	3514 ± 1715	2152 ± 606	**U=108, p<.001** d_{Cohen}= 1.356	**U=108, p=.007** d_{Cohen}= 0.907

Table 2. Performance of patients and controls on face and non-face recognition tasks. Values are shown as mean ± standard deviation. Independent t-tests' or Mann-Whitney U's results, as well as effect sizes (Cohen's d), are shown for each comparison between left MTLE/left NC groups and right MTLE/right NC groups. Significant values at p < .05 (two-tailed) are shown in bold. Acc = accuracy, RT = response times, Up = upright, Inv = inverted.

3.1.1. Face detection

Left and right MTLE patients did not differ in accuracy rates from their respective NC groups at the Mooney face detection test. Whereas left MTLE patients were not different from their NC in RT, right MTLE patients showed significantly longer RT.

3.1.2. Unfamiliar face and non-face individuation

Left and right MTLE patients did not differ in accuracy at the BFRT-c and CFMT from their respective NC groups. At the delayed matching task with pictures of cars, both patient groups showed normal accuracy performance compared to their NC groups. For faces, left MTLE patients performed in the normal range in accuracy. Right MTLE patients had a slightly (i.e., 4%) but significantly lower accuracy at matching upright faces only. However, there was no interaction with stimulus inversion, both patient groups showing normal face inversion indexes.

Right MTLE patients were significantly slower than their NC group on all measures (BFRT-c; delayed matching task with faces and cars, both orientations). In contrast, left MTLE patients were only slower on the delayed matching task with inverted cars. Interestingly, in both patient groups, RT on the BFRT-c correlated with the Coding test of the WAIS assessing visuospatial processing speed ($r = -0.56$, $p = .02$, and $r = -0.51$, $p = .01$, for left and right MTLE groups respectively) (**Tables 3 and 4**).

Correlations in left MTLE patients		**Age at inclusion**	**Age at epilepsy onset**	**Epilepsy duration**	**Number of AED**	**Total IQ**	**Processing speed (percentile Coding test)**
BFRT-c	**Acc**	r = 0.169, p = .517 $CI_{95\%}$ = -0.339 / 0.601	r = -0.023, p = .930 $CI_{95\%}$ = -0.498 / 0.463	r = 0.195, p = .453 $CI_{95\%}$ = -0.315 / 0.618	r = 0.315, p = .218 $CI_{95\%}$ = -0.195 / 0.691	r = -0.261, p = .312 $CI_{95\%}$ = -0.682 / 0.290	r = 0.003, p = .991 $CI_{95\%}$ = -0.510 / 0.514

		RT	r = 0.051, p = .846 $CI_{95\%}$ = -0.440 / 0.519	r = 0.273, p = .289 $CI_{95\%}$ = -0.239 / 0.666	r = -0.305, p = .234 $CI_{95\%}$ = -0.685 / 0.206	r = -0.046, p = .861 $CI_{95\%}$ = -0.515 / 0.444	**r = -0.497, p = .042 $CI_{95\%}$ = -0.804 / 0.020**	**r = -0.557, p = .020 $CI_{95\%}$ = -0.832 / -0.062**
Delayed Matching Task	Cars	Acc Up	**r = -0.544, p = .024 $CI_{95\%}$ = -0.812 / -0.086**	**r = -0.751, p = .0005 $CI_{95\%}$ = -0.905 / -0.423**	r = 0.446, p = .073 $CI_{95\%}$ = -0.044 / 0.763	r = 0.331, p = .194 $CI_{95\%}$ = -0.178 / -0.009	r = 0.341, p = .180 $CI_{95\%}$ = -0.207 / 0.726	r = 0.202, p = .437 $CI_{95\%}$ = -0.346 / 0.647
		Acc Inv	**r = -0.488, p = .047 $CI_{95\%}$ = -0.785 / -0.009**	**r = -0.577, p = .015 $CI_{95\%}$ = -0.828 / -0.133**	r = 0.274, p = .287 $CI_{95\%}$ = -0.238 / 0.667	r = 0.220, p = .396 $CI_{95\%}$ = -0.291 / 0.634	r = 0.358 p = .158 $CI_{95\%}$ = -0.189 / 0.735	r = 0.257, p = .319 $CI_{95\%}$ = -0.294 / 0.680
		RT Up	**r = 0.531, p = .028 $CI_{95\%}$ = 0.068 / 0.806**	r = 0.455, p = .066 $CI_{95\%}$ = -0.033 / 0.768	r = -0.074, p = .778 $CI_{95\%}$ = -0.536 / 0.422	r = -0.368, p = .146 $CI_{95\%}$ = -0.721 / 0.137	r = -0.037, p = .888 $CI_{95\%}$ =-0.539 / 0.484	r = -0.306, p = .232 $CI_{95\%}$ = -0.707 / 0.245
		RT Inv	r = 0.431, p = .084 $CI_{95\%}$ = -0.063 / 0.755	r = 0.287, p = .264 $CI_{95\%}$ = -0.225 / 0.674	r = 0.048, p = .855 $CI_{95\%}$ = -0.443 / 0.517	r = 0.351, p = .167 $CI_{95\%}$ = -0.156 / 0.711	r = -0.030, p = .909 $CI_{95\%}$ = -0.534 / 0.490	r = -0.315, p = .218 $CI_{95\%}$ = -0.712 / 0.235
		Index	**r = -0.560, p = .019 $CI_{95\%}$ = -0.820 / -0.108**	**r = -0.612, p = .009 $CI_{95\%}$ = -0.844 / -0.186**	r = 0.250, p = .333 $CI_{95\%}$ = -0.262 / 0.652	r = 0.058, p = .825 $CI_{95\%}$ = -0.435 / 0.524	r = -0.142, p = .587 $CI_{95\%}$ = -0.610 / 0.399	r = -0.165, p = .527 $CI_{95\%}$ = -0.624 / 0.379
	Faces	Acc Up	r = -0.127, p = .627 $CI_{95\%}$ = -0.573 / 0.377	r = -0.125, p = .633 $CI_{95\%}$ = -0.571 / 0.378	r = 0.039, p = .882 $CI_{95\%}$ = -0.450 / 0.510	r = -0.104, p = .691 $CI_{95\%}$ = -0.557 / 0.396	**r = 0.492, p = .045 $CI_{95\%}$ = -0.027 / 0.802**	**r = 0.598, p = .011 $CI_{95\%}$ = 0.123 / 0.850**
		Acc Inv	r = -0.120, p = .646 $CI_{95\%}$ = -0.568 / 0.383	r = -0.159, p = .542 $CI_{95\%}$ = -0.594 / 0.348	r = 0.090, p = .731 $CI_{95\%}$ = -0.408 / 0.547	r = 0.004, p = .988 $CI_{95\%}$ = -0.477 / 0.484	**r = 0.545, p = .024 $CI_{95\%}$ = 0.045 / 0.826**	**r = 0.650, p = .005 $CI_{95\%}$ = 0.206 / 0.872**
		RT Up	r = 0.199, p = .444 $CI_{95\%}$ = -0.311 / 0.620	r = 0.295, p = .250 $CI_{95\%}$ = -0.216 / 0.679	r = -0.189, p = .467 $CI_{95\%}$ = -0.614 / 0.321	r = -0.232, p = .370 $CI_{95\%}$ = -0.641 / 0.280	r = -0.291, p = .257 $CI_{95\%}$ = -0.699 / 0.260	**r = -0.545, p = .024 $CI_{95\%}$ = -0.826 / -0.045**
		RT Inv	r = 0.119, p = .649 $CI_{95\%}$ = -0.383 / 0.567	r = 0.263, p = .308 $CI_{95\%}$ = -0.249 / 0.660	r = -0.225, p = .385 $CI_{95\%}$ = -0.637 / 0.287	r = -0.273, p = .289 $CI_{95\%}$ = -0.666 / 0.239	r = -0.186, p = .475 $CI_{95\%}$ = -0.637 / 0.361	r = -0.331, p = .194 $CI_{95\%}$ = -0.721 / 0.218

		Index	r = -0.100, p = .702 $CI_{95\%}$ = -0.554 / 0.400	r = -0.069, p = .792 $CI_{95\%}$ = -0.532 / 0.426	r = -0.008, p = .975 $CI_{95\%}$ = -0.487 / 0.474	r = -0.260, p = .313 $CI_{95\%}$ = -0.658 / 0.252	r = -0.133, p = .611 $CI_{95\%}$ = -0.604 / 0.407	r = 0.088, p = .737 $CI_{95\%}$ = -0.444 / 0.574
CFMT Total		Acc	r = -0.172, p = .509 $CI_{95\%}$ = -0.603 / 0.336	r = -0.329, p = .197 $CI_{95\%}$ = -0.699 / 0.180	r = 0.260 p = .313 $CI_{95\%}$ = -0.252 / 0.658	r = -0.131, p = .616 $CI_{95\%}$ = -0.575 / 0.373	r = 0.206, p = .428 $CI_{95\%}$ = -0.342 / 0.650	r = 0.370, p = .144 $CI_{95\%}$ = -0.175 / 0.742

Table 3. Correlations in left MTLE patients. Correlations of clinical and demographic variables with the accuracy scores and response times of the face and non-face individuation tasks in left MTLE patients. Pearson r and associated p-values are displayed, as well as 95% confidence intervals. Values in bold are significant at p < .05 (not corrected for multiple comparisons). Acc = Accuracy, RT = response times, $CI_{95\%}$ = 95% Confidence intervals.

Correlations in right MTLE patients			Age at inclusion	Age at epilepsy onset	Epilepsy duration	Number of AED	Total IQ	Processing speed (percentile Coding test)
BFRT-c		Acc	r = -0.274, p = .185 $CI_{95\%}$ = -0.604 / 0.136	r = 0.285, p = .167 $CI_{95\%}$ = -0.124 / 0.611	**r = -0.425, p = .034 $CI_{95\%}$ = -0.702 / -0.036**	r = 0.034, p = .872 $CI_{95\%}$ = -0.366 / 0.423	**r = 0.454, p = .023 $CI_{95\%}$ = 0.072 / 0.720**	r = 0.163, p = .436 $CI_{95\%}$ = -0.248 / 0.524
		RT	**r = 0.476, p = .016 $CI_{95\%}$ = 0.099 / 0.733**	r = 0.070, p = .739 $CI_{95\%}$ = -0.334 / 0.453	r = 0.340, p = .096 $CI_{95\%}$ = -0.064 / 0.648	r = 0.294, p = .154 $CI_{95\%}$ = -0.114 / 0.617	**r = -0.478, p = .016 $CI_{95\%}$ = -0.734 / -0.102**	**r = -0.512, p = .009 $CI_{95\%}$ = -0.754 / -0.146**
Delayed Matching Task	Cars	Acc Up	**r = -0.563, p = .003 $CI_{95\%}$ = -0.784 / -0.216**	r = 0.159, p = .448 $CI_{95\%}$ = -0.252 / 0.521	**r = -0.569, p = .003 $CI_{95\%}$ = -0.787 / -0.224**	r = 0.140, p = .504 $CI_{95\%}$ = -0.270 / 0.507	r = 0.197, p = .345 $CI_{95\%}$ = -0.215 / 0.549	r = -0.077, p = .714 $CI_{95\%}$ = -0.458 / 0.328
		Acc Inv	**r = -0.537, p = .006 $CI_{95\%}$ = -0.769 / -0.180**	r = 0.277, p = .180 $CI_{95\%}$ = -0.133 / 0.606	**r = -0.636, p = .0006 $CI_{95\%}$ = -0.824 / -0.322**	r = -0.345, p = .091 $CI_{95\%}$ = -0.651 / 0.058	**r = 0.400, p = .047 $CI_{95\%}$ = 0.006 / 0.687**	r = 0.309, p = .133 $CI_{95\%}$ = -0.098 / 0.627
		RT Up	**r = 0.650, p = .0004 $CI_{95\%}$ = 0.343 / 0.831**	r = -0.017, p = .936 $CI_{95\%}$ = -0.409 / 0.381	**r = 0.543, p = .005 $CI_{95\%}$ = 0.188 / 0.772**	r = 0.339, p = .097 $CI_{95\%}$ = -0.065 / 0.647	r = -0.256, p = .217 $CI_{95\%}$ = -0.763 / -0.165	r = -0.382, p = .059 $CI_{95\%}$ = -0.675 / 0.015
		RT Inv	**r = 0.669, p = .0002 $CI_{95\%}$ = 0.372 / 0.842**	r = 0.005, p = .981 $CI_{95\%}$ = -0.391 / 0.399	**r = 0.544, p = .005 $CI_{95\%}$ = 0.190 / 0.773**	r = 0.313, p = .128 $CI_{95\%}$ = -0.094 / 0.630	r = -0.232, p = .256 $CI_{95\%}$ = -0.574 / 0.180	r = -0.385, p = .057 $CI_{95\%}$ = -0.677 / 0.012

		Index	r = 0.042, p = .842 $CI_{95\%}$ = -0.359 / 0.430	r = -0.152, p = .468 $CI_{95\%}$ = -0.516 / 0.259	r = 0.150, p = .474 $CI_{95\%}$ = -0.260 / 0.515	r = 0.066, p = .754 $CI_{95\%}$ = -0.338 / 0.449	r = -0.141, p = .501 $CI_{95\%}$ = -0.508 / 0.269	r = -0.153, p = .465 $CI_{95\%}$ = -0.517 / 0.258
	Faces	**Acc Up**	r = -0.328, p = .109 $CI_{95\%}$ = -0.640 / 0.077	r = 0.225, p = .279 $CI_{95\%}$ = -0.187 / 0.569	**r = -0.429, p = .032 $CI_{95\%}$ = -0.705 / -0.041**	r = -0.185, p = .376 $CI_{95\%}$ = -0.541 / 0.227	**r = 0.668, p = .0003 $CI_{95\%}$ = 0.371 / 0.841**	**r = 0.413, p = .040 $CI_{95\%}$ = 0.021 / 0.695**
		Acc Inv	r = -0.260, p = .209 $CI_{95\%}$ = -0.594 / 0.151	r = 0.173, p = .408 $CI_{95\%}$ = -0.238 / 0.532	r = -0.333, p = .104 $CI_{95\%}$ = -0.643 / 0.071	r = -0.241, p = .546 $CI_{95\%}$ = -0.581 / 0.170	r = -0.016, p = .939 $CI_{95\%}$ = -0.408 / 0.381	r = 0.036, p = .864 $CI_{95\%}$ = -0.364 / 0.425
		RT Up	r = 0.382, p = .059 $CI_{95\%}$ = -0.015 / 0.675	r = 0.042, p = .842 $CI_{95\%}$ = -0.359 / 0.430	r = 0.281, p = .174 $CI_{95\%}$ = -0.128 / 0.608	r = 0.083, p = .693 $CI_{95\%}$ = -0.323 / 0.463	r = -0.238, p = .252 $CI_{95\%}$ = -0.579 / 0.173	r = -0.319, p = .120 $CI_{95\%}$ = -0.634 / 0.087
		RT Inv	**r = 0.432, p = .031 $CI_{95\%}$ = 0.044 / 0.706**	r = 0.051, p = .809 $CI_{95\%}$ = -0.351 / 0.437	r = 0.315, p = .125 $CI_{95\%}$ = -0.091 / 0.631	r = 0.185, p = .376 $CI_{95\%}$ = -0.227 / 0.541	r = -0.226, p = .277 $CI_{95\%}$ = -0.570 / 0.186	r = -0.326, p = .112 $CI_{95\%}$ = -0.639 / 0.079
		Index	r = -0.003, p = .989 $CI_{95\%}$ = -0.398 / 0.393	r = 0.065, p = .757 $CI_{95\%}$ = -0.339 / 0.449	r = 0.049, p = .816 $CI_{95\%}$ = -0.353 / 0.436	r = 0.244, p = .240 $CI_{95\%}$ = -0.167 / 0.583	**r = 0.408, p = .043 $CI_{95\%}$ = 0.015 / 0.692**	r = 0.234, p = .260 $CI_{95\%}$ = -0.177 / 0.576
CFMT Total		**Acc**	r = -0.181, p = .386 $CI_{95\%}$ = -0.560 / 0.260	r = -0.016, p = .939 $CI_{95\%}$ = -0.435 / 0.408	r = -0.141, p = .501 $CI_{95\%}$ = -0.531 / 0.298	r = -0.194, p = .353 $CI_{95\%}$ = -0.569 / 0.248	**r = 0.413, p = .040 $CI_{95\%}$ = -0.010 / 0.711**	r = 0.307, p = .135 $CI_{95\%}$ = -0.132 / 0.645

Table 4. Correlations in right MTLE patients. Correlations of clinical and demographic variables with the accuracy scores and response times of the face and non-face individuation tasks in right MTLE patients. Pearson r and associated p-values are displayed, as well as 95% confidence intervals. Values in bold are significant at $p < .05$ (not corrected for multiple comparisons). Acc = Accuracy, RT = response times, $CI_{95\%}$ = 95% Confidence intervals.

3.1.3. Old/new recognition tasks

Both patient groups had lower accuracy than their NC on the old/new tasks both with face and bird stimuli. Right MTLE patients were also significantly slower than their NC on these two tasks while left MTLE were unimpaired (**Table 2**).

3.1.4. Famous face recognition and naming

Right MTLE patients showed lower performance than their NC in identifying famous people from their face (FRI, CELEB test) but had no difficulty in naming those that they could identify (NAI, CELEB test). In contrast, left MTLE patients did not differ in identifying famous people from their face but showed lower performance than their NC in naming famous faces. Right and left MTLE did not differ from their respective NC groups in RT on naming (correctly named famous faces).

3.2. Interim summary

The latter finding that left MTLE patients had difficulties at naming famous faces, while right MTLE patients were impaired at identifying famous persons from their faces, is consistent with previous studies (Drane *et al.*, 2008, 2013). Moreover, both right and left MTLE patients were impaired at explicitly learning face and bird images, in line with visual episodic memory deficits in MTLE (Chiaravalloti and Glosser, 2004; Helmstaedter, 2013). However, a novel aspect of the present study is that right and left MTLE patients had no difficulties at individuating pictures of unfamiliar faces (BRFT-c, CFMT, face matching), at least when accuracy only is considered. Right MTLE performed more slowly than NC in all tasks (except at naming famous faces in the CELEB test, after identification). This slowing down was not specific to faces since it was always found for both faces and non-face items, without any evidence of a more severe effect for faces. Moreover, right MTLE patients were also significantly slower than the left MTLE patients at the general Coding test.

3.3. Interindividual variability in unfamiliar face and non-face individuation tasks

Although no clear difference was found between patients and controls in unfamiliar face individuation tasks at the group level, there was an increase of interindividual variability for patients as compared to their NC for some of these tasks (BFRT-c, face and car delayed matching task and CFMT), as shown by Levene’s tests. Left and right MTLE patients had more variable accuracy on the delayed matching task with upright cars than their respective

NC (F = 4.175, p = .049, and F = 4.879, p = .032, respectively). Right MTLE patients also had more variable response times on the BFRT-c (F = 8.793, p = .005), delayed matching with inverted and upright cars (F = 7.659, p = .008, and F = 7.056, p = .011, respectively) and with inverted faces (F = 5.551, p = .023).

To further understand the nature of this interindividual variability in unfamiliar face and non-face individuation tasks (BFRT-c, CFMT, face and car delayed matching task), we correlated the patients' performance (accuracy and RT) on these tasks with their demographic and clinical characteristics (all correlations are found in **Tables 3 and 4** for left and right MTLE patients respectively). Note that in the following analysis, we did not correct our statistical threshold for multiple comparisons (6 × 13 = 78 comparisons for each patient group) because this led to a highly conservative threshold (FDR-corrected). This analysis should be interpreted with caution because of the weak statistical power due to the small sample of subjects, especially in the left MTLE group. However, we report confidence intervals for each correlation in Tables 3 and 4. In right MTLE patients, duration of epilepsy was significantly and negatively correlated with accuracy at the BFRT-c and delayed matching with upright faces and cars, and inverted cars (**Tables 3 and 4**). In left MTLE patients, no correlation was found between epilepsy duration and any of these individuation tasks. Total IQ was positively correlated with several scores in both left (delayed matching with faces) and right (BFRT-c, delayed matching with upright faces and inverted cars, face inversion index, CFMT) MTLE patients, indicating that patients with a lower IQ also had lower performance on these tasks.

There were also significant negative correlations of RT in the BFRT-c with total IQ and the Coding test in both left and right MTLE patients. A significant positive correlation was also found between age at inclusion and BFRT-c RT in right MTLE patients only (**Table**

4), indicating that older patients had longer RT. RT in the delayed matching task with faces and cars were not correlated with IQ or processing speed, except for the RT at matching upright faces which was correlated with processing speed in left MTLE patients only.

3.4. Do MTLE patients differ qualitatively from normal controls?

Although no clear difference was found between patients and controls in unfamiliar face individuation tasks at the group level (i.e., at a quantitative level), we explored the possibility that they differ qualitatively (i.e., accuracy or RT pattern across items). We therefore performed an item-by-item analysis on the second part of the BFRT-c (matching the target with its 3 corresponding probes). We focused on the BRFT-c for two main reasons: (1) normative data from 307 participants are available with this test, including mean accuracy and RT for each item (Rossion and Michel, 2018); (2) the BFRT-c is characterized by a large variability in difficulty across items (Rossion and Michel, 2018).

In the normative study of the test (Rossion and Michel, 2018), mean accuracy scores and RT across 307 typical participants were computed for each of the 16 items of the second part of the BFRT-c, ranking the items from the easiest to the most difficult. Here, we followed the same procedure as in Rossion and Michel (2018) and considered at the mean accuracy score and mean RT for each item of this second part (n = 16) in both patient and NC groups. Consistent with the results observed in Rossion and Michel (2018) (these results are shown in **Fig. 2A and 3A**), items with changes in head rotation (HR items) showed higher accuracy scores and lower RT than items with changes in lighting direction (LD items) in both left and right MTLE patients and in their NC (**Fig. 2B, 2C** for accuracy; **Fig. 3B and 3C** for RT). To statistically assess that the difference between LD and HR items was the same across patients and their matched NC, we calculated two indexes reflecting the difference in accuracy or response times between these two types of items for each participant. We subtracted the mean accuracy score of LD items from the mean accuracy score of HR items and divided it by the mean accuracy of all items. We followed the same principle with RT, but subtracted the mean RT of HR items from the mean RT of LD items, to obtain a positive index. We then compared the accuracy and RT difference indexes of the patients and their NC. No difference was found between the right MTLE patients and their NC (accuracy: $t = -0.780$, $p = .439$; RT: $t = 1.298$, $p = .202$), or between the left MTLE patients and their NC (accuracy: $t = -0.454$, $p = .653$; RT: $t = -0.554$, $p = .584$). The same comparison performed between MTLE patients and the 307 participants of the normative data did not reveal any difference between groups (accuracy indexes: $t = -0.390$, $p = .697$ and $t = 1.350$, $p = .189$ for the comparison of the normative data with left and right MTLE patients, respectively; RT indexes: $t = 1.445$, $p = .149$ and $t = -0.414$, $p = .682$ for left and right MTLE patients, respectively).

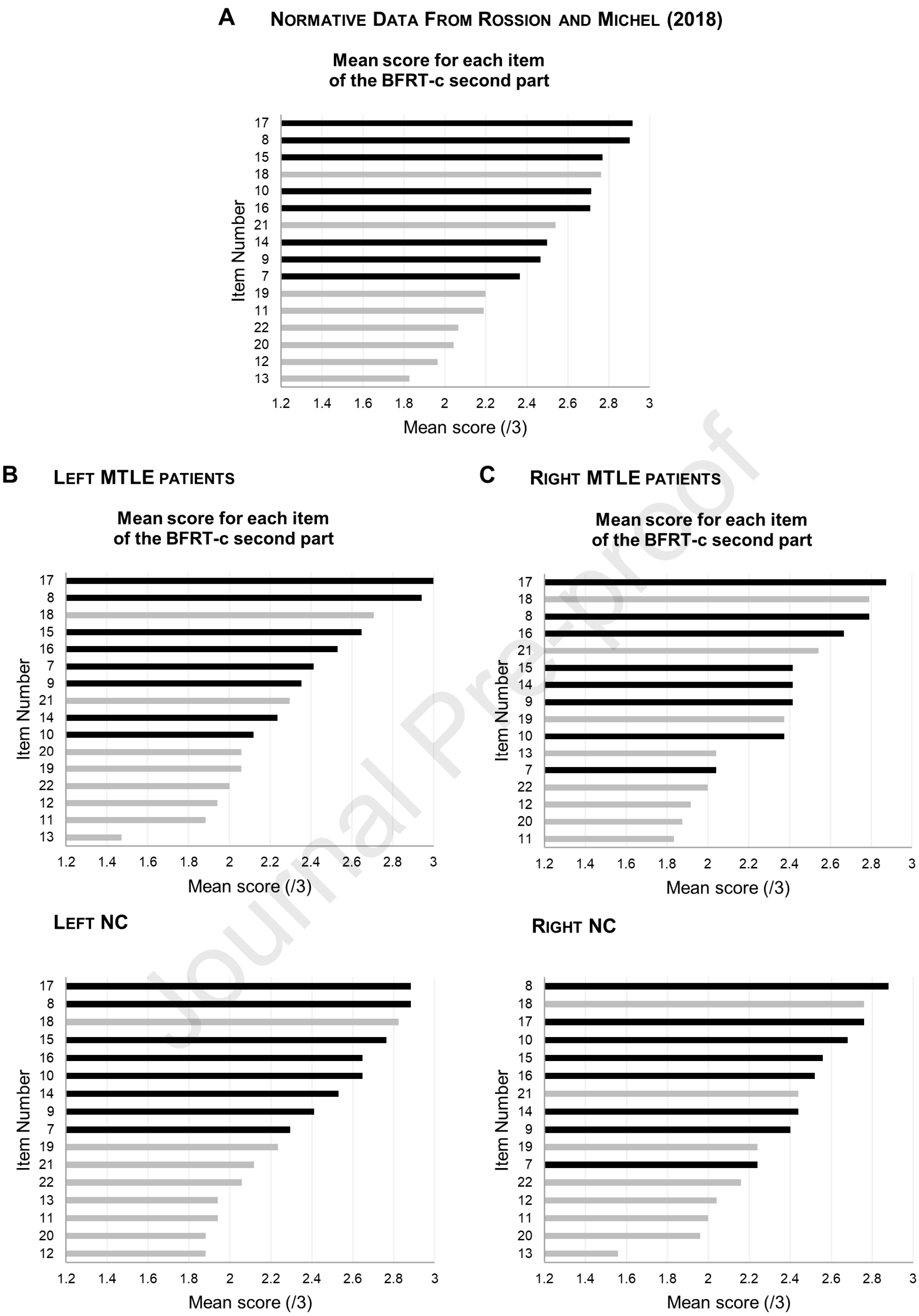

Fig. 2. Mean accuracy scores per item of the second part of the BFRT-c. Items are ordered from the highest to the lowest score. Light gray represents LD items, dark gray represents HR items. **A.** Normative data on 307 young adult participants from Rossion & Michel (2018). **B.** Mean accuracy scores per item in the left MTLE patients and their matched NC. **C.** Mean accuracy scores per item in the right MTLE patients and in their matched NC.

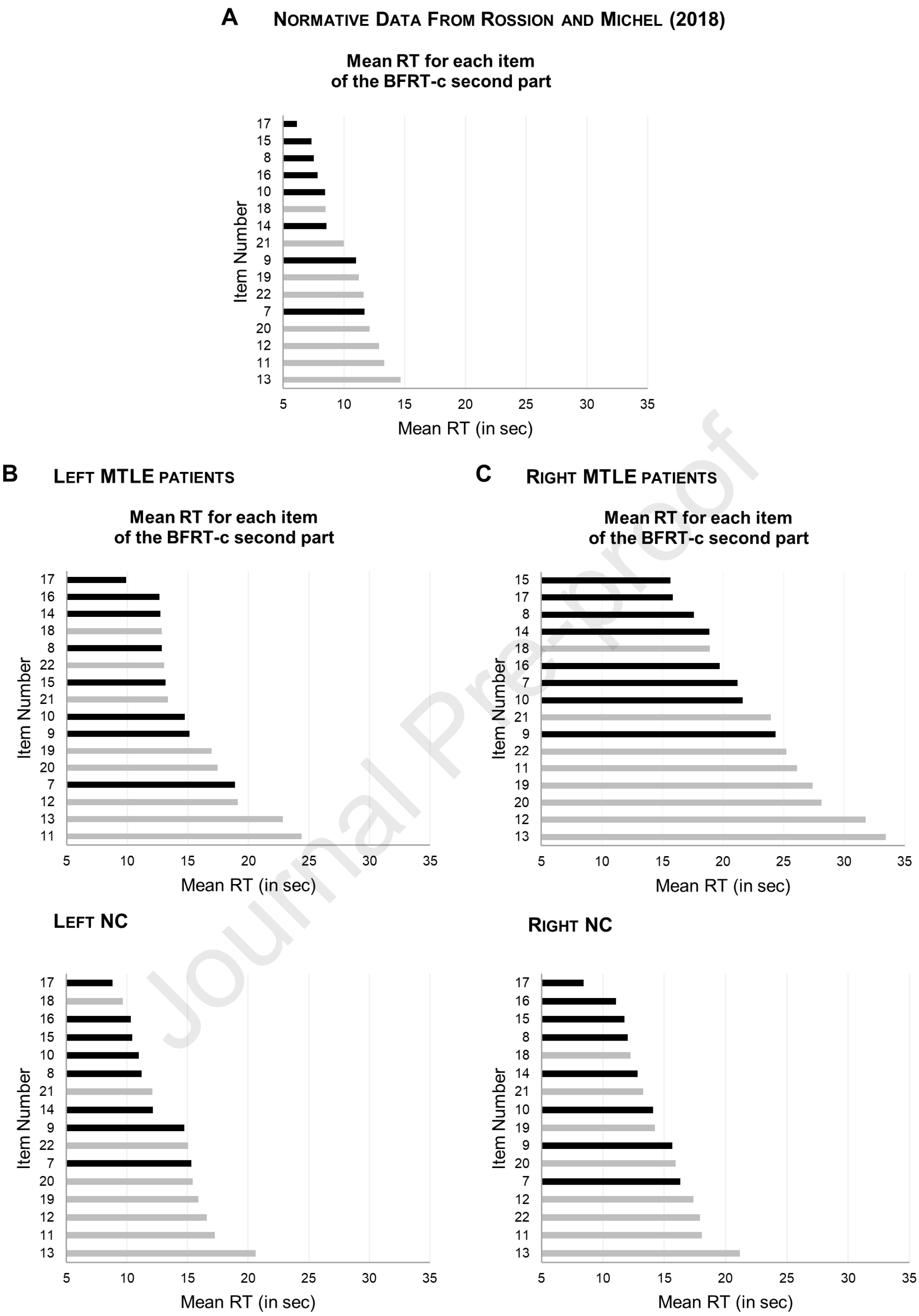

Fig. 3. Mean response times per item of the second part of the BFRT-c. Items are shown from the fastest to the slowest RT. Light gray represents LD items, dark gray represents HR items. **A.** Normative data on 307 young adult participants from Rossion & Michel (2018). **B.** Mean RT per item in the left MTLE patients and their matched NC. **C.** Mean RT per item in the right MTLE patients and in their matched NC.

Moreover, mean accuracy scores correlated negatively with mean RT in both left and right MTLE patients ($r = -0.760$, $p < .001$, and $r = -0.793$, $p < .001$, respectively), as well as in left and right NC ($r = -0.864$, $p < .001$, and $r = -0.880$, $p < .001$, respectively), indicating that items with the highest accuracy scores were also the ones with the shortest response times (see **Fig. 2 and 3**), as found in normative data (Rossion and Michel, 2018).

Finally, we calculated the inverse efficiency of each item for both patients and NC groups to take into consideration speed-accuracy trade-offs. This was done by dividing the RT by mean accuracy for each item in each group (Townsend and Ashby, 1978, 1983; see also Bruyer and Brysbaert, 2011). There was a strong positive correlation across items between patients and NC, for both left and right MTLE patients ($r = 0.91$, $p < .001$ and $r = 0.90$, $p < .001$, respectively), indicating that items that were better succeeded (high accuracy and low RT) in NC were also those that were better succeeded in MTLE patients (**Fig. 4A and B**). Results of both MTLE patient groups were also similar to the results of a larger sample of 307 younger participants from a recent normative study (Rossion and Michel, 2018) as shown by strong positive correlations between inverse efficiency scores of left MTLE and normative data ($r = 0.90$, $p < .001$), and right MTLE and normative data ($r = 0.97$, $p < .001$) (**Fig. 4C**). Altogether, these results show that MTLE patients do not differ qualitatively from normal controls at unfamiliar face individuation.

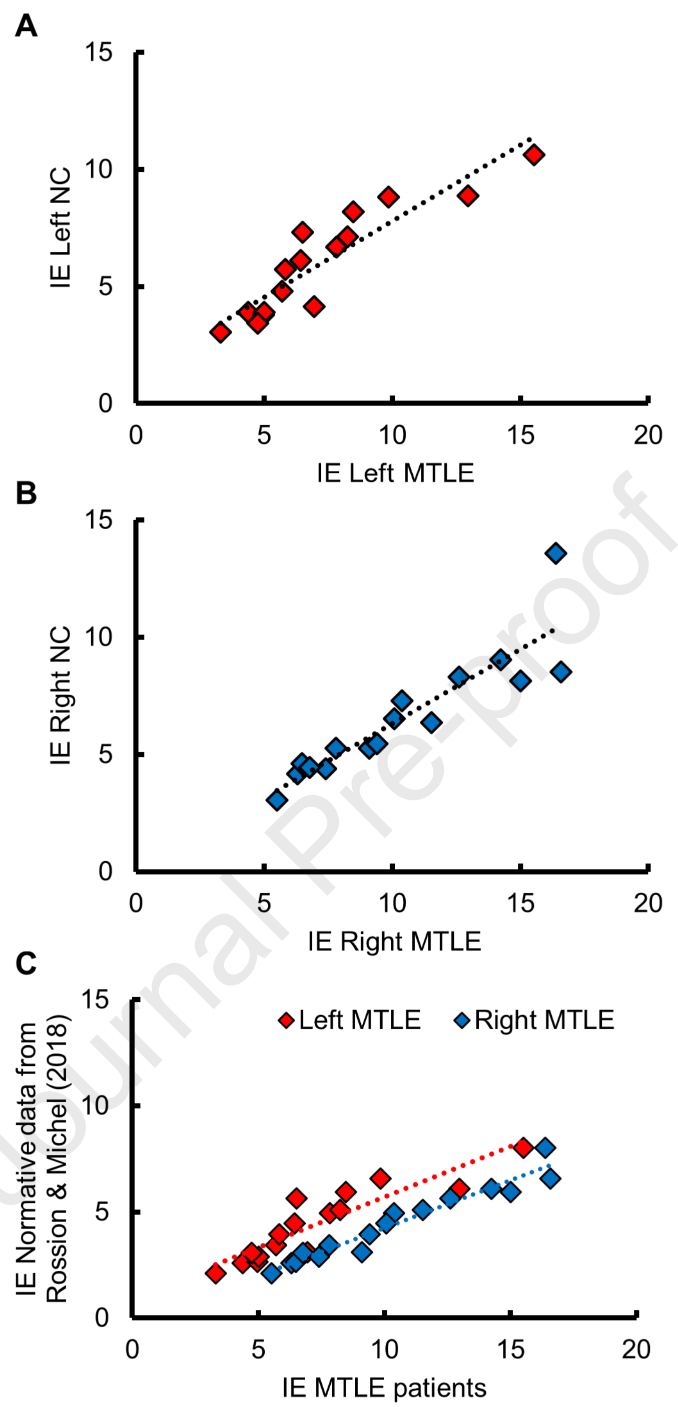

Figure 4. Correlations of inverse efficiency scores for each item of the second part of the BFRT-c. Each data point represents one of the 16 items of the second part of the BFRT-c. **A.** Correlation between inverse efficiency scores of left MTLE and their respective NC. **B.** Correlation between inverse efficiency scores of right MTLE and their respective NC. **C.** Correlation between inverse efficiency scores of left and right MTLE and inverse efficiency scores of 307 neurotypical participants from the normative data in Rossion and Michel (2018). IE = Inverse Efficiency.

4. Discussion

The present study is the first to systematically assess a range of face and non-face recognition abilities in patients presenting with left or right MTLE. Our main findings are that: (1) MTLE patients present with famous face identification and learning difficulties, in line with previous evidence (Chiaravalloti and Glosser, 2004; Drane *et al.*, 2008, 2013); (2) despite this, left and right MTLE patient groups do not differ on accuracy scores at unfamiliar face individuation tasks compared to their respective NC groups; (3) MTLE patients do not differ qualitatively from NC at unfamiliar face individuation; and (4) right MTLE patients show a general increase of RT in all tasks, suggesting a slowdown at explicit behavioral tasks for visual material, unspecific to unfamiliar face individuation.

4.1. Unfamiliar face individuation is preserved in MTLE patients

The most important and original finding of our study is that at the group level both left and right MTLE patients do not differ in accuracy compared to their NC on unfamiliar face and non-face individuation tasks (BFRT, CFMT and delayed face and car matching task). Importantly, there was no difference in accuracy between patient and NC groups on the two most widely used neuropsychological tests to investigate face recognition in the scientific literature, i.e. the BFRT and CFMT (Benton *et al.*, 1983; Duchaine and Nakayama, 2006). Only a significant 4% decrease in accuracy at matching upright faces was found in right MTLE patients at the delayed matching task. However : (1) this decrease, even if it is significant, remains very small (91.32% of correct responses in right NC compared to 86.79% in right MTLE patients), (2) it may be due to the nature of a task that, contrary to the BFRT, requires to hold individual face representations in memory for 1000ms, and (3) total IQ might play a role in this small decrease, knowing that we found a strong positive correlation between IQ and accuracy at matching upright faces in right MTLE patients, and that these patients had a mean IQ 10 points lower than left MTLE patients (even though the difference was not significant).

Although patient and NC groups did not differ on accuracy scores at the group level, some of the scores were correlated across individuals with clinical and neuropsychological characteristics (**Tables 3 and 4**). In right MTLE patients, both the upright face matching and the BFRT accuracy scores were negatively correlated with epilepsy duration, suggesting that a slightly lower performance at these two-face individuation tasks in some individuals could be associated with a longer epilepsy duration. More generally, total IQ was positively correlated with several scores in both left (delayed matching with upright and inverted faces) and right (BFRT-c, delayed matching with upright faces and inverted cars, face inversion index, CFMT) MTLE patients, suggesting that their performance may be related to difficulties to understand the instructions of explicit behavioral tasks.

4.2. MTLE patients do not differ qualitatively from normal controls

In the delayed face and car matching task, MTLE patients showed a classical face inversion effect (i.e., lower accuracy and higher RT for inverted faces compared to upright faces) with the same magnitude as their NC (similar index of face inversion effect between MTLE patients and their NC). Face inversion is known to dramatically affect behavioral individuation of faces in neurotypical human adults (Yin, 1969; Freire *et al.*, 2000; see Rossion, 2008 for review) and this effect is abolished in brain-damaged prosopagnosic patients (as reviewed in Busigny and Rossion, 2010). A preserved face inversion effect in left and right MTLE patients therefore provides strong evidence that this clinical population is not qualitatively impaired on unfamiliar face individuation. Moreover, the magnitude of the face inversion effect was higher than for non-face stimuli, as also is observed in neurotypical human adults (Busigny and Rossion, 2010; Rossion and Curran, 2010).

We further explored potential qualitative differences using the BFRT-c data. The normative study of Rossion and Michel (2018) showed a higher accuracy and lower RT items on HR items than on LD items. However, the well-known prosopagnosic patient PS, although she achieved a borderline score of 39/54 (Busigny and Rossion, 2010), showed almost no advantage for HR items compared to LR items at the BFRT-c (Liu-Shuang *et al.*, 2016; Rossion and Michel, 2018). Importantly, the same profile as in normal controls was found here in left and right MTLE as well as in their respective NC. Moreover, items that were better performed (high accuracy and low RT) by MTLE patients were also those that were better performed by their respective NC and by the normative population (N = 307, Rossion and Michel, 2018).

4.3. Semantic and episodic memory in MTLE patients

As in previous studies, we found that MTLE patients had lower performance at famous face recognition compared to normal controls (Seidenberg *et al.*, 2002; Viskontas *et al.*, 2002; Glosser *et al.*, 2003; Griffith *et al.*, 2006). Specifically, left MTLE patients were impaired at naming famous faces while right MTLE patients were impaired at explicitly recognizing famous faces (i.e. both by naming and providing semantic information from a face), consistently with previous studies (Drane *et al.*, 2008, 2013). Since the very same patients were not impaired at individuating unfamiliar faces, their famous face recognition deficit does not appear to be due to visual face individuation, but rather to a semantic memory impairment. This hypothesis is consistent with the functions of the ventral anterior and polar temporal cortex, which is affected in MTLE (Maillard *et al.*, 2004). Numerous neuroimaging and lesion studies have provided evidence for a strong involvement of the bilateral ventral anterior temporal cortex and temporal pole in semantic processing (Rice *et al.*, 2015, 2018*b*; Hoffman and Lambon Ralph, 2018). In particular, lesion studies (in patients after surgical resection of the anterior temporal lobe or presenting with a neurodegenerative disease such as semantic dementia) found relative differences in semantic performance depending on the side of the lesion (Snowden *et al.*, 2004, 2012; Butler *et al.*, 2009, Rice *et al.*, 2018*a*). Damage to the left ventral anterior and polar temporal regions has been shown to cause relatively more difficulties with verbal semantic processing (as naming) while damage to the right ventral anterior and polar temporal regions leads to more relative difficulties with non-verbal semantics (as recognizing famous faces). The differential involvement of left and right anterior temporal lobes in semantics is consistent with our results showing greater difficulties at naming famous faces in left MTLE patients and greater difficulties at explicitly recognizing famous faces in right MTLE patients.

Interestingly, we also found that both left and right MTLE patients had lower performance (around 10% less in accuracy compared to NC) at explicitly encoding and retrieving visual items. This decrease in performance affected both face and non-face (birds) items, showing that this impairment was not specific to faces. These results are consistent with well-known visual episodic memory deficits in this population (Helmstaedter, 2013; Brissart *et al.*, 2018; Ono *et al.*, 2019), related to dysfunctions of the hippocampus and rhinal cortex, which are always affected (to a greater or lesser extent) in MTLE. Moreover, the fact that both left and right MTLE patients present with visual learning difficulties is consistent with the view that there is no strict relationship between the lateralization of the epileptogenic focus and the performance at memorizing visual information (Lee *et al.*, 2002; Saling, 2009).

4.4. Response times increase in right MTLE patients

Right MTLE patients showed a general increase of RT in virtually all tasks that were tested in the present study. RT is an important variable to consider in individual face matching tasks, as it may reveal impairments beyond accuracy measures, for instance in patients with prosopagnosia (Davidoff and Landis, 1990; Farah, 1990; Delvenne *et al.*, 2004). However, and importantly, RT increases in right MTLE patients in the present study were not specific to the type of stimuli (increase in RT for face and non-face items) or to the task (increase in RT for detection, individuation and learning tasks). Right MTLE patients were also slowed down compared to left MTLE patients at a simple visuo-spatial task, evaluating general processing speed. Specifically for the BFRT-c, the performance on the Coding test was negatively correlated with the RT at this task, suggesting that the slowing down of right MTLE patients at the BFRT-c was partly related to a general slowing down in visuo-spatial processing speed rather than to difficulties at individuating unfamiliar faces. This is supported by the fact that the Coding test was not correlated with the RT on other face or non-face individuation tasks that require less visuo-spatial processing compared to the BFRT (2 images to explore in the delayed matching task, 3 in the CFMT, as compared to 6 in the BFRT).

Overall, our observations suggest that the general increase of RT in right MTLE patients does not reflect impairment at unfamiliar face individuation *per se* but rather a general slowdown at all visual tasks, related to the right hemispheric lateralization of the epilepsy. Cerebral asymmetry in RT in brain damaged populations has been previously demonstrated (see Benton, 1986). A plausible explanation for this asymmetry relies on the more prominent role of the right hemisphere in sustaining visuospatial attention. According to this hypothesis, the right hemisphere has a crucial role in maintaining directed attention towards a task (Heilman and Van Den Abell, 1979; Mesulam, 1981; Whitehead, 1991; Thiebaut de Schotten *et al.*, 2011), and a right-lateralized damage is thus more susceptible to cause attentional deficits (Mesulam, 1981). Consistently, early studies have shown that patients with right-lateralized lesions had increased RT on simple visual reaction tasks (e.g., pressing a button when a light appeared) compared to patients with left-lateralized lesions (Arrigoni and De Renzi, 1964; De Renzi and Faglioni, 1965; see Benton, 1986).

Another possibility to explain the slower RT of right MTLE patients is related to the intellectual efficiency. Although the difference was not significant, right MTLE patients exhibited in average a 10 points lower total IQ than left MTLE patients, which could be of importance when understanding instructions of the tasks and responding appropriately to them. This is in line with numerous studies showing a strong association between processing speed and intellectual efficiency and indicating that lower IQ scores are associated with longer response times during simple reaction tasks or choice reaction tasks (Deary *et al.*, 2001; Schweizer, 2001; Jensen, 2006; Sheppard and Vernon, 2008; see also Frischkorn *et al.*, 2019). Hence, the general slowing-down observed in our population of right TLE patients could be related to an alteration of visuospatial attentional networks or to more general cognitive factors (i.e., as measured by the IQ score; see **Table 4**) rather than visual face individuation processing *per se*.

A promising avenue to clarify this issue with MTLE patients in future studies is the use of implicit measures of face individuation, as provided by EEG frequency tagging (Norcia *et al.*, 2015). In particular, sensitive and objective measures of unfamiliar face individuation can be obtained in a few minutes of testing with an oddball paradigm (Liu-Shuang *et al.*, 2014; reviewed in Rossion *et al.*, in press) showing high test-retest reliability (Dzhelyova *et al.*, 2019) and specific sensitivity to severe impairment in face identity recognition (i.e. prosopagnosia, Liu-Shuang *et al.*, 2016). If the slowing down of right MTLE patients is not specific to visual individuation of faces *per se*, this population should present with typical frequency-tagged EEG responses in this paradigm.

4.5. The validity of iEEG recordings to understand visual face recognition

Over the last decade, iEEG recordings implanted in epileptic patients (either with subdural electrodes, ECoG, or with depth intracerebral electrodes, SEEG) in patients with epilepsy has become increasingly used to understand the neural basis of face recognition, and in particular the mechanisms of visual face individuation (Allison *et al.*, 1999; Davidesco *et al.*, 2014; Engell and McCarthy, 2014; Ghuman *et al.*, 2014; Jonas *et al.*, 2016; Kadipasaoglu *et al.*, 2016; Hagen *et al.*, 2020; Rangarajan *et al.*, 2020). Since iEEG recordings are performed in patients with drug-resistant epilepsy and MTLE is the most frequent focal epilepsy referred for epilepsy surgery (Schuele and Lüders, 2008; Spencer and Huh, 2008; see also Ladino *et al.*, 2014), MTLE patients are the most included patients in iEEG studies. Therefore, it is legitimate to ask whether iEEG recordings in epileptic patients provides a valid model to understand normal face recognition (Rossion *et al.*, 2018). Several sources of evidence provide support for the validity of human iEEG to inform about normal visual face individuation. For example, despite mixed evidence of general decreases of neuroimaging signal in some regions (Riley *et al.*, 2015), MTLE patients appear to show a typical localization of posterior cortical face-selective activations in fMRI (Jacques *et al.*, 2016; Weiner *et al.*, 2016). Moreover, in this population, the largest face-selective responses in iEEG are found in the lateral section of the right middle fusiform gyrus (Jonas *et al.*, 2016; Hagen *et al.*, 2020), as in typical brains in fMRI (Kanwisher *et al.*, 1997). The present behavioural study significantly adds to these sources of evidence by showing that left and right MTLE patients have normal quantitative and qualitative performance at individuating unfamiliar faces, suggesting that these patients present with a typical neurofunctional organization of face individuation.

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Declarations of interest

None.

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Highlights of « Typical visual unfamiliar face individuation in left and right mesial temporal epilepsy »

- A range of face recognition tasks is tested in a group of MTLE patients and controls
- MTLE have difficulties at recognizing famous faces and learning visual stimuli
- Individuation of unfamiliar faces is quantitatively and qualitatively preserved in MTLE
- Right MTLE patients are slowed down at all explicit tasks due to general factors