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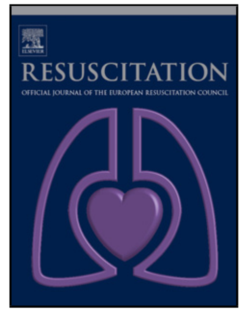

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TITLE PAGE

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ABSTRACT

Aim: To date, no clinical test is able to predict cognitive and functional outcome of cardiac arrest survivors. Improvement of auditory discrimination in acute coma indicates survival with high specificity. Whether the degree of this improvement is indicative of recovery remains unknown. Here we investigated if progression of auditory discrimination can predict cognitive and functional outcome.

Methods: We prospectively recorded electroencephalography responses to auditory stimuli of post-anoxic comatose patients on the first and second day after admission. For each recording, auditory discrimination was quantified and its evolution over the two recordings was used to classify survivors as "predicted" when it increased vs. "other" if not. Cognitive functions were tested on awakening and functional outcome was assessed at 3 months using the Cerebral Performance Categories (CPC) scale.

Results: Thirty-two patients were included, 14 "predicted survivors" and 18 "other survivors". "Predicted survivors" were more likely to recover basic cognitive functions shortly after awakening (ability to follow a standardized neuropsychological battery: 86% vs. 44%; p=0.03 (Fisher)) and to show a very good functional outcome at 3 months (CPC 1: 86% vs. 33%; p=0.004 (Fisher)). Moreover, progression of auditory discrimination during coma was strongly correlated with cognitive performance on awakening (phonemic verbal fluency: r_s=0.48; p=0.009 (Spearman)).

Conclusions: Progression of auditory discrimination during coma provides early indication of future recovery of cognitive functions. The degree of improvement is informative of the degree of functional impairment. If confirmed in a larger cohort, this test would be the first to predict detailed outcome at the single-patient level.

INTRODUCTION

Cardiac arrest affects yearly more than 350’000 people in the US [1]. Half of the hospital admitted patients survive to discharge, mostly after post-anoxic coma. Among those, about 50% may undergo some degree of long-term cognitive impairment [2,3]. In this condition, predicting survival, and especially cognitive and functional outcome, is a major concern for clinicians and relatives. To date, clinical evaluations during coma (such as clinical examination, neurophysiological tests, biochemical markers, and brain imaging) are used to predict poor outcome [4,5]. Previous studies investigating the contribution of these variables for the prediction of functional outcome are sparse and showed inconclusive results. Only one study reported that the S-100B protein (reflecting glial suffering) correlated to long-term cognitive performances [6], but these results have never been replicated.

In contrast to these clinical evaluations, assessment of auditory functions during coma showed promising results in predicting survival [7–12]. Patients’ auditory response is typically quantified by measuring the so-called mismatch negativity (MMN) component, elicited automatically upon occurrence of a deviant stimulus in a train of regularly repeated stimuli [13]. The presence of an MMN in comatose patients from various etiologies has been correlated with awakening from coma [14–16]. Using a multivariate EEG decoding algorithm, our group previously demonstrated that an improvement in auditory discrimination between the first and the second day of coma predicted survival at 3 months in patients treated with therapeutic hypothermia [10,11]. However, some survivors did not show any improvement in decoding performance. This raises two questions about the contribution of auditory discrimination to outcome prediction: (1) Is this difference informative of survivors' functional outcome? (2) Is the degree of improvement indicative of the degree of recovery?

In this study, we measured the evolution of auditory discrimination during acute coma and assessed cognitive functioning at awakening in a cohort of cardiac arrest survivors, hypothesizing that the progression of auditory discrimination during early coma mirrors brain recovery measured by neuropsychological and functional evaluations. More specifically, we expected that survivors showing improved auditory discrimination during coma would exhibit better cognitive and functional outcome, and postulated an association between the progression of auditory discrimination and outcome measures. To our knowledge, this is the first attempt to use the evolution of auditory processing during early coma for prediction functional status in this clinical setting.

METHODS

Study design and population

Between October 2012 and September 2015, 119 adult post-anoxic comatose patients were admitted to the Department of Intensive Care Medicine of the Lausanne University Hospital (CHUV). Ninety-six (81%) could be prospectively recorded with EEG on the first and second day of coma using the MMN paradigm. About half of them (49; 51% of tested patients) awoke from coma and 17 (37%) could not be tested neuropsychologically shortly after awakening, due to early transfer to other hospitals (see Figure 1). Therefore, the analysed cohort is constituted of 32 patients (9 women; mean age ± standard deviation: 56 ± 14 years).

All but five patients were treated with mild therapeutic hypothermia to 33-34°C for the first 24 hours, induced through ice packs and the Arctic Sun® system surface cooling device (Medivance, Louisville, CO, USA), in agreement with current guidelines [17]. Midazolam (0.1 mg/kg/h) and fentanyl (1.5 µg/kg/h) were given for sedation-analgesia, and vecuronium (0.1 mg/kg boluses) in case of shivering. Patients with myoclonus or electrographic epileptic seizures received intravenous, nonsedating anti-epileptic treatment (valproate, levetiracetam). Return to normal temperature was controlled at 0.5°C increase per hour until 37°C. Sedation was discontinued at 36°C. Four out of the five patients not receiving therapeutic hypotherma had targeted temperature management at 36°C for 24h, the remaining patient had no temperature control; all were sedated as the hypothermic patients. The decision to prescribe hypothermia was taken according to patient's clinical situation and following latest recommendations [18]. On the second day, all patients were normothermic.

Decision to withdraw intensive care was discussed interdisciplinary within 7 days after admission, based on a multimodal approach [19]. Extubation was decided based on the clinical status (oriented and reproducible motor response to commands), in absence of respiratory problems. Importantly, auditory discrimination was not used to take any of these decisions, and its results were not communicated to the healthcare teams.

This study received full approval from our Ethic Commission. Informed consent was obtained in the first days from a family member or a physician not involved in the research protocol. After awakening, agreement was asked again directly to the patient or to a close relative.

Mismatch Negativity paradigm

As described in details in a previous study [10], we used an auditory MMN paradigm including one standard and three types of deviant sounds (pitch, duration and location deviants). Stimuli were separated by a constant interval of 950 ms between the onsets of two sounds. Standards were 1000 Hz sinusoidal tones of 100 ms duration and 0 ms inter-aural time difference. Pitch deviants were at 1200 Hz, duration deviants lasted 150 ms, and location deviants had 700 ms inter-aural time difference (left ear leading). Standard sounds were presented in 70%, while each type of deviant was presented in 10% of trials. A sequence included 500 standard sounds and 50 of each type of deviant sounds organized in a pseudo-random order. The same sequence was used in three consecutive blocks. Auditory stimuli were displayed at 90dB via specialized ER4 Etymotic earphones (Etymotic Research, Inc.) using E-prime 2.0 software for patients included up to 2014 (Psychology Software Tools Inc., Pittsburgh, PA) or the Psychophysics Toolbox (Psychtoolbox-3) extensions in Matlab [20–22]. The procedure was identical for recordings on the first and second day of coma.

EEG acquisition and pre-processing

EEG recordings were performed as detailed previously [19,23] using a 19 electrodes montage following the international 10-20 system (Viasys Neurocare, Madison, WI, USA; sampling rate of 1024 Hz, online reference to Fpz). For each patient, two recordings were collected: on the first day after admission, during hypothermia or normothermia but always under active sedation, and on the second day of coma, during normothermic conditions (at least 35°C), after sedation weaning. The recording included the MMN paradigm, run after the routine clinical part lasting 20-30 minutes [10,11].

Preprocessing was performed using Cartool v.3.43 [24]. We extracted peri-stimulus epochs spanning 50 ms before to 500 ms post-stimulus onset. An artefact rejection criterion of ±100 µV was applied offline. Data were re-referenced offline to the common average reference, 0.18–40 Hz band-pass filtered, and 50 Hz notch filtered. No prestimulus baseline correction was applied.

Decoding of single-trial EEG

As in our previous studies, we analysed auditory evoked responses to standard and deviant sounds using a multivariate EEG analysis [25–27], extracting in a data-driven manner time periods and prototypical voltage topographies discriminating between the two conditions. This offers the advantage of being free of *a priori* hypotheses about electrode location where a stimulus-related activity would be expected, and is independent of any inclusion criteria aside from having sufficient artifact-free trials. Because this method is based on voltage topographies, an accurate performance results from activation of different underlying neural generators between experimental conditions [26].

We applied analyses separately for each patient and recording to discriminate the neural responses to standard versus deviants. Artifact-free trials were divided in a training dataset, used to model the distribution of voltage topographies by a Mixture of Gaussians, and a test dataset that applied the resulting model to classify each single-trial. The decoding performance was measured as the area under the receiver operating characteristic curve (AUC) [28], quantifying the difference in brain responses to standard versus deviants from 0 to 1 (1 = perfect decoding), and averaged across the three types of deviant sounds, to obtain a unique value for each recording. Progression of auditory discrimination was calculated as the difference between the second and the first recording.

Early cognitive functioning

Few days after awakening (defined as the extubation) and in a standard inpatient unit, cognitive functioning was tested by a neuropsychologist blinded to auditory discrimination results using a standardized neuropsychological battery during around 90 minutes. It included validated tests evaluating seven main cognitive domains: language, praxia, gnosia, long-term and short-term memory, executive functions, and attention (see Supplementary material for a detailed description). A cognitive domain was considered as affected when scores were severely impaired (performance below the 5th percentile) or when the patient was not able to perform the test.

Functional outcome

Long-term global outcome was assessed using the Cerebral Performance Categories scale (CPC; Booth, Boone, Tomlinson, & Detsky, 2004) at 3 months follow-up through a short semi-structured phone interview by a research nurse blinded both to auditory discrimination and cognitive testing. Outcomes categorized as “very good” for CPC 1 and “moderate” for CPC 2-3; no patient was vegetative (CPC 4).

Coma duration (time from admission to extubation; reflecting rapidity of brain function recovery), hospital stay duration (time from admission to discharge from any acute unit; reflecting recovery speed of global functions), and indication to neurorehabilitation were considered as additional variables of interest. Indication for intensive neurorehabilitative treatment reflects an interdisciplinary decision; since only patients with serious cognitive impairment were offered this option, this may be seen as a surrogate of the quality of recovery.

Relation between progression of auditory discrimination and outcome

We applied Spearman’s rank correlations to investigate this relationship. In order to test whether “predicted survivors” and “other survivors” differed in their outcome, we compared cognitive and functional measures, using two-sided non-parametric tests (Wilcoxon signed rank test) or categorical tests (Fisher exact test), as appropriate. We did not correct for multiple comparisons given the exploratory nature of this study. All analyses were run on Matlab 2011b.

RESULTS

Auditory discrimination results during coma

Among the 32 tested survivors, 14 (44%) showed an increase in auditory discrimination over the first two coma days (“predicted survivors”), while 18 did not improve (“other survivors”) (Figure 2). The mean (± SEM) decoding performance for the first recording was 0.60 ± 0.009 for “predicted survivors” and 0.63 ± 0.006 for “other survivors”, and 0.64 ± 0.009 and 0.59 ± 0.006 for the second recording, respectively. Nine of the 32 patients recovered minimal consciousness (still intubated but at times responding to commands) at the moment of the second recording (five in “predicted survivors”, four in “other survivors”).

Cognitive functioning on awakening

Neuropsychological testing took place on average 10 ± 7 days (here and in the following: mean ± standard deviation) after awakening (see Figure 3 for detailed test results). More than one third of patients (12/32; 38%) could not perform the whole battery, and 14 (44%) were not oriented to time. Phonemic verbal fluency was impaired in 15/29 tested patients (52%), while this was the case in 11/28 (39%) for semantic verbal fluency and in 4/31 (13%) for digit span forward

Functional outcome

At 3 months follow-up, 18 (56%) patients showed very good (CPC 1) and 13 (41%) moderate recovery (ten with CPC 2, three with CPC 3); one died few weeks after awakening (CPC 5) after decision to provide palliative care in a poor prognosis context related to severe comorbidities. Among the 20 patients who completed the whole neuropsychological examination on awakening, 16 (80%) had a CPC 1 and four (20%) a CPC 2; there was no patient with CPC 3. In comparison, only two (17%) out of the 12 patients who could not complete the neuropsychological assessment on awakening had a CPC 1; six (50%) had a CPC 2, three (25%) a CPC 3 and one (8%) died. The proportion of patients with very good recovery (CPC 1) vs. moderate recovery (CPC 2-3) was significantly different in these two groups ($p = 0.002$; Fischer exact test).

The average coma duration was 6 ± 5 days, and hospital stay was 22 ± 18 days; 12/32 (38%) patients were addressed to a specialized neurorehabilitation center.

To ensure that there was no selection bias in the present cohort, we also collected the CPC scores at 3 months in survivors not included (see Figure 1). Nine out of 17 (53%) displayed "very good" recovery, seven (41%) "moderate" (five with CPC 2, two with CPC 3), and one died after awakening. The proportion of patients with very good recovery was similar in included and not included subjects (i.e. 56% and 53% respectively; Fisher's exact test $p = 1$).

Relation between progression of auditory discrimination and outcome

We included in this analysis only cognitive measures available for most patients, i.e. ability to complete the whole battery, phonemic and semantic fluency, digit span forward, and orientation to time. Auditory discrimination progression during early coma and cognitive outcome measures showed significant positive correlations for both phonemic ($r_s = 0.48$, $p = 0.009$) and semantic verbal fluency scores ($r_s = 0.45$, $p = 0.02$), indicating that higher auditory discrimination improvement was associated with better cognitive performance (see Figure 4A and 4B respectively). Moreover, progression of auditory discrimination showed a negative relationship with both coma duration ($r_s = -0.4$, $p = 0.02$) and hospital stay duration ($r_s = -0.49$, $p = 0.005$): higher auditory discrimination improvement predicted shorter recovery time (Figure 5A and 5B respectively). These correlations survived when excluding possible outliers (coma duration: r_s =

-0.4, $p = 0.03$; hospital stay duration: $r_s = -0.49$, $p = 0.006$). No such significant relationship was found for digit span forward scores.

Table 1 compares "predicted survivors" to "other survivors" on clinical variables, cognitive performances and functional outcome. Clinical characteristics did not differ between groups with respect to demographics and hypothermia treatment. However, "predicted survivors" showed a tendency towards shorter cardiac arrest duration. Cognitive testing confirmed the above-mentioned correlations for phonemic and semantic verbal fluency, with higher scores for "predicted survivors". In addition, more patients in the "other survivors" group were not oriented to time and not able to perform the whole battery. Interestingly, time to cognitive assessment tended to be longer in the "other survivors" group, suggesting a slower recovery to a stable condition. At 3 months follow-up, more "predicted survivors" exhibited a very good recovery (Table 1: CPC 1). Finally, "other survivors" showed both longer coma and hospital stay duration and were more likely to need a specialized neurorehabilitation center.

DISCUSSION

Our results show that the dynamic of auditory processing during early coma in cardiac arrest survivors provides valuable information about detailed functional status after awakening state. The evolution of auditory discrimination over the first two days is informative of cognitive performances and rapidity of recovery. Grouping patients based on their progression of auditory discrimination yielded meaningful clinical inputs: "predicted survivors" exhibited better cognitive functioning on awakening, faster recovery, and very good functional outcome at 3 months (CPC 1), suggesting that the degree of progression of auditory discrimination could reflect a more general recovery of brain functions.

In comparison to the survival prediction, estimation of cognitive and functional outcome has received far less attention and is even more challenging, as most of clinical outcome predictors available during coma are predictive of death [4]. In contrast, auditory responses to mismatch negativity paradigms are more sensitive to survival [9,14], but have not been used to predict functional recovery despite encouraging results in healthy and psychiatric populations [30,31]. Compared to previous studies assessing auditory functions through mismatch negativity paradigms [8,9], here we took advantage of the whole EEG electrode montage to characterize the evoked brain activity. Its evolution over time has previously been reliably related with survival [10,11], but not with cognitive and functional outcome.

We characterized cognitive functioning using few measures available for the majority of patients according to their limited cognitive capacities shortly after awakening. In this context, ability to undergo the whole neuropsychological testing and orientation to time were interesting variables, reflecting the recovery of basic cognitive functions. In addition, the strong relationship between the ability to complete the whole neuropsychological assessment and CPC scores at three months suggests that early cognitive evaluation can be seen as a predictor of subsequent functional recovery, confirming results from previous studies [6,32]. Verbal fluency represents a complex measure covering multiple cognitive domains, including primarily executive functions (e.g. self initiation, switching, inhibition), and verbal abilities [33]. Semantic and phonemic verbal fluency differ regarding both the involved neuroanatomical substrates and the recruited cognitive processes, with more executive processes and frontal involvement in phonemic verbal fluency [34,35]. Combined together, we believe that these measures may constitute a global and parsimonious appreciation of cognitive functioning, which could be easily used in routine clinical evaluations to quickly assess patient's status. In addition, testing cognition shortly after awakening may have several advantages: influence of motivational and environmental factors that might appear later in time (e.g. external stimulations, targeted neurorehabilitative treatments) is reduced and there is less chance to lose patients at follow-up; moreover, early neuropsychological examination is of clinical value in the decision for appropriate treatments. Considering that the aim here was to determine if auditory discrimination during coma is related with cognitive functions at all, we feel that the present setting allows assessing more directly the relationship between acute cerebral processing and subsequent cognitive functioning in two groups of survivors with strictly identical conditions.

In contrast to previous outcome studies characterizing good outcome as CPC 1-2 and poor outcome as CPC 3-5 [4], here our cohort included only survivors with CPC 1-3 (there were no vegetative state patients at three months). As our aim was to predict very good outcome, we considered separately patients having no or minor neurological deficits (CPC 1) and the rest (CPC 2-3) as moderate. Combined with the fact that inter-rater variability [36] was not an issue as the same research nurse collected all CPC scores, we believe that this classification provides accurate information for our purpose. Even though coma and hospital stay durations can be influenced by many factors besides brain injury (e.g., infectious or cardiovascular complications), they proved to be consistent with other measures and reliable indicators of the recovery speed. In particular, the tendency of "other survivors" to undergo neuropsychological testing later, while still having worse cognitive performance, suggests that longer time to recover is indicative of poor outcome. In fact, coma duration has been previously associated with functional status, showing more complaints of cognitive functioning and worse quality of life in patients awakening later [37,38]. Indication to intensive neurorehabilitative treatment was also a marker of poor outcome.

Interestingly, cardiac arrest duration tended to be shorter in "predicted survivors", suggesting that a briefer insult correlates to a better recovery of brain functions assessed by progression of auditory discrimination. In previous studies, arrest duration has been related to survival [39], but, as far as we are aware, never with detailed outcome [40,41], except in one older report showing a significant association with long-term memory scores [42]. To the best of our knowledge, our study is the first to suggest that patients recovering auditory functions during coma (and later exhibiting better outcome) have lighter initial insult as attested by shorter time to ROSC.

This study has limitations. First, the overall number of included patients is relatively small. Even considering all cardiac arrest patients over three years in a university hospital, the considerable mortality rate represents the highest constraint. However, functional outcome at three months of the few patients that could not be included in the present analysis did not differ from those presented here, suggesting no selection bias. Therefore, we believe that our study represents a reliable sample of the population of cardiac arrest survivors. Second, some patients regained consciousness during the second EEG, but were almost equally distributed among the two groups; it seems thus unlikely that this influenced our results in a significant way. More importantly, results of auditory discrimination did not influence decisions on interruption of intensive care – minimizing risks of the so-called "self-fulfilling prophecy"; also, the neuropsychologist and nurse evaluating cognitive and functional outcome were blinded to them. Third, the severity of cognitive impairment may be over-estimated during hospital stay, in the acute setting [43], however this particularly applies to patients showing deficits. As stated above, we nevertheless believe that early neuropsychological testing was appropriate in our design, as it served as variable for the CPC outcome at three months. Fourth, there was no control group to provide "normal" cognitive performances, but using normalized tests and comparing patients with similar clinical condition provide a reliable control.

CONCLUSIONS

Progression of auditory discrimination over time during early coma seems to reliably predict the subsequent cognitive and functional outcome of cardiac arrest survivors. These findings, together with the consideration of time to ROSC and to extubation, may orient relatively early the clinical teams and proxy regarding the management of rehabilitation care. Confirmation of these results for detailed long-term outcome prediction in a larger cohort could contribute to more accurately orient early rehabilitation efforts and therefore improve patients' outcome.

Conflicts of interest

The authors declare no conflict of interest.

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Author contributions

Concept and study design: EJ, MDL, VB, MO, SC, AOR; Data acquisition and analysis: EJ, AT, VB, MDL; Drafting the manuscript and figures; EJ, MDL, AOR.

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FIGURE LEGENDS

Figure 1. Flow chart describing each step of patient's evaluation, from hospital admission to 3 months follow-up. Grey boxes indicate patients that could not be included in the final cohort. *MMN* Mismatch Negativity; *CPC* Cerebral Performance Category

Figure 2. Distribution of patients according to their progression of auditory discrimination during early coma, calculated as the difference of the decoding performance between the first and the second recording (respectively AUC_{Day1} and AUC_{Day2}). Patients showing an improvement of auditory discrimination are classified as "predicted survivors" while patients showing no improvement are categorized as "other survivors".

Figure 3. Overall proportion of patients impaired for each cognitive domain. Cognitive domains most frequently impaired were executive functions (53% of patients), long-term memory (35%) and attention (31%). Some cognitive domains could not be tested in all patients (praxia: n = 29, long-term memory: n = 31, short-term memory: n = 31). The majority of cognitive deficits came from patients not able to follow the whole neuropsychological testing (see Supplementary Figure for an overview).

Figure 4. Correlations between progression of auditory discrimination during early coma and cognitive scores on awakening. Positive correlations were found for both phonemic verbal fluency (panel A) and semantic verbal fluency (panel B).

Figure 5. Correlations between progression of auditory discrimination during early coma and functional outcome measures. Negative correlations were found both for coma duration (panel A) and hospital stay duration (panel B). Correlations remain significant without extreme values, indicated by empty rhombus (coma duration: r_s = -0.4, p = 0.03; hospital stay duration: r_s = -0.49, p = 0.006).

	Predicted Survivors n = 14	Other Survivors n = 18	*p* value	Z value	Test
Clinics					
Age (years)	57 ± 15	55 ± 15	0.82	0.22	Wilcoxon
Female gender	4 (29%)	5 (28%)	1		Fisher
Time to ROSC (min)	15 ± 6	24 ± 13	0.05	-1.97	Wilcoxon
Hypothermia treatment	12 (86%)	15 (83%)	1		Fisher
Cognitive functioning					
Cognitive testing delay (days)	8 ± 2	12 ± 9	0.07	-1.82	Wilcoxon
Whole NPS exam completed	12 (86%)	8 (44%)	0.03*		Fisher
Orientation to time failed	2 (14%)	12 (67%)	0.004*		Fisher
Phonemic verbal fluency (words)†	9 ± 4	4 ± 4	0.003*	2.95	Wilcoxon
Semantic verbal fluency (words)‡	16 ± 5	11 ± 7	0.02*	2.31	Wilcoxon
Digit span forward (span)¥	5 ± 1	5 ± 2	0.77	0.79	Wilcoxon
Functional outcome					
CPC 1 at 3 months	12 (86%)	6 (33%)	0.004*		Fisher
Coma duration (days)	4 ± 3	7 ± 5	0.01*	-2.51	Wilcoxon
Hospital stay duration (days)	15 ± 4	28 ± 22	0.003*	-2.93	Wilcoxon
Neurorehabilitation	1 (7%)	11 (61%)	0.003*		Fisher

Table 1. Results of clinical variables, cognitive tests and outcome measures (mean ± std) for patients grouped according to their progression of auditory discrimination during acute coma.

ROSC return of spontaneous circulation, *CPC* Cerebral Performance Category

* Significant at $p < 0.05$

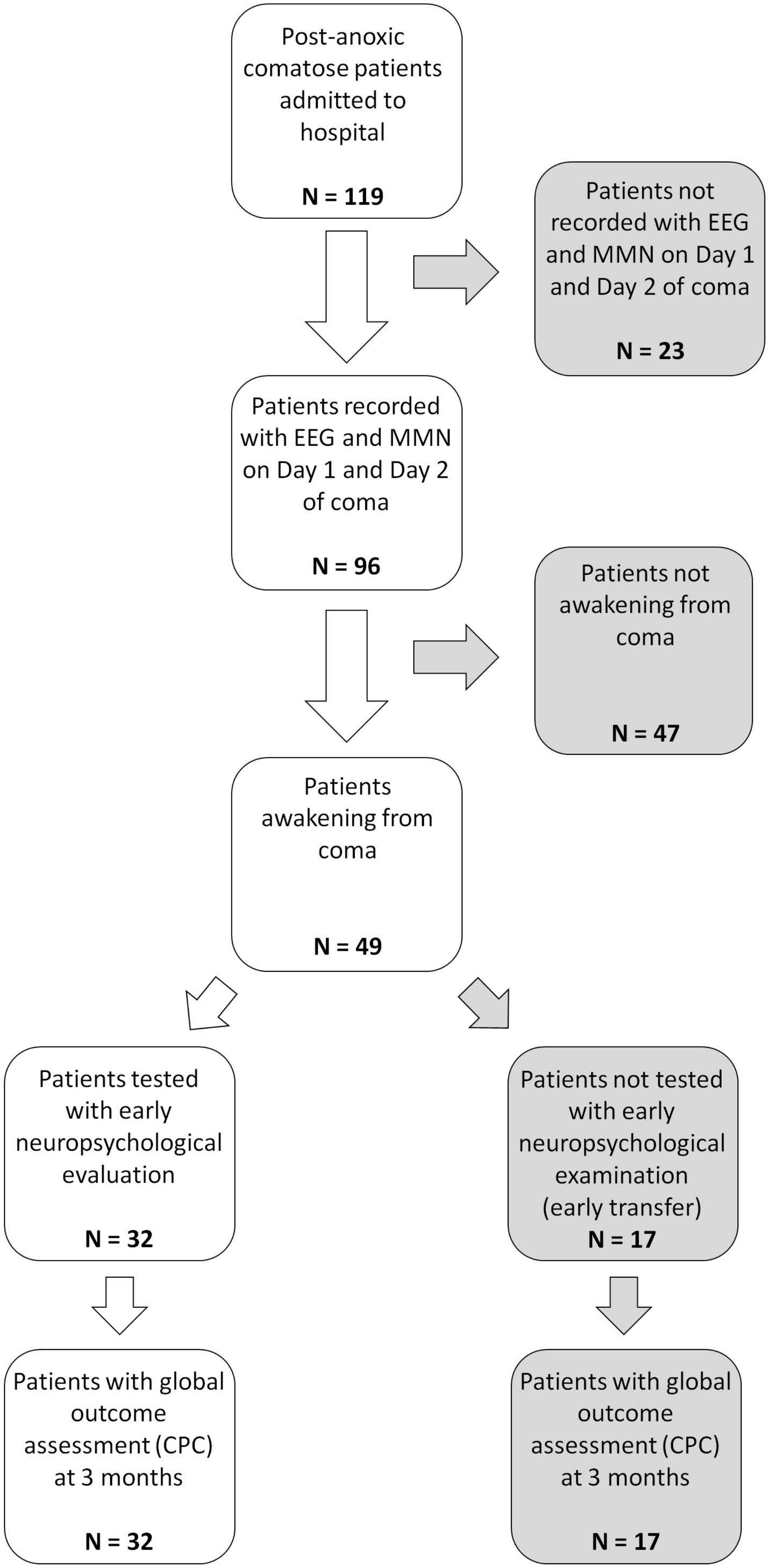
† Scores available for 29 patients (13 predicted survivors / 16 other survivors)

‡ Scores available for 28 patients (13 predicted survivors / 15 other survivors)

¥ Scores available for 31 patients (14 predicted survivors / 17 other survivors)

Cardiac arrest survivors were split in two groups according to the progression of auditory discrimination during coma ("predicted survivors" vs. "other survivors") and compared on several measures using appropriate statistical tests.
Detailed CPC results: in the "predicted survivors" group, two patients (14%) had a CPC 2 and no patient (0%) had a CPC 3; in the "other survivors" group, eight patients (44%) had a CPC 2, three (17%) had a CPC 3 and one died.

Figure 1



Post-anoxic comatose patients admitted to hospital
N = 119
Patients not recorded with EEG and MMN on Day 1 and Day 2 of coma
N = 23
Patients recorded with EEG and MMN on Day 1 and Day 2 of coma
N = 96
Patients not awakening from coma
N = 47
Patients awakening from coma
N = 49
Patients tested with early neuropsychological evaluation
N = 32
Patients not tested with early neuropsychological examination (early transfer)
N = 17
Patients with global outcome assessment (CPC) at 3 months
N = 32
Patients with global outcome assessment (CPC) at 3 months
N = 17

Figure 2

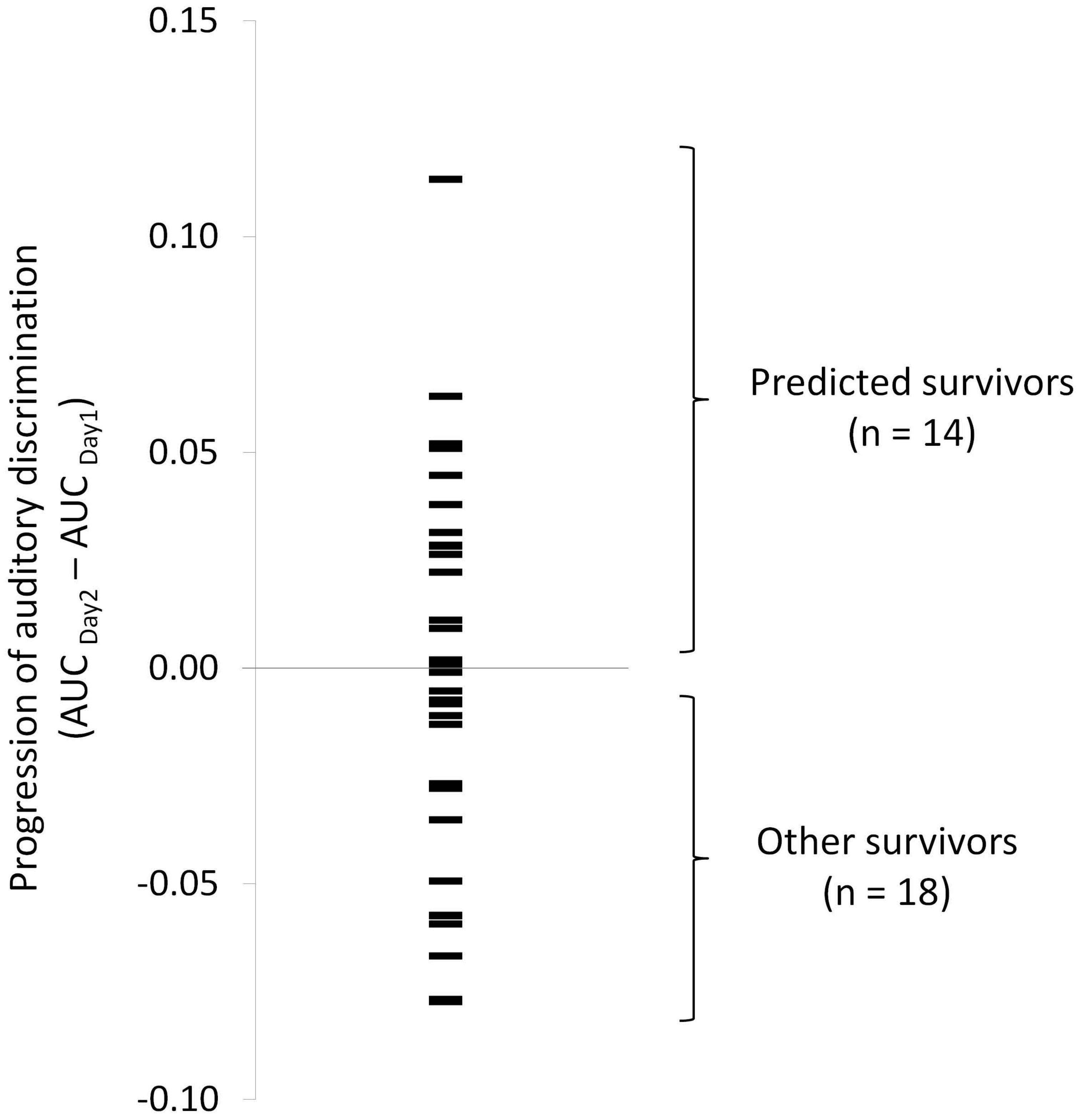
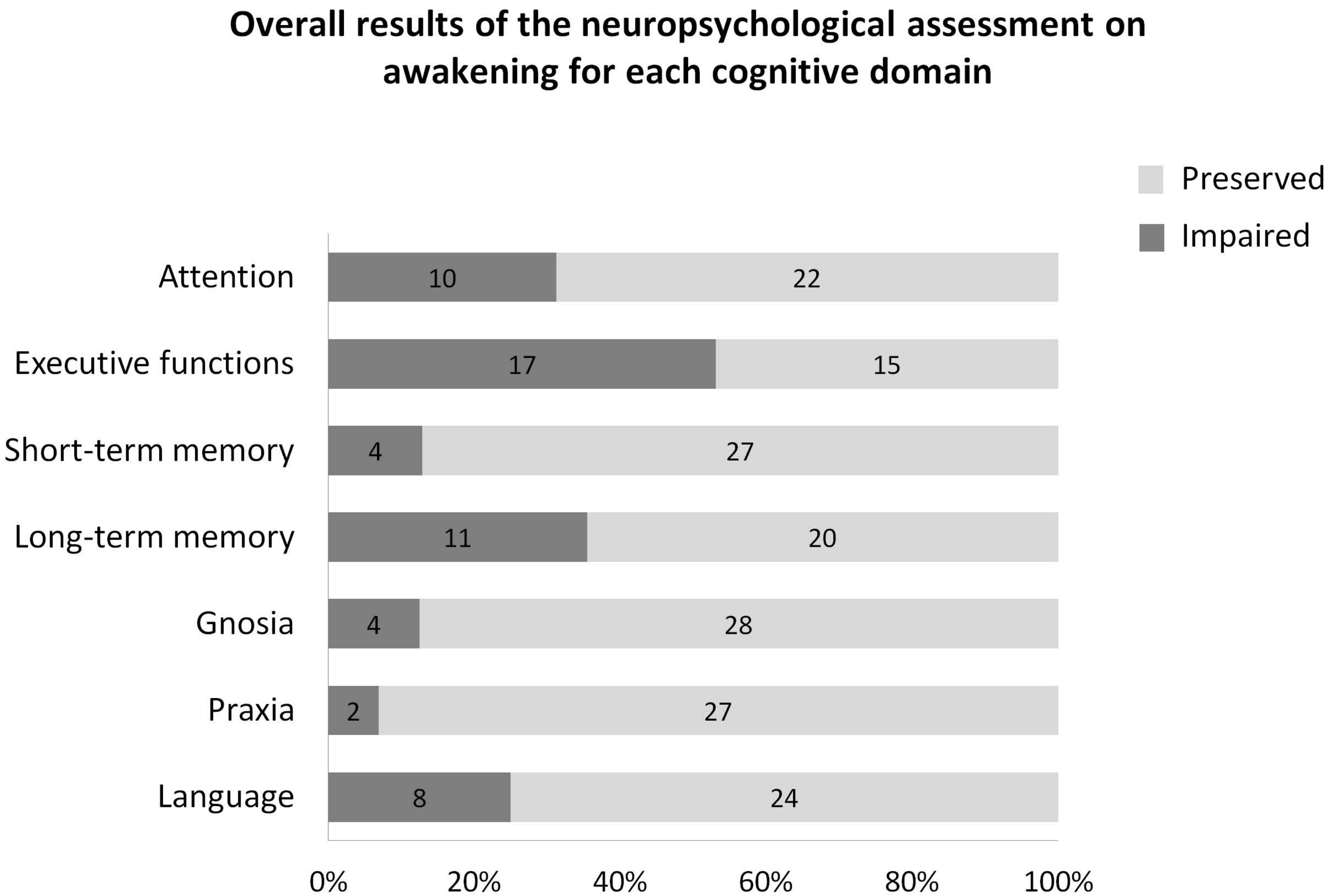

0.15
0.10
0.05
0.00
-0.05
-0.10
Progression of auditory discrimination
(AUC Day2 − AUC Day1)
Predicted survivors
(n = 14)
Other survivors
(n = 18)

Figure 3



Overall results of the neuropsychological assessment on awakening for each cognitive domain
Preserved
Impaired
Attention
10
22
Executive functions
17
15
Short-term memory
4
27
Long-term memory
11
20
Gnosia
4
28
Praxia
2
27
Language
8
24
0%
20%
40%
60%
80%
100%

Figure 4

Correlation between progression of auditory discrimination during coma and cognitive performances on awakening

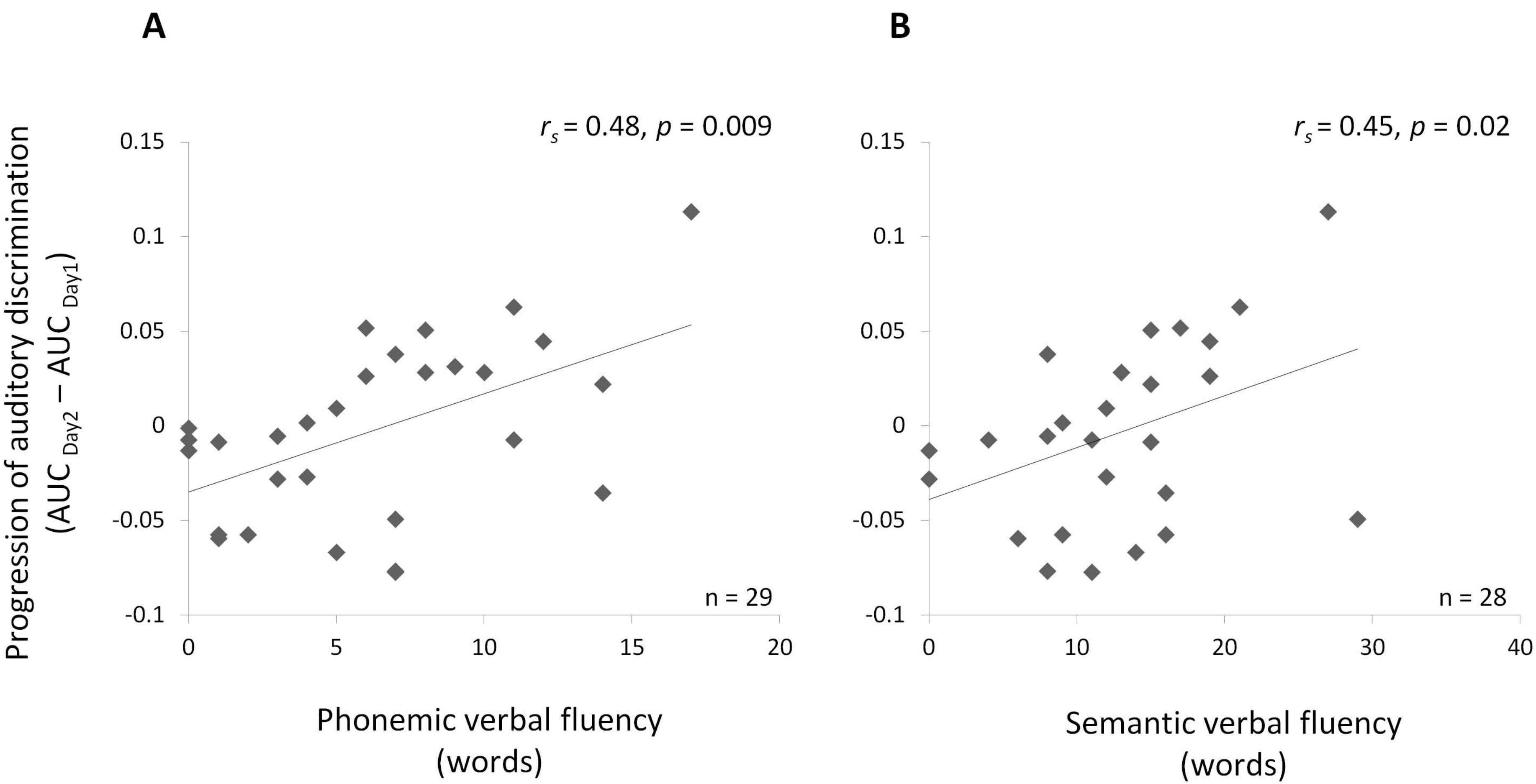


Figure 5

Correlation between progression of auditory discrimination during coma and functional outcome