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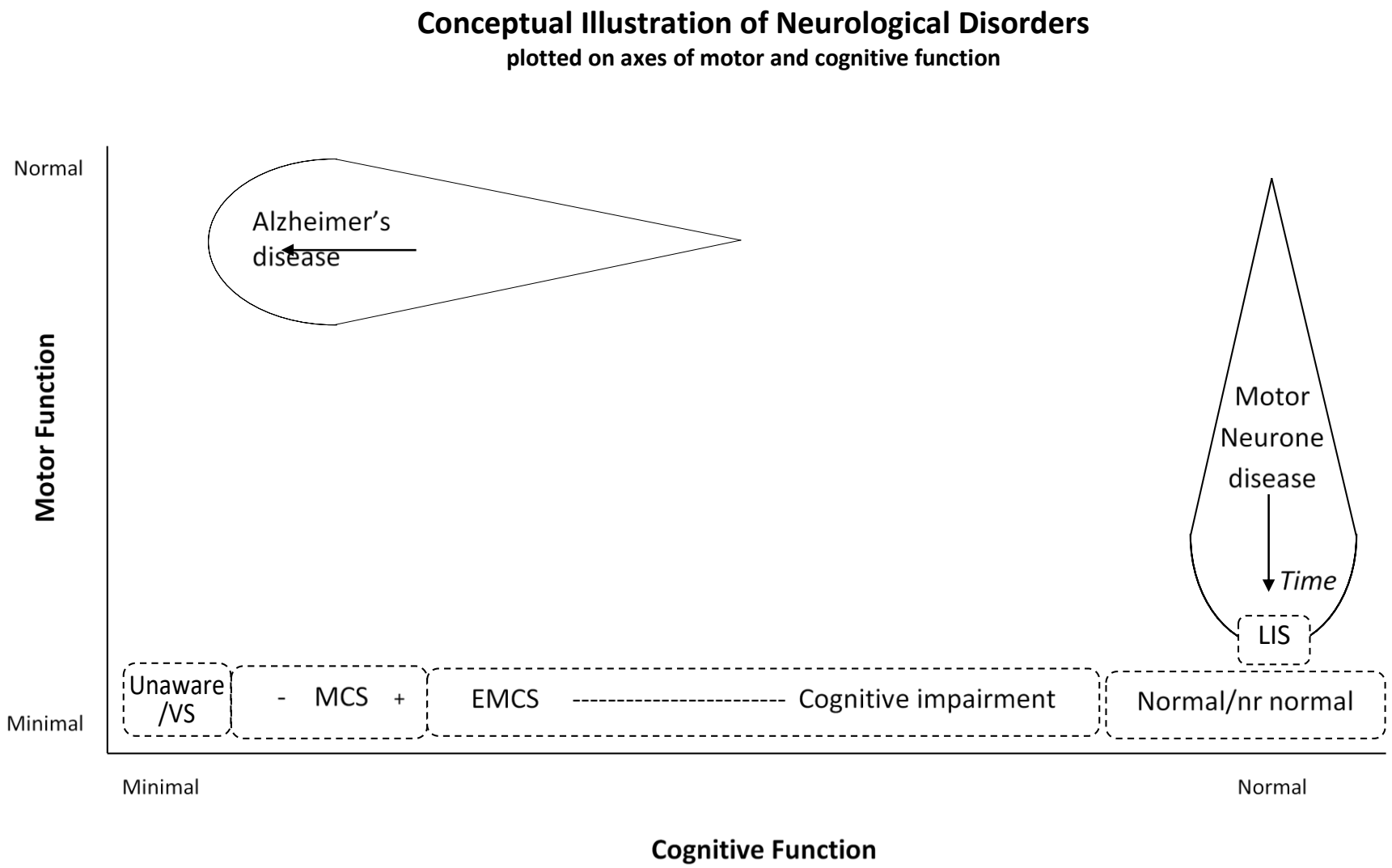
Cognitive functioning and multimodal neuroimaging interactions in patients with disorders of consciousness

Charlène Aubinet
Lesley Murphy
Olivia Gosseries
Steven Laureys

GIGA Consciousness
Coma Science Group
Université & CHU de Liège

www.giga.ulg.ac.be
www.comascience.org

Introduction



Aims

1. Cognitive assessment of people with disorders of consciousness:
   - MCS and EMCS
   - Framework for the clinician to carry out basic cognitive assessment
   - Not a rigid 'test'
   - Range of cognitive domains, (basic mood assessment, basic insight assessment)

2. Comparison of behavioral performance with neuroimaging

   Hypothesis:
   - Resting state networks' functional connectivity corresponds to behavioral performance at several subtests

Methods

- 3 patients
- Behavioral assessments
  - CAVE -
  - Output using eye movement

Royal Hospital for Neuro-disability

COGNITIVE ASSESSMENT BY VISUAL ELECTION

NAME: ..... WARD: ..... DATE: .....

A REAL OBJECTS				B NUMBERS				C WORDS			
1 Ball		**BUS**		1 **5**		8		1 **COMB**		Pen	
2 **CUP**		Comb		2 3		**9**		2 Bus		**CAR**	
3 Cow		**PIG**		3 1		**7**		3 **SPOON**		Cup	
4 Bus		**CAR**		4 **4**		2		4 **PEN**		Fork	
5 **PEN**		Fork		5 6		**3**		5 Car		**COW**	
6 Car		**COW**		6 **8**		4		6 Ball		**BUS**	
7 **SPOON**		Cup		7 **0**		5		7 **CUP**		Comb	
8 **COMB**		Pen		8 7		**2**		8 Pig		**BALL**	
9 **FORK**		Spoon		9 **6**		0		9 **FORK**		Spoon	
10 Pig		**BALL**		10 9		**1**		10 Cow		**PIG**	
Total Left		**Right**		**Total Left**		**Right**		**Total Left**		**Right**	
Grand total:				**Grand total:**				**Grand total:**			
Pass / Fail:				**Pass / Fail:**				**Pass / Fail:**			

D LETTERS				E PICTURES				F COLOURS			
1 H		**R**		1 Car		**COW**		1 **BLUE**		White	
2 **A**		L		2 Pig		**BALL**		2 Orange		**BLACK**	
3 B		**F**		3 **CUP**		Comb		3 Pink		**GREEN**	
4 G		**B**		4 Ball		**BUS**		4 **GREY**		Red	
5 **C**		W		5 **FORK**		Spoon		5 Green		**ORANGE**	
6 **L**		Z		6 **COMB**		Pen		6 Yellow		**PINK**	
7 F		**H**		7 Cow		**PIG**		7 **PURPLE**		Grey	
8 **R**		**G**		8 Bus		**CAR**		8 Black		**YELLOW**	
9 **W**		A		9 **PEN**		Fork		9 **RED**		Blue	
10 **Z**		C		10 **SPOON**		Cup		10 **WHITE**		Purple	
Total Left		**Right**		**Total Left**		**Right**		**Total Left**		**Right**	
Grand total:				**Grand total:**				**Grand total:**			
Pass / Fail:				**Pass / Fail:**				**Pass / Fail:**			

Methods

- 3 patients
- Behavioral assessments

  CAVE

  Extended CAVE:

– If P can read single words
→ orientation

– If P can identify pics/objects
→ semantic
→ picture recall

– If P can identify numbers
→arithmetic, digit span

COGNITIVE ASSESSMENT BY VISUAL ELECTION (extended)

NAME: ..... DATE .....

1. ORIENTATION
Administer if passed "Words"

Gender	Man	Woman
Year of birth	Target	Target+5
Surname	Distractor	Target
Marital status	Single	Married
Nationality	Target	Distractor
Place now	Hospital	Home
Time of day	Morning (am)	Afternoon (pm)
Type of day	Weekend	Weekday
Total correct:		
Pass/Fail:		

2. SEMANTIC USE
Use objects or pictures, according to highest score

Which is for transport?	Ball	BUS
Which is crockery?	CUP	Comb
Which is an animal?	Comb	PIG
Which is a writing utensil?	PEN	Fork
Which is an animal?	Car	COW
Which is cutlery?	SPOON	Cup
Which is for hair?	COMB	Pen
Which is a throwing toy?	BALL	Pig
Which is transport?	Spoon	CAR
Total Correct:		
Pass/Fail:		

3. PICTURE RECALL

PRESENT 1	PRESENT 2	
Elephant	ELEPHANT	Duck
Clock	Lamp	CLOCK
Banana	BANANA	Tomato
Spanner	SPANNER	Axe
Shoe	Hat	SHOE
Total:		
Pass/Fail:		

4. MENTAL ARITHMETIC

2 + 3		
4 + 5		
10 - 3		
6 - 2		
3 + 0		
5 + 3		
3 - 3		
7 - 5		
2 + 4		
8 - 7		
Total:		
Grand total:		
Pass/Fail:		

5. DIGIT SPAN

6 8 5		
7 2 9 3		
2 6 7 4 9		
5 2 4 1 6 3		
3 9 8 5 7 2 1		
Total:		
Grand total:		
Pass/Fail:		

Methods

- 3 patients
- Behavioral assessments
  - CAVE
  - Extended CAVE
  - Repeated CRS-R

Giacino et al, *Neurology*, 2002
Schnakers et al, *Brain Inj* 2009

JFK COMA RECOVERY SCALE - REVISED ©2004

Record Form

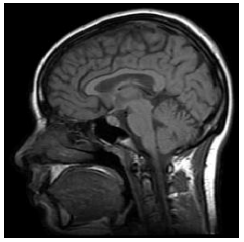
Patient: Date:								
AUDITORY FUNCTION SCALE								
4 - Consistent Movement to Command *								
3 - Reproducible Movement to Command *								
2 - Localization to Sound								
1 - Auditory Startle								
0 - None								
VISUAL FUNCTION SCALE								
5 - Object Recognition *								
4 - Object Localization: Reaching *								
3 - Visual Pursuit *								
2 - Fixation *								
1 - Visual Startle								
0 - None								
MOTOR FUNCTION SCALE								
6 - Functional Object Use †								
5 - Automatic Motor Response *								
4 - Object Manipulation *								
3 - Localization to Noxious Stimulation *								
2 - Flexion Withdrawal								
1 - Abnormal Posturing								
0 - None/Flaccid								
OROMOTOR/VERBAL FUNCTION SCALE								
3 - Intelligible Verbalization *								
2 - Vocalization/Oral Movement								
1 - Oral Reflexive Movement								
0 - None								
COMMUNICATION SCALE								
2 - Functional: Accurate †								
1 - Non-Functional: Intentional *								
0 - None								
AROUSAL SCALE								
3 - Attention								
2 - Eye Opening w/o Stimulation								
1 - Eye Opening with Stimulation								
0 - Unarousable								
TOTAL SCORE								

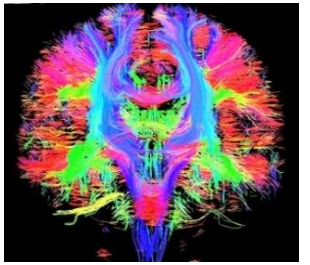
Denotes emergence from MCS †

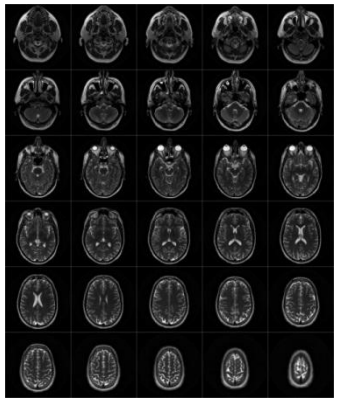
Denotes MCS *

Methods

- 3 patients
- Behavioral assessments
  - CAVE
  - Extended CAVE
  - Repeated CRS-R
- Neuroimaging assessments
  - Structural MRI
    - Voxel-based morphometry
    - Diffusion weighted imaging
  - Functional MRI
    - Seed-based resting state analysis







CASE 1
Patient data

Male

26 years old

16 months post-TBI

Functional communication (EMCS)

Right-handed

Visual pursuit and fixation

Presence of VEP

EEG → slow theta dysrhythmia on posterior and temporal derivations of left hemisphere

Results - CASE 1
Cognitive performance

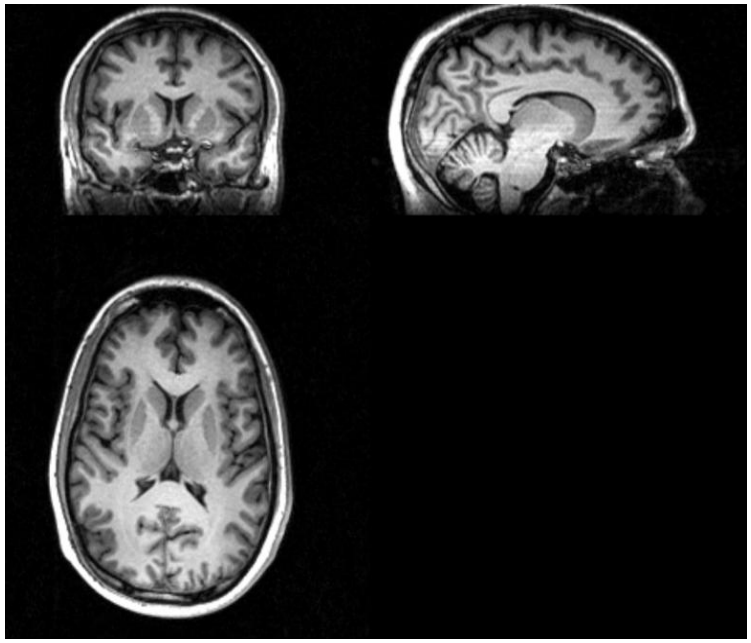
CAVE	Score	Interpretation
Real objects	9/10	OK
Numbers	9/10	OK
Words	9/10	OK
Letters	10/10	OK
Pictures	/	
Colors	/	
Left/right differences		**No**

Cut-off score = 8/10

Extended CAVE	Score	Interpretation
Orientation	5/6	OK
Semantics	8/9	OK
Picture recall	5/5 – 4/5	OK
Mental arithmetic	9/10	OK
Digit span	/	

Results - CASE 1
Structural MRI

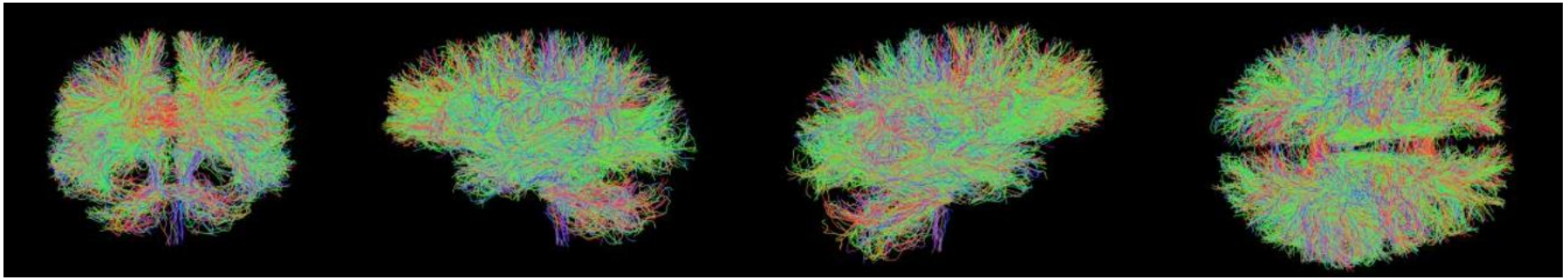
Control



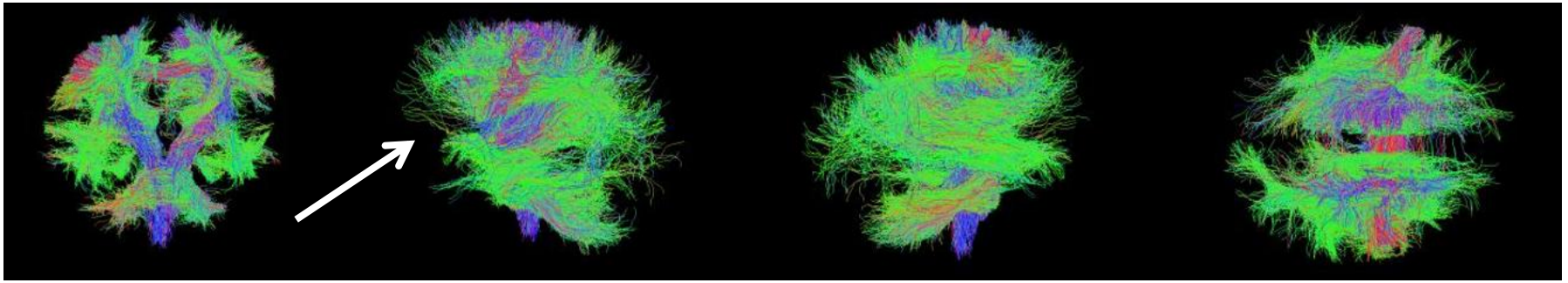
Patient

Results - CASE 1
Diffusion weighted imaging

Controls

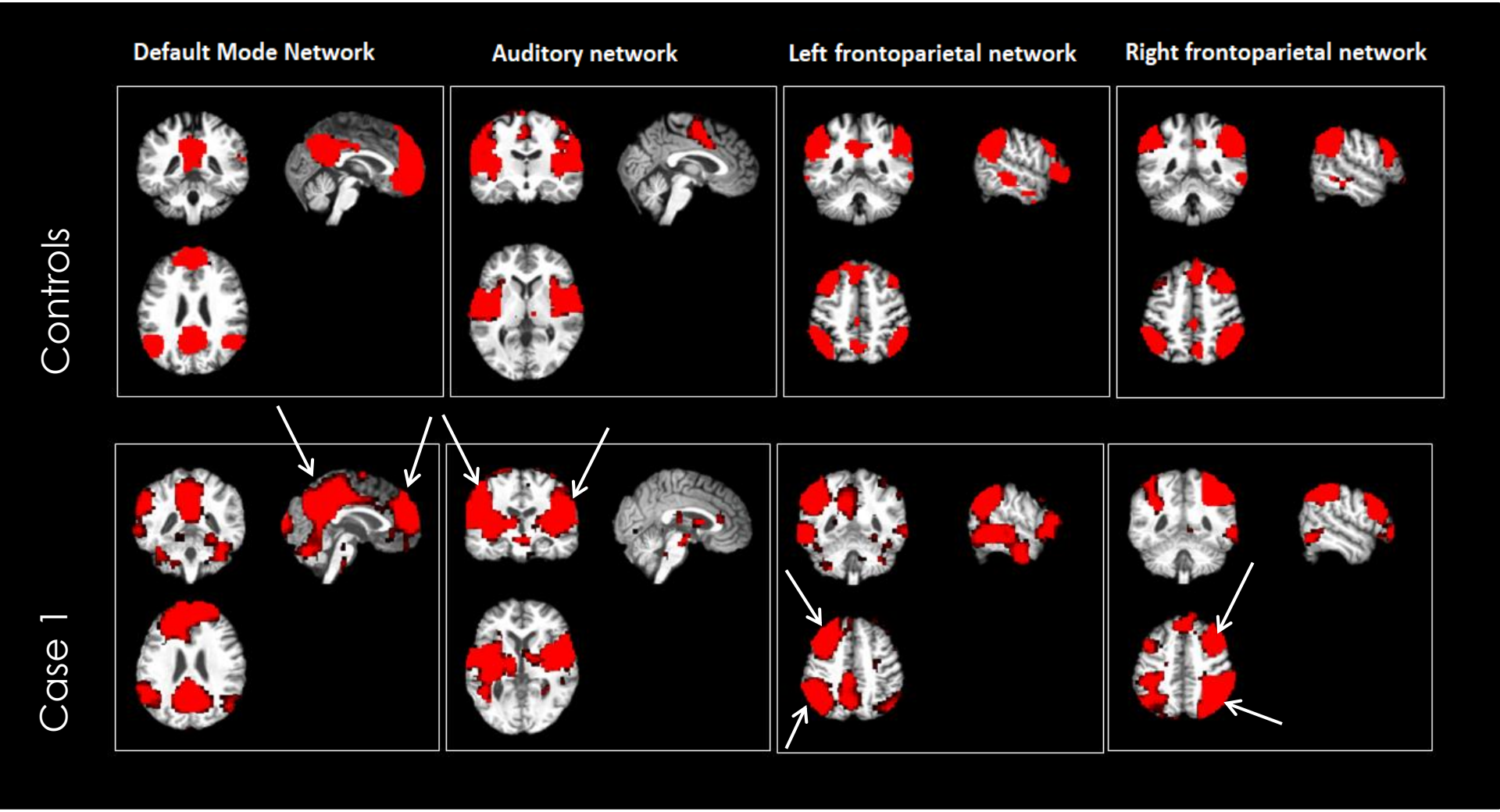


Patient



Results - CASE 1
Resting functional MRI

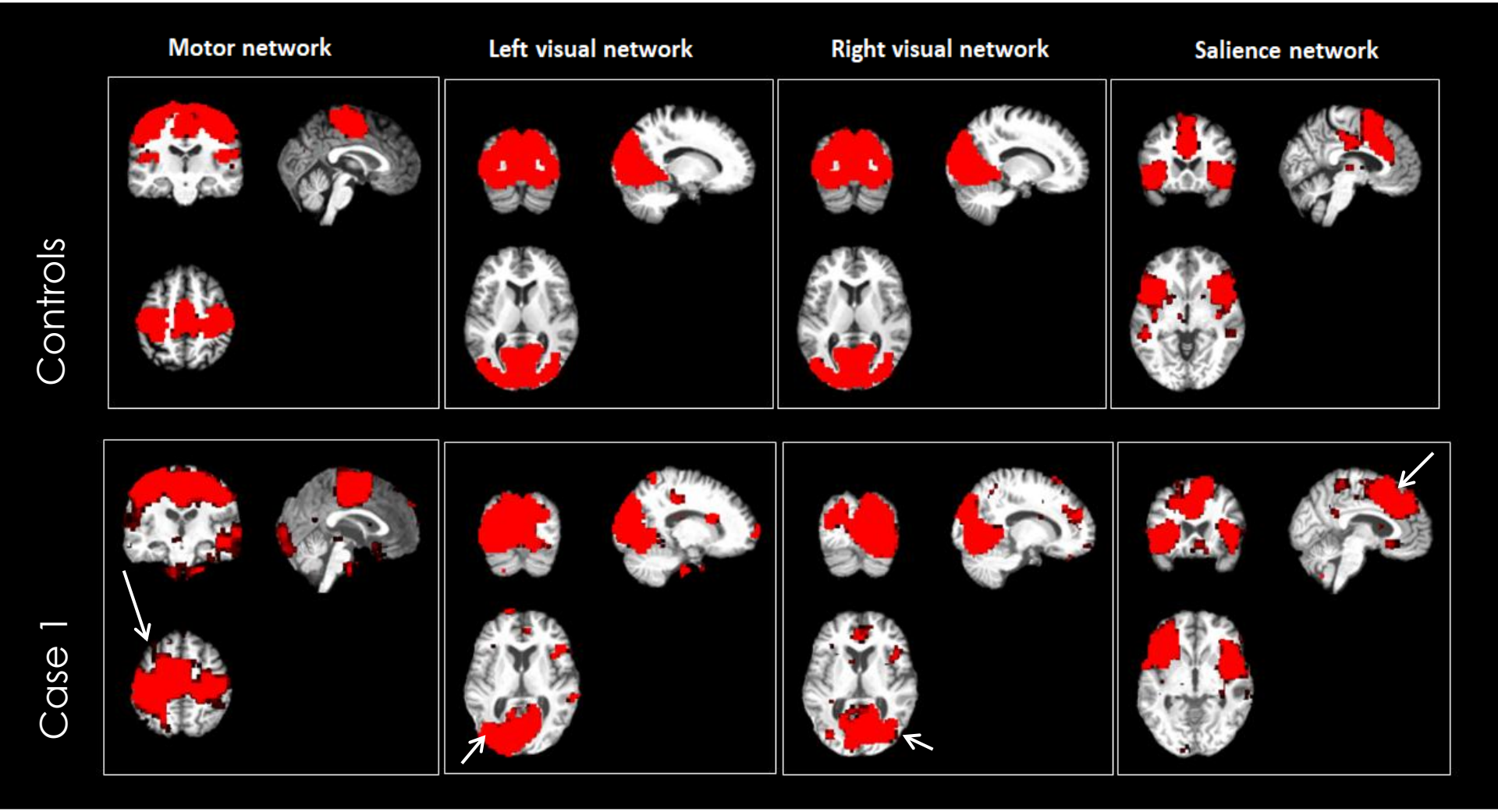
- Not sedated



Smith et al, 2009; Heine et al, 2013

Results - CASE 1
Resting functional MRI

- Not sedated



Smith et al, 2009; Heine et al, 2013

Conclusion - CASE 1
Cognitive performance

CAVE	Score	Interpretation
Real objects	9/10	OK
Numbers	9/10	OK
Words	9/10	OK
Letters	10/10	OK
Left/right differences		**No**

Visual network OK

Auditory network OK

Salience network OK

Left FPN OK

Right FPN OK

CRS-R
EMCS

DMN OK

Extended CAVE	Score	Interpretation
Orientation	5/6	OK
Semantics	8/9	OK
Picture recall	5/5 – 4/5	OK
Mental arithmetic	9/10	OK

CASE 2
Patient data

Male

20 years old

13 months post-TBI

Command following (MCS+)

Right-handed

Visual pursuit and fixation

Excellent VEP

Results - CASE 2
Cognitive performance

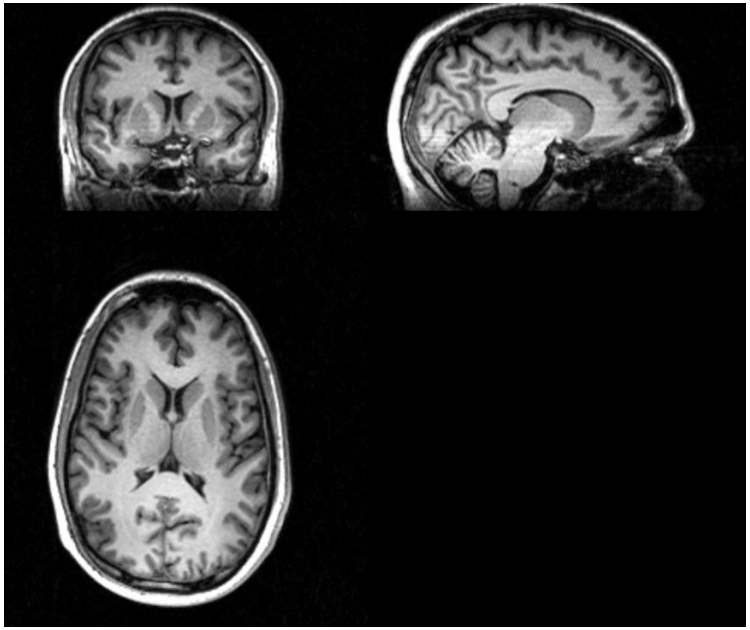
CAVE	Score	Interpretation
Real objects	10/10	OK
Numbers	8/10	OK
Words	1/10	X
Letters	7/10	X
Pictures	9/10	OK
Colors	5/10	X
Left/right differences		**No**

Cut-off score = 8/10

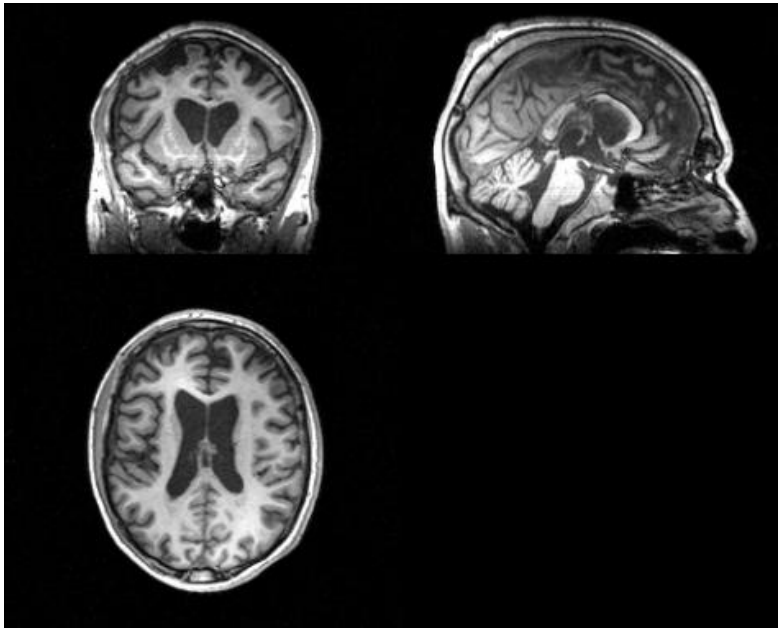
Extended CAVE	Score	Interpretation
Orientation	Not completed	X
Semantics	3/10	OK
Picture recall	1/5	OK
Mental arithmetic	/	
Digit span	/	

Results - CASE 2
Structural MRI

Control

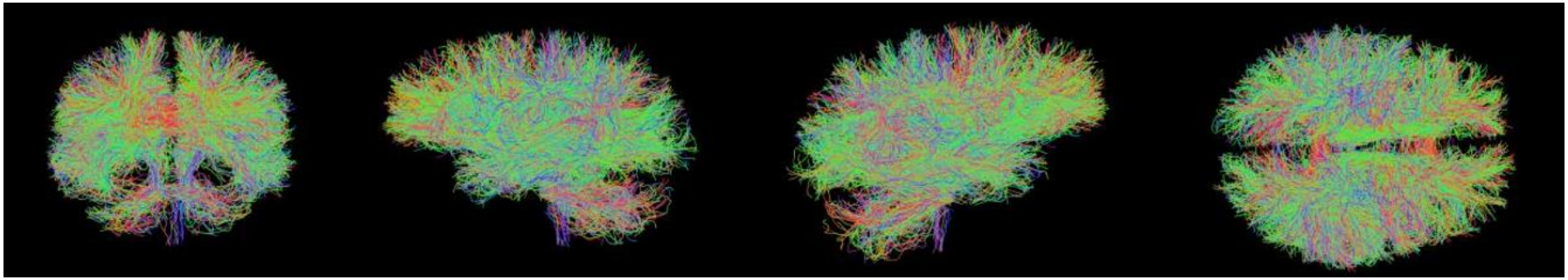


Patient

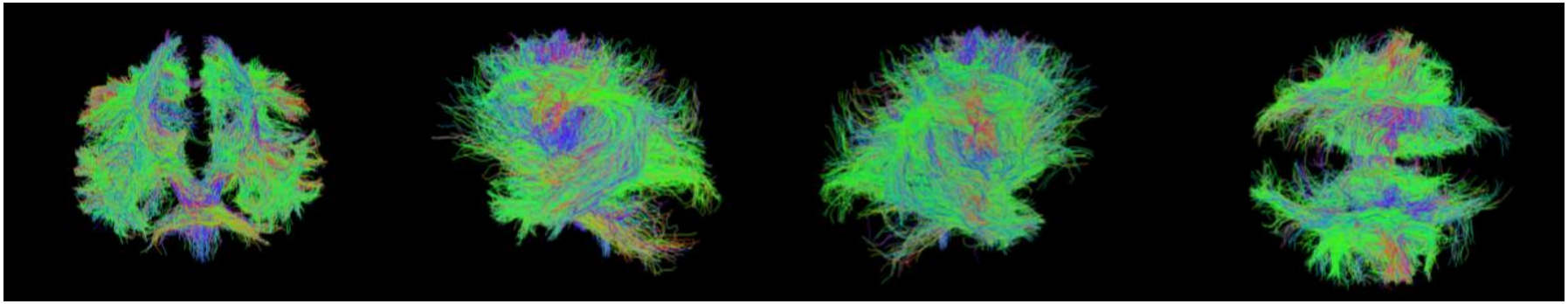


Results - CASE 2
Diffusion weighted imaging

Controls

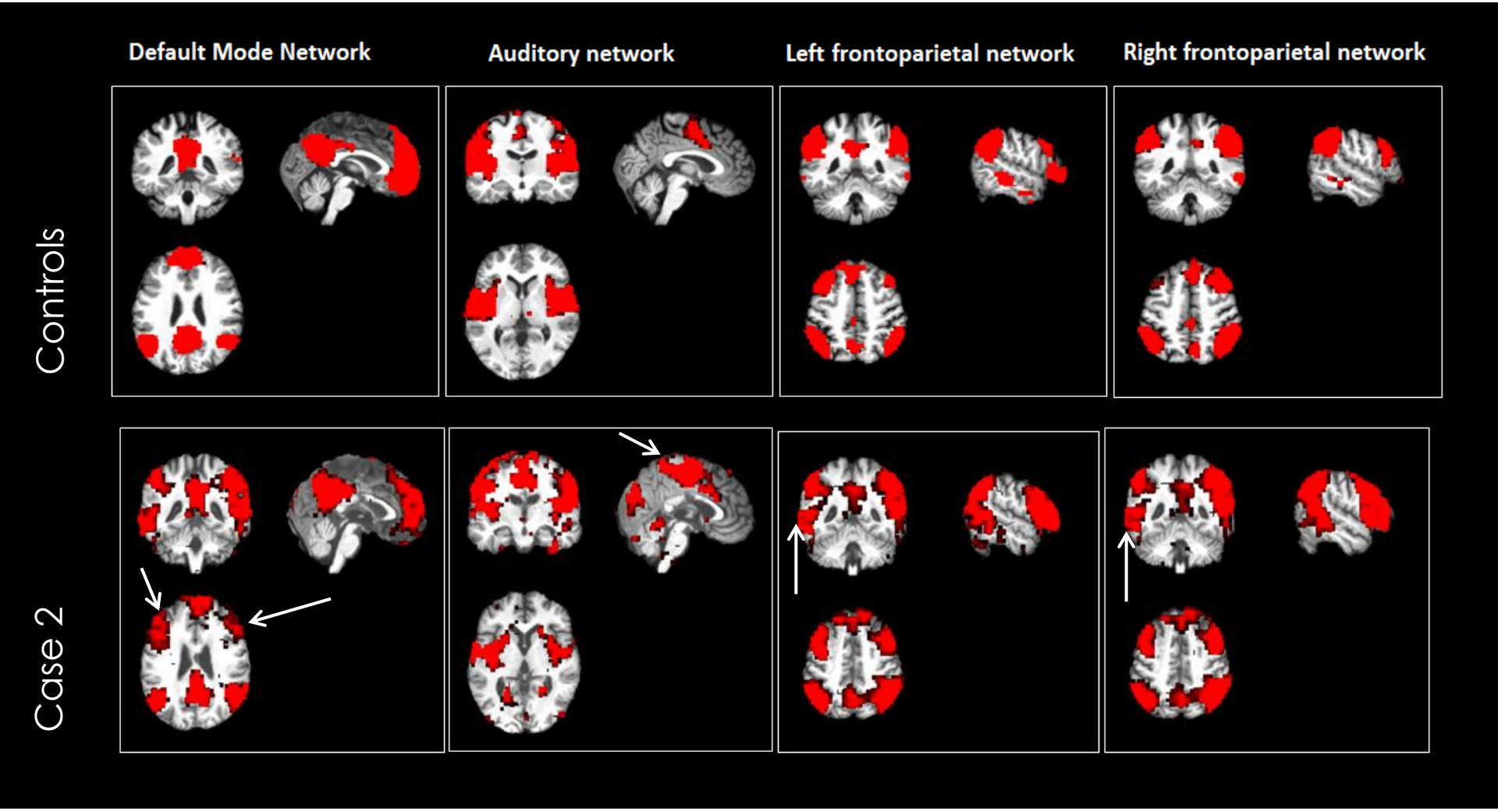


Patient



Results - CASE 2
Resting functional MRI

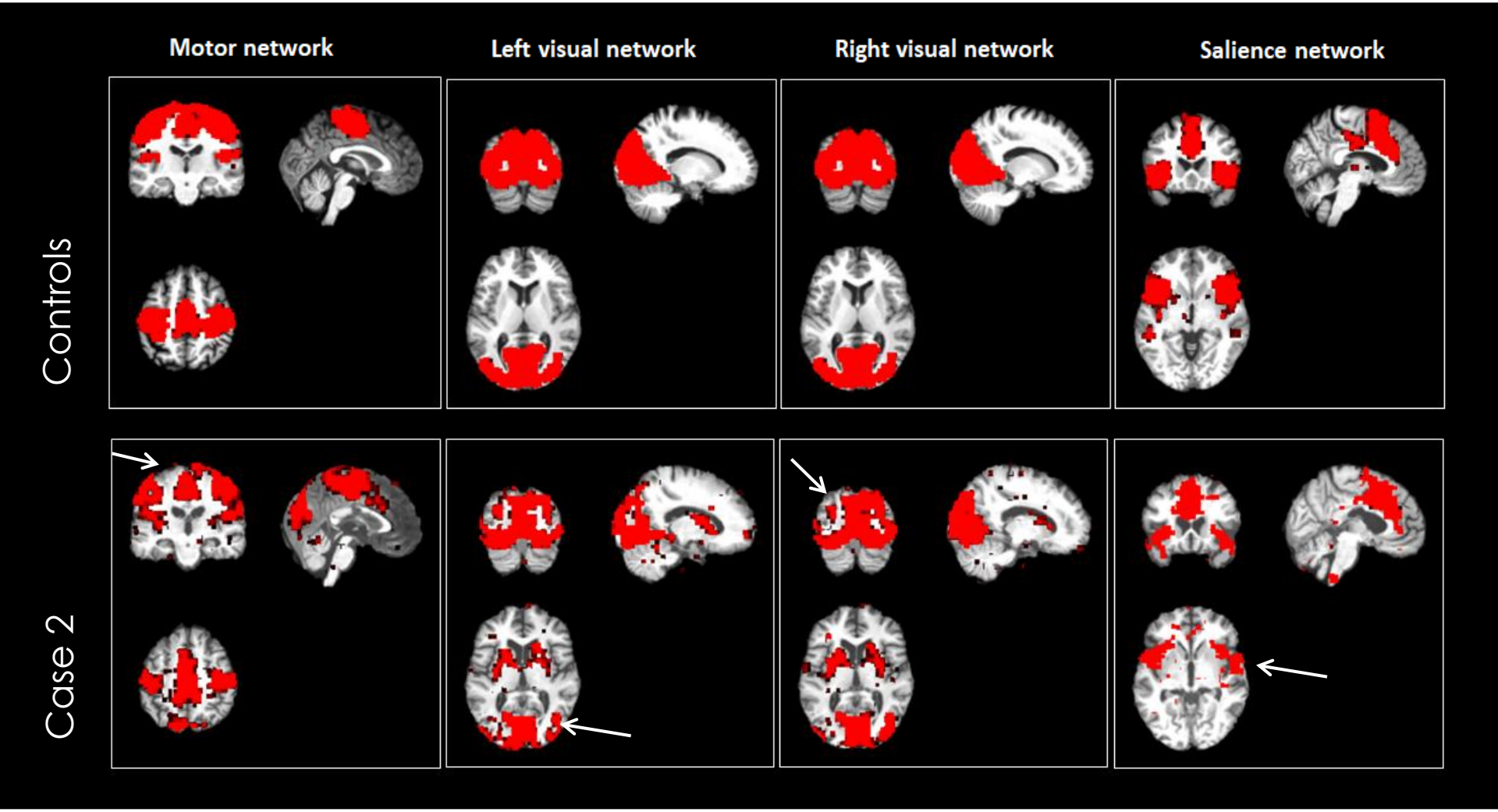
- Sedated



Smith et al, 2009; Heine et al, 2013

Results - CASE 2
Resting functional MRI

- Sedated



Smith et al, 2009; Heine et al, 2013

Conclusion - CASE 2
Cognitive performance

CAVE	Score	Interpretation
Real objects	10/10	OK
Numbers	8/10	OK
Words	1/10	X
Letters	7/10	X
Pictures	9/10	OK
Colors	5/10	X
Left/right differences		**No**

Visual network ↘ (+ diffuse)

Auditory network ↗

Salience network ↘

CRS-R
MCS+

DMN ↗

Left FPN ↗

Right FPN ↗

Extended CAVE	Score	Interpretation
Orientation	Not completed	X
Semantics	3/10	X
Picture recall	1/5	X

CASE 3
Patient data

- Male
- 66 years old
- 30 months post-stroke
- Functional use of objects (EMCS)
- Right-handed
- Visual pursuit and fixation
- Normal EVP
- EEG → Important left hemispheric damage (beginning encephalopathy)

Results - CASE 3
Cognitive performance

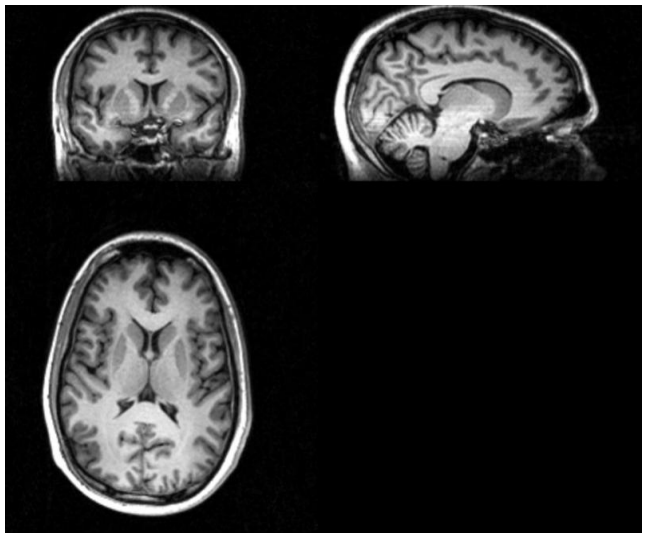
CAVE	Score	Interpretation
Real objects	7/10	X
Numbers	9/10	OK
Words	6/10	X
Letters	5/10	X
Pictures	10/10	OK
Colors	7/10	X
Left/right differences		**L>R!**

Cut-off score = 8/10

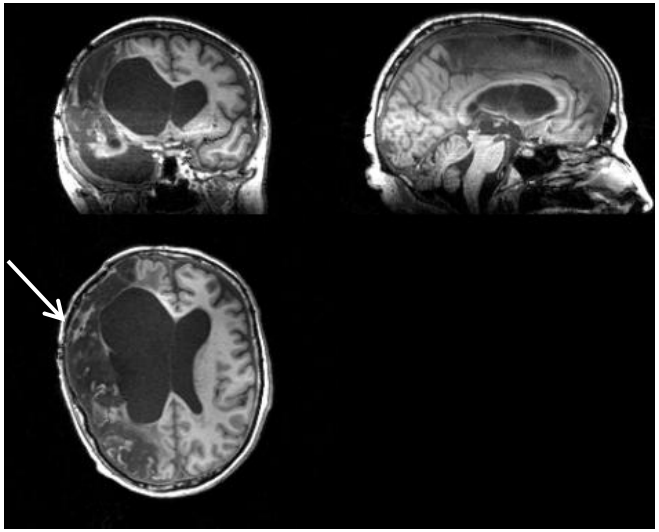
Extended CAVE	Score	Interpretation
Orientation	/	
Semantics	7/9	X
Picture recall	3/5 – 2/5	X
Mental arithmetic	0/5	X
Digit span	/	

Results - CASE 3
Structural MRI & VBM

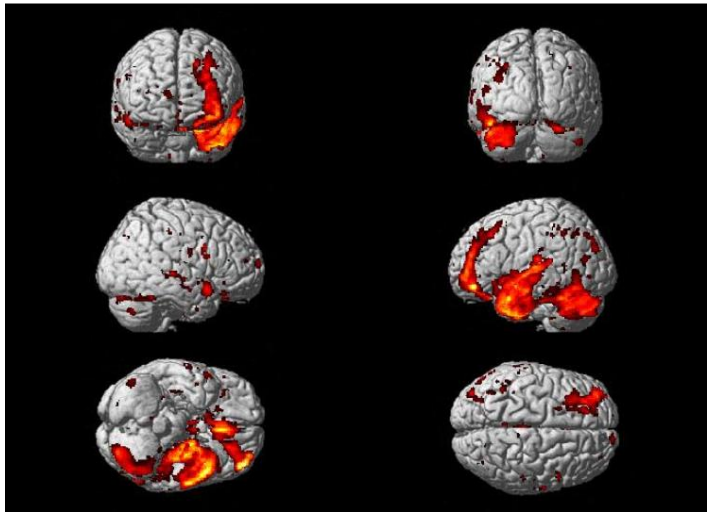
Control



Patient

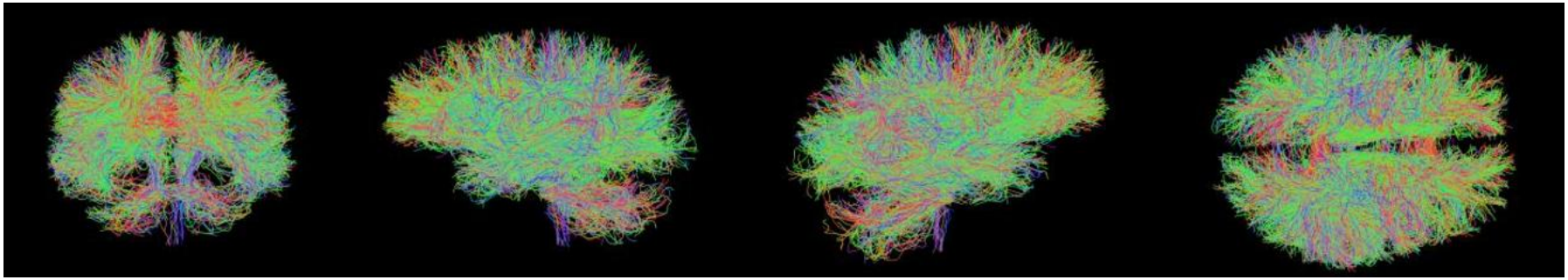


Patient < Controls

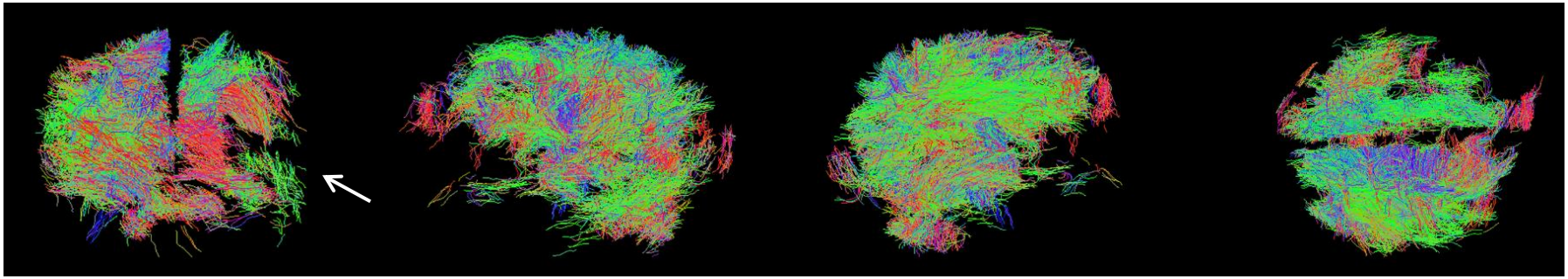


Results - CASE 3
Diffusion weighted imaging

Controls

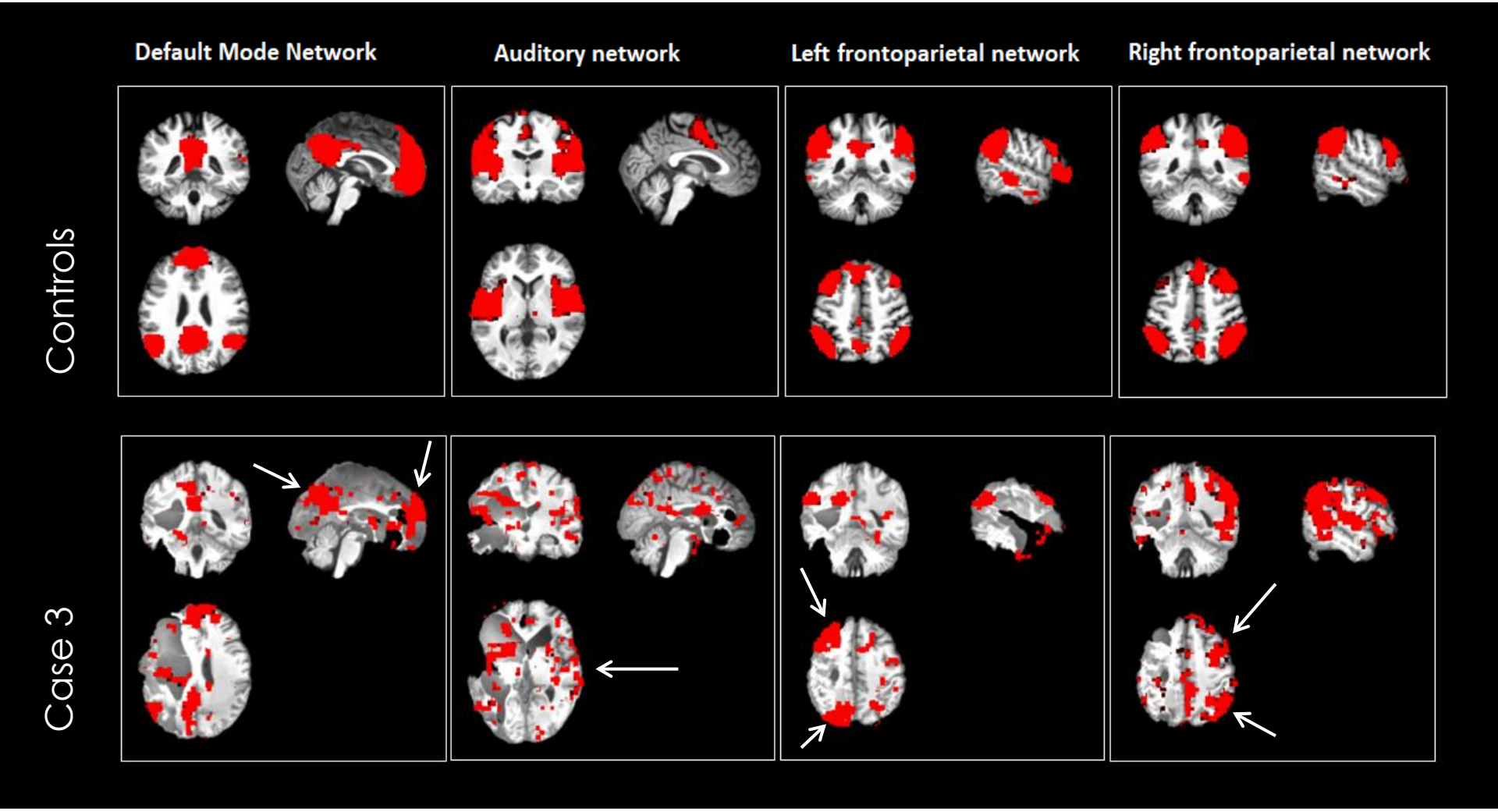


Patient



Results - CASE 3
Resting functional MRI

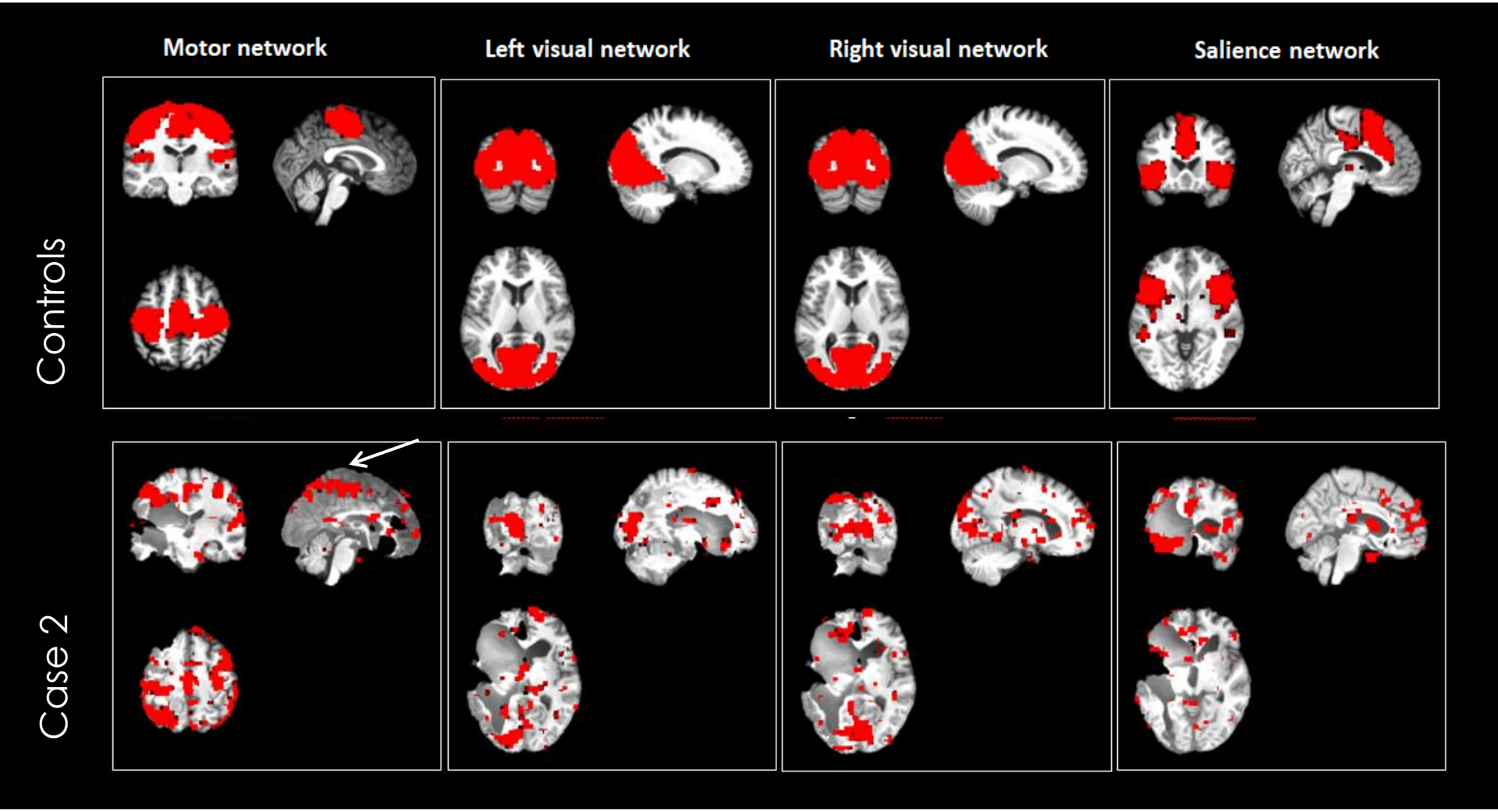
- Sedated



Smith et al, 2009; Heine et al, 2013

Results - CASE 3
Resting functional MRI

- Sedated



Smith et al, 2009; Heine et al, 2013

Conclusion - CASE 3
Cognitive performance

CAVE	Score	Interpretation
Real objects	7/10	X
Numbers	9/10	OK
Words	6/10	X
Letters	5/10	X
Pictures	10/10	OK
Colors	7/10	X
Left/right differences		**R>L!**

Visual network ↘↘

Auditory network ↘↘

Salience network ↘↘

CRS-R

EMCS

DMN ↘

Left FPN ↘

Right FPN ↘

Motor ↘

Extended CAVE	Score	Interpretation
Semantics	7/9	X
Picture recall	3/5 – 2/5	X
Mental arithmetic	0/5	X

Conclusions

- CASE 1: Good cognition // preserved FC
  CASE 2: Higher-level cognitive difficulties // atypical FC ?
  CASE 3: Impaired cognition // altered FC, mainly visual/auditory/salience networks, but caution!

→ Multimodal neuroimaging // CAVE assessment

- Extended CAVE harder ++
- /!\ visual/auditory impairment!
- Perspectives
  - Increase the sample!
  - Statistical comparisons with control group
  - Controlled order of subtests
  - Improvement of extended CAVE items

Thank you for your attention!

For additional information:
caubinet@ulg.ac.be
www.giga.ulg.ac.be
www.comascience.org

References

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