Behavioral signs of recovery from unresponsive wakefulness syndrome to emergence of minimally conscious state

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Abstract

Background

Precise description of behavioral signs denoting transition from unresponsive wakefulness syndrome/vegetative state (UWS/VS) to minimally conscious state (MCS) or emergence from MCS after severe brain injury is crucial for prognostic purposes. A few studies have attempted this goal but involved either non-standardized instruments, limited temporal accuracy or samples, or focused on (sub)acute patients.

Objectives

To describe the behavioral signs that led to a change of diagnosis, as well as the factors influencing this transition, in a large sample of patients with chronic disorders of consciousness after severe brain injury.

Methods

In this retrospective cohort study, 185 patients in UWS/VS or MCS were assessed with the Coma Recovery Scale Revised (CRS-R) five times within the two weeks following their admission to a neurorehabilitation center and then weekly until emergence from MCS, discharge or death.

Results

Of these 185 patients, 33 patients in UWS/VS and 45 patients in MCS transitioned to another state. Transition to MCS was mostly denoted by one behavioral sign (72%), predominantly visual fixation (57%), followed by localization to noxious stimulation (27%), visual pursuit (21%) and object manipulation (12%), and could be predicted by etiology, time post-injury and age. Emergence from MCS was characterized by one sign in 64% of patients and by two signs (functional communication and objects use) in the remaining cases, and could be predicted by time post-injury and number of behavioral signs at admission.

Conclusions

Repeated assessments using the CRS-R evidenced that transition from UWS to MCS was predominantly signaled by visual fixation and could be predicted by etiology, time post-injury and age. Emergence from MCS was mostly signaled by one sign and could be predicted by time post-injury and number of behavioral signs at admission. Clinicians should be therefore advised to pay particular attention to visual and motor subscales of the CRS-R to detect behavioral recovery.

Database registration

This study was registered at clinicaltrials.gov (NCT04687397)

Keywords

Disorders of Consciousness – Vegetative State - Unresponsive Wakefulness Syndrome – Minimally Conscious State – Brain injury – Coma Recovery Scale Revised

Introduction

Severe brain injuries of traumatic (TBI) or non-traumatic (non-TBI) etiologies can lead to prolonged periods of altered consciousness, which are generally gathered under the term « disorders of consciousness » (DOC) [1]. During coma, patients cannot be awaken and do not show any behavioral sign of self or environmental awareness [2]. Patients who recover from coma are considered in an unresponsive wakefulness syndrome (UWS) [3] if they open their eyes but only show reflexes [4], or in a minimally conscious state (MCS) if they show reproducible but inconsistent non-reflex cortically mediated behaviors in response to environmental stimuli (i.e. visual pursuit, command-following) [5,6]. Recovery of functional communication or appropriate use of objects are considered as indicators of emergence from MCS (EMCS) [7].

Important clinical decisions in terms of pain treatment, rehabilitation plans and end-of-life decisions are taken based on the diagnosis [8,9]. Several neurobehavioral scales have emerged during the last 15 years to provide standardized means to assess the level of consciousness and make an accurate diagnosis. Among them, the Coma Recovery Scale Revised (CRS-R) is considered as the gold standard [10]. This scale evaluates the auditory, visual, motor and oromotor/verbal functions as well as communication and arousal, and was specially designed for the differential diagnosis of UWS and MCS [11].

Identifying the first behavioral signs denoting a change of diagnosis (i.e., a transition from UWS to MCS or from MCS to EMCS) might facilitate and guide the clinical decision-making of specific therapeutic options. Yet, only a few studies have been conducted using standardized tools so far. Taylor and colleagues first documented the recovery profiles of 9 patients with TBI during their course of emergence from MCS, using the Western Neuro Sensory Stimulation Profile [12]. They showed that 55% (5/9) of them recovered both functional object use and communication at the same time, while the others recovered either functional communication or object use. This was confirmed by Noé and colleagues who followed 12 patients in UWS and 20 patients in MCS during one year of inpatient rehabilitation [13]. Seven patients in MCS and one in UWS emerged from MCS, which was mostly associated with the recovery of both functional communication and object use. Lesser chronicity and the presence of more than visual behavioral responses at admission significantly predicted the emergence. In another study, Bagnato and colleagues assessed 37 patients in UWS with and without TBI with the CRS-R up to 12 months after the admission to the rehabilitation centre [14]. Of the total group of patients, 21 evolved to the MCS, with around 90% of them recovering consciousness within three months. At the first diagnosis of MCS, about half of the patients showed signs denoting a transition from UWS to MCS in only one subscale: primarily the visual subscale, followed by the motor subscale. When two signs were detected concurrently, the visual and motor subscales were always involved. The high prevalence of visual and motor behaviors in the diagnosis of MCS was confirmed by two large studies documenting the most frequently observed signs of consciousness in patients in MCS using the CRS-R. In the first one, visual signs were identified in more than 80% of the cases, and motor signs in almost 60% of the cases [15]. The second study found visual fixation, visual pursuit and reproducible movement to command as the most frequently observed signs denoting a transition from UWS to MCS, with an occurrence in more than 50% of patients [16]. A recent retrospective observational study investigated the time course of recovery and the first behavioral signs that appeared in a sample of 79 (sub)acute patients with DOC biweekly assessed with the CRS-R [17]. Visual pursuit was the most common initial sign of MCS, followed by reproducible movement to command and automatic movements. Median time to recovery of consciousness was 44 days. Etiology did not significantly affect time to recovery of consciousness but motor signs were more likely to appear in first place in patients with TBI compared to other etiologies. Finally, Bareham and colleagues assessed 16 patients in UWS and 22 in MCS every three months with the CRS-R for a maximum of two years [18]. Of the 11 UWS who evolved to the MCS, 10 recovered a sign belonging to the visual subscale (two with visual fixation and eight with visual pursuit) and one recovered reproducible movement to command. Of the three patients with MCS who emerged from this state, two recovered functional communication and one recovered functional objects use.

Although these studies provide valuable clinical information, they also present some limitations that restrict the interpretation and generalization of their findings (i.e., poor temporal accuracy [13,14,18], limited sample size [12–14,18], use of non-standardized instrument [12] or inclusion of (sub)acute patients only [17]). In addition, the literature about EMCS is scant.

The objective of our study was to describe the first behavioral signs denoting a change of diagnosis (i.e., a transition from UWS to MCS, or from MCS to EMCS) as well as the demographic and clinical factors that might influence this transition, within a representative sample of patients with chronic DOC by means of weekly CRS-R assessments.

Methods

Participants

Demographic and behavioral data were retrospectively extracted from a database containing clinical data of patients with DOC admitted to an inpatient neurorehabilitation program comprising daily physical rehabilitation procedures and multimodal sensory stimulation. Participants met the following inclusion criteria: a) at least 18 years old; b) documented medical diagnosis of CRS-R–based diagnosis of UWS or MCS at admission to the neurorehabilitation program, and c) evidence of transition from one state to another during the inpatient rehabilitation stay.

The study was approved by Comité Ético de Investigación Clínica del Hospital Clínic Universitari de València (2019002) and was registered at clinicaltrials.gov (NCT04687397).

Written informed consent to participate in the study was obtained from the legal representative of all patients.

Procedure

All patients were assessed with the Spanish version of the CRS-R [13] five times in the following two weeks from admission and then weekly until emergence from MCS, discharge or decease. Assessments were conducted at the same time of the day, by an experienced neuropsychologist trained in the use of the CRS-R. Transitions between clinical conditions were confirmed by two consecutive assessments. All transitions were identified (from UWS to MCS or EMCS, and from MCS to EMCS). Data collection included the week of transition from the injury, the clinical condition and the behavioral sign(s) that led to the transition, retrieved from the available scores to the CRS-R.

Statistical analyses

The normality of the data was investigated using Shapiro-Wilk tests. Descriptive statistics (median and interquartile range [IQR]) were used to summarize demographic and clinical information. Percentages were used to show incidence rates for the first behavioral signs of MCS or EMCS observed at the time of transition. Differences in etiology, sex, age and time from injury to admission were assessed between patients who transitioned and those who did not using Chi-square and Mann-Whitney U tests. Differences between TBI and non-TBI patients in time to recovery of consciousness and the number of conscious behaviors observed at transition were assessed using Mann-Whitney U tests. A binomial logistic regression was performed to ascertain the effects of time since injury, age, etiology and sex (covariates) on the likelihood of transition to MCS (dependent variable). We also evaluated the effects of etiology, time since injury, age, sex, number of behaviors at admission and presence or absence of intentional communication at admission (covariates) on the likelihood of emergence from the MCS (dependent variable).

Results

Participants

Between May 2004 and October 2019, 197 patients with DOC after a severe acquired brain injury were admitted to the neurorehabilitation program. Twelve patients were excluded because they were under 18 years old. No evidence of transition to another state was observed in 107 of the remaining patients. The demographic and clinical data of the 88 patients initially diagnosed as UWS and the 97 patients initially diagnosed as MCS are summarized in Table 1.

The remaining 78 patients (42% of the initial sample) were included for analysis of the behavioral signs that led to a transition between states (Figure 1). From them, 33 patients, 25 men and 8 women, were in UWS after a traumatic (n=21) or non-traumatic injury (n=12), had a median age of 31 [23-39] years and a median time since injury of 96 days [54–145] at admission. In the last assessment of the 33 patients who transitioned, 23 had evolved to the MCS and 10 of them had further emerged from the MCS. This latter subgroup of patients included 9 men and a woman, had a median age of 26 [21-32] years and a median time since injury of 120 [88–198] days. All of these patients but one had a TBI. The remaining 45 patients who were analyzed were in MCS and emerged from this state. This group included 34 men and 9 women who had a traumatic (n=27) or non-traumatic injury (n=18), had a median age of 43 [26-54] years and a median time since injury of 85 [62–113] days at admission.

When all patients in UWS and MCS were analyzed as a whole, 49 of 81 patients with TBI (60%) transitioned, while only 29 of 104 (28%) patients with non-TBI did ($p<.001$). Time from injury to admission was significantly shorter in patients who transitioned compared to those who did not (88 [62-128] *vs* 121 [87-236] days; $U=2555$, $p<.001$). Patients who transitioned were also significantly younger than those who did not (37 [25-50.4] *vs* 47 [30.5-59]; $U=3016$, $p=.001$). No significant difference was found between men and women: 58 of 134 men transitioned (43%) compared to 20 of 51 women (39%) (p=.251).

Transition from unresponsive wakefulness syndrome to other states

Transition from UWS to MCS was evidenced by a single behavioral sign in 24 cases (73%), by two signs in eight cases (24%), and by three signs in the remaining case (3%) (Figure 2). Two patients directly progressed from the UWS to EMCS by showing functional communication. The median time since injury at the moment of transition from UWS to other states was 162 [103-222] days.

Among patients who exhibited one behavioral sign denoting a transition, 17 patients showed a visual sign (15 patients showed visual fixation and two patients showed visual pursuit), five showed a motor sign (localization to noxious stimulation), one showed an auditory sign (reproducible movement to command) and the remaining patient showed functional communication. All patients who concurrently exhibited two behavioral signs showed both visual and motor signs. Specifically, four patients showed visual pursuit and object manipulation, three showed visual fixation and localization to noxious stimulation and the remaining patient showed visual fixation and automatic motor response. The only patient who exhibited three concurrent signs showed visual pursuit, localization to noxious stimulation and functional communication.

From the 88 patients in UWS, 21 of 36 patients with TBI (58%) progressed to the MCS, whereas only 12 of 52 patients with non-TBI (23%) did (χ^2=11.282; p=.001). Patients with TBI were significantly younger than patients with non-TBI (U=58; p=.010). However, no differences in time from injury to transition (U=115.5; p=.593) or the number of behavioral signs at the time of transition were found between patients with and without TBI (U=124; p=.776). No significant difference was either found between sexes. Nine of the 26 women (35%) transitioned to MCS and

24 of the 62 men (39%) did (χ^2=.131; p=.717). UWS patients who evolved to MCS were significantly younger than those who did not (31 [23-39] *vs* 46 [30-58]; U=544; p=.002). Finally, time since injury to admission was not significantly different between patients who progressed to the MCS and those who did not (96 [54-145] *vs* 108 [84-187] days; U=741; p=.151).

The logistic regression model was statistically significant ($\chi^2(4)$=22.212, p<.000) with 30.4% of the variance of transition to MCS explained by the model and 77.3% of cases correctly classified. The time since injury (p=.039), age (p=.013) and etiology (p=.017) added significantly to the model. Increasing time since injury and age were associated with a reduction in the likelihood of transition to MCS, while a traumatic etiology was associated with an increased likelihood of transition to MCS (Table 2).

Transition from minimally consciousness state to emergence from minimally conscious state

The transition from MCS to EMCS was indicated by one behavioral sign in 35 patients (64%) and by two signs in 20 patients (36%) (Figure 3). Among patients who exhibited one behavioral sign, 18 showed functional communication and 17 showed functional object use. The median time since injury at the moment of transition was 172 days [59-668].

Emergence from MCS was more likely to occur among patients in MCS than among those in UWS (χ^2=27.099, p<.001). While 45 patients admitted in MCS (46%) emerged from this state, only 10 patients admitted in UWS (11%) did. The probability of emergence was significantly higher in patients with TBI, who had a rate of 36 over 54 cases (67%), than in patients with non-TBI, who had a rate of 19 over 53 cases (36%) (χ^2=10.169; p=.001). Patients with TBI were significantly younger than patients with non-TBI (U=500; p<.001). However, no differences in time from injury to emergence (U=323.5; p=.743) or number of behavioral signs at emergence were found between patients with and without TBI (U=339.5; p=.958). Comparable probability of emergence was found between men and women. Precisely, 43 men over 81 (53%) and 12 women over 26 (46%) (χ^2=.379; p=.538). Patients in MCS who emerged were also similar in terms of age to those who did not [38 (16) *vs* 46 (16); U=1018; p=.101]. Time from injury to admission was significantly shorter in patients who emerged from MCS compared to those who remained in that state [109 (72) *vs* 210 (174) days; U=717; p<.001]. The number of behavioral signs observed at admission was linked to probability of emergence from MCS (χ^2=20.019; p<.001). Patients showing one behavioral sign at admission had 33% likelihood to emerge from the MCS, compared to 51% likelihood when showing two signs, and 91% likelihood when showing three or more signs. Finally, patients displaying intentional communication at admission were more likely to emerge from the MCS (89% or 16 from 18) than those who scored zero at that subscale (44% or 39 from 89; χ^2=12.174; p<.001).

The logistic regression model was statistically significant ($\chi^2(7)$=65.811, p<.000), with 61.3% of the variance of emergence explained by the model and 83.2% of cases correctly classified. The time since injury (p=.006) and number of behavioral signs observed at admission (p=.013) added significantly to the model. A high number of behavioral signs present at admission was associated with an increased likelihood of emergence, while increasing time since injury was associated with a reduction in the likelihood of emergence (Table 3).

Discussion

The aims of this study were to document the recovery of patients with DOC by identifying the first behavioral signs denoting the transition between clinical states as well as the demographic and clinical factors that might influence this change of diagnosis. We examined a large sample of patients admitted to a long-term neurorehabilitation program including patients with UWS who transitioned to MCS or EMCS and patients with MCS who emerged from this state. Clinical examination was performed with the CRS-R five times within the two weeks following admission and then weekly until emergence from MCS, discharge or death. It is important to point out that this study only focused on behaviors comprised among the CRS-R items and therefore does not encompass all the possible intentional behaviors in DOC. Some studies indeed showed that observation of spontaneous motor behaviors (that may or may not be intentional) [19] or use of subjective approaches based on caregivers' collective intelligence [20] could help diagnose covert consciousness.

Transition from unresponsive wakefulness syndrome to other states

The higher chance to transition from UWS to other states by exhibiting one single sign is in accordance with the findings of Martens et al, who reported the same percentage [17]. The presentation of one single sign, although still most likely to occur, was reported to be lower in the study of Bagnato et al (52%) [14]. This emphasizes the importance of conducting repeated assessments in various time periods to minimize the chance of missing behavioral signs denoting a transition between states. In this regard, Wannez et al advised to perform at least five assessments with the CRS-R within a short time interval to counter behavioral fluctuations and thereby reduce misdiagnosis [21]. Consequently, although our patients were assessed repeatedly in our study (i.e., weekly), the data might have looked different if they had been evaluated daily.

Interestingly, the first four most prevalent behavioral signs observed at transition from UWS to MCS are identical to those found by Bagnato et al, although in a slightly different order [14]. Similarly to our findings, where visual fixation was the most frequently observed sign (57% of cases), followed by localization to noxious stimulation (27%), visual pursuit (21%) and object manipulation (12%), Bagnato and collaborators reported visual pursuit as the most commonly observed sign (43%), followed by visual fixation (33%), localization to noxious stimulation (28%)

and object manipulation (19%). The reduced temporal accuracy of this latter study, with assessments at 1, 2, 3, 6, and 12 months from admission, could explain the discrepancies with our study, as some of the patients who showed visual pursuit could have previously shown visual fixation between assessments. In contrast to these two studies, although Martens et al also observed visual pursuit as one of the most frequent signs denoting a transition from UWS to MCS (41%), reproducible movement to command (25%) and automatic movement (24%) ranked second and third [17]. These differences might be explained by the different time windows of the studies. Indeed, while Martens at al included (sub)acute patients presenting an early recovery, our study focused on recovery beyond three months post-injury. They might also be explained by fluctuations in the demonstration of behavioral signs that have, for instance, been reported in the auditory channel [22].

The high prevalence of visual fixation and pursuit in all these studies is concordant with previous reports supporting that diagnosis of MCS is predominantly done based on the visual subscale of the CRS-R [15,16]. Particularly, visual pursuit is considered as a key descriptor of MCS and has been documented as an early indicator of consciousness, as well as a good prognostic marker, especially in the acute stage [13,23,24]. Visual fixation would involve cortical and subcortical structures but require less complex coordination than saccades [25]. This might therefore support the recovery of visual fixation before visual pursuit and explain the higher prevalence of visual fixation over visual pursuit in our study. However, the reliability of visual fixation as a criterion of MCS is still a matter of debate [26,27]. Visual fixation might indeed be initiated reflexively (from the parietal eye field via the superior colliculus of the midbrain) or intentionally (from the frontal eye field via the paramedian pontine reticular formation) [25]. For this reason, international guidelines insist on the consistency and the sustained *vs* fleeting aspect of fixation [4,28]. Conversely, visual pursuit depends upon a widespread fronto-temporo-parietal network projecting on pontic and cerebellar structures [29]. The recovery of this behavioral sign would therefore reflect at least partial recuperation of brainstem-cortical interactions and overall brain arrangement, which is thought to be necessary to sustain consciousness [23].

The presence of localization of noxious stimuli and object manipulation among the commonest behavioral signs observed in our study is also in line with previous studies that highlighted the importance of visual and motor aspects when assessing the level of consciousness [13,15]. For instance, Noé et al found that 55% of patients were diagnosed as in MCS by showing only visual signs, while 20% of patients showed both visual and motor signs [13]. Similarly, in the study of Bagnato et al, when patients showed two concurrent behavioral signs on the CRS-R, it always concerned the visual and motor subscales [14]. Clinicians should therefore be advised to pay particular attention to the motor subscale in the presence of any visual impairment.

Our findings regarding the distinguishing characteristics between patients who transitioned from UWS to MCS and those who did not are supported by previous studies, which identified age [4,30–32] and etiology [4,13,33] as predictors of recovery in patients with UWS. However, conclusions must be drawn carefully because, although patients with TBI seem to be more likely to progress compared to other etiologies, they also tend to be younger than patients with non-TBI etiologies. Consequently, the higher probability of transition might not be attributed to the etiology but only or also to age. Our results also showed that time since injury is a predictive factor of transition to MCS, which is consistent with previous studies that identified it as an important predictor of both short [34] and long-term outcomes [32] in DOC. Finally, sex did not show to influence transition in our study, thus confirming previous findings [30,35,36].

Transition from minimally consciousness state to emergence from minimally conscious state

The 64% likelihood of emergence from MCS by showing one single behavioral sign is higher than that reported by two previous studies, which reported the presence of two signs in at least half of the cases [12,13], but lower than in the study of Bareham et al, who observed two signs in only one of four patients who emerged [32]. The results of these studies, however, should be taken carefully as they included less than ten patients who emerged from the MCS.

Considering patients who emerged from MCS by showing only one behavioral sign in our study, the proportion of functional communication or functional objects use was comparable to the findings of Taylor et al [12]. Functional communication was, in contrast, less common than in other studies, which identified this sign in 75% and 67% of the cases [13,32]. The absence of follow-up after discharge in our study prevented us from identifying predictive factors of a long-term good prognosis. Future studies should explore whether the type of behavioral sign that leads to EMCS (i.e., functional communication or objects use) influences the long-term clinical evolution.

As for the transition to MCS, differences in etiology and time since injury were found between patients who emerged and those who did not. The influence of time since injury on emergence from MCS is supported by Noe et al, who identified this factor as a predictor of EMCS [13], as well as by other studies [4,34,37]. We also found that patients displaying intentional communication and higher number of signs at admission had a higher probability of emergence from MCS. It would therefore be advisable that these patients receive continued attention through close monitoring to detect any sign of clinical progress. When using logistic regression analyses, however, only the time since injury and the number of behavioral signs observed at admission were found to be predictive factors of emergence from MCS. The absence of etiology is in line with the results of Steppacher et al showing that etiology could predict long-term outcome for patients with UWS, but not patients with MCS [30].

Conclusions

Transition from one consciousness state to another was predominantly signaled by only one behavioral sign, which supports the need to perform repeated evaluations at different time periods to increase the likelihood of detection of these signs. The evolution to the MCS was predominantly signaled by visual fixation, followed by localization to noxious stimulation, visual pursuit and objects manipulation, and could be predicted by etiology, time since injury and age. EMCS was likewise signaled by functional communication and functional object use and could be predicted by time since injury and number of behavioral signs at admission.

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Disclosure of interest

The authors declare that they have no competing interest.

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Figures

Figure 1. Flowchart of patients included in the study

The figure illustrates the inclusion of patients in the study. UWS: unresponsive wakefulness syndrome. MCS: minimally conscious state.

Figure 2. Number and types of behavioral signs that evidenced transition from unresponsive wakefulness syndrome to other states

The figure summarizes the number and types of behavioral signs that denoted transition from UWS to other states. UWS: unresponsive wakefulness syndrome. MCS: minimally conscious state.

Figure 3. Number and types of behavioral signs that evidenced transition from minimally consciousness state to emergence from minimally conscious state

The figure summarizes the number and types of behavioral signs that denoted transition from MCS to emergence from MCS. MCS: minimally conscious state

Table 1. Demographic and clinical data summary of the patients initially diagnosed as either unresponsive wakefulness syndrome or minimally conscious state

	UWS (N=88)		MCS (N=97)	
	Transition (N=33)	**No transition (N=55)**	**Transition (N=45)**	**No transition (N=52)**
Median days since injury [IQR]	96 [54-145]	108 [84-187]	85 [62-113]	141 [104-275]
Days between admission and transition	47 [32-71]	NA	53 [34-94]	NA
Sex	8 women	17 women	9 women	14 women
Median age in years [IQR]	31 [23-39]	46 [30-58]	43 [26-54]	48 [32-60]
Etiologies				
Traumatic brain injury	21	15	27	18
Anoxia	7	27	5	7
Hemorrhagic stroke	5	11	10	24
Ischemic stroke	-	1	-	1
Encephalitis	-	1	-	-
Intoxication	-	-	1	-
Infection	-	-	1	1
Tumor	-	-	1	1

Abbreviations: UWS=Unresponsive Wakefulness Syndrome; MCS=Minimally Conscious State; TBI=Traumatic Brain Injury, IQR=Interquartile Range; NA=Non Applicable.

Table 2. Logistic regression analysis for the transition to minimally conscious state.

	B	SE	Wald	df	p-value	Exp(B)	95% Confidence interval for Exp(B)
Time since injury	.006	.003	4.240	1	.039*	.994	.988 – 1.000
Age	-.046	.019	6.130	1	.013*	.955	.920 – .990
Etiology	-1.326	.555	5.702	1	.017*	.265	.089 – .788
Sex	.837	.619	1.827	1	.177	2.308	.686 – 7.766

**indicates significance at p<.05.*

Table 3. Logistic regression analyses for the emergence from minimally conscious state

	B	SE	Wald	df	p-value	Exp(B)	95% Confidence interval for Exp(B)
Etiology	.951	.696	1.868	1	.172	2.589	.662 – 10.125
Time since injury	-.016	.006	7.571	1	.006*	.984	.973 - .995
Intentional communication	1.053	1.518	.481	1	.488	2.866	.146 – 56.164
Number of signs at admission	1.218	.489	6.198	1	.013*	3.381	1.296 – 8.822
Sex	.887	.704	1.587	1	.208	2.428	.611 – 9.652
Age	-.025	.021	1.318	1	.251	.976	.936 – 1.017
Diagnosis at admission	23.438	10302.627	.000	1	.998	1.510E10	.000

**indicates significance at p<.05*

Figure 1

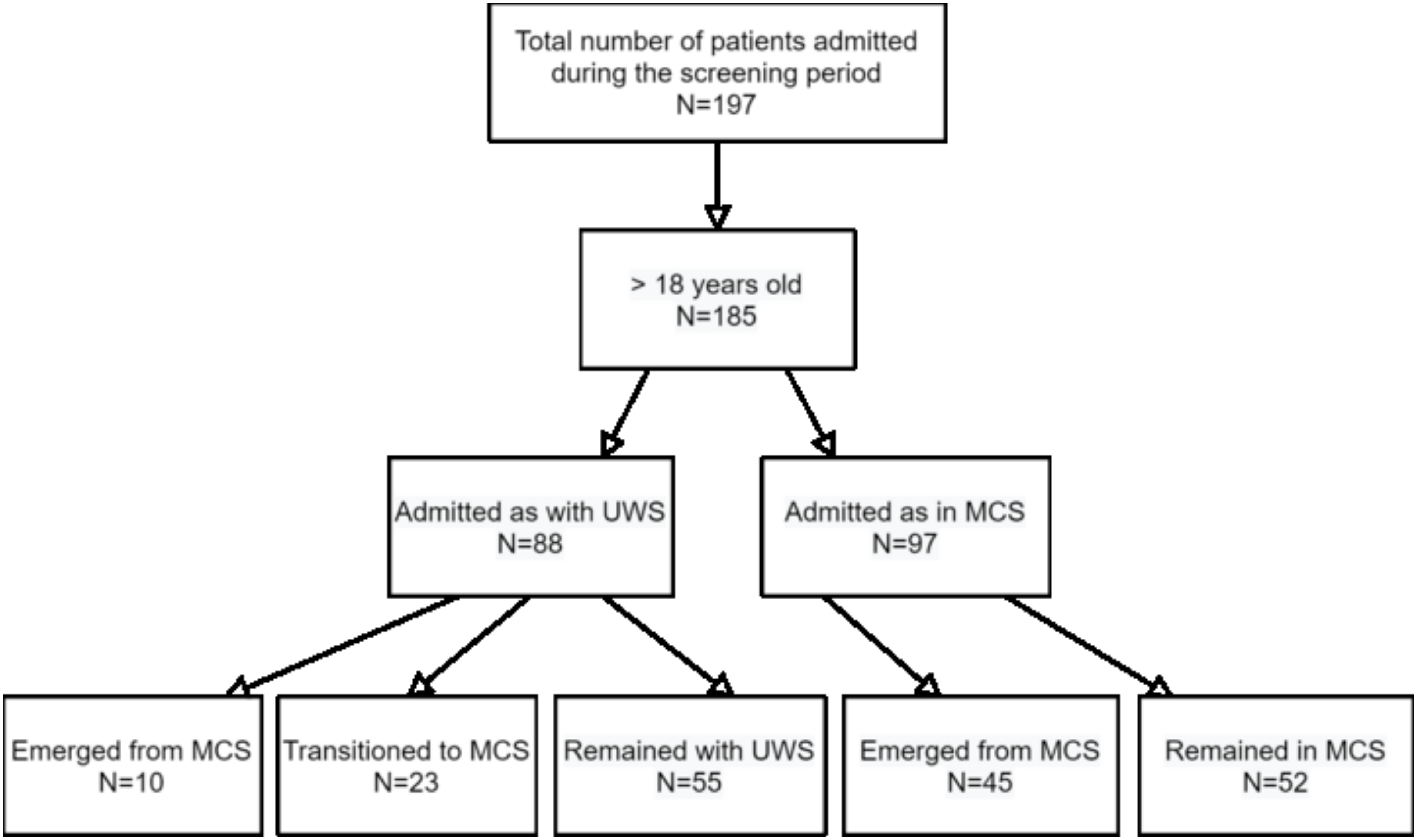
Total number of patients admitted during the screening period N=197
> 18 years old N=185
Admitted as with UWS N=88
Admitted as in MCS N=97
Emerged from MCS N=10
Transitioned to MCS N=23
Remained with UWS N=55
Emerged from MCS N=45
Remained in MCS N=52

Figure 2

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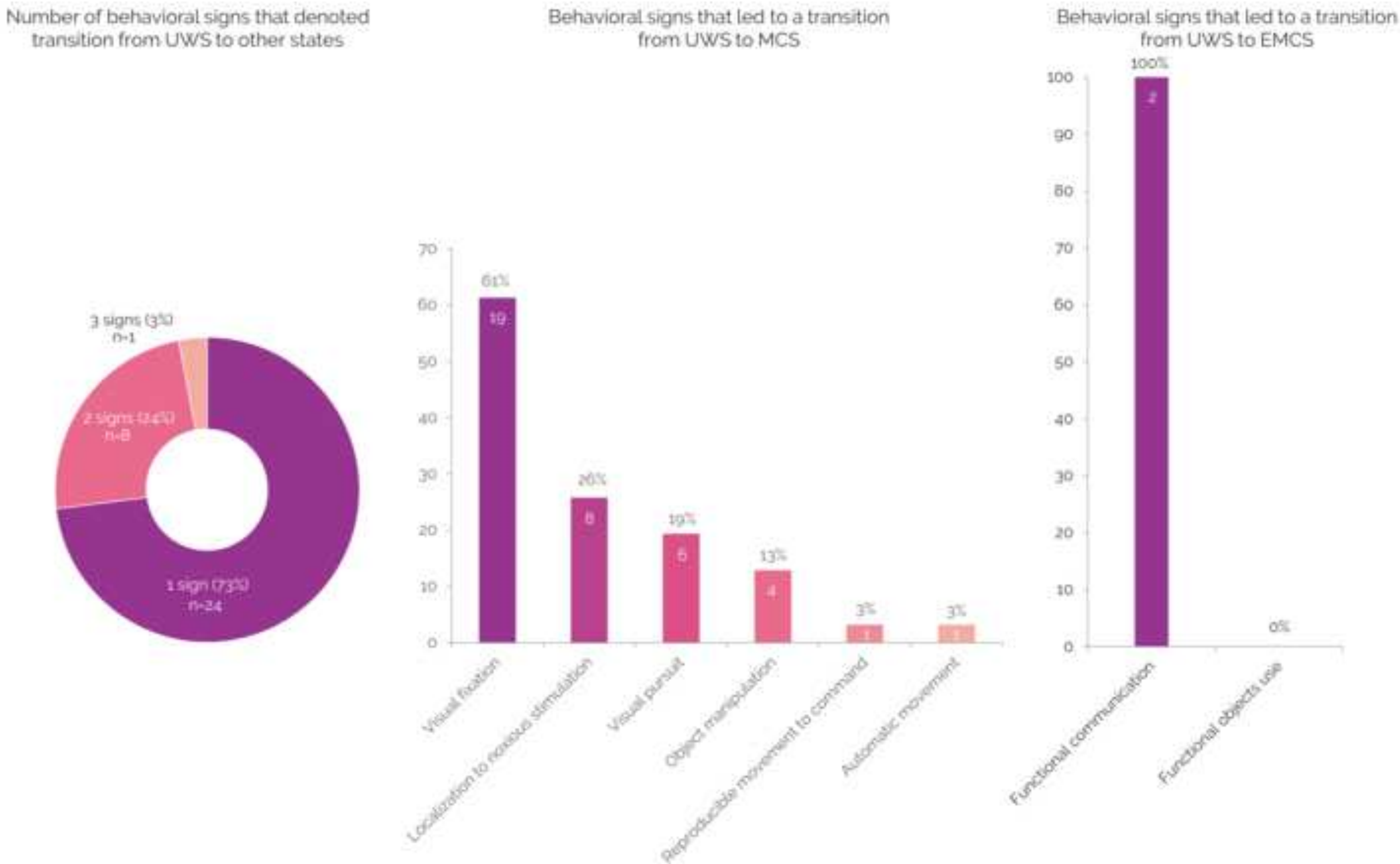

Figure 3

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