

# Supplementary material

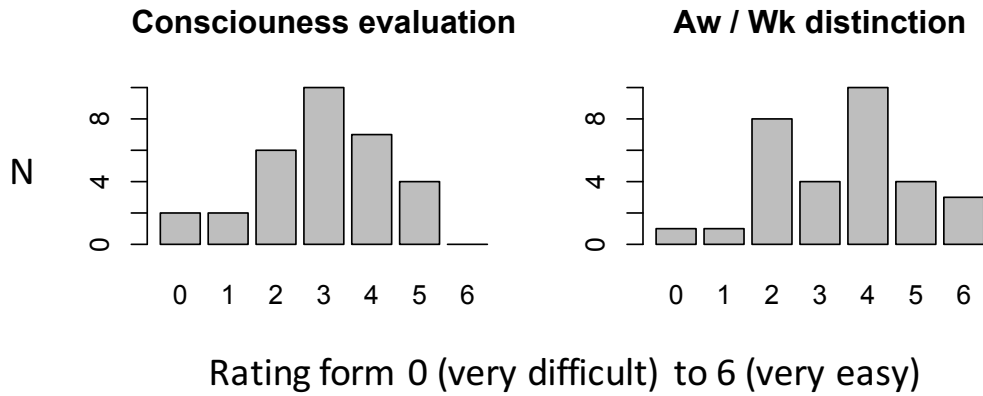
## Details regarding the design of DoC-feeling scale

### Assessment of the prior expertise of caregivers

In order to evaluate the expertise of caregivers and the further generalizability of our study, we assessed prior knowledge on consciousness state (Unresponsive Wakefulness Syndrome -UWS- and Minimally Conscious State -MCS) among the nursing staff before the beginning of inclusions through an online survey. First we asked caregivers to rate from 0 (very difficult) to 6 (very easy) how hard they considered assessing consciousness and disentangling wakefulness from awareness. They were then asked to rate wakefulness and awareness of UWS and MCS patients presented either as descriptive clinical vignettes or only with the state of consciousness label (e.g., “a MCS patient has an awareness: impaired / intermediate / preserved / no idea”).

Thirty-one team members completed the preliminary survey (18 nurses and 13 nurse assistants -NAs-). Evaluation of consciousness was rated as intermediate, difficult or very difficult by 20/31 (64%) of team members and distinction between awareness and wakefulness by 14/31 (45%) (Figure S1). Descriptive clinical vignettes tended to elicit more accurate answers than the same question asked using only the clinical labels (Table S1; e.g., 74% vs 58% of MCS patients rated as being in an intermediate level of awareness when asked in a clinical vignette or a label context respectively). However, in both conditions, awareness and wakefulness tended to be confounded (e.g.,

78% and 84% of UWS rated as having impaired wakefulness when asked in a clinical vignette or a label context respectively).



**Figure S1. Initial appreciation of consciousness assessment and wakefulness/awareness distinction difficulties.**

Wk: wakefulness; Aw: awareness.

**Table S1. Priors relative to wakefulness (Wk) and awareness (Aw) DoC patients.**

		Impaired	Intermediate	Preserved	No idea
<b>“UWS” label only*</b>	Wk	78%	19%	3%	0%
	Aw	78%	19%	0%	3%
<b>Case vignette of a UWS patient</b>	Wk	84%	16%	0%	0%
	Aw	97%	3%	0%	0%
<b>“MCS” label only</b>	Wk	29%	45%	7%	19%
	Aw	29%	58%	3%	10%
<b>Case vignette of a MCS patient</b>	Wk	13%	39%	45%	3%
	Aw	3%	74%	20%	3%

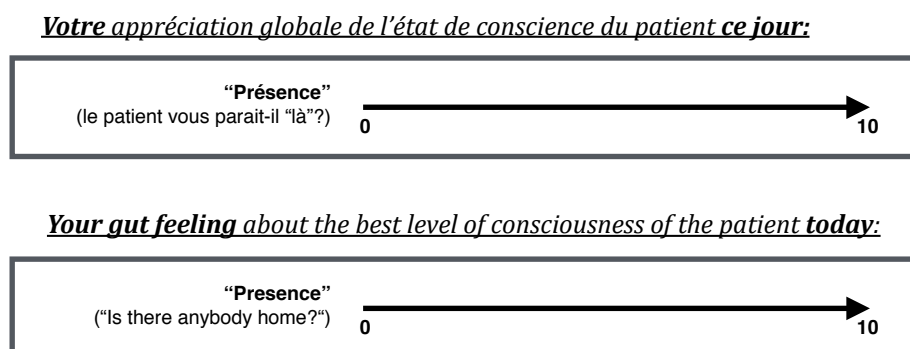
UWS: unresponsive wakefulness syndrome; MCS: minimally conscious state; Wk: wakefulness; Aw: awareness

\* we used the term “*état végétatif*” that corresponds to vegetative state (VS).

## Development of the scale

According to the results of the survey described above, we decided to use a global assessment of consciousness rather than the classical distinction between wakefulness and awareness. We chose to use a visual analogic scale (VAS) named “DoC-feeling”. VAS is a simple tool already known by all caregivers (for instance it is commonly used to assess conscious patients’ pain) although it is important to note that in our present study, it is the caregivers who use the VAS.

The choice of the framing of the question associated with the VAS converged toward the commonly used verbatim used by caregivers on daily basis when they share their observations related to the consciousness level of a patient (Figure S2) asking to rate the “presence” / “gut feeling” using a cross-section of the horizontal line of the VAS. The ratings were later manually measured using a 1 mm precision scale and collected into a database (in mm) for further analysis (the real size of the printed arrow, which could minimally vary across printers, was also measured in order to normalize the obtained value to 100 mm) [1].



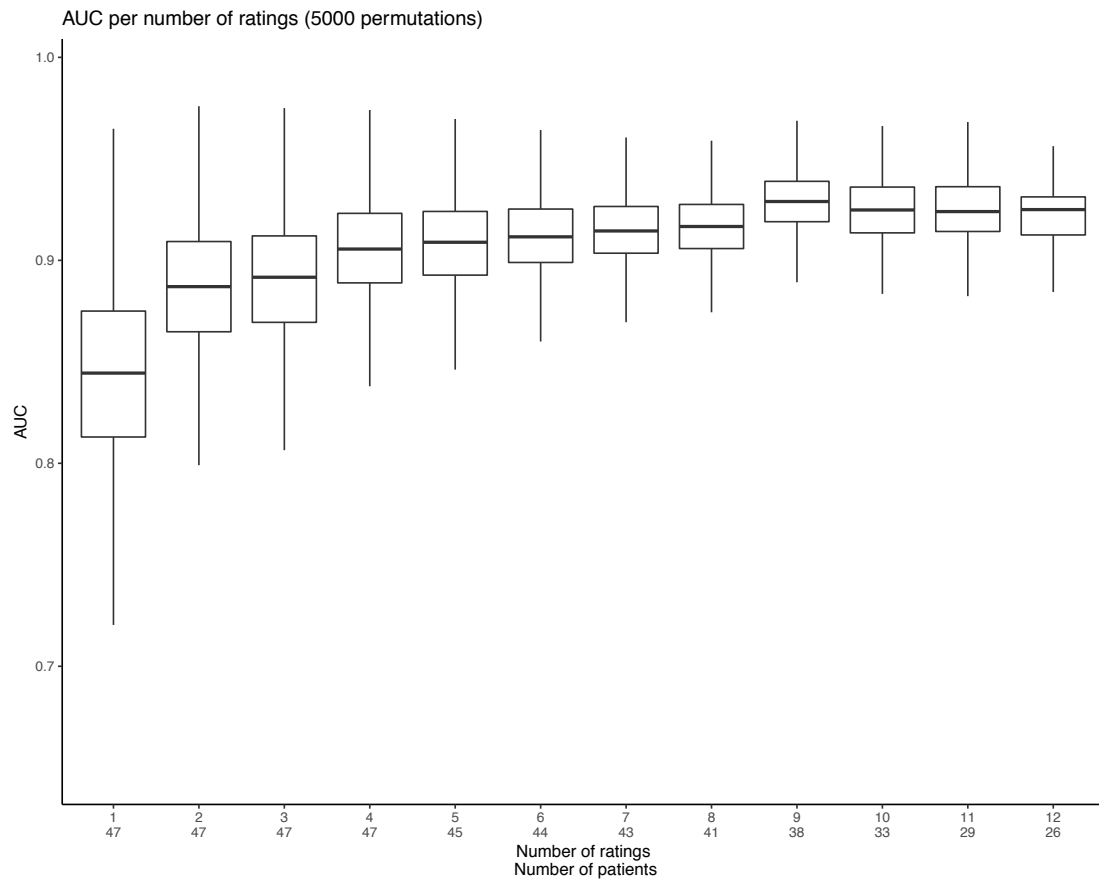
**Figure S2. DoC-feeling scale.** Original French version (top) and English translation of the DoC-feeling scale (bottom).

## Impact of the time and of the number of ratings on the accuracy of DoC-feeling score

To assess the impact of time that could have led to a convergence among caregivers over days, we compared the variability of individual ratings between the first and the second half of the evaluation' period. Variability tended to increase over time (median standard deviation in mm:11.8 [6-20.3] vs 16.2 [6.4-27.9]  $p=0.09$ ) which does not support the convergence hypothesis.

To assess the impact of the number of ratings on the accuracy of DoC-feeling score, we performed two different analyses. First, to estimate if repeated evaluation by the same rater was better than only one evaluation by rater, we computed the AUC of DoC-feeling score by taking only one rating per rater (the first one). This yielded an AUC of 0.89 [0.79-0.98]. Albeit lower than the AUC considering multiple ratings per rater, this difference was not significant ( $p=0.66$ ).

Secondly, to assess the effect of the number of ratings per patients on the AUC of DoC-feeling, we simulated AUCs using different number of randomly selected ratings per patients (from one to the median value of ratings per patient) over 5000 permutations. This analysis suggests that a number of 4 ratings is sufficient to reach an AUC over 0.9. (Figure S3, displays the maximum number of patients that had a given number of ratings. Therefore, the AUC were not computed using the same samples. However, the same analysis restricted to the 41 patients that had 8 ratings gave the same results with an AUC > 0.9 from  $\geq 4$  ratings).



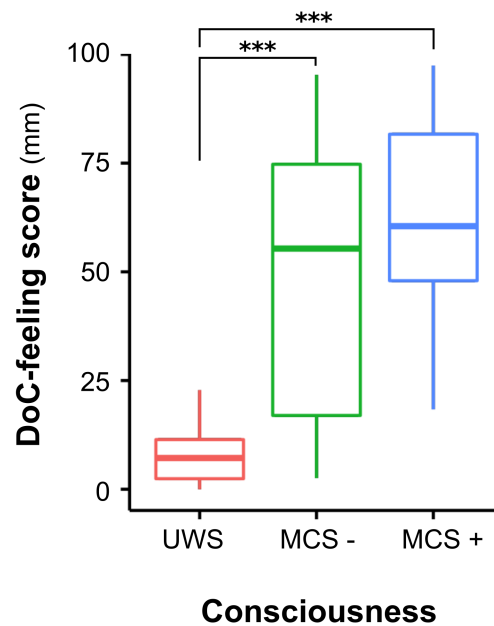
**Figure S3. AUCs of DoC-feeling score simulated for different number of ratings.** Obtained boxplots are represented for each number of ratings alongside the number of patients left in the analysis. For visualization purpose, outliers are not shown.

## Distinction between MCS “minus” and MCS “plus”

Recently, a distinction between MCS “minus” and MCS “plus” patients has been proposed. MCS “plus” patients are defined by at least one of the following: command following (score of 3 or 4 on the auditory function scale), intelligible vocalization (score of 3 on the oromotor/verbal scale) and/or not-functional but intentional communication (score of 1 on the communication scale) [2]. MCS “minus” patients are patients meeting lower CRS-R MCS criteria (e.g., fixation, visual pursuit or adapted motor reaction to pain) without any behavior defining the MCS “plus” subcategory. Eleven (23%) patients met the criteria of MCS “plus”.

A one-way ANOVA with DoC-feeling score as the dependent variable and state of consciousness (UWS, MCS “plus” and MCS “minus”) as the predictor revealed a main effect of state of consciousness on DoC-feeling score ( $F[df:2]=24.14$ ,  $p<0.0001$ ). Post-hoc pairwise comparisons found a significant difference for UWS vs. MCS “minus” and UWS vs. MCS “plus” (Bonferroni corrected p-values  $<0.001$ ,  $<0.0001$  and  $0.90$  respectively) but no significant difference for MCS “minus” vs. MCS “plus” (Figure S4).

**Figure S4. DoC-feeling score obtained in UWS, MCS “minus” (-) and MCS “plus” (+) patients.**  
\*\*\*:  $p < 0.001$ .



## Misclassified patients

We identified 6 misclassified patients according to DoC-feeling score using the cut-off of 16.7 mm: 3 UWS and 3 MCS. Their characteristics are shown in the supplementary Table S2.

Two of the 3 UWS patients according to the CRS-R but with a DoC-feeling score  $> 16.7$  mm evolved towards MCS over the next 6 months.

The 3 MCS patients according to the CRS-R but with a DoC-feeling score  $< 16.7$  mm were fluctuating between UWS and MCS “minus” during their stay. Moreover, none had a neural correlate of consciousness on the local-global auditory oddball paradigm [3,4] and each of them were classified as UWS by at least one of the following methods: multimodal EEG classification [5], 18-FDG-PET-TDM metabolism of the highest hemisphere [6] or resting state MRI functional connectivity analysis [7]. Finally, they were more chronic patients and none evolved towards a better state of consciousness over the next 6 months.

**Table S2. Characteristics of misclassified patients**

Patients	Age / sex Etiology / Delay	DoC-feeling score [n_ratings / n_raters]	CRS-R ratings → state	EEG	ERP	rs-fMRI	PET	Outcome (delay)
<b>Patients labelled as UWS by the CRS-R with DoC-feeling score &gt;16.7 mm</b>								
UWS_18	52 yo / F Anoxia / 724 days	18.3 [10/6]	6 [1-0-2-1-0-2] → UWS 6 [1-0-2-1-0-2] → UWS	UWS	LE+/GE-	UWS	-	MCS- (6 month)
UWS_19	32 yo / M Anoxia / 14 days	21.9 [20/9]	5 [0-0-2-1-0-2] → UWS 3 [0-0-1-1-0-1] → UWS 3 [0-0-1-1-0-1] → UWS	UWS	LE-/GE-	MCS	-	Dead/ WLST (1 month)
UWS_20	35 yo / M Hypoglycemia / 41 days	22.8 [20/13]	5 [0-0-2-1-0-2] → UWS 5 [1-0-1-1-0-2] → UWS 4 [1-0-1-1-0-1] → UWS	UWS	LE-/GE-	UWS	UWS	MCS- (4 month)
<b>Patients labelled as MCS by the CRS-R with DoC-feeling score &lt; 16.7 mm</b>								
MCS_1	41 yo / F Stroke / 778 days	6.6 [28/11]	9 [2-0-3-2-0-2] → MCS- 8 [2-0-3-1-0-2] → MCS- 7 [2-0-2-1-0-2] → UWS	MCS	LE-/GE-	NA	UWS	MCS- (6 month)
MCS_2	23 yo / M TBI / 619 days	9.7 [12/7]	8 [1-2-2-1-0-2] → MCS- 7 [1-2-2-1-0-1] → MCS- 7 [1-2-2-1-0-1] → MCS- 6 [1-1-2-1-0-1] → UWS 6 [1-1-2-1-0-1] → UWS 6 [1-1-2-1-0-1] → UWS	UWS	LE-/GE-	NA	UWS	MCS- (6 month)
MCS_3	29 yo / M TBI / 109 days	2.6 [8/7]	9 [1-3-2-1-0-2] → MCS- 9 [2-2-2-1-0-2] → MCS- 7 [1-1-2-1-0-2] → UWS	MCS	LE-/GE-	UWS	MCS	MCS- (6 month)

*Abbreviations:* F: female; CRS-R: coma recovery scale-revised; EEG: Multimodal EEG classification according to Sitt et al.[5]; ERP: local-global event-related potentials[3,4]; LE: local effect; GE: global effect; M: male; MCS: minimally conscious state; NA: not available; PET: 18-fluoro-deoxy-glucose positron emission tomography classification according to Stender et al.[6]; rs-fMRI: resting state functional MRI classification according to Demertzi et al.[7]; TBI: traumatic brain injury; UWS: unresponsive wakefulness syndrome; yo: years old.



## Secondary metrics

In addition to DoC-feeling score, and in order to allow for the identification of items that could better correlate with the CRS-R, we collected several secondary metrics using the same VAS approach after the collection of DoC-feeling rating (see full assessment form in the supplementary appendix).

We assessed the two classical components of consciousness: 1) wakefulness (*“ouverture des yeux”*; eye opening) and 2) awareness (*“le patient paraît-il conscient de lui même et/ou de son environnement ?”*; does the patient seem to be aware of himself and/or of his environment?).

We also collected behaviors that correlate with state of consciousness such as purposeful behavior (*“participation aux soins de nursing ?”*; does the patient participate to nursing care ?) response to command (*“mouvements sur ordre?”* does the patient follow command?) and pain reaction (*“réaction aux soins douloureux ? et si oui: ces réactions vous paraissent elles adaptées?”*; reaction to painful stimuli ? and if yes: does this reaction seem adapted?).

Finally, since the FOUR score is performed by nurses as standard of care in our unit, we also recorded the best FOUR score obtained during the day whenever a DoC feeling rating was performed.

The results of the secondary metrics (other VAS and FOUR-score) are presented in Table S3 using the same analyses as in the main manuscript: association of individuals' ratings with the state of consciousness (linear mixed model) and performances of aggregated metrics across raters for state of consciousness discrimination (group medians comparisons and AUCs). Only the VAS for awareness (does the patient seem to be aware of himself and/or of his environment?) reached a similar level of AUC than DoC-feeling,

although the comparison between VAS is not univocal since DoC-feeling was systematically performed first.

**Table S3. Secondary metrics**

LMM: linear mixed model; p: p-value; t: t-value; MCS: minimally conscious

	LMM	UWS	MCS	p*	AUC
	t/p				[95% CI]
Eyes opening (mm; n=688)	1.375/ 0.33	78.9 [63.1-93.9]	91.8 [75.4-94.8]	0.32	0.59 [0.41-0.75]
Does the patient seem aware of himself and/or of his environment? (mm; n=687)	6.200/ <.0001	3.6 [0.0-6.4]	42.9 [18.0-63.0]	<.0001	0.96 [0.88-1.00]
Does the patient participate to nursing care? (mm; n=677)	3.259/ 0.0030	0.0 [0.0-0.0]	1.5 [0.0-6.4]	<.0001	0.81 [0.71-0.91]
Does the patient follow commands? (mm; n=672)	4.339/ <.0001	0.0 [0.0-0.0]	4.0 [0.0-32.0]	<.0001	0.82 [0.71-0.92]
Does the patient react to painful stimuli? (mm; n=540)	4.538/ <.0001	42.6 [26.4-55.4]	86.1 [66.5-91.3]	<.0001	0.80 [0.66-0.92]
If yes, does this reaction seem adapted? (mm; n=482)	4.985/ <.0001	30.8 [6.1-50.3]	83.0 [73.9-93.3]	<.0001	0.86 [0.75-0.96]
FOUR score (n=467)	4.83/ <.0001	10.5 [9.5-13.5]	13.0 [12.8-13.3]	<.0001	0.78 [0.66-0.90]
FOUR score Eye Response subscale (n=477)	2.696/ 0.013	3.0 [3.0-3.0]	3.0 [3.0-3.8]	0.0092	0.68 [0.57-0.79]

state; UWS: unresponsive wakefulness syndrome; \*p: Wilcoxon-Mann-Whitney test p-value for UWS vs. MCS comparison; AUC: area under the receiver operating characteristic curve.

## References:

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- 2 Bruno M-A, Vanhaudenhuyse A, Thibaut A, *et al.* From unresponsive wakefulness to minimally conscious PLUS and functional locked-in syndromes: recent advances in our understanding of disorders of consciousness. *J Neurol* 2011;**258**:1373–84. doi:10.1007/s00415-011-6114-x
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- 6 Stender J, Mortensen KN, Thibaut A, *et al.* The Minimal Energetic Requirement of Sustained Awareness after Brain Injury. *Curr Biol* 2016;**26**:1494–9. doi:10.1016/j.cub.2016.04.024
- 7 Demertzi A, Antonopoulos G, Heine L, *et al.* Intrinsic functional connectivity differentiates minimally conscious from unresponsive patients. *Brain* 2015;**138**:2619–31. doi:10.1093/brain/awv169

## Supplementary Appendix:

### Doc-Feeling (évaluation de l'état de conscience par le personnel para-médicale en situation de soins courants)

Etiquette patient

Nom AS:

Date:

Heure:



- Réa    jour    garde    nuit  
 USC

### Feuille AS

#### Votre appréciation globale de l'état de conscience du patient ce jour:

**"Présence"**  
(le patient vous paraît-il "là" ?)   0 —————> 10

ouverture des yeux   0 —————> 10

le patient paraît-il conscient de lui même et/ou de son environnement?   0 —————> 10

Items secondaires :		Vous pouvez préciser les comportements observés dans remarques générale si nécessaire	
Participation aux soins de nursing ?	0	—————>	10
Mouvements sur ordre?	0	—————>	10
Réaction aux soins douloureux ? (prises de sang / pansement etc)	0	—————>	10
Si OUI ces réactions vous paraissent elles adaptées?	0	—————>	10

Remarques générales / fluctuations dans la journée? / Autre? :

Modifications éventuelles notées en présence des proches:

# Doc-Feeling (évaluation de l'état de conscience par le personnel para-médicale en situation de soins courants)

Etiquette patient

Nom IDE:

Date:

Heure:



- Réa     jour     garde     nuit  
 USC

## Feuille IDE

### Votre appréciation globale de l'état de conscience du patient ce jour:

<b>"Présence"</b> (le patient vous paraît-il "là" ?)	<div style="display: flex; align-items: center;"> <div style="margin-right: 10px;">0</div> <div style="flex-grow: 1; border-bottom: 2px solid black; position: relative;"> <div style="position: absolute; right: -10px; top: -5px;">➔</div> </div> <div style="margin-left: 10px;">10</div> </div>
ouverture des yeux	<div style="display: flex; align-items: center;"> <div style="margin-right: 10px;">0</div> <div style="flex-grow: 1; border-bottom: 2px solid black; position: relative;"> <div style="position: absolute; right: -10px; top: -5px;">➔</div> </div> <div style="margin-left: 10px;">10</div> </div>
le patient paraît-il conscient de lui-même et/ou de son environnement?	<div style="display: flex; align-items: center;"> <div style="margin-right: 10px;">0</div> <div style="flex-grow: 1; border-bottom: 2px solid black; position: relative;"> <div style="position: absolute; right: -10px; top: -5px;">➔</div> </div> <div style="margin-left: 10px;">10</div> </div>

Items secondaires :	Vous pouvez préciser les comportements observés dans remarques générale si nécessaire
Participation aux soins de nursing ?	<div style="display: flex; align-items: center;"> <div style="margin-right: 10px;">0</div> <div style="flex-grow: 1; border-bottom: 2px solid black; position: relative;"> <div style="position: absolute; right: -10px; top: -5px;">➔</div> </div> <div style="margin-left: 10px;">10</div> </div>
Mouvements sur ordre?	<div style="display: flex; align-items: center;"> <div style="margin-right: 10px;">0</div> <div style="flex-grow: 1; border-bottom: 2px solid black; position: relative;"> <div style="position: absolute; right: -10px; top: -5px;">➔</div> </div> <div style="margin-left: 10px;">10</div> </div>
Réaction aux soins douloureux ? (prises de sang / pansement etc)	<div style="display: flex; align-items: center;"> <div style="margin-right: 10px;">0</div> <div style="flex-grow: 1; border-bottom: 2px solid black; position: relative;"> <div style="position: absolute; right: -10px; top: -5px;">➔</div> </div> <div style="margin-left: 10px;">10</div> </div>
Si OUI ces réactions vous paraissent elles adaptées?	<div style="display: flex; align-items: center;"> <div style="margin-right: 10px;">0</div> <div style="flex-grow: 1; border-bottom: 2px solid black; position: relative;"> <div style="position: absolute; right: -10px; top: -5px;">➔</div> </div> <div style="margin-left: 10px;">10</div> </div>

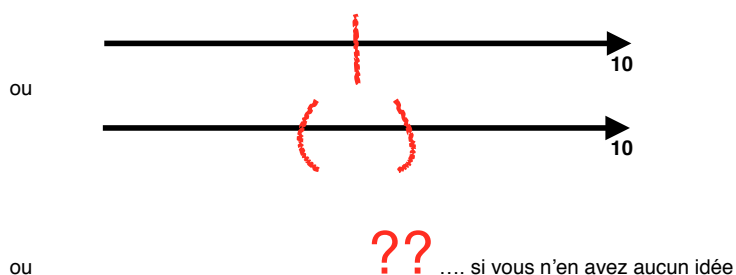
Remarques générales / fluctuations dans la journée? / Autre? :

Modifications éventuelles notées en présence des proches:

### **Consignes pour la saisie des données:**

- On inclut tous les patients "DOC" (bilan de conscience, max 1 en réa et 1 en UCS/ semaine). L'infirmière et l'aide soignant du patient remplissent tous les jours leurs parties dédiées en fin de roulement, au moment des transmissions (temps moyen <3min). Cela fera donc en tout 3 feuilles AS et 2 à 3 feuilles IDE / patient "DOC" et par jour.
- Noter tout d'abord **votre** appréciation globale de la "présence" du patient **ce jour** comme ceci:



- La "présence" est la donnée principale; l'ouverture des yeux (vigilance) et la perception du degrés de "conscience" sont des données secondaires.
- Remplir **dans un deuxième temps** les Items secondaires, en précisant si besoin ce que vous avez observé dans le cadre du bas
- Pour l'IDE, merci de recopier le **meilleur RASS et FOUR-score** observé ce jour, si il y a eu (ne rien faire en plus que de ce qui est prescrit par le médecin en charge ou fait habituellement)

Merci de votre participation!!

L'équipe **DOC-Felling**



Tous les détails de ce protocole sont disponibles sur notre **Slack** dans le channel **#doc-feeling**